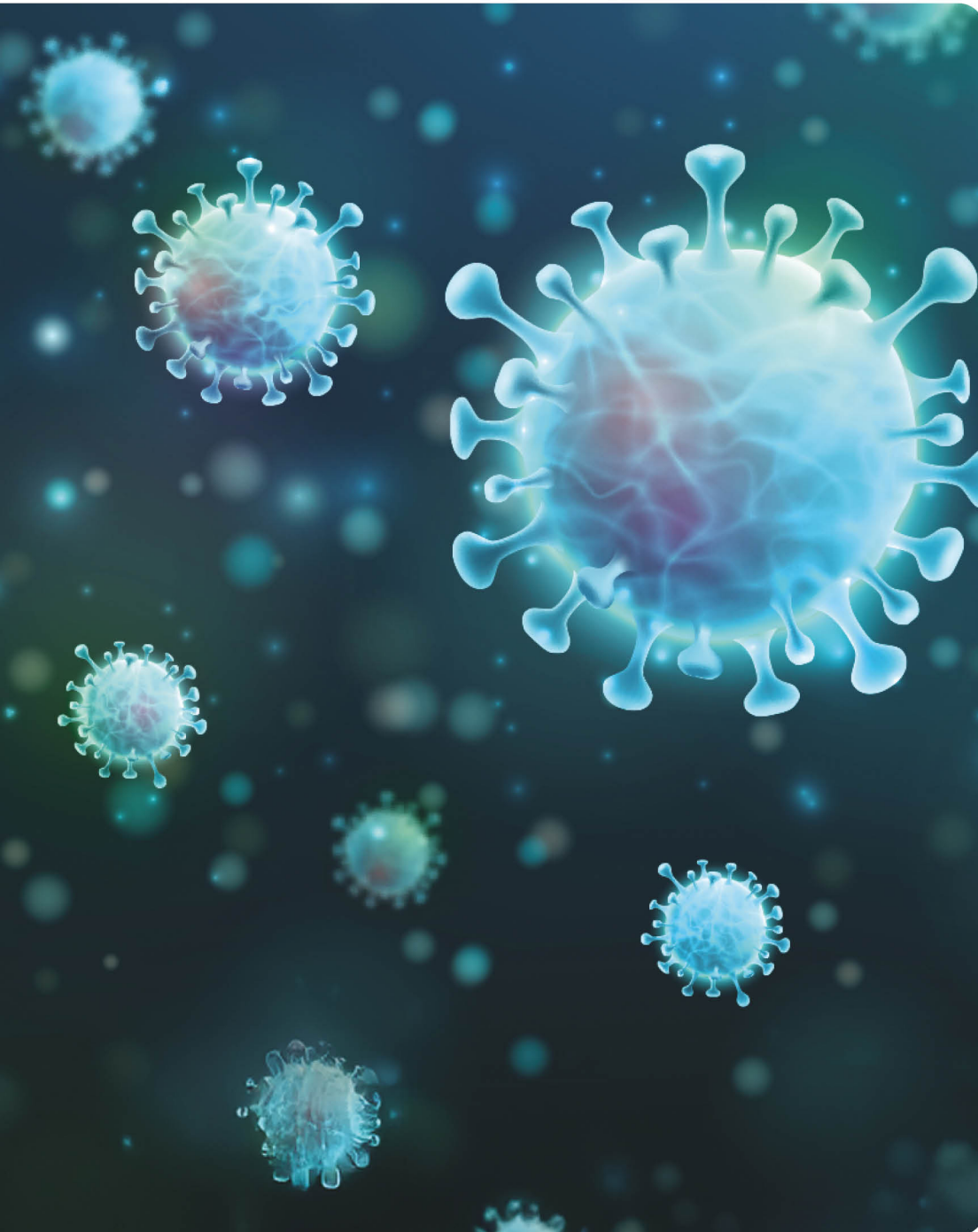


THE MAX MEDICAL JOURNAL

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ORIGINAL ARTICLES

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PATH-BREAKING CASES

THE IMAGES

STUDENTS' CORNER



FROM 'FEAR OF THE FACE' TO 'BEST FACE FORWARD':

A Remarkable 20-Year Journey After Complex Reconstruction of a Dangerous Facial Arteriovenous Malformation

In October 2005, a young man sought treatment at the Max Institute of Reconstructive, Aesthetic, Cleft & Craniofacial Surgery (MIRACLES) for a rare congenital arteriovenous malformation (AVM) that engulfed the entire right side of his face. The condition had forced his right eye shut and turned his face, his identity into his greatest source of fear. Years of social stigma had compounded the psychological burden of his medical condition. Several leading medical centres had deemed his case too dangerous to attempt.

Facial AVMs present unique challenges, combining both aesthetic and functional complexities. Without complete removal, recurrence is possible; however, aggressive surgery carries life-threatening risks, including massive bleeding and blindness. The Max team, led by Dr. Sunil Choudhary, adopted a meticulous, safety-focused approach. Advanced imaging techniques, including computed tomography (CT) angiography and Doppler studies, were used to map the abnormal vessels and plan the operation.

During the six-hour high-stakes surgery, the main external carotid artery was temporarily occluded to control bleeding. The AVM was carefully dissected away from vital facial nerve branches and muscles responsible for expression and eyelid movement, followed by reconstructive flaps to restore both function and appearance.

Nearly two decades later, he returned to MIRACLES, Saket to thank the team. Now serving as Director of Business Development for a multinational travel company in Singapore, his journey from '*fear of the face*' to '*best face forward*' stands as a powerful testament to perseverance, compassionate care, and the remarkable possibilities of reconstructive surgery.

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THE ANTI-CLOCK



“
Everyone desires long life,
not one old age.”

— Jonathan Swift

I have spent many Sundays glued to the television, and two Netflix series that I found fascinating were ‘Live to 100: Secrets of the Blue Zones’ and ‘Don’t Die: The Man Who Wants to Live Forever’. The former delves into the lives of five communities that live the longest and healthiest. These are residents of the ‘Blue Zones’ — Okinawa, Sardinia, Ikaria, Loma Linda, and Nicoya. Their secret lies in a plant-based diet, walking, gardening, focus on peace of mind, family bonds, and community support. The second series is a dichotomy and features a wealthy entrepreneur Bryan Johnson, and his obsession with anti-ageing. His wealth and energy are totally channelled into radical regimens including 54 dietary supplements, sleep regulation, exercise, gene therapy, plasma exchanges and gadgetry to reverse his biological clock and make him younger each day. He spends 2 million dollars each year to defy age and become 18 again. It raises questions about accessibility, ethics and psychological implications when I hear him talk. Two contrasting approaches towards the same goal — longevity and health.

Our genes are what we inherit. What we do after we are born is what we become. We don’t just want to live long, but we want to look youthful too. Youth has become a commodity. What we do not realise is that the actors and social media influencers often conceal their medical issues behind their exalted, glorified external appearances. Health and beauty are two sides of the same coin — they need to be unified.

The Brazilian butt lift (BBL) is the most popular and highly advertised cosmetic procedure, with Turkey being the murky hub for the same. Yet this dangerous surgery kills 3,000 people annually. A mother of five children in Gloucestershire died recently of a BBL. A well-known Indian actress died after a self-administered cocktail of anti-ageing injections. The beauty industry is booming. Around 50 billion dollars were spent on Botox, hyaluronic acid fillers, lasers, skin lifts and cosmetic procedures in 2024. India is vying with the United States (US), Brazil and Japan for the top spot in aesthetic procedures. Surgical procedures include breast augmentation, liposuction, nose jobs, hair transplants and dental procedures. Medical tourism is flourishing, and the mushrooming of substandard, unethical clinics continues to claim lives. It is unregulated and only a minimum standard of service exists. Anti-ageing cannot — and should not — be confused with longevity and health. Beauty is only skin deep. Gen-Z seems to be infatuated with fillers rather than with what fills their insides.

What causes ageing? Growing old is a ubiquitous, inevitable, ongoing phenomenon. Hippocrates and Aristotle blamed ageing on diminishing ‘vital heat’. Modern-day scientists have proposed that it is genomic damage, cell senescence, mammalian target of rapamycin (mTOR) pathway and a reduced pool of stem cells that make a person age. ‘Inflammaging’ is an interesting concept where the human body is in a constant low-grade ‘sterile’

inflammatory state due to oxidative stress. Sirtuins are a fascinating family of proteins responsible for deoxyribonucleic acid (DNA) damage repair and are the focus not just of longevity but also of anti-cancer research. The endocrine theory discusses hormonal changes, and the immune theory emphasises immunosenescence in biological ageing. Ageing is such a complex process beginning at birth and culminating in death. Ultimately, it is the genes and the environmental factors that together interplay to determine biological age versus chronological age.

There are two subsets of phenotypes which are generating considerable interest — the 'Metabolically unhealthy non-obese' (MUNO) and the 'Metabolically Healthy Obese' (MHO). We have all read about the 'YY paradox' where the thin-fat Indian, Dr. Yajnik, and the Caucasian Dr. Yudkin had identical body mass index (BMI) but the former had a much higher body fat content.

So, is it all genetic expression or are there environmental determinants too? Ageing starts by the third decade with reduced cardiac output, maximum attainable heart rate and aerobic capacity. The blood vessels begin to harden, and gradually the blood pressure creeps upwards. People develop a mid-life paunch and gain a couple of kilograms each year. One fine day you realise that your trousers no longer fit. The laboratory results come back with elevated lipids and sugars. The clock keeps ticking, and routine activities cause tiredness and breathlessness. It's not just the mid-life crisis that we are talking about. The muscle mass decreases, testosterone levels fall with reduced libido, and bones become brittle. Reflexes are slower, falls and accidents happen, sleep becomes fragmented, and memory lapses lead to awkward moments. It feels depressing to see our bodies age. These grim changes happen at a much faster pace in diabetics, cardiac and renal patients.

We cannot stop Father Time, but we can certainly slow down the ticking of the clock. English poet John Gay wrote, "Exercise thy lasting youth defends." In 1966, five healthy 20-year-olds in Dallas spent three weeks of their summer vacation in bed as part of the 'Dallas Bed Rest and Training Study'. Their metabolism and cardiac function worsened to men twice their age. Then they were subjected to eight weeks of intense exercise, and their body fat and cardiac indices were better than their baseline. They had actually reversed a part of their ageing. The moral of the story is to mobilise patients early after an illness or surgery. The same five volunteers were re-evaluated when they turned 50. After six months

of a structured endurance exercise programme, they lost substantial weight, improved aerobic capacity and managed to slow down — albeit not reverse — the clock. A sensible exercise programme has to include endurance exercises like walking, jogging, swimming or bicycling to improve the cardiac function. The machines in the gym are fine as long as we use them under supervision. Resistance exercises using light weights are vital for muscle and bone health. Yoga, stretching and balancing exercises protect the joints and maintain flexibility. The endorphins counteract anxiety and low mood. Rest is rust, movement keeps the body young. In a long-term follow-up of 16,936 Harvard Alumni, those who walked, climbed stairs and played sports had a 39% lower risk of heart disease and 24% lower risk of stroke than their sedentary classmates. The benefits of exercise include improvement in diabetes, hypertension, fatty liver, impotence, osteoporosis, depression, immunity and Alzheimer's, to name a few. It increases life expectancy by more than two years.

There are a number of magic concoctions on social media to reduce ageing, but consider these with a pinch of salt. An overdose of simple things like turmeric (haldi) can cause curcumin hepatotoxicity. Cut down the saturated fats and include monounsaturated fatty acids and omega-3 in your diet. Processed foods, salt, simple sugars, smoking and alcohol reduce years. Our diet lacks sufficient protein and needs more of these. Think before you order. It's not the carbs and the fat — it's the proteins that matter. Big biceps are not the same as muscle strength. An octogenarian loses around 8 kg of muscle mass. Sarcopenia causes falls and fractures.

Darwin proclaimed that it is 'survival of the fittest.' We may not be able to prevent cataracts from developing or prostates from enlarging, but we can age healthier, more gracefully and certainly slow down the tick-tock of the clock. We should target 'optimal' rather than 'normal' laboratory reports. Our prime focus has to be mental and metabolic health. You can't stop the clock and live forever.

"No one is so old that he does not think he could live another year." — Cicero

Dr. Monica Mahajan

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Demographics and Clinical Outcomes of Carcinoma Rectum Patients After Planned Neoadjuvant Chemoradiotherapy with Capecitabine-Based Regimen: A 3-Year Experience from a Private Tertiary Cancer Care Centre

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Abstract:

Rectal cancer incidence is increasing globally, both in developed and developing countries. Neoadjuvant chemoradiotherapy (NA-CTRT) followed by total mesorectal excision is the standard of care for locally advanced rectal cancer (LARC). NA-CTRT improves sphincter preservation, reduces local recurrence, and increases pathological complete response (pCR) rates. This study aims to report the demographics and clinical outcomes (overall survival [OS], progression-free survival [PFS], and pCR rates) in patients with carcinoma rectum receiving NA-CTRT at a private tertiary cancer care centre. The radiation planning database was screened for patients who presented to the Radiation Oncology Department from January 2021 to December 2023. Sixty-seven patients with histologically confirmed rectal adenocarcinoma were identified, of whom 44 who received NA-CTRT were included in the study. Retrospective data were collected via discharge summaries and hospital records. Analysis was conducted using SPSS software v20. The median age of the patients at diagnosis was 55.5 years, and 68.2% were males. The most common presenting complaint was bleeding per rectum (61.4%), with the majority of patients in Stage III (79.5%). Following NA-CTRT, 45.5% patients received neoadjuvant chemotherapy (NACT) prior to surgery. Only 23 patients underwent surgery, and the dropout percentage for surgery after NA-CTRT was 47.7% due to various reasons. Postoperative histopathology demonstrated that 45.4% of patients who underwent surgery had a complete or near complete response, and the pCR rate was 22.7%. The mean PFS and mean OS for the cohort were 38 months and 40 months, respectively. Multivariate analysis identified comorbidities and the surgery performed were found to be significant prognostic factors for OS.

NA-CTRT with capecitabine is a feasible and effective approach in LARC, achieving favourable tumour regression and survival outcomes in a real-world setting. However, high dropout rates post NA-CTRT and delays in surgical intervention point to systemic barriers that warrant attention. Institutional efforts to optimise patient adherence, improve multidisciplinary coordination, and expand access to supportive care are crucial for maximising treatment benefits in such settings.

Key words: Carcinoma Rectum, Rectal Adenocarcinoma, Neoadjuvant Chemoradiotherapy (NA-CTRT), Capecitabine-Based Regimen, Total Mesorectal Excision (TME), Pathological Complete Response (pCR), Progression-Free Survival (PFS), Overall Survival (OS), Locally Advanced Rectal Cancer (LARC).

Introduction

Rectal carcinoma is a significant global health burden, with an increasing incidence in both developed and developing countries. Colorectal cancer ranks third in terms of incidence and second in mortality, as per the GLOBOCAN 2022 data.¹ Over recent decades, treatment strategies for locally advanced rectal cancer (LARC) have evolved significantly, with multimodal approaches improving both local control and overall survival (OS). Neoadjuvant chemoradiotherapy (NA-CTRT), particularly when employing capecitabine as a radiosensitiser, has emerged as a standard therapeutic modality for LARC (Stage II and III), offering potential tumour downstaging, increased rates of sphincter preservation, and reduced local recurrence.²⁻⁴

Capecitabine, an oral prodrug of 5-fluorouracil (5-FU), has gained widespread acceptance due to its efficacy, ease of administration, and favourable toxicity profile.⁵ When combined with radiotherapy, it enhances radiosensitivity and mimics continuous infusion of 5-FU, making it a preferred agent in many institutional protocols.

Despite well-established guidelines, real-world evidence from private tertiary cancer centres, particularly in low-

and middle-income countries, is limited. Variations in patient demographics, treatment compliance, and access to multimodal care often influence outcomes in ways that may not be reflected in large clinical trials.⁶ Therefore, institution-specific analyses are essential for contextualising global standards within local practice environments.

This study presents a retrospective 3-year analysis of patients with carcinoma rectum treated with planned NA-CTRT using a capecitabine-based regimen at a private tertiary cancer care centre. The primary objectives are to evaluate the demographic profiles, clinical and pathological responses, and early outcomes of this cohort, thereby contributing valuable insights into the practical implementation and oncological effectiveness of this treatment approach in a real-world clinical setting.

Materials and Methods

We screened the radiation planning database for patients who came to the Radiation Oncology Department from January 2021 to December 2023 and found 67 histologically confirmed rectal adenocarcinoma patients. Out of 67, 44 patients received NA-CTRT and were taken for analysis in this study, as shown in Figure 1.

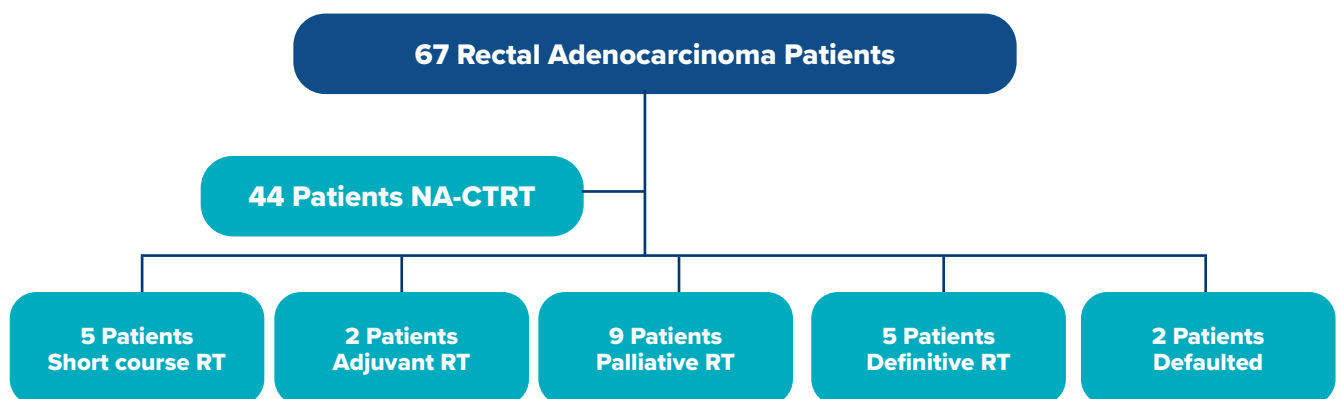


Figure 1: Consort diagram of patients who came to the Radiation Oncology Department.

Abbreviations: NA-CTRT: Neoadjuvant Chemoradiotherapy; RT: Radiotherapy.

All patients underwent contrast-enhanced planning computed tomography (CT) scans with slice thickness ranging from 2.5–3 mm. Non-contrast scans were performed in patients with renal impairment. Baseline magnetic resonance imaging (MRI) and positron emission tomography–computed tomography (PET–CT) scans were utilised for improved gross tumour delineation where feasible. Treatment included radiotherapy dose at either 45 Gy in 25 fractions followed by a boost of 5.4 Gy in 3 fractions, or 50 Gy in 25 fractions. The clinical target volume (CTV) encompassed the primary tumour, lymphadenopathy, and high-risk nodal areas, including the mesorectal, presacral, internal iliac, and obturator lymph nodes. Intensity-modulated radiotherapy (IMRT) was delivered using 6-MV photons through Tomotherapy or Clinac-IX machines, with on-board imaging systems for precise localisation and verification. Oral tablet capecitabine was administered concurrently at a dose of 625 mg/m² twice daily during NA-CTRT sessions, and dose adjustment was done on the basis of complete blood counts, liver function tests, kidney function tests, age, and general condition of the patient.

Post NA-CTRT, patients were evaluated for surgical resectability with an MRI/PET-CT approximately 8–12 weeks after the last radiotherapy. Preoperative chemotherapy (0–4 cycles) was administered after NA-CTRT according to the patient's condition and MRI assessment. Generally, radical surgery was carried out 7 to 14 weeks after the completion of NA-CTRT. Postoperative histopathology and tumour regression scores were recorded for response assessment. The follow-up details were obtained from the hospital computerised patient record system and through telephonic follow-ups. The analysis was conducted in April 2025, with a minimum follow-up period of 15 months to assess outcomes.

We aimed to report the pathological complete response (pCR) rate in patients receiving NA-CTRT and 4-year oncological outcomes for progression-free survival (PFS) and OS. PFS was defined as the duration from

the date of diagnosis to the date of 1st progression or death from any cause or censored at the last follow-up visit. OS was defined as the duration from the date of diagnosis to the date of death from any cause or censored at the last follow-up visit. Survival analysis was performed using the Kaplan–Meier method, and all statistical analyses were conducted using SPSS version 20 software (IBM Corporation, Armonk, New York, NY). A Cox proportional hazards regression model was used to perform multivariate analysis of prognostic factors.

Results

The cohort consisted of 44 patients, of whom 30 (68.2%) were males. The median age of the patients at diagnosis was 55.5 years. 61.4% patients were less than or equal to 60 years of age. Comorbidities were observed in 20 (45.5%) patients, including diabetes, hypertension, coronary artery disease (CAD), hypothyroidism, and/or chronic kidney disease (CKD). The most common presenting complaint was bleeding per rectum (PR), observed in 61.4% of patients, followed by altered bowel habits (40.9%), and perianal/abdominal pain (36.4%). Other symptoms included recurrent vomiting, pus discharge, perianal itching, loss of appetite/weight, faecal incontinence, anaemia, or generalised weakness. Diagnostic evaluations included colonoscopy/recto-sigmoidoscopy and biopsy, confirming adenocarcinoma in all patients. Moderate and poorly differentiated tumours (including signet ring histology) were seen in 29.5% and 18.2% patients, respectively. Based on the distance from the anal verge, 68.2% patients had low rectal disease (disease extension up to 5 cm from anal verge), 25% patients had middle rectal disease (> 5–10 cm from anal verge), and 6.8% patients had high rectal disease (> 10–15 cm from anal verge). Imaging modalities utilised for staging included MRI alone in 25% patients, PET–CT alone in 18.2% patients, and both MRI and PET–CT in 56.8% patients. Clinical staging revealed that the majority of patients were in Stage III (79.5%). The details are summarised in Table 1.

Characteristic (N = 44)	Percentage (n)
Gender: male/female	68.2% (30)/ 31.8% (14)
Median age at diagnosis (In years)	55.5
Mean (Range)	54.7 (20–88)
Age group	
≤ 60 years	61.4% (27)
> 60 years	38.6% (17)
Comorbidities present	45.5% (20)
Presenting complaints	
Bleeding per-rectal	61.4% (27)
Altered bowel habits	40.9% (18)
Pain (abdominal/perianal)	36.4% (16)
Other complaints	11.4% (5)
Histological grading	
Well-differentiated	38.6% (17)
Moderately-differentiated	29.5% (13)
Poorly-differentiated/signet ring	18.2% (8)
Not available	13.6% (6)
Investigations	
MRI alone	25.0% (11)
PET–CECT alone	18.2% (8)
MRI and PET–CECT	56.8% (25)
Colonoscopy/recto-sigmoidoscopy and biopsy	100% (44)
Average length of disease (in cm)	5.8 cm
≤ 6 cm	59.1% (26)
> 6 cm	40.9% (18)
Site of tumour involvement	
High rectal	06.8% (3)
Middle rectal	25.0% (11)
Low rectal	68.2% (30)
Clinical stage	
cT1/2/3/4	(0)/(6)/(26)/(12)
cN0/1/2	(9)/(17)/(18)
cM0/1a/1b	(44)/(0)/(0)
Group stage	
Stage II	20.5% (9)
Stage III	79.5% (35)

Table 1: Demography and baseline characteristics details.

Abbreviation: CECT: Contrast-Enhanced Computed Tomography; MRI: Magnetic Resonance Imaging; PET: Positron Emission Tomography.

Almost half of the patients (45.5%) received neoadjuvant chemotherapy (NACT) before surgery, the most common chemotherapy regimen used being modified FolFOX in 13 patients. Out of 44 patients, 23 patients underwent surgery, 7 patients denied surgery, 3 had progression, 2 were medically unfit for surgery, and 9 were lost to follow-up. The dropout rate for surgery after NA-CTRT was 47.7%. The 23 patients who underwent surgery had various surgical procedures as detailed in Table 2, and the average time duration to surgery after the last radiotherapy fraction was 11.9 weeks.

Treatment details	Percentage (n)
Radiotherapy dose (N = 44)	
50.4 Gy	61.4% (27)
50.0 Gy	38.6% (17)
Neoadjuvant chemotherapy (N = 44)	
Yes (FolFOX/CapOx/FolFlirinOx)	45.5% (13/6/1)
No	54.5% (24)
Post neoadjuvant chemoradiotherapy (N = 44)	
Underwent surgery	52.3% (23)
Patient denied surgery	15.9% (7)
Lost to follow-up	20.5% (9)
Progression	06.8% (3)
Not fit for anaesthesia	04.5% (2)
Surgical procedure (N = 23)	
LAR (Low anterior resection)	21.7% (5)
U-LAR (Ultra-low anterior resection)	08.7% (2)
APR (Abdomino-perineal resection)	60.9% (14)
ISR (Inter-sphincteric resection)	08.7% (2)
Average time to surgery after neoadjuvant chemoradiotherapy (in weeks)	11.9 (± 2.9)
Tumour regression score (N = 23)	
Score 0	22.7% (6)
Score 1	22.7% (5)
Score 2	40.9% (9)
Score 3	13.7% (3)

Table 2: Radiotherapy, chemotherapy, and surgical treatment details.

The postoperative histopathology and tumour regression scores showed that 45.4% patients had complete or near complete response, while 40.9% patients had partial response and 13.7% had poor/no response to NA-CTRT. The pCR rate was 22.7%. The mean PFS and mean OS for patients who received NA-CTRT were 38 months and 40 months, respectively, whereas median PFS and OS were not reached (Table 3 and Table 4). With the median follow-up of 21 months, the 4-year PFS and OS were 73% and 77% respectively, for all the patients as shown in Figure 2 and Figure 3, respectively.

Mean^a for Progression-Free Survival (PFS)

Estimate	Standard error	95% Confidence interval	
		Lower bound	Upper bound
37.995	2.895	32.321	43.669

Table 3: Mean progression-free survival (PFS). ^aEstimation is limited to the largest survival time if it is censored.

Mean^a for Overall Survival (OS)

Estimate	Standard error	95% Confidence interval	
		Lower bound	Upper bound
39.765	2.838	34.202	45.327

Table 4: Mean overall survival (OS). ^aEstimation is limited to the largest survival time if it is censored.

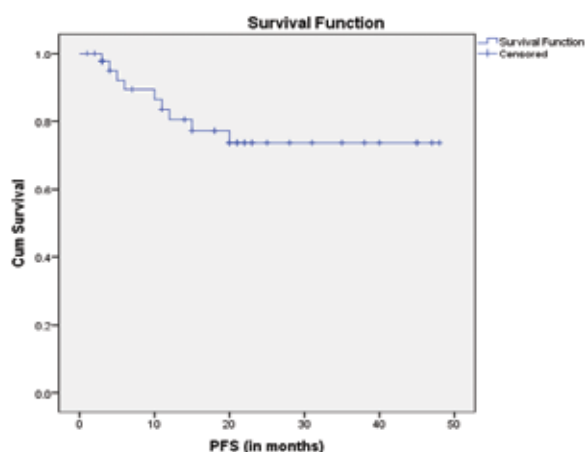


Figure 2: Kaplan–Meier survival curve for progression-free survival.

Abbreviation: PFS: Progression-Free Survival.

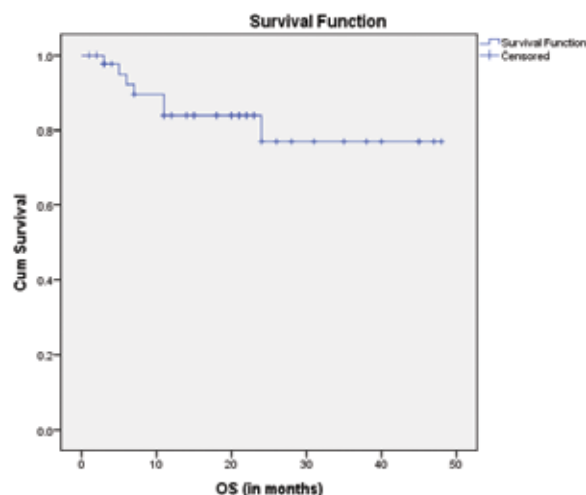


Figure 3: Kaplan–Meier survival curve for overall survival
Abbreviation: OS: Overall Survival.

A Cox proportional hazards regression model was used to perform multivariate analyses to identify different prognostic factors associated with OS (univariate analysis is shown in Table 5). Related factors for OS were investigated in univariate and multivariable analyses that included age group, gender, comorbidities, histological grade, disease length, distance of disease from anal verge, clinical tumour stage, clinical nodal stage, overall stage group, NACT before surgery, and whether surgical resection was performed. Univariate analysis of OS revealed that age group, comorbidities, distance of disease from anal verge, and NACT before surgery had $p \leq 0.05$. Surgical resection was not found to be significant on univariate analysis; however was included in multivariable analysis. After multivariate adjustment, comorbidities ($\chi^2 = 7.163$, $p = 0.007$), and surgery ($\chi^2 = 7.419$, $p = 0.006$) were found to be significant factors for OS.

Factors	Chi-square (χ^2)	p-values
Age group (> 60 years vs ≤ 60 years)	5.63	0.018
Gender (female vs male)	0.192	0.662
Comorbidities (present vs absent)	5.668	0.017
Histological grade	1.121	0.772
Disease length (> 6 cm vs ≤ 6 cm)	1.112	0.292
Distance of the disease from the anal verge	7.173	0.028
Clinical T stage	5.474	0.065
Clinical N stage	0.974	0.614
Stage (II vs III)	0.408	0.523
Neoadjuvant chemotherapy before surgery (given vs not given)	4.597	0.032
Surgery (done or not)	3.022	0.082

Table 5: Univariate analysis of overall survival.

Discussion

This study provides valuable real-world data on the demographic and clinical outcomes of patients with carcinoma of the rectum undergoing planned NA-CTRT with a capecitabine-based regimen in a private tertiary care setting in India. The results reflect both the effectiveness and challenges associated with multimodal therapy in a population often underrepresented in global clinical trials.

The majority of patients in our cohort were male (68.2%), with a median age of 55.5 years. This aligns with data from Indian population-based cancer registries, where colorectal cancers tend to present at a younger age than in Western cohorts.¹⁷ A notable 61.4% of our patients were ≤ 60 years of age, supporting the trend of earlier disease onset in South Asian populations, possibly linked to genetic predisposition and dietary/lifestyle risk factors.⁸ A significant proportion of patients (45.5%) presented with comorbidities, which may impact treatment decisions and overall outcomes.

Low rectal tumours predominated (68.2%), consistent with regional epidemiologic data showing a higher prevalence of low rectal involvement.⁹ Most patients presented with

advanced disease, with 79.5% in Stage III, underscoring the need for early detection strategies and timely referral.

All patients received intensity-modulated radiotherapy (IMRT), with 50.4 Gy or 50 Gy regimens, in combination with concurrent oral capecitabine. This is in line with standard international protocols and highlights the feasibility of implementing advanced radiotherapy techniques in private centres.¹⁰ The capecitabine dose (625 mg/m² twice daily) administered during radiation mirrors that used in major trials, such as NSABP R-04, where it demonstrated non-inferior outcomes to infusional 5-FU.¹¹

Almost half of the cohort (45.5%) also received NACT post-NA-CTRT but prior to surgery, mainly with modified FolFOX, reflecting an adaptation of total neoadjuvant therapy (TNT) concepts emerging in modern rectal cancer management.^{11,12} However, the post-NA-CTRT attrition rate was substantial — 47.7% of patients did not proceed to surgery. This is a concerning finding, with reasons including patient refusal (15.9%), disease progression (6.8%), medical unfitness (4.5%), and loss to follow-up (20.5%). These data highlight systemic and socio-economic barriers to comprehensive care, such as treatment-related fatigue, financial constraints, or inadequate patient counselling.¹³ This dropout rate is higher than in trial settings, where compliance is tightly monitored.

Among patients who underwent surgery, the pCR rate was 22.7%. These results are consistent with published pCR rates for capecitabine-based NA-CTRT, which typically range from 15%–30%.¹⁴ A favourable tumour regression score (TRG 0–1) was seen in 45.4% of patients, indicative of effective downstaging and radiosensitisation.

At a median follow-up of 21 months, 4-year PFS and OS were 73% and 77%, respectively. While these survival results are encouraging, interpretation is limited by the relatively short follow-up period and a significant proportion of patients being lost to surgical follow-up.

On univariate analysis, age > 60 years, presence of comorbidities, low tumour location, and receipt of NACT before surgery were all significantly associated with OS ($p \leq 0.05$). However, surgery showed only a trend toward significance ($p = 0.082$), but may have been underpowered due to the high dropout rate. Multivariate Cox regression revealed comorbidities ($\chi^2 = 7.163$,

$p = 0.007$) and surgery ($\chi^2 = 7.419$, $p = 0.006$) as independent predictors of OS. These findings reinforce that optimal patient selection, perioperative care, and management of coexisting conditions are essential to improving outcomes. Contrary to many studies, clinical T and N staging, and group stage were not statistically significant predictors in our multivariate model, which may be attributed to the relatively small sample size and dominance of Stage III patients in the cohort.

This study's strengths include the use of standardised treatment protocols, advanced radiotherapy techniques, and real-world demographic data from a private tertiary setting, which is underreported in the literature. However, several limitations — including its retrospective nature, relatively small sample size, high attrition, and loss to follow-up — should be acknowledged. Despite these, the study offers practical insights into the challenges and outcomes associated with NA-CTRT implementation in private oncology practice in India.

Conclusion

NA-CTRT with capecitabine is a feasible and effective approach in locally advanced rectal cancer, achieving favourable tumour regression and survival outcomes in a real-world setting. However, high dropout rates post-NA-CTRT and significant delays in surgical intervention point to systemic barriers that warrant attention. Institutional efforts to optimise patient adherence, improve multidisciplinary coordination, and expand access to supportive care are crucial for maximising treatment benefits in such settings.

Rashi Agrawal, Nelesh Aggarwal, Muskan Gupta, Vivek Mangla. Demographics and Clinical Outcomes of Carcinoma Rectum Patients After Planned Neoadjuvant Chemoradiotherapy with Capecitabine-Based Regimen: A 3-Year Experience from a Private Tertiary Cancer Care Centre. MMJ. 2025, September. Vol 2 (3).

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Prevalence of Sexual Dysfunction in Males (Erectile Dysfunction) and Females with Diabetes: Types, Associations, and Severity — An Observational Study from India

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Abstract:

Sexual well-being is integral to overall quality of life; however, diagnosing sexual dysfunction (SD) remains challenging, particularly in India. Diabetes mellitus (DM), a chronic and progressive condition, is intricately linked to physical, psychological, and sexual health issues, with its comorbidities acting as independent risk factors for SD. This study aimed to assess the prevalence, types, associations, and severity of SD among patients with diabetes.

This cross-sectional study, conducted at Max Superspeciality Hospital in New Delhi, included 340 participants diagnosed with DM. Participants were evaluated using the Arizona Sexual Experience Scale (ASEX), and males were additionally assessed via the International Index of Erectile Function (IIEF)-5. Among participants, 93.8% of males and 53.1% of females were willing to discuss their sexual health. The prevalence of SD was 68.5% in males and 72.5% in females. The most frequently reported SD was dissatisfaction with orgasm, affecting 83% of males and 82% of females. Proteinuria was detected in 94.8% of males and 78% of females. Elevated total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides were observed, alongside reduced high-density lipoprotein cholesterol (HDL-C) levels in males. Notably, 99.3% of males with SD reported erectile dysfunction (ED), with 9.6% experiencing severe ED. SD significantly impacts both genders, with females less inclined to discuss their experiences. Most SD cases involve dissatisfaction with orgasm, and males tend to develop ED and SD earlier in the course of diabetes. Education level, occupation, and smoking status were additional risk factors for SD in males.

Key words: Sexual Dysfunction, Prevalence, Diabetes, Erectile Dysfunction.

Introduction

Kama is a basic instinct, whereas sexual behaviour is learned. Ayurveda identifies *Dharma*, *Artha*, *Kama*, and *Moksha* as the four *Purusharthas* — life's essential goals

and fundamental human needs.¹ The sexual response cycle, as defined by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR), consists of four phases: desire, excitement (arousal), orgasm, and resolution. It describes the

physiological and psychological changes occurring in an individual during sexual arousal and activities such as intercourse and self-stimulation.² A positive correlation characterises the relationship between an individual's sexual well-being and quality of life.³

Sexual dysfunction (SD) can affect any phase of the sexual response cycle and includes problems with desire (libido), arousal (pelvic vasocongestion causing erections in males and lubrication in females), orgasm (pleasurable rhythmic contractions), and pain during sexual activity. Such pain may prevent individuals or couples from achieving sexual satisfaction. Identifying SD has been particularly challenging in India due to cultural factors. SD causes considerable physical, emotional, and relational distress, significantly impacting the well-being of those affected. Understanding these classifications is essential to addressing this complex and sensitive health issue.^{4,5}

Diabetes mellitus (DM) is a chronic, progressive disorder that can result in various medical, psychological, and SDs. DM is linked to SD in both males and females, with an elevated risk observed at a younger age.⁵ The prevalence ranges from 20% to 85%.⁶ Diabetes-related comorbidities such as vascular disease, hypertension, peripheral neuropathy, and obesity independently increase the risk of SD. Individuals with diabetes have a higher prevalence and severity of these conditions compared to the general population. Erectile dysfunction (ED) affects about 36% of diabetic males, nearly three times higher than in non-diabetics. Poor glycaemic control further worsens ED-related morbidity. These factors collectively contribute to the elevated rates and severity of SD in DM.⁷ Research also shows that individuals diagnosed with diabetes typically develop ED 10 to 15 years earlier than those without the condition.⁸ The prevalence of ED and premature ejaculation in males correlates with advancing age, hypertension, and diabetes.⁹

A study conducted by Yaylali *et al.* demonstrated a higher prevalence of female sexual dysfunction (FSD) in women with DM relative to those without the condition.¹⁰ Females with diabetes commonly experience SD, including reduced sexual desire, diminished satisfaction, orgasmic disorder, arousal disorder, and lubrication difficulties.¹¹ Evidence suggests that the somatic sensory system is altered in diabetes, with the introitus vagina, labium minora, and clitoris identified as the genital regions most adversely impacted. Neuropathy, vascular impairment, and

psychological issues are recognised factors contributing to the development of SD in women with diabetes.¹² In addition, endocrine changes can result in diminished vaginal lubrication. Research indicates that female patients with diabetes show a higher incidence of SD than their male counterparts. The presence of diabetes-related complications appears to exacerbate the severity of SD and associated concerns in affected patients.¹³

The prevalence of ED has been thoroughly examined in male populations because of DM. The phenomenon of SD in females is inadequately addressed in the current literature. SD is acknowledged as a significant health concern that impacts quality of life, significantly affecting both patients and their sexual partners.¹⁴ This research has implications for individual health outcomes and societal well-being, enhancing the understanding of patient profiles. ED frequently arises as a common concern in clinical settings. The evaluation of SD in females is often overlooked in clinical assessments. This study sought to assess the prevalence, classifications, and associations of SD in diabetic individuals of both genders, employing internationally recognised assessment instruments.

Methods

Study setting and population

This cross-sectional study was conducted at Max Super Speciality Hospital, New Delhi, between February and December 2017. Consenting outpatients aged 18 years and older with a diagnosis of DM and a history of sexual activity within the past year were eligible. Exclusion criteria included a history of pelvic surgery, pre-existing sexual disorders, spouses with sexual diseases, or any significant medical or psychological conditions.

Data collection

A total of 340 patients meeting the inclusion criteria were approached and those providing consent were enrolled. SD was evaluated using the validated Arizona Sexual Experience Scale (ASEX), which assesses libido, arousal, erection or lubrication, orgasm, and satisfaction. An ASEX score > 19 or specific item criteria, indicated dysfunction. All male participants also completed the International Index of Erectile Function (IIEF-5), a validated tool assessing ED severity across five domains, with National Institutes of Health (NIH)-defined cut-off values categorising ED into five severity levels. Both

questionnaires are validated tools administered as structured self-reports.

Sample size and statistical analysis

The sample size required to estimate SD prevalence with a 5% margin of error and 80% power was calculated to be 222, consistent with the findings of Marzieh *et al.* in Iran.¹⁴ Statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS) version 16.0. Continuous variables (age, body mass index [BMI], blood pressure, and fasting blood sugar) are presented as mean $\pm$ standard deviation, while categorical variables (gender,

education, job type), are summarised as percentages. Chi-square tests were used to assess the differences between male and female participants.

Results

A total of 340 patients with DM (210 males and 130 females) were screened over an 11-month period. Of these, 93.8% of males (197 out of 210) and 53.1% of females (69 out of 130) consented to discuss their sexual experiences. Figure 1 illustrates the study flow diagram.

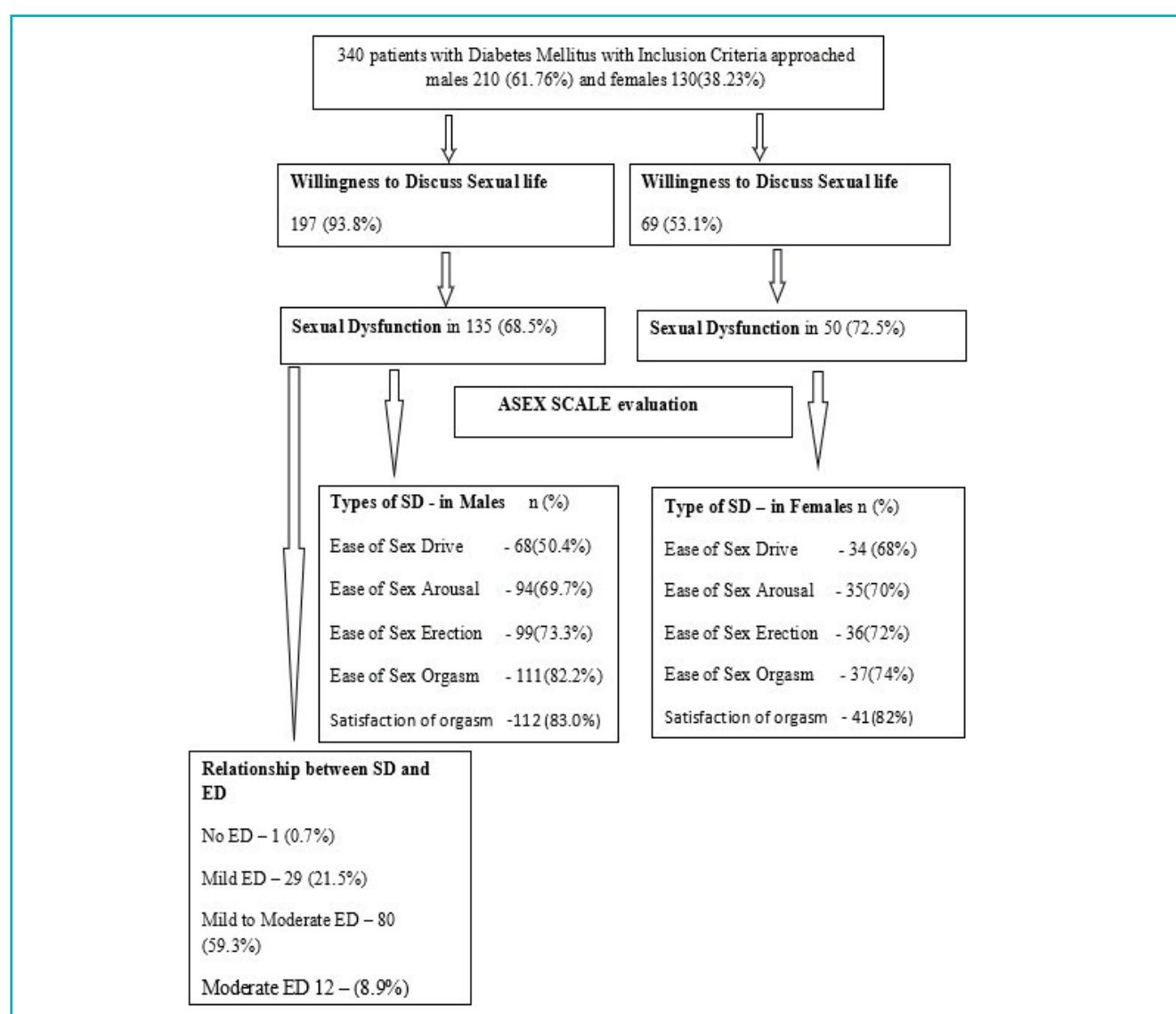


Figure 1: Study flow diagram and demographic characteristics of the study participants.

Abbreviations: ASEX: Arizona Sexual Experience Scale; ED: Erectile Dysfunction; SD: Sexual Dysfunction.

All participants were married, with mean ages of 43.0 ± 7.69 years for males and 43.23 ± 7.80 years for females. Most had type 2 DM (97.1% of males; 99.2% of females), with mean ages at diagnosis of 37.81 ± 7.65 years for males and 39.03 ± 7.71 years for females. Hypertension was present in 51% of males and 45.4% of females, while dyslipidaemia was reported in 49.5% and 45.4%, respectively. The primary method of diabetes management was diet and lifestyle modification (53.3%), followed by oral medications (50.8%). Higher education was achieved by 64.3% of males and 20% of females; 96.7% of males were employed full-time, while 58.5% of females were homemakers. Alcohol consumption (10%) and smoking (4.3%) were reported exclusively among males, and all participants identified as heterosexual.

Prevalence of SD

The prevalence of SD was 68.5% in males (135/197) and 72.5% in females (50/69). Dissatisfaction with orgasm was the most common issue (83% males; 82% females, $p = 0.019$), followed by difficulty achieving orgasm (82.2% males; 74% females, $p = 0.004$) (Table 1). Males with SD had a mean age of 42.9 ± 8.0 years (62.2% aged 30–45), while females averaged 46.9 ± 8.1 years (60% aged 46–60). Educational levels differed significantly ($p < 0.001$) — 66.7% of affected males held a college education versus 20% of females. Employment status also varied, with 95.6% of males in full-time employment and 58% females being homemakers.

Category n (%)	Male n=135	Female n=50	p-value
Lack of ease in sex drive	68 (50.4)	34 (68)	0.013
Lack of ease of arousal	94 (69.7)	35 (70)	0.003
Lack of ease of erection	99 (73.3)	NA	-
Lack of ease of wetness	NA	36 (72)	-
Lack of ease of orgasm	111 (82.2)	37 (74)	0.004
Dissatisfaction with orgasm	112 (83)	41 (82)	0.019

Table 1: Types of sexual dysfunction in male and female patients.

On comparing the metabolic profile, 94.8% of males and 78% of females had proteinuria. Although total cholesterol, LDL-C, and TGs were raised, HDL-C levels were lower in males as compared to females ($p < 0.001$) (Table 2).

	Patients with Sexual Dysfunction	Patients without Sexual Dysfunction	p-value
Age	43.09 ± 7.73	43.00 ± 7.70	
Fasting blood sugar (FBS)	181.28 ± 56.45	143.05 ± 9.26	< 0.001
Glycated haemoglobin (HbA1c)	8.77 ± 1.99	7.64 ± 1.56	< 0.001
Cholesterol	241.37 ± 27.27	192.54 ± 31.61	< 0.001
High-density lipoprotein-cholesterol (HDL-C)	35.78 ± 4.04	43.07 ± 4.78	< 0.001
Low-density lipoprotein-cholesterol (LDL-C)	114.57 ± 16.47	83.40 ± 20.78	< 0.001
Triglycerides (TG)	169.08 ± 29.62	113.28 ± 42.30	< 0.001

Table 2: Comparison of socio-demographic and clinical variables of patients with and without sexual dysfunction.

Patients with SD had significantly higher FBS, HbA1c, total cholesterol, and LDL-C, but lower triglycerides compared to those without SD (Table 3). Smoking ($p = 0.009$), hypertension ($p = 0.046$), and dyslipidaemia ($p = 0.05$) showed significant associations with SD, whereas mean ages did not differ between groups (43.09 ± 7.73 vs. 43.00 ± 7.70).

Variables	Male n=135	Female n=50	p-value
Socio-demographic variables			
Age (years)	42.89 ± 8.03	46.92 ± 8.07	0.003
Age group, n (%)			
30–45	84 (62.2%)	19 (38%)	0.013
46–60	49 (36.3%)	30 (60%)	
> 61	2 (1.5%)	1 (2%)	

Variables	Male n=135	Female n=50	p-value
Socio-demographic variables			
Occupation, n (%)			
House maker	0 (0%)	29 (58%)	< 0.001
Full-time	129 (95.6%)	9 (18%)	
Part-time	5 (3.7%)	11 (22%)	
Unemployed	0 (0%)	1 (2%)	
Retired	1 (0.7%)	0 (0%)	
Alcohol, n (%)			
Yes	11 (8.1%)	0 (0%)	0.037
No	124 (91.9%)	50 (100%)	
Smoking, n (%)			
Current smoker	2 (1.5%)	0 (0%)	0.049
Ex-smoker	13 (9.6%)	0 (0%)	
Non-smoker	120 (88.9%)	50 (100%)	
Clinical characteristics			
Type of diabetes mellitus, n (%)			
Type 1 diabetes mellitus	3 (2.2%)	1 (2%)	0.926
Type 2 diabetes mellitus	132 (97.8%)	49 (98%)	
Age at onset of diabetes (years)	37.78 ± 7.439	42.78 ± 7.939	< 0.001
Duration of diabetes, n (%)			
1–5 years	66 (49.6%)	29 (58%)	0.173
6–10 years	60 (44.4%)	21 (42%)	
> 10 years	9 (5.9%)	0 (0%)	

Variables	Male n=135	Female n=50	p-value
Treatment for diabetes, n (%)			
Diet/lifestyle and oral medications	77 (57%)	28 (56%)	0.899
Injectables (mainly insulin)	36 (26.7%)	21 (26%)	0.927
Injectables (mainly insulin) and oral medications	22 (16.3%)	1 (20%)	0.554
History of hypertension, n (%)	100 (74.1%)	13 (26.3%)	0.793
Dyslipidaemia, n (%)	73 (54.1%)	26 (52%)	0.423
Body mass index (BMI, kg/m²)	25.63 ± 1.615	25.52 ± 2.002	0.702
Systolic blood pressure	130.37 ± 5.439	130.16 ± 6.267	0.823
Diastolic blood pressure	79.75 ± 6.511	79.08 ± 6.240	0.532
Pulse rate	90.44 ± 5.914	90.02 ± 6.485	0.679
Biochemical laboratory parameters, %			
Fasting blood sugar (FBS, mg/dL)			
< 120	22 (16.3%)	15 (30%)	0.640
> 120	113 (83.7%)	35 (70%)	
Glycated haemoglobin (HbA1c)			
6%–8%	74 (54.8%)	29 (58%)	0.699
> 8%	61 (45.2%)	21 (42%)	
MAU, mcg/mg of creatinine			
< 30	7 (5.2%)	11 (22%)	0.001
30–300	128 (94.8%)	39 (78%)	

Variables	Male n=135	Female n=50	p-value
Total cholesterol	245.38 ± 22.51	230.56 ± 35.26	0.001
LDL	116.54 ± 13.14	109 ± 22.538	0.007
HDL	35.04 ± 3.31	37.76 ± 5.08	< 0.001
Triglycerides	171.64 ± 28.65	162.14 ± 31.35	0.052
Urea	14.93 ± 3.22	15.50 ± 3.20	0.283
Creatinine	0.78 ± 0.42	0.82 ± 0.39	0.534

Table 3: Socio-demographic factors, clinical characteristics, and laboratory parameters of males and females with sexual dysfunction.

Abbreviations: HDL: High-density cholesterol; LDL: Low-density cholesterol; MAU: Microalbuminuria.

Prevalence of ED

Among males with SD, 99.3% (134/135) reported ED. Based on IIEF-5 scores, 9.6% (13/135) had severe ED, while 59.3% (80/135) had mild to moderate ED. Even among males without SD, 81.6% still reported ED, mainly mild (63.2%). The mean age of males reporting ED was 43.05 ± 7.98 years.

Discussion

Female sexual dysfunction (FSD) in India is under-researched, partly due to conservative societal norms and women's traditional roles. While western studies report higher prevalence, Indian research often reports lower rates, likely due to fewer focused studies and the women's reluctance to discuss sexual health. In this cohort of 340 patients with diabetes, no significant gender difference in SD prevalence was observed, possibly reflecting the unequal gender distribution and female participants' hesitance to discuss sexual experiences. This reluctance may stem from their homemaking role and strong conservative cultural norms in the Indian society.

Among male participants, SD prevalence was 68.5%, slightly higher than the 59.8% reported in Ghanaian men⁹ and comparable to 63.6% in Chinese diabetic men.¹⁰ Female SD prevalence was 72.5%, exceeding

the Ghanaian rate of 61.5%⁹ but lower than the 83% reported by Yaylali *et al.*¹⁰ Other studies show variability, with rates ranging from 51.3% to 71% among women with diabetes.^{11,12} Such differences across studies may stem from variations in sample selection, SD definitions, assessment tools, and population characteristics such as ethnicity, geography, and diet.

In a 2010 Iranian study, Marzieh Ziaei-Rad *et al.* reported SD prevalence of 82.5% among diabetic patients, with a significant gender association.¹⁴ By contrast, our study reported a 69.5% overall prevalence, with orgasm satisfaction being the most common complaint in both genders (83% in males, 82% in females). Muniyappa *et al.* noted that diabetes affects desire, arousal, and orgasm, reducing genital sensation and causing vaginal dryness and dyspareunia.¹³ Our findings align, showing decreased arousal (70%), lubrication (72%), and orgasm (74%) among females with diabetes, underscoring the need to recognise and address FSD in diabetes management.

A vast majority (99.3%) of males with SD reported ED. Notably, 83.6% of males without self-reported SD still exhibited ED, reflecting that while SD is subjective, ED is an objectively measurable condition. SD prevalence was higher in older females compared to males (Table 2). Although many studies suggest SD increases with age, some report no significant age association. Diabetic males show earlier susceptibility to SD and ED, with incidence varying widely (20%–85%),¹⁴ often linked to longer diabetes duration. However, several studies report non-significant age correlations with SD, including ED.¹⁵

In our study, no significant correlation was found between diabetes duration and either gender or sexual function. SD was more prevalent in both sexes with shorter diabetes duration. Younger males (30–45 years) showed higher SD rates than females, possibly reflecting cultural factors that influence older males' attitudes toward sexual health. Male sexual function is strongly influenced by psychological and cultural factors, unlike females, who focus more pragmatically on caregiving roles. These findings contrast with some previous research showing a stronger link between diabetes duration and female SD, highlighting inconsistent evidence and the need for further longitudinal studies to clarify this relationship.^{16,17}

Occupation was significantly associated with SD in both sexes. More educated males in managerial or

professional roles reported higher SD, possibly due to greater awareness linked to education and occupation, a finding supported by an African study.¹⁷ Conversely, most females with SD were less educated homemakers. Additionally, SD prevalence was significantly related to diabetes treatment type, with most affected participants, both male and female, managing diabetes primarily through diet and lifestyle modification.

Our study found that males and females with poor glycaemic control exhibit higher rates of SD compared to those with good control, consistent with findings by Romeo *et al.*¹⁸ High glycaemic levels, which contribute to microvascular and macrovascular complications, likely underlie this association.¹⁸

Additionally, this study found a significant relationship between lipid abnormalities and SD — males with SD had higher total cholesterol and LDL-C, and lower HDL-C compared with females with SD. Smoking was also gender-related, with male smokers and ex-smokers more prone to SD. Patients rarely discuss SD with healthcare providers, often due to embarrassment or the assumption that providers will address it. Many participants reported negative impacts on relationships, psychological well-being, and overall quality of life. Males tended to view SD as a threat to masculinity, whereas females were more accepting of their condition. Poor partner understanding of SD may lead to marital and psychosocial difficulties.

Conclusion

The research evaluated SD in diabetic patients using validated measures, revealing significant effects in both genders. Females exhibited a lower propensity to engage in discussions regarding sexual issues compared to males. Orgasm dissatisfaction was prevalent in both genders, and most males with SD also reported ED. In males, SD was associated with an earlier onset of diabetes compared to females. The prevalence of SD varied by education, occupation, and employment type, with higher rates observed among more educated, professionally employed males. Lipid profiles also varied by gender, with males exhibiting elevated cholesterol levels and reduced HDL-C levels. Additionally, male smokers exhibited a higher prevalence of SD in comparison to females.

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Alterations in Serum Electrolyte Levels Among Enteric Fever Patients: A Study at Max Super Speciality Hospital, Saket, New Delhi

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Abstract:

Electrolyte disturbances are common yet under-recognised complications in patients with enteric fever and can lead to adverse clinical outcomes if not promptly managed. Enteric fever, caused by *Salmonella enterica* serovars Typhi and Paratyphi, remains a major public health challenge in developing countries like India. Despite its prevalence, limited research has focused on electrolyte imbalance patterns in affected patients. This study evaluated alterations in serum electrolyte levels — specifically sodium, potassium, chloride, and bicarbonate — among adult enteric fever patients admitted to a tertiary care center in New Delhi. A hospital-based cross-sectional analysis was conducted at Max Super Speciality Hospital, Saket, including 128 adult patients (≥ 18 years; 59 males, 69 females). Serum electrolytes were measured on admission and categorised as low, normal, or high. Descriptive statistics, including mean and standard deviation, were used to evaluate the distribution of electrolyte values, which were as follows: bicarbonate 21.37 ± 3.93 mmol/L, chloride 100.96 ± 4.18 mmol/L, potassium 4.21 ± 0.61 mmol/L, and sodium 133.70 ± 4.00 mmol/L. A significant proportion of patients exhibited hyponatraemia (58.6%) and low bicarbonate levels (57.8%), suggesting trends toward fluid-electrolyte imbalance and metabolic acidosis. In contrast, potassium and chloride levels remained largely within normal limits, with over 95% of patients maintaining normal potassium levels. The study highlights that mild to moderate hyponatraemia and metabolic acidosis (as indicated by low bicarbonate) are frequent findings among patients with enteric fever. Regular monitoring of electrolyte profiles should be integrated into the diagnostic and therapeutic workflow to mitigate potential complications and improve patient outcomes.

Key words: Enteric Fever, Serum Electrolytes, Hyponatraemia, Metabolic Acidosis, Adult Patients, Max Hospital.

Introduction

Enteric fever, encompassing both typhoid and paratyphoid fever, remains a pressing public health concern in many developing regions, including India. Caused primarily by *Salmonella enterica* serovar Typhi, this systemic illness is typically transmitted through the ingestion of contaminated food or water. Despite advances in hygiene and sanitation, the burden of enteric fever remains high. The World Health Organisation (WHO) estimates over

11 million cases globally each year, resulting in approximately 129,000 deaths, the majority occurring in South Asia and sub-Saharan Africa.¹

In India, enteric fever continues to be a significant cause of morbidity and mortality, particularly in urban slums and semi-urban regions with inadequate sanitation and poor water quality. According to the Surveillance for Enteric Fever in India (SEFI) study, the incidence of typhoid fever in urban India is estimated at 360–1,200 cases per 100,000

population annually, with children and young adults being the most affected demographic.² The National Centre for Disease Control (NCDC) reports that India accounts for an estimated 4.8 to 6 million cases of typhoid fever each year, with a mortality rate of approximately 0.5%.³ These alarming figures emphasise the urgent need for improved clinical monitoring and early detection of complications — such as electrolyte imbalance — that can significantly impact patient outcomes.

Electrolyte disturbances are frequently observed in systemic infections due to various factors such as prolonged fever, gastrointestinal losses (e.g., diarrhoea or vomiting), poor oral intake, and renal dysfunction. Among these, serum sodium and potassium imbalances are the most commonly reported abnormalities.⁴ Hyponatraemia, in particular, is widely recognised in patients with enteric fever and may result from syndrome of inappropriate antidiuretic hormone secretion (SIADH), third-space fluid losses, or renal salt-wasting.⁵ Additionally, metabolic acidosis due to low bicarbonate levels is often underappreciated but may significantly affect patient outcomes if left uncorrected.

While the clinical profile and antimicrobial resistance patterns of enteric fever have been extensively studied, there is a relative paucity of data specifically focusing on electrolyte imbalances in hospitalised adults. Previous studies, such as that by Ohanu *et al.*, have highlighted the diagnostic and prognostic relevance of serum electrolyte assessment in infectious conditions, underscoring the need for routine monitoring.⁶

This study, conducted at Max Super Speciality Hospital, Saket, New Delhi, aimed to identify and analyse patterns of serum electrolyte alterations — namely sodium, potassium, chloride, and bicarbonate — among adult patients diagnosed with enteric fever. By characterising the extent and type of electrolyte disturbances, this study aimed to contribute valuable clinical insights that can assist healthcare providers in optimising patient management and improving treatment outcomes.

Methods

This retrospective observational study evaluates alterations in serum electrolyte levels among enteric fever patients. Data were obtained from the laboratory information system at Max Super Speciality Hospital,

Saket, New Delhi, covering patients diagnosed between January 2023 to March 2024.

A total of 240 patient records were initially retrieved. After removing duplicates and cases with incomplete electrolyte profiles, 128 patients with complete values for all four major electrolytes (sodium, potassium, chloride, and bicarbonate) were included in the final analysis.

Only the first test results from each patient were analysed to standardise comparisons and reflect the early biochemical status on admission. All tests were performed as part of routine clinical evaluation using automated biochemistry analysers, following standard procedures.

Electrolytes measured

The study assessed four key electrolytes, each essential for maintaining physiological balance and commonly affected during febrile illnesses like typhoid fever.

Chloride:

Serum chloride concentration was determined using a colorimetric method, wherein chloride ions react with specific reagents to form a coloured complex. The absorbance of this complex, measured at a specific wavelength, is directly proportional to the chloride concentration.⁷

Potassium:

Potassium levels were analysed via turbidimetric analysis. In this method, the sample is treated with sodium tetraphenylborate, which forms a colloidal suspension with potassium ions. The resulting turbidity, measured spectrophotometrically, corresponds to the potassium concentration within the measurable range.⁸

Bicarbonate:

Serum bicarbonate was measured using an enzymatic method based on the modified Forrester procedure. In this assay, phosphoenolpyruvate reacts with bicarbonate in the presence of phosphoenolpyruvate carboxylase (PEPC) to produce oxaloacetate, which is then converted to malate-by-malate dehydrogenase (MDH). This conversion is coupled with the oxidation of nicotinamide adenine dinucleotide (NADH) to NAD⁺, and the rate of NADH depletion, measured spectrophotometrically, indicates the bicarbonate concentration.⁷

Sodium:

Sodium concentration was determined using ion-selective electrode (ISE) technology, which measures the potential difference generated by sodium ions across a selective membrane. This method allows for accurate and direct quantification of sodium in undiluted serum or plasma.⁷

Electrolyte reference ranges

To classify test results, the following reference ranges were adopted based on WHO clinical guidance and peer-reviewed literature (Table 1):

Electrolyte	Reference Range (mmol/L)	Clinical Source
Sodium (Na ⁺)	135–155	WHO Guidelines/ Ohanu <i>et al.</i> , 2016 ⁶
Potassium (K ⁺)	3.0–5.0	
Chloride (Cl ⁻)	98–108	
Bicarbonate (HCO ₃ ⁻)	22–32	

Table 1: Classification of serum electrolyte values among enteric fever patients.

Each electrolyte value was classified as low, normal, or high according to these reference ranges. The cleaned dataset was then analysed using descriptive statistics (mean, median, standard deviation), with distributions also assessed by gender.

Results

A total of 128 adult patients with confirmed enteric fever and complete serum electrolyte records were included in the analysis. Sodium, potassium, chloride, and bicarbonate levels were measured at admission.

Figure 1 illustrates the distribution of serum electrolyte levels (low, normal, high) across male and female patients for sodium, potassium, chloride, and bicarbonate. A notable proportion of females exhibited low bicarbonate and sodium levels compared to males.

