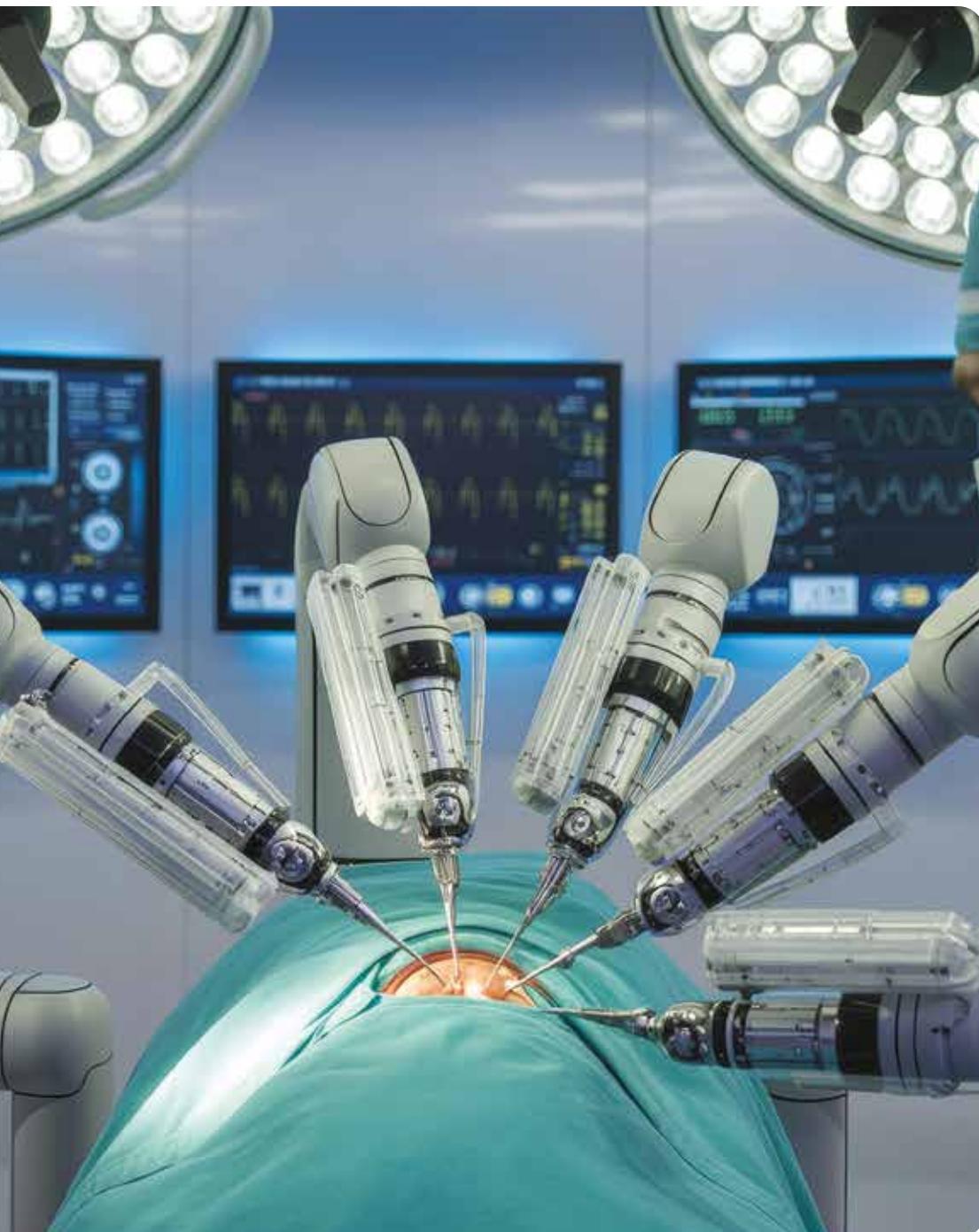


# THE MAX MEDICAL JOURNAL

Volume II | Issue IV December 2025



ORIGINAL ARTICLES

REVIEW ARTICLES

PATH-BREAKING CASES

THE IMAGES

STUDENTS' CORNER



## Living Donor Liver Transplantation for Acute Intermittent Porphyria in an Adolescent: India's First Reported Case

A fifteen-year-old boy arrived in critical condition with severe abdominal pain, persistent nausea, recurrent arrhythmias, seizures, altered sensorium, and neuropsychiatric symptoms. Diagnosis was difficult, as acute intermittent porphyria (AIP) mimics neurological, psychiatric, and gastrointestinal disorders. His urine turning red on standing provided the key clue. Elevated urinary porphobilinogen and genetic testing confirmed AIP with a heterozygous hydroxymethylbilane synthase (HMBS) mutation (c.160+5G>A).

Despite intensive therapy, his neurovisceral crises persisted, and liver transplantation was planned as the definitive cure. After family counselling, a living donor liver transplant was performed, making this one of fewer than 50 such cases reported worldwide and the first from the Indian subcontinent.

Perioperative management was highly complex. Continuous high-glucose infusion suppressed hepatic aminolevulinic acid (ALA) synthase, while tachycardia, arrhythmias, seizures, and syndrome of inappropriate antidiuretic hormone secretion (SIADH)-related hyponatraemia were carefully controlled. Drug selection was extremely cautious to avoid triggering porphyria crises. Surgically, the absence of portal hypertension posed technical challenges, necessitating a short anhepatic phase and close monitoring of hepatic arterial flow. Prophylactic anticoagulation and precise fluid management maintained adequate perfusion without overload.

Postoperatively, neurological recovery was gradual. With strong family support, biochemical values normalised, pain and hyponatraemia resolved, and neuropsychiatric symptoms improved. He was discharged haemodynamically stable on Day 14.

This case highlights the expertise required to diagnose a rare disorder such as AIP and the multidisciplinary effort that enabled a successful curative liver transplant.

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# THE MIND THAT WORKS THE NIGHT SHIFT



“

Each night, when I go to sleep, I die. And the next morning, when I wake up, I am reborn ”

— Mahatma Gandhi

What do Donald Trump, Margaret Thatcher, Benjamin Franklin, Thomas Edison, Nikola Tesla, Indra Nooyi, Elon Musk and Shah Rukh Khan have in common? These are all reputed personalities, known for barely sleeping 3–6 hours per night. When Edison was proclaiming that genius is one percent inspiration and ninety-nine percent perspiration, was he hinting at sleeping less and working longer? Today, we heatedly debate whether a 90-hour work week improves productivity and economic growth or whether it leads to a catastrophic work-life balance and burnout. However, no one seems to be debating how many hours of sleep are essential for physical and mental well-being. Ideally, we are meant to sleep eight hours a day. This would mean that one-third of our lives should be spent sleeping in order to recharge our minds and bodies. Recall, when was the last time you had a blissful, uninterrupted, refreshing sleep? Was it yesterday, last week, last month, last year or perhaps during your school summer vacation? Are you among those paranoid ones who check their phones multiple times at night to ensure that everyone under their care is alive and kicking? The fact of the matter is that sleep is the most neglected health issue. We rarely talk about it with our patients, friends or family.

Imagine a surgeon who starts following these celebrities and decides to work more and sleep less. Does it impact his decision-making, dexterity, technical skills, focus or attention span? Do the

operative times become longer, and do the error rates jump up? Sleep deprivation has a hand-in-glove relationship with burnout, depression, cynicism, apathy and lack of empathy. It leads to reduced appetite, exhaustion and a ‘paradoxical insomnia’. These make a silent entry through the back door and then become permanent residents. A 1972 study revealed that 80% of sleep-deprived residents had difficulty in executing planned manoeuvres and a diminished proficiency in carrying out routine procedures. The 1984 Libby Zion case was a moment of awakening. An 18-year-old patient was admitted to a New York hospital with complaints of fever and agitation. A sleep-deprived junior resident and an intern attended to her, and she died within a few hours. Her father, who was a lawyer, sued for medical negligence and impaired judgment because of the doctor’s fatigue. The case made media headlines, the hospital was held responsible for the residents, and ‘the Bell Commission’ emerged as the first regulatory order on work hours for residents. These were later adopted by the Accreditation Council for Graduate Medical Education (ACGME) for the entire American nation. The resident work hours were fixed: 80–88 hours per week and not more than 28 hours at a stretch. A meta-analysis of thirty-three studies has revealed that the technical skills of a sleepy surgeon decline by 11.9% to 32%. This does not have a strong association with age, seniority or proficiency. Hospitals require a

24 x 7 x 365 coverage, night shifts, and on-call rota depending on patient inflow, complexity of surgeries and manpower. The financial implications for an organisation include higher attrition rates, more litigation for errors, and reduced productivity.

Lack of proper sleep also disrupts the hypothalamic-pituitary-adrenocortical (HPA) axis, and the serum cortisol levels are higher even after one single night of sleep deprivation. These result in physiological derangements, including hypertension, impaired blood sugar, reduced immunity with decreased killer cell activity, as well as an early onset of dementia. It also takes a toll on personal lives with increased alcohol consumption, depression, higher divorce and suicide rates. Women residents have higher infertility and pregnancy-related complications.

The other end of the spectrum is a doctor who dozes off in the middle of a conference. It can only mean two things: either the speaker is too boring or that he himself is suffering from sleep apnoea. He needs to go home and check with his wife if he snores. If he looks like Mr. Pickwick from Dickens' novel, has a short neck, a potbelly and a constant feeling of fatigue after an entire night of sleep, he should straight away get a polysomnography done. It is not just impacting his marriage but also making him prone to strokes and heart attacks. When he laughs, the world laughs with him; when he snores, he sleeps alone.

Then, there are those who just can't fall asleep, stay asleep and wake up too early. There is a very high prevalence of insomnia amongst doctors and nurses. It has only worsened after the pandemic. A cross-sectional survey of 1004 participants in a tertiary care hospital in China showed that 47.7% of doctors and 51.3% of nurses suffered from insomnia. It is higher among those with no physical activity, who smoke, use alcohol and consume more than three cups of coffee per day. Exposure to patient suffering and death, as well as workplace violence, is also responsible. The other reasons may be jet-lag for the high-flying surgeon, late-night parties, binge-watching serials and an addiction to social media. Insomnia occurring thrice a week for at least three months or longer needs evaluation and definitive treatment. Check for gastro-oesophageal reflux, thyroid disorders, anxiety, depression, or medications that interfere with sleep.