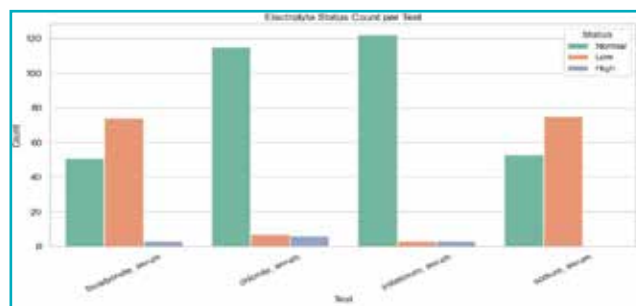


Figure 1: Distribution of electrolyte status by gender.

Electrolyte status distribution: Overall

Electrolyte abnormalities were most pronounced for sodium and bicarbonate. As shown in Table 2, 58.56% of patients had hyponatraemia, while 57.8% showed low bicarbonate levels, suggesting a trend towards metabolic acidosis. In contrast, potassium levels were largely preserved, with 95.3% of patients falling within the normal range, and only 4.7% presenting either low or high values. Similarly, chloride levels were predominantly normal (89.8%), with only a small proportion of patients presenting hypochloraemia or hyperchloraemia.

These findings further corroborate trends observed in the Ohanu *et al.*⁶ study, where sodium and bicarbonate disturbances were most common among typhoid patients, while potassium remained relatively unaffected. This emphasises the importance of monitoring sodium and bicarbonate closely during the early stages of enteric fever, particularly in patients with symptoms of dehydration or gastrointestinal loss.

Electrolyte	Low (n)	Normal (n)	High (n)	% Low	% Normal	% High
Serum bicarbonate	74	51	3	57.8%	42.5%	2.34%
Serum chloride	7	115	6	5.4%	89.8%	4.68%
Serum potassium	3	122	3	2.34%	95.3%	2.34%
Serum sodium	75	53	0	58.59%	41.4%	0.0%

Table 2: Distribution of electrolyte status.

Electrolyte	Mean (mmol/L)	Standard Deviation (mmol/L)
Serum bicarbonate	21.37	± 3.93
Serum chloride	100.96	± 4.18
Serum potassium	4.21	± 0.61
Serum sodium	133.70	± 4.00

Table 3: Mean and standard deviation of serum electrolytes.

The overall mean serum electrolyte concentrations are summarised in Table 3. Sodium exhibited the highest deviation with a mean value of 133.70 ± 4.00 mmol/L, slightly below the lower reference threshold, reinforcing the high prevalence of hyponatraemia observed earlier. Mean bicarbonate was 21.37 ± 3.93 mmol/L, marginally below the lower clinical cutoff of 22 mmol/L, indicating a general trend toward metabolic acidosis.

The potassium levels were within the expected reference range (4.21 ± 0.61 mmol/L), showing relatively tight clustering and further supporting the observation that potassium regulation remained stable in most patients. The mean chloride concentration was 100.96 ± 4.18 mmol/L, which lies within the normal physiological range, with only minor deviations observed in a few patients.

Gender	Test name	Mean	Standard Deviation
Female	Serum bicarbonate	19.82	± 4.57
Female	Serum chloride	101.39	± 3.70
Female	Serum potassium	4.36	± 0.59
Female	Serum sodium	132.20	± 6.18
Male	Serum bicarbonate	20.93	± 4.86
Male	Serum chloride	100.72	± 3.69
Male	Serum potassium	4.19	± 0.50
Male	Serum sodium	133.32	± 6.28

Table 4: Electrolyte distribution by gender.

Gender-specific patterns are detailed in Table 4. For bicarbonate, a greater proportion of female patients were observed in the low category, with fewer in the normal range. Conversely, male patients exhibited a relatively balanced distribution, skewing slightly toward the normal range. The mean bicarbonate level in females was 19.82 ± 4.57 , whereas in males it was 20.93 ± 4.86 , indicating a slightly higher average in males.

For chloride, both genders predominantly had normal values, with females recording a mean of 101.39 ± 3.70 and males 100.70 ± 3.69 reflecting minimal deviation, with very few individuals in the low or high categories.

Potassium levels were largely within the normal range for both genders, with slightly higher values in females (4.36 ± 0.59) compared with males (4.19 ± 0.50). The tight standard deviation values indicate a consistent distribution across the population.

Sodium levels showed a notable skew towards low values in females (132.20 ± 6.18), while males were more represented in the normal range (133.32 ± 6.28).

Overall, males tended to have higher mean values across most electrolytes and a more balanced distribution, whereas females showed a greater tendency towards low bicarbonate and sodium levels. These findings highlight potential gender-based differences in electrolyte status and may inform targeted clinical management strategies.

Discussion

This study investigated serum electrolyte alterations among 128 adult patients with enteric fever admitted to a tertiary care center. The most prevalent abnormalities observed were hyponatraemia (58.6%) and low bicarbonate levels (57.8%), while potassium and chloride levels were largely within normal limits.

The high prevalence of hyponatraemia aligns with prior studies and can be attributed to several mechanisms commonly associated with enteric fever. These include gastrointestinal losses (diarrhoea, vomiting), reduced oral intake, and in some cases, SIADH, which is known to occur in systemic infections. SIADH leads to water retention and dilutional hyponatraemia, even in the absence of overt fluid loss. The severity of hyponatraemia may also reflect the level of dehydration or delay in seeking care.

Similarly, the high frequency of low bicarbonate suggests a trend toward metabolic acidosis, which may result from volume depletion, poor tissue perfusion, and lactic acid accumulation in response to infection. The mean bicarbonate level (21.37 mmol/L) was slightly below the reference range, consistent with mild acidosis in this patient population. While arterial blood gases were not assessed, the biochemical pattern indicates a compensatory metabolic response to systemic illness.

In contrast, potassium and chloride remained largely unaffected, with over 95% of patients showing normal potassium concentrations, unlike other infections where hypokalaemia is common. This may suggest earlier presentation or less severe illness in our cohort.

Gender-based analysis revealed slightly lower average sodium and bicarbonate levels in female patients, possibly indicating a greater vulnerability to electrolyte shifts. Hormonal influences, hydration status, and differences in health-seeking behaviour may contribute to this variation and warrant further investigation.

These findings underscore the need for routine electrolyte monitoring in enteric fever management. Early detection and correction of sodium and bicarbonate imbalances can reduce complications such as seizures, confusion, or prolonged hospitalisation. Despite being an underexplored area in typhoid research, electrolyte assessment has strong clinical relevance and should

be integrated into diagnostic workflows, especially in endemic settings.

Limitations of this study include its single-center design, lack of clinical outcome correlation, and absence of statistical tests to confirm significance. Nonetheless, it highlights an important aspect of supportive care in febrile illness and offers a foundation for larger prospective studies.

Disclosures

The authors declare no conflicts of interest. Artificial Intelligence (AI) assistance (ChatGPT by OpenAI) was used for grammar correction, language enhancement, and formatting improvements during manuscript preparation. The study design, data collection, analysis, interpretation, and conclusions are entirely original and solely authored by the listed contributors.

Conclusion

This study demonstrates that significant alterations in serum electrolyte levels, particularly hyponatraemia and low bicarbonate levels, are common among patients with enteric fever. These disturbances likely result from gastrointestinal losses, systemic infection, and altered fluid balance. Among the electrolytes studied, sodium was the most frequently affected, emphasising the need for vigilant monitoring and prompt correction of electrolyte imbalances during the clinical management of enteric fever.

Our findings underscore the importance of incorporating routine electrolyte assessment in the diagnostic and therapeutic protocols for enteric fever, especially in endemic regions like India. Early recognition and management of these imbalances can reduce morbidity, shorten hospital stays, and improve patient outcomes. Further multi-centre studies with larger sample sizes are recommended to strengthen the generalisability of these results.

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Monitoring Physiotherapy in Peripheral Vascular Diseases: An Important Part of Patient Care

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Abstract:

Peripheral Arterial Disease (PAD), a progressive atherosclerotic disorder, significantly impairs blood flow to the lower extremities, leading to functional limitations such as intermittent claudication, fatigue, and decreased mobility. As PAD progresses, patients may experience pain at rest, ulcerations, or limb-threatening ischaemia. This review explores the critical role of physiotherapy monitoring in the management of PAD. Evidence suggests that physiotherapeutic interventions, including exercise therapy, wound care education, gait training, and patient education, contribute significantly to improving patient outcomes. The integration of physiotherapy into multidisciplinary PAD care helps restore functional mobility, reduce complications, and improve quality of life.

Key words: Peripheral Arterial Disease (PAD), Intermittent Claudication, Physiotherapy, Functional Mobility, Vascular Rehabilitation, Exercise Therapy, Patient Monitoring.

Introduction

Peripheral arterial disease (PAD) is a chronic vascular disorder resulting from atherosclerosis, primarily affecting the arteries of the lower limbs. It is characterised by arterial narrowing and occlusion that compromises peripheral blood flow.¹ A typical clinical manifestation is intermittent claudication, pain or discomfort in the lower extremities triggered by physical activity and relieved by rest. As the disease advances, symptoms can progress to critical limb ischaemia, with rest pain, and ulcerations. Reduced perfusion results in impaired skin integrity, delayed wound healing, muscle weakness, and limited

exercise tolerance, all of which negatively impact both the physical and psychological well-being of patients.^{2,3} Management of PAD extends beyond pharmacologic and surgical interventions. Physiotherapy plays an essential role in improving functional status, addressing exercise limitations, monitoring cardiopulmonary function, and preventing complications related to immobility and tissue breakdown. This review aims to highlight the significance of physiotherapy surveillance as an integral part of the comprehensive management of PAD.

Role of Physiotherapy in PAD

Early functional assessment and monitoring

Early physiotherapy evaluation enables timely identification of mobility limitations, impaired skin integrity, and cardiopulmonary compromise. Surveillance includes monitoring vital signs, oxygen saturation, pulse rate, and exertional symptoms during physical activity, ensuring that patients respond safely to rehabilitation.^{4,5}

Exercise rehabilitation

Supervised exercise therapy (SET) remains the first-line non-invasive treatment for intermittent claudication. Programs typically include treadmill walking, resistance training, and functional movement exercises to enhance lower limb perfusion and increase walking distance.⁶ Regular exercise stimulates collateral circulation, improves muscle metabolism, and delays the onset of claudication pain.

Wound care and skin integrity

Patients with PAD are prone to ulcers, delayed wound healing, and skin breakdown due to compromised perfusion. Physiotherapists play a role in wound prevention by educating patients on skin protection, proper footwear, and offloading techniques. Where applicable, they support wound healing through adjunctive modalities and mobility strategies.⁷

Cardiopulmonary considerations

PAD often coexists with coronary artery disease and pulmonary dysfunction. Physiotherapists assess and manage cardiopulmonary status both pre-surgery and post-surgery to prevent complications. Monitoring includes assessing haemodynamic responses to activity and adjusting intensity levels accordingly.⁸

Education and behavioural modification

Patient education is a cornerstone of PAD management. Physiotherapists educate patients on the disease process, importance of smoking cessation, safe mobility practices, and exercise adherence. This improves treatment compliance and enhances long-term outcomes.⁹

Psychosocial support and quality of life

PAD significantly affects patients' mental health due to chronic pain, reduced mobility, and social isolation.

Physiotherapists provide motivational support and help restore confidence through achievable physical goals, ultimately enhancing quality of life.¹⁰

Clinical application

A case analysis of a patient with chronic PAD revealed common challenges including intermittent claudication, poor cardiopulmonary reserve, and impaired skin integrity. Angiographic findings showed arterial narrowing at the common iliac artery. Physiotherapy interventions focused on:

- Cardiopulmonary monitoring during ambulation
- Exercise therapy for strength and endurance
- Patient education regarding PAD, medication adherence, and symptom tracking
- Referral for vascular surgery assessment

Post-discharge follow-up involved ongoing surveillance, therapy progression, and continued lifestyle modification education. This case illustrated the need for collaborative care among physiotherapists, vascular surgeons, and primary care physicians.

Discussion

PAD requires a comprehensive and interdisciplinary approach due to its systemic effects. The inclusion of physiotherapy in the management framework ensures that functional impairments are addressed early. Numerous studies have validated the effectiveness of supervised exercise therapy in increasing pain-free walking distance and reducing disease progression.^{6,9}

Physiotherapy's value extends to secondary prevention through education and monitoring. By identifying subtle functional changes, physiotherapists can intervene proactively, thereby reducing the risk of ulceration, amputation, and hospital readmission.

Despite these benefits, barriers such as lack of physiotherapy access or insufficient awareness among patients and clinicians can limit its impact. Therefore, healthcare systems should integrate physiotherapy as a routine part of PAD care pathways.

Conclusion

Physiotherapy monitoring plays a pivotal role in the holistic management of PAD. From early assessment to rehabilitation and education, physiotherapists significantly contribute to restoring mobility, preventing complications, and improving patient quality of life. Incorporating physiotherapy into standard PAD treatment protocols promotes optimal outcomes and underscores the importance of multidisciplinary collaboration in chronic vascular care.

Albert Paul Varghese, Anurag Ashok Luharia, Suhas Tiwaska, Shreya Naik, Ishiqua Vinay Patil, Arif Hussain Malla, Syed Asrar. Monitoring Physiotherapy in Peripheral Vascular Diseases: An Important Part of Patient Care. MMJ. 2025, September. Vol 2 (3).

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Percussion: You Remember?

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Abstract:

In this article, percussion is used symbolically to represent the bedside medical skills and practices that are fading from routine use. Clinicians must constantly remember "The Art & Science of Bedside Diagnostics." In the age of high-resolution imaging, the traditional art of percussion is gradually disappearing from routine clinical practice. However, bedside skills like percussion remain indispensable, particularly in situations where immediate imaging is unavailable or delayed. We present a case in which percussion played a pivotal role in diagnosing pleural effusion, reminding clinicians of the irreplaceable value of clinical examination. This article aims to reinforce the relevance of percussion for young doctors, medical students, and interns, and to encourage the revival of this fundamental yet underutilised skill.

Key words: Percussion, Clinical Skills, Physical Examination, Pleural Effusion, Medical Education, Bedside Diagnosis.

Introduction

Physical examination has long been a cornerstone of clinical practice, and inadequacies in physical examination are a preventable source of medical error.¹ Yet, with the growth of advanced diagnostic technologies, essential bedside skills like percussion are being neglected in everyday practice. Percussion allows clinicians to distinguish between normal, fluid-filled, or air-filled body cavities. Historically, it has been critical for diagnosing pleural effusions, pneumothorax, hydropneumothorax, mild ascites, and organomegaly; especially splenomegaly.

Training in medicine, even a couple of decades ago, involved a systematic approach with a thorough history and an elaborate physical examination, including inspection, palpation, percussion, and auscultation, after which one would shortlist the differential diagnoses. Diagnostic tests were useful in confirming or ruling out a diagnosis. This process lent our practice a certain charm and excitement that may have been lost over the years.

Today, when a clinician sees a patient, they are often already equipped with a large 'file' with multiple test reports, either confirming a diagnosis or informing further

tests. They are seldom required to perform a traditional physical examination. For example, how often do we now see a pleural effusion or thickening diagnosed using percussion? How often do we perform a percussion exam to diagnose ascites?

In this age of super specialists, and of course, social media and generative artificial intelligence (AI), clinicians spend significant time and effort answering highly specific questions about particular organs or diseases, often to the extent of having to justify their approach. This has also become important in preventing potential medico-legal issues. Thus, a heavy dependence on investigations has crept into practice.

Historical Perspective

Leopold Auenbrugger introduced percussion to clinical medicine in 1761, revolutionising the way physicians approached the diagnoses of internal diseases.² For over two centuries, percussion, coupled with inspection, palpation, and auscultation, were the mainstay of chest and abdominal assessments, providing diagnostic clues long before X-rays or computed tomography (CT) scans became available.

Case Report

A 52-year-old male, non-smoker, with hypertension, presented to the emergency department with breathlessness and left-sided chest heaviness. There was no history of trauma, fever, or cough. On presentation, his vital signs were as follows: respiratory rate 34/min, blood pressure 90/70 mmHg, SpO₂ 79% on room air, and pulse rate 112/min. The differential diagnoses considered were pulmonary embolism, acute coronary syndrome, and pleural pathology (effusion or pneumothorax). Due to an unforeseen technical failure, and anticipated delay in imaging, the physician proceeded with a detailed bedside examination.

Relevant clinical findings included tracheal shift to the right, and reduced chest expansion on the left. On percussion, there was a stony dullness over the left hemithorax, with the upper border at the 4th intercostal space, midclavicular line. On auscultation, breath sounds were absent over the dull area of the left hemithorax.

Based on percussion and auscultation, a massive left-sided pleural effusion was diagnosed clinically. Once the technical issue was resolved, a chest X-ray confirmed the diagnosis, validating the bedside findings. Emergency thoracentesis was performed, draining 1.5 litres of straw-coloured fluid, resulting in immediate symptom relief.

Discussion

Mechanisms and techniques of percussion

Percussion assesses tissue density based on sound transmission:

1. **Resonant:** Normal lung
2. **Dull:** Consolidation or mass
3. **Stony dull:** Pleural effusion
4. **Hyper-resonant:** Pneumothorax or emphysematous bullae

The technique highlights the use of the non-dominant hand as a pleximeter, with the middle finger of the dominant hand (the plexor finger) used to tap briskly on the pleximeter. Both sides should be compared systematically to ensure accurate interpretation.

Clinical applications

1. **Thoracic pathologies:** Pleural effusion, consolidation, pneumothorax and specially hydropneumothorax

2. **Abdominal assessment:** Hepatomegaly, splenomegaly, bladder distension, ascites (including demonstration of shifting dullness)
3. **Cardiac borders:** Pericardial effusion (rarely performed today but still valuable in certain situations) and cardiomegaly

Evidence-based utility

This involves emphasising the most important physical signs needed to determine an underlying medical condition or disease.³ Dr. Sapira also emphasised the role of percussion in bedside diagnosis.⁴

Why has percussion been forgotten?

- Overreliance on imaging (X-ray, ultrasound, CT scan)
- Fear of medico-legal cases
- Fear of missing diagnoses
- Decline in confidence in physical examination³

When can percussion save lives?

- Emergency triage when imaging is delayed
- Mass casualty situations or disasters
- Resource-limited or rural settings
- Rapid bedside diagnosis during acute deterioration
- Lack of importance given to medical sign

Limitations

- Operator-dependent; requires practice and experience
- Less effective for early pathology especially small effusions, minimal pneumothorax or mild organomegaly
- May miss subtle pathology without complementary techniques

Educational implications

Percussion should be actively taught and demonstrated during bedside rounds. Senior clinicians must role-model its use to ensure transfer of skills. It should be included in Objective Structured Clinical Examination (OSCEs) and clinical competency assessments. Studies have shown that pulmonary physical examination skills among medical students vary significantly and are often inadequate, highlighting the need for focused training.⁵

Conclusion

This case serves as a reminder that percussion remains an essential clinical tool, especially in acute care. When performed skilfully, it can provide rapid, cost-effective, and reliable diagnostic information at the bedside. Reviving this practice can enhance the synergy between technology and clinical acumen, benefitting patients and improving diagnostic efficiency.

In this article, percussion symbolises bedside medical skills and practices that are fading. One must remember that medical diagnosis is both an 'Art and a Science'!

We present below the quotes of senior clinicians teaching post graduate doctors:

- Dr. Nitin Rathod, Senior Consultant, HOD Internal Medicine, Training Programme Director IMT, at Nanavati Max Super Speciality Hospital, Mumbai: *"A clinical sign cannot be replaced every time by investigations. To investigate the patient, one must have a clinical diagnosis for ordering investigations."*
- Dr. Hemalata Arora, Senior Consultant, Internal Medicine at Nanavati Max Super Speciality Hospital, Mumbai: *"I would say, read Hutchison's Clinical Methods if possible and try eliciting just one sign daily. It will keep you engaged and interested in clinical signs. There is a huge sense of accomplishment when you diagnose based on clinical signs and confirm on diagnostics. That is the essence of medicine."*
- Dr. Sandeep Tamane, Consultant Internal Medicine at Deenanath Mangeshkar Hospital and Research Centre: *"Basic clinical skills are very important including thorough systemic examination. This will help diagnose many conditions clinically without the need for costly investigations. We must update our clinical skills."*

Learning Points

Percussion, a core bedside clinical examination, remains an important and cost-effective diagnostic skill. Despite technological advances, it warrants continued teaching and deliberate practice. Careful bedside assessment can sometimes pre-empt and guide imaging decisions, saving critical time. By strengthening clinical suspicion and judgement, unindicated or unnecessary investigations can be avoided.

Ashwini Jogade, Nitin Rathod, Andrea Janice. Percussion: You Remember? MMJ. 2025, September. Vol 2 (3).

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Oral Inflammation and Chronic Heart Failure: Is there a Risk Association?

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Abstract:

Periodontal disease (PD), a chronic oral inflammatory condition, has been associated with an increased risk of cardiovascular disease (CVD), including complications such as heart failure (HF). Patients with coronary artery disease (CAD) have a higher prevalence of PD, and conversely, individuals with PD are at increased risk of CAD, myocardial infarction, and stroke. HF and PD share common risk factors, such as smoking, diabetes mellitus, alcohol consumption, hypertension, and low socioeconomic status. Chronic inflammation is the primary aetiology for chronic HF regardless of its underlying cause. Increased oral inflammation caused by periodontitis exacerbates systemic inflammatory burden, thereby predisposing individuals to a higher risk of CAD and HF.

Key words: Cardiovascular Disease, Gum Disease, Chronic Heart Failure, Inflammation, Periodontitis, Oral inflammation, Oro-Systemic Inflammation.

Introduction

Heart failure (HF) is a severe manifestation occurring in the late stages of various heart diseases. It is a progressive syndrome characterised by structural and functional cardiac changes resulting in typical symptoms as exertional dyspnoea, ankle swelling, and fatigue. HF is considered a global pandemic, especially affecting the older population. It can be stratified by left ventricular systolic function into HF with preserved ejection fraction (HFpEF), HF with mildly reduced ejection fraction (HFmrEF), and HF with reduced ejection fraction (HFrEF).¹ An estimated 64.3 million people worldwide are affected by HF. In developed countries, the prevalence is generally 1%–2%. HF can lead to cardiac arrest and is associated with a high risk of mortality. Inflammation plays an important role in the pathogenesis of cardiovascular diseases (CVD), including HF.²⁻⁴ Studies have shown that inflammatory factors contribute to ventricular remodelling, which in turn affects the development of HF.⁵⁻⁷

Periodontitis is described as a chronic infectious inflammatory condition affecting the supporting tissues around the teeth. Severe periodontitis is a serious burden and has been linked to several systemic conditions^{8,9} including CVD, which may progress to HF.

Pathobiology Underlying Risk Association of Periodontitis and CVD

The invasion of oral bacteria (present in dental plaque) into the systemic circulation activates a series of immunoinflammatory responses, leading to a massive release of pro-inflammatory mediators such as interleukin-1 (IL-1), IL-6, tumour necrosis factor- α (TNF- α), and monocyte chemoattractant protein-1 (MCP-1), along with acute phase proteins, matrix metalloproteinases, C-reactive protein (CRP), fibrinogen, and free radicals.¹⁰ These inflammatory mediators impact the cardiovascular system by altering lipid metabolism, causing endothelial injury, and increasing the hypercoagulability of blood and platelets. This,

in turn, increases the risk of atherosclerosis, arterial calcification, fibrogenesis, and cardiovascular tissue

injury.¹¹⁻¹³ Pathway of how inflammatory mediators are linked to periodontitis and atherosclerotic CVDs is shown in Figure 1.

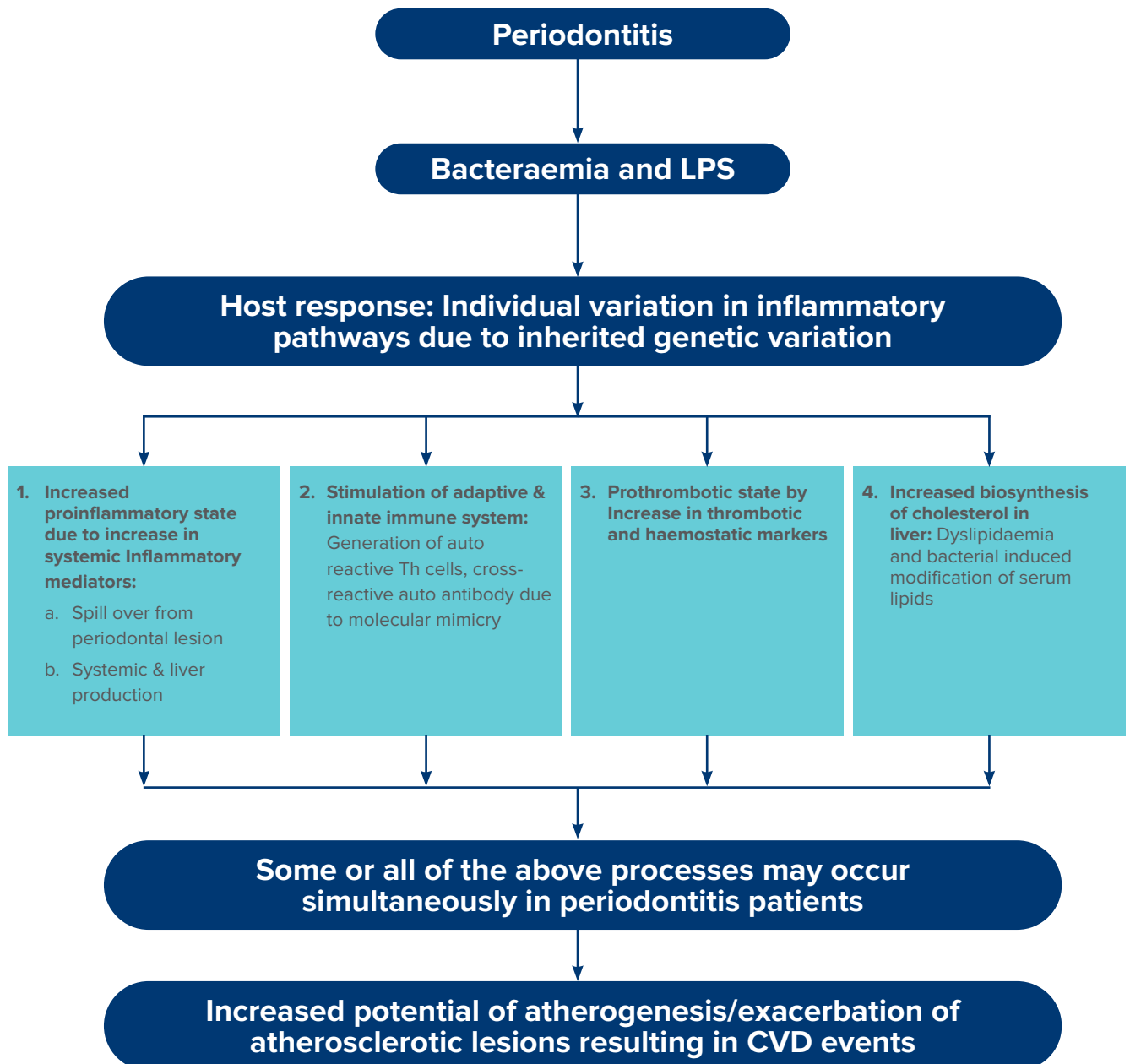


Figure 1: Inflammatory mechanisms linking periodontitis and atherosclerotic cardiovascular disease.³⁶

Abbreviations: CVD: Cardiovascular Disease; LPS: Lipopolysaccharide.

Studies have confirmed the link between increased oral bacterial load, bacteraemia and CVDs.¹⁴⁻¹⁸ Among oral microbes, bacteria associated with periodontal disease, particularly those belonging to the red and orange complexes, have been linked to systemic conditions such as CVDs.¹⁹ Furthermore, previous studies have reported the molecular mechanisms through which inflammatory factors contribute to CVDs

such as hypertension, atherosclerosis, and myocardial infarction.^{20,21}

Evidence-Based Data on the Association between Periodontitis, Coronary Heart Disease, and HF

Published data support the association between CAD and periodontitis. Oral pathogens have been identified in up to 44% of atherosclerotic plaques,²² and

a high antibody response against major periodontal pathogens appears to be associated with prevalent CAD.²³ Furthermore, dental-plaque bacteria such as *Streptococcus sanguis* can induce platelet aggregation by expression of the platelet aggregation-associated protein in vitro.²⁴ Intravenous infusion of these pathogens in rabbits has been shown to cause changes in electrocardiographic values, heart rate, blood pressure, and cardiac contractility.²⁵ Frohlich *et al.*, in their study on 71 patients with stable chronic HF reported the prevalence of gingivitis, moderate periodontitis, and severe periodontitis as present in 17 (24%), 17 (24%), and 37 (52%) patients, respectively. Severe periodontitis was more prevalent among chronic HF patients than in the general population. When assessing the relationship between periodontitis severity and HF symptoms, the authors concluded that the 6-minute walking distance (a test to assess physical activity capacity) was significantly lower in patients with severe periodontitis.²⁶

Yan *et al.*, in their population-based study (NHANES III), reported that the incidence of HF in participants with moderate or severe periodontitis was 5.72 times higher (95% CI: 3.76–8.72, $p < 0.001$). This risk was regardless of the presence or absence of hypertension, and the risk was higher in the non-hypertensive subgroup, suggesting that periodontitis may be an independent risk factor for HF.²⁷ Wood & Johnson were among the first to report this association, having evaluated over 17,000 people from NHANES III. They found that patients with periodontitis had a higher incidence of self-reported HF.²⁸ A large Asian study, using the Taiwan National Health Insurance Research Database, also reported a positive correlation between periodontitis and HF.²⁹

Although HF and periodontal disease differ in aetiology and pathophysiology, both are characterised by chronic, unregulated inflammatory processes, that contribute to myocardial damage, decreased cardiac function, and poor prognosis.^{30,31} The global cardiovascular mortality report states that many chronic infectious and inflammatory diseases such as periodontitis are associated with a significantly increased risk of cardiovascular adverse events, such as atrial fibrillation, myocardial infarction, and HF.³² Mucci *et al.*, in their study stated that periodontitis and HF have shared risk factors such as: age, gender, smoking, diabetes, hypertension, and hypercholesterolaemia. After adjusting for various confounding factors, they confirmed an independent association between periodontitis and the risk of HF.³³ Walther *et al.*, in a study of 6300 patients, reported that patients with periodontitis showed a higher burden of cardiovascular risk factors (e.g., older age, male sex, diabetes mellitus, hypertension) compared to those with no or mild periodontitis. Severe periodontitis was significantly associated with HFmrEF.³⁴

Molensky *et al.*, in their study involving 1,700 patients, reported that baseline periodontal disease and edentulism were associated with incident HF during a 13-year follow-up period. Periodontal status was associated with elevated levels of CRP and N-terminal pro-B-type natriuretic peptide (NT-proBNP). PD was associated with an increased risk for HFpEF and significantly increased risk for HFrEF. Edentulism was associated with unfavourable changes in both CRP and NT-proBNP, while PD was associated only with CRP.³⁵

Conclusion

Poor gum health (periodontal disease) is a potential precursor to systemic inflammation and is highly prevalent in patients with HF irrespective of the cause of HF. Therefore, neglect of oral health should not be overlooked by cardiologists. Cardiologists should be encouraged to refer their patients for dental screening.

Sangeeta Dhir, Viveka Kumar. Oral Inflammation and Chronic Heart Failure: Is there a Risk Association?

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Tracheal Stenting in Patients with Malignant Oesophageal Carcinoma: A Comprehensive Review

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Abstract:

Pulmonary complications in oesophageal carcinoma are well known and are a major cause of morbidity and mortality. They present as extrinsic compression, airway involvement due to local invasion, and tracheoesophageal fistula (TEF). Tracheal stenting has been effectively used as a treatment to help palliate symptoms and improve the general well-being of the patient. This review focuses on the spectrum of airway involvement in carcinoma of the oesophagus, site of involvement, and the treatment modalities available. The article then focuses on airway stenting and its effect on patients' symptoms, quality of life, and contribution to overall management while addressing the concerns associated with the stent and its attendant complications.

Key words: Tracheal Stenting, Airway Involvement in Carcinoma Oesophagus, Tracheoesophageal Fistula (TEF).

Introduction

Oesophageal cancer is a major global health challenge, including in India. Worldwide, it is the eighth most common cancer, with an annual incidence of 4.56 lakh new cases. Oesophageal carcinoma is the fourth most common cause of cancer-related deaths in India. Approximately 47 thousand new cases are reported each year in India. A retrospective cohort study from Christian Medical College Hospital, Vellore¹, showed that the majority of cancers affected the upper and middle one-thirds of the oesophagus at the mean age of 51.7 years. Countries with a high human development index (HDI) have a higher incidence of adenocarcinoma, whereas countries with low HDI, such as India, have a higher incidence of squamous cell carcinoma.

Pulmonary Involvement in Carcinoma of the Oesophagus: Review of Literature

Pulmonary complications in carcinoma of the oesophagus are well known and are a major cause of morbidity and mortality. In a study by Cheng *et al.*²,

the main presenting complaints in patients with airway involvement were acute respiratory failure (33.3%), dyspnoea (23.8%), recurrent aspiration pneumonia (19.0%), persistent cough (19.0%), and dysphagia (4.8%). Airway involvement in advanced oesophageal cancer can be in the form of tracheal obstruction, which can be classified as intrinsic or extrinsic. Airway invasion by the tumour may compromise luminal space and produce critical airway narrowing or be extrinsically compressed by the oesophageal growth. Formation of tracheoesophageal fistula (TEF) is also a recognised problem. TEF is an abnormal connection between the trachea and oesophagus seen in approximately 5% to 15% cases. Systemic therapies for the treatment of oesophageal cancer can also predispose to the formation of TEF. Over an 18-year study period, Wang *et al.*³ found that 26 patients (0.4%) developed airway gastric fistula among 6,316 consecutive patients who underwent oesophagectomy for oesophageal carcinoma. Junyang *et al.*⁴, in a retrospective study, found that previous radiotherapy was associated with an increased risk of airway involvement, including

TEF, which had poorer survival compared to TEF attributed to tumour invasion. A common complication of TEF is recurrent non-resolving aspiration pneumonia. Pulmonary sepsis causes fatality in about 6 to 12 weeks if not treated promptly.^{5,6} Also, these patients are at higher risk of pulmonary embolism and lung atelectasis. Junyang *et al.*⁴ retrospectively evaluated data from 804 patients with oesophageal cancer, of which 294 patients were found to have airway involvement. Among patients with airway involvement, 57.1% had airway invasion, 71.4% had compression, and 39.5% had both invasion and compression.

Airway involvement in oesophageal carcinoma can be complex, often involving multiple sites and types of involvement, with the left main bronchus being the most affected site due to its close anatomical relationship with the oesophagus. Nophol *et al.*⁵ retrospectively evaluated data of 37 patients who underwent airway stenting for locoregional involvement in patients with carcinoma of the oesophagus. The study showed tumours occurring in the mid oesophagus to be the most common site leading to airway involvement, the upper oesophagus was the second most common location (32.4%) as compared to other sites, followed by upper-middle oesophagus (8.1%), lower oesophagus (5.4%), and upper-middle-lower oesophagus (2.7%). A total of 36.6% of their patients had evidence of airway involvement. The most common site of airway involvement was the left main bronchus (48.6%), followed by the trachea in 12 patients (32.4%). A study by Junyang *et al.*⁴ showed a similar trend with mid-oesophageal tumours being associated with a higher risk of airway involvement. Whereas lower oesophageal cancers rarely affected the central airways.

Airway invasion is the most common involvement at 91.94% and 57.1%, as reported in cohort studies by Cheng *et al.*² and Junyang *et al.*⁴, respectively. Almost one-third of patients had 70%–90% luminal compression, and 10% patients had critical airway narrowing. Cheng *et al.*² reported TEF was present in 14 patients (37.8%), whereas Junyang *et al.*⁴ reported it as 35.7%. A 2020 retrospective study from a single gastroenterology centre in India⁷ evaluated data of the last 20 years and found 7% incidence of TEF. Mixed type of involvement (more than one type) was observed in 78.4% patients.³

A study by Junyang *et al.*⁴ found that patients with airway involvement had reduced survival from the time

of diagnosis (hazard ratio: 1.52) and had significantly more hospitalisations per year compared to those without airway involvement. TEF had shorter survival times compared to those with airway involvement but without TEF.

A ray of hope: Airway stenting

Tracheal stenting is a tested and necessary intervention for malignant central airway obstruction and tracheoesophageal fistula. Guidelines by the World Association for Bronchology and Interventional Pulmonology (WABIP) recommend airway stenting in patients with malignant central airway obstruction (MCAO) presenting with attributable symptoms.⁸

Successful stent deployment has been shown to improve patient's quality of life.⁹ Another single-centre study showed that timely airway stenting in MCAO resulted in a significant improvement in Medical Research Council (MRC) dyspnoea scale and Eastern Cooperative Oncology (ECOG) performance scores.¹⁰ In a retrospective, single-centre study¹¹, it was found that in patients with MCAO, a combination of airway stenting and external beam radiotherapy (EBRT) was associated with better survival rates compared to EBRT or stenting alone. Yonghua *et al.*¹², in a retrospective analysis of combined airway and oesophageal stent implantation for malignant tracheobronchial and oesophageal disease, found that both dyspnoea and dysphagia were significantly relieved, and the survival rates were 82.4%, 78.8% and 78.8% for 1, 3, and 5 years, respectively.

An ideal tracheal stent should be stable and strong to resist the external compressive forces and migration, biocompatible, easily deployed, and removable. The available stent materials include silicone, nitinol, stainless steel, and hybrid stents. Metallic stents made from nitinol and steel are preferred nowadays due to their strength and the ability to exert radial force to keep the airways open. Stents can be self-expandable metallic stents (SEMS) or fixed-diameter stents that may require balloon dilatation. Covered metallic hybrid stents have the advantage that they allow minimal tissue ingrowth and can be easily manipulated. In general, flexible bronchoscopy under local sedation is needed for deployment of these metallic stents.^{2,3,5}

The silicone stents, on the other hand, are versatile and can be easily removed and replaced, which serves a purpose in managing benign airway diseases. They usually require a rigid bronchoscopy and deeper

sedation for deployment. The most common silicone stents include Montgomery t-tube, tubular stent, and Y stent.¹³ Biodegradable stents are under evaluation but are currently not available in India.

The initial concern regarding stents affecting radiation is now being addressed. Early porcine model study by Evans *et al.*¹⁴ showed that metallic airway stents do not significantly affect radiation dose in the airway, and EBRT can be given in a patient with metallic airway stents without affecting the radiation delivered to the tissue.

Airway stenting remains a crucial intervention for patients with malignant airway involvement as it serves as a bridge to further cancer-specific therapy. Many patients who may be rendered non-treatable due to an underlying fragile condition and severe airway complications may improve post-stenting. Nophol *et al.*⁵ demonstrated this, where only 48.6% out of 56.7% patients — who received treatment after airway stenting — were found eligible to receive treatment before airway stenting. More patients were eligible to receive concurrent chemoradiation, post-stenting, as it improved their underlying general condition. Patients who received post-stenting treatment had longer survival time (139 days) than those without treatment (57 days). The median survival time after airway stenting was 97 days (interquartile range: 57–199 days). Specifically, airway stenting in treatment-naïve patients provided survival benefits, and adjuvant treatment after airway stenting was associated with significantly prolonged survival. The study strongly advocated that airway involvement is not a contraindication for chemoradiation, but airway management should be considered before chemoradiation. The study found that treatment-naïve patients and those who received treatment after airway stenting were associated with improved survival. In cases of respiratory failure requiring mechanical ventilation, it may facilitate extubation.

Airway stenting, oesophageal stenting, or both (double stenting) after TEF diagnosis were associated with

improved survival. They found that prior radiation was associated with increased risk of airway involvement, increased TEF incidence, and that airway stenting was associated with improved survival.⁴

A significant issue with airway stenting is the formation of granulation tissue, which can lead to restenosis or airway obstruction.^{15–17} Stent migration is another complication, particularly in dynamic airway regions, necessitating the regular monitoring of stent positioning.¹⁴ Of all the patients that received airway stents, 52.4% had stent-related complications such as mucus plugging (35.7%), tumour ingrowth (38.1%), and granulation tissue formation (7.1%). They found that the incidence of tumour ingrowth was significantly higher in this study (38.1%) when compared to previous data from different studies (5%–24%).

Case 1

We present the case of a 74-year-old female who was evaluated for dysphagia and difficulty in breathing. Upper gastrointestinal (GI) endoscopy showed an eccentric growth at 18 cm–22 cm, and a biopsy confirmed it to be squamous cell carcinoma of the oesophagus. A bronchoscopy was done to evaluate the airways, which showed extrinsic compression of the distal half of the trachea compromising approximately 80% of the tracheal lumen (Figure 1) and tracheal infiltration of the right and left main bronchus. Since the patient had worsening shortness of breath, a SEMS Y stent was placed to cover the lower half of the trachea and both the main stem bronchi (Figures 2 and 3). The patient's general condition improved along with improvement in breathlessness. The patient was started on weekly neoadjuvant chemotherapy (NACT) with injection carboplatin and paclitaxel. The patient was doing well, with significant improvement in symptom burden after 5 weeks since SEMS insertion.

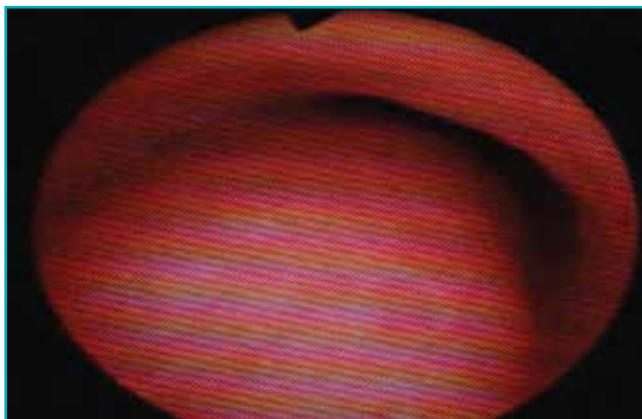


Figure 1: Bronchoscopic examination showing severe tracheal luminal narrowing due to extrinsic compression.

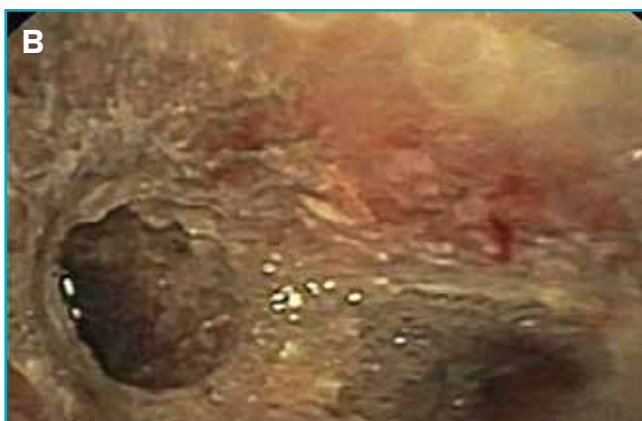


Figure 2(A and B): After the deployment of self-expandable metallic stent (SEMS) Y stent - Bronchoscopic examination showing near normal lumen of the lower trachea and bilateral mainstem bronchi.

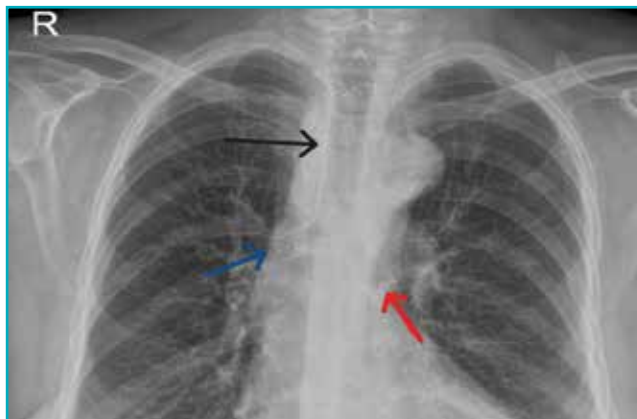


Figure 3: Chest X-ray showing self-expandable metallic stent (SEMS) Y stent placement. Black arrow — Indicates the tracheal limb of the Y stent. This portion is placed within the trachea above the carina; Blue arrow — Points to the right main bronchial limb of the Y stent. This extends into the right main bronchus; Red arrow — Marks the left main bronchial limb of the Y stent. This extends into the left main bronchus.

Case 2

We present a case of a 71-year-old female evaluated for dysphagia, weight loss, and cough while swallowing. Upper GI endoscopy showed an ulceroproliferative growth of 18 cm–27 cm from the upper incisor, completely obstructing the lumen. Biopsy showed well-differentiated squamous cell carcinoma of the oesophagus. Whole body positron emission tomography (PET) and computed tomography (CT) showed metabolically active circumferential wall thickening involving the mid-oesophagus, approximately 4.7 cm in length. In view of a persistent cough, bronchoscopy was done, which showed a fungating growth involving the posterior and right lateral wall of the lower trachea, causing luminal compromise (Figure 4). A SEMS Y-Stent placement was done (Figure 5). The patient was started on weekly chemotherapy with carboplatin + pacliaqualip. The patient's general condition improved, and was symptomatically better at 8 weeks after stent and chemotherapy treatment.



Figure 4: Bronchoscopy showing induration with slough in the post wall of the trachea overlying a tracheo-oesophageal fistula.

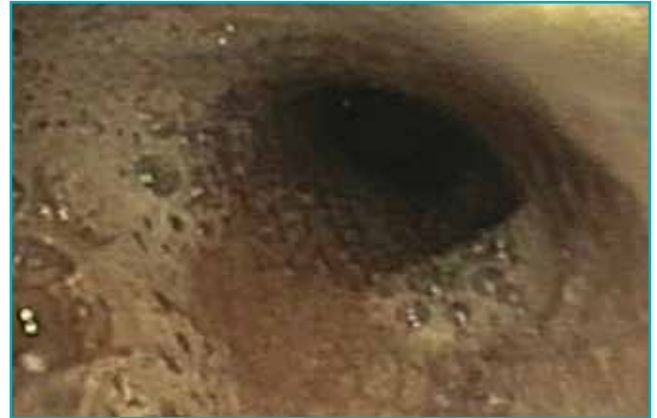


Figure 5: Fistula covered with the stent.

Conclusion

Airway stenting is an active need in patients with airway involvement in cases of advanced oesophageal cancers, which has proven time and again its safety record, amelioration of patient symptoms, improvement in quality of life, and facilitation of further systemic therapy.

Taha Nabeel, Stuti Gupta, Pritha Nayyar, Nikhil Tomar, Ashish Kumar Jain. Tracheal Stenting in Patients with Malignant Oesophageal Carcinoma: A Comprehensive Review. MMJ. 2025, September. Vol 2 (3).

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Emerging Add-Ons in In Vitro Fertilisation Laboratories: Scientific Evidence and Clinical Relevance

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Abstract:

For over a decade, in vitro fertilisation (IVF) laboratories have witnessed a substantial surge in innovative adjunct technologies and procedures — commonly referred to as “add-ons” — designed to optimise IVF reproductive outcomes. While many adjuvants promise improvements in fertilisation, embryo development, and subsequent implantation success, their scientific underpinnings and clinical efficacy remain varied. This review critically examines the most prominent emerging add-ons in IVF, assesses current evidence regarding their effectiveness, and discusses their relevance in clinical practice.

Key words: In Vitro Fertilisation (IVF), Adjuvants-Add On, Success Rates, Pre-Implantation Genetic Testing for Aneuploidy (PGT-A), Artificial Intelligence (AI), Embryo Glue, Assisted Hatching (AH).

Introduction

In vitro fertilisation (IVF) add-ons are supplementary techniques or products introduced alongside conventional IVF treatment protocols in IVF laboratories, and aim to improve IVF success rates. The most widely used IVF laboratory adjuvants — time-lapse imaging, embryo glue, pre-implantation genetic testing for aneuploidy (PGT-A), artificial intelligence (AI)-based embryo selection, and assisted hatching (AH) are aimed at improving implantation and live birth rates. With the increasing competition among fertility clinics, the demand for cutting-edge technologies is rising, often outpacing the evidence supporting them. Many of the new techniques are embraced enthusiastically. But regulatory bodies like the Human Fertilisation and Embryology Authority (HFEA) have warned that approximately 73% of patients in the UK use unproven add-ons, often with limited effectiveness and inadequate risk disclosure. This review article aims to analyse the scientific data behind emerging IVF add-ons and evaluate their actual benefits in clinical settings.

Prominent Emerging Add-Ons and Scientific Evidence

1. Integrated time-lapse imaging (TLI) based on AI and morphokinetics

Time-lapse monitoring systems, such as embryoscope, allow high-frequency continuous imaging of embryo development without disturbing the culture conditions of the embryos (Figure 1). AI-based algorithms are now being integrated to assess embryo quality and objectively rank embryos based on morphology and kinetics. AI models like Intelligent Data Analysis Score (iDAScore) for embryo evaluation and AIVF's Embryo Morphological Assessment (EMA) are using deep learning to interpret morphokinetics data. iDAScore versions 1.0 and 2.0 showed AI performance comparable to experts.¹ A retrospective Chinese cohort found that iDAScore-guided TLI improved predictive power for pregnancy. These systems may standardise embryo selection, though prospective randomised controlled trial (RCT) validation remains pending.²

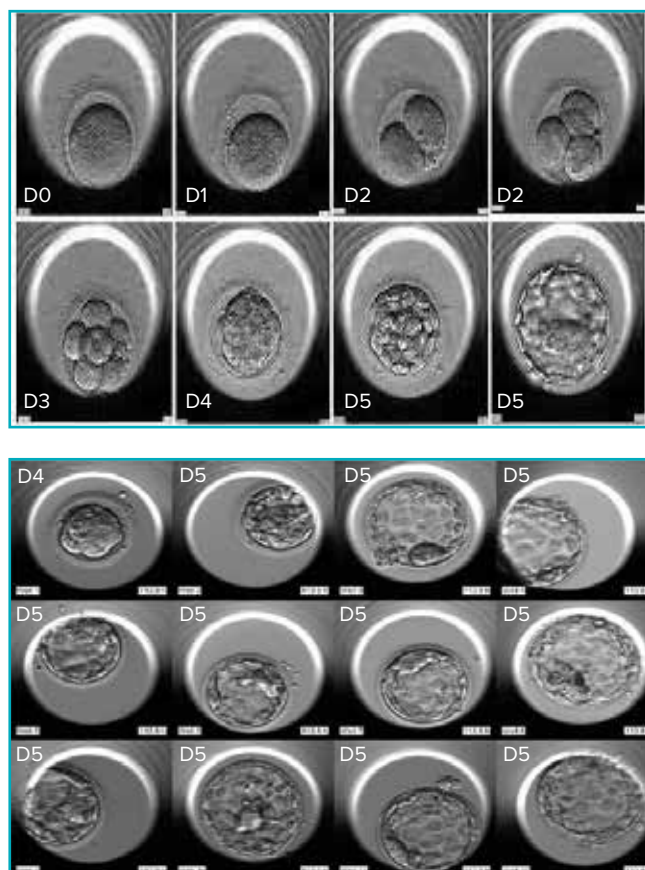


Figure 1: Illustration of the systematic development of human embryos in a time-lapse embryo monitoring system, depicting various stages, from zygote (Day 1 [D0]) to blastocyst (Day 5 [D5]) formation.

Scientific evidence: While TLI offers valuable morphokinetics data, meta-analyses show no consistent improvement in live birth rates compared to conventional embryo assessment.³ Preliminary findings suggest potential in improving consistency and predictive power in embryo selection, but more validated studies are needed.

Another major multicentre RCT (1,575 patients) found no significant improvement in live birth or pregnancy rates with approximately 33.7% TLI assisted live births vs 33%–36% control.⁴

- The American Society for Reproductive Medicine (ASRM) considers TLI an experimental technology. There is insufficient evidence to support the routine use of TLI system to improve IVF outcomes.
- European Society of Human Reproduction and Embryology (ESHRE) stated that while TLI provides detailed embryo development information, its clinical benefit remains unproven.

Clinical relevance: TLI is a non-invasive and helpful technique in selecting embryos, but not a standalone predictor of success. It is not yet proven to be superior to a skilled embryologist assessment and is evolving rapidly.

2. PGT-A

PGT-A is a transformative tool in assisted reproductive technology (ART), which involves prior screening of embryos for chromosomal abnormalities followed by implantation via biopsy and genetic testing, aiming to improve IVF outcomes. Abnormal chromosome count or aneuploidy is a primary cause of implantation failure and miscarriage, especially in women over 35 years of age. PGT-A employs technologies like fluorescence in situ hybridisation (FISH), array-comparative genomic hybridisation (aCGH), single-nucleotide polymorphism (SNP), and next-generation sequencing (NGS) to select euploid embryo transfer. NGS enhances the detection of mosaicism and segmental anomalies with superior accuracy compared to older methods. There are some challenges and limitations associated with PGT that may complicate its usage, like mosaicism, biopsy impact on embryo, false positives, false negatives, cost, and ethical concerns.

PGT procedure involves the culture of embryos till the blastocyst stage. At this stage, the embryo has two distinct parts: inner cell mass (ICM) and trophectoderm (TE). With the help of a laser pulse, a small opening is made in the zona pellucida (ZP), and using a biopsy pipette (Figure 2), a few of the TE cells (approximately 6–8) are gently aspirated.

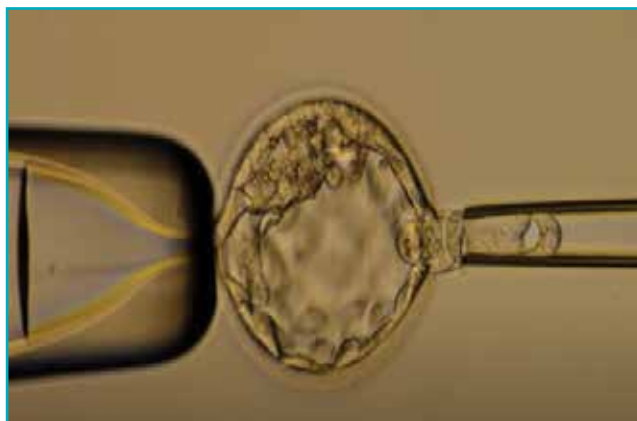


Figure 2: Illustration of human blastocyst (trophectoderm cells) biopsy — Day 5.

Types of PGT

- 1. PGT-A:** Screens for chromosomal aneuploidies, such as trisomy 21, Turner syndrome, Klinefelter syndrome, trisomy 13, and trisomy 18
- 2. Preimplantation genetic testing for monogenetic or single gene disorder (PGT-M):** Targets specific inherited disorders (e.g., cystic fibrosis, thalassaemia) in couples who are known carriers
- 3. Preimplantation genetic testing for structural rearrangements (PGT-SR):** Detects chromosomal structural abnormalities such as translocations and inversions, common in couples with recurrent pregnancy loss

Scientific evidence (Table 1): Although PGT-A may reduce miscarriage rates and improve implantation in certain age groups (e.g., advanced maternal age), as large RCTs suggest limited benefit in young patients with good prognosis.⁵

- American College of Obstetricians and Gynaecologists (ACOG 2020/ASRM 2024) does not recommend routine use of PGT-A and suggests its selective use in advanced maternal age (AMA) groups, recurrent miscarriage, or recurrent implantation failure after counselling on limitations.⁶

Patient Group	Live Birth Rate	Miscarriage Rate	Clinical Pregnancy
Women > 35 years with poor prognosis	↑Modestly	↓Significantly	↑Somewhat
General population (≤ 35 years)	No or ↓ benefit	↓ Low benefit	No Benefit
Known disease population	↑ Benefit	↓ Significant	↑ Improved by 5%–10%

▼
Table 1: Summary of outcomes by patient group.⁷

Clinical relevance: PGT-A offers clear benefits in older women (> 35 years) and those with recurrent loss or failure, reducing miscarriage and modestly improving live birth outcomes. It allows elective single embryo transfer (eSET), reducing multiple pregnancies. However, it does not benefit — and may harm —

younger patients or those with few embryos. Its routine use requires cautious, informed consent, and selection based on age and prognosis.

3. Embryo glue (hyaluronic acid-enriched transfer medium)

Embryo glue is a very specialised transfer medium containing hyaluronan to improve embryo adhesion to the endometrial wall. Hyaluronan is naturally elevated in the uterine environment during the implantation window, with roles in embryo adhesion (via CD44 receptors), trophoblast invasion, angiogenesis, and protection against expulsion by increasing medium viscosity. Commercially available embryo glue contains a high concentration of hyaluronan and recombinant albumin formulated to mimic uterine fluid.

Scientific evidence (Table 2): Some RCTs show a modest increase in implantation rates in patients having recurrent implantation failure, while others show negligible impact.⁸

- ESHRE (2023) categorises embryo glue as a “recommended” add-on for its moderate evidence.
- HFEA rates it “amber” (conflicting/moderate evidence).

Conditions	Evidence Summary
Fresh transfer	Live birth rate ↑ up to 28%; cleavage/blastocyst formation rate: +19%–22%
Frozen embryo transfer (FET)	No consistent benefit shown
RIF patients	Some benefit in clinical pregnancy; not universal
Safety	No increase in miscarriage or harm detected
Cost-effectiveness	Variable; low risk with marginal benefits; patient-informed choice needed

▼
Table 2: Summary of a systematic review and meta analysis.⁹

Abbreviations: FET: Frozen Embryo Transfer; RIF: Recurrent Implantation Failure.

Clinical relevance: Embryo glue may modestly increase live birth rate (approximately 20%) in fresh IVF cycles and possibly in implantation-challenged patients. Although the use of embryo glue is generally considered safe, its cost varies, and its benefits remain small. Thus, it is offered as an option rather than as a routine add-on. Transparent counselling on its likely marginal impact and cost aligns with current evidence-based practice.

4. Assisted hatching (AH)

Implantation failure remains a significant hurdle in ART. For implantation to occur, a blastocyst must hatch from the ZP — a glycoprotein shell surrounding an embryo. Assisted hatching is a micromanipulation technique used in IVF, which involves mechanical, chemical, or laser thinning of the ZP to aid in implantation. Some embryos, particularly from older women or those used after cryopreservation, may have difficulty hatching because of the thickness of the ZP. To address this, AH was developed to artificially weaken or breach the ZP, theoretically facilitating embryo escape and improving pregnancy outcomes.

Scientific evidence (Table 3): Based on various studies, the usage of assisted hatching shows mixed evidence. It could be beneficial in frozen embryo transfers and in patients with prior implantation failure.¹⁰

- ASRM: AH is not recommended routinely; mixed data in FET; caution advised.¹¹
- HFEA: Rates AH as “amber” (uncertain efficacy).
- ESHRE similarly endorses selective use of AH with informed consent.

Clinical relevance: The use of assisted hatching should be individualised based on patient age, the number of embryo transfer failures, and the thickness of the zona pellucida of embryos.

Future Directions

1. Robust RCTs targeting AI-integrated TLI and emerging sequencing platforms, focusing on live birth and neonatal outcomes across age, ovarian reserve, and embryo quality strata are needed.

Outcome	General Population/ Fresh Transfer	Recurrent Implantation Failure	FET/AM Age
Clinical pregnancy	Not significant	↑ in RIF	↑ FET and advanced age
Live birth	Non-significant difference	Slightly improved reported	Minimal benefit
Miscarriage	Uncertain	↓ in young cleavage transfers	Non-significant
Multiple pregnancies	Slight ↑	No ↑	No clear data

Table 3: Summary of a systematic review.¹²

Abbreviations: AM: Advanced Maternal; FET: Frozen Embryo Transfer; GP: General Population; RIF: Recurrent Implantation Failure.

2. Validation of AI models (e.g., iDAScore, EMA) across diverse clinics and patient subgroups is essential for generalisability. AI-based embryo assessment may complement genetic screening for better selection.
3. Explore non-invasive alternatives (niPGT) that use cell-free DNA from spent culture media to assess embryo genetics, avoiding biopsy. Combining genomics, transcriptomic, and metabolomic profiling for comprehensive embryo assessment.
4. Evaluate cost effectiveness, psychological impact, and health economics in diverse healthcare systems.

Guidelines and Recommendations

- **HFEA (UK):** Classifies add-ons with color-coded evidence rating (green=proven, red=not proven)
- **ESHRE:** Emphasises the need for high-quality RCTs before adopting new interventions
- **ASRM (USA):** Recommends personalised use of add-ons based on individual prognosis

Conclusion

The IVF field continues to evolve with innovative technologies aiming to enhance success rates. However, the clinical utility of many emerging add-ons remains under debate. While some add-ons may improve outcomes in selected patient groups, many lack robust, high-quality evidence. The widespread use of these technologies raises ethical concerns about informed consent, cost-effectiveness, and patient expectations. Add-ons often carry hefty price tags with unclear benefits. Clinics sometimes fail to disclose their effectiveness and risks. While technologies like AI-powered embryo selection and enhanced TLI hold great promise, current evidence does not conclusively support their routine use to improve live births. Ethical provision requires transparent patient counselling and prioritising interventions supported by rigorous data. Future trials must validate the potential of the AI platform to ensure add-ons shift from innovative hype to concrete clinical progress. A critical evaluation of scientific evidence and a personalised approach to add-on use are essential to ensure ethical and effective fertility care. Clinicians must prioritise evidence-based practice and transparent communication with patients.

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Vaginal Microbiota: A Critical Component of Reproductive Health and Pregnancy Outcomes

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Abstract:

The vaginal microbiota is a complex and dynamic ecosystem, predominantly composed of *Lactobacillus* species, which play a vital role in maintaining vaginal health and influencing broader reproductive and systemic health outcomes. This review discusses the protective roles of the microbiota in infection prevention, pregnancy, and sexual health, and explores emerging insights and therapeutic applications, including probiotics and vaginal microbiota transplants. As research continues to expand, the vaginal microbiota is proving to be central to the development of personalised medicine in women's health.

Key words: Vaginal Microbiota, *Lactobacillus*, Bacterial Vaginosis, *Gardnerella vaginalis*, *Atopobium vaginae*, *Prevotella Species*, Vaginal Dysbiosis.

Introduction

The vaginal microbiota is a complex ecosystem of microorganisms, including bacteria and fungi, that resides inside the vagina.¹ A healthy vaginal microbiota is typically dominated by *Lactobacillus* species, which produce various antimicrobial compounds such as lactic acid and hydrogen peroxide. These organisms form a homeostatic and mutualistic relationship with the human host,^{2,3} providing protection against pathogenic microbes in exchange for nutrients and shelter. This harmonious interaction supports a healthy vaginal environment, which is essential for reproductive and systemic health.⁴ However, the composition of vaginal microbiota is not uniform across all women.² The communities dominated by *Lactobacillus* are a common feature of many, yet there are those with mixed microbiota that show no symptoms.² While *Lactobacillus*-dominated communities are common, some women have a more diverse or mixed microbiota without exhibiting any symptoms. This variation challenges the definition of what constitutes a

'normal' vaginal microbiota and highlights the need for personalised therapeutic approaches.^{3,4}

Importance of Maintaining Vaginal Health

The female's vagina is a closely balanced and flexible ecosystem that relies on her interactions with existing living microbes, and can be disrupted by various intrinsic or extrinsic factors.⁵ Nowadays, women commonly choose to use intimate hygiene products to cleanse the vulvovaginal area as part of their daily routine.⁶ A national cross-sectional survey in Canada found that over 95% of respondents reported using at least one product in or around the vaginal area, including vaginal/genital moisturisers, anti-itch creams, feminine wipes, washes, suppositories, sprays, powders, and pubic hair removal practices.⁷ Vagina is a self-cleaning organ.⁸ The vaginal area and vulva are resilient and do not require special care; the key to maintain vaginal health is a perfect balance of pH and vaginal microbiome.⁹

Microbes and Their Role in Vaginal Health

1. *Lactobacillus* (most beneficial resident): The *Lactobacillus* species are gram-positive anaerobic microorganisms which naturally colonise the vaginal mucosal surface. They are essential in promoting vaginal health by inhibiting the overgrowth of potentially harmful microorganisms. This is mainly done in two ways, they stick with the epithelial cells that form the vaginal wall and they also secrete antimicrobial substances. Glycoproteins, such as fibronectin, on the surface of these cells facilitate the attachment of *Lactobacilli* to the vaginal epithelium, and the acidic nature of the vagina contributes to this attachment. Although further studies are required, it is believed that other components, such as host proteins, carbohydrates, glycoproteins, lipoteichoic acids, and certain metal ions, also play facilitating roles in this process. Lactic acid is one of the most significant protective substances secreted by *Lactobacillus* and it assists in maintaining the vaginal pH in the acidic range of approximately 3.5 to 4.5, which therefore, has the effect on inhibiting the growth of pathogenic organisms. In the vagina, the two primary sources of lactic acid are the vaginal epithelium (contributing an estimated 10%–20%) and the microbiota, mainly *Lactobacillus* species (estimated to provide 80%–85%). These bacteria metabolise glycogen to produce lactic acid: *Lactobacilli* produce both the L and D isomers, but the ratio of the two forms depends on these species. Oestrogen controls the synthesis of glycogen in vaginal epithelial cells, and when these cells are shed through a process known as desquamation, the glycogen is degraded into glucose, which is then converted into pyruvate and subsequently into lactic acid. Moreover, glycogen stores in the vaginal lumen are converted into smaller sugars by enzymes such as alpha-amylases and lactate-dehydrogenase then utilises them to produce lactic acid. This sustained production of acid is required to uphold the acidic vaginal pH and favours the overall microbial equilibrium. Besides lactic acid, hydrogen peroxide (H₂O₂) is produced by certain *Lactobacillus* strains and is capable of inhibiting opportunistic pathogens, such as sexually transmitted pathogens. Bacteriocins are small polypeptide bactericidal compounds that have demonstrated activity under

laboratory conditions. These bacteriocins constitute another type of protective substance produced by *Lactobacillus*, and their effects have primarily been studied in vitro. Collectively, these mechanisms highlight the complex role of *Lactobacillus* in preserving vaginal homeostasis, providing defence against infection, and positively influencing overall reproductive health.¹⁰

2. *Gardnerella vaginalis* (G. vaginalis: problematic opportunist): *G. vaginalis* is a facultative anaerobic, Gram-variable rod-shaped bacterium that, together with several other predominantly anaerobic bacteria, is implicated in bacterial vaginosis (BV) in some women. This condition results from disruption of the normal vaginal microflora. The acidic environment of the vagina is maintained by the resident facultative anaerobic *Lactobacillus* population. When this normal flora is displaced by anaerobic bacteria, treatment with prescription antibiotics targeting anaerobes may be required to restore the vaginal ecosystem's homeostasis. *G. vaginalis* is not the sole cause of BV but rather functions as a sentinel organism indicative of an altered microbial community marked by the proliferation of multiple bacterial strains. While *G. vaginalis* is commonly isolated from genital specimens, it can also be detected in blood, urine, and pharyngeal samples. Despite being a predominant species in BV, *G. vaginalis* may also be present in asymptomatic women without any signs of infection.¹¹

3. *Atopobium vaginae* (secondary invader in BV): *Atopobium vaginae* is a relatively recent discovery, commonly found in women with BV. The name *Atopobium*, meaning 'strange living thing' in Greek, was established in 1992 to reclassify certain bacteria formerly included in *Lactobacillus* and *Streptococcus*. It belongs to the corio-bacteriaceae family and includes species such as *A. minutum*, *A. rimae*, and *A. parvulum*. *A. vaginae* was first isolated in 1999 from a healthy woman in Sweden. These bacteria are anaerobic, non-motile, gram-positive, and range from elliptical to rod-shaped. They mainly produce lactic acid, along with acetic and formic acids. *A. vaginae* is strongly linked with BV symptoms, including abnormal discharge, raised vaginal pH, and clue cells. In high quantities, especially alongside *Gardnerella vaginalis*, it has been associated with miscarriage and preterm birth. Studies indicate

A. vaginae can stimulate the immune system via toll-like receptor 2 (TLR2), promoting proinflammatory mediators such as interleukin-6 (IL-6), interleukin-8 (IL-8), and antimicrobial peptides. This suggests it plays a role in BV development. Due to its strong association with BV, diagnostic methods detecting both *A. vaginae* and *G. vaginalis* are being considered to enhance diagnostic accuracy.¹²

4. *Prevotella* species (anaerobic disruptors):

Prevotella species are anaerobic microbes that usually participate in BV. The glucose, which may be derived by host enzyme degradation of glycogen, is fermented to produce short-chain fatty acids (SCFAs) including acetic, propanoic, and butyric acid. Although these acids have a minor effect in lowering vaginal pH, they are considerably less potent than lactic acid, and without the predominance of *Lactobacilli*, they are unable to maintain an acidic environment. This helps raise the pH characteristic of BV. Under glucose-depleted conditions, particularly in low-oestrogen conditions, *Prevotella* reliance is on readily available amino acids that are shed by the host epithelium or provided via bacterial enzyme activity.¹³ This leads to generation of alkaline by-products such as ammonia that increases vaginal pH and provides an excellent environment to anaerobes. Other by-product substances are putrescine and cadaverine which create the fish odour that BV has and hydrogen sulfide which is the cause of tissue irritation and bad smells. Such metabolic processes also disrupt vaginal homeostasis and inhibit the good *Lactobacilli*. *Prevotella* is another bacterium that forms biofilms in most cases alongside other bacteria like *G. vaginalis*. Biofilms also enable bacteria to resist antibiotics and the immune system, making BV more persistent. The stabilisation of these microbial communities through the production of extracellular polysaccharides, combined with enzymes that weaken the epithelial barriers — such as sialidases and proteases — facilitates the shedding of nutrients that contribute to inflammation and promote further bacterial proliferation.¹⁴ *Prevotella* tends to be synergistic with other BV-associated bacteria

e.g. *G. vaginae* and *Fannyhessea vaginae*. When they are combined, they enhance the synthesis of toxic substances such as ammonia, biogenic amines, hydrogen sulphide, SCFAs, which favour a toxic and alkaline milieu, thus altering the vaginal microbiome and worsening the BV symptoms.¹⁵

Putative Model for the Establishment of BV

Healthy vaginal microbiome is dominated by *Lactobacillus* species (Figure 1). *Lactobacilli* enhance the vaginal secretions with lactic acid that decrease its pH and defends against invading or pathogenic bacteria or pathobionts. In healthy epithelial cells, antimicrobial peptide (e.g. secretory leukocyte protease inhibitor [SLPI]) and cytokine secretion is constitutive. Moreover, epithelial and immune cells contribute to homeostasis in production of anti-inflammatory cytokines (e.g. interleukin-1 receptor antagonist [IL-1RA]) (Figure 1A). *G. vaginalis* is the first step in the initiation of vaginal dysbiosis, and the enterococcal facultative anaerobe is normally introduced through sexual exposure. *G. vaginalis* infects the epithelial cells of the vagina, displaces *Lactobacilli* and gives biofilm foothold. Subsequent to *G. vaginalis* colonisation the strict anaerobe, *Prevotella bivia*, is recruited into the biofilm. The metabolism of ammonia and amino acids promotes the growth of the *G. vaginalis* and *P. bivia*. Both *G. vaginalis* and *P. bivia* have the ability to produce enzymes, e.g. sialidase, that can help in mucus degradation and destruction of barriers. No active inflammation is noted; therefore, it may be assumed that these two species of bacteria can avoid host immunity via some unknown ways (Figure 1B). The biofilm has other secondary colonisers recruited e.g. *A. vaginae* and *Sneathia* species. This point involves in shedding of the epithelial cells which are covered with the polymicrobial biofilm. They are identified in vaginal fluid wet mounts and are involved in the Amsel criteria, these are also called as clue cells. The synthesis of biogenic amines and additional metabolites generated by BV-related microbes is supposed to cause high vaginal pH and BV symptoms that include foul odour. Pro-inflammatory cytokines and chemokines are created by epithelial cells and recruited immune cells, and these molecules might cause genital inflammation (Figure 1C).¹⁶

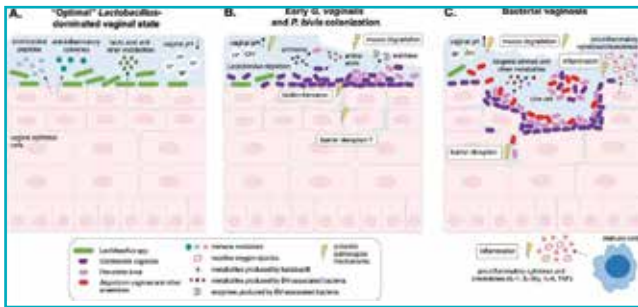


Figure 1: Depiction of a putative model for the establishment of bacterial vaginosis and immunologic/physiological changes related to host-microbe interactions.¹⁶ A. Optimal *Lactobacillus*-dominated vaginal state, B. Early *G. vaginalis* and *P. bivia* colonisation C. Bacterial vaginosis.

Abbreviations: IL: Interleukin; TNF: Tumour Necrosis Factor.

Pregnancy and Reproductive Outcomes

A healthy vaginal microbiome is essential in the maintenance of pregnancy. These imbalances correlate with preterm labour risks, miscarriage, and other complications. Microbiota dominated by *Lactobacillus* influence immune activity and enhance mucosal barriers, which are particularly important to a healthy gestational environment. Recent research indicated that microbiota profiling could help diagnose painless and pregnancy-related complications, stating that early dysbiosis detection could help predict and prevent pregnancy complications, thus it can be used in prenatal care.¹⁷

Preterm birth: Preterm birth is the biggest cause of mortality in children below five years old all over the world and those who survive are often afflicted throughout their lifetime due to motor, sensory, cognitive, and respiratory conditions. The spontaneous prelabour membrane rupture before 37 weeks of gestation and prior to the onset of labour known as preterm prelabour rupture of membranes (PPROM) is associated with up to 30% of preterm births. Infection is the core mechanism of pathogenesis of membrane rupture as well as morbidity of the mother and newborns thereafter. The ability of pathogenic bacteria to colonise the vagina may initiate an inflammatory process that compromises the strength of foetal membranes causing rupture. After rupture, 80% of women give birth in 9 days, thereby exposing the foetus to an ascending infection and complications like chorioamnionitis and funisitis.¹⁸

During pregnancy, the vaginal microbiota is typically dominated by a stable, low-diversity community of

Lactobacillus species, which help to prevent infections. However, domination by *L. iners* or an absence of *Lactobacillus*, combined with polymicrobial colonisation, are recognised risk factors for PPROM, preterm birth, and histological chorioamnionitis. Despite this, there is a paucity of literature examining the vaginal microbiota specifically in PPROM cases, and much of the available data are limited to small cohorts of women with previously ruptured membranes. The management of PPROM involves balancing the extension of pregnancy with the risk of infection. The ORACLE I trial has informed current standard practice, which includes administration of corticosteroids and a 10-day course of erythromycin as prophylaxis. Nevertheless, the long-term benefits of erythromycin are contentious; critics argue that it may not provide adequate coverage of all pathogens and that its use is associated with increased antibiotic resistance and adverse effects such as cerebral palsy, epilepsy, asthma, and obesity.¹⁹

Miscarriage: Miscarriage is a common issue in obstetrics, complicating about 25% of pregnancies worldwide and leading to an estimated average of 44 pregnancy losses per minute.²⁰ Miscarriages can be divided into two categories based on the time point of occurrence: early miscarriages, happening before 12 weeks gestation, and late miscarriages, happening between 12 weeks and 22 weeks of gestation. Also, recurrent miscarriage, defined as three or more consecutive miscarriages, constitutes another variation of the condition.²¹ The relationship between the vaginal microbial landscape and miscarriage was the focus of many studies. First, women who have a miscarriage tend to develop a vaginal microbiome with greater diversity and richness relative to those with successful current pregnancies. This heterogeneity may be attributed to variations in the abundance rates of *Bacteroides plebeius*, *B. breve*, *G. vaginalis*, *M. girerdii*, *L. iners*, *Gardnerella*, and *Prevotella*. Furthermore, a moderately large prospective analysis noted that first and second trimester miscarriage are related to *Lactobacillus* type decline and high bacterial mix precedes miscarriage diagnosis.²²

Gestational diabetes mellitus (GDM): GDM poses a significant challenge not only to the health of the pregnant woman but also to the healthcare system, with an estimated prevalence of 5%–20%. Part of the pathophysiology of GDM involves changes in the hormonal and metabolic profile during pregnancy, which lead to

reduced insulin sensitivity and may occasionally result in the development of glucose intolerance and GDM.²³ During pregnancy, the vaginal microbiome undergoes significant changes. In cases of GDM, alterations in the microbial composition have been observed, including increased bacterial diversity and a higher presence of certain genera. Additionally, women with GDM tend to exhibit a more diverse fungal community, with increased richness and evenness compared to typical pregnancy. However, findings on these associations remain inconsistent, with some evidence suggesting no significant differences in the vaginal microbiome between women with GDM and those without.²⁴

Preterm premature rupture of membranes (PPROM): The prevalence of PPRM varies globally from 1%–4% and its association with preterm birth has been well established, contributing to virtually 30%–40% of premature births. One study attempted to provide insight into the relationship between the characteristics of the vaginal microbiome and PPRM. The bacterial composition in the context of alpha diversity analysis differed significantly in richness, evenness, and diversity between the two groups. Also,

increased relative abundance of *L. iners*, *G. vaginalis*, *P. bivia*, *Ochrobactrum* species, *Prevotella timonensis*, and *Ureaplasma parvum*, and decreased relative abundance of *L. gasseri* were correlated with PPRM.²⁵

Preeclampsia: Vaginal dysbiosis may contribute to abnormal placental development. Pathogenic bacteria from the vaginal tract can ascend to the upper reproductive system, causing inflammation at the maternal-foetal interface. A study published showed that 12.7% of placental samples from women with preeclampsia contained bacteria such as *Prevotella* and *Sneathia*, while none were detected in the control group.²⁶

Ectopic pregnancy: In ectopic pregnancy, there is an association of the disease with chronic inflammation of the fallopian tubes due to dysbiosis common pathogens. This has the capacity of ruining cilia and tubal structure putting more risk of implantation, outside uterus. A meta-analysis revealed that women with BV were exposed to an additional risk of ectopic pregnancy by 54% and colonisation of the cervix with pathogens increased this risk by 16%.^{11,18}

Conclusion

The vaginal microbiota functions both physically and centrally in determining systemic as well as reproductive health in a woman by preventing infections, regulating immunology, and retaining pregnancy as well. The beneficial microbiota is enriched by *Lactobacillus* species and induces a protective low-pH environment by the production of lactic acid, hydrogen peroxide and bacteriocins. These mechanisms of antimicrobials maintain the vaginal homeostasis and prevent the colonisation as well as the growth of pathogenic organisms. Any imbalance in this balance, also known as vaginal dysbiosis, may be quite serious, at least when a woman is pregnant.

Dysbiosis is strongly associated with the negative development during pregnancy, such as preterm birth, PPRM, miscarriage, preeclampsia, and ectopic pregnancy. For example, overgrowth of *G. vaginalis*, *A. vaginae*, *Prevotella* and *Sneathia* has been shown to impair the mucosal barrier, trigger pro-inflammatory responses, and compromise the integrity of reproductive tissues. Such alterations enable the development of ascending infections, weaken foetal membranes, and make it possible to disrupt placental formation, which is linked to such complications as premature labour or a miscarriage. Particularly, microbial colonisation in the placenta of women affected by pre-eclampsia was observed in 12.7% of cases, compared with zero in the controls, and BV increased the susceptibility to ectopic pregnancy by up to 54%.

The knowledge of the composition and dynamics of vaginal microbiota contributes to new possibilities of clinical interventions. The prevention of complications and the enhanced outcomes of pregnancy might be prevented by observing dysbiosis at an early stage in terms of microbial profiling and intervening promptly with specialised therapeutic measures, including probiotics or vaginal microbiota transplantation. Finally, the addition of microbiome monitoring to prenatal care can open a new frontier in the field of individualised medicine when it comes to women's health and would offer a preventative model of reproductive health management and the elimination of pregnancy-related morbidity and mortality.

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Emporiatics: The Science and the Art of Safe Travel

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Abstract:

With a global boom in travel, it becomes imperative to ensure that the journey is safe, the traveller remains healthy, accidents are avoided, and the trip is a memorable experience rather than a health disaster. Emporiatics, or travel medicine, is a fascinating, challenging and upcoming branch of medicine. It involves pre-travel consultation, discussion of the itinerary, risks of travel, precautions, immunisation, medical prescriptions, and first aid advice. The physician educates the traveller about insect bite avoidance, protection against heat and cold exposure disorders, and food and water precautions. Individualised advice is provided for special travellers, including pregnant women, infants, and patients with diabetes. The specific medical challenges during adventure travel need to be addressed. Lastly, fever in a person returning from distant lands remains a medical mystery to be solved.

Key words: Emporiatics, First Aid Kit, Yellow Fever Vaccine, Malaria Chemoprophylaxis, Motion Sickness, Jet Lag, Venous Thromboembolism, Altitude Sickness, Decompression Sickness, Heat Stroke, Frost Bite, Traveller's Diarrhoea, In Flight Emergencies, Insect Bites, Fever.

Introduction

"You cannot swim for new horizons until you have courage to lose sight of the shore" — William Faulkner

According to the United Nations World Tourism Organisation, 1.4 billion people travelled internationally in 2024.¹ This was 99% of pre-pandemic numbers, representing the indomitable spirit of humans and their unquenchable thirst for travel. Emporiatics is a highly dynamic and niche branch of medicine focusing on pre-travel advice, and the prevention and management of medical problems faced by international travellers. The word "emporiatics" originates from two Greek words "emporos" meaning someone who travels by sea and "iatrike" meaning medicine. It is an emerging multi-disciplinary branch that includes specialities like family medicine, tropical medicine, infectious diseases, internal medicine, epidemiology and public health policy. The key aspects of emporiatics are:²

- Pre-travel consultations, including assessment of potential health risks based on the travel plans,

and providing individualised advice for vaccination, medications, and preventive measures

- Risk assessment to identify and evaluate health hazards associated with travel, including diseases like malaria, food- and water-borne illnesses, and injuries
- Prevention strategies, including immunisation
- Management of post-travel health issues
- Repatriation of sick travellers and liaison with medical insurance providers
- Public health considerations, including the spread of diseases across borders and monitoring emerging and re-emerging diseases

A Basic Travel Health Kit (Table 1)

First-aid kits are available online, but it makes better sense to customise them as per individual requirements.

Travellers should be able to self-manage minor injuries, scrapes, cuts, burns, sore-throat, travellers' diarrhoea, motion sickness, jet lag, and sunburn. Used or expired items must be replaced before each trip.³ Countries like the United Arab Emirates and Dubai have very strict laws that prohibit travellers from carrying any narcotic or psychotropic drugs. This includes medicines like diazepam, clonazepam, tramadol, and codeine.

Contents of a First Aid Kit

Basic items: Adhesive tape, bandages, crepe bandage, sterile gauze, gloves, antiseptic ointment, sunscreen, insect repellent, hand sanitiser, surgical masks, thermometer, scissors, tweezers, safety pins, rubber tourniquet, cigarette lighter (for starting a fire), Swiss military knife, extra batteries, first-aid manual

Medical supplies: Antipyretics, antihistamines, motion sickness medications, antacids, anti-diarrhoeal, laxatives, anti-emetics, aspirin, melatonin, basic antibiotics, malaria prophylaxis, acetazolamide (for high altitude), antibiotic cream, steroid ointment, pain relief spray, calamine lotion, oral rehydration salts, condoms, water purification tablets

Personal medication: Sufficient (and extra) supplies, along with a doctor's prescription mentioning diagnosis, allergies, and medicines. Include any special medicines such as an epinephrine auto-injector pen (EpiPen) if prone to allergies

Personal devices: Hearing aids with extra batteries, contact lenses with solution, glucometer, ankle or knee brace, etc

Emergency information card: Include your address, family physician's details, emergency contact details, travel insurance details, and an International Certificate of Vaccination or Prophylaxis (ICVP or Yellow Card)

Table 1: First aid kit.

Pre-Travel Vaccinations

The vaccines for travellers are categorised as routine, required, and recommended. A pre-travel consult is a good time to update routine vaccinations. The yellow fever (YF) vaccine for visits to Africa and Amazonian regions of South America, and the quadrivalent meningococcal vaccine for Hajj and Umrah, are categorised as 'required' vaccines. Other vaccines which are recommended for travel purposes, but not mandatory, include Hepatitis A, Hepatitis B, influenza, typhoid, Japanese encephalitis, and rabies vaccines.^{4,5}

Yellow fever (YF) vaccine

YF occurs in tropical and sub-tropical Africa and South America. As per the World Health Organisation (WHO), African countries include Angola, Benin, Cameroon, Central African Republic, Chad, Republic of Congo, Democratic Republic of Congo, Cote d'Ivoire, Guinea, Ethiopia, Gabon, Gambia, Ghana, Kenya, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, South Sudan, Sudan, Togo, and Uganda. The South American countries with YF include Argentina, Brazil, Colombia, Trinidad and Tobago, Venezuela and others as per the updated WHO list.

YF is a viral infection transmitted by the *Aedes aegypti* mosquito. In the majority of the patients, it is a self-limiting illness with myalgia and fatigue. In about 15% of individuals, it causes jaundice (hence the name) and can lead to fulminant hepatic failure and death.

The YF vaccine is a live attenuated vaccine, given as a single 0.5 mL subcutaneous dose to all travellers above 9 months of age intending to travel to countries with YF. It can only be administered, and a valid certificate issued, by authorised centres under the International Health Regulations. In 2014, the WHO recommended that a single dose provides 100% immunity, and a booster dose is not required.⁶ The 'International Certificate of Vaccination or Prophylaxis' (ICVP) has lifelong validity. It must be administered at least 10 days before travel to build sufficient immunity and be considered valid. Conception should be avoided for at least one month following vaccination. It is contraindicated in cases of severe allergy to egg, chicken, or gelatine proteins. Being a live vaccine, it is also contra-indicated in immunocompromised travellers, including those with bone marrow or solid organ transplants, cancer, thymoma or thymectomy, and human immunodeficiency virus (HIV). These travellers must obtain an exemption certificate but may still be subject to quarantine on return depending on country policies. Side effects of the YF vaccine include fever, myalgia, and, rarely, encephalitis. It must not be administered with any other live vaccine.

Malaria Chemoprophylaxis (Table 2)

Visitors to malaria-endemic regions are at high risk and should be educated about mosquito-bite avoidance, chemoprophylaxis, symptoms of the disease and the need for urgent treatment.⁷ In a meta-analysis of 52 studies, the pooled prevalence of severe imported malaria was 12.5%, with deaths attributable to the disease being 5.1%.

Drug	Dose (Adult)	Dose Regimen	Beginning of Prophylaxis	End after Exposure	Side-Effects
Atovaquone-proguanil	250 mg/100 mg	Daily	1 day	7 days	Mild nausea, headache
Mefloquine	250 mg	Weekly	1–3 weeks	4 weeks	Hallucinations, seizures
Doxycycline	100 mg	Daily	1–2 days	4 weeks	Photosensitivity, abdominal pain, contraindicated in children and pregnant females
Primaquine (check Glucose-6-phosphate dehydrogenase [G6PD])	30 mg base (usually two tablets)	Daily	1 day	3–7 days	Contraindicated in G6PD deficiency and pregnancy
Chloroquine	300 mg base (500 mg salt)	Weekly	1 week	4 weeks	Blurred vision, tinnitus

Table 2: Malaria chemoprophylaxis.

For children, options include mefloquine and chloroquine. For pregnant and breastfeeding travellers, chloroquine, hydroxychloroquine, or mefloquine may be used.

Motion Sickness

“Basically, it’s a mismatch” — Dr. Kellye Knuepell

Travelling becomes a nightmare if a person is prone to motion sickness. The word “nausea” has its Greek roots — “naus” meaning a ship. Motion sickness can develop during a car or bus ride, train journey, flight, choppy sea cruise, roller coasters in adventure parks, 3-D movies and virtual reality games.

Symptoms

The symptoms include nausea, vomiting, dizziness, drowsiness, sweating and headache. Other symptoms may include hyperventilation, yawning, increased salivation and blurring of vision.

Mechanism of motion sickness

When the body is in motion, the central nervous system gets neural inputs from the eyes, ears, spinal cord and joints. The cerebellum interprets these cues to decipher the spatial orientation of our head with respect to our body. It is easy to understand these inputs while walking on level ground. When we are

travelling in a vehicle there is a mismatch in these visual and vestibular signals and an imbalance between the actual versus the perceived motion. These incongruous signals cause motion sickness.

Risk factors for motion sickness

Female sex (hormonal influences such as menstruation, pregnancy, or oral contraceptive pills), children aged 7–12 years, co-morbidities including migraine and Meniere’s disease, and psychological factors (e.g., travellers who are convinced they will experience travel sickness).

Counter-measures for motion sickness

Focusing on the horizon or looking at a stationary object in the distance, choosing the best seat (front seat in cars, over the wings in planes, lower deck midship on ships, or a front-facing seat in trains), driving the vehicle, listening to music or audiobooks instead of reading or using a phone, sipping liquids intermittently, taking frequent breaks, dietary supplements like ginger, habituation and desensitisation techniques, and avoiding strong food odours, petrol fumes, sleep deprivation, alcohol and smoking.

Pharmacotherapy (Table 3)

Drugs prescribed for motion sickness include antimuscarinics like scopolamine or H1 antihistamines

like dimenhydrinate. Other antihistamines like fexofenadine or cetirizine, are ineffective as they do not cross the blood-brain barrier. Ondansetron may prevent vomiting but is ineffective for motion sickness.^{8,9} Promethazine is the most sedating option. Scopolamine patches may cause dry mouth and urinary retention and are contraindicated in glaucoma or benign prostatic hypertrophy (BPH). These patches need to be replaced every 72 hours, and should not be cut as this interferes with the release mechanism. For short-term motion exposure (< 6 hours), meclizine or dimenhydrinate are preferred. For longer journeys, or in severe symptoms, promethazine or scopolamine may be used. These medicines should be used with caution in children, as they may cause sedation, hallucinations, or agitation.

Drug	Dose	Route
Scopolamine (Transdermal patch)	1–1.5 mg	Transdermal, oral, intramuscular (IM)
Promethazine (Phenergan)	25–50 mg	Tablet/IM/Suppository
Dimenhydrinate (Dramamine)	50–100 mg	Tablet
Meclizine (Antivert)	25–50 mg	Tablet
Cinnarizine (Stugeron)	15–30 mg	Tablet

Table 3: Drugs used for motion sickness.

In-hospital management

Involves ruling out central and peripheral causes of vertigo, administering intravenous (IV) fluids, IV electrolytes and intramuscular promethazine (25–50 mg) or rectal suppositories.

Mal de Débarquement (MdDS) (Cha, 2009)

Persistence of motion sickness or a rocking sensation even after a journey ends is called Mal de Débarquement Syndrome (disembarkment syndrome). This “drunken sailor syndrome” or “land sickness” can last from a few hours to a few days.¹⁰

Jet Lag

“You define a good flight by negatives: you didn’t get hijacked, you didn’t crash, you didn’t throw up, you weren’t late, you weren’t nauseated by the food. So, you are grateful.” — Paul Theroux

Even at the end of a good flight, you can still experience jet lag. Airlines enforce strict rules for their pilots and crews because of constant travel across time zones and disruption to the sleep-wake cycle.

Definition

Jet lag is a sleep disorder in travellers on arriving at their destination due to travel across multiple time zones (at least two). This causes a temporary desynchronisation between the body clock and the local time at the destination.

Time zones

Each time zone is 15 degrees of longitude in width. Since the globe is curved, time zones are maximum at the equator and zero at the poles. For example, the width of the time zone is 1,035 miles in Kenya and 675 miles in Alaska.

Impact and diagnostic criteria for jet lag¹³

Jet lag impacts the performance of professional athletes,^{11,12} confuses bankers and businessmen, and makes the international faculty and audiences sleep during conferences. Diagnosis requires the presence of all three criteria listed below:

1. Insomnia or excessive sleepiness along with reduced sleep time due to trans-meridian travel across at least 2 time zones
2. Negative impact on daily functions, malaise, abdominal symptoms within 1–2 days after travel
3. Not attributable to any other medical, neurological, mental or sleep disorder, medication use or substance abuse

Circadian rhythm and travel

Our circadian rhythm regulates the sleep-wake cycle. Travel across time zones exposes us to different daylight hours, and our internal body clock cannot adapt quickly to these external light-dark cues. This disruption affects sleep, appetite, and bowel movements. The intensity of jet lag is directly proportional to the number of time zones traversed, rather than the duration of the flight, as time zone widths vary.¹⁴

Eastward travel, generally causes more jet lag than westward travel, as we ‘lose’ time rather than ‘gain’ it. Jet lag varies from person to person but typically lasts 1–1.5 days per time zone travelled. Symptoms are usually more intense in the elderly.

Preventing jet lag

Preventing jet lag consists of several strategies:

- Planning a flight that arrives at a time to offer sufficient timed light exposure to reset the sleep-wake cycle
- Returning the sleep cycle to match the sleep period at the destination (for eastwards journey, prepone sleep time by one hour each night for a few nights and for westwards journey, reset your watch to the destination time and then follow the meal and sleep timings based on the destination time)
- Hydrating oneself, as this helps counter jet lag, whereas caffeine and alcohol cause dehydration and can worsen it
- Sleeping only when it is nighttime at your destination (avoiding sedatives with a long half-life)
- Self-exposure to natural daylight after arrival helps the circadian cycle to adapt to the new time zone
- Taking short daytime naps of 20–30 minutes if needed
- Stopping caffeine intake at least 6 hours before your planned sleep time
- Pharmacological measures include:

Melatonin: Melatonin is produced by the pineal gland and regulates the sleep-wake cycle. When the light intensity is lowest at night, the melatonin production is at its maximum with highest levels at 3–4 am. Levels are lowest in daytime.¹⁴ Timing of melatonin as a medication is important. For eastward travel, take melatonin at bedtime; for westward travel, take it when the natural clock thinks it's the next morning. A dose of 3 mg is usually sufficient, and melatonin tends to be more effective for eastward travel.

Stimulants and hypnotics: Stimulants such as caffeine and modafinil improve wakefulness.¹⁴ Sedatives and hypnotics like zolpidem, midazolam, etizolam, and eszopiclone may be prescribed, but care should be taken regarding their half-life and potential side effects, such as residual drowsiness (hangover) and confusion.

Venous Thromboembolism (VTE)

VTE refers to deep vein thrombosis (DVT), pulmonary embolism (PE), or both.

Pathogenesis

Virchow's triad explains thrombosis through three mechanisms: venous stasis, vessel wall damage, and hypercoagulability. Prolonged sitting during flights causes venous pooling and stasis, which can in turn injure the vessel wall. Hypoxia and low cabin pressure further exacerbate these changes.

Risk factors for VTE during flight

Includes obesity, height < 1.6 m (excess seat pressure) or > 1.9 m (reduced leg space)¹⁵, ageing, oral contraceptives or hormone replacement therapy, pregnancy and postpartum, recent surgery or immobilisation, malignancy, thrombophilia, history of VTE, and medical conditions such as heart failure, connective tissue disorders, or inflammatory bowel disease.

Symptoms

DVT: Pain, swelling, and redness in the calf

PE: Pleuritic chest pain, dyspnoea, and haemoptysis

Diagnosis

Doppler ultrasound for DVT; Computed tomography pulmonary angiography (CTPA) or ventilation-perfusion (V/Q) scan for PE.

Treatment of VTE

Includes heparin (unfractionated or low molecular weight), fondaparinux and oral anticoagulants (apixaban, rivaroxaban, dabigatran, warfarin).

Air travel after VTE

The British Thoracic Society (BTS) 2022 recommends avoiding air travel for at least 2 weeks after a diagnosis of DVT/PE.¹⁶ The International Air Transport Association (IATA) allows travel after 5 days if the patient is on a stable anticoagulant dose and maintains adequate oxygen saturation on room air.¹⁷

Prevention of VTE

Measures include properly fitted below-knee compression stockings (15–30 mmHg) during flights,¹⁸ choosing an aisle seat, performing calf muscle

exercises, and, for high-risk individuals, administering enoxaparin 40 mg or 1 mg/kg subcutaneously four hours before the flight.

Altitude Sickness

“It is not the mountains we conquer, but ourselves.”
— Sir Edmund Hillary

Altitude sickness occurs when travelling to elevations above 8000 ft (2438 m) above sea level, and the probability increases when the rate of ascent is more than 1000 ft per day. The three forms of altitude sickness include: acute mountain sickness (AMS), high-altitude pulmonary oedema (HAPE) and high-altitude cerebral oedema (HACE) (Table 4).

Risk factors for altitude sickness

Include climbing too fast, higher sleeping altitude, over-exertion and failure to acclimatise, living close to sea level, a previous history of altitude sickness, genetic predisposition, and age > 50 years.

Acclimatisation

The human body takes 3–5 days to adjust to the high-altitude hypoxia by compensatory mechanisms

such as increased ventilation, improved oxygenation and changes in cerebral circulation, all of which help prevent altitude sickness. Travellers should allow one extra night for acclimatisation for every 100 metres of gain in sleeping altitude.

Pathogenesis

The percentage of oxygen in air remains constant at higher elevations. However, atmospheric pressure decreases, causing a fall in partial pressure of oxygen, to about half that at sea level at 5800 m and to about one-third at 8848 m (Mt. Everest).¹⁹ Altitude sickness affects between 25% and 85% of high-altitude travellers.

- AMS develops slowly and may be due to activation of the trigeminovascular system.
- HACE has a more acute onset and results from hypoxaemia leading to blood-brain barrier leakage and subsequent raised intracranial pressure.
- HAPE is caused by hypoxia-induced pulmonary hypertension, resulting in pulmonary oedema, capillary leak, and sympathetic overdrive.

Feature	Acute Mountain Sickness (AMS)	High-Altitude Cerebral Oedema (HACE)	High-Altitude Pulmonary Oedema (HAPE)
Clinical Features	Headache, giddiness, weakness, fatigue, lightheadedness, nausea, vomiting, sleeping problem, anorexia	Altered mental status, ataxia	Dyspnoea, chest pain, cough, tightness on exertion, congestion, decreased exercise capacity, respiratory distress, cyanosis
Timing	Within hours and lasts 1–2 days	Transitions from AMS, worsening to HACE	Within 1–4 days
Elevation	5000–8000 ft	Mostly > 12,000 ft (can occur > 8000 ft)	> 8000 ft
Physical Exam	Normal	Truncal ataxia, papilloedema, retinal haemorrhage, cranial nerve palsies	Tachycardia, tachypnoea, haemoptysis, cyanosis, inspiratory crackles
Imaging	Normal	MRI: hyperintensities in corpus callosum, cerebellar oedema	CXR: Bilateral patchy infiltrates, perivascular oedema, right ventricular strain
Lab Findings	Normal	Normal	↑ WBC, raised CRP, increased pulmonary artery pressure on ECHO

Table 4: Comparison of altitude illnesses.

Abbreviations: AMS: Acute Mountain Sickness; CRP: C-Reactive Protein; CXR: Chest X Ray; ECHO: Echocardiography; HACE: High-Altitude Cerebral Oedema; HAPE: High-Altitude Pulmonary Oedema; MRI: Magnetic Resonance Imaging; WBC: White Blood Count.

Role of acetazolamide (Diamox)

Acetazolamide is a carbonic anhydrase inhibitor, which leads to bicarbonate diuresis, resulting in metabolic acidosis. This counters the respiratory alkalosis that occurs at high altitude, stimulates ventilation, and improves oxygenation. It promotes acclimatisation and is used for both the prevention and treatment of AMS and HACE. Acetazolamide also helps control periodic breathing and improves sleep quality at high altitude.²⁰

- **Dose:** 125 mg every 12 hours beginning a day prior to ascent and continuing throughout exposure.

- **Side effects:** Include paraesthesias, excessive urination, and blurred vision.
- **Contraindication:** History of sulpha allergy.

Oxygen therapy

Oxygen supplementation is useful in the management of high-altitude illness and can be provided using a hand-held canister, oxygen tank, oxygen concentrator, or a portable pressurisation bag with a pump, known as a Gamow bag.

Altitude Illness	Medication	Preventive Dose	Therapeutic Dose	Side Effects
Headache	Acetaminophen	Oral: 1 g/6h	Oral: 1 g/6h	Gastric bleeding
Headache	Ibuprofen	Oral: 400 mg/8h	Oral: 400 mg/8h	Gastric bleeding
AMS/HACE/HAPE	Acetazolamide	Oral: 125 mg/12h	Oral: 250 mg/12h	Paraesthesia, nausea, diuresis, visual blurring
AMS/HACE	Dexamethasone	Oral: 2 mg/6h 4 mg/12h	Oral, IM or IV 16h (Loading dose 8 mg) F/B 4 mg/6h	Hyperglycaemia, psychiatric symptoms
HAPE	Nifedipine	Oral: 20 mg/8-12h	20 mg/8-12h	Flushing, headache, hypotension
AMS (Severe), HACE, HAPE	Oxygen	Supplement hyperbaric oxygen	Use if descent not possible	Barotrauma, seizures

Table 5: Medications for prevention and treatment of altitude illness.

Abbreviations: AMS: Acute Mountain Sickness; F/B: Followed by; HACE: High-Altitude Cerebral Oedema; HAPE: High-Altitude Pulmonary Oedema; IM: Intramuscular; IV: Intravenous

The seven golden rules to prevent altitude sickness

“Reaching a summit is optional, coming down is mandatory.” — Ed Viesturs

1. Do not ascend higher
2. Descend if the symptoms are persistent
3. Rest and keep warm
4. Avoiding sedative pills, alcohol
5. Hydrating well so that the urine is colourless
6. Using appropriate medication like acetazolamide, dexamethasone, and nifedipine
7. Not to ignore red flags like ataxia or dyspnoea at rest

Heat Stress (Table 6)

“Live in the sunshine, swim the sea, drink the wild air” — Ralph Waldo Emerson

But sometimes, excessive sun can ruin a perfect holiday, with hikers and bikers being at highest risk. Heat stress illness can range from the seemingly innocuous prickly heat to the life-threatening heat stroke. Older adults and infants are more vulnerable. Certain medications, including diuretics, beta blockers, antipsychotics, and alcohol may interfere with the body's ability to lose heat. High ambient temperatures and humidity can further worsen symptoms.

Heat cramps

Heat cramps are painful muscle contractions that typically occur during intense physical activity in hot and humid conditions. They result from dehydration, electrolyte imbalances, and excessive sweating, which

deplete sodium, potassium, and magnesium levels in the body. Prevention of heat cramps involves staying hydrated by drinking plenty of fluids, especially water and electrolyte-rich drinks, before, during, and after physical activity. Wearing lightweight, light-coloured clothing, taking breaks in cool environments, and gradually acclimatising to heat are also essential steps to reduce risk.

Treatment of heat cramps

Treatment involves stopping physical activity, moving to a cooler area, and drinking fluids with electrolytes. Gentle stretching and massaging of the affected muscles can help alleviate pain. If cramps persist, medical attention may be required to manage dehydration and electrolyte disturbances.

Heat exhaustion

Heat exhaustion is a condition caused by prolonged exposure to high temperatures, often accompanied by dehydration, resulting in weakness, dizziness, nausea, and heavy sweating. Prevention involves staying hydrated by drinking water regularly, taking frequent breaks in cool, shaded areas, and using fans or air conditioning to stay cool, especially in hot weather, and wearing loose, lightweight clothing.

Treatment of heat exhaustion

Treatment for heat exhaustion includes moving the affected person to a cooler place, ideally an air-

conditioned room or a shaded area. They should be encouraged to rest in an air-conditioned area and drink electrolyte solutions, to rehydrate. It's important to monitor for worsening symptoms, as untreated heat exhaustion can lead to heat stroke, which requires immediate medical attention.²¹

Heat stroke

Heat stroke is a life-threatening medical emergency that occurs when the body's temperature regulation system fails, leading to a dangerous rise in body temperature (above 104°F or 40°C). It usually follows prolonged exposure to extreme heat. Prevention of heat stroke involves staying well-hydrated, avoiding strenuous activities during the hottest parts of the day, wearing lightweight and light-coloured clothing, and taking frequent breaks in cool or shaded areas.

Treatment of heat exhaustion

If you suspect someone has a heat stroke, call emergency services immediately. While waiting for help, move the person to a cooler area, remove excess clothing, and cool them rapidly using methods such as applying cold, wet clothes or immersion in cool water. Offering fluids should be avoided if the person is unconscious or confused. Medical professionals focus on cooling the body effectively and addressing complications such as dehydration, electrolyte imbalance, and organ dysfunction to prevent serious complications or death.

Feature	Heat Cramps	Heat Exhaustion	Heat Stroke
Definition	Painful, involuntary muscle cramps during/after heat exposure	Failure of thermoregulation with intact CNS function	Complete thermoregulation failure with CNS dysfunction
Typical Setting	Hot, humid conditions; after exertion	Hot environments; labourers, elderly, athletes	Extreme heat + exertion or cooling failure
Precipitating Factors	Sodium + fluid loss from sweating + hypotonic fluids	Water and sodium depletion from sweating or dehydration	High heat/humidity + impaired heat dissipation
Key Symptoms	Muscle cramps, profuse sweating	Dizziness, fatigue, headache, nausea, orthostatic hypotension	Confusion, coma, seizures, hot/dry or sweaty skin
Temperature	Normal or slightly high	Usually < 40.5°C (105°F)	> 40.5°C; often > 42°C (107.6°F)
Lab Findings	↓Na ⁺ , ↓Cl ⁻ , possibly ↓K ⁺	↓Na ⁺ , ↓Cl ⁻ , ↑LFTs, ↑urine Na ⁺ /Cl ⁻	↑LFTs, CK, LDH, coagulation issues, hypoglycaemia, rhabdomyolysis

Feature	Heat Cramps	Heat Exhaustion	Heat Stroke
Treatment	Oral electrolytes (e.g., 0.1% saline), rest	IV fluids, rest, cooling, correct deficits over 1–2 days	Immediate rapid cooling, IV fluids, CVP monitoring
Complications	Rare (e.g., rhabdomyolysis)	Can progress to heat stroke	SIRS, DIC, multiorgan failure, death
Special Notes	Self-limiting; due to sweating and salt loss	Diagnosis of exclusion; mild GI/neurologic symptoms	CNS dysfunction is key; can resemble sepsis or toxicosis

Table 6: Comparison table — Heat cramps vs heat exhaustion vs heat stroke.

Abbreviations: CK: Creatine Kinase; Cl: Chloride; CNS: Central Nervous System; CVP: Central Venous Pressure; DIC: Disseminated Intravascular Coagulation; IV: Intravenous; K: Potassium; LDH: Lactate Dehydrogenase; LFT: Liver Function Test; Na: Sodium; SIRS: Systemic Inflammatory Response Syndrome.

Cold Stress

Tourists, mountaineers and pilgrims are exposed to snow, icy winds, rain, yet may be inadequately clad. Proper base layers of clothing and snow boots are frequently lacking. Non-freezing cold injuries include chilblains, trench foot, and urticaria, while freezing injuries result in frostbite.

Frostbite (Figure 1)

Frostbite is a condition that occurs when the skin and underlying tissues freeze after prolonged exposure to extremely cold temperatures, often affecting the fingers, toes, ears, and nose. Prevention involves dressing in layers to retain body heat, covering exposed

skin, and avoiding prolonged exposure to cold weather. Additionally, staying dry and ensuring proper circulation by avoiding tight clothing or footwear can further help reduce the risk.

Treatment of frostbite

Treatment of frostbite requires immediate action to prevent further tissue damage. The affected area should be slowly warmed using warm (not hot) water, around 37–39°C (98.6–102.2°F), for about 30 minutes. Avoid rubbing or massaging the frostbitten areas, as this can worsen the injury. Once rewarming is complete, the skin may appear red or swollen. It is essential to seek medical attention promptly.²²

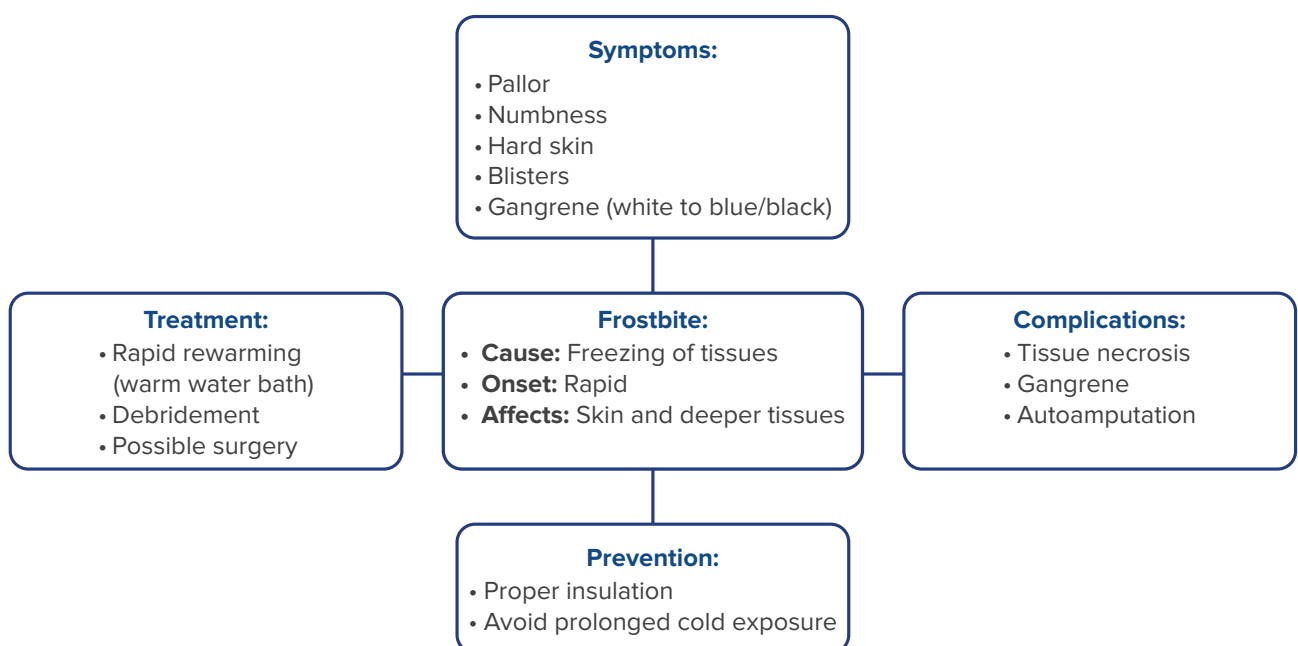


Figure 1: Frostbite.

Chilblain (Figure 2)

Chilblains are painful, itchy lesions that develop on the skin after exposure to cold, damp conditions, typically affecting the fingers, toes, ears, and nose. Prevention involves keeping the body warm and dry during cold weather by wearing insulated clothing, gloves, socks, and shoes. It's important to avoid sudden temperature changes as it increases the risk of chilblains.

Treatment of chilblain

Treatment for chilblains involves warming the affected area slowly, but gently, by moving to a warmer environment. Applying soothing creams containing corticosteroids can help reduce inflammation and alleviate itching.

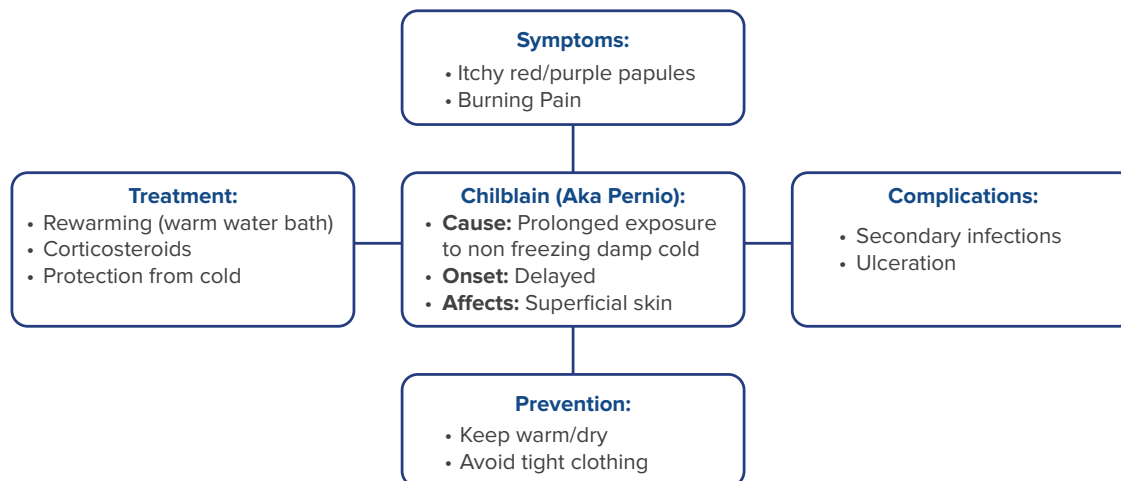


Figure 2: Chilblain.

Trench foot (Figure 3)

Trench foot, also known as immersion foot, is a condition caused by prolonged exposure of the feet to cold, wet conditions, leading to damage of the skin and underlying tissues. Prevention involves keeping the feet dry and warm, as well as avoiding prolonged exposure to cold, damp environments.

Treatment of trench foot

Treatment for trench foot involves gradually warming the affected feet, gently drying and keeping clean to prevent infection. If the skin appears swollen, blistered, or discoloured, it's essential to seek medical attention.

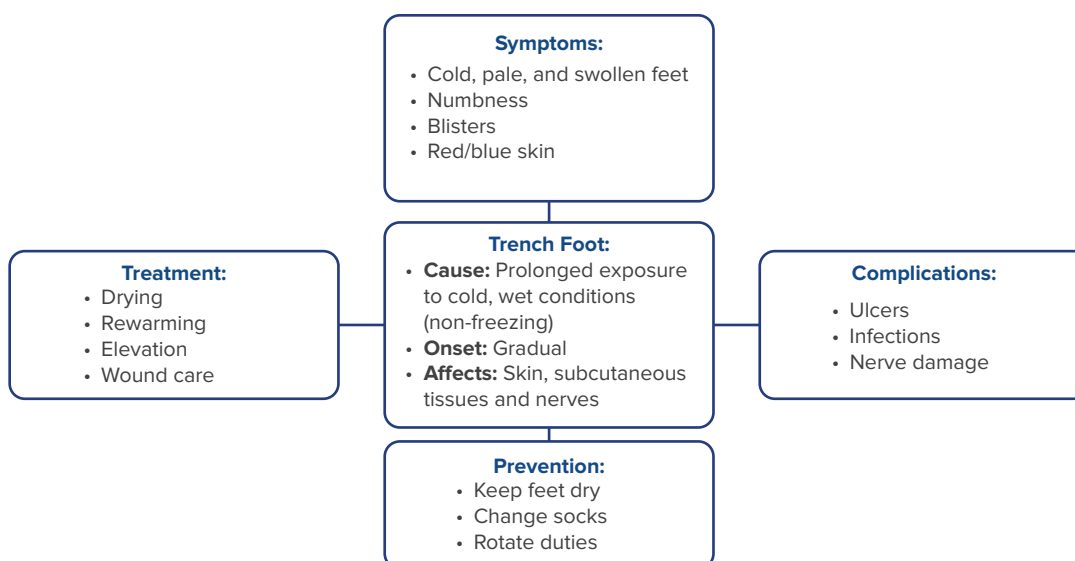


Figure 3: Trench foot.

Triaging patients with cold injury (Figure 4)

This involves rapid assessment of both the severity and type of cold injury — such as frostbite, chilblains, or hypothermia — prioritising life-threatening conditions like systemic hypothermia or deep frostbite. Patients with signs of circulatory compromise, infection, or altered mental status should be prioritised for urgent care.

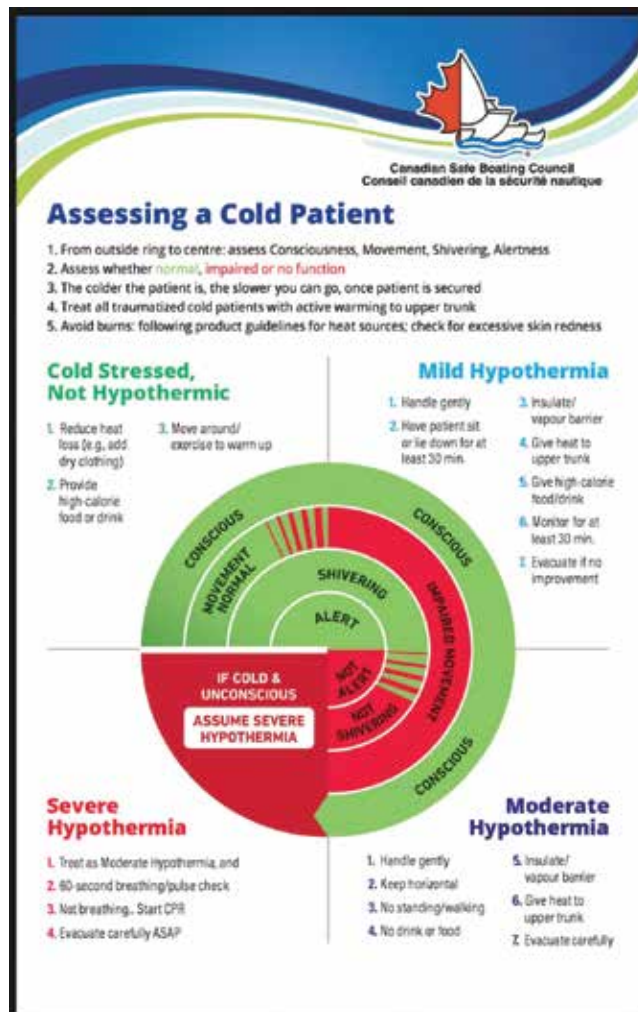


Figure 4: Assessment of hypothermia.²³

Travellers' Diarrhoea

Gastroenteritis can be broadly categorised based on the setting and causative agents:

- **Community-acquired gastroenteritis:** Occurs in individuals within the home or local environment. Common viral causes include norovirus and rotavirus (especially in children). Bacterial causes include *Campylobacter jejuni*, *Salmonella* species, *Shigella* species, and *Escherichia coli* (non-travel related strains).²⁴
- **Travellers' diarrhoea:** Defined as ≥ 3 loose/watery stools in 24 hours accompanied by symptoms such as abdominal cramps, fever, nausea, vomiting, or blood in the stool. It typically occurs within a few days of travel to high-risk areas (South Asia, Africa, Latin America).
 - o **Most common cause:** Enterotoxigenic *Escherichia coli* (ETEC)
 - o **Other bacterial pathogens:** *Shigella*, *Campylobacter*, *Salmonella*, and enteroaggregative *Escherichia coli*
 - o **Less common causes:** Viruses (e.g., norovirus), protozoa (*Giardia lamblia*, *Entamoeba histolytica*)
- **Acute food poisoning:** Refers to rapid onset (< 6 hours) of nausea, vomiting, and diarrhoea due to ingestion of preformed toxins rather than active infection.
 - o *Staphylococcus aureus*
 - o *Bacillus cereus*
 - o *Clostridium perfringens*: Produces enterotoxin causing diarrhoea typically 8–12 hours after ingestion of improperly cooked or stored meat dishes

Infection	Key Points
<i>Escherichia coli</i>	1. Common cause of bacterial gastroenteritis, especially in children and travellers 2. Mild watery diarrhoea to severe bloody diarrhoea and abdominal cramps within 12–48 hours of exposure 3. Treatment involves supportive care with oral rehydration to prevent dehydration. Antibiotics are avoided due to increased risk of haemolytic uraemic syndrome (HUS)
Giardiasis (caused by <i>Giardia lamblia</i> , a protozoan parasite)	1. Transmitted through contaminated water, food, or person-to-person contact 2. Commonly affects children and travellers after 7 days of exposure, leading to symptoms such as watery or greasy foul-smelling diarrhoea, bloating, flatulence, and abdominal cramps leading to malabsorption and weight loss 3. Treatment includes rehydration and antiprotozoal medications, with metronidazole, tinidazole, or nitazoxanide 4. Prevention involves good hygiene and drinking safe, treated water
Salmonellosis (Enteric/Typhoid Fever)	1. Caused by ingestion of contaminated food, especially undercooked poultry, eggs, or unpasteurised dairy 2. Presents with fever, abdominal cramps, nausea, vomiting, and watery or sometimes bloody diarrhoea, typically within 12–48 hours of exposure 3. Treatment is focused on hydration and electrolyte replacement. Antibiotics such as ciprofloxacin or azithromycin are reserved for severe cases, infants, or elderly 4. Prevention includes proper food handling and cooking
<i>Shigella</i>	1. Transmitted via contaminated food, water, or direct contact 2. Commonly affects young children and causes symptoms like fever, abdominal cramps, and bloody or mucus-filled diarrhoea (dysentery) within 48–72 hours of exposure 3. Treatment involves oral rehydration and in moderate to severe cases, antibiotics such as ciprofloxacin or azithromycin 4. Good hand hygiene and sanitation are key to prevention
<i>Staphylococcus aureus</i>	1. Caused by ingestion of preformed enterotoxins produced by <i>S. aureus</i> in improperly stored or handled food 2. Symptoms begin rapidly, within 1–6 hours, and include nausea, vomiting, abdominal cramps, and watery diarrhoea 3. Treatment is supportive as it is self-limiting, primarily focusing on oral rehydration to prevent dehydration 4. Prevention involves proper food handling, storage, and hygiene
<i>Campylobacter</i>	1. Usually contracted through consumption of undercooked poultry, unpasteurised milk, or contaminated water 2. Presents with a flu-like prodrome within 48–72 hours of exposure which is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody; may mimic appendicitis 3. Self-limiting and resolves within a week with supportive care, including oral rehydration

	4. Antibiotics such as azithromycin or ciprofloxacin are used for severe cases
<i>Bacillus cereus</i>	1. Caused by ingestion of contaminated food, commonly reheated rice, pasta, or meat 2. Produces two types of illness: a. Emetic form occurs within 1–6 hours of consumption of contaminated fried rice b. Diarrhoeal form occurs within 8–16 hours, presenting with diarrhea and abdominal cramps without vomiting 3. Usually mild and self-limiting and resolves within 24 hours 4. Treatment focuses on supportive care with oral rehydration; antibiotics are typically not required
Amoebiasis (caused by <i>Entamoeba histolytica</i>)	1. Characterised by gradual onset (> 7 days) of abdominal pain, bloody or mucus-laden diarrhoea, and tenesmus 2. Transmission occurs via ingestion of cysts in contaminated food or water, particularly in areas with poor sanitation 3. Treatment involves metronidazole or tinidazole to eradicate tissue-invasive forms, followed by a luminal agent such as paromomycin to eliminate intestinal cysts and prevent recurrence

▼
Table 7: Travellers' diarrhoea.

In Flight Medical Emergencies (Table 8)

More than 3.5 billion passengers travelled in commercial flights in 2022. In-flight medical emergencies (IME) are estimated to occur in 1 per 604 commercial flights. The most frequent IMEs include syncope or pre-syncope (32.7%), gastrointestinal (14.8%), respiratory (10.1%) and cardiovascular (7.0%).²⁵ In these situations, doctors, nurses, and other healthcare providers may be called upon to assist with medical emergencies. In-flight cardiac arrest is rare, occurring in only 0.2% of IMEs. Around 90% of flights continue onwards after an IME, while 10% may require an emergency landing.

Pathophysiology

Commercial aircrafts fly at altitudes of 30,000 to 40,000 feet. The pressurised cabin can cause expansion of gas in the sinuses and middle ear as well as non-physiological gas buildup in compartments (e.g., pneumothorax). Additionally, while the lower partial pressure of oxygen in the cabin, leads to mild hypoxia in all passengers, it can have a more deleterious impact in those with pre-existing medical conditions and respiratory compromise. The latter individuals may need medical certification for a portable oxygen concentrator during flight. Hypoxia and prolonged immobility can lead to VTE. The dehumidified and dry cabin air can

cause dehydration. Recycled air can expose travellers to allergens and airborne communicable pathogens.

In-flight medical equipment

In-flight medical equipment is typically scaled to the number of passenger seats, with larger aircraft carrying multiple medical kits. Automated external defibrillators (AEDs) are present on most U.S. and European flights, though not mandatory on all. Supplemental oxygen is available on larger commercial flights, ensuring basic support for respiratory issues and other in-flight medical emergencies until landing.

The contents of the medical kit include, but are not limited to, swabs, tapes, bandages, splints, scissors, sphygmomanometer, stethoscope, airway, masks, gloves, intravenous set, syringes, needles, and a glucometer. The medicines commonly found in such kits include non-narcotic analgesics, antihistamines, aspirin, antacids, bronchodilators, epinephrine, lidocaine, nitroglycerine, 50% dextrose, and saline. Additionally, some kits may also include a thermometer, umbilical cord clamp, tourniquet, and pulse oximeter.

Category	Conditions
Neurological	Syncope, presyncope, transient ischaemic attack, stroke, migraine, loss of consciousness, hypoglycaemia
Cardiac	Angina, acute coronary syndrome, accelerated hypertension, aortic dissection, arrhythmia (ventricular tachycardia, ventricular fibrillation, asystole), cardiac arrest
Pulmonary	Asthma, chronic obstructive lung disease, pulmonary embolism, pneumonia, pneumothorax
Gastrointestinal	Gastritis, diarrhoea, pain abdomen, pancreatitis, food poisoning
Obstetric	Pre-term labour, pre-eclampsia, eclampsia, miscarriage, ectopic pregnancy
Urological	Retention of urine
Allergic Reaction	Anaphylaxis, urticaria, pruritus
Psychiatric	Anxiety, depression, psychosis, mania, post-traumatic stress disorder
Substance Abuse	Misuse or withdrawal of drugs and alcohol

Table 8: In-flight medical emergencies.

Obstetric emergencies

Women beyond 36 weeks of gestation (single pregnancy) or 32 weeks (multiple gestation) are generally not permitted to fly.

Obstetric emergencies constitute 0.7% of IME. For pain in the abdomen or vaginal bleeding before 20 weeks of pregnancy, medical services can be provided on arrival. Beyond 20 weeks, any complication — including pre-term labour — require ground medical support and may require flight diversion.

The role of medical volunteers and ground support

Medical personnel who volunteer in-flight services need not carry their professional license documents. However, they should not volunteer if they have consumed a significant amount of alcohol. The contents of the medical kit may be used only after consulting

the ground physician. Final decision-making lies with the ground medical team and in-flight care should be a collaborative effort. Various laws including the Good Samaritan's Protection, the Warsaw Convention, and the Montreal Convention provide legal protection to the volunteer.²⁶

Scuba Diving and Decompression Sickness (Table 9)

SCUBA is an acronym for 'self-controlled breathing apparatus'. It is a popular recreational activity as well as a profession for marine biologists, underwater archaeologists, rescue divers and military personnel. The recent advances include rise of 'Enriched Air Nitrox' (EANx), which has a higher oxygen concentration, thereby reducing the nitrogen absorption and further chances of decompression sickness.

Condition/Disorder	Examples
Cardiac disorders	Coronary artery disease, cardiac stent or coronary artery bypass, cardiac ventricular arrhythmias, valvular lesions, pacemaker implantation, heart failure, intra-cardiac shunts
Pulmonary disorders	Asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), bullae, spontaneous pneumothorax
Neurological disorders	Epilepsy, stroke, cerebral aneurysm, spinal injury, previous neurosurgery with deficit
Ear Nose Throat (ENT) disorders	Tympanic membrane perforation, otitis media, hearing impairment, temporo-mandibular joint dysfunction, previous ear surgery (e.g., myringotomy, stapedectomy)
Gastrointestinal disorders	Severe gastroesophageal reflux, hernia, fistulae, inflammatory bowel disorder
Endocrine disorders	Obesity, diabetes
Orthopaedic conditions	Chronic back pain, scoliosis, amputations
Mental disorders	Panic disorder, phobia, alcohol and substance abuse
Others	Pregnancy, chronic kidney disease, anaemia, polycythaemia

Table 9: Medical contraindications for scuba diving.

Decompression Sickness (DCS)

Decompression sickness, commonly known as “the bends” or “Caisson’s disease”, is a life-threatening condition arising from the formation of gas bubbles (generally nitrogen) in body tissues and the bloodstream. This results from a rapid reduction in ambient pressure. It commonly affects deep-sea divers, aviators, astronauts performing experiments outside the space station, and workers in compressed-air environments.