There are some of us who are movers and shakers. We have an incessant desire to shake our legs at night. Our neurology colleagues call it restless leg

syndrome. Then there are those like comedian Jimmy Kimmel who can sleep at the wrong places at the wrong time due to narcolepsy. In this instance, the brain is unable to regulate the sleep-wake cycle, causing sleep attacks. It may be associated with sudden muscle weakness and falls (cataplexy). Sleepwalking, sleep-talking, bed-wetting, night terrors and circadian rhythm disorders are forms of parasomnias.

Does this sound like my story or yours? Perhaps what is needed urgently is to develop a sleep-wake schedule for weekdays and weekends. Remove the clutter from the bedroom. Your bedroom is to be shared with your spouse, not with your laptop and your mobile. Cricket and over-the-top (OTT) platforms are more addictive than alcohol and smoking. Caffeine is fine in medical college for burning the midnight oil, but not in routine life. Pooris, paranthas and alcohol cannot be part of the dinner menu. Supper is a good idea. Exercise, reading, music and a warm bath do help. Over-the-counter medication may be used as a short-term measure, but beware of addiction potential. Melatonin has been recommended as a good option, but a recent paper cautions against long-term regular use, which 'may be associated with heart failure'. Cognitive Behavioural Therapy (CBT) may help fight disruptive thoughts. Don't feel embarrassed to seek help if you think you have sleep apnoea. Polysomnography and Multiple Sleep Latency Test (MSLT) are required to diagnose sleep disorders. The best solution for sleep apnoea is weight reduction and avoidance of alcohol. Otherwise, custom-made oral appliances and continuous positive airway pressure (CPAP) have made the quality of sleep so much better. The CPAP machines have become compact, efficient and easy to carry along on an international trip too.

Our work is demanding. Fortunate are those who sleep soundly.

## Dr. Monica Mahajan

Editor-in-chief,  
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# Serum Magnesium Levels as a Predictor of Morbidity and Mortality in Critically Ill Patients: An Observational Study in a Tertiary-Care Intensive Care Unit

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**Abstract:**

Magnesium plays a crucial role in numerous physiological processes. In critically ill patients, both hypomagnesaemia and hypermagnesaemia have been implicated in adverse outcomes. This study investigates the association of serum magnesium levels with morbidity and mortality in Intensive Care Unit (ICU) patients. A prospective observational study was conducted in a tertiary-care ICU in Central India over 18 months. Serum magnesium levels were measured within 24 hours of admission in 150 patients. Patients were categorised into hypomagnesaemia (<1.7 mg/dL), normomagnesaemia (1.7–2.3 mg/dL), and hypermagnesaemia (>2.3 mg/dL). Outcomes assessed included Acute Physiology and Chronic Health Evaluation II (APACHE II) score, ICU stay, need/duration of ventilation, and mortality. Hypomagnesaemia was observed in 49.3% of patients and hypermagnesaemia in 8.7%. Patients with abnormal magnesium levels had significantly higher APACHE II scores, longer ICU stay, higher ventilation needs, and increased mortality. Median APACHE II scores were highest in hypermagnesaemia (52.0), followed by hypomagnesaemia (28.0) and normomagnesaemia (16.0). Mortality was 53.8% in hypermagnesaemia, 37.8% in hypomagnesaemia, and 1.6% in normomagnesaemia. Disturbances in serum magnesium are associated with higher disease severity and poorer outcomes. Regular monitoring and timely correction of magnesium imbalances in ICU settings may improve patient prognosis.

**Key words:** Magnesium, APACHE II Score, ICU Mortality, Hypomagnesaemia, Critical Illness, Ventilatory Support.

## Introduction

Magnesium is the fourth most common cation in the body after sodium, potassium, and calcium. It is also the second most common intracellular cation after potassium, yet its deficiency in critically ill patients is frequently overlooked. Magnesium is essential for human health, and ionised magnesium is involved in the interaction of more than 300 enzyme reactions and is important for electrolyte homeostasis, membrane stability, cell division, and the generation of action potentials. Magnesium disturbance is a common problem in both critical care settings and in the general

population. Magnesium dysregulation mainly impacts neuromuscular and cardiovascular functions. The incidence of hypomagnesaemia varies from 20%–65% in intensive care unit (ICU) patients. Hypomagnesaemia may present as tetany, vertigo, reversible psychiatric aberrations, seizures, cardiac arrhythmias, hypertension, muscular weakness, acute cerebral ischaemia, and asthma. In addition, critically ill patients have several potential risks of magnesium dysregulation. It was significantly associated with increased and prolonged need for mechanical ventilation, difficulty weaning, prolonged ICU stay, and increased mortality in critically ill patients. The critically ill patient population is one

of the most vulnerable groups in modern medicine, requiring swift and efficient management in the ICU. A myriad of biochemical parameters have been studied as predictors of outcomes in these patients, and emerging evidence suggests that serum magnesium levels might play a critical role in determining both morbidity and mortality. Hence, it has gained attention as a potential prognostic biomarker in critically ill patients.

Recent studies have indicated that aberrations in serum magnesium — whether hypomagnesaemia or hypermagnesaemia — are not merely reflective of the underlying disease state but could actively influence the duration of ICU stay and overall clinical outcome. For instance, a study by Khan *et al.* (2023)<sup>1</sup> demonstrated that hypomagnesaemia was independently associated with increased length of ICU stay and a higher incidence of acute complications, emphasising the fundamental role of magnesium in maintaining bioelectrical stability and metabolic function under critical conditions. Additionally, Smith *et al.* (2024)<sup>2</sup> provided evidence supporting the theory that magnesium supplementation in patients with low serum levels may reduce ICU length of stay, potentially through improved myocardial performance and attenuation of inflammatory responses.

In a tertiary care setting, where patients often present with multifactorial critical illness, understanding the correlation between serum magnesium levels and ICU stay can have significant implications for clinical management. The interplay between magnesium and other electrolytes, such as calcium and potassium, further complicates the metabolic milieu in these patients. This complex relationship necessitates comprehensive studies that not only examine serum magnesium in isolation but also as part of a broader electrolyte and metabolic profile. Recent advancements in critical care research have also shed light on the molecular mechanisms by which magnesium influences cellular function. Magnesium has been observed to modulate the activity of several enzymes that are critical for maintaining homeostasis during systemic inflammatory responses and sepsis — the latter being a leading cause of prolonged ICU stays. Moreover, the role of magnesium in modulating stress responses at the cellular level, including the regulation of cytokine release, further underscores its significance in critical illness.

Given the growing evidence, it is crucial to examine the relationship between serum magnesium levels and ICU stay duration in a tertiary care setting. This study aims to assess the correlation between serum magnesium levels and APACHE II scores at admission and to evaluate magnesium's potential as a predictor of morbidity and mortality in critically ill patients.

## Materials and Methods

This was a prospective observational study conducted in a tertiary care ICU in Central India over 18 months. A total of 150 critically ill patients aged over 18 years with at least one organ failure were included. Patients with pre-existing magnesium supplementation, chronic alcoholism, or pregnancy were excluded. Serum magnesium levels were measured within 24 hours of ICU admission and categorised as hypomagnesaemia (< 1.7 mg/dL), normomagnesaemia (1.7–2.3 mg/dL), and hypermagnesaemia (> 2.3 mg/dL).

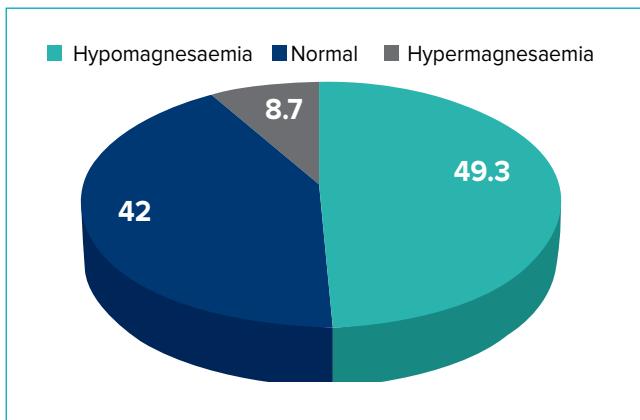
The primary outcome was correlation with the APACHE II score. Secondary outcomes included ICU stay duration, ventilation needs, and mortality. Statistical analysis was performed using the statistical package for the social sciences (SPSS) v25, with  $p < 0.05$  considered significant.

## Results

Out of 150 patients, 74 (49.3%) had hypomagnesaemia, 63 (42.0%) had normomagnesaemia, and 13 (8.7%) had hypermagnesaemia (Table 1) (Figure 1).

Status	Serum magnesium level (mg/dL)	No. of cases	% of cases
Hypomagnesaemia	≤ 1.69	74	49.3
Normomagnesaemia	1.70–2.40	63	42.0
Hypermagnesaemia	> 2.40	13	8.7
<b>Total</b>		<b>150</b>	<b>100.0</b>

**Table 1:** Distribution of prevalence of hypomagnesaemia and hypermagnesaemia in the study group.

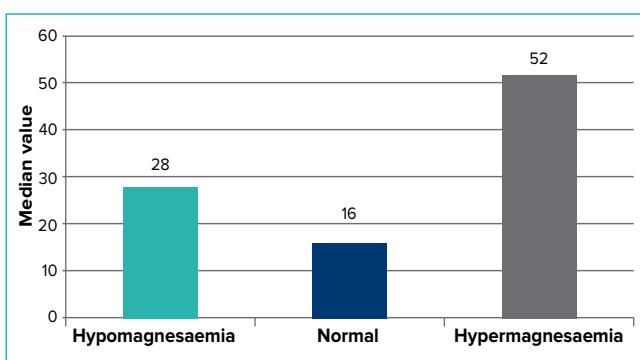


**Figure 1:** Distribution of prevalence of hypomagnesaemia and hypermagnesaemia in the study group.

	Hypomagnesaemia (n=74)		Normal (n=63)		Hypermagnesaemia (n=13)		P-value
	Median	Min–Max	Median	Min–Max	Median	Min–Max	
APACHE II	28.00	15–64	16.00	10–62	52.00	14–68	0.001***

P-value by Kruskal-Wallis H test (Non-Parametric ANOVA). p < 0.05 is considered to be statistically significant.  
\*\*\*p < 0.001.

**Table 2:** Distribution of median APACHE II score according to levels of serum magnesium.  
**Abbreviations:** ANOVA: Analysis of Variance; APACHE II: Acute Physiology and Chronic Health Evaluation II.