Pathophysiology of DCS

During scuba diving, the diver inhales extra oxygen and nitrogen from the air tank. The former gets utilised whereas the latter remains dissolved in the body tissues and blood due to increased partial pressure. When the diver ascends too rapidly, the pressure is reduced too quickly. The nitrogen gets insufficient time to separate from the blood and forms microbubbles in the bloodstream or the body tissues. Extreme pain causes the person to literally ‘bend’. Nitrogen is an inert gas, but the bubbles cause vascular obstruction and organ damage. Risk factors for DCS include obesity, dehydration, congenital heart defects, injury, cold-water diving, alcohol or tobacco intake, advanced age, and male sex.

Symptoms of DCS

- **Bends:** Joint pain (commonly in shoulders, elbows, knees) and ‘dysbaric osteonecrosis’ (DON) due to pressure-induced bone damage
- **Chokes:** Cough, dyspnoea, wheeze, chest pain and right sided heart failure (“air-lock”)
- **Staggers:** Neurological deficits such as headache, blurred vision, paraesthesias, ataxia, behavioural changes, seizures, spinal cord injury, and altered sensorium

Classification of DCS

- **Type 1 DCS:** ‘Simple’ DCS with mottled skin and musculoskeletal involvement
- **Type 2 DCS:** ‘Serious’ DCS with CNS or other organ involvement

Treatment of DCS

The ideal treatment is hyperbaric oxygen therapy in a recompression chamber.²⁷ This therapy pushes back the nitrogen bubbles from the tissues into the bloodstream and improves oxygenation. The duration of treatment may range from four hours to multiple sessions. Beware of seizures and temporary myopia due to oxygen toxicity. The patient is treated in the Trendelenburg position. IV fluids and anti-inflammatory drugs are administered.

Prevention of DCS

1. Avoid rapid ascent.
2. Use dive tables. Ascent speed of > 20 metres per minute increases the chances of DCS.
3. Avoid flying for a minimum of 12 hours after a single dive and 18 hours after multiple dives.

Management of Bites and Stings

Travellers are often exposed to various arthropod and animal bites or marine stings depending on the destination. Prompt first aid and appropriate medical treatment can prevent serious complications.

Management of insect bites

Includes washing the affected area thoroughly with soap and water, removing the stinger or insect with a pair of tweezers and applying a topical antihistamine or low-potency corticosteroid cream to reduce itching and swelling. Oral antihistamines and analgesics may be prescribed.

Management of animal bites

Includes immediately washing the wound with soap and running water for at least 15 minutes, administering tetanus prophylaxis if not up to date, initiating rabies post-exposure prophylaxis (PEP) immediately as rabies is 100% fatal. Consider starting empirical antibiotics such as amoxicillin-clavulanate, especially for deep or high-risk wounds.

Management of marine stings

Includes using topical jellyfish sting inhibitor lotions for prevention. For jellyfish stings, rinsing the area with vinegar to neutralise nematocysts, immersing the affected limb in hot water (40–45°C) for 20–30 minutes to relieve pain or taking a hot bath to get rid of the nematocysts, picking off tentacles with a tweezer, gloves or towel-wrapped hand is recommended. Seeking emergency medical care in case of systemic symptoms such as difficulty breathing, chest pain, muscle spasms, or hypotension develops is important. Anti-venom is administered IV for box jellyfish stings as mortality is high. Injectable analgesics are needed for ‘Irukandji syndrome’ (chest, back, or abdominal pain with high blood pressure).

Condition	Key Travel Advice
Pregnancy	Avoid travel after 36 weeks, carry prenatal card, avoid Zika zones, avoid dehydration, use compression stockings, prefer aisle seat, use seatbelt extender, use wheelchair or electric cart at terminal. Don’t travel if diagnosed with pre-eclampsia, gestational diabetes, anaemia, or twin gestation
Infants	Maintain hydration and immunisation, protect from bites, carry over the counter (OTC) emergency medicines, don’t leave unsupervised near pool or water bodies
Parkinson’s disease	Adhere to medication timing, avoid stress, use wheelchair assistance
Dementia	Travel with caregiver, wear medical bracelet, avoid crowds
Diabetes	Carry glucometer, adjust insulin as per activity and time zone, carry snacks, avoid extra carbs, don’t walk barefoot
Human Immunodeficiency Virus (HIV)	Adhere to antiretroviral therapy (ART) and safe sex practices; avoid food or water risk

Table 10: Travel advice for special populations.

Fever in a Traveller Returning Home

Nearly 43%–79% of travellers to low and middle-income countries (LMICs) fall sick during or on return from travelling to these places. Since the incubation period of disease is variable, a detailed travel and exposure history and a syndromic approach becomes pertinent. Table 10 represents travel advisory for infants, during pregnancy, and other specific conditions

Triaging the patient

Some diseases are highly contagious and when these are suspected or confirmed, use of personal protective equipment (PPE) and isolation of the patient is needed. High Consequence Infectious Diseases (HCIDs) include ‘Contact’ diseases like Ebola, Lassa fever, Marburg disease, and Crimean Congo Haemorrhagic Fever. The ‘Respiratory’ HCIDs include Mpox (Clade 1 only), Avian Influenza A (H5 and H7), Nipah virus, Pneumonic plague and severe acute respiratory syndrome (SARS). These are all notifiable diseases.²⁸

For all other patients, outpatient treatment is advisable unless they are haemodynamically unstable and require hospitalisation. The threshold for admission should be low as these patients can worsen rapidly. Malaria, especially *P. falciparum*, should be rapidly ruled out. *P. knowlesi* is an emerging species causing malaria on exposure to macaque monkeys.

Differential diagnoses

- Malaria: Most important and potentially life-threatening; should always be ruled out first
- Dengue, Chikungunya, Zika virus: Common in tropical and subtropical areas
- Enteric (typhoid) fever: Especially in South Asia
- Rickettsial infections: Eschar, rash, thrombocytopenia
- COVID-19, influenza: Depending on outbreaks and exposure
- Leptospirosis, Schistosomiasis: Freshwater exposure, animal contact
- ‘Undifferentiated’ fevers with no localising symptoms or signs e.g., Epstein–Barr virus, cytomegalovirus, toxoplasmosis

Most of these illnesses have a short incubation period of up to two weeks e.g., dengue, influenza, travellers' diarrhoea. Some diseases with an incubation period of 2–6 weeks include acute viral hepatitis, typhoid, malaria, leishmaniasis, malaria, and acute HIV infection. Other diseases like tuberculosis, schistosomiasis, filariasis, and strongyloidiasis can have a variable incubation period of a few months to years. Malaria has an incubation periods ranging from days to months.

Relevant history taking

The following questions need to be asked:

1. Time of onset of symptoms
2. Geographical location: When the symptoms started, destination, transit or on return
3. Destination, itinerary: Adventure sports, leisure activities, water exposure, bites (mosquito, ticks, sandflies), sexual exposure, tattoos
4. Consumption of raw or undercooked food, seafood, unfiltered water
5. Use of insect repellents, nets, malaria prophylaxis compliance
6. Whether vaccinated for vaccine preventable diseases: Hepatitis A, Hepatitis B, typhoid, influenza
7. Treatment received prior to consult

Suggested workup

Includes complete blood count (CBC) with differential count, liver function tests (LFTs), blood cultures, urine routine and culture, stool culture, malaria rapid diagnostic test (RDT), and peripheral smear (thick and thin), dengue NS1 antigen/IgM antibodies, typhoid Widal test/blood culture, chest X-ray if respiratory symptoms are present, tests for rickettsioses, leptospirosis, HIV testing and multiplex PCR respiratory panel.

Management principles

- Administer antipyretics such as paracetamol
- Apply isolation precautions if a contagious infection is suspected
- Initiate specific treatment based on confirmed diagnosis (e.g., antimalarials, antibiotics, supportive care)

Additional resources

The Centre for Disease Control (CDC), Travellers' Health website, WHO GeoSentinel²⁹ network and the International Society of Travel Medicine (ISTM) provide useful resources for updating physicians about geographical distribution of diseases and outbreaks. Post COVID-19 pandemic, telemedicine has provided a platform for a convenient pre-travel and post-travel consults.

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A Series of Challenging and Interesting Cases for Anaesthesia Management

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Background:

Anaesthesia management begins with the pre-anaesthetic checkup and continues throughout the perioperative treatment. It requires not only determining the appropriate type of anaesthesia for the surgery but also taking into account the patient's various abnormalities and comorbidities, their severity, progression and ongoing treatment. This presents a significant challenge and varies from case to case.

Challenges may include haemodynamic stress due to cardiac changes, respiratory changes, renal impairment, or other systemic abnormalities.

The surgeon's requirement must also be considered. For instance, the surgeon may require relaxation of the operating field, or conversely, may request no relaxant to monitor nerve integrity. Surgical demands related to operative exposure, patient positioning, or intraoperative monitoring can themselves present additional challenges — for example, fiberoptic intubation, one lung anaesthesia, prevention of ocular injury in the prone position, avoidance of optic nerve damage or cerebral oedema in extreme Trendelenburg positioning, as well as preventing hypothermia or inducing it when required.

Drug interactions and the implications of concurrent treatments must also be carefully evaluated, with the end goal of delivering safe anaesthesia. All factors must be anticipated, planned, and executed systematically to achieve an optimal outcome. In this paper, we present seven challenging cases, each requiring individualised anaesthetic management.

Case Report – 1

Intraoperative manifestation of superior vena cava syndrome (SVCS) in a renal transplant recipient with an indwelling haemodialysis catheter.

Introduction

SVCS arises from obstruction of venous return from the upper body to the heart, typically caused by extrinsic compression or intraluminal thrombosis. It is most commonly associated with malignancies like bronchogenic carcinoma, lymphoma, or with prolonged

chemotherapy.^{1,2} However, with the increasing use of central venous catheters (CVC) for long-term dialysis, non-malignant causes like catheter-induced thrombosis have become more prevalent.³⁻⁵ SVCS presents with facial and upper-limb oedema, dyspnoea, and engorged neck veins.^{6,7} The anaesthetic implications are profound, especially when SVCS is first diagnosed intraoperatively, as it may precipitate airway obstruction, cardiovascular collapse, or cerebral hypoperfusion.⁷ This case report describes the intraoperative diagnosis and management of SVCS in a 45-year-old woman undergoing a living-donor renal transplant.

Case discussion

A 45-year-old woman with end-stage renal disease (ESRD) on maintenance haemodialysis for one year via a right subclavian Permacath was scheduled for a living-donor renal transplant. Her medical history included hypertension, hypothyroidism, anaemia of chronic kidney disease, and a prior episode of infective endocarditis caused by *Providencia rettgeri*.

Because of a positive crossmatch, the patient received rituximab therapy and underwent plasmapheresis one week prior to surgery. Post-plasmapheresis, she developed hypocalcaemia and hypokalaemia, both of which were corrected. She underwent a routine dialysis one day before surgery. Preoperative evaluation showed stable vitals (heart rate [HR]: 78 beats per minute [bpm], blood pressure [BP]: 100/60 mmHg, SpO₂: 98%), normal airway assessment, and clear lung fields on auscultation. Investigations, including complete blood count (CBC), kidney function test (KFT), liver function test (LFT), prothrombin time (PT), activated partial thromboplastin time (APTT), international normalised ratio (INR), thyroid function tests (TFT), electrocardiogram (ECG), and chest X-ray (CXR) were within normal limits.

Patient was premedicated preoperatively with intravenous (IV) ranitidine, metoclopramide, and methylprednisolone. Anaesthesia was induced with IV fentanyl (100 µg), propofol (100 mg), and cisatracurium (10 mg). A 7.0-mm cuffed endotracheal tube (ETT) was inserted, with correct placement confirmed by bilateral equal air entry. Intraoperatively, invasive haemodynamic monitoring was instituted using left radial arterial cannulation for blood pressure and central venous pressure (CVP) measurement by the existing right subclavian Permacath. Simultaneously, an abdominal ultrasound was performed to evaluate fluid status; the inferior vena cava (IVC) measured 1.5 cm in diameter with more than 50% collapsibility during intermittent positive pressure ventilation (IPPV), findings consistent with functional hypovolaemia.

The CVP was initially maintained between 10–14 cm H₂O. However, over the next two hours, after administration of only 200 mL of IV fluid, the CVP rose progressively to 35–45 cm H₂O. This was accompanied by profound hypotension that was unresponsive to further fluid resuscitation, along with the sudden onset of facial and upper limb swelling. Intraoperative transoesophageal

echocardiography (TEE) revealed impaired right atrial filling, a dilated SVC with a thrombus, and an empty left ventricle, confirming the diagnosis of SVCS.

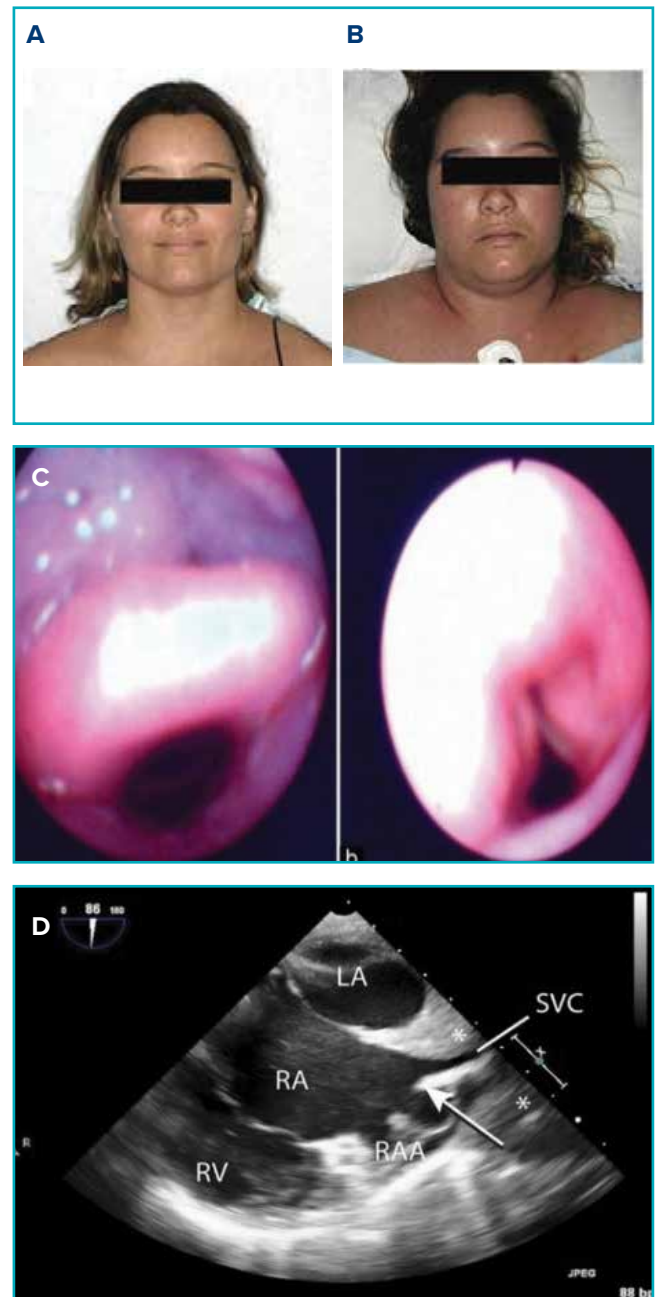


Figure 1A–D: Clinical and intraoperative findings of superior vena cava syndrome (SVCS) in a renal transplant recipient: A. Preoperative appearance with no significant swelling, B. Perioperative onset of facial puffiness suggestive of venous congestion, C. Bronchoscopic image showing oedematous airway secondary to upper body venous obstruction, D. Intraoperative transoesophageal echocardiography (TEE) demonstrating a dilated superior vena cava (SVC) with intraluminal thrombus.

Major anaesthetic challenges included airway oedema with risk of obstruction, haemodynamic instability, central venous access difficulties, preservation of renal perfusion, and the potential for cerebral and pulmonary complications.

Management

The patient was placed in a head-up tilt position to reduce venous congestion. Invasive arterial blood pressure (IBP) and CVP monitoring were used to guide therapy. Femoral vein cannulation was performed to avoid unpredictable circulation times through upper-extremity lines. Haemodynamic instability was managed with cautious fluid administration and a norepinephrine infusion. Corticosteroids were given to reduce airway oedema. Ventilation was managed using low tidal volumes and high fraction of inspired oxygen (FiO_2) to minimise intrathoracic pressure and optimise oxygenation. Postoperative imaging and vascular team review confirmed SVCS secondary to thrombotic occlusion associated with the indwelling catheter. The right subclavian Permacath was removed, and the patient was started on anticoagulation therapy. Gradual improvement in urine output and renal function was observed.

Conclusion

This case illustrates the critical importance of early recognition and prompt intraoperative management of catheter-associated SVCS in a renal transplant recipient. Although the patient was asymptomatic preoperatively, general anaesthesia and positive pressure ventilation unmasked a latent venous obstruction, leading to sudden haemodynamic collapse and airway compromise. This highlights how central venous thrombosis can remain clinically silent until physiological changes during surgery precipitate acute decompensation.

Case Report – 2

Anaesthetic challenges in a patient with a large ventricular septal defect (VSD) and pulmonary hypertension

undergoing emergency lower segment caesarean section (LSCS).

Introduction

Anaesthesia management in parturients with a large VSD and pulmonary hypertension (World Health Organisation [WHO] risk class IV cardiac disease) involves many challenges.^{1,2} These patients are at risk of haemodynamic stress due to cardiocirculatory changes, contributing to maternal morbidity and mortality.¹⁻³ Effective management involves an understanding of the type, severity, and progression of the underlying disease. We report the case of a term primigravida with a previously undiagnosed large VSD who underwent emergency LSCS under general anaesthesia (GA) with a successful maternal and neonatal outcome.

Case discussion

A 31-year-old primigravida presented to the emergency department at 36 weeks of gestation with dyspnoea at rest and active labour. She had a two-month history of progressive exertional breathlessness (New York Heart Association [NYHA] III) that had not been investigated.

The preoperative pre-anaesthesia check-up (PAC) revealed a pansystolic murmur best heard at the cardiac apex. Her vital signs recorded were as follows: HR 107 bpm, BP 138/92 mmHg, SpO_2 97% on room air, and respiratory rate 54 per min. Routine laboratory investigations were within normal limits. The ECG showed a right bundle branch block (RBBB) with right ventricular hypertrophy. Bedside 2D echocardiography (Figure 2) demonstrated a large perimembranous VSD measuring 2.2 cm with a left-to-right shunt, left ventricular ejection fraction (LVEF) 50%–55%, pulmonary valve thickening with a peak gradient of 140 mmHg, moderate tricuspid regurgitation (TR), and biventricular hypertrophy. High-risk consent was obtained (American Society of Anaesthesiologists [ASA] class IV E) and the patient was immediately shifted to the operation theatre for emergency LSCS.



Figure 2: Parasternal long-axis view on 2D echocardiography showing a perimembranous ventricular septal defect (VSD) with mosaic flow jet from the subaortic region of the left ventricle to the right ventricle.

Abbreviations: Ao: aorta; LA: Left Atrium; LV: Left Ventricle; RV: Right Ventricle; VSD: Ventricular Septal Defect.

Ranitidine and metoclopramide were administered IV stat for aspiration prophylaxis. A 15° left lateral tilt was maintained to prevent supine hypotension. The patient was preoxygenated with 100% oxygen for three minutes followed by rapid sequence induction (RSI) using etomidate 16 mg IV and succinylcholine 150 mg IV. The patient was intubated with a 6.5 mm cuffed oral ETT and put on volume-controlled ventilation (VCV). Milrinone (phosphodiesterase-3 inhibitor), norepinephrine, and epoprostenol were kept ready to manage pulmonary hypertension.

Anaesthesia was maintained with sevoflurane in oxygen and air at minimum alveolar concentration (MAC) 1. Cisatracurium IV (8 mg, 50% of the intubation dose) was administered for neuromuscular blockade. Oxytocin 3 international units (IU) bolus followed by 10 IU in 500 mL Ringer's lactate (RL) was given after delivery. Fentanyl 120 µg IV and paracetamol (PCM) 1 g IV were also administered after delivery. RL was infused at 60 mL/hour intraoperatively using a dial flow. Urine output at the end of surgery was 300 mL.

A live male infant weighing 2.4 kg was delivered within 8 minutes of induction of GA, with an Apgar score of 8 and 10 at 1 and 5 min, respectively. An arterial blood gas (ABG) analysis performed prior to extubation revealed no significant abnormalities. Esmolol 10 mg IV was given to attenuate tachycardia. The patient was extubated successfully, awake, responding to verbal commands, and breathing spontaneously.

Conclusion

The incidence of cardiac disease in pregnant patients in developing countries ranges from 3% to 5%, with around 44% of affected women developing pulmonary oedema in the third trimester.¹ In this case, the patient presented at term with a large perimembranous VSD (2.2 cm²) left-to-right shunt and moderate pulmonary hypertension that had previously gone undiagnosed. Such patients are at greatest risk of maternal mortality during labour, delivery, and the first month postpartum, when venous return is diminished and right ventricular filling decreases.³ GA was selected for better control of ventricular and airway pressures.

Case Report – 3

Combined spinal-epidural (CSE) anaesthesia for bipolar hemiarthroplasty in a patient with hypertrophic obstructive cardiomyopathy (HOCM) and recent lower respiratory tract infection (LRTI).

Introduction

HOCM is a genetic disorder of the myocardium that carries significant perioperative risk due to dynamic left ventricular outflow tract (LVOT) obstruction, particularly when compounded by acute respiratory infections.¹⁻³ We report the successful use of CSE anaesthesia for bipolar hemiarthroplasty in a high-risk patient with HOCM (resting LVOT gradient 55 mmHg) and recent LRTI. The anaesthetic challenges include a high incidence of intraoperative LVOT obstruction, diastolic dysfunction, myocardial ischaemia, and atrial arrhythmias.⁴

Case discussion

An 80-year-old woman with a history of type 2 diabetes mellitus (DM), hypertension (HTN), and coronary artery disease (CAD) presented with a fractured neck of the femur following a fall. She was planned for bipolar hemiarthroplasty after orthopaedic assessment. The patient had a recent LRTI that was clinically resolving at admission. She had received antibiotics for 5 days and had remained afebrile for 48 hours, with no clinical signs of active infection.

On examination, her HR was 88 bpm, BP 130/80 mmHg, and SpO₂ was 95% on supplemental oxygen at 2 L/min via nasal prongs. Preoperative workup included CBC, LFT, KFT, cardiac assessment, and respiratory evaluation.

A CSE technique was selected as the preferred anaesthetic approach to optimise perioperative haemodynamic stability. A femoral nerve block was performed to attenuate the nociceptive response to positioning for the CSE. An epidural catheter was placed to allow for titrated postoperative analgesia and controlled sympathectomy, further enhancing haemodynamic stability. Phenylephrine was selectively administered to maintain systemic vascular resistance (SVR) without increasing myocardial contractility, thereby reducing the risk of dynamic LVOT obstruction (Figure 3).

The patient received comprehensive postoperative management focused on analgesia and respiratory support. Continuous epidural analgesia was maintained using 0.125% bupivacaine, supplemented by a transdermal fentanyl patch delivering 25 µg/hr to ensure adequate pain control. This multimodal analgesic approach effectively managed surgical pain while minimising systemic opioid requirements.

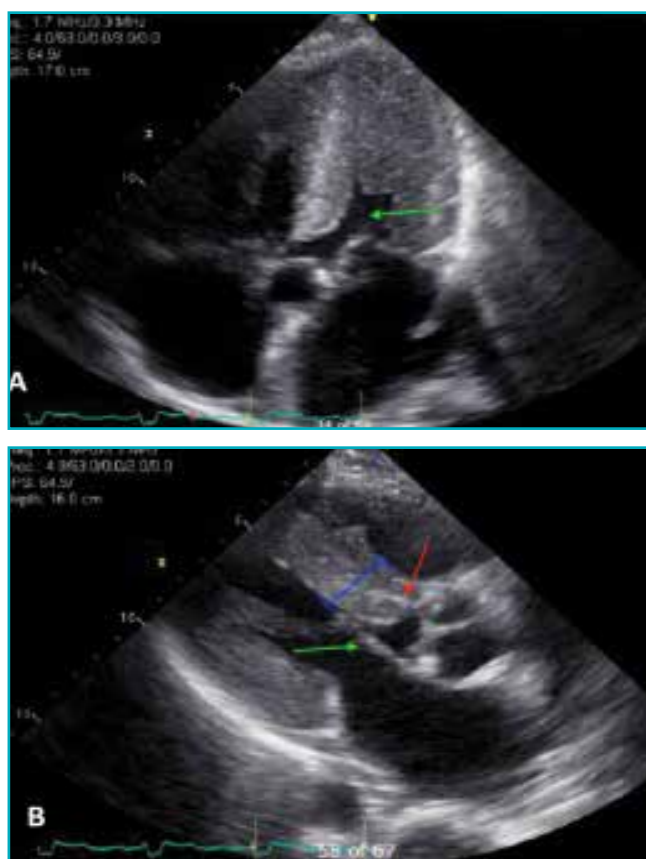


Figure 3A–B: Echocardiographic view. A. Marked left ventricular hypertrophy (LVH) with a narrow chamber (green arrow), B. Irregular septal hypertrophy with partial left ventricular outflow tract (LVOT) obstruction (blue line), systolic anterior motion (SAM) causing LVOT (green arrow), and a speckled or granular myocardial appearance (red arrow).

Conclusion

HOCM presents significant anaesthetic challenges due to its complex pathophysiology, dynamic LVOT obstruction, diastolic dysfunction, myocardial ischaemia, and arrhythmogenic potential. This case highlights the critical importance of comprehensive anaesthetic planning for patients with HOCM and systolic anterior motion (SAM) undergoing non-cardiac surgery. CSE anaesthesia represents an optimal approach in such complex cases, offering dual benefits of maintaining haemodynamic stability while minimising respiratory risks associated with GA in a patient with LRTI.

Case Report – 4

Anaesthesia management of a child with Rett syndrome undergoing open reduction and internal fixation (ORIF) of the femur.

Introduction

Rett syndrome is a rare genetic neurodevelopmental disorder that can present with unique challenges in the perioperative period such as difficult airway management, seizure disorder, DM, heightened sensitivity to anaesthetic agents, prolonged QT interval, and risk of sudden death.^{1,2} This case report describes the anaesthetic management of a 15-year-old girl with Rett syndrome scheduled for ORIF of the femur. It also outlines the associated organ system involvement and discusses anaesthetic strategies tailored to this patient population.

Case discussion

A 15-year-old female weighing 30 kg with RETT syndrome was scheduled for ORIF of the left femur. PAC was done the day before surgery and included a detailed history obtained from her mother. Birth history revealed she had full-term normal delivery with an uncomplicated antenatal period. She had normal developmental motor milestones (walked without support) till 24 months of age, followed by regression of motor and language milestones. By 34 months, genetic testing confirmed Rett syndrome. Six months prior, lumbar scoliosis was diagnosed, and she was started on physiotherapy during which she sustained a left femoral fracture.

On examination, the child was pale, spoke only occasional monosyllabic words, and had lumbar scoliosis with multiple limb contractures (both upper and lower

limbs). Laboratory investigations revealed anaemia (haemoglobin 7.9 g/dL); other investigations were normal. One unit of packed red blood cell was transfused the day before surgery.

Total IV anaesthesia (TIVA) using target-controlled infusion (TCI) was planned, along with an ultrasound guided supra-inguinal fascia iliaca block for postoperative pain relief. Preoperatively, IV glycopyrrolate 0.2 mg and IV midazolam 1 mg were administered via an existing peripheral line. GA was induced with IV fentanyl 60 µg (2 µg/kg) followed by propofol TCI. Bag-mask ventilation was provided without difficulty, followed by neuromuscular blockade with IV atracurium 15 mg (0.5 mg/kg). Intubation was done with C-MAC and a 5.5 mm cuffed ETT was placed.

Tranexamic acid was administered for the prevention of fibrinolysis (50 mg/kg bolus, followed by 5 mg/kg/hr infusion). Crystalloids were given as maintenance fluid. Positioning of the patient was done with utmost care due to the presence of multiple contractures. Surgical duration was around 90 minutes with minimal blood loss and uneventful. She was then transferred to the post-anaesthesia care unit and monitored closely. She remained hospitalised for three days without any further complications and was subsequently discharged in stable condition.

Conclusion

Rett syndrome is a neurodevelopmental disorder that affects the grey matter of the brain. It is caused by mutations in the methyl-CpG-binding protein 2 (MECP2) gene, which is located on the X chromosome.³ Because MECP2 is essential for survival, the condition is usually fatal in males before birth, making Rett syndrome primarily a disorder seen in females.³

Special consideration should be given during anaesthesia administration for these patients due to airway challenges, autonomic instability, seizure risk, and abnormal sensitivity to anaesthetic drugs. In this case, preoperatively midazolam and intraoperatively propofol were used due to their anticonvulsant properties.¹⁻³

Case Report – 5

Locked jaw, high stakes: Navigating anaesthesia in paediatric temporomandibular joint (TMJ) ankylosis.

Introduction

Anaesthetic management of patients with TMJ ankylosis poses significant challenges due to limited or absent mouth opening, which restricts access for conventional intubation techniques. Children with TMJ ankylosis often exhibit retrognathia, mandibular hypoplasia, and altered oropharyngeal anatomy, making direct laryngoscopy, supraglottic airway insertion, and even bag-mask ventilation challenging. These factors increase the risk of airway obstruction, hypoxia, and failed intubation, especially under GA with muscle relaxation. In such cases, awake fibreoptic intubation is the preferred technique, as it enables controlled airway access while preserving spontaneous respiration and airway reflexes. In our case, it was further compounded by our patient being an international patient with a language barrier. Sedation with propofol, opioids, or benzodiazepines carries a risk of respiratory depression and airway obstruction.¹ Dexmedetomidine, an α_2 -adrenergic agonist, provides anxiolysis, sedation, and modest analgesia without significant respiratory depression, allowing the patient to remain calm and arousable with preserved airway reflexes.

Case discussion

A 10-year-old international patient, weighing 22 kg, presented with congenital restricted mouth opening and feeding difficulties. The child was referred for further evaluation and management. On examination, child had misaligned dentition along with severely hypoplastic left mandible. The mouth opening was 8 mm and the Mallampatti grading assessment was not possible due to limited oral aperture (Figure 4). All preoperative lab investigations were within normal limits. After multidisciplinary discussion, right TMJ release with right interpositional arthroplasty was planned.

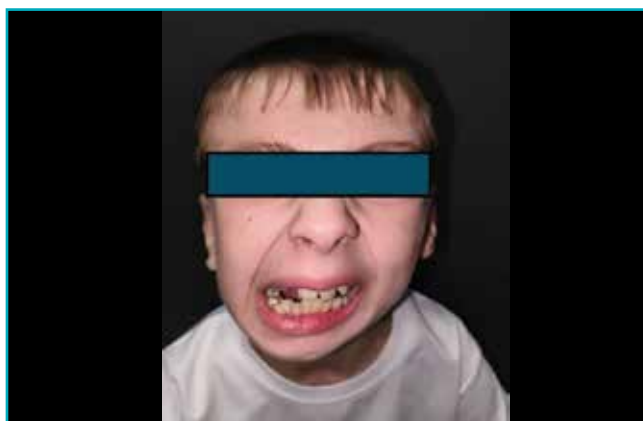


Figure 4: Preoperative photographs depicting restricted mouth opening and retrognathia.

Preoperatively, IV access was secured, and IV glycopyrrolate 0.2 mg, ranitidine 25 mg, dexamethasone 2 mg, and ondansetron 2 mg were administered. Nebulisation of the airway was done with 2 mL of 2% lignocaine in the preoperative room. A loading dose of dexmedetomidine (3 µg/kg) was infused over 10 minutes. Oxygen enrichment was done with a face mask held just above the child face. The fiberoptic bronchoscope was introduced without difficulty and clear visualisation of the glottic opening was achieved. Lidocaine 1% was sprayed onto the vocal cords, and a lubricated 5.0 flexometallic ETT was advanced over the bronchoscope into the trachea. Correct tube placement was confirmed using capnography and bilateral chest auscultation.

Anaesthesia was maintained with an admixture of oxygen and nitrous oxide (50:50) with sevoflurane, while muscle relaxation was achieved with cisatracurium. Multimodal analgesia included IV paracetamol and diclofenac. At the end of the procedure, check laryngoscopy was performed to confirm adequate mouth opening, and to ensure preparedness for potential reintubation if

required. Thorough oral suctioning was carried out, and after confirming adequate muscle tone, limb power, and protective airway reflexes, the patient was extubated with a satisfactory air blast (Figure 5).



Figure 5: Postoperative Day 1 after the corrective surgery.

Conclusion

Airway management in paediatric patients with TMJ ankylosis poses significant challenges due to restricted mouth opening and the potential for difficult mask ventilation and intubation.² The combination of dexmedetomidine and ketamine has proven effective for fiberoptic intubations in such scenarios, due to their ability to maintain spontaneous ventilation and airway reflexes.³ This approach maintained spontaneous ventilation, provided adequate sedation and analgesia, and avoided the need for more invasive techniques. The combination of these agents may be considered in similar challenging paediatric airway scenarios.

Case Report – 6

Anaesthetic management of a 65-year-old female posted for total conservative parotidectomy with facial nerve monitoring under TIVA.

Introduction

Parotidectomy procedures present unique anaesthetic challenges, particularly when intraoperative facial nerve monitoring is required.^{1,2} Management of parotid masses typically involves imaging, diagnostic needle aspiration, and surgical excision.^{1,2} Depending on the aetiology, surgical approaches range from extracapsular excision to radical parotidectomy with facial nerve sacrifice, with facial nerve injury being a feared complication. The use of TIVA

ensures minimal interference with neuromonitoring.^{2,3} We present the perioperative management of a 65-year-old obese, diabetic female with anaemia and a predicted difficult airway who underwent total conservative parotidectomy under TIVA, with intraoperative facial nerve monitoring.

Case discussion

A 65-year-old female with a history of type 2 DM, chronic hepatitis C infection, and anaemia (haemoglobin: 10.5 g/dL) was scheduled for right total parotidectomy for a suspected neoplasm. The patient was obese (weight: 75 kg, height: 156 cm, BMI: 30.8 kg/m²), and a difficult airway was anticipated (Mallampati Grade-III). Preoperative evaluation was unremarkable apart from her comorbidities. After standard monitoring was established, anaesthesia was induced using fentanyl 2 µg/kg, propofol 2 mg/kg, and 10% lignocaine spray was applied orally to blunt the intubation reflex. Anaesthesia was maintained with TIVA using TCI of propofol (plasma concentration: 2–3 µg/mL), supplemented with fentanyl 50 µg/hr for analgesia. A right-sided total parotidectomy was performed. Intraoperative facial nerve stimulation (IFNM) confirmed intact responses in all five branches (Figure 6) of the facial nerve. A rotational flap was placed for contour restoration at the surgical site. Postoperatively, facial nerve function was evaluated and found to be intact in all branches.



Figure 6: Intraoperative facial nerve monitoring (IFNM).

Conclusion

Parotidectomy carries an inherent risk of facial nerve injury due to the nerve's anatomical course through the gland. Complications can range from transient paresis to permanent paralysis, depending on factors such as surgical technique, anatomical variations, or accidental

trauma. The use of IFNM (Figure 6) has significantly improved nerve preservation, reducing permanent deficits to under 2% in experienced centres.^{2,3}

Case Report – 7

Neuraxial anaesthesia in Lutembacher syndrome — a rare case.

Introduction

Lutembacher syndrome is a rare cardiac condition defined by the coexistence of a congenital atrial septal defect (ASD) and mitral stenosis (MS).^{1,2} The ASD may be either an ostium primum defect, or more commonly, an ostium secundum defect. It affects females more frequently than males.^{1,2} It is reported to be more prevalent in developing countries where incidence of rheumatic fever is high.¹⁻³

We also encountered a 65-year-old female with Lutembacher syndrome, left ventricular dysfunction, and a low ejection fraction of 30%, who was posted for modified radical mastectomy (MRM). The main challenge was the patient and attendant's refusal for GA. This report highlights the perioperative anaesthetic management and its outcome in this case.

Case discussion

A 65-year-old lady posted for right MRM presented to the PAC room. She had history of rheumatic heart disease, 40 years back, and was diagnosed with Lutembacher syndrome with an ostium secundum ASD and MS. She also had heart failure with a reduced ejection fraction of 30%. Additional comorbidities included chronic liver disease (CLD) and Hepatitis C virus (HCV) positivity, though there was no evidence of portal hypertension, oesophageal varices, ascites, or drug allergy.

On physical examination, she appeared afebrile and clinically stable. Her vital signs were within normal range, with BP 110/70 mmHg, and HR 90 bpm. Respiratory examination was unremarkable. Cardiovascular examination revealed irregular pulse on radial artery palpation. Further evaluation with TTE showed: mitral valve area of 0.9 cm², LVEF 30%, dilated left atrium, and thickened mitral valve (Figure 7). A CXR revealed cardiomegaly. On head and neck examination, she had Mallampati Grade I, with mouth opening of > 3 finger breadths, thyromental distance of > 6 finger breadths and adequate neck movement.

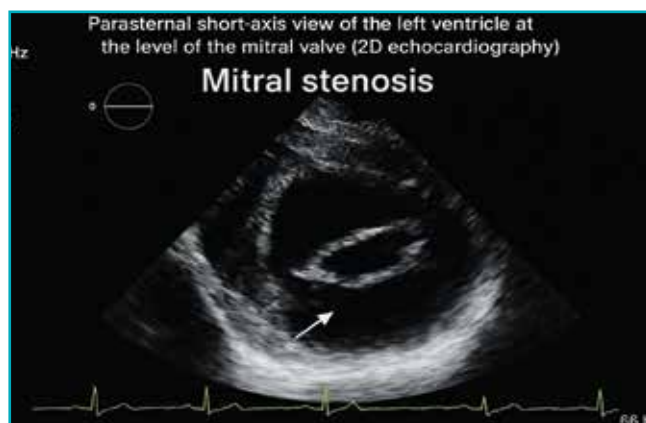


Figure 7: Two dimension (2D) echocardiography showing mitral stenosis and reduced valve area.

After painting and draping, the surgery was commenced under GA. A bolus of 5 mL of 2% lignocaine was administered prior to incision. Intraoperatively, BP remained stable around 110/70 mmHg with a HR of 75–80 bpm. At 30 minutes, a bolus of 5 mL of 0.5% bupivacaine was given to maintain the block. The surgery lasted 1.5 hrs and was completed uneventfully. Only 200 mL of IV Kabilyte was required intraoperatively. The postoperative period was uneventful.

Conclusion

Administration of GA in patients with Lutembacher syndrome can be unpredictable due to complex intracardiac shunting and compromised ventricular function.^{2,3} Epidural anaesthesia offers several advantages:³

- Graded sympathetic block, minimising sudden drop in SVR, which can worsen shunting or compromise coronary perfusion
- Slow onset permits better BP control compared to spinal or GA induction agents
- Good analgesia, reducing stress induced tachycardia. It provides continuous pain relief postoperatively, it reduces the catecholamine surges, which increases peripheral vascular resistance (PVR) and HR
- Beneficial for patients with underlying lung conditions, like chronic obstructive pulmonary disease (COPD) and restrictive lung diseases, where GA carries high risk

The successful use of epidural anaesthesia in a patient with Lutembacher syndrome highlights the importance of individualised anaesthetic planning based on the patient's unique cardiac physiology.

Arun Puri, Vikky Jaiswal, Smriti Sahu, Manoj Sinha, Naveen Gupta, Devender Dua, Mallika Kulkarni, Anurag Chaturvedi, Sony Mathew, Anoop VP, B Kanmani, Deepak, Nishant Sood, Prachi Sharma, Satish Gajula, Sanjeev Sharma, Pragya Singh. A Series of Challenging and Interesting Cases for Anaesthesia Management. MMJ. 2025, September. Vol 2 (3).

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A Case Report of Cholesterol Granuloma in Mastoid Cavity

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Abstract:

Cholesterol granulomas are benign granulomatous lesions caused by a tissue reaction to a foreign body. Lesion formation is caused by cholesterol crystals and occurs secondary to insufficient ventilation, drainage disorder, haemorrhage, and/or chronic inflammation. Cholesterol granulomas may involve the middle ear, the mastoid bone, and the petrous apex. However, cholesterol granulomas presenting as a mass obstructing the external ear canal are relatively rare and can be a diagnostic challenge, especially in a post-mastoidectomy case.

We report a case of cholesterol granuloma occupying the roof of the mastoid cavity and presenting as a mass in the external auditory canal (EAC). Temporal bone computed tomography showed a soft tissue mass along the roof of the mastoid cavity with rarefaction of the tegmen mastoideum/roof of the mastoid air cells. The cholesterol granuloma was removed surgically, and characteristic pathological findings confirmed the diagnosis.

Key words: Cholesterol Granuloma, External Auditory Canal (EAC), Mastoid Cavity, Post-Mastoidectomy.

Introduction

Cholesterol granuloma can occur anywhere in the body, with the most common site being the temporal bone.¹ Cholesterol granuloma, or cholesterol cyst, is a clinical entity that was first reported by Manasse in 1894.^{2,3} Cholesterol granulomas are benign granulomatous lesions caused by a tissue reaction to a foreign body.³ These lesions develop secondary to insufficient ventilation, drainage disorders, haemorrhage or chronic inflammation. Cholesterol granulomas have been reported in various regions of the body where cholesterol crystals may form, such as the lungs, breast, peritoneum, mediastinum, liver, spleen, thyroid, kidneys, lymph nodes, testis, facial skeleton, skull and temporal bone. Within the temporal bone, cholesterol granuloma is known to occur most commonly in the petrous apex.⁴ Very few cases of cholesterol granuloma presenting as a mass in the external auditory canal (EAC) have been reported, and occlusion of the entire EAC by a cholesterol granuloma is rare.

Case Report

A 50-year-old male presented to the Ear, Nose and Throat (ENT) outpatient department with complaints of bilateral ear discharge and decreased hearing for the past few months. He had no history of ear pain, tinnitus, vertigo, headache or any neurological complaints. He had a history of hypertension, left mastoidectomy 20 years earlier, and right mastoidectomy 18 years ago. On otomicroscopic examination, the right tympanic membrane could not be visualised due to a mass completely obstructing the EAC (Figure 1). The left ear showed a mastoid cavity with discharge, with an intact and normal tympanic membrane. The remaining ENT examination was within normal limits, including the facial nerve. The audiogram showed bilateral moderate conductive hearing loss. High-resolution computed tomography (HRCT) of the temporal bone showed a well-defined abnormal soft tissue along the roof of the mastoid cavity, measuring approximately

1.5 cm in cephalo-caudal extent (Figure 2) and 1.8 cm x 1.6 cm in maximal axial dimension (Figure 3).



Figure 1: Otomicroscopic examination — mass obstructing the external auditory canal (yellow arrow).



Figure 2: High-resolution computed tomography of the temporal bone — coronal section, showing cephalo-caudal extension of the mass in the external auditory canal (yellow arrow).

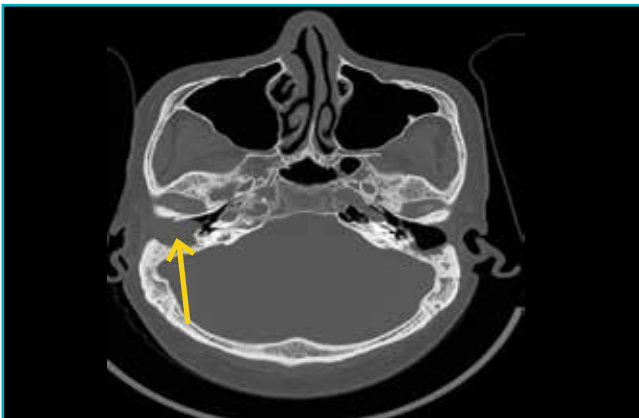


Figure 3: High-resolution computed tomography of the temporal bone — axial section, showing the horizontal extent of mass in the external auditory canal (yellow arrow).

Rarefaction of the tegmen mastoideum (roof of the mastoid air cells) was seen. Post-mastoidectomy status was noted in both ears, with non-visualisation of the ossicular chain except for the footplate of the stapes and handle of the malleus. Mucosal thickening was noted in both mastoid cavities. The preoperative blood work-up was normal.

Based on the diagnosis of cholesterol granuloma from medical imaging, revision mastoidectomy under general anaesthesia was performed via a postauricular approach. A cystic lesion containing dark, chocolate-coloured fluid was found in the operated mastoid cavity, extending to the EAC. The cyst wall of cholesterol granuloma was removed along the EAC, and a large cholesteatoma was cleared from the mastoid air cells and middle ear cavity (Figure 4). The mastoid cavity smoothed. Ossiculoplasty was performed, and the attic was repaired using conchal cartilage. After the mass was completely excised, the meatal flap was repositioned.



Figure 4: Cyst wall of cholesterol granuloma.

The post-operative period was uneventful. The excised tissue was sent for histopathological examination. The histopathology report confirmed the diagnosis of cholesterol granuloma. The cyst had a fibrous lining and contained cholesterol crystals, haemosiderin and fibrin, which were surrounded by foreign body giant cells. Follow-up of the patient during the postoperative course was uneventful, with no neurological complications.

Discussion

The first theory about the pathogenesis of cholesterol cyst was proposed by Friedman in 1974, according to which haemorrhage and the catabolism of haemoglobin produce cholesterol crystals and iron.⁵ Sade, in 1979, emphasised the role of low ventilation and hypoxia. Many more theories have since been formulated.⁶ Summarising, there are three major factors regarded as responsible for the formation of cholesterol granuloma — local haemorrhage occurring during an inflammatory process, obstruction of ventilation and poor drainage of cavities.⁷

Cholesterol granuloma represents the most common cystic lesion of the temporal bone. It is often found in young to middle-aged patients with a history of chronic otitis media, temporal bone surgery, or temporal bone trauma.⁸ When a ventilation problem occurs, oedema of the mucosal membrane and rupture of blood vessels may result, secondary to the negative pressure created in the closed space. The degradation products of haemoglobin may then be exposed to the surrounding tissue, causing a foreign body-type reaction.⁹ With repeated inflammatory reactions and additional haemorrhage, a cholesterol granuloma can form. In our patient, a cholesterol granuloma formed a large mass in the EAC, which appears to support the local haemorrhage theory proposed by Friedman. The lesion may have originated inside the tympanic bone of EAC and expanded into the mastoid and EAC.⁴

Microscopically, the cyst presents with cholesterol clefts (the cholesterol dissolving during tissue processing)

that are surrounded by histiocytes and foreign body giant cells.⁷ In fact, cholesterol crystals stimulate the accumulation of giant cells, which are responsible for the tissue reaction.¹⁰

Patients with cholesterol granuloma may present with hearing loss (conductive when concerning the middle ear or sensorineural when located in the petrous apex), tinnitus, vertigo, cranial nerve deficits, headache, facial pain/numbness, diplopia, and cerebrospinal fluid (CSF) leak.⁷ Clinically, the differential diagnosis in a post-operated ear with a bulge in the EAC includes cholesteatoma and brain herniation. Computed tomography (CT) scan and magnetic resonance imaging (MRI) play a significant role in the diagnosis of cholesterol granuloma. The cholesterol granuloma appears as a well-margined lesion on CT, isodense with brain tissue, with no significant contrast enhancement, while bone erosion may be present.

Cholesterol granulomas do not routinely require surgery. However, surgical intervention may be considered based on the size and location of the lesion, the presence of symptoms and the need for diagnostic confirmation.^{4,11-13} In this case, the mass was excised through mastoidectomy. The patency of the EAC was maintained without postoperative complications such as necrosis and stenosis.

This case highlights the importance of long-term follow-up after cholesteatoma surgery.

Conclusion

Cholesterol granulomas are benign granulomatous lesions caused by cholesterol crystals, which occur secondary to haemorrhage, chronic inflammation, and/or insufficient ventilation. They may involve the middle ear, mastoid bone, and the petrous apex. Cholesterol granulomas of the mastoid cavity presenting as a mass obstructing the EAC are a rare entity, particularly in post-mastoidectomy patients. This case underscores the importance of considering cholesterol granuloma in the differential diagnosis of EAC masses, especially when associated with a history of chronic otitis media or prior ear surgery. Early imaging with HRCT and, when necessary, MRI can aid in prompt diagnosis, while surgical excision remains a safe and effective treatment for symptomatic or diagnostically uncertain lesions. Long-term postoperative follow-up is essential to monitor for recurrence and to preserve auditory function.

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Early-Onset *Pneumocystis jiroveci* Pneumonia During the Periengraftment Phase in Haploidentical Haematopoietic Stem Cell Transplantation

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Abstract:

Pneumocystis jiroveci pneumonia (PJP) remains a critical opportunistic infection in haematopoietic stem cell transplantation (HSCT) recipients, traditionally occurring late post-transplant. This report presents two rare cases of early-onset PJP during the peri-engraftment phase in high-risk patients undergoing haploidentical HSCT — one a paediatric case with inborn error of immunity due to dedicator of cytokinesis 8 (DOCK8) deficiency and the other, an adult with Janus kinase 2 (JAK2) positive primary myelofibrosis. Both patients developed acute respiratory symptoms and characteristic radiographic findings within 10–22 days post-transplant. PJP was confirmed through bronchoalveolar lavage (BAL) and direct immunofluorescence assay. Prompt initiation of trimethoprim-sulfamethoxazole (TMP-SMX) in therapeutic doses led to clinical improvement and successful haematological recovery. These cases underscore the potential for PJP to emerge earlier than expected, challenging existing guidelines that recommend prophylaxis primarily after engraftment. Earlier initiation of TMP-SMX may be associated with a risk of delayed engraftment and graft failure. These cases highlight that the timing of prophylactic interventions, potentially initiating before or during the engraftment period, may enhance patient outcomes. Radiological imaging and early bronchoscopy remain essential for timely diagnosis. Further multicentric studies and registry analyses are warranted to inform evidence-based prophylaxis protocols and improve early detection strategies in this vulnerable patient population.

Key words: *Pneumocystis jiroveci* Pneumonia, Haematopoietic Stem Cell Transplantation, Early Onset, Haploidentical Transplant, Trimethoprim-Sulfamethoxazole (TMP-SMX) Prophylaxis.

Introduction

Pneumocystis jiroveci pneumonia (PJP), formerly known as *Pneumocystis carinii* pneumonia (PCP), is a potentially fatal opportunistic fungal infection predominantly affecting immunocompromised individuals, particularly those undergoing haematopoietic stem cell transplantation (HSCT). Despite significant advances in supportive care and antimicrobial prophylaxis, PJP remains a substantial cause of morbidity and mortality in this vulnerable population. The profound immunosuppression resulting

from myeloablative conditioning regimens, prolonged neutropenia, graft-versus-host disease (GVHD), and the use of corticosteroids or other immunosuppressive therapies contributes to a high susceptibility to PJP in HSCT recipients.¹

The clinical presentation of PJP in HSCT patients often diverges from that seen in human immunodeficiency virus (HIV) infected individuals, typically manifesting as an acute, rapidly progressive pneumonia characterised by non-productive cough, dyspnoea, hypoxaemia, and

bilateral interstitial infiltrates on imaging. These atypical and rapidly evolving features often delay diagnosis, underscoring the need for high clinical suspicion and timely diagnostic interventions, such as bronchoalveolar lavage (BAL) and polymerase chain reaction assays.²

Prophylactic strategies, particularly trimethoprim-sulfamethoxazole (TMP-SMX) or cotrimoxazole, have proven highly effective in reducing the incidence of PJP, yet challenges remain in determining optimal duration and managing drug-related toxicities.³ Recent reports also indicate emerging resistance and breakthrough infections, even in the context of prophylaxis, highlighting the importance of vigilance and reassessment of existing protocols.⁴

We present unusual cases of early-onset of this potentially life-threatening opportunistic infection that can occur during the peri-engraftment period following HSCT.

Case 1

A 7-year-old girl, a case of hyper-immunoglobulin E (IgE) syndrome with chromosome 9 deletion and dedicator of cytokinesis 8 (DOCK8) deficiency, presented with a history of recurrent episodes of pneumonia and ear infections since the age of 1 year. Subsequently, she developed bronchiectasis with pulmonary hypertension at the age of 6 years and was on sildenafil and torsemide. The patient also developed multiple crusted skin lesions and erythema of the skin since the age of 1 year. Serum IgE was markedly elevated at 2230.37 IU/mL (normal < 100). The immunodeficiency panel was normal, showing natural killer (NK) and T-cell populations with a preserved cluster of differentiation 4:cluster of differentiation 8 (CD4:CD8) ratio, normal neutrophil and monocyte populations, and a reduced B-cell population. Baseline complete blood count (CBC) prior to HSCT showed haemoglobin 11.2 g/dL, total white blood cell (WBC) count $25.3 \times 10^3/\text{L}$, and a differential cell count comprising neutrophils 58%, lymphocytes 7%, monocytes 6%, eosinophils 28%, and a platelet count $263 \times 10^3/\text{L}$.

The patient underwent haploidentical HSCT from the mother as the donor, who did not have any pathogenic variant on genetic evaluation. The patient received fludarabine $150 \text{ mg}/\text{m}^2$, treosulphan $42 \text{ g}/\text{m}^2$, and total body irradiation (TBI) 2 Gy as myeloablative conditioning and post-transplant cyclophosphamide

100 mg/kg and tacrolimus/mycophenolate mofetil based GVHD prophylaxis. The patient was transfused with $10.9 \times 10^6/\text{kg}$ peripheral blood stem cells from the mother as donor.

On Day +10 of HSCT, she developed high-grade fever, sudden onset of breathlessness, tachypnoea, tachycardia, and was placed on non-invasive ventilation. HRCT of the chest (Figure 1A and 1B) revealed diffuse, bilateral ground-glass opacities with mosaic attenuation, predominantly in perihilar, middle, and lower lung zones, along with thin-walled cysts. It also showed atelectatic changes with traction bronchiectasis. The patient was evaluated for infective aetiology and bronchoscopy with BAL performed on Day +12, in which direct immunofluorescence assay was positive for *Pneumocystis jiroveci* cysts and trophozoites.

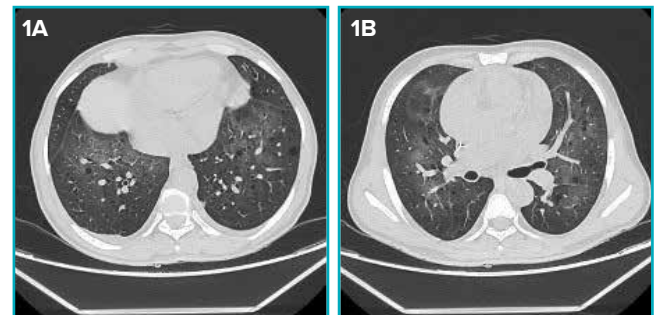


Figure 1A and 1B: High-resolution computed tomography (HRCT): A. Axial HRCT chest showing diffuse, bilateral ground-glass opacities with mosaic attenuation, B. Coronal HRCT chest showing diffuse, bilateral ground-glass opacities with thin-walled cysts and traction bronchiectasis.

The patient was treated with a therapeutic dose of injectable TMP-SMX from Day +14 for PJP for 1 week and later changed to oral when the patient became haemodynamically stable and given for a total duration of 3 weeks. Neutrophil engrafted on Day +14 of HSCT. The patient showed symptomatic improvement after 6 days of non-invasive ventilation. The patient's post-engraftment chimerism on Day +20 and Day +60 was 99% with normal haematological recovery.

Case 2

A 53-year-old male with a case of primary myelofibrosis, Janus kinase 2 (JAK2) positive, presented with a history of left hypochondrium pain, early satiety, significant weight loss and progressive generalised weakness for a year. The patient received thalidomide and ruxolitinib and did not show any significant improvement and was planned for HSCT.

The patient underwent haploidentical HSCT with fludarabine 150 mg/m², busulphan 6.4 mg/kg, TBI 2 Gy reduced-intensity conditioning and post-transplant cyclophosphamide 100 mg/kg and tacrolimus/mycophenolate mofetil-based GVHD prophylaxis. Increased bronchovascular markings were seen in both lungs on the chest X-ray (Figure 2A), indicating that the bronchial tubes in the lungs were more visible than usual. The patient was transfused with 10.2 x 10⁶/kg peripheral blood stem cells from his brother as a donor. The patient developed Grade III gut and oral mucositis and neutropenic fever.



Figure 2A: Normal chest X-ray with increased bronchovascular marking.

Neutrophil engrafted on Day +19. On Day +20, the patient developed a sudden onset of breathlessness, cough with haemoptysis, hypoxemia and bilateral crackles. HRCT chest (Figure 2B) was suggestive of patchy and confluent areas of ground-glass opacities in bilateral lungs with relative peripheral sparing, with multiple thin-walled air-filled cysts scattered in bilateral lung parenchyma. Sputum direct immunofluorescence assay positive for *Pneumocystis jiroveci* cysts and trophozoites. The patient was started on injectable TMP-SMX followed by oral treatment at therapeutic doses total of 3 weeks. His post-engraftment chimerism on Day +30 was 94% and Day +60 was 95%. The patient had mild cytopenia, which improved following completion of PJP treatment.

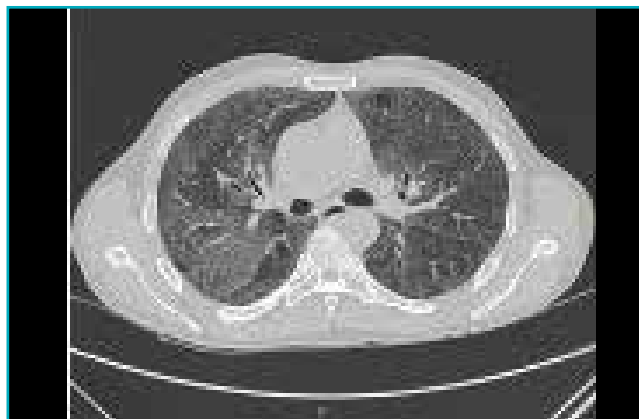


Figure 2B: Patchy and confluent areas of ground-glass opacities in bilateral lungs with relative peripheral sparing with multiple thin-walled air-filled cysts.

Discussion

PJP remains a significant opportunistic infection in HSCT recipients, typically manifesting late in the post-transplant course — often beyond 100 days — particularly in patients receiving prolonged immunosuppression, corticosteroids, or with chronic GVHD. The American Society for Transplantation and Cellular Therapy (ASTCT) and European Society for Blood and Marrow Transplantation (EBMT) guidelines recommend PJP prophylaxis — preferably with TMP-SMX for at least 6–12 months post-transplant and until the cessation of immunosuppressive therapy.⁵ However, the occurrence of PJP during the peri-engraftment phase, as seen in our cases, is exceptionally rare and underreported.

Both patients in this report developed PJP within the first 3 weeks post-transplant, during the neutropenic and engraftment phases. The early onset raises concern about a vulnerable period before prophylaxis is typically initiated or becomes effective. Nazir *et al.* reported similar early-onset cases in haploidentical transplant recipients with familial haemophagocytic lymphohistiocytosis (HLH), suggesting that profound immune dysregulation and mucosal barrier damage during conditioning may permit early fungal invasion.⁶ Additionally, the EBMT Paediatric Diseases Working Party has highlighted that atypical pathogens, including PJP, may present even within the first 30 days, particularly in high-risk patients or those with prior pulmonary compromise.⁷ Studies estimate PJP incidence in HSCT recipients at 3%–5% without prophylaxis, but lower with routine TMP-SMX use.⁸ However, breakthrough infections have been noted, possibly due to suboptimal

absorption, emerging resistance, or atypical immune responses.⁹

A retrospective cohort analysis from the Multidisciplinary Digital Publishing Institute (MDPI) Journal of Clinical Medicine described ground-glass opacities and cystic changes in PJP similar to those seen in our HRCT findings, underlining the importance of radiographic suspicion even early post-transplant.¹⁰ These cases underscore the need to revisit current prophylactic protocols and consider pre-engraftment initiation of TMP-SMX, particularly in

high-risk scenarios. Both of our cases showed timely haematological recovery following haploidentical HSCT, with no persistent cytopenia observed after therapeutic administration of TMP-SMX. Moreover, heightened clinical suspicion, early BAL, and polymerase chain reaction (PCR)-based diagnostics are crucial for timely diagnosis. Multicentric surveillance and data from HSCT registries are imperative to better understand the incidence and optimal preventive timing for early PJP.

Conclusion

PJP can occur unusually early in the post-transplant course of HSCT, even during the peri-engraftment phase, especially in high-risk HSCT settings like haploidentical HSCT. The two cases presented highlight the critical need for heightened clinical vigilance and early diagnostic measures in high-risk patients. These findings challenge current prophylactic practices, emphasising the potential value of initiating TMP-SMX before engraftment in select populations. Imaging and timely bronchoalveolar diagnostics played a pivotal role in rapid identification and successful treatment. Multicentre studies and registry-based surveillance are essential to optimise prevention strategies and improve outcomes in this vulnerable cohort.

Neelkumar Patel, Sanjeev Sharma, Anamika Bakliwal, Viral Jain, Kumar Animesh. Early-Onset *Pneumocystis jirovecii* Pneumonia During the Periengraftment Phase in Haploidentical Haematopoietic Stem Cell Transplantation. MMJ. 2025, September. Vol 2 (3).

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Endometriosis Presenting as Pneumothorax: Rare Entity of Thoracic Endometriosis Syndrome — A Case Report and Review of Literature

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Abstract:

Endometriosis affects roughly 10% (190 million) of women and girls of reproductive age globally, having significant social, public health and economic implications. It can decrease quality of life due to severe pain, fatigue, depression, anxiety and infertility. It can present as varied symptoms but presentation as pneumothorax is not only rare but difficult to diagnose. We report a case of a 45-year-old female presenting with recurrent right-sided pneumothorax coinciding with her menstrual cycle. Surgical exploration confirmed the diagnosis. The patient underwent a right-sided video-assisted thoracoscopic surgery (VATS) with repair of diaphragmatic fenestrations and pleurodesis. There was no recurrence of symptoms on follow-up. This case highlights the importance of a high index of suspicion in reproductive-aged women with recurrent pneumothorax. This entity is also termed as catamenial pneumothorax (CP).

Key words: Catamenial Pneumothorax, Thoracic Endometriosis, Diaphragmatic Fenestration, Video-Assisted Thoracoscopic Surgery (VATS), Hormonal Therapy.

Introduction

Catamenial pneumothorax (CP) is one of the manifestations of thoracic endometriosis syndrome (TES), a rare presentation of endometriosis. TES includes catamenial haemothorax, catamenial haemoptysis, and pulmonary nodules predominantly affecting women of reproductive age and usually presenting as right-sided pneumothorax closely associated with the onset of menstruation. The aetiology remains multifactorial, involving retrograde menstruation, prostaglandin-induced bronchospasm, and diaphragmatic fenestrations.¹ Given its rarity and often subtle radiologic findings, the diagnosis requires a combination of clinical suspicion, imaging, and intraoperative findings.

Case Report

A 45-year-old female presented with two episodes of sudden-onset right-sided pleuritic chest pain and breathlessness over the past eight months. Both episodes occurred in close association with her menstrual period. No radiological investigations were done at the time of the first episode, and she improved within 2–3 days of conservative management from a local medical practitioner. She denied any history of trauma, smoking, or previous lung disease. During the present episode, she developed sudden and severe shortness of breath, with exacerbation on walking, and was referred to us for further management. Clinical examination during this episode revealed decreased breath sounds in the right hemithorax. Chest radiograph revealed a moderate

right-sided pneumothorax (Figure 1). A high-resolution computed tomography (HRCT) scan of the thorax showed no bullous lung disease or parenchymal abnormalities, but confirmed the pneumothorax. Given the recurrent nature and clear association with menses, CP was suspected.



Figure 1: Right-sided pneumothorax with complete collapse of the underlying right lung.

The patient underwent video-assisted thoracoscopic surgery (VATS) under general anaesthesia. Intraoperative findings included multiple small fenestrations in the central tendon of the right diaphragm and brownish deposits on the diaphragmatic surface (Figure 2). The deposits were not large enough for a biopsy. A right-sided VATS-guided suture repair of diaphragmatic fenestrations with pleurodesis was performed (Figures 3 and 4).



Figure 2: Intra-operative view of diaphragmatic fenestrations with small brownish deposits of endometriosis.

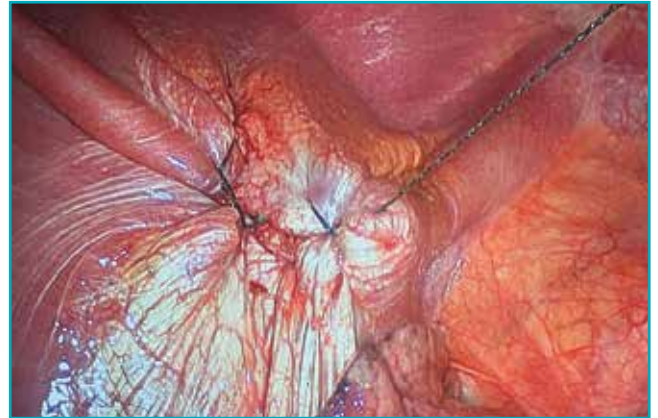


Figure 3: Intra-operative view after diaphragmatic plication of the affected portion of the diaphragm.



Figure 4: Intra-operative view after diaphragmatic plication and talc pleurodesis.

Postoperatively, the patient recovered well and was discharged on the third postoperative day after removal of the chest tube. She is on regular follow-up and prescribed gonadotropin-releasing hormone (GnRH) analogues for 6 months, as per the advice of the gynaecologist.

Review of Literature

CP is a rare but increasingly recognised clinical entity, first described by Maurer *et al.* in 1958. It is considered the most common manifestation (3%–6%) of TES, which also includes catamenial haemothorax, catamenial haemoptysis, and pulmonary nodules associated with menstrual cycles. CP typically presents as spontaneous pneumothorax occurring within 72 hours of menstruation onset, primarily affecting women of reproductive age, and exhibits a striking right-sided predominance in over 90% of cases.^{1,2}

The pathogenesis of CP is multifactorial and remains incompletely understood. The most widely accepted theories include:

- Transdiaphragmatic migration theory, where endometrial tissue traverses diaphragmatic fenestrations to implant on the pleural surface.
- Microembolisation theory, which suggests haematogenous or lymphatic spread of endometrial tissue to thoracic structures.
- Hormonal hypothesis, where high levels of prostaglandins or hormonal influences lead to vasospasm and alveolar rupture.
- Metaplasia theory, positing that coelomic epithelium differentiates into endometrial tissue under hormonal stimulation.²⁻⁴

Surgical findings frequently reveal diaphragmatic defects, fenestrations, and endometrial implants on the pleura or diaphragm. Alifano *et al.* conducted a pivotal study highlighting that diaphragmatic involvement is present in a majority of surgically treated CP cases, and emphasised the need for thorough inspection of the diaphragm during VATS.¹

Joseph and Sahn, in their analysis of 110 cases, provided a framework for the clinical diagnosis of TES, emphasising the importance of menstrual correlation with recurrent pneumothorax.¹ Visouli *et al.* further reinforced the clinical variability of CP in their case series, noting the frequent misdiagnosis and underreporting due to low clinical suspicion.⁵

Radiologic imaging may be non-specific, with occasional visualisation of diaphragmatic discontinuities or pleural nodules on computed tomography (CT) scans. However, diagnosis is most reliably achieved through thoracoscopic exploration and histopathological confirmation of endometrial glands or stroma, often positive for oestrogen and progesterone receptors.^{3,6}

Management strategies include both surgical and medical approaches. Surgical intervention typically consists of VATS with pleurodesis, pleurectomy, and repair or resection of diaphragmatic lesions, as detailed by Marshall *et al.* in their treatment algorithm.⁶ Hormonal suppression using GnRH analogues, progestins, or oral contraceptives helps reduce recurrence by inducing endometrial atrophy.^{6,7} The recurrence rate following surgery alone is higher compared to combined surgical and hormonal therapy, underscoring the importance of a multidisciplinary approach involving both thoracic surgeons and gynaecologists.^{5,6}

Despite increasing awareness, CP remains an underdiagnosed cause of recurrent pneumothorax. Timely recognition and appropriate combined treatment significantly reduce morbidity and improve long-term outcomes.

Declarations

Patient Consent: Obtained.

Funding: None.

Conflict of Interest: None.

Conclusion

CP, though rare, should be considered in reproductive-age women with recurrent right-sided pneumothorax. Early diagnosis and a combination of surgical and hormonal treatment can effectively prevent recurrence and improve quality of life.

Saraansh Bansal, Pramoj Jindal. Endometriosis Presenting as Pneumothorax: Rare Entity of Thoracic Endometriosis Syndrome — A Case Report and Review of Literature. MMJ. 2025, September. Vol 2 (3).

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A Rare Case of Rapidly Progressive Diffuse Parenchymal Lung Disease

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Abstract:

We present a case of a 56-year-old man with progressive dyspnoea and dry cough for over one month, initially treated as community-acquired pneumonia without improvement. Despite antibiotics and steroids, his respiratory function worsened, accompanied by haemoptysis and escalating oxygen needs, necessitating intubation. Laboratory evaluation revealed elevated C-reactive protein (CRP), negative infectious disease panel, a positive myositis panel (anti-PL-12), and SSA/Ro52 antibodies. Chest computed tomography (CT) showed extensive subpleural ground-glass opacities consistent with rapidly progressive interstitial lung disease (ILD). Given the diagnosis of anti-synthetase syndrome (ASS), high-dose pulse methylprednisolone (500 mg intravenous [IV] for 3 days) and rituximab (1 g IV, two doses) were instituted. The patient exhibited marked clinical and radiologic improvement, achieving extubation on Day 10. Post-therapy imaging demonstrated near resolution of ground-glass opacities, leaving reticulations indicative of chronic fibrosis.

This case underscores the significance of early recognition and aggressive immunomodulation in ASS-associated ILD. High-dose steroids and rituximab may offer critical benefits in refractory, rapidly progressive lung involvement. A multidisciplinary approach remains essential, and further research is needed to establish standardised treatment protocols.

Key words: Anti-Synthetase Syndrome, Interstitial Lung Disease (ILD), Rapidly Progressive ILD, Anti-PL-12 Antibody, Rituximab Therapy.

Introduction

Diffuse parenchymal lung disease (DPLD), also known as interstitial lung disease (ILD), is classified on the basis of shared clinical, radiographic, physiological, or pathological features. The complexity in comprehending this category of diseases arises from the intricate terminology used. In reality, the pathogenic progression entails a sequence of inflammation and fibrosis that extends beyond merely affecting the interstitial bed, as suggested by the name ILD. In DPLD, the pathology alters the lung parenchyma, encompassing the alveoli, alveolar ducts, and bronchioles.¹

One condition in which ILD occurs is anti-synthetase syndrome (ASS). It is an autoimmune disease

characterised by antibodies directed against an aminoacyl transfer t-RNA synthetase, along with clinical features that can include ILD, myositis, Raynaud's phenomenon, and arthritis.² ASS is categorised as an idiopathic inflammatory myopathy (IIM), and is more likely to be associated with ILD than other IIMs, such as dermatomyositis (DM) and polymyositis (PM), with which it shares similar features. The ILD observed in individuals with ASS is frequently intense and progresses rapidly, thus contributing significantly to the elevated morbidity and mortality linked to this syndrome.³

Case Report

A 56-year-old male presented to the emergency department with complaints of shortness of breath and dry cough for one month. The patient had no history of fever, weight loss, or haemoptysis, and was admitted to the ward. He denied any other symptoms, and reported no relevant family history. The patient had previously been treated elsewhere as a case of community-acquired pneumonia based on clinical and radiological findings (Figure 1A).

On examination, the patient was dyspnoeic; the heart rate was 92/min, blood pressure was 110/70 mmHg, and room-air oxygen saturation was 90%, with bilateral crepitations on auscultation. He was initially managed with intravenous (IV) antibiotics, oxygen supplementation, and other supportive measures.

Despite treatment, his respiratory distress worsened, with new onset haemoptysis and increasing oxygen

requirements. The patient was intubated and started on invasive mechanical ventilation. Investigations were sent (enlisted in Tables 1 and 2), and a repeat computed tomography (CT) scan of the chest was performed (Figure 1B) on Day 5 that showed increase in ground-glass opacities indicating worsening of condition.

Upon investigation, the patient tested positive for elevated C-reactive protein (CRP), myositis panel (anti-PL-12), and SSA/Ro52 antibodies, and therefore met the diagnostic criteria (Table 3) for ASS. As the patient was not responding to the initial line of treatment involving antibiotics and steroids, on Day 5 he was subsequently treated with IV methylprednisolone 500 mg/day for three doses and 1 gm rituximab for two doses, two weeks apart. Following this, the patient showed significant improvement and was extubated on Day 10. A CT scan was repeated post extubation to assess for sequelae (Figure 1C).

Investigations	Values
Haemoglobin	13.8 g/dL (Normal)
TLC	6100/microlitre (Normal)
PLT count	271/microlitre (Normal)
SGPT	26 U/L (Normal)
SGOT	16 U/L (Normal)
BUN	22.9 mg/dL (Normal)
Serum creatinine	0.8 mg/dL (Normal)
Urine routine microscopy	Normal
Blood and urine culture	Sterile
CRP	17.12 mg/dL (Increased)
Procalcitonin	0.07 µg/L (Normal)
D-Dimer	17.12 ng/mL (Normal)
Troponin I	0.01 ng/mL (Normal)
NT- ProBNP	88.7 pg/mL (Normal)
Creatinine phosphokinase	Normal
HIV	Negative
CMV titre	Negative
2D echocardiography	Normal
DVT Screen	Normal
Bronchoalveolar lavage for a. PCR, b. Gram stain, c. AFB stain, d. Fungal stain and culture, e. PJP, f. Mucor PCR, g. Galactomannan	Negative

Table 1: Blood and basic investigation.

Abbreviations: AFB Stain: Acid-Fast Bacilli Stain; BUN: Blood Urea Nitrogen; CMV Titre: Cytomegalovirus Antibody Titre; CRP: C-Reactive Protein; DVT: Deep Vein Thrombosis; HIV: Human Immunodeficiency Virus; NT-proBNP: N-terminal pro-B-type natriuretic peptide; PCR: Polymerase Chain Reaction; PJP: *Pneumocystis jirovecii* pneumonia. PLT: Platelet; SGOT: Serum Glutamic-Oxaloacetic Transaminase; SGPT: Serum Glutamic Pyruvic Transaminase; TLC: Total Leucocyte Count.

Serum ANA	Negative
ANA by IF - Nuclear pattern	Negative
Cytoplasmic pattern	Linear fibrillar
Aldolase	Positive
NCV, EMG	Normal
Myositis panel	Positive for PL-12
Vasculitis panel	Negative
Hypersensitivity pneumonitis panel	Negative
Extended autoimmune profile	Positive for SSA/Ro52

Table 2: Specific investigations done for the patient.

Abbreviations: ANA: Anti-Nuclear Antibody; EMG: Electromyography; IF: Indirect Immunofluorescence; NCV: Nerve Conduction Velocity.

Solomon et al. Diagnostic Criteria ⁴	Connors et al. Diagnostic Criteria ²
Definitive: the presence of ARS autoantibody	Definitive: the presence of ARS autoantibody
Plus, two major or one major and two minor criteria a. Major: 1. Interstitial lung disease 2. Dermatomyositis or polymyositis by Bohan and Peter criteria b. Minor: 1. Arthritis 2. Fever 3. Mechanic's hands	Plus, one or more of the following: • Interstitial lung disease • Arthritis • Raynaud's phenomenon • Fever • Mechanic's hands

Table 3: Diagnostic criteria to diagnose anti-synthetase syndrome.

Abbreviations: ARS: Aminoacyl t-RNA Synthetase.

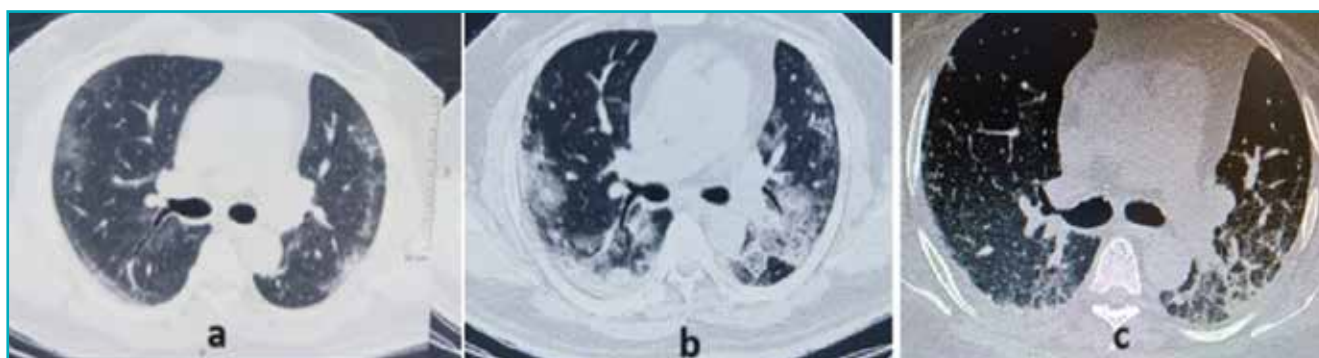


Figure 1: Computed tomography (CT) of the chest: A. A small focal area of patchy ground-glass opacity in the subpleural area of the lateral segment of the right middle lobe. Curvilinear ground-glass opacities with stranding in subpleural areas of the superior segment of bilateral lower lobes, B. Day 5: In comparison to prior high-resolution computed tomography (HRCT), an increase in size and attenuation of the ground-glass opacities in the subpleural areas of the superior segments of bilateral lower lobes. Focal ground-glass opacity in the lateral segment of the right middle lobe also shows an increase in attenuation, C. Day 10: Scan shows near complete resolution of the ground-glass opacities in both lower lobes with increased reticulations and strandings representing chronic fibrotic changes post pulse therapy.

Discussion

ASS is a rare, multisystemic autoimmune disease with variable symptoms ranging from myositis, ILD, and non-erosive arthritis. The diagnosis of ASS can be facilitated by employing the precise criteria outlined by Solomon *et al.*, and Connors *et al.* (Table 3).^{2,4}

Six anti-aminoacyl transfer RNA (t-RNA) synthetase autoantibodies have been associated with ASS: anti-histidyl-tRNA synthetase (anti-Jo-1), anti-isoleucyl-tRNA (anti-OJ), anti-threonyl-tRNA (anti-PL7), anti-alanyl-tRNA (anti-PL12), anti-glycyl-tRNA (anti-EJ), and anti-asparaginyl-tRNA (anti-KS). Amongst these, the most common and well-recognised antibody is anti-Jo-1, detected in approximately 20%–30% of such patients.⁵

Essential components of the diagnostic process include high-resolution computed tomography (HRCT) imaging, which may show nodules, micronodules, linear opacities, irregular interfaces, ground-glass opacities, fibrosis with or without honeycombing, consolidation, traction bronchiectasis, and bronchiectasis.⁶ Among the observed patterns, nonspecific interstitial pneumonitis (NSIP) is the most common, followed by organising pneumonia.⁷ Bronchoscopic or muscle biopsy may seldom be required; however, if the patient's condition permits, a bronchoscopic lavage prior to initiating immunosuppression may be performed to rule out secondary infection.

Currently, there are no established treatment protocols or guidelines for individuals affected by this condition. The first-line of treatment is corticosteroids. Other immunosuppressants such as azathioprine, mycophenolate mofetil, tacrolimus, rituximab, and cyclophosphamide may be used in conjunction with steroids as augmentative therapy for pulmonary and muscular movement. Due to the rarity of the disease, no large-scale treatment trials have been conducted. The available medical literature primarily consists of

individual case reports and small case series, with no head-to-head trials. Some reports comparing cyclophosphamide with rituximab have found rituximab to be associated with better progression-free survival at two years, leading some authors to consider it a first-line option.^{8,9} The use of pulse steroids as a last resort in refractory autoimmune conditions is well-established and may be a viable option in this setting, even though the evidence for its use in ASS remains scarce.¹⁰

Contribution

All the authors were involved in the literature search, planning, conducting, writing the original manuscript draft, and editing. All the authors have agreed with the submitted manuscript. Dr. Nikhil Raj is the corresponding author and guarantor for all.

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Conflicts of interest

The authors declare no conflicts of interest regarding the current study.

Funding

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Availability of data and material

The clinical data and the study materials are available from the corresponding author upon reasonable request.

Patient consent

Written informed consent has been obtained from the patient or their legally authorised representative.

Conclusion

High doses of immune suppression remain the cornerstone therapy for refractory ASS, and insufficient recognition of ASS among primary care physicians leads to delayed referrals to specialists, contributing to the advancement of the illness. Larger studies are needed to standardise therapy for ASS.

Vivek Nangia, Nikhil Raj, Navin Dalal, Anshul Mittal, Amina Mobashir, Manu Madan, Parth Rajdev, Swapnil Pathak. A Rare Case of Rapidly Progressive Diffuse Parenchymal Lung Disease. MMJ. 2025, September. Vol 2 (3).

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Preoperative Embolisation and Surgical Resection of a Giant Anterior Skull Base Meningioma

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Abstract:

Anterior giant skull base meningiomas are technically challenging tumours to treat because of their deep vascular supply that can preclude early devascularisation during resection. Preoperative embolisation of these arterial feeders is thought to decrease blood loss and facilitate resection, especially in these large-sized lesions. It is essential that both the endovascular and skull base neurosurgeons understand the potential benefits of preoperative embolisation. We present a case which highlights the applicability and benefits of pre operative embolisation in the surgical resection of a giant skull base meningioma.

Key words: Meningioma, Embolisation, Skull Base.

Introduction

Skull base meningiomas can be highly vascular tumours, and their vascularity may complicate or limit resection because of intraoperative blood loss.^{1,2} Surgical devascularisation can be challenging in practice, particularly for tumours arising along the skull base in locations that prevent access to the vascular pedicle until later stages of the resection.^{3,4} Embolisation of meningiomas may be performed preoperatively when surgical devascularisation is expected to be challenging. Preoperative embolisation of meningiomas has been advocated to facilitate intraoperative resection by decreasing surgical blood loss through occlusion of feeding arteries, as well as by shrinking, softening, and sometimes inducing necrosis in the tumour in ways that sometimes facilitate mechanical removal and reduced operative duration.³

Case Report

A 45-year-old female patient presented with complaints of headache and personality changes for the past two months. She also had difficulty in perceiving smell. On

examination, she had anosmia, 6/6 vision in both eyes, and fundus examination revealed bilateral papilloedema. The rest of the clinical examination was unremarkable. Magnetic resonance imaging (MRI) revealed a large, contrast-enhancing lesion arising from the anterior skull base involving the crista galli, planum sphenoidale and tuberculum sellae, suggestive of a giant anterior skull base meningioma (Figure 1A–C).

In view of the large size of the lesion, the decision to perform a pre-operative digital subtraction angiography (DSA) with tumour embolisation was taken. Diagnostic angiographic runs, from the right external carotid artery, revealed feeders from the accessory middle meningeal artery (MMA) (distal branch of internal maxillary artery) giving rise to a characteristic tumour blush (Figure 2A–B). A similar tumour blush was noted from the left accessory MMA.

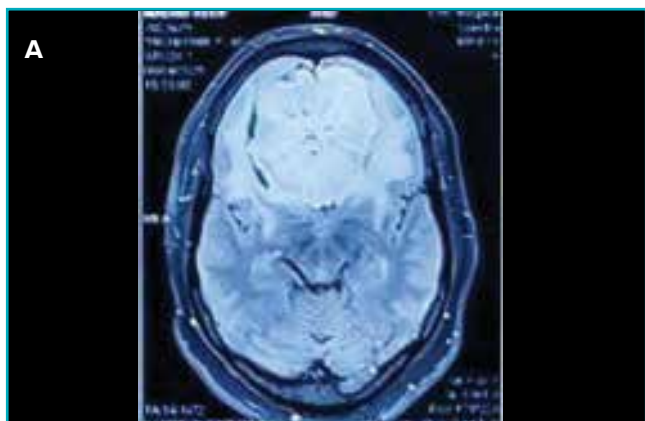


Figure 1A: Preoperative magnetic resonance imaging (MRI) axial view showing a giant, contrast-enhancing anterior skull base lesion involving the crista galli, planum sphenoidale, and tuberculum sellae, suggestive of a meningioma.

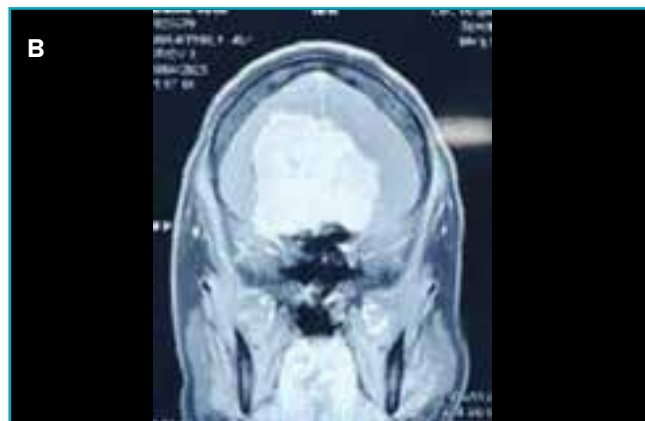


Figure 1B: Preoperative magnetic resonance imaging (MRI) coronal view demonstrating the extent of the anterior skull base meningioma with significant mass effect.



Figure 1C: Preoperative magnetic resonance imaging (MRI) sagittal view depicting the large anterior skull base tumour with superior extension.

Superselective cannulation of the accessory MMA was done using a microcatheter (on both right and left sides), and feeders were embolised with lipiodol and nectacryl glue (n-Butyl cyanoacrylate) (Figure 2A and B).

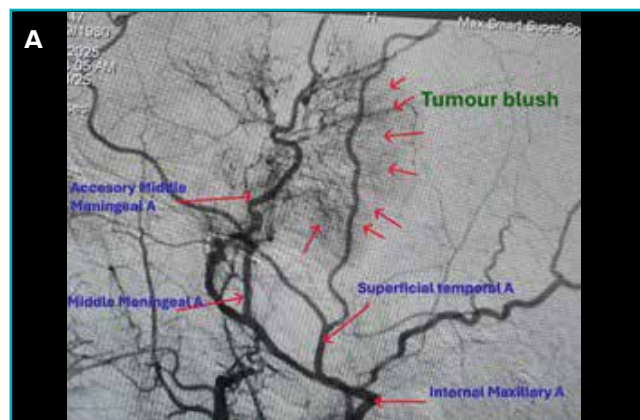


Figure 2A: Selective digital subtraction angiography (DSA) showing tumour blush from branches off the external carotid artery.

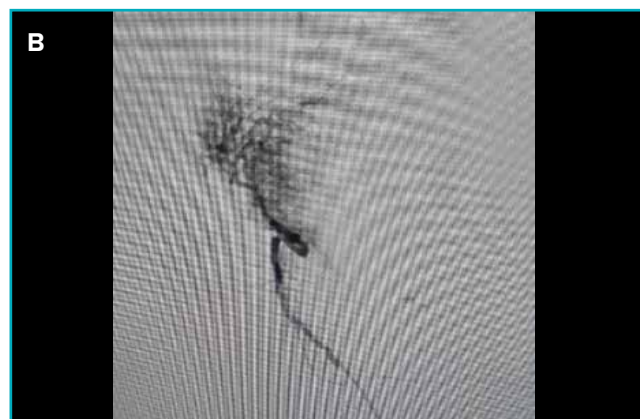


Figure 2B: Super selective shoot from the accessory meningeal artery through a microcatheter.



Figure 3: Postembolisation status.



Figure 4A: Postembolisation magnetic resonance imaging (MRI) axial view revealing hypointense areas with decreased contrast uptake, indicating reduced tumour vascularity.

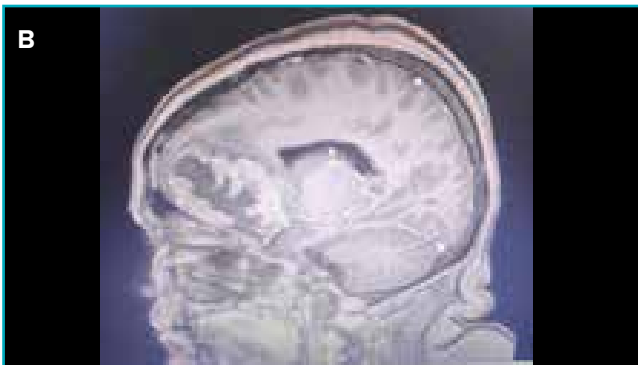


Figure 4B: Postembolisation magnetic resonance imaging (MRI) coronal view showing further reduction in contrast enhancement, consistent with successful embolisation.

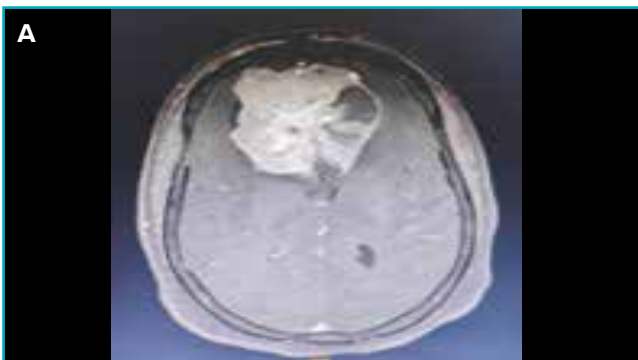


Figure 5A: Postoperative computed tomography (CT) axial view demonstrating satisfactory removal of the anterior skull base meningioma following bifrontal craniotomy.



Figure 5B: Postoperative computed tomography (CT) coronal view confirming near-complete tumour resection with no significant residual lesion.

Postembolisation of feeders revealed the disappearance of tumour blush on both sides, indicating satisfactory tumour embolisation (Figure 3). Postembolisation MRI showed hypointense areas of decreased contrast uptake suggestive of decreased tumour vascularity (Figure 4).

Post endovascular embolisation, the patient underwent definitive surgery (bifrontal craniotomy) and tumour decompression via subfrontal approach. Intraoperatively, there was a significant reduction in tumour vascularity, which contributed to a near complete tumour resection (Figure 5) along with decreased blood loss. Postoperatively, the patient was stable with no new neurological deficits and was discharged subsequently.

Discussion

Anterior skull base meningiomas can have a varied and complex vascular supply. The anterior and/or posterior ethmoidal arteries are the major arterial feeders in more than 13% of skull base meningiomas. The vascular supply of meningiomas in the olfactory groove and planum sphenoidale can arise from dural, transosseous, and even pial feeders.¹ These tumours may also be fed by arteries that supply the anterior branch of the MMA, the recurrent meningeal branches of the ophthalmic artery (OphA) and lacrimal artery, the meningeal branches of the internal carotid artery (ICA), the tentorial branch of the meningohypophyseal trunk (MHT), and the terminal branches of the internal maxillary artery (IMA), accessory meningeal artery.^{1,5} Super selective embolisation of

these feeders is done through special microcatheters. However, aggressive embolisation can be fraught with permanent postprocedural neurological deficits in view of external and internal carotid artery anastomoses, which may sometimes not be visible.

Tumour embolisation decreases the tumour vascularity and initiates tumour necrosis, making the tumour consistency soft and more amenable to surgical resection. The necrotic areas can be identified on the postembolisation MRI as hypointense areas of decreased contrast uptake, which were noted in this case.

Conclusion

Preoperative embolisation of skull base meningiomas is increasingly used to improve surgical time, reduce bleeding, and enhance the neurosurgeon's confidence while minimising the manipulation of healthy brain tissue during the surgical procedure. Endovascular approaches using super selective embolisation of the tumour feeders form the baseline treatment in these cases.

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Large Uterine Mass with Multiple Myomas Mimicking Malignancy: A Rare Case Report

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Abstract:

A 46-year-old perimenopausal woman, with a history of previous three caesarean sections, presented with progressive abdominal distension, heavy and prolonged menstrual bleeding, and fatigue over several months, accompanied by poor appetite and lower abdominal discomfort. She experienced two episodes of severe vaginal bleeding with syncope, resulting in very severe anaemia and thrombocytopenia, necessitating multiple transfusions of packed red blood cells (PRBCs) and fresh frozen plasma (FFP). Clinical examination revealed pallor, tachycardia, and a massive firm, irregular abdominopelvic mass with hepatosplenomegaly. Laboratory investigations confirmed anaemia, thrombocytopenia, and hyperbilirubinemia. Imaging identified a massive uterine fibroid (measuring up to 32.2 × 28.4 cm) with degenerative changes and heterogenous fluorodeoxyglucose (FDG) uptake, associated with ureteric compression, hepatosplenomegaly, and mild ascites. Multidisciplinary evaluation, including bone marrow biopsy excluded marrow suppression. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO) and liver biopsy. Intraoperatively, a large, lobulated uterine mass with multiple fibroids and myxoid degeneration was confirmed, weighing 8.3 kg; intraoperative frozen section and final histopathology confirmed benign leiomyomas. Liver biopsy and ascitic fluid cytology were negative for malignancy. The postoperative course was uneventful, with close monitoring and supportive transfusions. This case highlights a rare presentation of giant uterine leiomyomas causing life-threatening anaemia and coagulopathy, mimicking malignancy and necessitating a multidisciplinary approach with definitive surgical management.

Key words: Perimenopausal, Thrombocytopenia, Fibroid, Hepatosplenomegaly.

Introduction

Uterine fibroids are the most prevalent benign tumours in women of reproductive age, often asymptomatic or presenting with menorrhagia and pelvic pressure.¹ They arise from the smooth muscle cells of the uterus and are usually diagnosed by ultrasound or pelvic examination. Rarely, massive degenerative myomas may mimic malignant neoplasms both clinically and radiologically, posing significant diagnostic challenges.^{1,2} Their unusual presentation can include cystic, myxoid, or red degeneration, leading to large, heterogeneous pelvic masses with features suggestive of sarcomas or ovarian malignancies.

This case report highlights a rare presentation of a degenerative fibroid, clinically resembling a malignant pelvic mass. Diagnostic complexity was further compounded by severe anaemia, thrombocytopenia, and indirect hyperbilirubinemia, occurring in the background of hepatosplenomegaly, suggestive of hypersplenism. Such haematologic abnormalities — especially in the presence of splenomegaly — raised suspicion for systemic disorders such as lymphoproliferative disease or chronic liver pathology, requiring a broad differential diagnosis. Such a constellation of findings is unusual in benign gynaecologic conditions and raises concern for underlying haematologic or systemic pathology, necessitating a multidisciplinary diagnostic approach.

Through this case, we emphasise the importance of thorough clinical evaluation, appropriate imaging, and histopathological correlation to accurately distinguish benign from malignant pelvic masses, particularly when atypical systemic manifestations coexist.

Case Report

A 46-year-old perimenopausal woman presented with progressive abdominal distension, heavy and prolonged menstrual bleeding, and fatigue over several months. She also complained of poor appetite and lower abdominal discomfort, with no significant weight loss. On 20th May 2025, she experienced heavy vaginal bleeding followed by syncope, and was admitted to a local hospital in Bareilly, from 20th to 25th May. Her haemoglobin was 4.8 g/dL and platelet count 60,000/ μ L, requiring transfusion of two units of packed red blood cells (PRBCs). She was discharged in a stable condition on 25th May.

On 26th May she again experienced profuse vaginal bleeding with extreme weakness and reported to our hospital. On examination, she appeared pale, with a pulse rate of 116 beats per minute (bpm) and blood pressure of 90/60 mmHg. Abdominal examination revealed a firm, irregular, non-tender abdominopelvic mass extending up to the xiphisternum. Pelvic examination confirmed a large irregular uterine mass, and hepatosplenomegaly was also noted. Obstetric history included three caesarean sections, the last 12 years ago. There was no history of chronic medical illness, malignancy, liver disease, or haemolytic disorders.

Initial laboratory investigations showed haemoglobin 8.8 g/dL, platelet count 61,000/ μ L, total bilirubin 2.77 mg/dL and direct bilirubin 1.54 mg/dL. Magnetic resonance imaging (MRI) of the whole abdomen demonstrated a large uterine fibroid measuring 21.5 $\times$ 32.2 $\times$ 28.4 cm with degenerative changes, extending into the subphrenic region. Hepatosplenomegaly and mild ascites were also noted. Bilateral ovaries were not clearly visualised.

A positron emission tomography–computed tomography (PET–CT) scan revealed a large soft-tissue lesion with necrotic areas and heterogeneous fluorodeoxyglucose (FDG) uptake measuring approximately 23 $\times$ 28 $\times$ 29 cm, occupying the abdomen and pelvic cavity, with ureteric compression. A multidisciplinary team including haematology and surgical gastroenterology was consulted. Bone marrow

biopsy demonstrated trilineage haematopoiesis, ruling out marrow suppression.

Subsequently, the patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH–BSO) and liver biopsy on 30th May 2025. Intraoperatively, mild ascites was present, and fluid was aspirated for cytological evaluation. A large, irregular, lobulated mass consistent with a 36-weeks pregnant uterus was visualised. Multiple fibroids with cystic and degenerative changes were noted, distorting the uterus (Figure 1). The adnexa appeared grossly normal but were elongated and distorted due to the size of the fibroids.

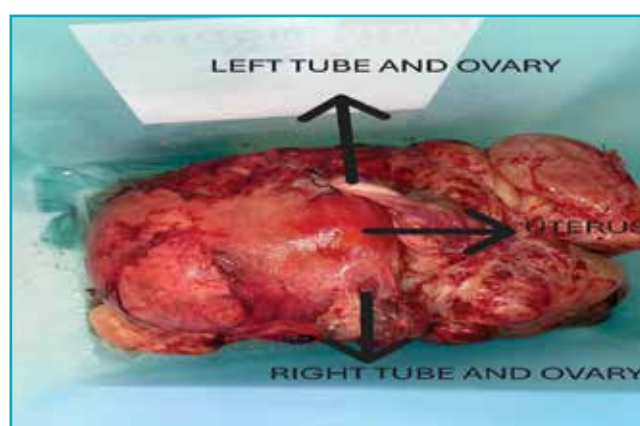


Figure 1: Multiple fibroids distorting the uterus.

Intraoperative frozen section analysis of a suspicious fibroid confirmed a benign leiomyoma, prompting completion of the planned TAH–BSO. A urologist assisted with bladder dissection and DJ stenting because of severe adhesions from three previous caesarean sections and distorted pelvic anatomy due to large multiple fibroids. The surgical specimen weighed 8.3 kg (Figure 2).



Figure 2: Multiple fibroids forming a huge mass involving the uterus, fallopian tubes, ovaries and cervix.

The patient was transferred to the intensive care unit (ICU) postoperatively for 3 days. Histopathological examination confirmed multiple benign leiomyomas with myxoid degeneration. Liver biopsy and ascitic fluid cytology were negative for malignancy. Her postoperative course was largely uneventful, with close monitoring of haematological parameters and liver function.

During her hospital stay, she received 11 units of leucodepleted PRBCs (LDPRBCs), 12 units of fresh frozen plasma (FFP), 10 units random donor platelets (RDP), and 10 units of single donor platelets (SDP). Following stabilisation, she was transferred to the ward.

The patient was discharged on 7th June 2025 in a stable condition, with haemoglobin of 9 g/dL and platelet counts recovered to over 300,000/ μ L. The patient has been on regular follow up for the last one month and is doing well.

Discussion

Multiple uterine fibroids uterus exhibiting cystic and degenerative changes can mimic malignancy, and can be associated with multifactorial anaemia, hyperbilirubinemia (suggestive of haemolysis), thrombocytopenia, and hepatosplenomegaly (indicative of underlying hypersplenism).²⁻⁴

Uterine fibroids are the most common benign pelvic tumours in women. Only a very small percentage of fibroids undergo malignant change or red degeneration. With the widespread use of ultrasound in clinical practice, uterine fibroids are generally diagnosed early and are usually not missed. Hence, the development of an unusually large myoma is rare.⁵

Pre-operative imaging is essential to determine the extent of the fibroid and to assess the likelihood of malignancy, particularly in cases of infiltrative growth.⁵

The differential diagnosis in this case included uterine leiomyosarcoma, ovarian neoplasm, lymphoproliferative disorder, haematological malignancy, and chronic liver disease with secondary hypersplenism.^{4,6}

The prognosis was favourable, as histopathology confirmed benign myomas with myxoid degeneration. The haematologic abnormalities improved after surgery with resolution of splenic sequestration. This confirms that the mass effect of the fibroid on surrounding organs likely contributed to hypersplenism and reactive cytopenias, which normalised following tumour removal.

Conclusion

This case highlights that large uterine fibroids with cystic and degenerative changes, can closely mimic malignancy, both clinically and radiologically. When associated with systemic features such as anaemia, thrombocytopenia, hyperbilirubinemia, and hepatosplenomegaly, the diagnostic complexity increases, raising suspicion for malignancy or haematologic disorders. It is crucial to maintain a broad differential diagnosis including benign aetiologies. A multidisciplinary approach, incorporating imaging, laboratory evaluation, and definitive histopathology, remains essential to accurately diagnose and appropriately manage such rare and complex cases.

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Simplifying Laparoscopic Totally Extraperitoneal Inguinal Hernia Repair with V-Technique

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Abstract:

Laparoscopic surgery for inguinal hernia repair has become the gold standard in the treatment of inguinal hernias in patients who are fit to undergo general anaesthesia. The total extra-peritoneal (TEP) technique is a preferred approach; however, it may be difficult for beginners. In this paper, we describe the “tri-compartment, V-Technique” for simplifying the understanding of extra-peritoneal space into three distinct compartments in a systematic manner. This technique involves precise and accurate partitioning of the medial, lateral, and central compartments, ensuring a clear view and effective mesh placement with minimal blood loss which can lead to improvised patient response and fewer complications.

Key words: V-Technique, Tri-Compartment, Laparoscopy, Totally Extra-Peritoneal, Inguinal Hernia.

Introduction

Ger *et al.* were the first to report laparoscopic surgery for inguinal hernia repair.¹ McKernan was the first to report a complete extra-peritoneal laparoscopic repair method, called total extra-peritoneal (TEP) hernia repair.² In TEP inguinal hernia repair, the principal concept is similar to that promoted by Stoppa, in which a large mesh is placed in the pre-peritoneal space to cover all potential hernia defects. This distributes intra-abdominal pressure over a wide area and requires little fixation. The operative steps for performing TEP and transabdominal pre-peritoneal (TAPP) repairs are very similar.³

Simplifying TEP with the V-technique essentially involves compartmentalising the pre-peritoneal space into three compartments, as shown in Figure 1, through laparoscopic dissection under clear vision. This approach provides a bloodless field and helps prevent vascular or nerve injuries.⁴

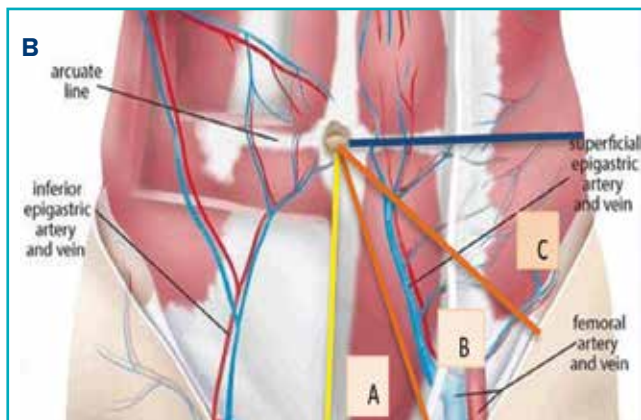
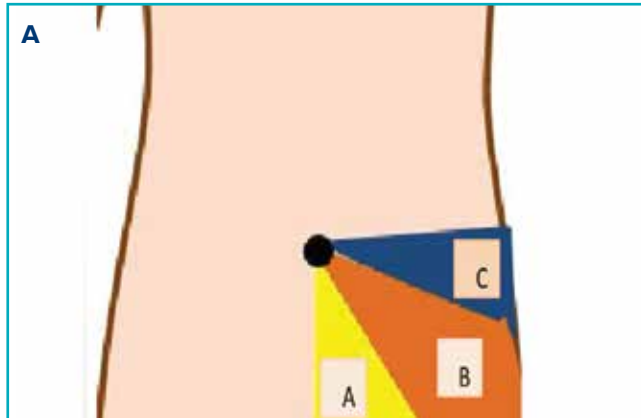


Figure 1A and B: Representation of the tri-compartment dissection for total extra-peritoneal inguinal hernia repair: a. Medial dissection, b. Central dissection, c. Lateral dissection in the pre-peritoneal space.

Generally, balloons or blunt instruments are used to create the pre-peritoneal space, a process that is usually not performed under direct vision. This often causes bleeding, which can obscure the anatomy of the pre-peritoneal space and increase the risk of complications.⁵

Technique: The tri-compartment V-technique includes the following steps:

A standard infra umbilical transverse incision of 2 cm, dissecting the adipose tissue, a transverse of 1.5 cm anterior rectus sheath incision is made and a rectus abdominis muscle is retracted laterally to expose the posterior sheath, and then, the Hassan's trocar is placed in that space, after which a telescope (10 mm, 0 degree) is introduced.⁶ Then, insufflation is done after insertion of the camera under vision so that proper extra-peritoneal space is created, as shown in Figure 2.

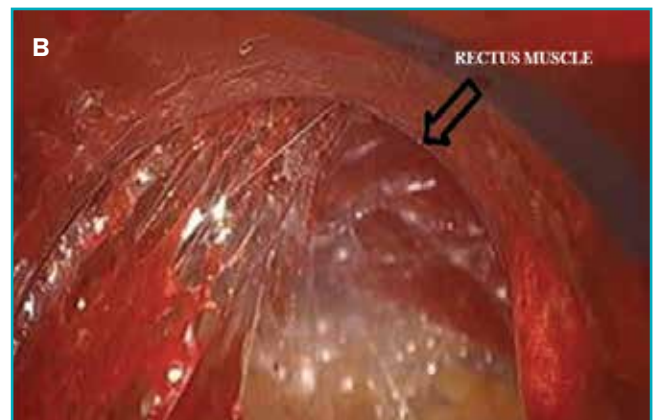
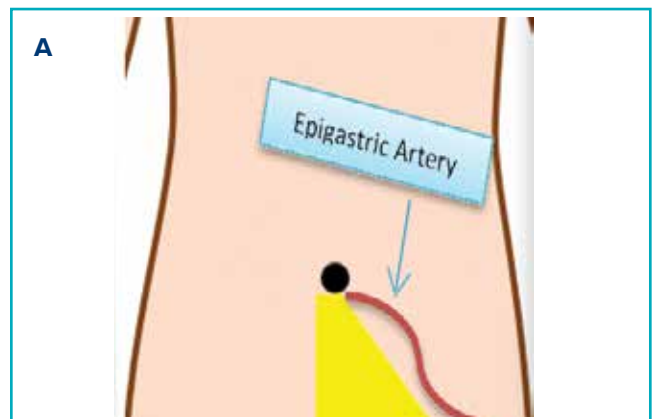


Figure 2: A. Pre-insufflated view, B. Post-insufflated view.

Firstly, surgical dissection in a medial compartment is done, using the telescope. The dissection is initiated posterior to the rectus muscle, cephalo-caudally up to the pubic crest, and then into the Retzius' space as shown in Figure 3.⁷



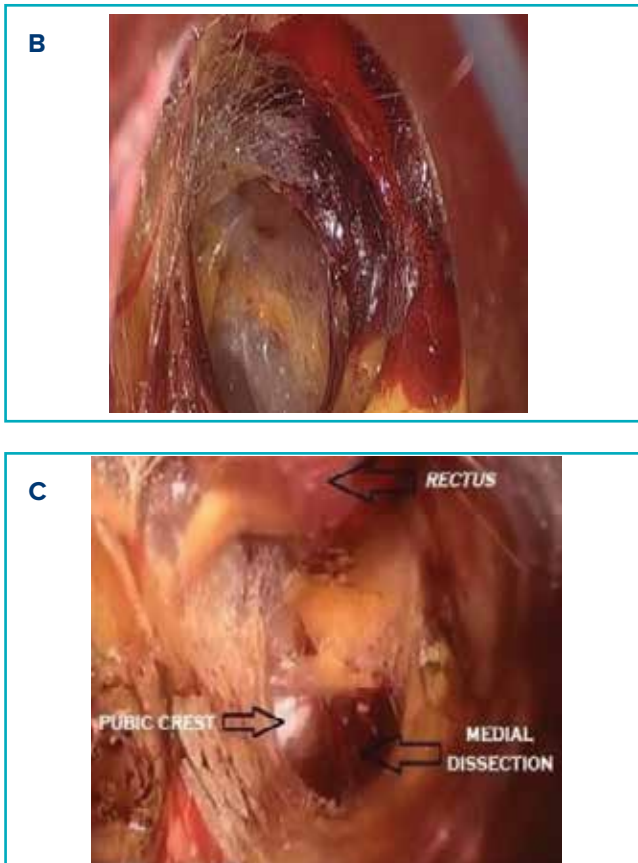


Figure 3: A. Showing the Retzius' space and representation of medial dissection, B. Initial view of medial compartment, C. Dissected medial compartment.

After completing medial dissection secondly, the lateral compartment dissection (Bogros' space) is done. This is achieved by dissecting laterally preserving the inferior epigastric vessels (IEV). The IEV should always be under direct vision to avoid any injury to them, once the IEV is preserved, lateral compartment space is created and the dissection completed up to the peritoneal reflection⁸ as shown in Figure 4. Posteriorly, the Psoas muscle should be visible and the lateral nerves must be preserved.

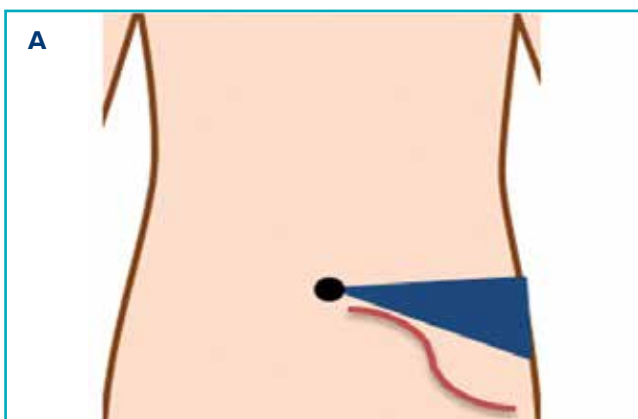


Figure 4: A. Showing the Bogros' space, B. Representation of lateral dissection

Lastly, the central compartment dissection (iliac vessel, the hernia sac and cord structure) as shown in Figure 5 is completed with gentle blunt dissection of the adipose tissue which is closely adherent to the inferior epigastric vessels away from the peritoneum posteriorly, the epigastric vessels are left undisturbed along with the anterior abdominal wall.⁹

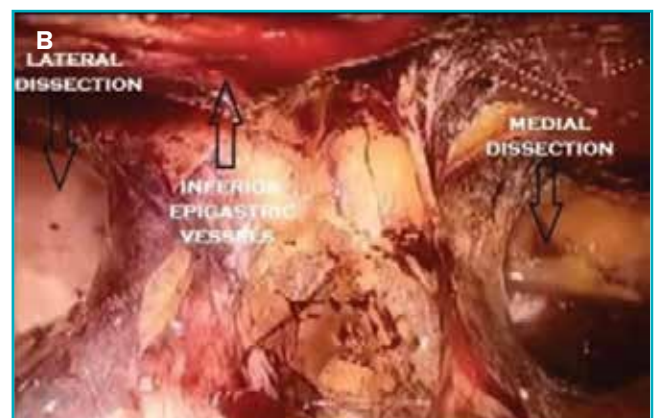
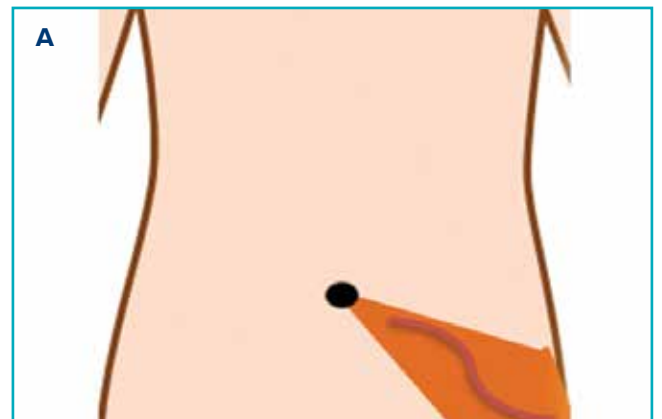


Figure 5: A. Showing the epigastric vessels' space, B. Representation of central dissection.

Then, the inguinal hernia surgery is completed in a conventional manner, reducing and dissecting the sac in front of the cord structures. Finally, a standard polypropylene mesh is placed comfortably as sufficient space is created and there is less chance of folding.

Discussion

Laparoscopy for inguinal hernia repair is now considered a gold-standard technique; however, it has a steep learning curve. The laparoscopic inguinal anatomy can be difficult for new surgeons to grasp, as the pre-peritoneal space offers few landmarks and is both narrow and enclosed. The technique described by the author aids in understanding the extra-peritoneal inguinal anatomy by compartmentalising it into three areas and addressing each compartment systematically. This makes it easier to understand and

perform the extra-peritoneal dissection, which is the most important aspect of the surgery. This technique is comparatively simple to perform and is cost-effective, making it an easy technique for experienced surgeons and those who are new to laparoscopic technique.¹⁰ This is performed entirely under the direct vision of the surgeon, which minimises the risk of errors. The anterior peritoneal space can be accessed by various methods such as mirror push method, ballooning, finger separation method and retropulsion.¹¹ However, TEP repair results in complete separation of the anterior peritoneal space through the extra-peritoneal cavity without entering into the abdominal cavity. When both TEP and TAPP are compared, they show similar outcomes in terms of recurrence rates, hospital stay, and complications.¹²

Conclusion

Laparoscopic extra-peritoneal technique using the V-technique, and addressing the inferior epigastric vessels as well as the major iliac vessels, can further minimise blood loss compared with other conventional techniques. This results in quicker recovery and reduces the risk of complications.¹³ It also clearly defines the pre-peritoneal space, which helps the surgeon to locate significant areas like the "triangle of doom" and "triangle of pain".¹⁴ A surgeon should create enough space for proper mesh placement, which is crucial for hernia repair.¹⁵ The V-technique allows easy understanding of inguinal anatomy which results in better visualisation of extra peritoneal anatomical structures and having better control to reduce any complications.

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Beyond Joint Pain: When Arthritis is a Harbinger of Leukaemia

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Abstract:

Acute lymphoblastic leukaemia (ALL) can present atypically, mimicking rheumatic conditions and causing significant diagnostic delays. This case details a 12-year-old boy initially diagnosed with juvenile idiopathic arthritis (JIA) due to persistent right shoulder and elbow pain and swelling, despite normal initial blood work. Initial evaluation, including physical examination, blood tests (normal complete blood count [CBC], elevated erythrocyte sedimentation rate/C-reactive protein [ESR/CRP]), and even rheumatoid factor positivity, pointed towards JIA. However, escalating nocturnal pain unresponsive to treatment, persistently high acute phase reactants, and bone oedema on magnetic resonance imaging (MRI) ultimately triggered a bone marrow aspiration, revealing a diagnosis of precursor B-cell ALL. This case emphasises the crucial need for high clinical suspicion and thorough investigation, including bone marrow examination, when children present with atypical or treatment-resistant musculoskeletal pain, particularly with features like worsening night pain and bone oedema on imaging, to avoid detrimental delays in diagnosing life-threatening conditions like ALL.

Key words: Leukaemia, Arthritis, Bone Marrow, Biopsy.

Introduction

Acute lymphoblastic leukaemia (ALL) is the most common childhood malignancy, often presenting with fever, pallor, fatigue, and bleeding.¹ However, a significant subset of children with ALL may initially exhibit musculoskeletal symptoms, mimicking rheumatic conditions like juvenile idiopathic arthritis (JIA).² This diagnostic challenge poses a serious risk, as delays in identifying and treating ALL can lead to adverse patient outcomes.³ Musculoskeletal complaints, including bone pain and arthritis, are present in a notable percentage of children with malignancies, highlighting the need for heightened clinical suspicion.⁴ This case report details the challenging diagnostic journey of a 12-year-old boy whose symptoms initially mimicked JIA, but ultimately revealed an underlying ALL.

Case Report

A 12-year-old boy, with no significant past medical history, presented to a paediatric rheumatology outpatient clinic with a four-week history of severe right shoulder pain and swelling. Notably, he denied any constitutional symptoms such as fever, loss of appetite, fatigue, weight loss, or night sweats. His medical history included a prior episode of bilateral knee pain and swelling that resolved with non-steroidal anti-inflammatory drug (NSAID) treatment, followed by right shoulder pain and swelling that also regressed with NSAID treatment. On physical examination, the patient exhibited swelling, pain, and a restricted range of motion in his right shoulder and elbow joints. Other joint and systemic examinations, including assessment for lymphadenopathy and hepatosplenomegaly, were unremarkable. Initial laboratory tests were surprisingly normal: haemoglobin 11.2 g/dL; white blood cell

(WBC) count 8400/mm³; absolute neutrophil count 5820/mm³; platelet count 2.86 lakh/microl; erythrocyte sedimentation rate (ESR) 55 mm/h; C-reactive protein (CRP) 105; and lactate dehydrogenase (LDH) 224 U/L. The peripheral blood smear revealed no atypical cells, and serological tests for viral and bacterial aetiologies were negative. Direct radiographs of both hands and feet were also normal. Following the detection of rheumatoid factor positivity, a preliminary diagnosis of migratory JIA was made, and naproxen sodium treatment was initiated. Magnetic resonance imaging (MRI) of the right shoulder unveiled diffuse bone oedema and mild periarticular fluid in the shoulder and elbow joints. An ophthalmological evaluation was conducted to rule out uveitis, which also turned out to be normal. Repeated peripheral blood smears consistently showed no atypical cells. However, the patient's condition did not improve. During follow-up, acute phase reactants remained elevated, and his pain, particularly at night, intensified significantly. His arthritis remained unresponsive to naproxen sodium treatment. Due to the persistent and unsettling joint pain that frequently disrupted his sleep, he was referred to haematology for further evaluation. Despite the continued absence of atypical cells in the peripheral blood smear, the severity of his joint and bony pain prompted a bone marrow aspirate. The bone marrow aspirate yielded a shocking revelation: suggestive evidence of leukaemia, with a staggering 55% blasts. The biopsy further confirmed near-total replacement of the bone marrow by blasts. Flow cytometry analysis identified a cluster of cells within the blast window on the cluster of differentiation 45/side scatter (CD45/SSC) plot. These cells displayed bright expression of cluster of differentiation 10 (CD10) (~97%) along with moderately bright cluster of differentiation 34 (CD34) (~94%), cluster of differentiation 19 (CD19) (~96.5%), cytoplasmic cluster of differentiation 22 (cCD22) (~88%), cytoplasmic cluster of differentiation 79a (cCD79a) (~97.2%), cluster of differentiation 58 (CD58) (~99%), human leucocyte antigen – DR isotype (HLA-DR) (~98%), and cluster of differentiation 38 (CD38) (~98%), along with heterogeneous dim expression of cluster of differentiation 20 (CD20) (~37.4%). This immunophenotypic profile was highly suggestive of precursor B-cell acute lymphoblastic leukaemia (Pre-B-ALL). Patient was started on Berlin-Frankfurt-Münster (BFM) 2009 protocol for ALL, which included steroids, resulting in the complete disappearance of pain in 4–5 days.

Discussion

ALL, the most common childhood malignancy, accounts for around 40% of childhood cancers in individuals under 20 years of age.⁵ While its precise aetiology

remains elusive, environmental, immunological, and genetic factors are believed to play a role.⁶ Although patients often present with classic symptoms like fever, pallor, fatigue, night sweats, lymphadenopathy, hepatosplenomegaly, and bleeding manifestations, monoarthritis or polyarthritis can be the initial manifestation of leukaemia, posing a significant diagnostic challenge.^{7,8} When evaluating arthritis in children, a thorough history regarding the number of affected joints, duration and pattern of pain, relationship to daily activity, previous infections, and potential triggering factors is crucial. In cases of monoarthritis, infectious aetiologies like septic arthritis or osteomyelitis should be carefully considered and excluded. In polyarthritis, initial differentials commonly include acute rheumatic fever, systemic and articular JIA, systemic lupus erythematosus, other connective tissue diseases, and vasculitis. Mechanical causes were excluded in our patient, given the absence of trauma history and unremarkable radiographs. The presence of polyarthritis for over six weeks, rheumatoid factor positivity, and persistently elevated acute phase reactants initially suggested inflammatory causes like systemic and articular JIA. However, the possibility of haematological malignancy, though initially considered less likely, remained in the differential diagnosis. Patients with suspected leukaemia presenting with musculoskeletal complaints, but normal baseline complete blood counts (CBCs) and peripheral blood smears, can be mistakenly diagnosed with a rheumatological condition, potentially delaying appropriate treatment.⁹ Several warning signs can help distinguish between haematology-oncological malignancies and rheumatic diseases. In leukaemia patients, bone pain is often described as deep, disproportionate to the degree of arthritis, worsens at night (independent of joint pain), and may not respond to analgesics.¹⁰ In contrast, JIA typically involves multiple joints with morning stiffness, swelling, and milder pain. Furthermore, peripheral blood smears in JIA often show a predominance of neutrophils, while leukaemia may present with lymphocytosis, or, as in our patient's case, even an initial neutrophilic dominance. The absence of morning stiffness has also been suggested as a more robust warning sign for malignancy.¹¹ Stoll *et al.* emphasised the need to re-evaluate the diagnosis in patients with joint pain that worsens at night and is unresponsive to treatment, particularly in the context of decreasing leucocyte and platelet counts and a significant increase in LDH values.¹² Although antinuclear antibody (ANA) positivity is a known indicator of autoimmune diseases, it's not always helpful in excluding malignancies. In our patient, the worsening nocturnal pain and elevated acute phase reactants, despite a consistently normal peripheral blood smear, were crucial factors that prompted further investigation.

Conclusion

This case report underscores the critical importance of considering malignancy, particularly ALL, in the differential diagnosis of children presenting with persistent musculoskeletal pain, even when initial laboratory findings, including CBCs and peripheral blood smears, appear normal. The patient's progression to severe, night-time bone pain, coupled with elevated acute phase reactants and bone oedema on MRI, ultimately led to the life-saving bone marrow aspirate that revealed the underlying leukaemia. Delayed diagnosis of ALL can have devastating consequences, impacting treatment efficacy and long-term prognosis. Therefore, in patients with atypical JIA, or those presenting with monoarthritis or polyarthritis accompanied by intense night pain, markedly elevated acute phase reactants, and bone oedema on MRI, bone marrow aspiration should be strongly considered before initiating or continuing treatment for presumed rheumatic conditions, even if rheumatoid factor or ANA positivity is present. A high index of suspicion and a thorough diagnostic approach are essential to ensure the timely and accurate diagnosis of ALL, improving the chances of favourable outcomes for these vulnerable patients. Avoidance of steroids till complete diagnosis is made is very crucial, as steroids can mask the diagnosis, further delaying the treatment. In our case, the rheumatologist who had seen the child earlier did not start steroids, which proved extremely beneficial.

Anamika Bakliwal, Jatin Munjal, Mousumi Kar, Aditi Mittal, Anil Handoo, Rachna Sharma, Sanjeev Kumar Sharma. Beyond Joint Pain: When Arthritis is a Harbinger of Leukaemia. MMJ. 2025, September. Vol 2 (3).

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Case Report: Lower Respiratory Tract Infection with Cardiac Tamponade in a Patient with Bronchial Carcinoid and History of Tuberculosis Infection

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Abstract:

Cardiac tamponade is a life-threatening condition that requires urgent diagnosis and intervention. Its occurrence in patients with complex pulmonary histories, such as bronchial carcinoid and previous tuberculosis (TB) infection, is rare and clinically challenging. We report the case of a 76-year-old male with a prior history of endoscopically treated bronchial carcinoid and treated pulmonary TB (2016), who presented with acute breathlessness, restlessness, chest discomfort, and gastrointestinal symptoms. He had a background of chronic productive cough and recurrent lower respiratory tract infections. On admission, he was tachycardic, tachypnoeic, hypotensive, and hypoxic. Clinical examination and two-dimension (2D) echocardiography confirmed massive pericardial effusion causing cardiac tamponade. Emergency pericardiocentesis drained 300 mL of turbid yellow pericardial fluid, which showed lymphocytic predominance. Imaging revealed bilateral pleural effusion, atelectasis, and left lung collapse. The patient was managed with intravenous antibiotics (meropenem and targocid), vasopressors, bronchodilators, supportive care, and empiric antitubercular therapy. His condition improved significantly, and follow-up echocardiography showed only mild residual effusion without tamponade. He was discharged in stable condition with a comprehensive treatment plan and scheduled follow-up.

Key words: Cardiac Tamponade, Pericardial Effusion, Pericardiocentesis, Bronchial Carcinoid, Tuberculosis Infection, Bronchial Carcinoid, Elderly Patient.

Introduction

Lower respiratory tract infections (LRTIs) are among the most common and potentially serious infections affecting the lungs and airways. When combined with rare complications such as cardiac tamponade, a life-threatening condition where fluid builds up around the heart, the risks increase significantly.¹ This report analyses a complex medical case involving a patient with a bronchial carcinoid tumour and a history of tuberculosis (TB) infection, who developed both a LRTI and cardiac tamponade. By examining the interactions between these conditions, this report aims to shed light

on how overlapping respiratory and cardiac issues can complicate diagnosis and treatment, especially in individuals with a history of lung disease. The goal is to provide insight into the medical challenges of such cases in an understandable way.

Case Report

A 76-year-old male with a known history of bronchial carcinoid status post-endoscopic removal and treated TB infection (2016) presented with an acute onset of breathlessness, restlessness, chest discomfort,

and gastrointestinal symptoms, including nausea, vomiting, and abdominal pain. He had a background of recurrent LRTIs and chronic productive cough. On admission, he exhibited tachycardia, tachypnoea, hypotension, and desaturation. Clinical evaluation and two-dimension (2D) echocardiography revealed a massive pericardial effusion causing cardiac tamponade (Figure 1). Approximately 300 mL of turbid yellow-coloured pericardial fluid was drained via pericardiocentesis after insertion of a sheath (Figure 2). The fluid analysis showed lymphocytic predominance. Chest imaging further revealed bilateral pleural effusion, atelectasis, and left lung collapse. Initial management included intravenous (IV) vasopressors, meropenem, targocid, supportive care, and bronchodilator therapy. The patient was also started on antitubercular therapy, considering his history and clinical findings. Serial monitoring showed clinical improvement and stabilisation of vital signs. A follow-up 2D echo showed only mild residual pericardial effusion without signs of tamponade (Figure 3). Computed tomography (CT) of the chest was carried out which revealed bilateral pleural effusion and left lung collapse (Figure 4). The patient was discharged in a vitally and haemodynamically stable condition with a comprehensive medication plan and advised follow-up after one week.



Figure 1: Chest X-ray on admission showing bilateral pleural effusion with left lung collapse.



Figure 2: Chest X-ray after pericardiocentesis demonstrating resolution of cardiac silhouette enlargement.



Figure 3: Chest X-ray at discharge showing significant improvement in lung expansion and reduced pleural effusion.

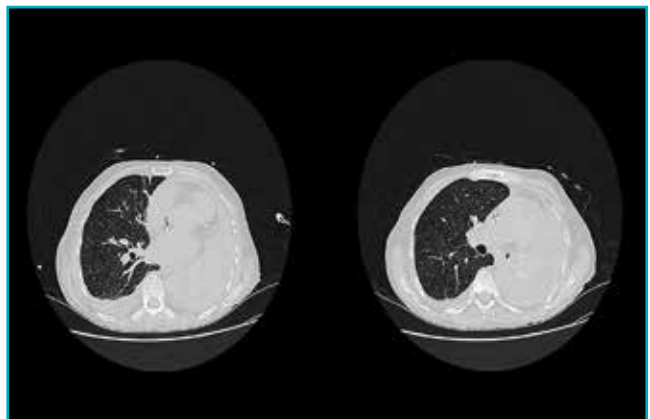


Figure 4: Computed tomography (CT) chest revealing bilateral pleural effusion, atelectasis, and left lung collapse.