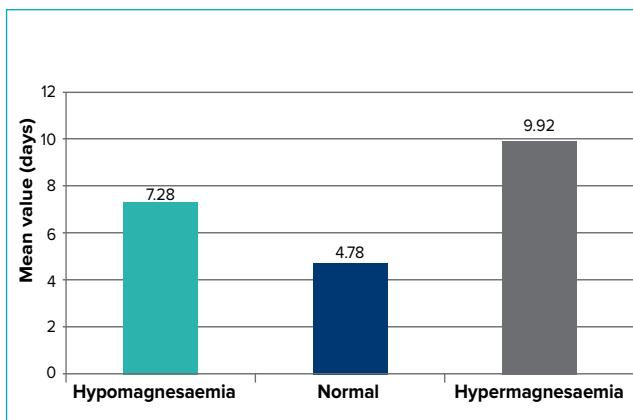
**Figure 2:** Distribution of median acute physiology and chronic health evaluation II (APACHE-II) score according to levels of serum magnesium.

	Hypomagnesaemia (n=74)		Normal (n=63)		Hypermagnesaemia (n=13)		P-value
	Mean	SD	Mean	SD	Mean	SD	
ICU duration (days)	7.28	4.29	4.78	1.83	9.92	3.43	0.001***

P-value by ANOVA (F test). p < 0.05 is considered to be statistically significant. \*\*\*p < 0.001.

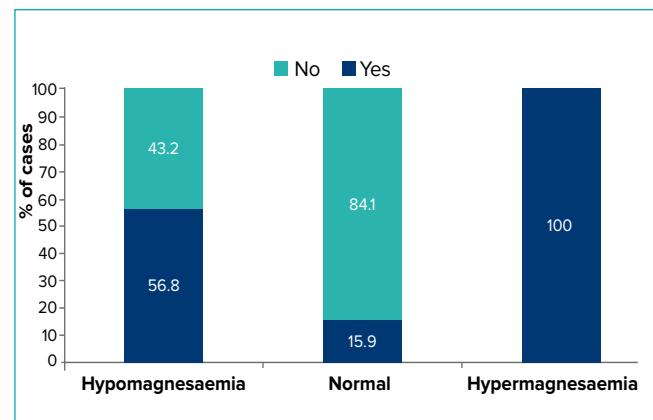
**Table 3:** Distribution of mean ICU duration according to levels of serum magnesium.  
**Abbreviations:** ANOVA: Analysis of Variance, ICU: Intensive Care Unit.

The distribution of mean duration of ICU stay differs significantly across various levels of serum magnesium ( $p < 0.001$ ). The distribution of mean duration of ICU stay is significantly higher among the group of cases with abnormal serum magnesium levels compared to the group of cases with normal magnesium levels in the study group ( $p < 0.001$ ).



**Figure 3:** Distribution of mean intensive care unit (ICU) stay duration according to levels of serum magnesium.

Out of the 74 cases with hypomagnesaemia, 42 (56.8%) required ventilation. Among the 63 cases with normal serum magnesium levels, 10 (15.9%) required ventilation. All 13 cases with hypermagnesaemia required ventilation (Table 4) (Figure 4).



**Figure 4:** The distribution of incidence of need for ventilation according to levels of serum magnesium.

	Hypomagnesaemia (n=74)		Normal (n=63)		Hypermagnesaemia (n=13)		Total (n=150)		P-value
	n	%	n	%	n	%	n	%	
Yes	42	56.8	10	15.9	13	100.0	65	43.3	0.001***
No	32	43.2	53	84.1	0	0.0	85	56.7	
<b>Total</b>	<b>74</b>	<b>100.0</b>	<b>63</b>	<b>100.0</b>	<b>13</b>	<b>100.0</b>	<b>150</b>	<b>100.0</b>	

P-value by Chi-Square test.  $p < 0.05$  is considered to be statistically significant. \*\*\* $p < 0.001$ .

**Table 4:** The distribution of incidence of need for ventilation according to levels of serum magnesium.

The distribution of incidence of requirement of ventilation differs significantly across various serum magnesium levels in the study group ( $p < 0.05$ ). Significantly higher proportion of cases in hypomagnesaemia and hypermagnesaemia groups had higher incidence of requirement of ventilation compared to the group of cases with normal serum magnesium levels ( $p < 0.05$ ).

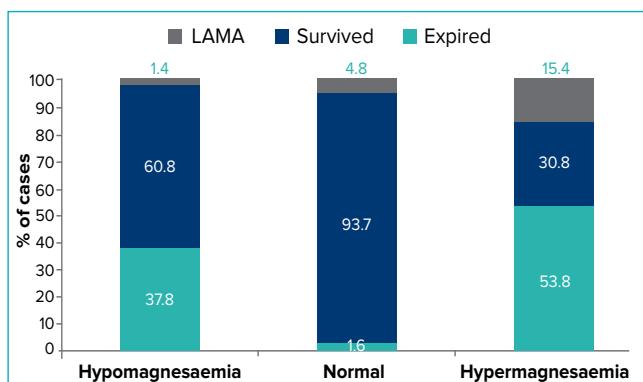
Among the 74 cases that had hypomagnesaemia, 28 (37.8%) expired. Out of the 63 cases that had normal serum magnesium levels, 1 (1.6%) expired. and of the 13 cases who had hypermagnesaemia, 7 (53.8 %) expired (Table 5) (Figure 5).

	Hypomagnesaemia (n=74)		Normal (n=63)		Hypermagnesaemia (n=13)		Total (n=150)		P-value
Mortality	n	%	n	%	n	%	n	%	
Expired	28	37.8	1	1.6	7	53.8	36	24.0	0.001***
Survived	45	60.8	59	93.7	4	30.8	108	72.0	
LAMA	1	1.4	3	4.8	2	15.4	6	4.0	
<b>Total</b>	<b>74</b>	<b>100.0</b>	<b>63</b>	<b>100.0</b>	<b>13</b>	<b>100.0</b>	<b>150</b>	<b>100.0</b>	

P-value by Chi-Square test. p < 0.05 is considered to be statistically significant. \*\*\*p < 0.001.

**Table 5:** The distribution of incidence of mortality according to levels of serum magnesium. **Abbreviation:** LAMA: Leave Against Medical Advice.

The distribution of incidence of mortality differs significantly across the three magnesium levels in the study group (p < 0.05). Significantly higher proportion of cases in hypomagnesaemia and hypermagnesaemia groups had higher incidence of mortality compared to the group of cases with normal serum magnesium levels (p < 0.05).



**Figure 5:** The distribution of incidence of mortality according to levels of serum magnesium. **Abbreviation:** LAMA: Leave Against Medical Advice.

## Discussion

This study highlights the prognostic value of serum magnesium levels in critically ill patients. Both hypo- and hypermagnesaemia were associated with worse clinical outcomes. Hypomagnesaemia, found in nearly half of the cohort, was linked to increased ventilation requirements and prolonged ICU stays. Hypermagnesaemia, though less prevalent, showed the highest mortality rate. These findings align with previous research suggesting magnesium's role in

cellular stability, cardiovascular health, and inflammatory response modulation. The results advocate for routine monitoring of serum magnesium in ICU protocols. It is well documented that older adults are at a higher risk of magnesium deficiency due to factors such as decreased dietary intake, reduced intestinal absorption, and increased renal excretion.<sup>3</sup>

In our study, we observed that individuals with hypomagnesaemia had a median APACHE-II score of 28, with a range of 15 to 64. This suggests that patients with low serum magnesium levels tend to have a higher severity of illness. Magnesium plays a crucial role in cellular metabolism and immune function, and its deficiency is associated with increased inflammatory responses, oxidative stress, and critical illness severity.<sup>4</sup> Patients with normal magnesium levels had a significantly lower median APACHE-II score of 16, ranging from 10 to 62. This indicates that maintaining normal magnesium levels may be associated with less severe illness. Normal magnesium levels contribute to physiological stability, including neuromuscular function, cardiovascular regulation, and immune response, which may contribute to better clinical outcomes.<sup>5</sup>

Interestingly, individuals with hypermagnesaemia had the highest median APACHE-II score of 52, with a range of 14 to 68. This suggests that excessive magnesium levels may also be associated with severe illness. Hypermagnesaemia is often seen in critically ill patients with renal impairment or those receiving

excessive magnesium supplementation, which can contribute to neuromuscular dysfunction, hypotension, and arrhythmias.<sup>6</sup> The high APACHE-II scores in this group may reflect the presence of severe underlying conditions that result in magnesium accumulation.

The high mortality rate in hypomagnesaemic patients may be attributed to several factors, including cardiovascular instability, increased incidence of sepsis, and neuromuscular dysfunction. Hypomagnesaemia has been associated with arrhythmias, increased inflammation, and impaired immune response, which can contribute to adverse outcomes and increased

mortality risk. Similarly, the highest mortality rate in hypermagnesaemic patients may be due to magnesium-induced neuromuscular blockade, leading to respiratory depression, hypotension, and cardiac conduction abnormalities.<sup>7,8</sup> Hypermagnesaemia can suppress the central nervous system, impairing haemodynamic stability and further complicating patient outcomes. Conversely, patients with normal magnesium levels had a significantly lower mortality rate (1.6%), emphasising the potential protective role of maintaining magnesium homeostasis in critically ill patients.<sup>11</sup>

## Conclusion

Magnesium is an essential cation involved in a variety of biological processes, including myocardial energy metabolism, electrical conductivity, and vascular tone regulation. In critically ill patients, especially those with ischaemic heart disease (IHD) admitted to ICUs, altered magnesium homeostasis has been implicated in poorer outcomes.

Significant association observed between serum magnesium levels and clinical outcomes in critically ill patients. Both hypomagnesaemia (low magnesium) and hypermagnesaemia (high magnesium) were found to correlate with worse clinical parameters, prolonged ICU stays, and increased need for ventilatory support, emphasising the critical role of magnesium homeostasis in patient prognosis. Early recognition and correction of these imbalances may contribute to improved patient outcomes.

Nitin Dambhare, Al Ameen M. Serum Magnesium Levels as a Predictor of Morbidity and Mortality in Critically Ill Patients: An Observational Study in a Tertiary Care Intensive Care Unit. MMJ. 2025, December. Vol 2 (4).

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# Polydrug Toxicity: Diagnostic Complexity and Critical Care Strategies

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**Abstract:**

Methamphetamine is a highly addictive psychostimulant drug derived from amphetamine. It can produce euphoria and stimulant effects like those caused by other stimulants such as cocaine. This case report describes a 22-year-old female who was brought to the hospital emergency department with agitation, tachycardia, hyperthermia, altered mental status, profuse perspiration, and vomiting. The symptoms observed in cases of polydrug toxicity fall into multiple toxicodromes, making it a diagnostic dilemma. In this case, the patient was diagnosed with methamphetamine and cocaine toxicity and developed acute liver and kidney injury. She required haemodialysis with specialised filters and prolonged Intensive Care Unit (ICU) stay, but eventually recovered to full strength. This case emphasises the importance of early extracorporeal therapy for multiorgan support and multidisciplinary approach involving various specialties along with the critical care team, to enhance recovery in toxicity cases.

**Keywords:** Polydrug, Toxicity, Extracorporeal.

## Introduction

Substance abuse is a deeply entrenched and multifaceted health issue that causes hundreds of fatal and non-fatal intoxications worldwide. Drug-related deaths most often occur due to polydrug toxicity, typically involving combinations of illicit opioids, other illicit drugs, and benzodiazepines consumed for recreational purposes, which together cause or contribute to the fatal outcomes.<sup>1</sup> Toxicological analysis plays a crucial role in identifying the real cause of intoxication, making the implementation of up-to-date good practices essential in toxicology laboratories.<sup>2</sup> Accordingly, effective toxicological screening and confirmatory analytical methods should be focused to detect and quantify multiple drug classes within a single analytical protocol.<sup>3</sup> In managing such cases, it is crucial to consider both the individual and combined toxic effects of drugs to devise an appropriate treatment plan.

This case report details the complex clinical management of multi-organ dysfunction resulting from polydrug toxicity in a 22-year-old female.

## Case Report

A 22-year-old female resident of Delhi attending an international music concert in Mumbai, presented to the emergency care centre of the concert with complaints of vomiting, profuse sweating, and altered mental status. Immediate intravenous (IV) access was obtained, and the patient was administered antiemetics and IV fluids before being transferred to the emergency department of Nanavati Max Super Speciality Hospital, Mumbai, Maharashtra.

On arrival at the emergency department, the patient was agitated and disoriented. Her vital signs were as follows: pulse rate 180 beats per minute (bpm), blood pressure 100/50 mmHg, oxygen saturation on room air 93% (indicating hypoxia), and temperature 102°F. Pupils were bilaterally 3 mm and sluggishly reacting to light. Her Glasgow Coma Scale (GCS) score was E2V3M5. In view of the poor GCS and continuous vomiting, the patient was immediately intubated for airway protection. As the patient was in altered sensorium and unaccompanied by family, with only friends present at the concert, no reliable past

medical history or exact course of the events leading up to her symptoms could be obtained.

Patient was shifted to the intensive care unit (ICU), where routine investigations and a urine toxicology screen were performed. The differential diagnosis considered included suicidal poisoning, recreational drug abuse, central nervous system (CNS) stroke, encephalitis, and postictal state.

The Day 1 laboratory investigations revealed: haemoglobin 11.7 g/dL, platelet count 1,67,000/ $\mu$ L, prothrombin time (PT)/international normalised ratio (INR) 14 sec/1.3, serum glutamic-oxaloacetic transaminase (SGOT) 120 U/L, serum glutamic-pyruvic transaminase (SGPT) 53 U/L, serum creatinine 2.1 mg/dL, creatine phosphokinase (CPK) 9,082 U/L, and serum ammonia 159 mg/L.

The patient was managed with IV fluids and prophylactic anti-epileptic medication. In view of deranged liver function tests (LFTs), N-acetylcysteine (NAC) infusion was started. Vasopressor support was administered to maintain adequate mean arterial pressure (MAP). Empirical antibiotics (ceftriaxone and doxycycline) were started in view of fever, hypotension and the possibility of atypical infection. Magnetic resonance imaging (MRI) brain was performed, which was essentially normal.

The urine toxicology screen, received the following morning, tested positive for amphetamines, methamphetamine and cannabinoids. Based on the

clinical picture and laboratory findings, a diagnosis of serotonin syndrome was established.

The patient fulfilled Hunter's criteria for serotonin toxicity, which include the presence of spontaneous clonus, inducible clonus with agitation or diaphoresis, ocular clonus with agitation or diaphoresis, tremor and hyperreflexia, or hypertonia with a temperature above 38°C (100.4°F) and ocular or inducible clonus.

The Day 2 investigations indicated worsening multi-organ dysfunction: haemoglobin 13.4 g/dL, platelet count 53,000/ $\mu$ L, PT/INR 47 sec/4.5, SGOT 15,414 U/L, SGPT 8,312 U/L, serum creatinine 2.8 mg/dL, CPK 19,648 U/L, lactate dehydrogenase (LDH) 11,067 U/L, and ferritin 6,331  $\mu$ g/L.

The patient developed oliguria with progressive renal and hepatic impairment, necessitating initiation of continuous renal replacement therapy (CRRT).

Given the markedly elevated liver enzymes and evidence of systemic inflammation, haemoperfusion using specialised HA 330 filter was performed on Day 3 and Day 6. The HA 330 extracorporeal haemoperfusion device, containing neutral macroporous resin, is proven to specifically adsorb medium- to large-sized inflammatory mediators, including cytokines such as Interleukin (IL)-1, IL-6, IL-8, and tumour necrosis factor-alpha (TNF- $\alpha$ ), thereby reducing the cytokine burden. The serial laboratory parameters summarised in Table 1.

Day of illness	Day 3	Day 4	Day 5	Day 6	Day 8	Day 9	Day 10
Haemoglobin	10.1	8.38	9.1	6.3	8.2	7.1	7.6
Platelet count	30	28	35	44	46	78	116
Prothrombin time (PT)	61	45	-	14	-	-	-
International normalised ratio (INR)	6	4.3	-	1.2	-	-	-
Partial thromboplastin time (PTT)	37000	94	82	46	33	30	-
Serum glutamic-oxaloacetic transaminase (SGOT)	15711	3752	1173	-	-	240	180
Serum glutamic-pyruvic transaminase (SGPT)	5813	3427	2723	-	-	700	476
Creatinine	2	2.5	2.6	3.4	-	2	2.4
C-reactive protein (CRP)	6	4	-	-	-	28	-
Creatine phosphokinase (CPK)	12017	6509	1560	1147	-	-	-
Ammonia	107	86	96	-	-	-	-
Ferritin	-	6331	-	-	-	-	-
Myoglobin	-	622	-	-	-	-	-
Procalcitonin (PCT)	1.72	-	-	-	-	2	-
Lactate dehydrogenase (LDH)	-	2637	-	-	-	-	-

**Table 1:** Laboratory reports from Day 3 to Day 10.

The patient required multiple blood and blood product transfusions during the course of the illness.

From Day 5, sedation holidays were initiated. The patient remained drowsy but was able to obey commands and move all limbs.

On Day 6, the patient developed hypotension with low-grade fever. Pan cultures were sent, and antibiotics were escalated to meropenem and teicoplanin. On the same day, a second HA 330 filter was used. With continued CRRT, the patient's liver and kidney functions showed gradual improvement, along with haemodynamic stabilisation. Urine culture grew *E. faecium*, which was vancomycin-resistant but linezolid-sensitive. The antibiotic therapy was then modified accordingly.

On Day 9, furosemide trial was given during ongoing CRRT, to which she responded well, allowing gradual weaning off CRRT. Once haemodynamically stable and with improving laboratory parameters, she was initiated on spontaneous breathing trials and successfully extubated on Day 11.

There was gradual improvement in liver enzymes and creatinine over the next 10 days. The patient was discharged on Day 20 with oral linezolid and supportive medications.

## Discussion

Methamphetamine is a highly addictive psychostimulant drug chemically related to amphetamine. It produces intense euphoria and stimulant effects similar to those of cocaine. Owing to its ease of synthesis from inexpensive and readily available chemicals, methamphetamine abuse has become widespread across the world.

The global use of methamphetamine and amphetamine has increased rapidly in recent years. The high

accumulation of methamphetamine, a potent stimulant drug, in multiple body organs is likely to contribute to the medical complications associated with methamphetamine abuse.<sup>6</sup>

In the CNS, amphetamines act by blocking presynaptic reuptake of catecholamines, resulting in hyperstimulation at selected postsynaptic receptors. Their indirect sympathomimetic effects arise from blockade of presynaptic vesicular storage and inhibition of cytoplasmic destruction of catecholamines by inhibition of mitochondrial monoamine oxidase.<sup>4,5</sup> Methamphetamine is absorbed readily from the gastrointestinal tract, airway, nasopharynx, muscle, placenta, and vagina. Peak plasma levels are observed approximately 30 minutes after IV or intramuscular routes and within 2–3 hours after oral ingestion. Rapid tissue redistribution occurs, with steady-state cerebrospinal fluid concentrations reaching about 80% of plasma levels. Metabolism occurs primarily in the liver via conjugation pathways involving glucuronide and glycine, followed by urinary excretion of metabolites.

Immediate supportive care is essential and includes airway protection, oxygenation and ventilatory support, and appropriate monitoring. Electrocardiographic (ECG) monitoring and prompt treatment of arrhythmias are crucial. Rhabdomyolysis, causing acute kidney injury (AKI) is a common complication and warrants appropriate medical treatment and early initiation of dialysis, if required.

Use of extracorporeal filters and CRRT for liver and kidney injury should be considered early, as they help to maintain electrolyte and hemodynamic balance.

During prolonged hospitalisation and extracorporeal therapy, common hospital-acquired infections should not be missed, and antibiotic therapy should be guided by the hospital antibiogram.

## Conclusion

Drug overdose cases present significant therapeutic challenges, as specific antidotes are unavailable for most substances and many drugs undergo complex, multi-pathway metabolism. Management should prioritise rapid stabilisation of airway, breathing and circulation. Timely initiation of therapies affecting drug pharmacodynamics and adequate multi-organ support is key to the treatment of acute intoxication and crucial to improving patient outcomes.

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# Living with Life After Stroke: Navigating Rehabilitation, Relationships, Resilience

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**Abstract:**

Stroke is a major cause of long-term disability, with millions of people worldwide being affected. Post-stroke survivors are strong physically, mentally, and emotionally and require much care, adaptation to normal life and a lot of mental power to endure. This paper is a comprehensive analysis of life after a stroke (evidence-based rehabilitation methods, the importance of changing the dynamics of personal relationships over time, and the methods to promote resilience). The narrative review included clinical trials, meta-analyses, qualitative studies, and patient-reported outcomes from PubMed, Google Scholar, and Consensus. We found that rehabilitation, a multidisciplinary procedure, must be done individually. The acknowledgement of others is significant in recovery, whereas psychological resilience assists survivors in making adaptations to living with a disability. The most significant problems are motor impairment, communication disorders, stress of the caregiver, and emotional distress. Person-centred, long-term rehabilitation, relational support, and resilience-building approaches are critical to the best recovery and reintegration.