Discussion

Pericardial effusion can lead to cardiac tamponade, a life-threatening condition in which fluid accumulation within the pericardial sac exerts pressure on the heart, impairing ventricular filling, especially during diastole, and reducing cardiac output.^{2,4} This can result in shock or cardiac arrest if not promptly addressed. Clinical signs of tamponade include hypotension, muffled heart sounds, and jugular venous distension (Beck's triad), and require urgent diagnosis via echocardiography and intervention such as pericardiocentesis.^{2,4} In this case, the patient initially presented with features of an LRTI, which can, especially when bacterial or viral, extend to the pericardium either through direct

spread or haematogenous dissemination, leading to pericarditis and subsequent effusion. The systemic inflammatory response associated with infection may further contribute to fluid accumulation.⁵ This case highlights how an LRTI can mask evolving pericardial complications and underscores the need for heightened vigilance in deteriorating patients, particularly elderly individuals with multiple comorbidities.^{5,6} Cardiac tamponade, although uncommon, can develop rapidly in such vulnerable populations and necessitates timely, life-saving intervention.⁵ In this instance, pericardiocentesis was crucial, and a multidisciplinary approach involving cardiology and pulmonology played a key role in ensuring the patient's optimal recovery.

Conclusion

This case highlights the importance of prompt recognition and management of pericardial effusion leading to cardiac tamponade, particularly in elderly patients with a complex medical history including prior pulmonary infections and malignancy. Timely intervention with pericardiocentesis and appropriate antibiotic and supportive therapy resulted in significant clinical improvement. Comprehensive evaluation and a multidisciplinary approach played a crucial role in the successful stabilisation and recovery of the patient. Regular follow-up and adherence to prescribed treatment are essential to prevent recurrence and monitor for potential complications.

Hemalata Arora, Pritisha Pillai. Case Report: Lower Respiratory Tract Infection with Cardiac Tamponade in a Patient with Bronchial Carcinoid and History of Tuberculosis Infection. *MMJ*. 2025, September. Vol 2 (3).

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Tubular Oesophageal Duplication: A Difficult Truth to Swallow in a Child with Stunted Growth, Unravelling with Imaging

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Abstract:

Congenital oesophageal duplications are rare anomalies classified under foregut malformations. They represent approximately 20% of all gastrointestinal (GI) duplications, which occur in about 1 in 4,500 live births. Among GI duplications, ileal duplications are the most common, while oesophageal duplications are relatively uncommon, and occur with equal frequency in males and females. The clinical presentation depends on the size and location of the duplication. Many children exhibit non-specific symptoms such as poor weight gain, stunted growth, feeding difficulties, dysphagia, or respiratory issues due to compression of adjacent structures. Early diagnosis through imaging and appropriate surgical management is crucial to prevent complications.

We report the case of a 5-year-old male child weighing 10 kg who presented with stunted growth and progressively worsening dysphagia, more pronounced for solids than liquids, over four years. Imaging findings from thin barium swallow demonstrated a dilated upper oesophagus with stricture at the junction of the upper and mid oesophagus, along with a large hiatal hernia causing upward displacement of the gastro-oesophageal junction and narrowing at this level in the upright position; in the supine position, the paraoesophageal contrast extended up to C5, while the duodenal and proximal bowel loops appeared normal. Contrast-enhanced computed tomography (CECT) of the neck, chest, and upper abdomen revealed partial duplication of the proximal and mid oesophagus, with a midline fold or membrane extending approximately 6 cm from C5 to D7, in addition to a dilated lower oesophagus. Cross-functional imaging enabled a non-invasive diagnosis of this rare anomaly and provided crucial anatomical details for planning surgical correction, highlighting the potential for definitive treatment with minimal mediastinal complications.

Key words: Foregut Malformations, Tubular Oesophageal Duplication, Oesophageal Stenosis, Hiatus Hernia.

Introduction

Congenital foregut malformations arise from abnormal embryogenesis of the foregut. Among these, oesophageal duplication is an extremely rare anomaly, accounting for approximately 20% of all alimentary tract duplications, which themselves occur in about 1 in 4,500 live births. Morphologic variants of oesophageal duplications include cystic, tubular and diverticular forms. These anomalies may be associated with other

spinal or vertebral malformations and, rarely, congenital diaphragmatic hernia.

This case report describes the imaging evaluation of a tubular oesophageal duplication in a 5-year-old male child presenting with dysphagia and recurrent lower respiratory tract infection (LRTIs). The imaging findings were crucial in pre-operative planning to facilitate

surgical management while minimising mediastinal complications.

Case Report

A 5-year-old male child weighing 10 kg presented with failure to thrive and a gradually progressive difficulty in swallowing, more pronounced for solid foods than liquids, for the past four years. This was associated with occasional cough and recurrent LRTIs during the same period. There was no history of prior surgery, corrosive ingestion, or trauma. The child was born at full term via normal vaginal delivery, with an uneventful postnatal course.

On thin barium swallow (Figure 1), there was a dilated upper oesophagus with a stricture at the junction of the upper and mid oesophagus. A hiatus hernia was noted, with upward displacement of the gastro-oesophageal junction (GEJ) and narrowing at this level in the standing position. In the supine position, paraoesophageal contrast was seen extending up to the C5 vertebral level, approximately over a length of 7 cm. The remaining bowel loops appeared normal.

On contrast-enhanced computed tomography (CT) of the neck, chest, and upper abdomen (Figures 2 and 3), partial duplication of the proximal and mid oesophagus was seen, with a midline fold or membrane extending approximately 6 cm from the C5 to the D7 vertebral level. The lower oesophagus was dilated. A large hiatal hernia was also identified, along with oesophageal dilatation proximal to the stricture at the junction of the upper and mid oesophagus.

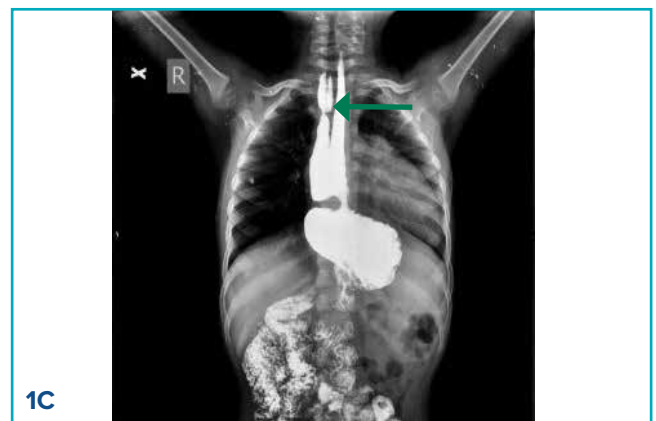
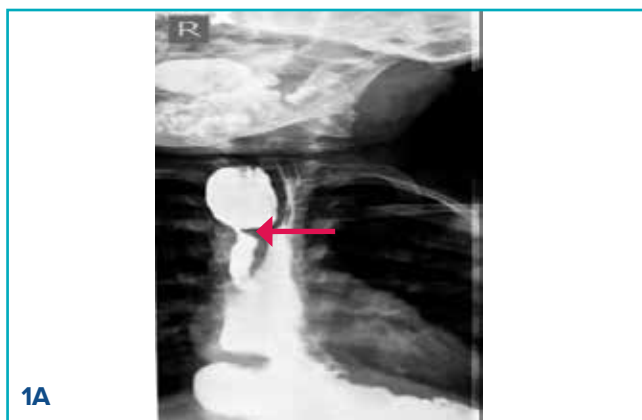


Figure 1A–C: A. Barium anteroposterior (AP) view shows a dilated proximal oesophagus due to stricture (red arrow), B. Barium swallow right anterior oblique (RAO) view shows a large hiatus hernia (blue arrow) with the gastro-oesophageal junction (GEJ) located above the diaphragm, C. Barium AP view shows duplicated oesophagus in all 3 radiographs with hiatus hernia and normally visualised small bowel loops (green arrow).





Figure 2A–C: A. Axial section shows dilated oesophageal lumen separated by thick fibrous septa (blue arrow), B. Shows luminal narrowing caused by a stricture (blue arrow), C. Maximum intensity projection (MIP) coronal images show hiatus hernia stricture (red arrow) and oesophageal duplication (yellow arrow).

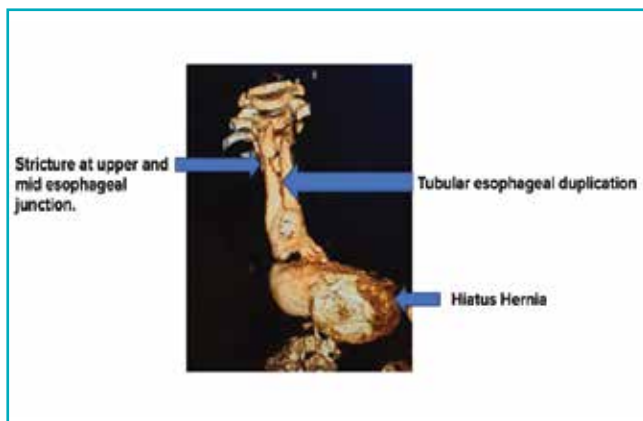


Figure 3: Computed Tomography (CT) neck, chest and upper abdomen with oral contrast using maximum intensity projection (MIP) images confirms the barium swallow findings with no associated vertebral or spinal anomalies.



Figure 4: Endoscopy via gastrotomy shows septum/membrane between the duplicated oesophagus.



Figure 5: Post endoscopic stapler septotomy.

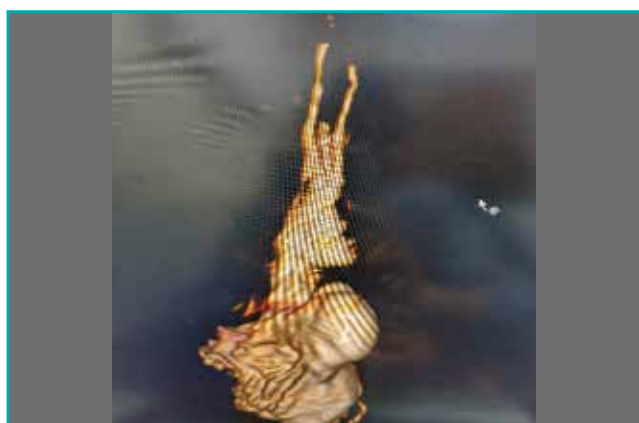


Figure 6: Post-operation virtual reality thoracoscopy (VRT) images reveal resolution of stricture with partial duplication.

Discussion

Congenital foregut malformations are among the rarest developmental anomalies, with gastrointestinal (GI) duplications occurring in approximately 1 in 4,500 live births. Of these, only about 20% involve the oesophagus, making oesophageal duplications particularly uncommon.^{1,2} They result from aberrations during embryogenesis of the foregut. Although the exact mechanisms of oesophageal duplications are not fully understood, two accepted theories include the diverticular theory and the canalisation defect theory. During the solid stage of foetal intestinal development, around the 6th gestational week, incomplete vacuolisation progressing from the cranial to caudal direction may lead to duplication.³

Oesophageal duplications may be associated with oesophageal atresia, tracheoesophageal fistula (TOF), or vertebral anomalies, such as scoliosis, hemivertebrae, or spina bifida, in up to 20% of cases. Rarely congenital diaphragmatic hernia may also coexist. The condition occurs equally in males and females. Symptoms usually appear early in life, with most patients presenting before the age of 2 years. Clinical presentation of foregut duplication depends on four main factors:

1. The anatomic level or location of the lesion
2. Mass effect of the lesion
3. Complications secondary to luminal secretions
4. Cyst infection

Patients become symptomatic due to respiratory symptoms secondary to airway compression from the mass effect.^{3,4}

There are three morphological types of oesophageal duplication:^{3,5}

- **Cystic (most common):** May communicate or remain non-communicating with the oesophageal lumen
- **Tubular (rare):** Communicates with the true oesophageal lumen, often sharing a long segment of its wall, separated by a thick fibrous septum
- **Diverticular (rarest):** This variant is rarely observed

Oesophageal duplication may occur in the cervical, thoracic or abdominal oesophagus. Tubular duplication can originate in either the thorax or abdomen but are usually located in the lower oesophagus within the posterior mediastinum, projecting into the right or left thorax.¹

Histologically, thoracic oesophageal duplication contain purely GI epithelium, even when located remote from the native oesophagus.⁵

Management depends on the patient's symptoms. Symptomatic oesophageal duplication cysts are typically excised through thoracoscopy. For partial tubular oesophageal duplications endoscopic stapler septotomy has emerged as a novel, minimally invasive surgical technique (Figures 4, 5 and 6).⁵ With the advent of newer modalities robotic thoracoscopic excision of oesophageal duplication cysts has also been reported as a valuable option.⁶

Conclusion

Tubular oesophageal duplication is a rare congenital anomaly of the foregut. Oesophageal duplications are classified into three types: cystic, tubular and diverticular. Symptoms usually arise when complications develop. A barium swallow is the first-line investigation for a child presenting with dysphagia, while contrast-enhanced CT is the investigation of choice for definitive diagnosis.

Abhishek Avalli, Pran Purohit, Neemish Kamat, Mitusha Verma, Deepak Patkar. Tubular Oesophageal Duplication: A Difficult Truth to Swallow in a Child with Stunted Growth, Unravelling with Imaging. MMJ. 2025, September. Vol 2 (3).

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Novel Technique of In-Situ Reduction of a Deceased Donor Small Intestine Graft to Improve Access in Donor–Recipient Mismatch

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Abstract:

Small intestine transplantation remains a complex but definitive treatment for patients with irreversible intestinal failure, particularly in settings where parenteral nutrition (PN) services are limited. One of the critical challenges is achieving size compatibility between the donor organ and the recipient's abdominal domain. We describe a 50-year-old man, 160 cm in height and 65 kg in weight (body mass index [BMI] 25.3 kg/m²), who suffered from massive bowel gangrene due to thrombosis. He underwent resection of the entire small bowel 10 cm distal to the duodenojejunal (DJ) flexure. He had two episodes of central venous line-related sepsis, multiple hospital admissions, and lost 30 kg in 2 months. He underwent a novel technique of in-situ reduction of a deceased donor intestinal graft, based on the principles of living donor intestinal transplant (LDIT), wherein approximately 200 cm of the distal ileum was retrieved. The patient was extubated on the table and discharged with stable graft function. Regular follow-up for 3 months was uneventful. Recipients of other organs were stable at discharge. The success of this case highlights the technique's feasibility, safety, and effectiveness. This innovative strategy could substantially expand the donor pool, particularly in resource-limited settings where paediatric or size-matched donors are scarce.

Key words: Deceased Donor Intestinal Transplant, Parenteral Nutrition, In-Situ Reduction, Small Bowel Gangrene, Donor–Recipient Size Mismatch.

Introduction

Patients suffering from progressive intestinal failure are at increased risk for significant complications associated with its management. These include intestinal failure or total parenteral nutrition (TPN)–associated liver disease, progressive loss of central vein access, and repeated

life-threatening central venous catheter-associated infections requiring critical care¹ Overall, the number of patients undergoing small intestine transplantation has decreased in Western countries. This is multifactorial, including a better understanding of intestinal failure, post-

resection intestinal reconstruction procedures, newer intravenous lipid emulsions with improved tolerance to parenteral nutrition (PN), dedicated intestinal rehabilitation services, home TPN services, intestinal growth factors like teduglutide, and better central venous lines with antibacterial locks.²⁻⁴ In contrast, in South-East Asian countries, including India — where TPN services are not readily accessible — patients with intestinal failure have a dismal prognosis without intestinal transplantation. However, donor–recipient size discrepancies have limited the available pool of ideal donor organs, with the acceptable donor–recipient body weight ratio ranging from 0.76–1.1. This is especially true for smaller patients.⁵ Additional factors compounding this size discrepancy include the loss of abdominal domain, often resulting from multiple surgeries, meshes, or enterocutaneous fistulas that frequently occur in these patients.⁶ Attempts to use relatively larger grafts in recipients with a small abdominal domain can result in the development of compartment syndrome and vascular complications, including venous outflow obstruction. Strategies to overcome this issue include mesh or abdominal wall grafts to increase domain. The living donor intestinal transplant (LDIT) technique was described by Beneditti *et al.*⁷ However, in-situ reduction of the small intestine during deceased donor procurement and transplantation has not been described previously. We report the first case utilising this technique and describe the methodology of procurement and recipient outcomes herein.

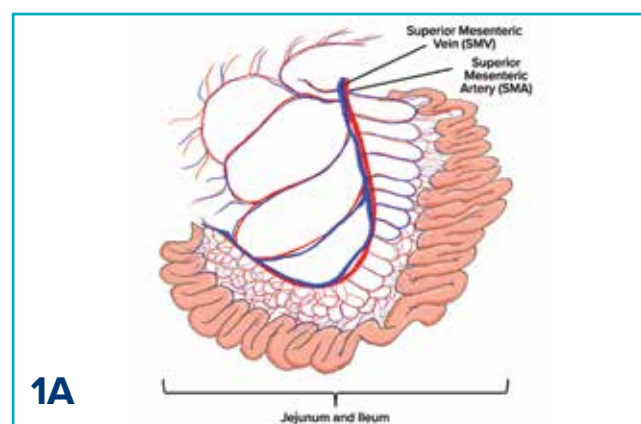
Case Report

A 50-year-old patient, 160 cm in height and 65 kg in weight (body mass index [BMI] 25.3 kg/m²), suffered from massive bowel gangrene due to superior mesenteric artery (SMA) thrombosis. He underwent emergency exploratory laparotomy, where the entire small bowel 10 cm distal to the duodenojejunal (DJ) flexure up to the proximal ascending colon, was resected. The proximal jejunum was brought out as an end jejunostomy, and the ascending colon was brought out as a distal mucous fistula at another hospital. His hospital stay was prolonged, complicated by two episodes of central venous line-related sepsis, after which a chemoport was inserted in the right internal jugular vein for administering TPN. He was discharged after 46 days of hospital admission, maintained on an alimetal diet and PN. He required multiple hospital readmissions due to dehydration, and he lost 30 kg within 2 months. He was referred to our centre for small intestine transplantation. He was evaluated and listed for a deceased donor small intestine transplantation. Within 2 months of listing, he received 3 organ offers,

but all of them had to be declined owing to his small abdominal size and weight. At this stage, his weight had decreased to 35 kg (BMI 13.67 kg/m²), and the abdomen appeared smaller compared to the initial admission. Finding an appropriately sized donor seemed challenging as most Indian adult donors on average weigh between 60–85 kgs. It was therefore decided to proceed with a reduced graft for the patient rather than waiting for an appropriate size-matched donor. Due to the unit's experience in performing living donor intestinal transplants, the retrieval was planned in the same manner as is done in case of a living donor, wherein approximately 200 cm of the distal ileum is retrieved. The patient received an offer from an 18-year-old female donor weighing 85 kg.

Donor surgery

The bowel was inspected and found to be appropriate for retrieval. A Cattell–Braasch manoeuvre was performed. The root of the mesentery was looped by creating a window on either side. The superior mesenteric vein (SMV) and the SMA were dissected and looped (Figure 1).



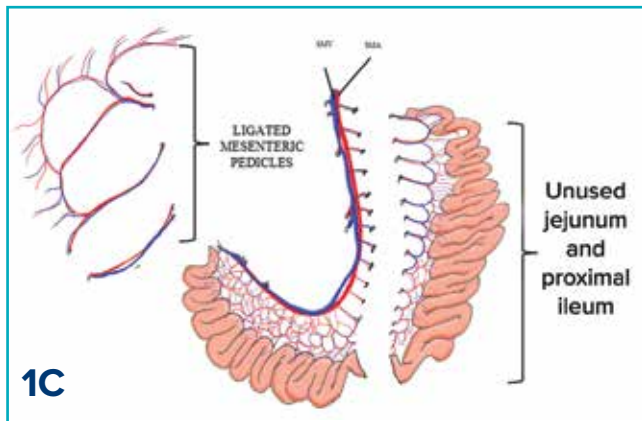


Figure 1A–C: Deceased donor intestinal graft before reduction.

Abbreviations: SMA: Superior Mesenteric Artery; SMV: Superior Mesenteric Vein.

Two hundred centimetres of terminal ileum were measured, and the mesentery was divided carefully by ligating the branches of the vessels not supplying the graft on either side, with the apex at the looped mesenteric vessels (Figure 2).

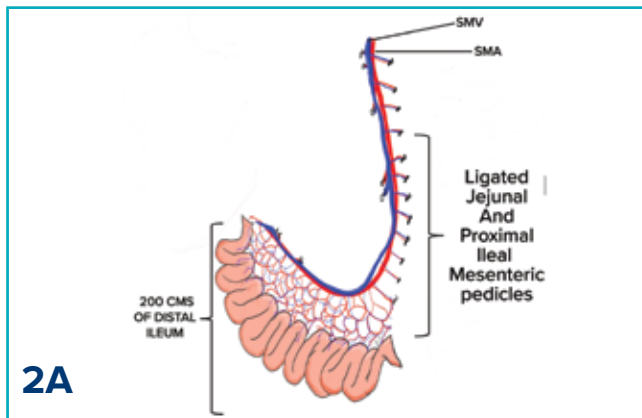


Figure 2A and B: In-situ reduced deceased donor intestinal graft after ligating the mesenteric vessels.

Abbreviations: SMA: Superior Mesenteric Artery; SMV: Superior Mesenteric Vein.

The lymphatics of the ileal mesentery were preserved to ensure maintenance of the lymphatic drainage. The proximal end of the bowel was marked using a Prolene stitch for later identification at the bench. The distal SMA and SMV were clamped and divided prior to cross-clamp to retrieve the graft, which was perfused immediately with cold University of Wisconsin (UW) solution on the back table, as is done in the case of a living donor intestine graft. Retrieval of other organs, including heart, lungs, liver, and kidneys, proceeded as planned without affecting intestinal procurement. The operative duration for intestinal retrieval was 90 minutes. The donor tolerated the procedure well, with a pulse rate of 86/min, blood pressure of 130/80 mmHg, maintained on nor-adrenaline infusion at 0.08 mcg/kg/min, and arterial blood gas analysis showing lactate of 2 mmol/L. The graft was packed in a sterile container and shifted to the base hospital (Figure 3).

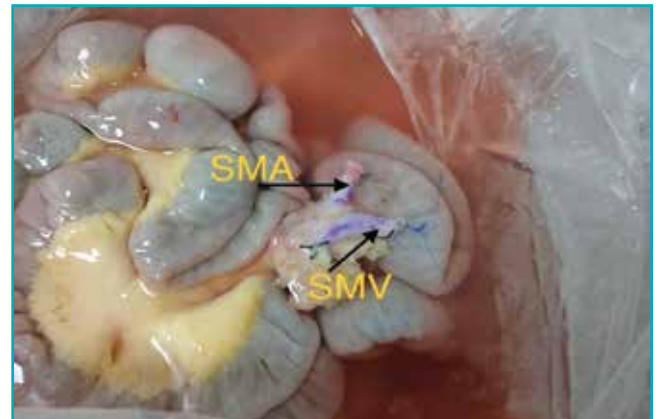


Figure 3: Benchling: Superior mesenteric artery (SMA) and superior mesenteric vein (SMV) are marked for orientation.

Recipient surgery

In the recipient, the abdomen was explored. The infrarenal aorta and inferior vena cava (IVC) were exposed (Figure 4).



Figure 4: Recipient bed where the aorta and inferior vena cava (IVC) is looped.

Vascular conduits using the iliac artery and vein were used on the aorta and IVC. The graft was transplanted by anastomosing the SMA and SMV to the vascular conduits (Figure 5).



Figure 5: Implantation of graft superior mesenteric artery (SMA) and superior mesenteric vein (SMV) into recipient aorta and inferior vena cava, respectively.

The bowel was well perfused, and the proximal and distal bowel anastomoses were performed, and a loop ileostomy was created proximal to the distal anastomosis. The mesenteric edges were sutured retroperitoneally to secure the graft and prevent rotation of the vascular pedicle. As the lymphatic drainage of the graft was kept intact up to the edge of the graft mesentery, spontaneous collateral formation with native retroperitoneal lymphatics was expected post-transplantation. Abdominal closure was completed immediately, with peak ventilator pressures unchanged following closure. The patient was extubated and shifted to the intensive care unit (ICU).

Postoperative course

Standard triple immunosuppression comprising tacrolimus, mycophenolate, and steroids was administered. The stoma began functioning on postoperative day (POD) 3, after which oral feeds were introduced progressively as per tolerance. The post-operative course was complicated by an anastomotic bleed on POD 7, due to dual anticoagulation (low molecular weight heparin [LMWH] and Ecosprin), which resolved by conservative management. Weekly protocol biopsies showed no rejection. Complete enteral autonomy was achieved on POD 18, after which the patient was discharged with stable graft function. Regular follow-up for 3 months was uneventful. The patient continues to be at home with stable graft function. Recipients of other organs were also stable at discharge.

Discussion

Small intestine transplantation remains a complex but definitive treatment for patients with irreversible intestinal failure, particularly in settings where PN services are limited or ineffective. One of the most critical technical challenges in this procedure is achieving size compatibility between the donor organ and the recipient's abdominal domain. This becomes particularly relevant in smaller adult or paediatric recipients, where transplantation of a full-sized intestinal graft from a standard adult donor can result in abdominal compartment syndrome, compromised graft perfusion, and even loss of the graft.

Traditionally, to address size mismatch, options include the use of prosthetic meshes for abdominal wall closure or vascularised composite grafts such as the rectus abdominis muscle. While these techniques can enable closure, they carry significant risks, including mesh infection, hernia formation, increased operative time, and potential for additional graft-related complications such as rejection of the vascularised flap.^{8,9}

An alternative and increasingly attractive approach is graft size reduction. Prior studies, including those by Heaton *et al.*, have described ex-situ reduction methods, where the small bowel is tailored during the back-table preparation by resecting a jejunal segment.¹⁰ However, ex-situ techniques may carry risks of inadvertent vascular or lymphatic injury, increased cold ischaemia time, and unanticipated bleeding during reperfusion.

In this case, we describe a different in-situ reduction technique, modeled on principles of living donor intestinal transplantation, as described by Beneditti *et al.*⁷ The familiarity of the transplant team with living donor procedures allowed for precise vascular ligation under direct vision in a warm setting, ensuring preservation of critical vasculature and lymphatic drainage. Key advantages of this method include:

- Controlled reduction of the graft tailored to the recipient's abdominal capacity
- Early procurement of the intestinal graft without interfering with the retrieval of other abdominal organs
- Reduction of back-table benching time, thereby shortening cold ischaemia and improving graft perfusion post-revascularisation
- Preservation of mesenteric lymphatics, facilitating spontaneous lymphatic drainage and reducing the risk of postoperative chyle leak

The patient had already lost substantial body mass and experienced repeated sepsis and central venous access complications. The in-situ reduction approach provided a critical solution in an otherwise high-risk scenario,

permitting primary abdominal closure and excellent graft function. The patient achieved full enteral autonomy by POD 18 and has maintained stable graft function without signs of rejection.

Conclusion

To the best of our knowledge, this is the first reported case in the literature of an in-situ reduction of a deceased donor small intestinal graft. The success of this case highlights the technique's feasibility, safety, and effectiveness. This innovative strategy could substantially expand the donor pool by making larger adult donor grafts usable for smaller recipients, particularly in resource-limited settings like India, where paediatric or size-matched donors are scarce. Additionally, this case demonstrates that the technique can be done without a significant impact on the procurement of other organs.

Gaurav Chaubal, Hunaid Hatimi, Aditya Nanavati, Amith Pakkala, Deepti Ramachandra, Amith Sreekanth, Harshit Chakshota, Premal Narkhede, Blossom D'souza, Pallavi R Kumar, Samir Shah, Uday Sanglodkar, Alisha Chaubal, Hardik Shah, Tejas Joshi, Abdul S Ansari, Tejaswini Ranade, Radhika Ruhatiya, Prateek Gupta, Saranya Narayanan, Uttkarsha Nikale, Wasim Khot. Novel Technique of In-Situ Reduction of a Deceased Donor Small Intestine Graft to Improve Access in Donor–Recipient Mismatch. *MMJ*. 2025, September. Vol 2 (3).

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Abbreviations

TPN: Total parenteral nutrition

BMI: Body mass index

DDIT: Deceased donor intestinal transplant

LDIT: Living donor intestinal transplant

SMA: Superior mesenteric artery

SMV: Superior mesenteric vein

IVC: Inferior vena cava

DJ: Duodeno-jejunal

UW: University of wisconsin

LMWH: Low molecular weight heparin

POD: Post-operative day

A Rare Triad: Chikungunya-Associated Myocarditis and Guillain–Barré Syndrome — A Case Report

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Abstract:

Chikungunya is a mosquito-borne viral disease caused by the chikungunya virus, typically presenting with a sudden onset of fever and severe joint pain. While the disease generally follows a benign course, it can lead to severe complications like myocarditis, encephalitis, and Guillain–Barré syndrome (GBS). We report the case of a 53-year-old male with a history of hypertension and diabetes mellitus, who was recently diagnosed with chikungunya infection. He presented with shortness of breath and fever and was subsequently diagnosed with chikungunya-associated myocarditis. During his hospital stay, he developed GBS. He was managed with corticosteroids, diuretics, intravenous immunoglobulin (IVIG), and supportive care. This case highlights the rare but severe neurological and cardiac complications that may arise in the course of chikungunya infection.

Key words: Chikungunya, Myocarditis, Guillain–Barré Syndrome (GBS), Viral Complications, Case Report.

Introduction

Chikungunya is a mosquito-borne viral disease caused by the chikungunya virus (CHIKV), a ribonucleic acid (RNA) virus belonging to the *Alphavirus* genus of the *Togaviridae* family. It is primarily transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes, which can also transmit dengue and Zika viruses.¹

The incubation period ranges from 2 to 12 days, with symptom onset typically occurring between 4 and 8 days post-infection. The disease is characterised by an abrupt onset of fever and severe joint pain, which may persist for weeks to months.¹

Although most cases are self-limiting, chikungunya can lead to serious complications involving the eyes, heart, and nervous system. Neurological manifestations include Guillain–Barré syndrome (GBS),

acute disseminated encephalomyelitis (ADEM), and oculomotor nerve palsy. Cardiac involvement, such as myocarditis, has also been reported.^{2–4}

This case report presents a rare and severe manifestation of chikungunya infection involving both myocarditis and GBS in a single patient.^{3,4}

Case Report

A 53-year-old male with a history of hypertension, diabetes mellitus, and obstructive sleep apnoea presented to the Emergency Department of Max Super Speciality Hospital, Nagpur, with complaints of progressive shortness of breath and fever for one day. He tested positive for CHIKV via reverse transcriptase–polymerase chain reaction (RT–PCR) (Figure 1).

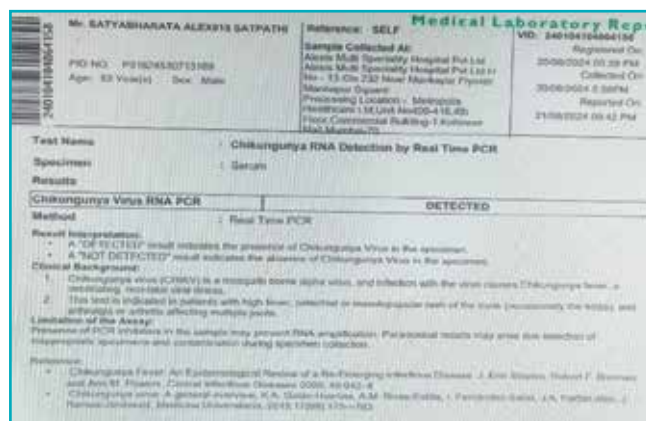


Figure 1: Chikungunya virus ribonucleic acid (RNA) reverse transcriptase–polymerase chain reaction (RT–PCR) report showing virus detected in serum.

On examination, the patient was tachycardic with a heart rate of 116 beats per minute (bpm), tachypnoeic with a respiratory rate of 36 breaths per minute, and dyspnoeic with an oxygen saturation of 92% on room air. Blood pressure was 140/80 mmHg. Laboratory investigations revealed a haemoglobin level of 12.6 g/dL, total leucocyte count of 10,300/mm³, and platelet count of 1.66 lakh/mm³. Inflammatory markers were significantly elevated, with a C-reactive protein (CRP) level of 178.2 mg/L and ferritin at 1045.8 ng/mL. Cardiac markers showed elevated levels, with high-sensitivity troponin I (Trop-I hs) at 314.22 pg/mL and N-terminal pro-B-type natriuretic peptide (NT-proBNP) at 1602 pg/mL. D-dimer was markedly elevated at 2380 ng/mL. Serum creatinine was 1.4 mg/dL, while liver enzymes were within normal limits, with serum glutamic-oxaloacetic transaminase (SGOT)/Serum glutamic pyruvic transaminase (SGPT) levels of 32/11 U/L.

Pulmonary embolism was suspected due to elevated D-dimer and tachycardia; however, computed tomography (CT) pulmonary angiography ruled out embolism. The patient was started on antiplatelets, anticoagulants, statins, diuretics, bronchodilators, and nasal oxygen. Despite treatment, respiratory distress persisted. CT of the chest and abdomen revealed trace bilateral pleural effusion and multiple large ground-glass opacities (Figure 2).



Figure 2: Computed tomography (CT) thorax showing ground-glass opacities and trace bilateral pleural effusion (right side) compared to previous scan (left side).

Differential diagnosis included:

- Pulmonary oedema secondary to acute coronary syndrome
- Viral pneumonia

A flu panel was sent, and oseltamivir was initiated. The patient developed atrial fibrillation with a pulse rate of 150 bpm, followed by desaturation. He was started on amiodarone and non-invasive ventilation. Injectable steroids were added due to worsening respiratory distress. Viral serology was negative.

Mechanical ventilation was initiated. Post-intubation CT of the thorax showed multiple large bilateral ground-glass opacities and pleural effusion, suggestive of pulmonary oedema. Viral myocarditis was suspected, and serum ferritin was elevated at 1045.8 ng/mL. Intravenous methylprednisolone and a diuretic infusion were started. The patient improved and was weaned off the ventilator.

Following transfer to the ward, he developed lower limb weakness and was unable to lift his legs. Deep tendon reflexes were absent. Electroencephalography (EEG) and nerve conduction studies confirmed acute demyelinating inflammatory polyradiculopathy, consistent with GBS. He was treated with intravenous immunoglobulin (IVIg) for 5 days with clinical improvement. The remainder of his hospital stay was uneventful except for intermittent low-grade fever.

Discussion

CHIKV is known for its classical presentation of fever and arthralgia, but rare complications such as myocarditis and GBS can occur.^{1,2} Myocarditis may result from direct viral invasion or immune-mediated injury, while GBS is thought to be triggered by post-infectious autoimmune mechanisms.^{3,4}

This case is unique due to the simultaneous occurrence of two serious complications — myocarditis and GBS — in a single patient.^{3,4} Early recognition and multidisciplinary management were crucial for recovery. The use of corticosteroids, IVIG, and supportive care proved effective.^{3,5}

Conclusion

This case highlights the importance of considering rare complications in chikungunya infection. Clinicians should maintain a high index of suspicion for myocarditis and GBS in patients presenting with respiratory distress and neurological symptoms.²⁻⁵ Timely diagnosis and appropriate treatment can significantly improve outcomes.

Nitin Wadaskar, Hitisha Agrawal. A Rare Triad: Chikungunya-Associated Myocarditis and Guillain–Barré Syndrome — A Case Report. *MMJ*. 2025, September. Vol 2 (3).

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Atypical Presentation of Classical Hodgkin Lymphoma Mimicking Disseminated Infection or Metastatic Disease in a Young Female

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Abstract:

Classical Hodgkin lymphoma (cHL) typically presents with localised lymphadenopathy with contiguous spread. Rarely, it can mimic infections or disseminated malignancies, leading to diagnostic delays. We report a case of a 25-year-old female with extensive systemic involvement and massive ascites resembling disseminated tuberculosis or metastatic disease. Diagnosis was confirmed via lymph node biopsy and immunohistochemistry. The patient responded well to combined immunotherapy and chemotherapy using nivolumab with doxorubicin, vinblastine, and dacarbazine (AVD). This case underscores the importance of considering cHL in the differential diagnosis of systemic symptoms in young adults and highlights the evolving role of immunotherapy in frontline treatment.

Key words: Hodgkin, Lymphadenopathy, Immunotherapy.

Introduction

Classical Hodgkin lymphoma (cHL) is a B-cell lymphoid malignancy characterised by the presence of Hodgkin and Reed-Sternberg (HRS) cells within a reactive cellular milieu. It shows a bimodal age distribution and is most commonly observed in adolescents and young adults. While most cases present with painless peripheral lymphadenopathy, atypical, disseminated presentations complicating diagnosis are rare but clinically significant.^{1,2}

Case Report

A 25-year-old female student presented with intermittent fever and unintentional weight loss over six months, progressing to abdominal distension and cervical/axillary swelling in the last two months. The initial complete blood

count (CBC) was within normal limits. Empirical antibiotic therapy provided only transient relief, and symptoms recurred, prompting further evaluation.

Investigations

Her haemogram revealed haemoglobin 7.8 g/dL, white cell count: 55,400/ μ L with neutrophilic leucocytosis (Figure 1), platelets 203,000/ μ L. Peripheral blood smear demonstrated macrocytic anaemia, and elevated lactate dehydrogenase (LDH) 314.7 U/L. She also had prolonged prothrombin time and activated partial thromboplastin time (APTT). Abdominal ultrasound (USG) revealed hepatosplenomegaly and abdominal lymphadenopathy. Whole-body positron emission tomography (PET)-computed tomography (CT) scan revealed fluorodeoxyglucose (FDG)-avid lymphadenopathy in the cervical, mediastinal, abdominal, and pelvic regions; FDG-avid lesions in the liver, spleen, and right lung nodule; bilateral pleural effusions; and gross ascites (Figure 2).

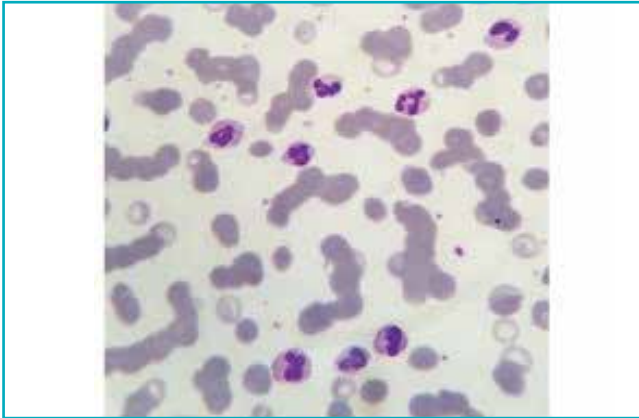


Figure 1: Peripheral blood smear showing neutrophilic leucocytosis with left shift and toxic granulation, indicative of systemic inflammatory response.

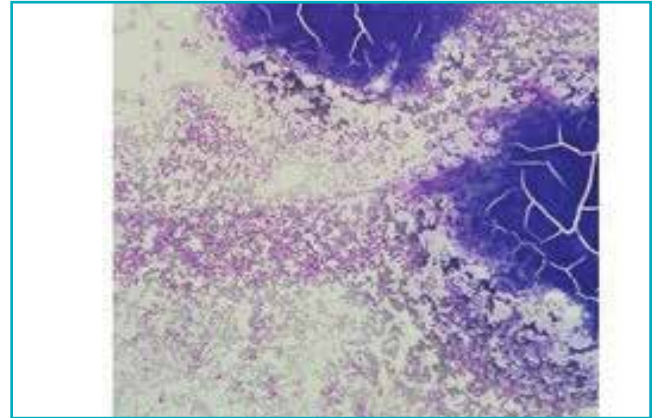


Figure 3: Bone marrow aspiration smear (low power view) showing increased cellularity with areas of haemophagocytosis.

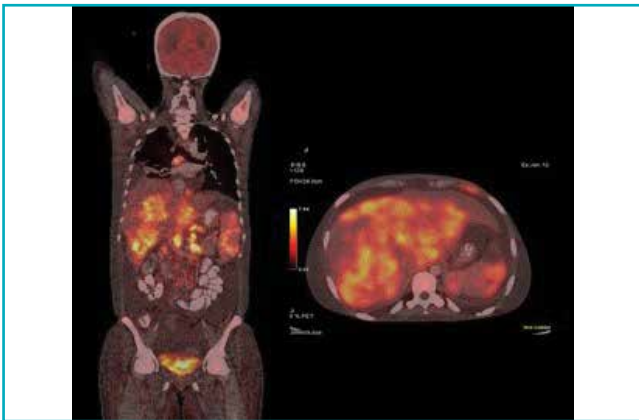


Figure 2: Baseline positron emission tomography (PET)–computed tomography (CT) scan showing widespread fluorodeoxyglucose (FDG)-avid lymphadenopathy and visceral involvement.

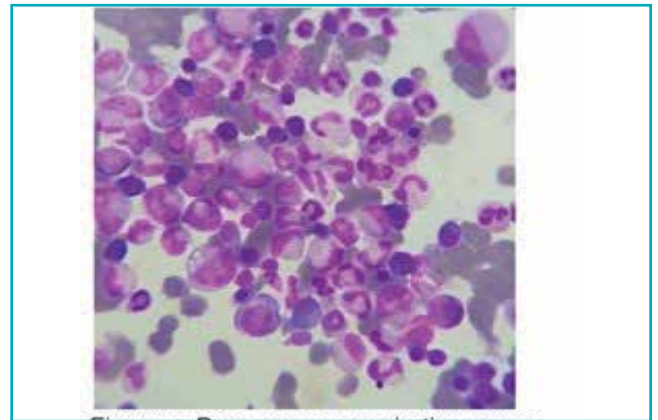


Figure 4: Bone marrow aspiration smear (high power view) demonstrating reactive features and scattered mononuclear cells.

The differential diagnoses included disseminated tuberculosis, haematolymphoid malignancy (lymphoma, leukaemia), fungal infection, solid tumours (germ cell tumour, carcinoma of unknown primary), or rare conditions such as haemophagocytic lymphohistiocytosis (HLH) or Castleman disease. Excisional biopsy of supraclavicular lymph node with immunohistochemistry revealed HRS cells positive for cluster of differentiation 30 (CD30) and cluster of differentiation 15 (CD15), weakly positive for paired box protein 5 (PAX5), multiple myeloma oncogene 1 (MUM1) positive, and negative for cluster of differentiation 3 (CD3), Cluster of differentiation 20 (CD20), Epstein–Barr virus (EBV). The final diagnosis was nodular sclerosing cHL. Bone marrow aspiration and biopsy showed reactive changes with haemophagocytosis. Echocardiography demonstrated an ejection fraction of 40%–45% with mild pericardial effusion (Figures 3–5).

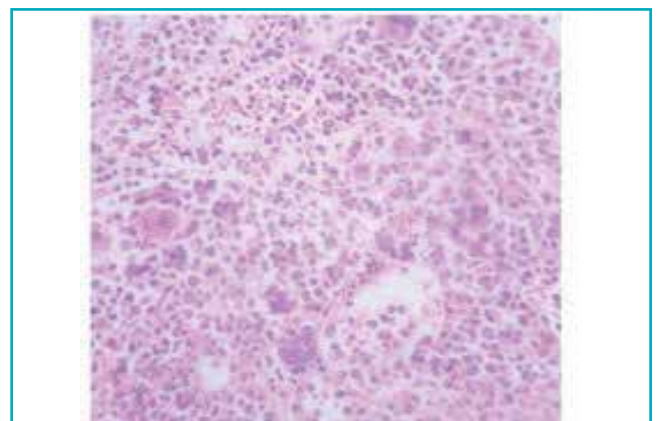


Figure 5: Bone marrow biopsy (Haematoxylin and Eosin stain) displaying increased cellularity with reactive changes and haemophagocytosis.

Treatment

The patient was started on immunochemotherapy using nivolumab with doxorubicin, vinblastine, and dacarbazine (AVD). Interim PET–CT, after 3 cycles, showed metabolic resolution of lymphadenopathy, liver and spleen lesions, and reduction of pleural effusion and ascites (Figure 6).



Figure 6: Interim positron emission tomography (PET)–computed tomography (CT) after 3 cycles of nivolumab with doxorubicin, vinblastine, and dacarbazine (AVD) showing Deauville Score 3 and significant metabolic response.

Discussion

cHL is characterised by its unique tumour microenvironment, where few HRS cells orchestrate a rich inflammatory infiltrate.^{1,4} This case highlights the disease's potential for widespread organ involvement and clinical masquerade. The patient, presenting with persistent abdominal distension, was initially treated for disseminated tuberculosis. Histologically, the nodular sclerosis subtype — characterised by lacunar variant HRS cells and collagen bands — is most prevalent in young females.^{2,3,5} CD30 and CD15 positivity, along with weak PAX5 expression and loss of B-cell markers, are diagnostic immunophenotypic hallmarks.³

Checkpoint blockade using programmed cell death protein 1 (PD-1) inhibitors like nivolumab has revolutionised the management of relapsed/refractory cHL, and recent trials now demonstrate efficacy in first-line settings.^{1,4,6} This case supports these findings, showing early metabolic response and symptom relief. The patient has completed six cycles of chemo-immunotherapy and returned to her usual routine.

Conclusion

cHL can rarely present with features mimicking disseminated infections or malignancies. High clinical suspicion, histological confirmation, and evolving therapies like immune checkpoint inhibitors are critical to achieve optimal outcomes.

Viral Jain, Sanjeev Kumar Sharma, Anamika Bakliwal, Neelkumar Patel. Atypical Presentation of Classical Hodgkin Lymphoma Mimicking Disseminated Infection or Metastatic Disease in a Young Female. MMJ.

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THE IMAGES

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Art and Artistry of Three-Dimensional Nasal Reconstruction

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Abstract:

The nose is not only an important part of human appearance but also performs important functions, including olfaction, humidification, and breathing. The history of nasal reconstruction dates back to 600 BC (Sushruta, India), and the Indian method using a forehead flap remains to this day the criterion standard for large defects. The art of nasal reconstruction has travelled across many countries and continents and benefited from their surgical contributions. An understanding of nasal subunits, arterial anatomy, and knowledge of skin zones is critical in planning any reconstruction. A stepwise logical planning process helps in deciding the right choices for reconstruction. It is vital to recreate all three layers of the nose, namely skin, skeletal support, and nasal lining. Local nose and facial flaps form the backbone of nasal reconstruction. Skeletal support is vital to providing shape and stability to any nasal construct. Nasal lining restoration is important for maintaining the patency of the airways. Patience, persistence, and the use of reliable techniques can make nasal reconstruction a predictable and rewarding experience for every plastic surgeon.

Key words: Nasal Reconstruction, Forehead Flap, Bilobed Flap, Dorsal Nasal Flap, Nasal Lining Flaps, Nasal Subunits, Nasal Skin Zones, Nasal Anatomy.

Introduction

The nose is hugely relevant to us in both form and function. Physiologically it helps in olfaction, along with the humidification and filtration of inhaled air by forming an entrance to the respiratory passage.

It is of immense emotional value to humans as well. It is a known fact that although we are constantly looking at our nose, our brain always chooses to ignore it. So, you may think that if human beings were not able to see themselves in the mirror, they would never have become conscious of the way their nose looks! This, however, would not have stopped others from seeing it.

It might be rare for anyone to get compliments for a beautifully proportionate nose, but it is almost impossible for an onlooker to keep their focus away from a disfigured or abnormal nose. Such a nose can make the owner

suffer from self-consciousness about appearance and damage their confidence and self-esteem.¹

Tissue loss of soft or skeletal elements of the nose can result from trauma, animal bites, human bites, infective necrosis, or carcinoma. The objective of this article is to simplify the reconstructive approaches to such nasal defects and discuss the nuances of various surgical techniques to achieve a 'near-normal' nose.

History of Nasal Reconstruction

While the eyes are often regarded as a defining feature of the face, the nose remains equally important as the most prominent and projecting structure.

It is thus no wonder that the nose has been traditionally equated with one's honour. Across cultures, history is full of descriptions of nasal amputation being used to disgrace or punish offenders. In India, this led to the development of the Indian method of nasal reconstruction using the forehead flap, believed to be the first in the world. Even today, this remains the foremost method of nasal reconstruction for tissue loss.

It is, in general, attributed to the revered ancient Indian surgeon Sushruta (600 BC). The method described in his treatise 'Sushruta Samhita' used a cheek flap, modified perhaps by an unknown disciple to the forehead flap.

In 1793, two British surgeons — Thomas Cruso and James Findlay — witnessed restorative surgery of the nose of a bullock-cart driver named Cowasjee and his four associates by the Indian potter-surgeons using the ancient 'Indian forehead flap' in Poona (Pune). They first published this in 'The Madras Gazette' in 1793, and later the same description was published in 'The Gentleman's Magazine', describing the technique step by step. This

caught the attention of British army surgeon J.C. Carpue, who — after practicing on cadavers first — used it on live subjects in 1889.

Important milestones of nasal reconstruction can be listed in the following interesting chronological order.²⁻⁴

600 BC

- **Indian Method:** The first documented evidence of nasal reconstruction comes from India in the Ayurvedic surgical treatise 'Sushruta Samhita' (Sanskrit: Suśrutasaṃhitā), wherein cheek or forehead skin was used for nasal reconstruction. The author Sushruta is rightly called the 'Father of Plastic Surgery'. He belonged to the potter clan of Varanasi, on the banks of the holy River Ganges. He taught surgical skills to his students on various simulation models like vegetables (such as watermelon, gourd, cucumber) for incisions (Figure 1).

Sushruta lived 150 years before Hippocrates in Greece and vividly described a variety of surgical techniques, including the first nasal reconstruction, in his treatise Sushruta Samhita (c. 600 BCE).



Figure 1: Artistic rendition of Sushruta performing nasal reconstruction surgery in 600 BCE (digital art by the authors based on images in the public domain).

1442 AD

- **Italian Modification of Indian Method:** It is widely acknowledged that plastic surgery in Europe as practiced in the medieval ages, was a direct descendant of classical Indian techniques. Italian surgeon Branca de'Branca introduced the Indian method (which came from India, probably via Arabia) of nasal reconstruction in Italy in 1442.
- He later modified this with delayed flaps from the arm and passed on this knowledge to his son, Antonio. This was the Italian Method.
- **Italian Method:** 100 years later, Tagliacozzi modified and popularised the Italian method by transferring an arm flap to the nose in 6 stages in 4 weeks (Figure 2A and B).



Figure 2: A. The second stage of nasal reconstruction with the 'Tagliacozzi' Italian method is shown in this figure. In the first stage, a bi-pedicled vertical flap was raised from the medial arm, and the proximal end was detached after 6 weeks, then attached to the nasal defect for reconstruction, B. The Tagliacozzi flap was detached after another 6 weeks in the third stage to achieve the final shape of the nose.

1793 AD

- 'The Madras Gazette' published the Indian forehead technique after witnessing the procedure in Pune, India. A year later, the same technique was published in 'The Gentleman's Magazine' of London by a British engraver Barak Longmate ('B.L.') while he was visiting India. He had observed such reconstruction on a bullock-cart driver named Cowasjee. This famous letter inspired the English surgeon Joseph Carpue (1764–1846) to practice the Indian method of nasal reconstruction, first on cadavers and later on two officers of the British Army.
- It is a lesser-known fact that 100 years before this famous letter, the Venetian adventurer Niccolao Manucci (1639–1717) had already witnessed and documented the Indian method of nasal reconstruction in his memoirs describing the history of the Mughal Empire (Storia do Mogor) in 1690 AD.

1818 AD

- **German Method:** This was described by German surgeon Karl von Gräfe, wherein a free skin graft from the arm was used instead of a delayed flap.

1834 AD

- **French Method:** This method used a trilobed flap from adjoining tissues and was introduced by the French surgeon Pierre Auguste Labat.

1845 AD

- German surgeon Johann Friedrich Dieffenbach described rhinoplasty in 'Operative Chirurgie'. He also described secondary revision to enhance outcomes.

1887 AD

- John Roe, an American otolaryngologist, first described aesthetic rhinoplasty techniques.

1889 AD

- Indian surgeon Tribhovandas Motichand Shah published his record-breaking 300 cases of forehead flap for nasal reconstruction in 'The Indian Medical Gazette'. This was a year before the British Surgeon J.C. Carpue had performed his first live forehead flap.

1913 AD

- Harold Delf Gillies, during World War I, recommended the forehead flap for nasal reconstruction and described it in his book 'Plastic Surgery of the Face'.

1946 AD

- Kazanjian popularised the median forehead flap in the United States. Several modifications were contributed by many to prevent external nasal deformities due to contracture. Attention was also given to the intranasal lining and its significance.

1986 AD

- Burget and Menick refined the art of nasal reconstruction with the paramedian forehead flap and introduced the concept of nasal lining flaps as the 'fourth dimension'. Their seminal articles on this subject should be read by every enthusiastic nasal reconstruction surgeon.

computer-aided manufacturing (CAM) technique have become an aid for planning and are replacing the clay models that were used previously. Bioengineered tissues are being experimented upon and tested for minimal donor site morbidity.

Relevant Clinical Anatomy**Subunits**

The nose has a complex topographic shape that can be easily divided into nine subunits based on the contour lines and skin type. The aesthetic nasal subunits were first illustrated by González-Ulloa in 1957, but the 'subunit principle' for nasal reconstruction was first described by Burget and Menick in 1985.⁵ Its subunits are divided into three paired and three unpaired structures. The unpaired subunits are the dorsum, columella, and nasal tip. The nasal sidewall, soft triangle, and ala comprise the paired subunits. The nine aesthetic nasal subunits are shown in Figure 3.

Future of nasal reconstruction

- Present-day three-dimensional (3D) reconstruction models with computer-aided design (CAD)/

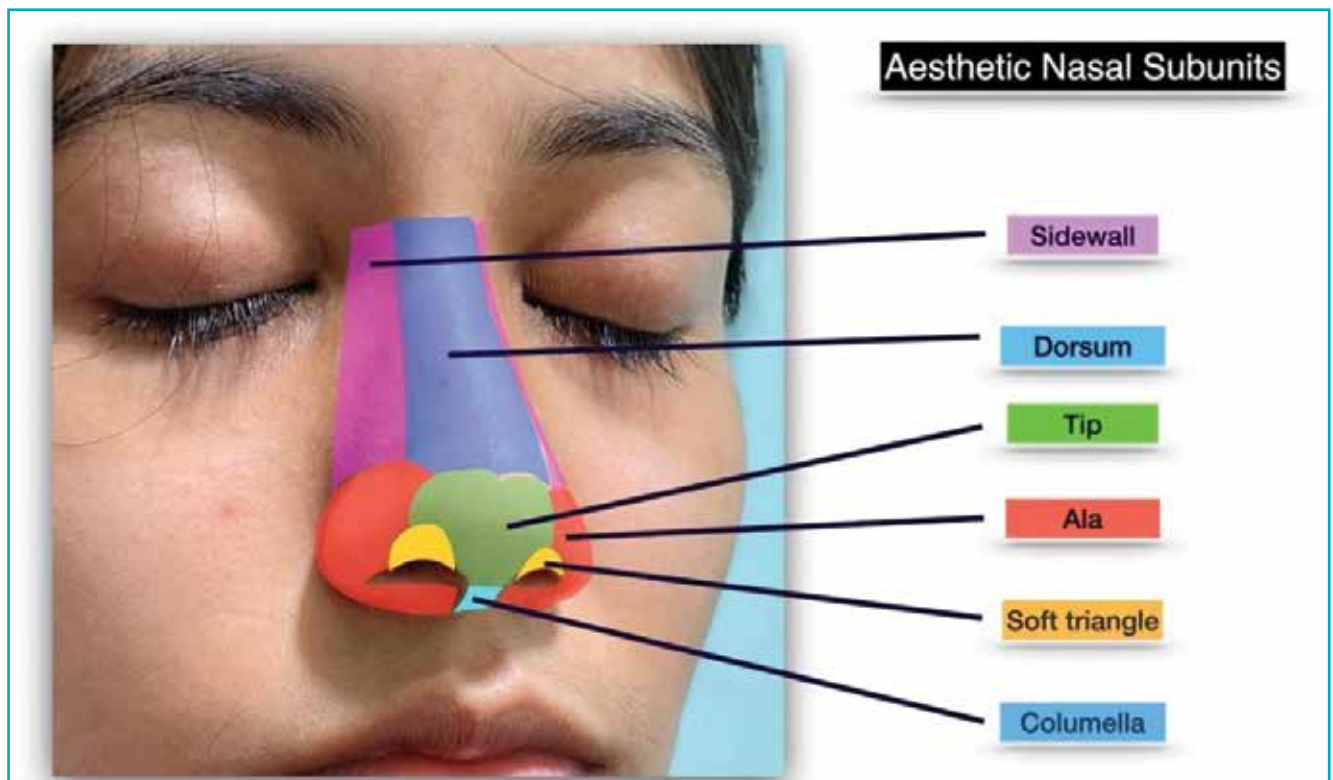


Figure 3: Nine topographic aesthetic subunits of the nose based on contour lines and skin zones of the nose.

Skin zones

The quality and texture of skin can be used to describe three distinct zones of the surface of the nose. This is useful in planning reconstruction as skin pliability is a deciding factor in the design of local flaps. Figure 4

illustrates the three skin zones of the nose and Table 1 describes the three zones based on skin type and their relevance.

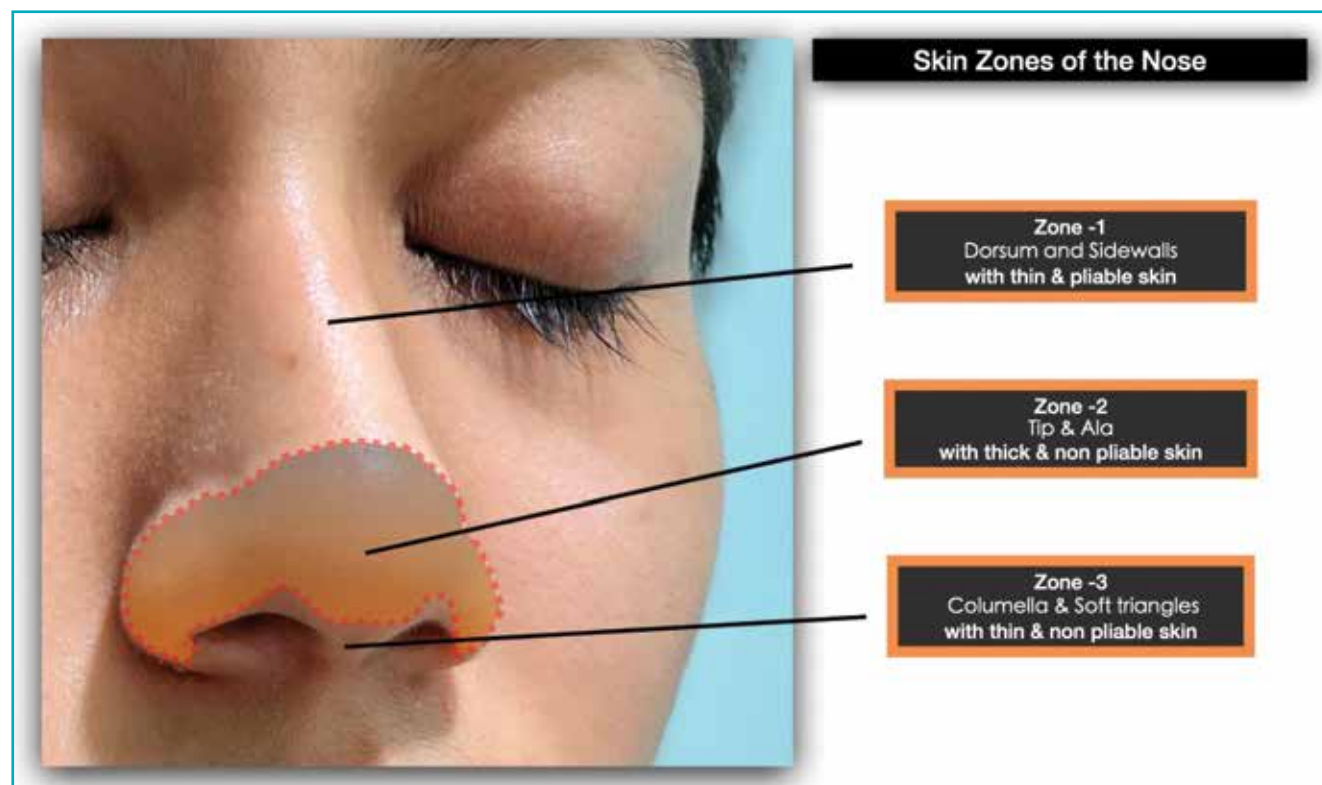


Figure 4: Three skin zones of the nose based on thickness and skin pliability.

Zone 1 — Dorsum and Sidewall
Mobile pinchable smooth skin
Full thickness skin grafts or single lobe flap can be effective
Zone 2 — Tip and Ala
Thick, sebaceous, non-pliable skin
Usually needs bilobed or complex design local flap
Zone 3 — Columella and Soft triangles
Thin but non-pliable skin
Difficult to reconstruct
Avoid undermining and reconstruct with the tip as a subunit or use small local flaps or composite grafts from the anterior helical rim of the ear

Table 1: Characteristics and relevance of the three skin zones of the nose.

The choice of reconstruction thus depends on the nature of the tissue to be replaced. The structural support is given by bone cranially and cartilage caudally. The upper lateral part is supported by the nasal bone and the frontal process of the maxilla, followed by upper and lower lateral cartilage inferiorly. The midline is held by a bony and cartilaginous septum constituted by the perpendicular plate of the ethmoid and vomer, and quadrangular cartilage, respectively. The ala and tip are supported by lower lateral cartilages, which are folded on themselves twice at the medial and the lateral genu, thus dividing it into lateral, middle, and medial crus. The lining is formed by the mucosa.

Blood and nerve supply of the nose

The blood supply and its anatomy help in identifying the potential donor sites to raise local flaps to cover various nasal defects. The venous drainage is largely through the

anterior facial and ophthalmic veins for the external nose. The septum has a rich plexus of blood vessels formed by branches of the ophthalmic artery (anterior and posterior

ethmoidal arteries), maxillary artery (sphenopalatine branches), and facial artery (superior labial artery). The arterial supply of the nose is illustrated in Figure 5.

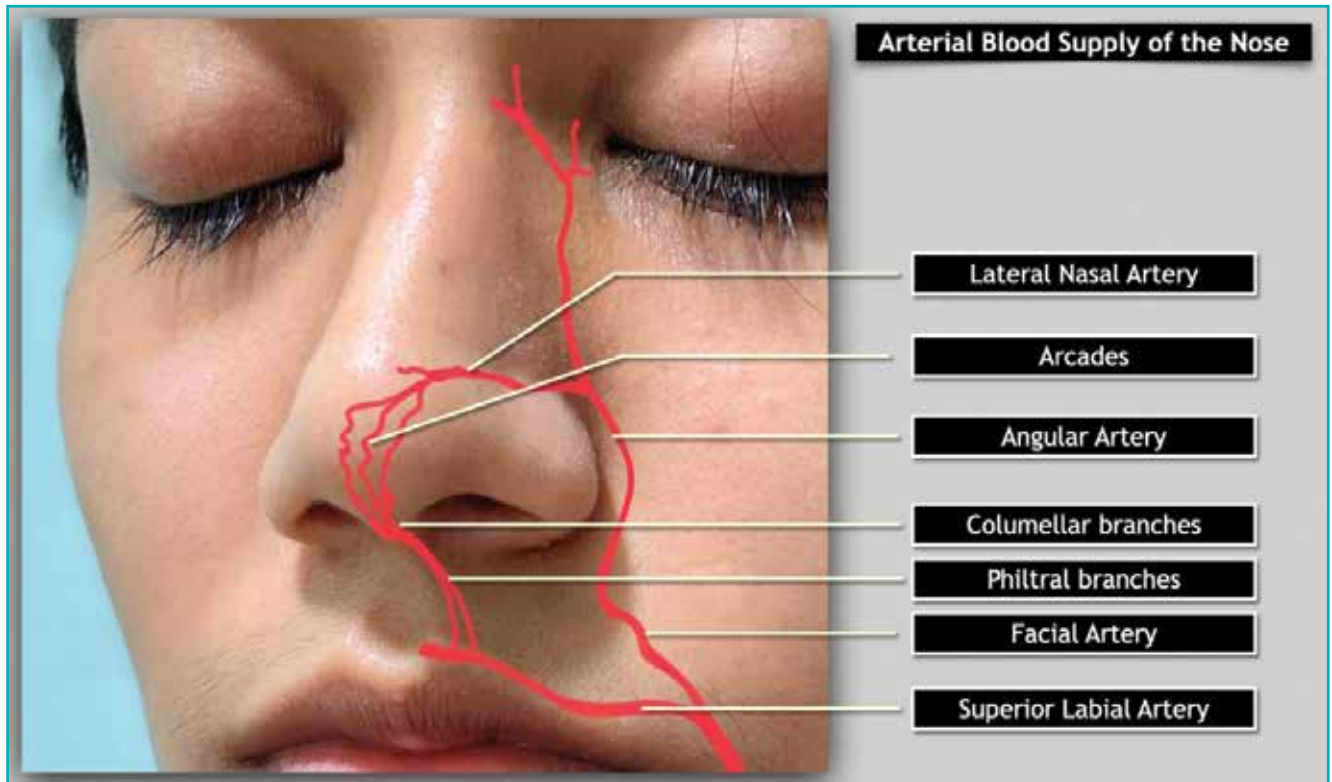


Figure 5: Arterial blood supply of the nose.