**Key words:** Stroke Survivorship, Rehabilitation, Caregiver, Resilience.

## Introduction

Stroke is one of the most common and significant causes of death and disability globally, and the long-term effects of this condition go far beyond the period of hospitalisation. Stroke is the fourth major cause of death and the fifth major cause of disability in India.<sup>1</sup> The Global Burden of Disease (GBD) study highlights that stroke was accountable for over 6.6 million deaths and 143 million disability-adjusted life years (DALYs) in 2019.<sup>2</sup> Rising frequency of strokes especially in the low-middle income countries (LMICs) such as India is due to modifiable risk factors, such as hypertension, obesity, high blood glucose levels, air pollution, and poor diet (Figure 1).<sup>3</sup> In fact, 70% of strokes are experienced in LMICs.<sup>4</sup> The gender distribution shows that males have an increased incidence than females, although this difference varies by geography and age group (Figure 2).<sup>5,6</sup> The survivors of stroke live with some degree of physical, cognitive, and emotional disabilities that linger long after

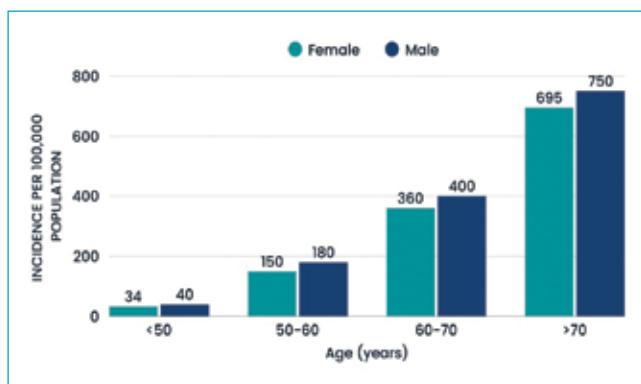
the original medical crisis has taken place. The idea of life after a stroke involves more than medical rehabilitation. It also involves adaptation, resilience, re-establishing self-identity and redefining familial and social connections in the presence of new constraints. Past studies have discovered that resilience is a key predictor of recovery outcomes.<sup>7</sup> But resilience is not created in a vacuum, but is shaped by rehabilitation access, interpersonal support and systems of the healthcare system.

This paper reviews the emerging literature on stroke survivorship to trace a comprehensive trajectory of life after stroke. The research analyses the effects of rehabilitation, relationships, and resilience on patient outcomes. It pays a critical focus on health care systems, policy outlooks, and forthcoming stroke recovery research prospects.



**Figure 1:** Risk factors of stroke in young adults, highlighting modifiable contributors.

**Source:** Conceived and guided by Dr. (Prof.) Man Mohan Mehndiratta, hand-drawn by Anushka Khatana.



**Figure 2:** The graph shows distinct patterns across different age groups and sexes. Men had a higher incidence of stroke than women in the younger (15–49 years) and middle-aged (50–69 years) groups. However, in the older age group (70+ years), the incidence rates for women approached and were similar to those of men. This indicates that while younger and middle-aged men are more at risk, older women face nearly the same risk of stroke as men.

**Source:** Behera DK, Rahut DB, Mishra S, et al. *Sci Rep.* 2024;14(1):22640.<sup>6</sup>

## Rehabilitation Pathways

Rehabilitation serves as the foundation for functional improvement following stroke.

**1. Physical rehabilitation:** Physical therapy, occupational therapy and speech-language therapy are the most evidence-based treatments to restore movement, hand skills, and verbal abilities. Early intervention optimises neuroplasticity and increases functional autonomy. Specific regimens frequently incorporate task-specific training, repetitive movement practice, and adaptable equipment. Special emphasis is placed on the investigation of emerging technologies and

developments in stroke rehabilitation. From robots, virtual reality and neurostimulation approaches, the evolving landscape of rehabilitation technology presents a great opportunity for improving outcomes and quality of life for stroke patients. These inventions have demonstrated the ability to alter rehabilitation techniques and enhance outcomes for stroke patients.<sup>8</sup>

**2. Cognitive rehabilitation:** The survivor usually has difficulties in their memory, attention and decision-making capabilities. The systematic cognitive training techniques enhance thinking skills, concentration, day-to-day activities and quality of life. Research suggests that, in most situations, the challenges with thinking are strongly correlated with loss of independence rather than movement impairment. Cognitive rehabilitation methods, like other rehabilitation concepts, can be divided into two types: restorative and compensatory approaches. Restorative techniques aim to repair or restore degraded function. Compensatory techniques teach and transfer new tactics, skills, or accommodations to compensate for impairments when the original function may not be entirely regained.<sup>9</sup>

**3. Technological aids:** Innovative technological aids are transforming rehabilitation by improving access and engagement. Remote rehabilitation, robotic applications, and immersive online therapy are becoming useful, particularly among those survivors who have limited physical ability to access face-to-face therapy. The training of robot-assisted arms enhances specific motor skills, whereas immersive online spaces expand engagement and attention during the sessions. Immersive online environments and virtual reality platforms are increasingly used to simulate real-world tasks, expand patient engagement, and provide robust feedback during therapy sessions. These technologies help bridge gaps due to distance, resource constraints, and individual limitations.<sup>10,11</sup>

**4. Barriers to rehabilitation:** Several significant barriers prevent effective stroke rehabilitation. Stroke survivors and caregivers report that the quality of available services is not adequate. There are barriers to rehabilitation such as limited resources (especially in resource-limited areas), inadequate infrastructure, poor quality of services, unavailable rehabilitation staff, high costs and geographical disparities. There are also gaps in continuity of care beyond the initial

months after stroke in most healthcare networks. Lack of information and awareness regarding stroke and stroke rehabilitation services was highlighted as a significant barrier to access among stroke survivors and their families.<sup>12</sup>

## Relationships and Social Reintegration

Stroke increasingly affects the personal and community relationships of the survivors, which changes the arrangement of the house and social interaction.

- Family and caregiving dynamics:** Family relations have a pivotal role in the recovery process of stroke survivors. Survivors experience a shift from self-reliance to the necessity of being helped with routine chores and in family roles. Caregivers often face emotional strain, stress and financial strains. This can cause a strain in marital relationships, but in other cases, caregiving could even make relationships stronger as a joint will to power is built.<sup>13</sup> When families actively participate in caregiving and rehabilitation, survivors experience enhanced emotional adjustment and motivation, which leads to better results and quality of life. In contrast, dysfunctional family dynamics — characterised by poor communication, unresolved disputes, or an overwhelming caregiver burden — can impede recovery, resulting in higher psychological distress, less therapy involvement, and slower rehabilitation progress.<sup>14</sup>
- Intimacy and relationships:** Complications after a stroke often disrupt closeness, physical intimacy, and partner communication. Survivors have identified the difficulty in expressing love and sustaining past patterns of relationships.<sup>15</sup> Professional advice and open discussion aid in improving relationship quality. Social support, affection, and open discussions are protective mechanisms, and patients who maintain strong social and emotional networks after stroke report improved relational satisfaction. A large amount of recent evidence has been released proving the critical significance of sexual function restoration to be as crucial to functional recovery as any other aspect in the context of rehabilitation.<sup>16</sup>
- Community and social reintegration:** Reintegration of patients after an episode of stroke into normal living is synonymous with their functional status, which is the individual's average daily performance. Community support markedly enhances post-stroke social reintegration by facilitating recovery across physical, psychological, and social domains. Survivors

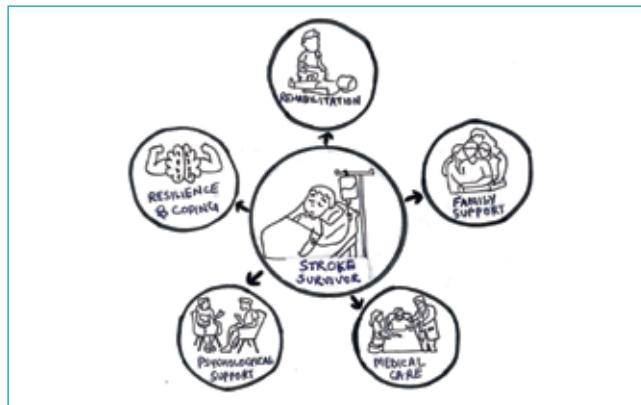
complain of feeling isolated because of loss of jobs, moving around or difficulty in speaking. Mutual support networks, local programs, social support from friends, family, and the local community also mitigate their isolation and help foster motivation, which not only helps manage depression and anxiety but also empowers survivors to resume meaningful social roles and relationships.<sup>17</sup>

## Resilience in Stroke Survivors

A key factor in long-term stroke healing is resilience, which refers to the ability to "bounce-back" and to adjust constructively in the face of difficulty. Resilience, as opposed to the professional emphasis on functional recovery, places more emphasis on psychological and social adaptability, assisting survivors and caregivers in reestablishing fulfilling lives despite ongoing difficulties.

- Psychological factors:** Survivors who are more hopeful, tolerant, and confident about their abilities experience better life satisfaction. Optimism, adaptive confrontation coping, and maintaining a sense of humour help patients adjust better to post-stroke challenges and support active participation in rehabilitation, while anxiety and depression can undermine resilience and slow recovery. When a stroke patient experiences difficulties, familial and social support might help him or her re-adjust or restore the balance of physical and mental health.<sup>18</sup>
- Role of social support:** Survivors who have good relationships with family and their peers have favourable coping skills, motivation, and fare well when reintegrating into the community. Social support serves as a buffer to stress and promotes resilience. Changes in relationships with spouses and children have a deep impact on both patients and caregivers.<sup>19</sup> High levels of social support are closely linked to faster and more complete functional recovery after a stroke. Studies suggest that patients with robust support systems had considerably higher increases in daily living skills and independence than those with minimal support, regardless of the initial severity of the stroke (Figure 3).<sup>20</sup>
- Faith and purpose discovery:** It is the religious beliefs, personal meaning, and rebuilding story that are important in strength development. Research has also revealed that caregivers who attempted positive religious coping measures had better relations with stroke survivors, and a lower level of depression was observed. More favourable responses are shown by

stroke victims who view stroke as a challenge and not a result.<sup>21</sup>



**Figure 3:** Stroke survivor support model.

**Source:** Conceived and guided by Dr. Abhishek Dixit, prepared by Anushka Khatana.

## Healthcare Systems and Policy Perspectives

The structure of the healthcare system has a great impact on recovery outcomes.