The nerve supply of the nose is via the nasociliary and infratrochlear branches of the ophthalmic nerve and the infraorbital branches of the maxillary nerve. The septum is innervated by the nasociliary branch of the ophthalmic nerve, the alveolar branch of the maxillary nerve, the nerve of the pterygoid canal, and the nasopalatine, anterior palatine, and nasal branches of the sphenopalatine ganglion.

The Stepwise Approach to Nasal Reconstruction

When confronted with the reconstruction of a complex 3D facial feature like the nose, it is best to use a logical planning process, as illustrated in Table 2. The whole process is simplified into four essential steps:

Step 1:

Visualise the 3D defect of the nose and account for the missing layers, namely skin, skeletal support, and mucosal lining. This is important as often different means of reconstruction have to be employed to reconstruct

each layer, e.g., local flap for the skin, cartilage graft for support, and nasal mucosal flap for the inner lining.

Step 2:

Map the defect in terms of the missing subunits. The subunits have been described and illustrated earlier. According to the subunit principle proposed by Burget and Menick for defects with more than 50% of a subunit missing, it was advised to replace the whole subunit by converting the partial defect into a complete subunit defect, provided a suitable method of reconstruction is available.⁵ It is not always advisable to apply this principle of subunit reconstruction fully, and maximum native skin preservation may be advisable in many cases. Exceptions to the classical subunit principle may include the elderly (to keep it simple), children (due to a lack of excess lax skin), very large defects (due to paucity of available tissues), and medically unfit patients (to keep the surgery short and simple). The surgeon should never use a cookie-cutter approach with any of these guidelines and instead use their judgement based on personal knowledge and

experience to customise the most suitable approach. They should also not hesitate to perform staged refinements in flap contour and bulk, as the excellent vascularity of the area allows for repeated elevation and thinning of the flaps. Restoration of nasal contour without sacrificing the whole subunit can yield good results, and subsequent scar treatments with dermabrasion and fractional lasers can further help in the restoration of contour and blending of scar lines.⁶

Step 3:

The timing of nasal reconstruction is very relevant and is dependent on local disease control. Reconstruction should be:

- Immediate if the wound is free of infection and disease (e.g., malignancy)
- Delayed in cases of infection, animal or human bite, incomplete or unconfirmed oncological margins, or poor medical condition, etc.

Step 4:

The final step is the execution step, wherein the selection of the most suitable techniques to reconstruct the nose will logically flow from the information gathered in the first three steps.^{7,8} Assess the local available sites for potential flaps and choose the appropriate donor site depending on the availability of adjacent tissues with a good match. Sometimes the presence of old scars may not allow the raising of a forehead flap due to previous surgeries or injury. For small defects less than 1.5 cm, one usually resorts to local nasal skin flaps only. There may be a combination of techniques involved in the reconstruction of various layers of structures like the lining, cartilaginous or bony framework, and external skin defect, depending on the subunit involved. A defect less than 1.5 cm without cartilage deficiency is considered small. Autologous materials are best for nasal reconstruction whenever possible, as artificial implants and allografts have higher risks of infection.

Stepwise Planning Process for Nose Reconstruction			
STEP 1	STEP 2	STEP 3	STEP 4
Visualise the 3-dimensional defect (3 layers)	Map the aesthetic subunit defect	Time the reconstruction	Choose available donor sites and best technique
• Skin defect • Skeletal defect • Lining defect	• Defect if more than 50% may be better reconstructed as a whole subunit by excising the entire subunit in selected cases • Exceptions are elderly and children, difficult reconstruction, very large defects, medically unfit patients, etc.	• Immediate if wound is free of infection and disease (e.g., malignancy) • Delayed in cases of infection, animal or human bite, incomplete or unconfirmed oncological margins, poor medical condition, etc.	• Assess available local sites • Local nasal single or bilobed flaps • Forehead flap • Meso/nasolabial flap • FTSG (postauricular) • Free flap • Lining flaps • Grafts - Ear cartilage, costal graft or Iliac bone graft • Dermal matrices

Table 2: Stepwise planning of nasal reconstruction.

Abbreviation: Full-Thickness Skin Graft.

Choice of Reconstructive Techniques and Available Options

It is important to remember that the ideal template for reconstruction is the opposite side, which can be mirrored in cases of unilateral defects with the help of simple paper or foil patterns. Nowadays, surgeons are using modern 3D planning and printing technologies, especially in larger defects where the opposite side is not available for mirroring.⁹ Artificial intelligence tools can help in reconstructing a virtual nose, and 3D models may be generated by CAD/CAM technique and printed for intraoperative planning. 3D surface scanning is also helpful in designing a prospective nasal structure suitable for the face and for designing prosthetic models. A 2D template may be generated from this scan, which can be used to design the flap with a calculated slight overcorrection to account for the 'fourth dimension' of healing, contraction, and flap perfusion.

Various common options available for the nasal reconstruction are discussed below in order of increasing complexity:

1. Tissue-engineered dermal matrices

Different artificial dermal substitutes are available in the market, and they can be used conveniently as an off-the-shelf option for small defects up to 1 cm in diameter with good results. If the defect is deep, they can be stacked with a delay of 7–10 days once the first matrix has vascularised. The biggest advantage is the lack of donor site morbidity. They can also be used for pre-lamination of forehead flaps for nasal lining as dermal matrices mucosalise very fast once inside the nose.¹⁰

2. Healing with secondary intention

Wounds that are less than 1 cm in diameter and less than 0.5 cm in depth, located in non-sebaceous areas and natural concavities like alar grooves, heal best by secondary intention. They can be improved further by modalities like laser, platelet-rich plasma, or subcision, etc., a few weeks post-healing.¹¹

3. Primary closure

Midline wounds less than 1 cm with good skin laxity, such as in the elderly, may be closed with simple elliptical excision. Vertical orientation is preferred for

small elliptical excisions and primary closures in the tip and supra-tip areas to avoid alar distortions. The surgeon should not limit the length of the ellipse to shorten the scar, as this may result in the formation of permanent, aesthetically undesirable dog-ear deformities. The dorsal aesthetic lines should be restored whenever possible. The nasal side walls form a normal cleavage line between the cheek and the nose, and linear primary closures in this area yield good results for small defects. Due to the zone of adherence, the base of the nasal side wall can take the tension of the mobile cheek flap with the help of marginal quilting dermal sutures. However, to avoid any unwanted ectropion of the lower lid, the linear closure should be obliquely placed with an upward slant, aiming towards the nasal side.

4. Full-thickness skin graft (FTSG) and split skin grafts

FTSGs can be good choices for simple skin defects of Zone 1 nasal dorsum, lateral walls, and especially for the inner canthal areas, where the flaps would be unacceptably thick. They are not usually a good match for thick Zone 2 areas as they cannot match the thick sebaceous skin, but may still be a simple option in elderly, unfit patients.

Preauricular, post-auricular, supraclavicular area, forehead hairline, and medial arm sites have all been used due to their hairless, smooth texture. FTSGs go through a prolonged phase of healing, can suffer partial take, and often undergo epithelial loss before healing. An FTSG should not be put on denuded cartilage but may take if the perichondrium or periosteum is well preserved. The final colour of these can be variable, especially in coloured skin, as they can suffer from post-inflammatory hyperpigmentation (PIH) and contracture.

Split skin grafts can also be used for nasal skin defects but often leave a depressed contour and are prone to contractures, which may deform the nose in the long term. FTSGs are preferred over split skin grafts for these reasons.

5. Composite grafts

Zone 3 defects of the columella and nasal rim in young patients, particularly children, can be well-suited to reconstruction by composite grafts. These

can be harvested from the anterior helical rim of the ear lobule as part FTSG and part composite graft with the helical cartilage. They can be used for Zone 3 defects for reconstruction of the nostril rim and columellar defects, usually up to 1 cm in width.¹² The graft take is enhanced if a large portion of their 'skin alone' part is in contact with the nasal bed. They often undergo a prolonged healing phase and turn into a black eschar before separating in a few weeks, leaving a well-healed tissue underneath.

Attention to accurate edge-to-edge approximation, good skin-bed contact and avoiding disturbance to the composite graft with a light bolster dressing can increase their take. The success rate is variable, with a higher risk of failure in smokers, the elderly, and in those with uncontrolled medical conditions or large-sized defects.

6. Single lobe flaps

Single lobe flaps are best suited for small skin defects less than 1.5 cm. These are simple subcutaneous random Banner-style or rhomboid flaps. They are best suited for the pliable, thin, superior nose Zone 1 defects.¹³

7. Dorsal nasal flap

The dorsal nasal flap can slide the entire nasal dorsum from the glabella down to the tip like a big vertical pillar with incisions along the dorsal wall aesthetic lines with V-Y design. It can fill in the defects of the tip and dorsal subunits (Figure 6A–C). It includes the nasalis muscle and is elevated in the loose areolar supraperiosteal plane. Various modifications, like the laterally based hatchet glabellar V-Y design can incorporate a Z-plasty superiorly to avoid dog-ear formation. The islanded, skin-only V-Y design is based on the nasalis muscle with bilevel undermining. This flap is capable of easily resurfacing defects upto 2 cm. The main disadvantage is extensive dissection and the resulting long scars.^{14,15}

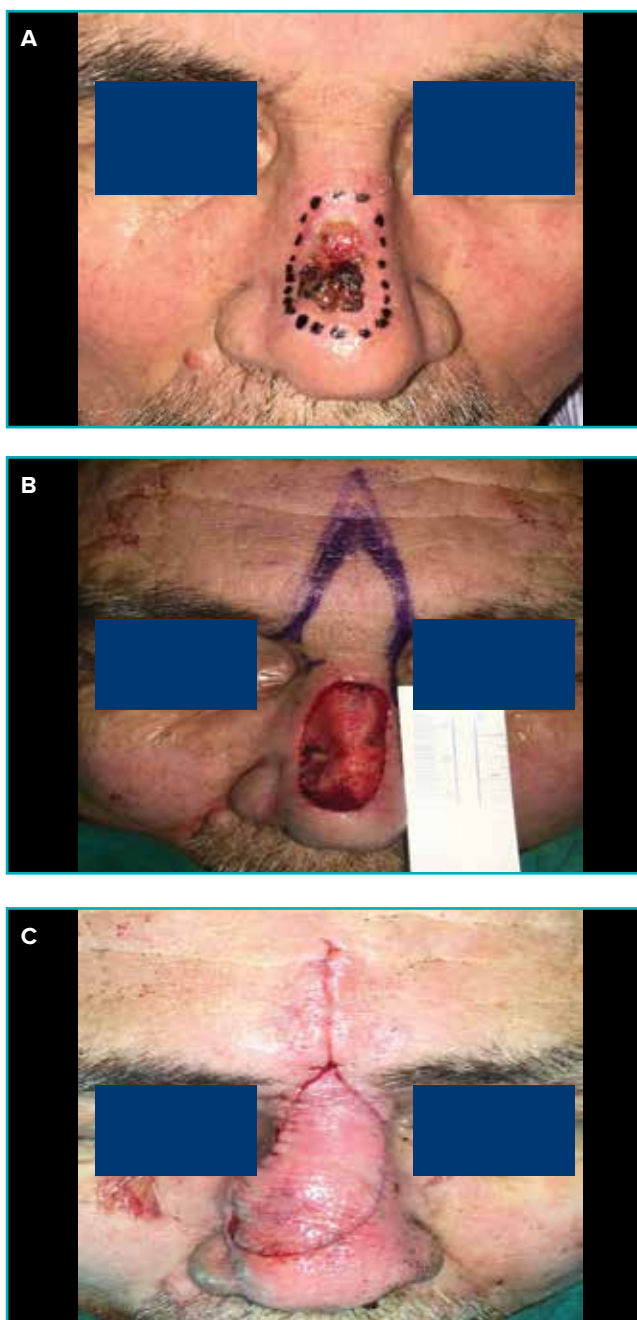


Figure 6: A. Large basal cell carcinoma of the nasal dorsum, B. Wide local excision defect of approximately 3.5 x 2 cm, C. Reconstruction with a sliding V-Y islanded dorsal nasal glabellar flap.

8. Bilobed flap

The bilobed flap is a double transposition flap and an excellent option for Zone 2 thick skin defects of the tip and ala (inferior nose), especially for defects located at least 0.5 cm away from the nostril rim. As the nasal skin in this zone is stiff, inflexible, and adherent, the 'bilobed principle' is applied to transfer skin from the thin, pliable superior nasal area by means of two adjacent flaps.

After the defect is triangulated by excising Burow's triangle, the first lobe flap is transposed from the adjacent thick skin of almost the same size and a contiguous second flap is used from the pinchable flexible superior nose skin, usually of a slightly longer length (to avoid dog-ears) but half the width to fill the space left by the first lobe flap. This efficiently transfers the skin laxity from the superior to the inferior nose in an effective manner. The flap should include the underlying muscle for a robust blood supply.

Most surgeons use the geometric design described by Zitelli, wherein each adjacent flap rotates in an arc-like fashion by 45°, bringing the final rotation to 90–100°. These are useful for defects up to 1.5 to 2 cm (Figure 7A and B). Small cartilage defects may not need any separate cartilage grafts, as the flap is quite thick.¹⁶



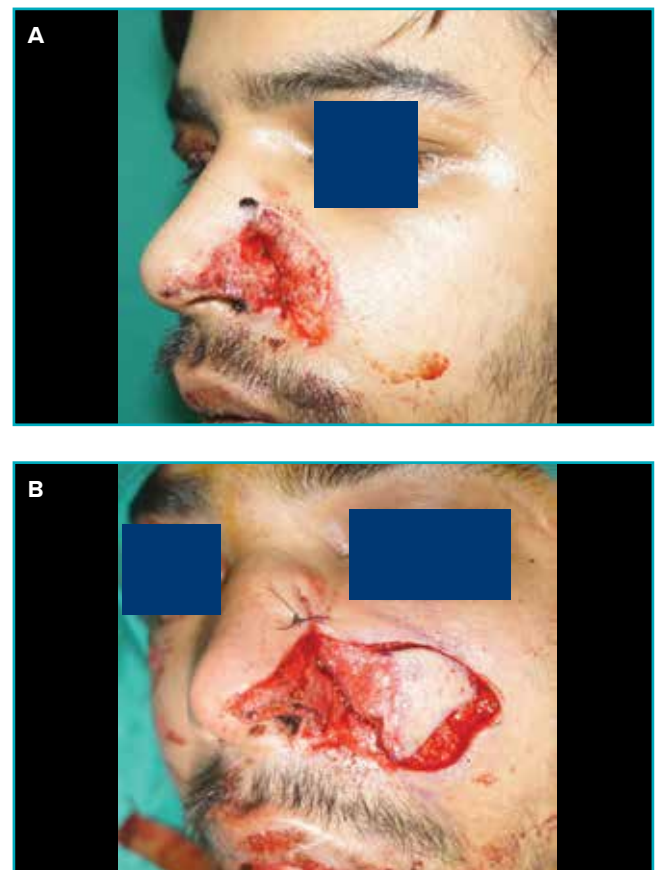
Figure 7: A. Right alar basal cell carcinoma planned for a wide local excision and reconstruction with a medially based bilobed flap using Zitelli's design, B. Final appearance of bilobed flap reconstruction.

Medially based design is used for alar defects, and laterally based design is used for tip defects. The second flap donor site should be closed first, and any dog-ear should be excised. This makes the further inset of the two flaps essentially tension-free. Accurate layered closure is important to avoid future 'pin-cushioning' of the scar. The main disadvantages are extensive dissection and scars that can pin-cushion or become hypertrophic.

9. Nasolabial and melolabial flap

The adjacent area of the cheek or the nasolabial area provides natural skin laxity along the resting lines of tension to raise a melolabial or nasolabial flap, respectively.^{17,18} Both are based on perforators emanating from the terminal branches of the facial artery. They can be used for large adjacent ala and sidewall nasal defects of up to 2 to 3 cm.

For adjacent defects, both flaps can be used as a pedicled transposition or an islanded flap (Figure 8A–E). If the flap is bulky, a second stage for thinning and alar groove or lateral wall contouring can be performed after 3 weeks. Cartilage grafts can be placed underneath in the very first stage.



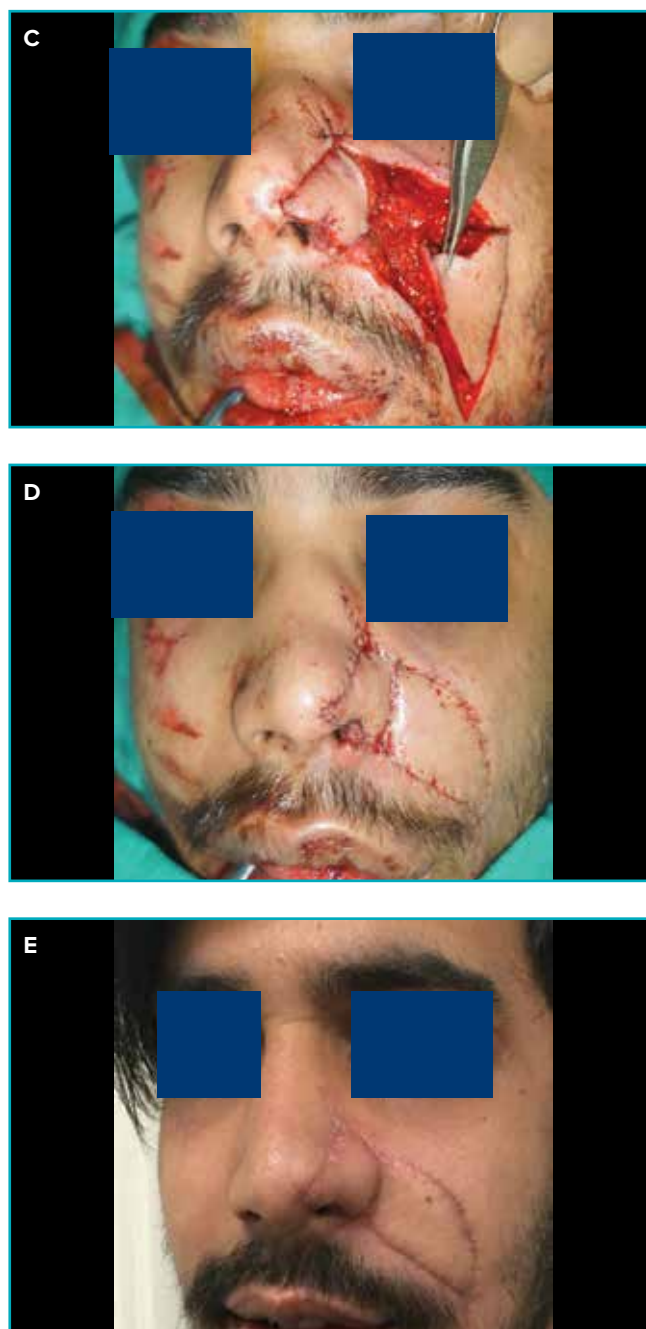


Figure 8: A. Traumatic loss of the left ala and cheek tissue, B. Adjacent mesolabial flap being raised as an island design (after verifying the arterial supply from the angular artery superiorly using a Doppler probe), C. V-Y island nasolabial flap raised to fill the donor defect of the mesolabial flap, D. Mesolabial flap inset to the left alar defect and nasolabial V-Y flap advanced to close the donor defect simultaneously. The two flaps successfully reconstructed a complex ala–cheek defect in this case, E. 2 months postoperative result. The patient was advised to undergo fractional laser resurfacing for further scar modulation.

Larger defects of the ala and tip or columella can also be reconstructed with two-stage pedicled nasolabial flaps. The main facial artery, which runs deep to the muscle, needs to be included in large-sized flaps; for smaller defects, however, island perforator-based flaps minimise donor site morbidity.

The width of the flap can vary from 2 to 4 cm, depending on cheek skin laxity, and is an excellent choice in elderly patients, for sidewall, ala, and composite inferior nose side defects due to its simplicity and reliability. In younger patients, the nasolabial flap is often limited to a maximum 2 cm width due to tight skin and a higher incidence of hypertrophic scars.

10. Forehead flap

The forehead flap is the best reconstructive option in large, complex defects involving the nose.¹⁹⁻²² It offers an excellent tissue match with acceptable donor site morbidity. It may be harvested based on the supratrochlear vessels as the paramedian flap or based on canthal and paracentral vessels as the midline flap. Apart from these two designs, many variations have been described, such as oblique, sickle, and converse scalping flaps. However, the vertical paramedian forehead flap has continued to enjoy immense popularity for hundreds of years due to its reliable vascularity, great skin texture match, large tissue availability, and good flap reach with minimal donor site morbidity.

Paramedian forehead flap is a workhorse flap for nasal reconstruction and is mostly performed in two stages, wherein the pedicle base and inset is performed in 3 weeks' time. The pedicle must always be at least 1.5 cm wide and may be rotated to the ipsilateral or contralateral side. If required, the flap can be extended to include the hair-bearing area, especially in short foreheads. Such patients benefit from hair removal with diode laser sessions later. The flap's reach can be extended by incising the medial margin of the flap below the brow hairline. Another method to increase the reach is to score the galea or frontalis without damaging the pedicle. This may give an extension of about 1 cm.

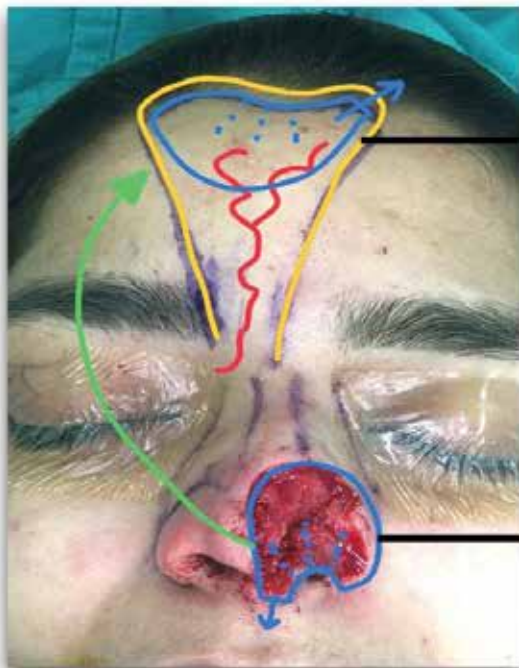
The subunits requiring reconstruction should be marked first. A foil or paper template of the defect can be made and transposed 180° to design the flap. The supratrochlear vessels are marked with the help of a handheld Doppler probe and are anatomically located just lateral to the frown crease. The exact pattern of the defect is marked on the forehead, which may include the hairline depending on the length of the flap required. The flap is elevated in the loose areolar plane from cranial to caudal direction towards the pedicle. Although the superior tip of the flap can be elevated in the subcutaneous plane to

reduce the bulk, more than two-thirds of the inferior flap must include the frontalis muscle, and the lower 2 cm must also include the periosteum to prevent inadvertent division of the tightly coursing pedicle vessels, which lie closely against the periosteum at the superior orbital rim. Skeletal support in the form of costal or auricular cartilage grafts can be implanted at the very first stage in most cases. It is often combined with turnover flaps or nasolabial flaps for the inner lining of large defects (Figure 9A–K).



Use of template to design the forehead flap to fit into the nasal defect

C

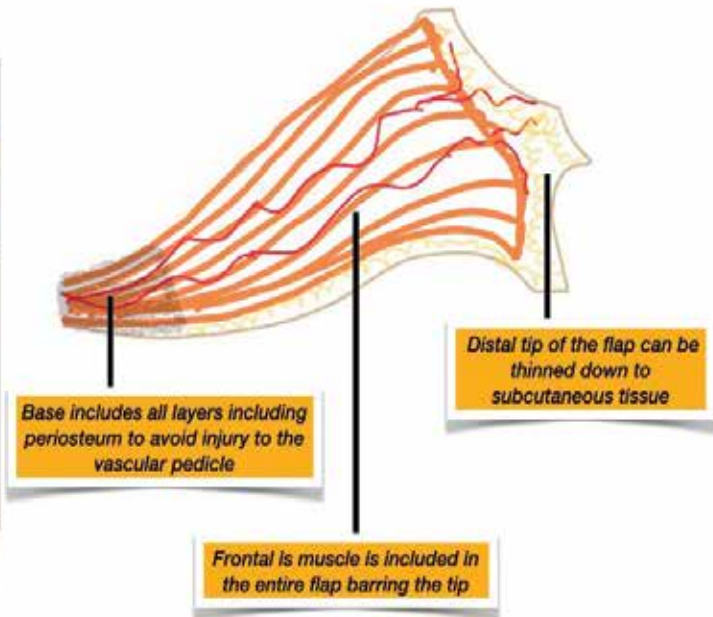


Template turned 180 degrees and incorporated in the forehead flap outline

Template drawn around the defect with a paper or a foil with orientation arrow

Underside of pedicled forehead flap showing various components

D



E



F



G



H





Figure 9: A and B. Showing a composite dorsum, left ala, tip, and columella defect secondary to a dog bite, C. Paramedian forehead flap drawn on the contralateral pedicle based on the defect template. Dorsal turnover flaps are used for alar lining, D. Underside of raised forehead flap showing inclusion of various deep components in different parts of the flap, E. Flap inset to reconstruct the nasal defect. The pedicle is protected with a nonadherent foam dressing, F. Stage 2 of flap division and inset at 3 weeks after the first stage, G and H. Stage 3 after another 3 months, showing further nasal lining addition with a full-thickness postauricular skin graft and septal extension and tip cartilage graft, I, J and K. Final result of nasal reconstruction with the forehead flap after one year.

Donor forehead closure may be achieved primarily in smaller cases; in larger defects, partial areas may be left for healing by secondary intention. This is preferred to split skin graft as secondary healing scars are excellent in the forehead area and the scalp, and do not suffer any contracture in the long term. The majority of surgeons prefer the 3-week period for the

second stage of pedicle division, but the duration can be shortened to 2 weeks if good vascularity of the distal flap can be validated with indocyanine green angiography, whilst temporary pedicle occlusion is performed with a gentle vascular clamp or rubber tourniquet (Figure 10A and B).

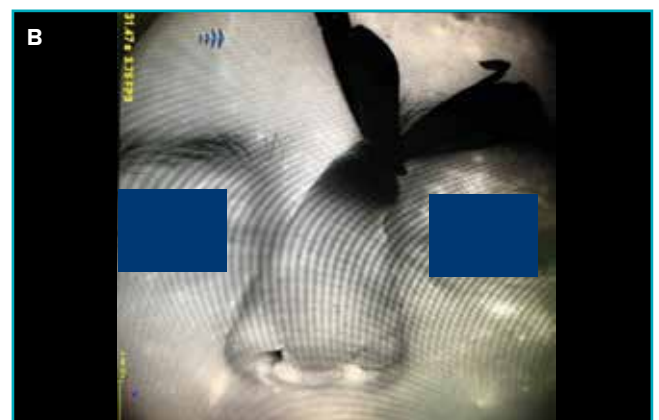
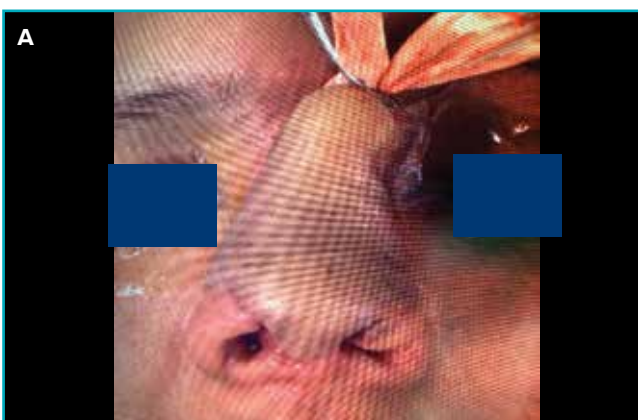


Figure 10: A. Glove tourniquet is tied at the forehead flap pedicle base on the forehead side. This flap is 2 weeks post-first stage, and indocyanine green (ICG) angiography will be performed to see if the distal part of the attached flap is well perfused from the nasal side, B. Bright white fluorescence of ICG angiography clearly demonstrates excellent flap vascularity despite the pedicle being occluded with a tourniquet. This indicates that the flap has started to derive full vascularity from the nasal side, and the pedicle can be safely divided at the base.

In smokers, elderly patients, or those with vasculopathies, no flap thinning should be done, and the duration of the second stage division should be increased to 4–5 weeks for safety. The flap can also be performed in three stages with an intermediate stage at 2–3 weeks for cartilage grafting, flap thinning, or contouring.

When faced with partially scarred foreheads or small foreheads, tissue expansion can be used before elevating the flap to increase its size. However, this is generally not a preferred option as it thins out the subcutaneous tissue and may result in later contraction on the nose, thus compromising the result. Forehead flap also lends itself to prelamination with a skin graft or a dermal matrix for the inner lining.

11. Radial artery forearm (RAFA) free flap

When no local options are available for nasal reconstruction due to failed previous reconstructions or scarred local sites, the RAFA free flap is quite the saviour.²³ It can reconstruct all subunits of the nose. It is preferred over other free flaps because of its long pedicle and thin, pliable tissue that can

easily be moulded to the desired shape and size. However, the colour match is not as good as the forehead flap, especially for coloured skin. It can also be used for nasal lining in large central defects and may be combined with a forehead flap for external cover. Cartilage or bone grafts should be sandwiched between two layers when necessary. It has the added advantage of bringing vascularity to severely scarred areas, besides promoting healing. In cases of large septal defects, a dorsal cantilever graft can be used for support without any formal attempt at reconstructing the septum, as the large septal fistula provides enough room for adequate airflow without stenosis.

The flap may also be prefabricated or prelaminated with cartilage graft on the forearm and later transferred to the recipient site.²⁴ The skin paddles may be longitudinally arranged like a string of pearls and placed according to the defect to restore the lining, floor, and columella separately. Attention must be paid to flap design and orientation of the pedicle to avoid kinking and vascular compromise to the skin paddle (Figure 11A–C).



◀ **Figure 11:** A. Patient with loss of the entire tip and nostrils from a bomb blast injury. The forehead flap was previously used unsuccessfully to reconstruct elsewhere, B. Radial artery forearm (RAFA) free flap raised and crafted whilst still attached in the forearm to make the nostril lining and the nasal tip complex. The construct was sutured over appropriately sized paediatric endotracheal tubes, which were also used as internal splints. The flap was anastomosed to the facial vessels, C. Excellent reconstruction of composite nostril tip complex along with internal lining with the RAFA free flap. Patient is advised to wear nasal splints for 3 months to prevent contracture. Patient will undergo further revision for refining the eternal nasal profile.

Structural Support Reconstruction

Stable nasal architecture, shape, function, and sturdiness of the reconstruction rest firmly on skeletal integrity. Split cranial grafts or rib grafts can be used for large nasal bone defects. Most nasal reconstructions require only the cartilage framework, for which septal, ear or costal cartilage grafts can be used.

Septal cartilage is easily available and provides good support, but its use may be limited in cases of large structural requirements. Ear cartilage is another site providing excellent tip and alar grafts. It is, however, rarely used for constructing a linear columella or dorsal graft owing to its curved nature and limited quantity. The ear cartilage is harvested from the conchal bowl using an anterior, or preferably a posterior technique in patients with keloid tendencies.

Costal rib cartilage is an excellent and almost unlimited source of cartilage grafts for a depleted nose. The sixth, seventh, and eighth rib cartilages are reliable donor sites when a large amount of structural reconstruction is necessary. Floating ribs can be used as a cantilever graft. The rib grafts often warp in the future, causing delayed deformation and deviation of the reconstructed nose. To prevent this, the cartilage is carved based on Gibson's principle of balance — equal carving on the sides of the core to prevent warping. Keeping the half-carved cartilage immersed in a bowl of sterile saline solution for half an hour can also make the future warping obvious and thus allow for pre-emptive corrections. Another method to minimise warping is to harvest half bone and half cartilage. A costochondral graft can be used as an L-shaped construct with a columellar strut for stable projection. The graft should be fixed securely to the remnant structures in the midline to prevent deviation. Additional K-wire fixation for 10 days can also be done. Anatomically shaped costal cartilage grafts can be used to reconstruct the septum, lateral nasal walls, tip, and alar regions just like in a standard open rhinoplasty approach (Figure 12).^{19,25}



Figure 12: Rib cartilage grafts used as a dorsal cantilever graft with a columellar strut and bilateral cartilage grafts. External nasal skin cover is restored with a paramedian forehead flap seen as being harvested (it is vital to fix all the grafts with the remaining base in a stable way at multiple points).

Split calvarial, ischial crest bone, and rib grafts can be used as cantilever grafts, which are fixed to the nasal radix with a screw but may suffer from absorption and dislodgement. Lack of columellar fixation is a weak link in the entire cantilever construct.

Artificial materials such as silicone and porous polyethylene implants are usually not preferred for complex nasal reconstruction as they are associated with high risks of extrusion and infection.

Nasal Lining

Nasal lining is important for maintaining a patent airway. Small defects can be reconstructed with a bi-pedicled nasal lining flap or even an inferior turbinate mucosal flap. Larger defects may be covered by a septal mucosal pivot flap based on the septal branch of the superior labial artery. The midvault lining may be obtained from a contralateral septal hinge mucosal flap based on the superior ethmoidal vessels, passed through an incision in the ipsilateral septum dorsally.⁸

Turnover skin flaps from the defect rim, folded forehead flap, nasolabial flap, or, in severe deficiency, a microvascular RAFA free flap can all be used as needed for the nasal lining.

It is also possible to use FTSG or a dermal matrix sutured to the underside of the forehead or a nasolabial flap.

Post-Operative Rehabilitation

Prevention of nostril stenosis, airway collapse, and skin contracture is essential in all major reconstructions. Sequential conforming silicone nasal retainers may need to be worn for a few months to prevent collapse and fibrosis (Figure 13).



Figure 13: Nostril retainer is advised to be worn for at least 3 months after nostril reconstruction, and retainers are worn in incremental sizes till the opening has been over-dilated by 10%–15%. In this particular case left side nostril retainer-dilator can be seen in place.

In extended forehead flaps that transfer hair-bearing skin to the nose, laser hair removal is hugely beneficial.

Fractional resurfacing lasers — such as carbon dioxide lasers — are helpful in improving scar appearance and texture. Triamcinolone intralesional injections may be needed to treat scar hypertrophy.

In patients for whom surgical reconstruction is not possible due to poor medical conditions or personal preference, an external removable or osseointegrated nasal prosthetic can be an option. They often become loose and need replacement. The side seams need regular cleaning and may develop crusting and infection.²⁶

Face transplant may be indicated in patients with severe facial deformity when autologous reconstruction and prosthetics are not possible. The entire face or midface may be transplanted, especially in patients with large neurofibromas and extensive facial trauma. The challenge is to obtain an ideal donor. There is, of course, the risk of rejection before and after the procedure, and lifelong immunosuppression is required. Composite tissue allotransplantation is a debatable procedure, as failure due to rejection leaves very little choice and often leaves the patient in a condition worse than their original state. In any case, given the lack of donors for such a procedure, it will always remain within the domain of advanced research institutes with unlimited resources.²⁷

Conclusion

The nose is a unique part of human appearance and identity. The reconstruction of a natural-looking and harmonious nose not only restores form and function, but also reinstates human dignity. An artistic blend of techniques, along with stepwise logical planning and layer-by-layer restoration of skin, skeletal support, and nasal lining, is the key to a good result. Local flaps, especially the ‘old-is-gold’ forehead flap, still retain their winner status in this arena. The aim is to make a good-looking nose that rests above a beautiful smile!

Take home messages

- The nose has a complex topographic shape that can be easily divided into 9 subunits based on the contour lines and skin type. In defects with more than 50% of a subunit missing, it is often best to replace the whole subunit by converting the partial defect into a complete subunit defect, provided a suitable method of reconstruction is available.
- Quality and texture of skin can be used to describe 3 distinct zones of the nasal surface. This is useful in planning reconstruction as skin pliability is a deciding factor in the design of local flaps.
- When confronted with the reconstruction of a complex three-dimensional facial feature like the nose, it is best to use a logical stepwise planning process focusing on restoration of all three anatomical layers.
- Bilobed flap is an excellent option for Zone 2 thick skin defects of the tip and ala (inferior nose).
- The paramedian forehead flap is the workhorse flap for large, complex defects involving the nose. It provides an excellent tissue match for nasal skin. It lends itself beautifully to moulding in multiple stages and the addition of skeletal grafts and other inner flaps. Scars on the donor forehead also settle well.
- Nasal lining flaps and skeletal support are vital to give stability and predictability to any nasal reconstruction.

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Multiple Choice Questions (MCQs)

- The 'Italian modification' of Indian nasal reconstruction secret was guarded and modified by:**
 - Tagliacozzi
 - Alessandro Benedetti
 - Pfalzpaint
 - Antonio Branca
- Which is the most important layer when performing a total nasal reconstruction?**
 - Skin
 - Structural support
 - Lining
 - Cartilage
- A bilobed nasal flap is best suited for:**
 - Defects of the tip and ala with thick skin
 - Defects of Zone 3 nasal skin
 - Defects of the dorsum and side walls with thin skin
 - Nasal lining
- Which of the following statements is incorrect regarding the nasolabial flap?**
 - It is the best flap for ala reconstruction
 - It can be used as a nasal lining flap
 - Its blood supply is from the superficial temporal artery
 - It can be used as a single-stage reconstruction
- A patient who is a smoker underwent nasal reconstruction with a forehead flap. The base of the flap needs to be divided for inset at three weeks, but the surgeon is concerned about the flap survival as the patient has a history of smoking. What is the best imaging modality to assess the vascularity prior to dividing the flap?**
 - Computed tomography (CT) angiography
 - Magnetic resonance (MR) angiography
 - Indocyanine green (ICG) angiography
 - Duplex Doppler
- According to Burget and Menick, what is the best time to provide skeletal nasal support in nasal reconstruction?**
 - Prior to skin reconstruction as prelamination
 - At the time of reconstruction, at the first stage itself
 - 3 to 4 weeks after skin flap reconstruction
 - Any time after the flap seems to have healed
- Which is the best form of nasal lining in total nasal reconstruction following gunshot injury with a palatal and nasal defect and intact maxillary arch?**
 - Prelamination with skin grafts and staged forehead flap reconstruction
 - Single radial forearm flap with separate skin paddles for lining with external cover
 - Radial forearm flap for lining and forehead flap for external skin cover
 - Mid-face transplant

8. Which of the following statements regarding tissue expansion is true?

- A. There is a rebound contracture of the flap
- B. Tissue expansion is commonly done for nasal reconstruction
- C. There is no need to excise the capsule
- D. The flap can be easily prelaminated

9. Which of the following is not a modification of the forehead flap?

- A. Scalping flap (converse)
- B. Gull Wing flap
- C. Washio flap
- D. Juri flap

10. Burget's principles of nasal reconstruction include all except:

- A. Restore the normal shape, contour, and texture of tissue
- B. Three-dimensional planning of tissues using computer-aided design (CAD)/computer-aided manufacturing (CAM) technique
- C. Replace like with like tissues
- D. Replace the entire subunit whenever practical

- 2. (C) Lining. It determines the final outcome. Without a lining, the reconstruction will collapse. It should be vascular, supple, and thin to support the cartilage and or bone.
- 3. (A) Defects of the tip and ala less than 1.5 cm can be easily covered with a bilobed flap, as the skin of this area is thick and immobile. The bilobed flap effectively transfers the skin laxity from the superior to the inferior nose in an efficient manner.
- 4. (C) Nasolabial flap is supplied by branches of the facial artery.
- 5. (C) Indocyanine green angiography (ICG angiography) is a simple and accurate imaging modality to assess the vascularity of the forehead flap before dividing the pedicle (a temporary glove tourniquet is tied to the pedicle). It is capable of showing dynamic cutaneous vascularity on the table intraoperatively. If the distal part of the flap fails to light up with the fluorescence, then it is not ready for pedicle division, and a further period of 1–2 weeks should be given before attempting division of the flap.
- 6. (C) According to Burget and Menick, 3–4 weeks post first stage nasal reconstruction with forehead flap is the preferred time to add skeletal support in the form of cartilage or bone grafts. They would divide the pedicle subsequently at the third stage 3–4 weeks later.
- 7. (C) In a severe gunshot injury, there is extensive damage resulting in scarred residual nasal and oral mucosa with a large palatal and midface defect. The palatal defect and nasal lining can both be reconstructed with a double paddle radial forearm flap. The best skin match for the external cover can be provided by the forehead flap.
- 8. (A) Rebound contraction of the flap is an unfavourable outcome seen with expanded forehead flaps, mainly used if the defect skin size is huge and the donor's forehead is small. This leads to contraction of the lining. Expanded flaps are better suited when nasal lining reconstruction is not required. The capsule is usually excised during transfer. Skeletal support is also always inserted at the first stage to limit flap skin contracture.

MCQ Answers

- 1. (D) Antonio Branca. The Italian family Branca de'Branca guarded the secret of nasal reconstruction with the Indian method. Later, Antonio Branca modified the reconstruction using a forearm flap in the fourteenth century. Alessandro Benedetti first reported the Italian method 100 years before Tagliacozzi. In the mid-fifteenth century, a similar technique was described by Pflazpaint (a German surgeon).

9. (D) Juri flap is a temporal scalp flap based on temporal artery branches, mainly used for the treatment of male pattern baldness. The other options are forehead flap modifications. The scalping flap has a skin paddle designed on the lateral forehead. It can be used to reconstruct large nasal defects. It requires a bi-coronal incision and leaves a large secondary scalp defect to be covered with a skin graft. Washio flap utilises post auricular and mastoid skin based on the lateral forehead and temporal area and is supplied by the superficial temporal artery and retroauricular artery. The Gull Wing flap was designed by Millard using a median forehead flap. It is used for columella reconstruction.
10. (B) Three-dimensional planning, as described by Burget and Menick, involves using a foil or an empty suture packet as a source for configuration.

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Quadri-Paddle Anterolateral Thigh Flap for Complex Maxillo-Mandibular-Cheek Defect in Vessel-Depleted Neck

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Abstract:

The anterolateral thigh flap has been the workhorse flap for coverage of soft-tissue defects in the head and neck for decades. However, the reconstruction of multiple and complex soft-tissue defects in head and neck with multi-paddled anterolateral thigh (ALT) or chimeric flaps is still a challenge for reconstructive surgeries, particularly for total maxillectomy defects, as it requires reconstruction of nasal lining, palatal reconstruction, cheek mucosa, and even skin defect reconstruction, if any created by the oncosurgeon. Here, we report a clinical case in which a multi-paddled anterolateral thigh flap was used for a complex soft-tissue defect created after onco-resection for recurrent squamous cell carcinoma of the maxilla. In this case, total maxillectomy with hemimandibulectomy was done along with excision of the skin of the lower half of the face of that side. Most branches of the external carotid artery, along with the internal jugular vein (IJV) were ligated in previous surgery. The availability of a vascular pedicle was also a challenge. Here, reconstruction was performed using a large ALT flap that was divided into four paddles based on three perforators for reconstruction of all linings, including a de-epithelised skin paddle for orbital floor reconstruction.

Key words: Free Anterolateral Thigh (ALT) Flap, Maxillectomy, Mandibulectomy, Head and Neck Onco-Reconstruction.

Introduction

Complex soft-tissue defects of the head and neck that involve multiple and nonadjacent anatomic sites can arise after radical surgery for advanced-stage malignancies or multiple lesions of the upper aerodigestive tract. Immediate flap reconstruction is the gold standard for the surgical treatment of these defects after tumour ablation. However, functional and aesthetic reconstruction of complex and multiple defects in the head and neck remains a major surgical challenge, because the reconstruction of multiple and nonadjacent defects requires a flexible and feasible flap with a multiplanar configuration consisting of multiple paddles.¹ For multiple and complex soft-tissue defects, reconstruction with three-

dimensional microvascular flaps is often the preferred alternative. The free anterolateral thigh (ALT) flap, first described by Song *et al.*² in 1984, is a versatile and reliable reconstructive option. This flap has become a workhorse for head and neck reconstruction in recent decades.^{3,4} The advantages of ALT flap include consistent and reliable anatomy, long vascular pedicle, feasibility to create multiple skin paddles by recruiting additional perforators, the flexibility to reconstruct composite defects by recruiting different tissue types, and low donor site morbidity. Based on multiple cutaneous perforators originating from the descending branch of the lateral circumflex femoral artery (LCFA), free ALT flap can be

harvested with multiple skin paddles for multiple and complicated soft-tissue defects, which can eliminate the need for two or more separate flaps and vascular anastomosis.⁵⁻⁷ In this study, we present our experience with free multi-paddled ALT flap for functional and aesthetic reconstruction of complex head and neck soft-tissue defects involving multiple nonadjacent anatomic sites in a single operation.

Challenging reconstructive cases occur in a previously treated neck following either surgery, radiation (with or without chemotherapy), or a combination of both. Patients with these prior interventions have cervical anatomy with distorted tissue planes, inflammation, and scarred vessels, leaving the neck depleted of suitable recipient vessels. A vessel-depleted neck (VDN) occurs in around 7% of all patients receiving microvascular reconstructions in the head and neck.⁸

Case Report

Our patient was a 60-year-old lady who was diagnosed with recurrent cancer of the right-sided buccal mucosa. The patient was a known diabetic and hypertensive (controlled on regular medications), with wide excision and primary closure of right buccal mucosal squamous carcinoma performed about 5 years earlier, along with a right neck dissection.

She presented with a mouth opening of less than one finger and recurrence of carcinoma at the same location, thus a total maxillectomy with hemimandibulectomy was performed by the oncosurgeon. On the same side of the neck, all branches of the external carotid were ligated, and the internal jugular vein (IJV) was also excised and ligated at the base of the neck.

Reconstruction was a challenge as there was a defect involving the floor of the right orbit, right lateral nasal wall, palate (two-thirds of the soft and hard palate were excised), right posterior pharyngeal wall, buccal mucosa, floor of mouth, and skin of cheek and mandibular area (Figures 1 and 2).



Figure 1: Front view — Post excision defect.



Figure 2: Lateral view (Day 5) — Reconstruction with single anterolateral thigh (ALT) flap.

On Doppler (handheld), two prominent perforators were found along the line of ALT flap, thus a flap with the full thigh length (26 cm x 9 cm wide) of skin paddle was planned, including a good bulk of vastus lateralis muscle. After the anterior skin incision, two septocutaneous and one musculocutaneous perforators were found. The flap was harvested, saving all perforators and taking a good bulk of muscle.

After getting three good perforators, the division of the flap into three parts was planned:

1. Lowermost skin paddle – 13 cm x 9 cm – for external skin defect
2. Skin paddle above No. 1 – 6 cm x 9 cm – for intraoral defect
3. Uppermost skin paddle was used in two parts:
 - a. 3 cm x 4 cm – terminal part de-epithelised to support orbit
 - b. 3 cm x 5 cm – for lateral nasal wall

After partial inset of flap in the oral cavity (Figures 3 and 4), vascular anastomoses were done in the following sequence:

Flap artery – external carotid – end to side

Two flap veins – IJV – end to end with closure of middle part of the IJV. Reconstruction with free ALT flap is shown in Figure 3 (lateral view) and Figure 4 (frontal view).



Figure 3: Lateral view — Defect after wide excision of right total maxillectomy, right hemimandibulectomy with skin of upper lip, lower lip, and cheek.



Figure 4: Front view (Day 5) — Reconstruction with free anterolateral thigh (ALT) flap.

Vascularity of the flap was excellent, as there was no marginal necrosis of the flap of even a millimetre at any margin. There was some fat necrosis of the facial skin leading to wound dehiscence, so debridement and secondary suturing were done on post-operative Day 14. The tracheostomy tube was kept for a longer period as a large part of the oral and nasal cavity was formed by the flap, leading to difficulty in breathing while attempting removal of the tracheostomy tube. The tube was removed with a gradual decrease in size of the uncuffed tube.

Discussion

In India, the majority of head and neck cancers present as locally advanced Stage III/IV disease.⁹ As the incidence and diagnosis of oral cancer increase, excision of the head and neck cancers will frequently yield large, complex three-dimensional defects. These defects test the limits of the reconstructive surgeons and thereby obligate imaginative planning and surgical astuteness. Since its description in 1984 by Song *et al.*¹⁰, ALT flap has become the preferred flap for reconstruction in varied settings. Other good options for these extensive defects are the flaps on the scapular or parascapular axis, but these require a change in position. Deep inferior epigastric artery, vertical rectus abdominis flaps, and second free flap are also other feasible options in this situation. Chimeric flaps are also described in the literature for reconstruction of such defects, taking the antero-medial thigh (AMT) along with the ALT flap.

In our case, we have achieved all the desired goals: providing support for the eyeball, lining of lateral nasal wall and posterior pharyngeal wall with buccal mucosa, and reconstruction of a large skin defect in a vessel-depleted post-radiation neck.

Conclusion

The ALT flap is a versatile and commonly used flap in reconstructive surgery, especially for covering defects of the head and neck, trunk, and lower extremities. It is valued for its large size, reliable pedicle, and relatively low donor-site morbidity, and has served as the workhorse flap for head and neck soft-tissue reconstruction for decades. However, the reconstruction of multiple and complex soft-tissue defects in the head and neck with multi-paddled ALT or chimeric flaps remains a challenge for reconstructive surgeries, particularly for total maxillectomy defects. Here, we report a clinical case in which a multi-paddled ALT was used to address a complex soft-tissue defect created after onco-resection for recurrent squamous cell carcinoma of the maxilla.

Anurag Pandey. Quadri-Paddle Anterolateral Thigh Flap for Complex Maxillo-Mandibular-Cheek Defect in Vessel-Depleted Neck. MMJ. 2025, September. Vol 2 (3).

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The Great Masquerader

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Abstract:

Young adults presenting with progressive neurological deficits and systemic features such as weight loss and night sweats pose a significant diagnostic challenge. Imaging that reveals widespread lytic skeletal lesions with a solitary pulmonary nodule often directs clinical suspicion towards an underlying malignancy. A previously healthy 24-year-old male presented with gradually progressive bilateral lower limb weakness, preceded by back pain, along with significant weight loss, loss of appetite, night sweats, and chronic dry cough. Neurological examination revealed paraparesis with areflexia in the lower limbs. Magnetic resonance imaging (MRI) of the spine showed multiple lytic lesions and a compression fracture at T10–T11 with significant nerve root compression. Fluorodeoxyglucose (FDG) positron emission tomography (PET)–computed tomography (CT) demonstrated a right middle lobe pulmonary nodule, mediastinal lymphadenopathy, and diffuse FDG-avid skeletal lesions. A malignancy workup, including bone marrow biopsy, was non-contributory. A CT-guided sternal biopsy revealed necrotising granulomatous inflammation, but no malignant cells or acid-fast bacilli. Pending culture results, the patient was started on empirical therapy based on the most probable aetiology. Gradual clinical improvement was observed, and definitive microbiological confirmation followed after 34 days. This case underscores the complexity of differentiating between infectious and malignant causes in patients presenting with systemic illness and multifocal bony lesions. High clinical suspicion, combined with histopathological and microbiological correlation, remains vital for accurate diagnosis.

Key words: Paraparesis, Multifocal Bony Lesions, Malignancy.

Introduction

Spinal involvement by systemic disease presents a broad differential diagnosis, ranging from infections to malignancies. When young adults present with progressive paraparesis, weight loss, and constitutional symptoms, metastatic malignancy is often high on the clinician's radar — especially when imaging reveals lytic spinal lesions and a solitary pulmonary nodule. However, in tuberculosis (TB)-endemic regions such as Southeast Asia, certain infections can mimic malignancies both clinically and radiologically.

TB of the spine (Pott's disease) accounts for approximately 50% of skeletal TB cases.¹ Atypical presentations — such as multifocal non-contiguous vertebral involvement, absence of classical constitutional symptoms, or isolated

pulmonary nodules — can obscure the diagnosis. Moreover, fluorodeoxyglucose (FDG) positron emission tomography (PET)–computed tomography (CT), though sensitive in detecting metabolically active lesions, does not reliably distinguish between infection and malignancy due to overlapping uptake patterns.²

We report a case of a young, immunocompetent male with rapidly progressive paraparesis, systemic features, and imaging highly suggestive of metastatic cancer, which ultimately revealed a very different aetiology. This case exemplifies the diagnostic dilemma posed by infections that masquerade as malignancies.

History

A 24-year-old male college student from Myanmar, belonging to a lower-middle socioeconomic background, presented to the outpatient department with the chief complaint of progressive bilateral lower limb weakness over the past two months.

He had been apparently well until six months prior, when he began experiencing lower back pain, initially dull and localised around the hip region, with no history of trauma, falls, lifting heavy objects, or exertion. The pain gradually progressed, radiating bilaterally to the lower limbs — from the hips to the feet — and worsened with movements and activities that increased intra-abdominal pressure, such as coughing or sneezing. Nonsteroidal anti-inflammatory drugs (NSAIDs) provided partial relief. Over time, the pain evolved into intermittent sharp, shooting pain, significantly impairing sleep.

Two months after the onset of back pain, he developed bilateral lower limb weakness, which was insidious in onset and gradually progressive. Initially, he could carry out daily activities independently, but over time required support and eventually became bedbound. The weakness involved both lower limbs equally, with no diurnal variation or fluctuation. He also reported tingling sensations in both lower limbs without numbness. There was noticeable muscle mass reduction, more prominent in the thighs than in the legs.

There was no involvement of the upper limbs and no history suggestive of bladder or bowel dysfunction. He denied symptoms of postural dizziness, gastrointestinal disturbances, autonomic dysfunction, palpitations, seizures, altered sensorium, speech disturbances, or cranial nerve involvement.

Associated systemic symptoms included unintentional weight loss of approximately 15 kg over six months, with decreased appetite and night sweats, a chronic

intermittent dry cough persisting for six months and persistent chest discomfort localised to the sternum for the same duration.

The patient had no history of fever, haemoptysis, chest pain, dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea, rash, joint pain, or constitutional features such as fatigue or malaise. There was no recent history of vaccination, foreign travel, or contact with known TB patients, nor any exposure to animals or pets. The patient also did not report any urinary, ear, nose, or throat (ENT), or gastrointestinal complaints. Past medical history was significant for treatment of pulmonary TB at 1.5 years of age; the strain was reportedly rifampicin-sensitive, and the patient had completed a six-month course of treatment with both symptomatic and radiological resolution. There was no history of diabetes, hypertension, asthma, prior malignancy, or major surgeries. Family history revealed no known neurological or infectious disorders; however, it was notable that the patient's elder brother was treated for adenocarcinoma of the lung at the age of 30. In terms of personal and social history, the patient was a non-smoker, did not consume alcohol, and had no history of illicit drug use. The patient was non-vegetarian and had experienced sleep disturbances due to pain. This constellation of progressive neurological symptoms with systemic features prompted further evaluation.

Examination

General physical examination revealed no pallor, icterus, cyanosis, clubbing, lymphadenopathy, or oedema. Oral hygiene was normal, and the thyroid examination was unremarkable. Vital signs were stable. Systemic examination of the respiratory, cardiovascular, and abdominal systems was normal. The central nervous system examination is as mentioned in Table 1.

1.	Higher mental function	Normal
2.	Cranial nerve examination	Normal
3.	Motor system	Upper limbs: Normal Lower limbs: 1. Power – 3/5 B/L 2. Tone – Decreased B/L 3. Attitude – Normal 4. Bulk – B/L wasting without any deformities 5. No involuntary movements 6. Straight leg raising test ++
4.	Reflexes	Upper limbs: Normal Lower limbs: 1. Superficial reflexes – Normal (flexor plantar response) 2. Deep tendon reflexes – Absent knee and ankle jerk B/L
5.	Sensory system	Primary sensations – Normal Secondary sensations – Normal
6.	Cerebellar function	Normal
7.	Meningeal signs of irritation/ANS	Normal
8.	Spine/skull deformity	Absent

Table 1: Examination of central nervous system.

Abbreviations: ANS: Autonomic Nervous System; B/L: Bilateral.

Hospital Course and Investigations

The patient was admitted for further evaluation of bilateral lower limb weakness and systemic complaints. Initial baseline investigations, including complete blood count (CBC), liver function tests (LFT), renal function tests (RFT), and procalcitonin, were all within normal limits. Paired blood and urine cultures showed no growth, and there were no laboratory signs of ongoing infection.

Given the progressive paraparesis with back pain, a magnetic resonance imaging (MRI) of the spine was performed. It revealed the following:

- Multiple lytic lesions with abnormal patchy marrow signals involving the cervical, thoracic, and lumbosacral spine, raising suspicion of metastases versus infection
- A compression fracture at T10–T11, with significant nerve root compression, suggestive of radiculoneuropathy

In view of the extensive lytic lesions, constitutional symptoms (notably significant weight loss), and a family history of lung carcinoma, a whole-body ^{18}F FDG PET–CT scan was done which revealed the following:

- A 1.5 cm FDG-avid pleural-based nodule in the right middle lobe, with adjacent pleuro-pericardial thickening
- FDG-avid mediastinal lymphadenopathy
- Increased FDG uptake in the sternum
- Multiple FDG-avid lytic lesions throughout the spine (Figure 1), including the T10–T11 region with associated compression fracture (Figure 2)

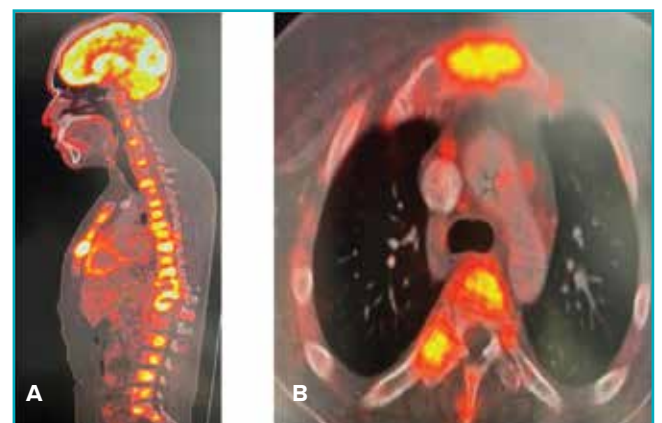


Figure 1: ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography (PET): A. Multiple FDG avid lytic lesions through spine, B. Sternal FDG enhancement.

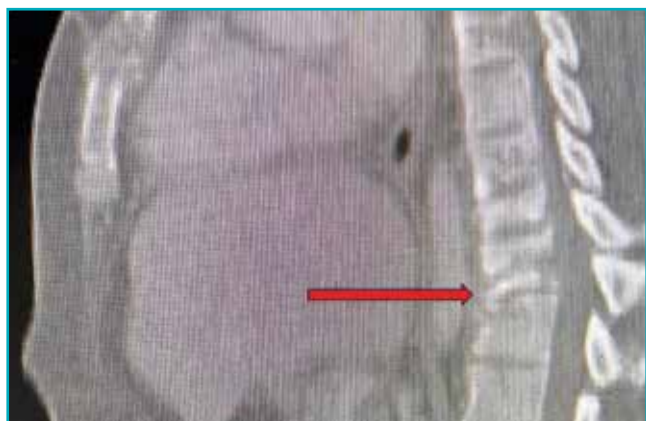


Figure 2: Compression fracture of vertebrae T10–T11 indicated by red arrow.

These findings were strongly suggestive of a primary lung malignancy with skeletal metastases. An oncology referral was made, and the provisional diagnosis was carcinoma of the lung with diffuse skeletal metastases and pathological vertebral fracture causing paraparesis.

To obtain histopathological confirmation, a CT/MRI-guided biopsy from one of the spinal lytic lesions and bone marrow aspiration and biopsy were planned.

Due to the patient's severe osteoporosis and high fracture risk, spinal biopsy was deferred. Bone marrow examination was performed and returned normal, with no evidence of haematological malignancy or metastases.

Given the diagnostic uncertainty, further evaluation included:

- Cerebrospinal fluid (CSF) analysis via lumbar puncture, which showed:
 - o Normal glucose
 - o No cells or red blood cells (RBCs)
 - o Elevated protein (94 mg/dL) with albuminocytological dissociation, suggestive of possible arachnoiditis
 - o GeneXpert for *Mycobacterium tuberculosis* (MTB), adenosine deaminase (ADA), and acid-fast bacilli (AFB) stain: Negative
 - o CSF BioFire, bacterial/fungal cultures, and malignant cytology: All negative
- Contrast-enhanced MRI brain: Normal

- Workup for multiple myeloma (serum protein electrophoresis [SPEP], serum free light chains, fluorescence in situ hybridisation [FISH] cytogenetics): Negative
- Serum calcium, vitamin D3, and parathyroid hormone (PTH) levels: Normal
- Extended infectious panel (sputum for AFB/GeneXpert, venereal disease research laboratory (VDRL), viral markers, urine *Histoplasma* antigen, serum galactomannan, and β -D-glucan): All negative
- Antinuclear antibody by immunofluorescence (ANA-IF): Negative

To obtain a histological diagnosis, a CT-guided sternal biopsy was pursued for its accessibility. Histopathology showed (Figure 3):

- Necrotising granulomatous inflammation
- No AFB
- No malignant cells

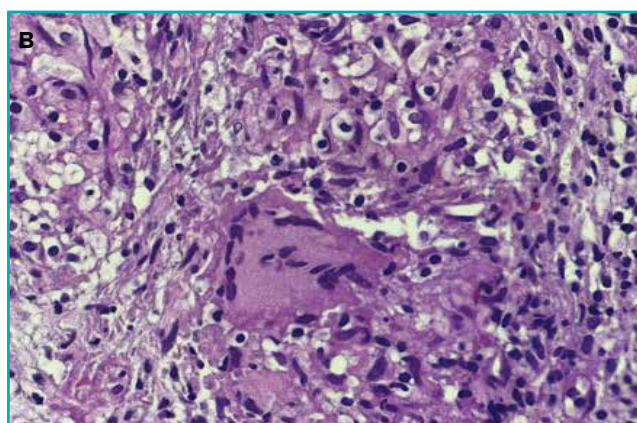
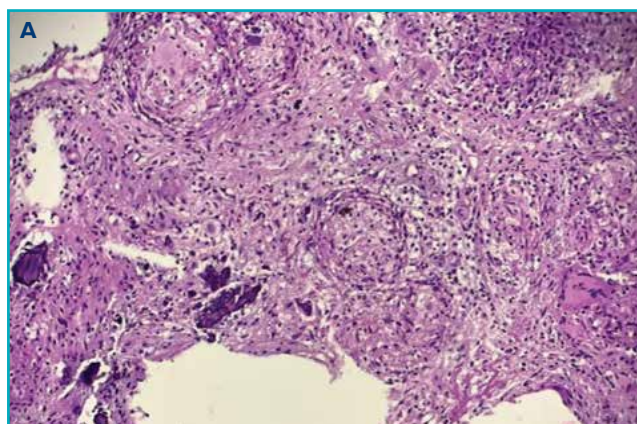


Figure 3: Necrotising granulomatous inflammation — haematoxylin and eosin stain: A. 10X, B. 40X.

Given the absence of malignant cells and the histological picture, empirical anti-TB therapy (ATT) was initiated at low doses while awaiting mycobacterial culture results. The patient was also managed conservatively for the vertebral compression fracture with spinal bracing and analgesics per neurosurgical advice.

After 34 days, culture of the sternal biopsy in BACTEC Mycobacteria growth indicator tube (MGIT) grew MTB complex, rifampicin-sensitive. By this time, the patient had already shown marked clinical improvement, including recovery of power in the lower limbs.

Final Diagnosis

- Pulmonary TB — Drug sensitive (presenting as a solitary pulmonary nodule)
- Pott's spine — Multifocal skeletal TB (MSTB) with compression fracture at T10–T11 causing paraparesis

Treatment Initiated

The patient was started on standard first-line ATT comprising HRZE:

- H: Isoniazid 300 mg once daily (OD)
- R: Rifampicin 450 mg OD
- Z: Pyrazinamide 1000 mg OD
- E: Ethambutol 800 mg OD

Additionally, pyridoxine 20 mg OD was given for neuroprotection.

The planned treatment duration included an intensive phase of 2 months and a continuation phase of 10 months (with weight-based regimen modification).

Discussion

This case exemplifies the diagnostic complexity encountered when TB masquerades as metastatic malignancy, particularly in TB-endemic regions such as Southeast Asia.¹ The constellation of findings — progressive neurological deficits, constitutional symptoms, and imaging showing widespread lytic skeletal lesions with a solitary pulmonary nodule — created a compelling picture strongly suggestive of malignancy, highlighting the challenges clinicians face in differentiating these conditions.

TB has long been recognised as a great mimicker of various diseases, particularly malignancy. In this case, several factors contributed to the initial diagnostic confusion. The patient's presentation with progressive bilateral lower limb weakness, significant weight loss (15 kg over 6 months), night sweats, and chronic cough, combined with imaging showing extensive lytic lesions,

created a clinical picture highly suggestive of metastatic disease. The family history of lung adenocarcinoma in the patient's elder brother further reinforced clinical suspicion towards malignancy.

FDG PET–CT, while highly sensitive for detecting metabolically active lesions, has significant limitations in TB-endemic regions. Active TB granulomas demonstrate intense FDG uptake due to the high glucose metabolism of inflammatory cells, including macrophages, epithelioid cells, and lymphocytes surrounding the central necrotic nucleus. Studies have shown that TB causes false-positive results in 9 out of 11 staging cases and 12 out of 14 restaging cases when evaluated for malignancy.³ The maximum standardised uptake value (SUV_{max}) values often overlap significantly between TB and malignant lesions, with TB lesions commonly exceeding the traditional diagnostic threshold of 2.5.⁴ Some studies suggest that an SUV_{max} cut-off of 8.45 may be more appropriate for distinguishing TB from lung cancer in endemic areas.⁴

MSTB is an uncommon presentation, accounting for less than 5% of all bone TB cases.⁵ It typically occurs in immunocompromised individuals, making its occurrence in apparently immunocompetent patients, as in this case, particularly unusual.⁵ The condition can involve multiple non-contiguous vertebrae and other skeletal sites, making differentiation from skeletal metastases extremely challenging both clinically and radiologically. The rarity of this presentation contributes to diagnostic delays, as clinicians may not initially consider TB in the differential diagnosis of multifocal lytic lesions.

The histopathological finding of necrotising granulomatous inflammation without AFB initially presented a diagnostic challenge. However, studies have shown that the presence of necrotising granulomatous inflammation is highly suggestive of TB, with 85% of patients with necrotic granulomatous tissue having TB compared to only 14% with non-necrotic lesions.⁶ The absence of visible AFB does not exclude TB, as mycobacterial culture remains the gold standard for definitive diagnosis.⁶

The 34-day delay in culture confirmation underscores the challenges of rapid TB diagnosis. The use of BACTEC MGIT culture systems has improved detection rates and reduced diagnosis time compared to conventional methods. The eventual growth of rifampicin-sensitive MTB complex confirmed the diagnosis and guided appropriate therapy.

Myanmar ranks among the 30 countries with the highest TB burden globally and continues to face substantial barriers to effective TB control.⁷ High rates of untreated and drug-resistant TB present significant challenges to effective diagnosis. In such endemic settings, TB should always be considered in the differential diagnosis of

destructive spinal processes, even when clinical and radiological features suggest malignancy.

The patient's history of successfully treated pulmonary TB at 1.5 years of age raised questions about possible reactivation versus reinfection. While childhood TB treatment typically provides some immunity, reactivation or reinfection can occur, particularly in endemic areas with continued exposure risk.

Pott's disease accounts for approximately 50% of skeletal TB cases. The thoracic spine involvement, as seen in this patient with T10–T11 compression fracture, is particularly prone to neurological complications due to the narrow spinal canal and limited space for cord accommodation. The progressive paraparesis with areflexia in the lower limbs is consistent with the typical presentation of thoracic spine TB.

The decision to initiate empirical ATT based on necrotising granulomatous inflammation, despite negative

microbiological studies, proved appropriate. The marked clinical improvement observed before microbiological confirmation supported the diagnosis. This approach is often necessary in TB-endemic regions where high clinical suspicion exists, particularly when tissue biopsy shows characteristic histopathological features.

The planned 12-month treatment duration (2 months intensive phase, 10 months continuation phase) follows standard recommendations for bone and joint TB, which typically requires longer treatment than pulmonary TB due to the avascular nature of bone tissue and slower drug penetration.

This case highlights that in regions where TB is endemic, the traditional clinical maxim 'when you hear hoofbeats, think horses, not zebras' may not always apply — TB often mimics other conditions. Continued clinical vigilance and comprehensive diagnostic evaluation are essential to ensure accurate diagnosis and optimal patient care.

Conclusion

This case highlights the formidable challenge of distinguishing TB from metastatic malignancy, particularly in endemic regions where the disease often presents with atypical and deceptive features. MSTB with spinal involvement can closely mimic disseminated malignancy, both clinically and radiologically, leading to significant diagnostic uncertainty. Early recognition, careful integration of clinical, radiological and histopathological findings, and timely initiation of empirical therapy remain crucial for favourable outcomes. The patient's clinical improvement prior to microbiological confirmation underscores the importance of maintaining a high index of suspicion for TB in similar presentations. Ultimately, this case reinforces the need for vigilance, multidisciplinary collaboration and context-specific diagnostic strategies to prevent misdiagnosis and ensure appropriate management.

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Through the Veil: Magnetic Resonance Imaging Mapping of Placenta Percreta with Bladder Invasion in a Scarred Uterus

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Abstract:

Magnetic resonance imaging (MRI) plays a pivotal role in antenatal diagnosis of placenta percreta, particularly when ultrasound findings are equivocal. Timely intervention improves maternal and foetal outcomes. We present a case of a 35-year-old gravida 2, para 1, live 1 (G2P1L1) woman with a history of prior lower segment caesarean section (LSCS) at 31 weeks of gestation with leaking per vaginum. This was a rare but life-threatening case of placenta percreta diagnosed antenatally by MRI in a patient with preterm premature rupture of membranes. MRI revealed features of placenta percreta, including loss of the uteroplacental interface, placental bulge, and bladder invasion. Caesarean delivery and hysterectomy were performed with intraoperative management of massive haemorrhage and bladder invasion. With this case study, we aim to emphasise the value of prompt imaging in maternal-foetal outcomes.

Key words: Placenta Percreta, Magnetic resonance imaging (MRI), Placenta Accreta Spectrum (PAS), Bladder Invasion, Obstetric Haemorrhage, Hysterectomy.

Introduction

Placenta accreta spectrum (PAS) includes placenta accreta, increta, and percreta — defined by progressive degrees of abnormal placental adherence and invasion into the myometrium and adjacent pelvic organs. With the global rise in caesarean deliveries, PAS incidence has surged from 1 in 2500 to nearly 1 in 533 pregnancies.¹ Early and accurate diagnosis is crucial for reducing maternal morbidity and mortality associated with massive haemorrhage and organ injury during delivery. Ultrasound remains the initial imaging modality, but magnetic resonance imaging (MRI) is increasingly recognised for its superior soft tissue contrast and ability to delineate the depth of invasion.²

Case Report

A 35-year-old gravida 2, para 1, live 1 (G2P1L1) woman with a prior lower segment caesarean section (LSCS)

presented at 31 weeks of gestation with complaints of leaking per vaginum since morning. The patient informed us that her last menstrual period was on 25th October 2024. She had been diagnosed with gestational diabetes mellitus a month prior and was on metformin 500 mg daily.

Foetal movements were normal, and baseline investigations, including complete blood count (CBC), coagulation profile, renal and liver function tests, were within normal limits.

Ultrasound investigation

Antenatal ultrasound showed an anterior placenta with grade II–III maturity. Multiple placental lakes were visualised. The myometrial-placental interface was poorly visualised in the lower uterine segment, raising concern for PAS. Colour Doppler studies revealed normal resistive

indices. Mild polyhydramnios was also present. Based on these findings, MRI was advised to further evaluate suspected placental invasion (Figure 1).



Figure 1: Antenatal ultrasound showing an anterior placenta with placental lake indicated by a red star and loss of the myometrium and placental junctional complex indicated by the blue arrow.

MRI investigation

MRI performed on a 3T scanner revealed a single live intrauterine gestation in cephalic presentation. The anterior placenta demonstrated heterogeneous signal intensity, with loss of the uteroplacental interface and a placental bulge measuring 12.9 cm (superoinferior [SI]) × 12 cm (transversely [TR]). Numerous placental lacunae and prominent intra placental flow voids were seen. Importantly, there was a loss of the fat plane between the placenta and urinary bladder, with mild irregularity at the interface, strongly suggesting bladder invasion, consistent with placenta percreta (Figures 2–6).

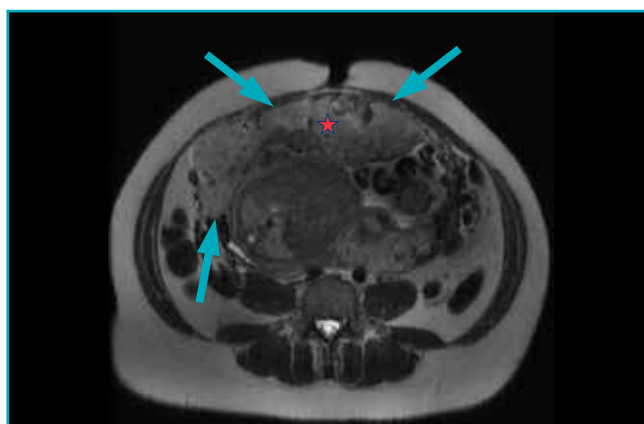


Figure 2: Axial T2-weighted magnetic resonance imaging (MRI) showing placental bulge with heterogeneous signal intensity indicated with a red star and loss of uteroplacental interface indicated by blue arrows.

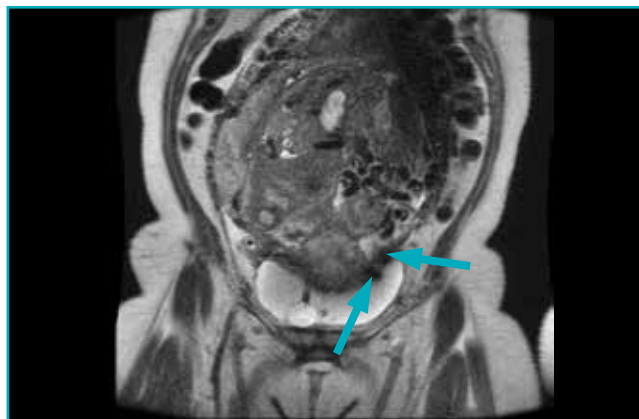


Figure 3: Coronal T2 magnetic resonance imaging (MRI) showing bladder wall invasion with prominent blood vessels indicated by blue arrows.

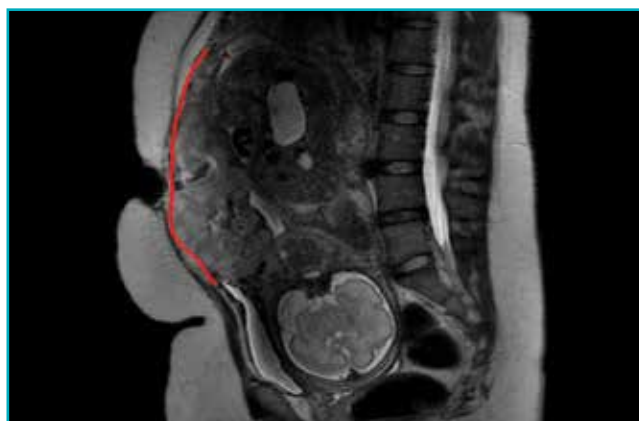
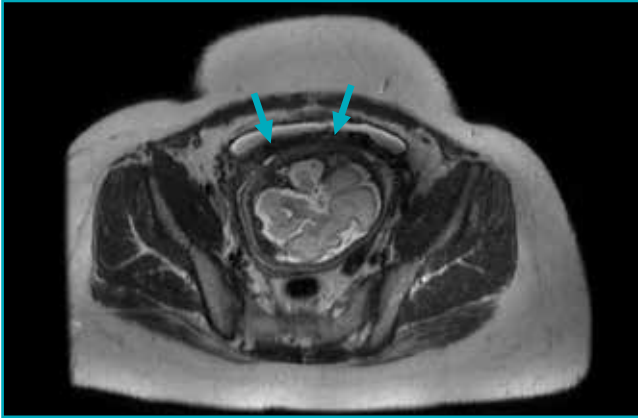


Figure 4: Sagittal magnetic resonance imaging (MRI) showing absence of myometrium along the entirety of the anterior placental margin, represented by a red line.



Figure 5: Sagittal magnetic resonance imaging (MRI) showing placental extension beyond the uterine serosa with obliteration of the fat plane between placenta and bladder (indicated by red star) as indicated by blue arrows.



▼ **Figure 6:** Axial T2-weighted magnetic resonance imaging (MRI) showing loss of the bladder interface with bladder wall invasion (blue arrows).

Surgical and postoperative management

The patient underwent emergency caesarean section followed by an obstetric hysterectomy. Dense invasion of the posterior bladder wall by the placenta was confirmed intraoperatively (Figure 7). Multidisciplinary involvement of cardiovascular and urology teams was necessary. Bilateral internal iliac artery ligation was performed to control haemorrhage. The invaded bladder segment was partially resected and repaired. Estimated blood loss was 7.5 litres; the patient received multiple blood products. The neonate was stabilised in the neonatal intensive care unit (NICU).

Postoperatively, the patient required intensive care monitoring but had an uneventful recovery and was discharged on Day 10.



▼ **Figure 7:** Intraoperative image showing completely thinned out myometrium with the underlying placenta, along with bulging vessels.

Discussion

Placenta percreta is the most severe form of PAS and can result in catastrophic haemorrhage, bladder injury, and maternal death if not diagnosed preoperatively.³ Risk factors include previous caesarean section, placenta praevia, advanced maternal age, and multiparity. In this case, the presence of a scarred uterus from prior LSCS and an anterior placenta raised the index of suspicion.

Role of imaging

Ultrasound is the first-line modality for PAS screening. The key features include:

- Loss of clear zone between placenta and myometrium
- Multiple placental lacunae ("swiss-cheese" appearance)
- Myometrial thinning (< 1 mm)
- Bladder wall interruption on colour Doppler⁴

However, ultrasound has limitations, especially in posterior placentas or when the lower uterine segment (LUS) is obscured. In such cases, MRI serves as a powerful adjunct. It offers:

- High soft tissue resolution
- Multiplanar evaluation
- Detailed depiction of the depth and lateral spread of invasion
- Better visualisation of posterior placentas, bladder interface, and extrauterine extension^{5,6}

In this patient, MRI demonstrated with clarity:

- Uteroplacental interface loss
- Placental bulge and heterogeneity
- Flow voids (indicative of increased vascularity)
- Loss of bladder fat plane with irregularity — predictive of bladder invasion, later confirmed surgically

MRI findings in PAS have shown high specificity (82%–100%) and positive predictive value (90%–100%), especially for placenta percreta and bladder involvement.⁵

Multidisciplinary planning

MRI allows surgeons to plan the extent of surgery, anticipate intraoperative challenges, and arrange blood products and multidisciplinary teams. The preoperative diagnosis enabled prompt involvement of urologists and vascular surgeons in this case, crucial in managing massive bleeding and bladder resection.

Acknowledgements

We thank the Departments of Obstetrics, Anaesthesia, and Urology for intraoperative support and the NICU staff for neonatal care.

Conclusion

This case underscores the critical role of MRI in the evaluation of PAS, particularly placenta percreta. MRI not only enhances diagnostic accuracy but also facilitates optimal surgical planning, reduces intraoperative surprises, and improves maternal-foetal outcomes. Integration of MRI into protocols for suspected PAS is strongly recommended, especially in high-risk patients.

Nikita Singh, Mitusha Verma, Deepak Patkar. Through the Veil: Magnetic Resonance Imaging Mapping of Placenta Percreta with Bladder Invasion in a Scarred Uterus. MMJ. 2025, September. Vol 2 (3).

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Revealing the Hidden Pathogen: The Role of Positron Emission Tomography in Diagnosing Amoebic Liver Abscess in an Immunocompetent Patient

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Abstract:

A 26-year-old male reported with high-grade fever accompanied by chills and rigours persisting for four days, followed by vomiting and dull, aching pain in the right hypochondrium. Laboratory investigations revealed leucocytosis with raised procalcitonin levels. An abdominal ultrasound (USG) showed no liver parenchymal abnormalities. As the patient's symptoms persisted despite antibiotic therapy, a comprehensive pyrexia of unknown origin (PUO) workup was undertaken. Serological tests for *Toxoplasma*, Epstein-Barr virus (EBV), anti-capsid antibodies, tropical fever panel, cytomegalovirus (CMV) immunoglobulin G (IgG) and immunoglobulin M (IgM), as well as blood cultures (aerobic and anaerobic), proteinase-3 (PR-3, cytoplasmic antineutrophil cytoplasmic antibody [c-ANCA]), and myeloperoxidase (MPO, perinuclear antineutrophil cytoplasmic antibody [p-ANCA]) were all negative. Anti-nuclear antibody (ANA) testing showed cytoplasmic speckled positivity. A positron emission tomography-computed tomography (PET-CT) scan revealed a liver abscess (amoebic) with marked hepatomegaly and an abscess in segment VIII of the liver. Intravenous (IV) metronidazole 750 mg three times daily and oral hydroxychloroquine 200 mg once daily were immediately started. CT-guided drainage of the abscess yielded around 210 mL of anchovy-sauce-like pus, which tested positive for *Entamoeba histolytica* (EH). The patient improved clinically, remained haemodynamically and vitally stable and was subsequently discharged.

Key words: Right Hypochondrial Pain, USG Abdomen, Anchovy Sauce, Intravenous Metrogyl, CT-Guided Drainage of Abscess.

Introduction

Amoebic liver abscess (ALA) is a parasitic infection resulting from *Entamoeba histolytica* (EH), an intestinal protozoan. Transmission typically occurs through the consumption of food or water contaminated with the cyst form of EH, which is the infective stage. These cysts withstand gastric acidity and travel to the distal ileum, where they excyst to release trophozoites — the active, feeding form of the parasite. In over 90% of infected

individuals, trophozoites remain confined to the intestinal lumen, feeding on bacteria and mucosal cells without causing clinical symptoms. However, in less than 1% of cases, the trophozoites invade the intestinal mucosa and spread to the liver via the portal circulation, leading to the formation of liver abscesses. Among the various clinical presentations of amoebiasis, ALA is the most prevalent and carries the highest risk of mortality. It continues to

be the leading cause of liver abscess in developing and resource-limited settings.¹

Although asymptomatic EH infections occur at similar rates in both genders, invasive amoebiasis, particularly ALA, is significantly more common in males, who are four to nine times more likely to develop the condition than females. This gender disparity has been documented even among travellers from non-endemic regions. The heightened susceptibility in males is believed to be associated with hormonal influences — particularly testosterone — as well as higher rates of alcohol consumption. Once EH trophozoites invade the colonic mucosa, they can reach the liver through the portal venous system. The right lobe of the liver is most frequently affected, likely because it receives the majority of portal blood via the superior mesenteric vein, which drains the caecum — the primary site of trophozoite invasion.²

Each year, EH is responsible for an estimated 40,000 to 100,000 deaths worldwide, making it the second leading cause of mortality among parasitic infections, surpassed only by malaria. Although invasive amoebiasis develops in less than 10% of infected individuals, once the parasite overcomes the host's innate immune defences, it can lead to serious complications such as amoebic colitis and liver abscesses. At the molecular level, EH employs a key virulence factor known as the Gal/GalNAc lectin to facilitate tissue invasion. This lectin plays a dual role: it enables the parasite to adhere to and invade host tissues and simultaneously triggers an antibody response that can inhibit further adherence, offering some degree of protection against recurrent or severe disease.³

Clinically, amoebiasis presents in two primary forms: intestinal and extraintestinal. The intestinal form, which is the most common, arises when EH invades the colonic mucosa — typically in the caecum or ascending colon. Clinical manifestations range from mild abdominal discomfort to severe ulcerative colitis, characterised by bloody and mucus-laden stools, also known as

amoebic dysentery. On the other hand, extraintestinal amoebiasis occurs when the parasite spreads beyond the gastrointestinal tract, affecting other organs. Among these, hepatic amoebiasis (liver abscess) is the most frequent, followed by pulmonary involvement, making the liver and lungs the two most commonly affected sites in extraintestinal disease.⁴

Case Report

A 26-year-old male patient presented with complaints of high-grade fever with chills and rigours persisting for four days, followed by vomiting containing food particles (non-bilious, non-blood stained) and dull aching, continuous, abdominal pain in the right hypochondrial region. The patient had a recent history of outside food consumption. There were no complaints of loose stools, haematochezia, or malaena. There was no significant past medical history, drug allergies, chronic illnesses or chronic drug use.

On presentation, the patient's vitals were as follows: he was febrile with a temperature of 101.9°F, blood pressure 110/70 mmHg, pulse rate 114 beats per minute (bpm), and SpO₂ 98% on room air. Physical examination revealed intercostal tenderness in the right hypochondrial region. Bowel sounds were normal, and the rest of the systemic examination was unremarkable. The patient was empirically started on intravenous (IV) levofloxacin 500 mg once daily and ceftriaxone 1 g twice daily, along with other supportive measures.

Initial laboratory investigations indicated an infectious aetiology, as shown by leucocytosis (white blood count [WBC] 13,150) and raised procalcitonin (1.6). Imaging studies, including abdominal ultrasonography (USG), suggested partial gallbladder distension but no liver parenchymal involvement. Chest X-ray was normal. The prothrombin time/international normalised ratio (PT/INR) was 14.6/1.34. Urine routine was normal. Laboratory investigations are shown in Table 1.

Day of Admission	Hb (g/dL)	WBC (/μL)	Platelets	Na (mEq/L)	K/Cl (mEq/L)	Creatinine (mg/dL)	PCT (ng/mL)	SGOT/SGPT (U/L)
Day 1	12.2	13150	237000	133	4.0/97	0.8	1.6	
Day 2	12.1	15330	259000					
Day 3	12.3	16820	270000			0.9	1.87	33.8/42.7
Day 4	12.4	18080	309000	136	4.0/100	0.85		
Day 5	12.6	23390	354000			1.64		
Day 7	11.4	25790	377000					
Day 9	11.2	21680	447000	136	3.33/101		0.63	
Day 10	11.2	15580	581000	133.4	3.4/97.4			

Table 1: Laboratory investigations.

Abbreviations: Cl: Chloride; Hb: Haemoglobin; K: Potassium; Na: Sodium; PCT: Procalcitonin; SGOT: Serum Glutamic-Oxaloacetic Transaminase; SGPT: Serum Glutamic-Pyruvic Transaminase; WBC: White Blood Cell.

Considering persistent fever and abdominal symptoms, and as the patient did not respond to antibiotics, further investigations for pyrexia of unknown origin (PUO) were conducted. Serologies for *Toxoplasma*, Epstein–Barr virus (EBV), anti-capsid antibodies, and a tropical fever panel were all negative. Further investigations revealed cytomegalovirus (CMV) immunoglobulin G (IgG) at 11 (negative) and immunoglobulin M (IgM) non-reactive; blood cultures (aerobic and anaerobic) showed no growth, proteinase-3 (PR-3, cytoplasmic antineutrophil cytoplasmic antibody [c-ANCA]) and myeloperoxidase (MPO, perinuclear antineutrophil cytoplasmic antibody [p-ANCA]) were negative, antinuclear antibody (ANA) showed cytoplasmic speckled positivity; ferritin was elevated at 739 ng/mL; lactate dehydrogenase (LDH) was 185 U/L, and triglycerides were 113 mg/dL.

A positron emission tomography–computed tomography (PET–CT) scan was subsequently performed to determine the fever aetiology, which revealed findings consistent with a liver abscess (amoebic) (Figures 1 and 2). There was marked hepatomegaly and an abscess in segment VIII of the liver. The cupola of the right diaphragm was elevated, secondary to hepatomegaly. The liver measured about 17.0 cm in the long axis and extended below the right costal margin. A large, peripherally enhancing lesion in segment VIII, extended to the hepatic capsule, measuring 8.0 x 7.6 cm in maximal axial dimension, with a cephalocaudal extent of about 7.3 cm and an approximate volume of 220 cm³. The wall thickness ranged from 5 to 9 mm. It was surrounded by a hypoattenuating zone of hepatic oedema, exhibiting metabolic activity with maximum standardised uptake value (SUV_{Max}) of 7.0.

Periportal hypoattenuation was suggestive of periportal oedema, with no dilatation of the intrahepatic biliary radicals. The intrahepatic vasculature was normal.

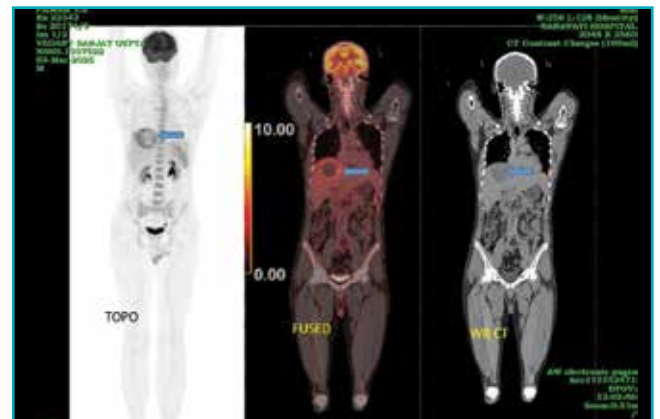


Figure 1: Positron emission tomography–computed tomography (PET–CT) imaging with blue arrows showing the amoebic liver abscess.

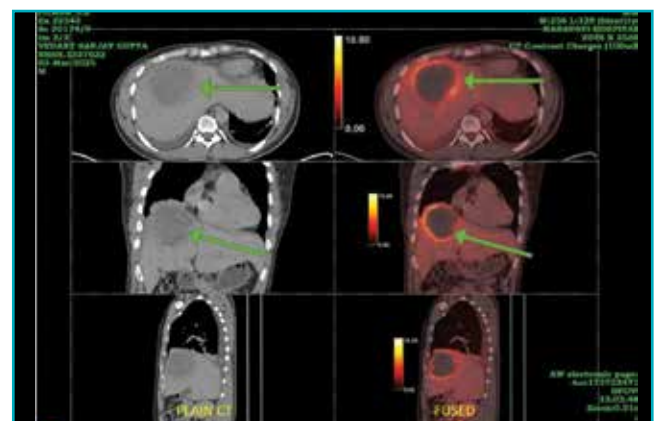


Figure 2: Positron emission tomography–computed tomography (PET–CT) imaging with green arrows showing the liver abscess.

Intravenous metronidazole 750 mg thrice daily and oral hydroxychloroquine 200 mg once daily were immediately started. CT-guided drainage of the abscess was performed, and around 210 mL of pus resembling anchovy sauce was drained. The pus was sent for further examination which confirmed EH.

The patient's fever gradually resolved, and his symptoms improved. He responded well to treatment, becoming afebrile and haemodynamically stable. Hence, he was discharged after seven days of IV antibiotics, with advice to continue oral metronidazole 400 mg twice daily and hydroxychloroquine 200 mg once daily for a further 14 days. At follow-up in the outpatient department, the patient was asymptomatic and haemodynamically stable.

Discussion

The term amoebic liver abscess (ALA) is somewhat misleading, as cavity formation and liquefaction do not result from suppuration but rather from a distinctive type of necrosis. The necrotic tissue appears as though chemically dissolved, leading to the early belief that EH secretes a toxin capable of lysing hepatocytes — hence the species name *histolytica*. However, it is now understood that proteolytic enzymes released primarily by inflammatory cells, play the central role in hepatic tissue destruction.

The gross morphology of ALA varies according to disease stage and severity. In the early phase, lesions consists of a central area of liquefied necrotic tissue, often described as chocolate-coloured sterile pus. This liquefied material within the abscess contains red blood cells (RBCs), leucocytes, and disintegrated hepatocytes, producing the classic reddish-brown appearance often likened to chocolate sauce or anchovy sauce. This necrotic core is surrounded by a zone of partially liquefied and solid tissue, giving the abscess wall a ragged or shaggy appearance. Notably, a mature fibrous capsule is absent at this stage. The surrounding hepatic tissue is typically congested, compressed, and oedematous, and mass effect may cause pressure on adjacent liver parenchyma or the hepatic capsule. In fatal cases, venous thrombosis and ischaemic infarction are frequently observed.

Clinically, ALA manifests in three forms:

- Subacute mild ALA (~80%) is the most common form. It develops over 2–4 weeks with low-grade

symptoms like fever, right upper quadrant pain, and hepatomegaly. Symptoms usually resolve rapidly with medical treatment. A characteristic finding on physical examination is localised tenderness over the right intercostal spaces. Organ dysfunction is minimal or absent.

- Acute aggressive ALA (~13%) is severe and rapidly progressive, presenting with high-grade fever, chills, and pronounced right upper quadrant tenderness due to exquisitely tender hepatomegaly. One of the hallmark features of this form is spontaneous abscess rupture, which may be the initial presentation in up to 57% of cases. Free intraperitoneal rupture frequently results in generalised peritonitis, necessitating hospitalisation, abscess drainage, and carries high mortality. Due to its severity, hospitalisation is required in up to 90% of cases, and around 13% may necessitate intensive care unit (ICU) admission. Misdiagnosis is common, as clinical features overlap with acute cholecystitis, appendicitis, or bowel perforation. Unlike in subacute disease, medical therapy alone is often insufficient. In most cases, abscess drainage — either via needle aspiration or catheter insertion — is required to achieve clinical improvement.
- Chronic indolent ALA (~10%–20%) is prolonged and milder, presenting with dull pain, systemic symptoms like weight loss, and complications like secondary infection. A history of previous medical therapy or even prior needle aspiration is frequently reported. Imaging plays a key role in evaluation.

Imaging plays a critical role in differentiating these clinical forms. Contrast-enhanced CT is particularly valuable, as it differentiates viable hepatic tissue from necrotic areas, allowing better distinction between chronic necrotic masses and active, aggressive abscesses. Acute ALA (Type 1) typically appears as ragged-edged lesions; subacute ALA (Type II) shows rim-enhancing walls with a thin rim of perilesional oedema, producing a “halo sign”; chronic ALA (Type III) demonstrates thick, non-enhancing fibrotic walls.¹

ALA has a highly variable presentation, causing diagnostic difficulties. Uncommon manifestations occur due to abscess rupture into neighbouring cavities — pleura, pericardium, peritoneum — or compression of tubular

structures in the hepatic hilum, or distant embolic dissemination.⁵ The diagnosis of ALA is confirmed by microscopic examination of aspirated pus, which characteristically resembles anchovy sauce. Aspiration is particularly indicated when the abscess exceeds 10 cm, shows a thin rim of liver parenchyma suggesting impending rupture, or demonstrates rapid enlargement.⁶

The laboratory diagnosis of amoebiasis relies on a combination of parasitological, serological, and molecular methods. Parasitological techniques, such as microscopy and culture, remain foundational, with microscopic detection of EH in stool, tissue, or body fluid samples still considered the diagnostic gold standard. However, microscopy is limited by low sensitivity and specificity, especially in distinguishing EH from non-pathogenic species. Serological tests such as enzyme-linked immunosorbent assay (ELISA), indirect haemagglutination assay (IHA), and latex agglutination are widely used for diagnosing extraintestinal amoebiasis, where stool microscopy often fails. In recent decades, the

polymerase chain reaction (PCR) technique has emerged as a highly sensitive and specific tool for detecting EH deoxyribonucleic acid (DNA). In addition, imaging modalities such as USG, CT, magnetic resonance imaging (MRI), and radiography have become valuable adjuncts for diagnosing hepatic and other extraintestinal forms of amoebiasis, aiding in localisation, characterisation, and monitoring of abscesses and other lesions.⁴

Metronidazole remains the most effective agent, with cure rates approaching 90%.¹ It is typically administered IV at 750 mg three times daily for 7–10 days. In severe cases, other agents such as emetine, dehydroemetine, and chloroquine may be considered. The risk of complications increases with larger abscess size and multiplicity of abscesses. Autopsy studies reveal that up to 60% of fatal cases involve multiple abscesses, often measuring 10 to 15 cm. Comparative data from Southeast Asia report a higher incidence of large (> 5–10 cm) and multiple abscesses in approximately 50% of cases, highlighting geographic variation.¹

Conclusion

Liver abscess is usually diagnosed by USG abdomen as a hypoechoic lesion; however, in its early stages, it may appear isoechoic and thus be missed. Hence, in early stages if sonography is inconclusive, particularly in patients with PUO, CT or PET imaging should be performed to facilitate early diagnosis.

Nitin Rathod, Andrea Janice Fonseca, Rajat Shende, Harsh Jani. Revealing the Hidden Pathogen: The Role of Positron Emission Tomography in Diagnosing Amoebic Liver Abscess in an Immunocompetent Patient.

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Research Methodology and Biostatistics
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A Note to Future Clinicians – **Ranee Thakar**

Research Methodology and Biostatistics Series VII – Guard Against Biases for Validity of the Findings

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Abstract:

Various biases, knowingly or unknowingly can creep into medical research, affecting the validity of findings and often lead to disappointing results when applied in real-world settings. This article provides a concise overview of more than 30 types of biases that can adversely influence research outcomes. The objective is to raise readers' awareness of these biases so that pre-emptive actions can be taken to ensure study validity, and thereby enhance the credibility of the findings.

Key words: Biases in Research, Validity of Findings, Selection Bias, Data Bias, Analysis Bias, Minimising Bias.

Introduction

Random errors occur due to sampling fluctuations and other uncontrollable factors, whereas biases are systematic errors that can, at least in part, be avoided, or controlled. Biases tend to invalidate the results and give false findings. They affect validity and should not be confused with reliability.

The concepts of reliability and validity were explained in the second article of this series. While reliability refers to the consistency of results when studies are repeated in the same or similar population, validity on the other hand, concerns whether the study truly measures or reflects the intended target. A study can be reliable — producing the same results each time — but still invalid if those results are consistently wrong. Both reliability and validity contribute to the credibility of research findings, but validity is more important. Without validity, findings may deviate from reality, rendering the entire effort futile.

Since biases affect validity, it is important to give them full consideration during the planning and execution of

a study and to avoid them wherever possible. It may not be possible to eliminate all biases, but any bias that persists despite best efforts should be explicitly stated as a study limitation, allowing for cautious interpretation of the findings.

Biases in medical investigations can occur at multiple stages. For convenience, they may be divided into 4 categories:

1. When conceptualising the problem and defining the study population
2. During the selection of cases and controls
3. At the data collection stage
4. During analysis and interpretation.

This article briefly describes these biases — further details can be found in Indrayan and Holt¹ — and concludes with practical steps to avoid or minimise bias and control its impact on results.

Biases in Concepts and Definitions

I regularly see proposals comparing two procedures to determine which is better for a particular differential diagnosis, but the gold standard is not specified. The assessment of 'better' cannot be done without a clear reference. If the gold standard is as straightforward as a regular clinical assessment, then the value of evaluating a new procedure is questionable. Although no medical procedure is 100% accurate, the gold standard should be as close as possible to this ideal. Moreover, the gold standard should be relatively more complex or expensive than the procedure under evaluation to make the research more meaningful. Imprecisely defining the research problem at the outset leads to difficulties later, often without being recognised until too late.

Take, for example, studies on diabetes. Will you include cases with fasting blood glucose (FBG) level ≥ 126 mg/dL or glycated haemoglobin (HbA1c) ≥ 6.5 or both? How will you classify patients with elevated FBG but normal HbA1c? Similarly, for hypertension, will you define cases as those with systolic blood pressure (BP) level ≥ 140 mmHg and diastolic BP ≥ 90 mmHg, or just one or the other. What about a case with systolic BP of 138 mmHg and diastolic BP of 92 mmHg? Some studies might even use thresholds of 135/85 or 160/95. The results will vary depending on the chosen definition. If one study uses 140/90 and another uses 135/85, their results are not directly comparable, although both are evaluating cases of hypertension. A target population must be sharply defined with strict inclusion and exclusion criteria that are applied consistently when recruiting participants.

Similar issues arise when defining cancer populations. If you decide to study colon cancer cases, are you including only those who present to a hospital — some at an early stage and others at an advanced stage? Findings could differ significantly between these groups. Likewise, in studies of elderly patients, even specifying "age 70 years and above", may be inadequate. Patients aged 80 or 90 years often respond very differently than those of age 70 years because of age-related degeneration. Pooling these groups without stratification may lead to results that fail to hold in practice. All these aspects should be clearly specified to avoid biased findings.

Another common source of bias is an ill-defined outcome measure. Merely stating that the outcome is "response" or "improvement after a regimen" is insufficient unless the

exact measurement criteria are specified. For example, a reduction in pain by at least three points on the visual analogue scale (VAS), ability to walk without assistance for at least two meters at a fixed time-point after treatment initiation, duration of hospitalisation, mortality rate, or any such event. Even mortality assessment must include the time frame, since all patients eventually die, but the research interest may lie specifically in hospital mortality. Additionally, old age is a major confounding factor in any mortality analysis and must be accounted for during analysis.

Many researchers, particularly at postgraduate level, fail to define outcomes with the necessary precision. Without explicit criteria, subjectivity creeps in, undermining the study validity.

Biases in Selection of Subjects

An obvious bias occurs when the results derived from hospitalised cases are generalised to all cases of a disease. Patients admitted to hospital tend to be more severe and also represent those who have the means — financial, social, or logistical — to access hospital care. Socioeconomic factors can further distort outcomes; for example, differences in nutrition status across social classes may significantly influence results. To reduce such bias, it is highly recommended to draw a random sample from the target population. The sample size must be large enough to represent the full cross-section of subjects from the target population. A small sample, even if random, risks coverage bias.

Similarly, results from studies conducted on specific groups, such as employees of a company, or teachers, may not be applicable to the general population, as these groups may have different health or nutritional profiles. Studies based on convenience samples (subjects who are readily available or who volunteers) can also lead to bias.

Survival bias is another issue in studies on older populations: the individuals available for study are those who have already survived to that age and may therefore be healthier than those who died earlier and are no longer represented.

Mixing newly diagnosed cases with those who are already undergoing treatment can distort findings, as treatment modifies response patterns. In field studies, men may be underrepresented if they are away at work during data collection, leading to sex-related bias.

In case-control studies, controls must be matched to cases for all relevant factors except the disease itself. In practice, this matching is rarely assured in clinical studies. Historical controls can also introduce bias, as diagnostic methods and treatment strategies may have improved in the intervening period. In clinical trials, baseline imbalances between test and control groups can skew results; that is why random allocation is advocated.

Before–after study designs are particularly vulnerable to bias from the placebo effect and confounding factors over time. Such biases cannot be corrected without repeating the study using parallel control groups. For this reason, before–after studies are of limited value and, ideally, should be avoided altogether.

Finally, ethical considerations require obtaining an informed consent from all participants. However, individuals who are apprehensive, severely ill, or exceptionally healthy may refuse participation. This can introduce unintentional bias, and the results from such studies should be interpreted with caution.

Biases in Data Collection

Most biases occur at the stage of data collection. The tools and instruments used for assessment must be checked for their validity. Laboratory investigations should ideally be conducted in an accredited laboratory, preferably using automated equipment. For biochemical measurements such as creatinine, the analytical method (e.g., Jaffe Kinetic) must be specified, as alternative methods may yield different results. If a tool such as a questionnaire is used, it must be pretested and validated, and designed to avoid leading questions that suggest a particular answer. Interviewers must be adequately trained to establish rapport and get accurate responses. Similarly, scoring systems if used, must be validated for the specific patient group under study.

In clinical assessments, differences in assessor skill can distort results. Some clinicians are more proficient than others and cognitive bias — where an assessor's values or preferences influence judgement — can easily creep in. This risk is not limited to humans; similar bias can appear in large language models² currently being developed. Blinding is therefore frequently employed in clinical trials to obtain unbiased responses. Another issue is that some assessors reach conclusions too quickly, which may subsequently be found to be inadequate or incorrect.

All cases must be assessed at the same stage of disease progression, such as at onset, or at a fixed follow-up point (e.g., 3 months post-discharge). The varying time gap between onset and detection or admission in different cases, called length bias, may influence the results. Differences in disease severity between patients must also be statistically adjusted to avoid bias.

Non-adherence and non-response (partial or full) commonly introduce bias in the findings. Subjects may feel disillusioned, cheated, fatigued or overwhelmed by sustained questioning or intensive investigations. In follow-up studies, dropouts are common. Unequal or differential care — for example, when some patients are treated by one clinician and others by another — can bias findings, as can the pooling of data from patients who receive different treatments.

Telephonic interviews, sometimes done for follow-up of patients, are particularly prone to error: patients may be unavailable despite repeated calls, or they may provide careless or inaccurate information. High non-response rates produce serious bias. Even when patients are physically recalled, those who feel better may fail to attend, while those who deteriorate may move to other facilities.

Recall bias is common in patient interviews: some patients remember every event in detail, whereas others forget minor episodes and recall only major ones. Confounding bias³, —where the effects of two or more factors become inextricably mixed — can sometimes be identified but often remains hidden, especially when knowledge is limited. Many patients, particularly older ones, take multiple treatment or supplements, and these can affect responses if not properly documented. Co-existing illnesses — whether treated or not — can also skew findings. Fortunately, statistical methods can help account for these biases when the number of variables is limited, and the study design is robust.

Another subtle source of error is digit preference, particularly documented in BP measurement.⁴ Observers tend to favour terminal digits such as 0 and 5, recording, for example, both 139 and 141 as 140. This reduces the standard deviation and biases results. To address this, BP categories such as 125–134, 135–144 are advocated instead of the usual 120–129, 130–139.

Biases in Analysis and Interpretation

While the use of inappropriate analytical methods is a concern, a more insidious issue is dredging — sometimes described as “torturing the data till it confesses”. Investigators may try multiple forms of analysis and selectively report whichever method produces the desired result.

Even simple factors can be manipulated in this way. Take anaemia, its impact may be analysed using haemoglobin values as a continuous variable or by applying a threshold to classify patients as anaemic or not. The choice of threshold — 10 mg/dL versus 9 mg/dL or 11 mg/dL — can substantially alter results. Occasionally, thresholds are deliberately chosen to fit the investigator’s hypothesis, a practice that often goes unnoticed by readers.

P-values are among the most widely used statistical measures to draw conclusions. In very large samples, even trivial differences can produce $p < 0.05$, giving a false impression of importance. Some statisticians recommend using $p < 0.001$ for extremely large samples⁵ to minimise errors, but this is rarely followed. Moreover an excessive use of statistical significance has overshadowed clinical or medical significance of the results. Encouragingly, awareness about the difference between statistical and medical significance, and the need to consider effect size — whether it is large enough to change current practice — is gradually rising, though progress is slow.

A common mistake in today’s era of prediction models is using sensitivity, specificity, and the area under the receiver operating characteristic (ROC) curve for assessing the predictive performance of a model and accepting the model if these indices are good. This approach is flawed for several reasons:

1. These indices evaluate classification of known cases (disease present vs absent), not the prediction of disease in patients whose status is unknown.
2. An ROC area of 0.70 — often deemed “acceptable” — still implies an error rate of up to 30%, which is far too high for clinical decision-making.
3. These metrics apply to groups of patients, not individuals. The appropriate method is one-to-one agreement within clinical tolerance, which is seldom used.

Unfortunately, this same error is now being carried into the evaluation of artificial intelligence (AI)-based models, perpetuating biases in evaluation. There are many other such biases that routinely occur without anyone raising a question.

Lastly, do we know enough about the interaction of human body with mind and soul on one hand and with the environment on the other? One paradigm says, “what we do not know is much larger than what we know.” While this ignorance propels research, it rarely brings humility in our reporting. Without such humility, conclusions are prone to bias.

Publication bias is also well known: studies with positive findings get published more easily than those reporting negative results. This skews the literature towards favourable outcomes and creates a distorted picture during evidence reviews. The imbalance may also tempt investigators to overwork their data to achieve positive findings that will be publishable. Perhaps negative findings deserve twice the weight in publication decisions to correct this distortion.

Fortunately, awareness of analytical bias is increasing, and many researchers are now more careful. Unfortunately, these lessons are often ignored by some researchers, particularly at the post graduate level, laying a weak foundation that carries to the next generation of researchers.

Steps to Minimise Bias

Indrayan and Malhotra⁶ have suggested several actions to minimise bias in medical research results. Some of these, along with the related type of bias, have been highlighted in this article.

The foremost responsibility of a researcher is to recognise that research is a pursuit of truth — a goal that can only be achieved with personal honesty and a willingness to invest the necessary effort. A non-judgemental frame of mind is needed to accept whatever findings the research reveals. Failing to confirm a hypothesis is not a failure; it simply indicates that the truth lies elsewhere, or else the design, data, or analysis may have been inadequate. This provides an important lesson for future research. Journal editors and reviewers must also cultivate a similar attitude.

It is always desirable to multiple checks to assess validity. Peer review is one such measure. Statistically, the results

should be checked for internal validity by splitting the sample into training and validation sets, while external validity should be assessed by replicating the results on another sample from the same or a similar population. Variations should remain within the limits of random sampling fluctuations. If discrepancies arise, the process, data, and analysis must be revisited to identify the problem and take corrective steps. Valid, unbiased results require deliberate effort, which is sometimes lacking due to an eagerness for quick recognition.

While statisticians often recommend large sample sizes, and these can indeed help address several problems, their importance is sometimes overstated. Large samples may lead to sloppy data collection caused by carelessness, fatigue, or limited resources, which can reduce the validity of the results in some situations. In contrast, intensive and in-depth investigations of even a small number of cases can yield highly valuable insights. Many Nobel Prize-winning studies have relied on the depth of investigation rather than a large sample size.

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A Note to Future Clinicians

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I often reflect on the journey that brought me here — a journey shaped by culture, purpose, and an unwavering belief in equitable care. Born in the United Kingdom (UK) to an Indian doctor and a Welsh midwife, I spent much of my early childhood in rural India, where my parents built a hospital from the ground up. In a community with no healthcare infrastructure, their commitment to service, resilience, and high clinical standards shaped the very core of my values. They taught me that compassionate and equitable care should not be a privilege — it should be a right.

After completing my medical training in India, I returned to the UK, never imagining that three decades later I would be the first woman of colour — and only the third woman overall — to serve as President of the Royal College of Obstetricians and Gynaecologists (RCOG). I am deeply honoured to hold this position and proud to be a part of the progress we are making in advancing women's health across the globe.

Throughout my career as a Consultant Obstetrician and Urogynaecologist at Croydon University Hospital, and as an Honorary Senior Lecturer at St. George's University of London, I have worked to improve clinical standards, promote equity, and elevate the voices of women from all backgrounds.

I'm particularly proud to have recently been appointed as Honorary Professor of Women's Health at the University of Liverpool. I am truly passionate about championing women's health, and this is another fantastic opportunity to collaborate with incredible people and organisations dedicated to making a difference to the lives of women and girls around the world.

One of the most rewarding aspects of my role as RCOG President is engaging with our members right across our global community. This includes engaging with colleagues in our international accreditation partnerships, like Max Healthcare Institute. Together, we're delivering an RCOG-accredited training programme that brings UK-standard obstetrics and gynaecology education to clinicians across five hospitals in Delhi. With Membership of the Royal College of Obstetricians and Gynaecologists (MRCOG) examinations, e-portfolio access, and expert-led teaching, this programme allows trainees to develop core competencies and clinical skills that benefit their career progression in obstetrics and gynaecology. I look forward to seeing this partnership develop further and am confident that the trainees joining the programme this summer will make significant strides in advancing their careers and contributing to the field. I wish them all the best on this exciting journey ahead and look forward to seeing their continued growth and success.

To students and early-career clinicians considering a future in obstetrics and gynaecology — this is a field of deep purpose. It demands skill, compassion, and resilience — but it also offers the opportunity to make a real difference in people's lives. Let your lived experiences inform your practice. Stay curious, stay grounded, and never lose sight of why you chose this path.

Together, we can shape a future where every woman — regardless of her background or identity — receives the care and dignity she deserves.

Max Institute of Medical Education Announcements

August and September – 2025

Max Institute of Medical Education (MIME) is an educational division of Max Healthcare Institute Ltd. MIME was established to meet and enhance the training needs of all medical/non-medical staff working in various healthcare organisations. The Institute is committed to ensuring that medical, nursing, and paramedical professionals gain the confidence to use their skills with practiced ease, maintaining the highest standards in an environment that is also safe for the patients.

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Max Healthcare Institute Ltd. is recognised by the National Board of Examinations to permit practical training for students undergoing DNB courses in broad and super-specialities in India, across more than 40 disciplines. Currently, we have 618 DNB residents in our group of network hospitals.

INTERNATIONAL AFFILIATED PROGRAMMES



POST GRADUATE PROGRAM IN INTERNAL MEDICINE — IMT

A three-year, full-time postgraduate training in Internal Medicine incorporating full Membership of the Royal Colleges of Physicians of the United Kingdom (MRCP-UK). This Programme is a partnership between Max Healthcare and the Joint Royal College of Physicians Training Board (JRCPTB-UK). The structured programme provides physician training of international standard, equivalent to that delivered in the UK, with the same curriculum and assessments. Our consultants, fully trained by the Royal College of Physicians, deliver this training. Currently, we have 60 residents enrolled in our IMT training across Max Hospitals in Delhi and Mumbai.

Eligibility: MBBS with a valid NMC/ State Medical registration

TRAINING LOCATION:

- Max Super Speciality Hospitals, New Delhi
- Nanavati Max Super Speciality Hospital, Mumbai



RCOG-MHC OBSTETRICS & GYNAECOLOGY PROGRAMME (RCOG)

A joint programme by Max Healthcare Institute Limited (MHIL) and the Royal College of Obstetricians and Gynaecologists (RCOG), United Kingdom. This training is equivalent to the Basic (ST 1–2) and Intermediate training (ST 3–5) in the UK. The training programme is underpinned by the RCOG Curriculum, MRCOG Examinations, use of the RCOG e-Portfolio, and an annual review of competence progression (ARCP) process with UK externality. We have 10 residents currently enrolled in our RCOG training programme.

Eligibility: MBBS with valid NMC/ State Medical registration

TRAINING LOCATION:

- Max Super Speciality Hospitals, New Delhi



MEM GWU INTERNATIONAL

A 3-year residency program in emergency medicine. The Max Emergency Medicine–George Washington University (MEM–GWU) is a skill-building training program conducted by MIME in collaboration with The Ronald Reagan Institute of Emergency Medicine (USA), under The George Washington University Medical Center. This programme aims to enrich the residents of Max Healthcare in knowledge, skills, and compassion needed for effective and efficient emergency medical care. Currently, 90 residents are enrolled in the ongoing programme.

Minimum Eligibility: MBBS with valid NMC/State Medical registration

Duration Of Course: 3 years

TRAINING LOCATION:

- Max Hospitals in Delhi, UP, Dehradun, Mohali, Lucknow, Mumbai, and Nagpur



Admissions open for
FY 2025-2028 Session



Admissions open for
FY 2025 Session



Admissions open for MEM
GWU FY 2025-2028 Session

Fellowship Courses (Non-NBE):

We offer medical training in various specialities to build the competency of physicians through our fellowship courses. The duration of the fellowship ranges from 6 months to 2 years.

- Abdominal and Transplant Imaging
- Aesthetic Medicine and Surgery
- Bariatric Anaesthesia
- Breast Imaging
- Critical Care Medicine
- Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)
- Emergency Department
- Dialysis
- Orthopaedic Oncology and Reconstruction of Foot and Ankle
- Gastroenterology
- General Nephrology
- Gynaecological Onco-Surgery
- Gastrointestinal (GI) Endoscopy
- Head and Neck Surgery
- Hip and Knee
- Pulmonology
- Radiology
- In Vitro Fertilisation (IVF)
- Robotic and Renal Transplant
- Neuro Imaging
- Non-invasive Cardiology
- Pain Management
- Rheumatology
- Robotics
- Spine Surgery
- Surgical Oncology
- Transplant Hepatology
- Ultrasound-Guided Regional Anaesthesia (UGRA)
- Uro-Oncology and Robotic Surgery
- Women's Imaging and more

Open fellowships:

- Fellowship in Clinical Cardiology
- Cross-Sectional Imaging
- Cardiac Anaesthesia
- Ultrasound-Guided Regional Anaesthesia
- Neuro Imaging
- Neuro Anaesthesia
- Endo-Urology and Renal Transplant

Master of Science (MSc.) Courses:

Max Institute of Medical Education (MIME) is offering two-year full-time Master's courses at Max Healthcare Institute Ltd. These programmes are a post-graduate-level degree that allows students to acquire knowledge and skills. In addition, the course will prepare them to work with specific populations and communities to improve health — through education, awareness, policy, and real-time exposure.

Provide career advancement and 100% placement opportunities through these Master's programs:

- **Master of Public Health:** Certified by the Academy of Scientific and Innovative Research (AcSIR)
- **Master of Healthcare Quality Management:** Certified by the AcSIR
- **MSc. in Clinical Research:** Certified by the Regional Centre for Biotechnology (RCB)

Minimum Eligibility: Bachelor's Degree/Graduation in Science

Duration: 2 years full-time

Admissions are open for the session 2025-2027

Observerships

MIME offers Medical Observership Programs in various clinical departments, wherein the Head of the Department reviews the applications from Indian and international students and accepts candidates based on departmental criteria. Observerships are customised training programs designed to develop the skills and knowledge of medical graduates, allowing them to learn as an observers.

Post-Graduate (PG) Diploma Courses:

MIME is offering one-year full-time PG Diploma courses at Max Healthcare Institute Ltd.

- **PG Diploma of Public Health:** Certified by AcSIR
- **PG Diploma in Clinical Research:** Certified by RCB
- **PG Diploma in Healthcare Quality Management:** Certified by AcSIR

Minimum Eligibility: Bachelor's Degree/Graduation in Science

Duration: 1 year full-time

Admissions are open for the session 2025-2026

Internships

Internships are provided to expose the students to the industry and give hands-on expertise to enhance their skills and knowledge. Internship duration can be 1-6 months.

Allied:

- Physiotherapy
- Dietetics
- Psychology

Support Services:

- Biomedical Engineering
- Service Excellence
- Human Resource
- Finance
- Medical Records Department
- IT
- Fire and Safety
- Healthcare Supply Chain Management

Upcoming Courses Announcement

Life saver training programmes & bespoke/workshop

Max Healthcare Institute is certified as an International Training Centre for American Heart Association and offers short courses in emergency/resuscitation.



**Basic Life Support
Provider Course (BLS) -**
Provider and Instructor



**Advanced Cardiac Life
Support Provider Course
(ACLS) -** Provider and
Instructor



**Paediatric Advanced Life
Support Course (PALS) -**
Provider and Instructor

Upcoming BLS and ACLS training:

Aug 2025

- Max Super Speciality Hospital, Saket**

4th Aug: BLS Provider
5th/6th Aug: ACLS Provider (Traditional)
25th Aug: BLS Provider
25th/26th Aug: ACLS Provider
27th Aug: ACLS Provider

- Max Super Speciality Hospital, Nagpur**

4th Aug: BLS Provider
5th/6th Aug: ACLS Provider (Traditional)
11th Aug: BLS Provider
18th Aug: BLS Provider
19th Aug: BLS Provider
20th Aug: BLS Provider
26th Aug: BLS Provider

Sept 2025

- Max Super Speciality Hospital, Saket**

8th Sep: BLS Provider
9th/10th Sep: ACLS Provider (Traditional)
22nd Sep: BLS Provider
22nd/23rd Sep: ACLS Provider (Traditional)
24th Sep: BLS Instructor
25th Sep: ACLS Instructor

- Max Super Speciality Hospital, Nagpur**

2nd Sep: BLS Provider
3rd/4th Sep: ACLS Provider (Traditional)
9th Sep: BLS Provider
22nd Sep: BLS Provider
23rd/24th Sep: ACLS Provider (Traditional)
29th Sep: BLS Provider

Bespoke/Certificate Courses:

Courses Name	Duration	Mode
Certification Course in Paediatric Cardiac CT	8 weeks	Full-time
Certification Course in Mammography Reporting	8 weeks/ 2 weeks/ 1 week	Full-time
Certification Course in Liver Transplant Donor Evaluation Imaging	3 days	Full-time

Foreign Medical Graduate (FMG) Clinical Skills Courses

These courses enable students to enhance their clinical skills and become familiar with Indian healthcare delivery standards. One of the important factors contributing to the failure of FMGs to clear the licensure exam in India is a lack of clinical skills. Our experience shows that sufficient hands-on training and clinical exposure can lead to success in FMG exam. With the upcoming NEXT exam, the need to build clinical skills will be further enhanced. We propose a program with the aim of bridging this gap and providing students with an opportunity to advance their careers in the field of medicine.

Eligibility: Foreign Medical Graduates

Duration:

- Basic – 15 Days**
- Advanced – 20 Days**
- Batch Commencement – 19th Aug 2025**

MIME Online Courses

MIME brings online training courses for healthcare professionals, including doctors, nurses and paramedics. These online courses have been curated by our stellar faculty, keeping in mind the needs of the learners and the healthcare industry.

Mode: Self-paced online learning (Hybrid)

Successful candidates will be awarded a certificate by MIME.

Online Fellowship Courses

- Diabetes Management
- Infectious Disease
- Emergency Medicine
- Critical Care
- Bariatric Anaesthesia
- Management of Liver Disorder

Online Certificate Courses

- Aesthetic Medicine and Surgery
- Healthcare Quality Management
- Public Health
- Clinical Research
- Bariatric Nutrition
- Acute Liver Failure (ALF)
- Geriatrics Care
- Difficult Airway Management

For more information, contact us:

Max Institute of Medical Education (MIME)

Max Healthcare Institute Ltd, Press Enclave Road, Saket, New Delhi- 110017

Call: +91 8826 600 461, 9999 853 797

E-mail: education@maxhealthcare.com/ jay.prakashpandey@maxhealthcare.com

Website: www.maxhealthcare.in



Scan for more details

About Max Healthcare

Max Healthcare Institute Limited (Max Healthcare) is one of the largest integrated healthcare providers in the country. We own, operate and provide medical services to facilities in Delhi NCR, Mumbai, Punjab, Uttar Pradesh and Uttarakhand. Max Lab supplements our commitment towards patient care by providing accurate testing and diagnostics. We are also revolutionising the care-continuum through Max@Home, ensuring treatment options are available to our patients in the comfort of their homes. Our continued emphasis on patient-centric care accompanied by our patients' trust has strengthened our position to become one of India's top private healthcare providers.

FACILITIES - **22**

BED CAPACITY - **~5,200**

CLINICIANS - **5,400+**

EMPLOYEES - **37,000+**

4 JCI accredited hospitals

3 AACI accredited hospitals

19 NABH accredited hospitals

12 NABL accredited labs

650+ ongoing clinical research projects

2,500+ high index journal research publications till date

~1 Lakh students enrolled in various courses every year

OUR FACILITIES

SOUTH DELHI

Max Super Speciality Hospital (East Block), Saket

(A Unit of Devki Devi Foundation)
2, Press Enclave Road, Saket,
New Delhi - 110 017
Phone: +91-11-2651 5050

Max Super Speciality Hospital (West Block), Saket

1, Press Enclave Road, Saket,
New Delhi - 110 017
Phone: +91-11-6611 5050

Max Smart Super Speciality Hospital, Saket

(A Unit of Gujarmal Modi Hospital and Research Centre for Medical Sciences)
Mandir Marg, Press Enclave Road, Saket,
New Delhi- 110017
Phone: +91-11-7121 2121

Max Multi Speciality Centre, Panchsheel Park

N - 110, Panchsheel Park,
New Delhi - 110 017
Phone: +91-11-4609 7200

Max Institute of Cancer Care, Lajpat Nagar

(A Unit of Devki Devi Foundation)
26 A, 2nd Floor, Ring Road,
Lajpat Nagar,
New Delhi - 110 024
Phone: +91-11-4720 3000

Max MedCentre, Lajpat Nagar

26 A, 1st Floor, Ring Road, Lajpat Nagar,
New Delhi - 110 024,
Phone: +91-11-4720 3030

CENTRAL DELHI

BLK-Max Super Speciality Hospital

Pusa Road, Rajendra Place,
New Delhi - 110 005
Phone: +91-11-3040 3040

EAST DELHI

Max Super Speciality Hospital, Patparganj

(A Unit of Balaji Medical and Diagnostic Research Centre)
108 A, Indraprastha Extension, Patparganj,
New Delhi - 110 092
Phone: +91-11-4303 3333

NORTH WEST DELHI

Max Super Speciality Hospital, Shalimar Bagh

FC - 50, C & D Block, Shalimar Bagh,
New Delhi - 110 088
Phone: +91-11-6642 2222, 7194 1000

SOUTH WEST DELHI

Max Super Speciality Hospital, Dwarka

(A Unit of Muthoot Hospitals Pvt Ltd)
Plot No. 1, Sector 10, Dwarka,
New Delhi - 110 075
Phone: +91-11-3511 3511

NCR

Max Super Speciality Hospital, Vaishali

(A Unit of Crosslay Remedies Ltd.)
W-3, Sector - 1, Vaishali,
Ghaziabad - 201 012, (U.P.)
Phone: +91-120-4173 000, 4188 000

Max Hospital, Gurugram

(A Unit of ALPS Hospital Ltd.)
Opposite HUDA City Centre Metro Station,
B - Block,

Sushant Lok - I, Gurgaon - 122 001
Phone: +91-124-6623 000

Max Super Specilaity Hospital, Noida

Wish Town, Sector-128, Noida - 201 303
Phone: +91-120-4122 222

Max Multi Speciality Centre, Noida

(A Unit of Crosslay Remedies Ltd.)
A-364, Sector - 19, Noida - 201 301
Phone: +91-120-662 9999

MAHARASHTRA

Nanavati Max Super Speciality Hospital, Mumbai

S.V. Road, Vile Parle (West),
Mumbai - 400 056
Phone: +91-22-6836 0000

Max Super Speciality Hospital, Nagpur

(A Unit of Alexis Multispeciality Hospital Pvt. Ltd.)
Survey No. 232, House No. 1313,
Mankapur Square, Koradi Road,
Nagpur - 440030, Maharashtra
Phone: +91-712-7120 000

PUNJAB

Max Super Speciality Hospital, Mohali

(A Unit of Hometrail Buildtech Pvt. Ltd.)
Near Civil Hospital, Phase - 6, Mohali,
Punjab - 160 055
Phone: +91-172-521 2000

Max MedCenter, Mohali

Plot No - A-19, Industrial Area Phase VI,
S.A.S Nagar, Mohali - 160 055
Phone: +91-172 521 2000

Max Super Speciality Hospital, Bathinda

(A Unit of Hometrail Buildtech Pvt. Ltd.)
NH - 64, Near District Civil Hospital, Mansa
Road, Bathinda,
Punjab - 151 001
Phone: +91-164-521 2000

UTTARAKHAND

Max Super Speciality Hospital, Dehradun

Near Indian Oil Petrol Pump, Malsi,
Mussoorie Diversion Road,
Dehradun - 248 001
Phone: +91-135-7193 000

UTTAR PRADESH

Max Super Speciality Hospital, Lucknow

(A Unit of Starlit Medical Centre Private Limited)
Viraj Khand, Gomti Nagar,
Lucknow - 226 010, U.P.
Tel.: +91-522-6780 001, 6780 002



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CIN: L72200MH2001PLC322854

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or visit www.maxhealthcare.in

Submit your articles for the December 2025 edition by 31st October 2025.
Email us at mmjeditorialboard@maxhealthcare.com