- Disparities in access:** Disparities in access to stroke therapy are primarily driven by socioeconomic inequality, with lower-income patients facing considerable disadvantages throughout the rehabilitation process. The poor survivors have a lower chance of receiving comprehensive or protracted care. The resulting cycle of disability, dependency, and medical impoverishment highlights the need for targeted policy reforms, such as subsidised services, expanded healthcare infrastructure, and equity-focused innovations like tele-rehabilitation, to bridge this gap and promote just outcomes for all stroke survivors.
- Integrated care models:** Evidence-based research indicates the benefits of multidisciplinary teamwork of physical therapists, occupational specialists, mental health professionals, and social workers to meet the physical and emotional needs of post-stroke patients. Recent systematic reviews and meta-analyses show that integrating these varied disciplines improves patients' health-related quality of life, allows improvements in everyday activities, and reduces depressive symptoms. Furthermore, integrated care frameworks that include both health and social care services promote long-term reintegration into home and community settings, improve caregiver support, and lower total healthcare costs.

**3. Policy implications:** Long-term care, assistance programs available to caregivers, and remote healthcare provision have to be sustained. Community-based policies that reinforce reintegration and peer networks have also been found to be effective in minimising the caregiver burden and enhancing the independence of survivors. Policies that promote community reintegration not only improve survivors' functional outcomes but also their emotional well-being by facilitating social connectedness and meaningful participation. Paid family and medical leave regulations, tax incentives for caregiving expenses, and the inclusion of informal caregivers as active partners in care delivery all guarantee that caregivers have the support, education, and resources they need to effectively handle complicated care demands.

## Future Directions

Several promising trends can shape post-stroke treatment in the future:

- Personalised rehabilitation using AI:** Machine learning may be used to improve treatment plans to monitor patient progress and, based on the results, generate personalised and dynamic recovery paths.
- Neuroregeneration and pharmacological interventions:** Advances in neuroscience are examining medications and cell-based methods that have the potential to spur neural repair and enhance recovery.
- Digital and virtual platforms:** Immersive technology, monitoring devices, and game-based rehabilitation have great promise to enhance engagement and reach, especially in underserved groups.
- Community-based resilience programs:** Structured resilience-building programs, teaching mindfulness, and peer support might be beneficial to the traditional therapeutic methods.
- Global policy innovation:** Models that would incorporate hospital care, community rehabilitation, and caregiver support would help reduce inequalities and enhance international outcomes.

## Discussion

Stroke recovery is not an easy process. It entails medical, psychological, and even social elements. Recovery programs cannot be effective without supportive

relationships and strength-building strategies, and are needed to restore their functioning. There are significant changes in relationships among the survivors, and their emotional stress may increase or decrease depending on family support. Personal, social, and system-level factors all influence resilience development. However, challenges such as disproportional access to rehabilitation, disrupted healthcare services, and a lack of caregiver support curtail

recovery outcomes. New innovations, particularly those based on machine learning, digital health solutions, and treatments grounded in resiliency, can help to fill these service gaps. The decision-makers are encouraged to focus on long-term models of care that extend beyond hospital stays in an emergency to the daily life of the survivors.

## Conclusion

Life after a stroke is a life-long process that has its challenges and yet presents opportunities to adjust and survive. The functions of rehabilitation are restorative, relationships offer emotional and social support, and resilience enables survivors to seek sense and purpose amidst adversity. Healthcare systems and policies should evolve to encourage holistic and long-term recovery. Integrating medical and psychosocial methods with the systemic methods will help society to ensure that the stroke survivors are not only surviving but also doing well in life after the stroke.

Anushka Khatana, Abhishek Dixit, Navya Jaitly, Tanzeel Wani, Parul Molhotra, Man Mohan Mehndiratta. Living with Life After Stroke: Navigating Rehabilitation, Relationships, Resilience. MMJ. 2025, December.

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# Personalised Communication with Patients and Relatives: An Essence Even in the Digital Era

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**Abstract:**

Patient-physician communication has undergone a profound transformation in recent decades, particularly with the ascent of digital technologies and the internet. Health information technology (health IT) has provided patients with unparalleled electronic access to information, facilitating communication, but has also introduced challenges such as information overload and misinformation. These phenomena, if unaddressed, risk undermining optimal health outcomes. In the present era, it is critical to integrate health IT with patient empowerment, robust doctor-patient relationships and shared decision-making to ensure effective and safe communication.

Recent research has emphasised the necessity of strategies that unite the technical capabilities of artificial intelligence (AI) with a deep appreciation of communication principles, behavioural science, and social theory. Despite advances in AI-driven processes, truly personalised communication — grounded in empathy, honesty, and individualisation — remains indispensable for effective interactions between healthcare providers and patients or their families. Such relationships foster understanding, collaborative decision-making, emotional support, and satisfaction, resulting in outcomes unachievable by technology alone.

**Key words:** Doctor-Patient Relationship, Communication, Personalised Communication, AI, Digital.

**Introduction**

Empathetic and clear communication is foundational to medical practice and underpins shared decision-making, trust, and emotional reassurance for patients and families. Personalised communication tailored to each patient's needs has been shown to improve satisfaction and clinical outcomes compared to standardised interactions. While recent advances in technology and artificial intelligence (AI) platforms can enhance clinical efficiency, these tools must complement, not replace, essential human skills such as active listening and compassion.

**Discussion**

Effective frameworks, including the Calgary-Cambridge<sup>1-3</sup> and SPIKES<sup>4</sup> models, foster outcomes like comprehension, emotional well-being, trust, and family engagement in clinical settings. The integration of these models in clinical routines demonstrates improved patient experiences and staff confidence. However, literature shows that AI and digital solutions may disrupt patient-centred relationships, potentially supporting autonomy but also risking paternalism if not guided by multiple contextual values. This could give rise to a new form of paternalism in which the AI makes decisions on behalf of patients and doctors.<sup>5</sup>

Even when digital innovation saves time, there is uncertainty about whether that benefit translates into more empathetic care or further system-driven efficiencies. Systematic reviews and expert consensus establish personalised communication as a primary marker of healthcare quality — particularly in diverse hospital environments. While technological tools can reduce burdens and support communication tasks, they cannot substitute human empathy, direct counselling, or emotional support during complex medical encounters. Training programs for motivational interviewing, empathy-based communication, and family engagement consistently show reductions in patient distress and improvements in provider effectiveness. Adoption of validated frameworks such as Calgary-Cambridge and SPIKES into daily workflow has clear evidence-based benefits for communication quality.

Recent long-term narrative reviews highlight the essential need for clinicians and healthcare systems to balance digital innovation with preservation of medicine's humanistic and relational core. As technical tasks are increasingly managed by digital solutions, clinicians will need to serve in roles emphasising care navigation, counselling, and responsible information curation. The collective approach by clinicians, health systems, and society toward these new tools will determine future care quality and social health outcomes.

It is important to note that this review did not involve patient and public involvement (PPI) in its conduct. Upcoming research should incorporate robust PPI strategies, as patient and public engagement provides valuable real-world insight and increases research relevance. As artificial intelligence becomes more prevalent, thoughtful implementation guided by ethical principles and stakeholder consensus is essential to strengthen — not supplant — the doctor-patient relationship.

## Results

- Communication models such as Calgary-Cambridge and SPIKES that embed personalised counselling demonstrate tangible benefits for patient understanding, shared decision-making, and family participation. The Calgary-Cambridge model integrates structured interviews with exploration of patient emotions and needs to foster active engagement and satisfaction. The SPIKES protocol's emphasis on empathy facilitates the delivery of difficult news and supports comprehension and trust.
- Interventions focusing on empathetic listening, emotional validation, and tailored communication consistently reduce anxiety and decisional conflict, particularly in intensive care and oncology settings.<sup>6,7</sup>
- Core human traits — empathy, non-verbal sensitivity, and cultural competence — remain essential for effective therapeutic communication.<sup>8-10</sup>
- Communication failures are associated with medical errors, lower patient satisfaction, increased distress, and subpar outcomes.<sup>1,7</sup>
- AI tools may reduce administrative burden and assist in drafting communication, but they cannot replace the nuanced, empathetic counselling required to navigate complex emotions and ethical dilemmas.<sup>2,8</sup>
- The comprehensive narrative review of digital transformation in patient-physician communication emphasises that, notwithstanding technological advancements, human-centred principles should remain at the heart of care to safeguard patient engagement and quality.<sup>2</sup>

## Conclusion

Personalised communication, composed of skilled counselling and empathetic, patient-centred dialogue, remains central to hospital-based care. Investment in communication training must accompany the adoption of technological solutions to optimise both clinical and psychosocial outcomes. Realising the potential of AI in healthcare will require broad, inclusive dialogue about fundamental values and meticulous design of clinical systems to guarantee that digital transformation enhances, rather than diminishes, relationship-centred care. The 25-year narrative review on digital age transformation in patient-physician communication further contextualises these shifts, highlighting the enduring importance of human factors.<sup>10</sup> Taking an interdisciplinary approach and integrating AI technologies with theoretical and practical insights will enable health marketers to improve engagement, advance health equity through personalised and accessible communications, and ultimately contribute to the development of healthier communities globally.<sup>11</sup>

Ashwini Jogade Pandhare. Personalised Communication with Patients and Relatives: An Essence Even in the Digital Era. MMJ. 2025, December. Vol 2 (4).

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# Managing Total Pain: The Crucial Role of Psychologists in Palliative Care

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**Abstract:**

Palliative care emphasises holistic well-being and the alleviation of suffering in patients with life-limiting illnesses. The concept of "total pain," introduced by Dame Cicely Saunders, underscores that pain is not merely physical but also psychological, social, and spiritual. This paper explores the indispensable role of psychologists in addressing these dimensions of suffering. Through psychological assessment, therapeutic interventions, and existential counselling, psychologists contribute significantly to improving patient comfort, emotional resilience, and quality of life. The integration of psychological care into palliative settings remains limited in India, necessitating urgent advocacy for a multidisciplinary model that treats total pain with equal attention to the mind and body.

**Key words:** Palliative Care, Total Pain, Psycho-Oncology, Psychological Intervention, Existential Distress, Cognitive Behavioural Therapy, Quality of Life, End-of-Life Care.

## Introduction

Palliative care, by its very nature, is designed to provide relief from the symptoms and stress of life-limiting illnesses. While much attention is often given to the medical management of pain, there is a growing recognition that pain in such contexts is seldom just physical. It encompasses emotional, psychological, social, and spiritual suffering — a concept widely known as "total pain", first articulated by Dame Cicely Saunders, the founder of modern hospice care.

In India, where cultural, familial, and existential concerns often intertwine with end-of-life experiences, addressing total pain requires a comprehensive, multidisciplinary approach. Among the key professionals in this effort are clinical psychologists, whose role, though often underemphasised, is fundamental.<sup>1</sup>

## Understanding the Multidimensional Nature of Pain

Patients facing terminal illnesses often report pain that persists despite optimal medical treatment. This is not due to inadequate medication but rather because the pain is compounded by psychological distress — fear of death, unresolved conflicts, anxiety about the future of loved ones, and a deep sense of loss or meaninglessness. These psychological and existential burdens not only intensify the perception of pain but may also render pharmacological interventions less effective. For many patients, untreated emotional suffering translates into physical discomfort, and vice versa.<sup>2</sup>

## Psychologists as Pillars in the Palliative Care Team

Psychologists bring to the palliative setting a skillset focused on understanding, assessing, and alleviating emotional and mental distress. Their contributions are varied and vital:

**Psychological assessment:** Identifying clinical depression, anxiety disorders, and cognitive changes that may go unnoticed in purely medical evaluations.

**Therapeutic interventions:** Providing counselling and evidence-based therapies such as cognitive behavioural therapy (CBT), which help patients reframe negative thought patterns that exacerbate suffering.

**Pain coping strategies:** Teaching relaxation techniques, mindfulness, and imagery to help patients manage pain perception and regain a sense of control.

**Supporting families:** Addressing the emotional toll on caregivers and facilitating open, meaningful conversations between patients and their loved ones.

**Existential counselling:** Assisting patients in finding peace, purpose, and dignity in their final days, often bridging the gap between psychological and spiritual care.

## A Public Health Imperative

Despite the documented benefits of psychological support in palliative care, mental health professionals remain scarce in Indian hospices and cancer centres. The stigma surrounding mental illness, coupled with limited training in psycho-oncology, further limits access.

Yet, data from global palliative care models show that patients who receive integrated psychological care report reduced pain levels, improved mood, and better quality of life, even when facing terminal diagnoses. Their families, too, experience fewer complications during the grieving process<sup>3</sup>

## Conclusion

As India moves towards a more inclusive and patient-centred healthcare model, psychological care must be recognised as an integral part of pain management in palliative care. Addressing "total pain" is not just a matter of clinical responsibility, but of human compassion.

In the final stretch of life, every effort must be made not only to extend life, but to enhance its dignity and meaning. It is here that the presence of a psychologist can make a world of difference.<sup>4</sup>

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# Triumph of India's Historic 2025 Female Cricket World Cup

## Women's Leadership in Healthcare: Lessons from India's Historic 2025 Female Cricket World Cup Triumph

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**Abstract:**

The landmark victory of the Indian women's cricket team at the 2025 World Cup symbolises resilience, dedication, and the breaking of traditional barriers — qualities deeply relevant to women's leadership in healthcare. Despite progress, gender disparities persist across healthcare leadership globally. This commentary explores parallels between female sports leadership and healthcare, emphasising strategies to empower women clinicians and administrators, promote equitable representation, and foster transformational leadership. Evidence from indexed journals highlights the positive impact of diverse leadership on healthcare outcomes and organisational culture, reinforcing the urgency of emulating the Indian team's spirit and teamwork in healthcare leadership development.

**Keywords:** Leadership, Healthcare, Women Leadership.

### Introduction

Women constitute a growing proportion of healthcare professionals worldwide, yet their representation in senior leadership positions remains disproportionately low. The historic victory of Indian women's cricket team in 2025 offers a powerful metaphor and motivation for addressing gender inequities in healthcare leadership. Both domains demand resilience, vision, and teamwork amid often male-dominated environments. This article discusses the importance of enhancing women's leadership in healthcare, learning from cross-sector success stories, with a focus on Indian healthcare systems and beyond.<sup>1-3</sup>

### Discussion

#### Women's leadership in healthcare: Current status

According to the World Health Organisation's (WHO) 2021 policy action paper, *Closing the leadership gap: gender equity and leadership in the global health and care workforce*, women made up nearly 70% of the global health and social care workforce, yet held only around 25% of senior positions. Updated 2024 data from the National Health Workforce Accounts indicate that women now make up 67.2% of the global health workforce.

Batson *et al.* reaffirms this imbalance, showing that women hold just 5% of top leadership roles globally.<sup>4,5</sup> In India, even with increased numbers of women medical graduates, leadership roles remain scarce due to sociocultural and structural barriers.<sup>3,6</sup>

## Lessons from sports leadership

The Indian women's cricket team's victory exemplifies inclusive leadership, teamwork, mentorship, and overcoming stereotypes. These attributes align with effective healthcare leadership models, providing transferable strategies to foster women leaders in medicine.

Women healthcare leaders often face gender bias, lack of mentorship, work-life balance conflicts, and restricted access to leadership development programs.<sup>1,2,7</sup> As organisations work to strengthen talent across all workforce levels, the continued underrepresentation of women in leadership roles has driven a growing demand for Women's Leadership Development Programmes (WLDPs) in recent years. These tailored initiatives, alongside organisational commitment to gender equity, flexible working environments, and increased visibility of women role models play a crucial role in improving

representation and strengthening leadership effectiveness within healthcare organisations.<sup>8,9</sup>

Research links gender-diverse leadership with improved patient outcomes, innovation, employee satisfaction, and improved organisational performance, emphasising the direct benefits of promoting women leaders in healthcare.<sup>10</sup>

## Disclaimer

The author gratefully acknowledges the support of family, society, mentors, and the organisation throughout her career. The views expressed herein are personal and intended to draw symbolic parallels between the achievements of the Indian women's cricket team and women's leadership in healthcare. They are general reflections meant to inspire and do not represent the official positions of any institution or organisation.

## Conclusion

The Indian women's cricket team's historic World Cup win in 2025 offers a compelling narrative to inspire efforts towards gender equity in healthcare leadership. Embracing inclusive leadership models, dismantling systemic barriers, and fostering women's leadership development should remain top priorities to strengthen healthcare leadership and improve health outcomes. Greater diversity in global health leadership ensures varied perspectives shape policies and priorities, advancing equitable healthcare worldwide.<sup>5</sup> Interventions promoting behavioural change and addressing gender bias will support career advancement of women in academic medicine and healthcare management.<sup>2,6</sup>

Ashwini Jogade Pandhare. Triumph of India's Historic 2025 Female Cricket World Cup. Women Leadership in Healthcare: Lessons from India's Historic 2025 Female Cricket World Cup Triumph. MMJ. 2025, December. Vol 2 (4).

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# Adjuvant Therapy in Adrenocortical Carcinoma: Review of Evidence and Evolving Perspectives

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**Abstract:**

Adrenocortical carcinoma (ACC) is a rare, aggressive malignancy with high recurrence rates even after complete resection. The role of adjuvant therapy remains controversial, owing to the scarcity of prospective data and disease heterogeneity. This article synthesises current evidence regarding the efficacy, indications, and evolving role of adjuvant mitotane and radiotherapy in resected ACC. A comprehensive literature review was conducted encompassing retrospective analyses, multi-institutional studies, meta-analyses, and recent prospective trials evaluating adjuvant mitotane and radiotherapy in ACC. Studies were analysed for recurrence-free survival (RFS), overall survival (OS), and toxicity outcomes. Mitotane, the only approved systemic therapy for ACC, shows benefit primarily in high-risk patients (European Network for the Study of Adrenal Tumours [ENSAT] stage III, R1 resection, Ki-67 > 10%). The ADIUVO trial demonstrated no significant improvement in RFS or OS for low- to intermediate-risk disease, supporting a risk-adapted approach. Ongoing trials (ACACIA, ADIUVO-2) are exploring combination chemotherapy with mitotane in higher-risk cohorts. Increasing evidence supports adjuvant radiotherapy (RT) in improving locoregional control, particularly in margin-positive or locally advanced cases. Meta-analyses confirm significant reductions in locoregional recurrence (Hazard ratio [HR] = 0.34) and improvements in OS (HR = 0.6), with modern conformal RT demonstrating favourable toxicity profiles. Adjuvant therapy remains critical in optimising outcomes for high-risk resected ACC, with current data supporting selective mitotane use and adjuvant RT in appropriately chosen patients. Future prospective, risk-stratified trials integrating systemic and locoregional modalities are essential to refine treatment paradigms and improve survival in this rare malignancy.

**Key words:** Adrenocortical Carcinoma, Mitotane, Adjuvant Radiotherapy, Recurrence-Free Survival, ENSAT, High-Risk.

**Background**

Adrenocortical carcinoma (ACC) is a rare and aggressive malignant tumour of the adrenal cortex, with an incidence of approximately 1–2 cases per million population annually.<sup>1–3</sup> It is more common in women (55%–65%) than in men (35%–45%) and exhibits a heterogeneous clinical behaviour that can range from indolent growth to rapid progression.<sup>4</sup> In contrast

to benign adrenal tumours — which are among the most common human neoplasms with a prevalence exceeding 3% in adults over 50 years — ACC carries a markedly poor prognosis.<sup>5</sup> Reported 5-year survival rates vary significantly with disease stage: 65%–82% for European Network for the Study of Adrenal Tumours

(ENSAT) stage I, 58%–68% for stage II, 41%–55% for stage III, and only 10%–20% for stage IV disease.<sup>3,6</sup>

Complete surgical excision remains the primary curative approach for localised and selected locally advanced disease. Despite complete macroscopic resection, recurrence in ACC remains alarmingly common. Reported rates after adrenalectomy range from 60% to 80%, underscoring the aggressive biology of the disease. Even when negative surgical margins are achieved, up to one-third of patients will develop local recurrence. The risk is substantially higher in cases with positive margins, where local failure rates can reach approximately 60%.<sup>7-9</sup>

This has fuelled interest in adjuvant therapies aimed at reducing relapse risk and improving survival outcomes. Mitotane, an adrenolytic agent, has long been used in the adjuvant setting, supported by retrospective analyses and some prospective data, though its optimal use, duration, and patient selection remain subjects of debate. Additionally, radiotherapy — once considered of limited value in ACC — has gained attention in select high-risk postoperative patients, particularly those with margin positivity or adverse pathological features, with emerging evidence suggesting improved local control.

In this review, we summarise current evidence and expert perspectives on adjuvant therapy in ACC, discuss key prognostic factors influencing treatment decisions, and outline evolving strategies that aim to improve patient outcomes in this challenging malignancy.

### Risk Stratification<sup>3</sup>

**Low risk:** ENSAT stage I or II and Ki-67≤ 10%.

**Standard risk:** ENSAT stage I or II and Ki-67 between 11% and 30%, or ENSAT stage III and Ki-67 < 30%.

**Very high risk:** Any of the following:

- Ki-67 ≥ 30%
- Large tumour thrombus in the vena cava
- Stage IV
- R1 resection

### Prognostication<sup>3</sup>

The Grade, Resection Status, Age, and Symptoms (GRAS) score is used. A modified version of this score also includes stage (S-GRAS).

### Stage:

- The risk of relapse at 5 years is estimated at 18%–47%, 36%–62%, 50%–81%, respectively, for stages 1, 2, or 3.
- The 5-year survival varies according to the stages, from 63%–88% for stages 1 to 38%–73% for stage 2, 19%–54% for stage 3, and 0%–21% for stage 4.
- Recent data show that nodal involvement has an unfavourable prognosis identical to stage 4.

### Grade (Weiss score/Ki-67):

- Higher Ki-67 levels are consistently associated with poor prognosis.
- Threshold levels of 10% and 20% have been considered for discriminating low from high Ki-67 labelling indices.
- Weiss score > 6 is considered high (The Weiss score is a histopathological scoring system used to assess the malignant potential of adrenocortical tumours).

**Resection:** Positive surgical margins (R1 resection) are a risk factor for worse outcomes in ACC and are associated with shorter overall survival (OS) and recurrence-free survival (RFS) compared to patients with negative margins (R0 resection).

**Age:** Age is an independent prognostic factor; older adults (more than 50 years of age) usually have a poorer prognosis.

### Symptoms:

- Hormonally functional status is a predictor of poor prognosis.
- Of all the types of hormonally active tumours, glucocorticoid tumours have the poorest prognosis.

### Current Evidence

#### Role of mitotane:

Mitotane is an adrenolytic drug with selective toxicity toward adrenal cortical cells. To date, the only drug specifically approved for the treatment of ACC is mitotane. It acts by inhibiting adrenal cortical function, both through direct suppression and, in some cases, by causing cellular destruction. It is a derivative of the insecticide dichlorodiphenyltrichloroethane (DDT), is currently the only drug specifically approved for the

treatment of ACC. Its pharmacologic effects include suppression of corticosteroid synthesis and alteration of peripheral steroid metabolism, resulting in increased urinary excretion of 17-hydroxycorticosteroids and 17-ketosteroids.<sup>10</sup>

The role of mitotane following curative-intent surgery for ACC continues to generate debate, largely due to the scarcity of high-quality prospective data. Interpretation of available studies is often complicated by methodological limitations and patient selection biases.<sup>11</sup>

A retrospective analysis was conducted involving 207 patients who underwent resection of ACC at 13 institutions across the United States, of whom 88 received adjuvant mitotane. In this cohort, adjuvant mitotane was associated with shorter RFS and OS. However, causality could not be established, as the mitotane group appeared to have a higher baseline risk of recurrence, reflecting treatment selection bias, which could not be completely accounted for despite statistical adjustment.<sup>12</sup>

A multicentre, case–control study was conducted in Italy and Germany, which compared outcomes of 47 patients treated at four Italian centres where adjuvant mitotane was routinely administered with two control groups: 55 patients from other Italian centres and 75 from German centres where adjuvant therapy was not standard practice. A key methodological strength was that treatment allocation was based on institutional policy rather than individual patient characteristics, minimising selection bias. Baseline characteristics were well matched between the mitotane group and the first control group, although the second control group included older patients and a greater proportion with early-stage disease. With a median follow-up exceeding 10 years, median RFS was significantly longer in the mitotane group (42 months) compared with control group 1 (17 months) and control group 2 (26 months). Median OS was also significantly prolonged compared with control group 1 (161 vs 65 months), although the difference versus control group 2 (92 months) did not achieve statistical significance.<sup>13,14</sup>

The most definitive prospective evidence comes from the ADIUVO trial (NCT00777244), the first and only randomised controlled study on adjuvant mitotane in ACC. This multicentre, open-label, Phase III trial enrolled patients with completely resected, low- to intermediate-risk ACC (ENSAT stage I–III, R0 resection, Ki-67 ≤ 10%) and randomised them to adjuvant mitotane for two

years or active surveillance. Due to slow accrual, only 91 patients were randomised (45 mitotane, 46 surveillance) over a decade, leaving the trial underpowered. At a median follow-up of 48 months, 5-year RFS was 79% with mitotane and 75% with surveillance (hazard ratio [HR] 0.74, 95% confidence interval [CI] 0.30–1.85), while 5-year OS was 95% versus 86% (HR 0.46, 95% CI 0.08–1.92) — differences that were not statistically significant. Recurrence occurred in 16% of mitotane-treated patients versus 24% under surveillance. No subgroups showed a clear differential benefit. A parallel prospective observational cohort of 95 patients managed according to patient preference confirmed these findings. The ADIUVO trial demonstrated that in patients with low-grade, localised ACC at low to intermediate recurrence risk, prognosis with surveillance alone is favourable, with 5-year RFS approaching 75%. In this group, the modest and non-significant differences in outcomes, combined with mitotane's toxicity, suggest that routine use is unwarranted. These findings, however, should not be extrapolated to higher-risk ACC, where adjuvant mitotane remains supported by retrospective evidence and expert consensus guidelines.<sup>15</sup>

While retrospective analyses and the ADIUVO trial have shaped current practice, ongoing trials aim to address key gaps in evidence and refine adjuvant treatment strategies for ACC.

The ACACIA trial (NCT03723941) is a Phase II randomised controlled study involving patients with localised, resected ACC (ENSAT stages I–III), stratified by recurrence risk. It compares the standard of care — which may be observation or mitotane — with combination therapy using etoposide, cisplatin, and mitotane (EP-M). The primary endpoint is disease-free survival (DFS). ACACIA seeks to determine whether early systemic therapy can confer benefit even in localised disease, potentially expanding the role of combination chemotherapy beyond high-risk groups.<sup>16</sup>

The ADIUVO-2 trial (NCT03583710) is a Phase III, randomised, international registry study enrolling high-risk patients after complete resection — such as those with R0/R1 resection, Ki-67 > 10%, or ENSAT stage III disease. Participants are randomised to receive either adjuvant mitotane alone or mitotane combined with platinum-based chemotherapy (cisplatin and etoposide). The primary endpoint is RFS. By focusing on a population at the highest risk of relapse, ADIUVO-2 is expected to provide the first prospective evidence on whether adding systemic chemotherapy to

mitotane improves outcomes compared with mitotane monotherapy.<sup>17</sup>

Together, these studies are expected to clarify the optimal role of mitotane monotherapy versus combination regimens, help define risk-adapted strategies, and guide future guideline recommendations.

#### **Considerations in the use of adjuvant mitotane:**

Mitotane therapy in ACC is associated with several practical challenges that influence its use in the adjuvant setting. Access can be limited due to its manufacture by only a few companies and restricted distribution pathways, which may delay treatment initiation. The drug has a narrow therapeutic window, necessitating regular plasma level monitoring to ensure efficacy while avoiding toxicity. Adverse effects are frequent and often significant, including gastrointestinal intolerance, neurotoxicity, hepatotoxicity, dyslipidaemia, skin changes, and endocrine disturbances that may require long-term hormone replacement. Its long half-life results in a delayed onset of action, with therapeutic levels sometimes taking weeks to months to achieve, which can be problematic in patients with rapidly progressive disease. Furthermore, the need for frequent laboratory monitoring, careful dose adjustments, and multidisciplinary follow-up, coupled with its impact on quality of life — such as fatigue and cognitive changes — makes patient selection and counselling essential before initiating mitotane.<sup>11</sup>

#### **Role of radiation therapy (RT):**

While ACC has long been considered relatively resistant to radiation, emerging data challenge this perception.

At MD Anderson Cancer Center, Habra *et al.* retrospectively analysed 58 patients with ACC treated between 1983 and 2011, of whom 20 received adjuvant RT after surgical resection. The primary aim was to evaluate the impact of postoperative RT on local recurrence-free survival (LRFS). Patients in the RT group had more adverse features, including higher stage and positive or close margins, compared with those managed with surgery alone. Despite these imbalances, adjuvant RT was associated with a significantly reduced risk of local recurrence (3-year LRFS 79% vs 45%,  $p = 0.03$ ) and a non-significant trend toward improved OS. Toxicity was generally mild to moderate, with no unexpected late effects. The authors concluded that postoperative RT should be considered in patients at elevated risk of locoregional relapse, particularly those with margin-positive resections.<sup>18</sup>

Sabolch *et al.* conducted a multi-institutional retrospective analysis encompassing 360 patients from 13 United States (U.S.) centres, of whom 58 received adjuvant RT after complete macroscopic resection. The study sought to determine whether RT conferred a local control or survival advantage. Using propensity score matching to balance high-risk factors between groups, adjuvant RT significantly improved locoregional control (LC) (5-year LC 76% vs 44%,  $p < 0.001$ ) and demonstrated a trend toward improved disease-specific survival. The benefit was most notable in patients with ENSAT stage III disease or R1 margins. Acute toxicity was primarily grade 1–2 gastrointestinal or constitutional symptoms, and severe late toxicity was rare, reflecting the adoption of modern conformal techniques.<sup>19</sup>

Nelson *et al.* analysed the National Cancer Data Base (NCDB) data from 2004–2013 to assess the impact of adjuvant RT in non-metastatic ACC following surgery. Among 1,184 patients identified, 171 (14.4%) received adjuvant RT. While demographic characteristics were similar between groups, those receiving RT were significantly more likely to have positive margins (37.4% vs 14.6%;  $p < 0.001$ ), vascular invasion (14.0% vs 5.1%;  $p = 0.05$ ), and concurrent chemotherapy (57.3% vs 28.8%;  $p < 0.001$ ). On multivariable analysis, positive margin status was the only independent predictor of RT use (odds ratio [OR] 3.84, 95% CI 1.95–7.56). In the overall cohort, RT was not associated with improved median OS; however, in the subset with positive margins, adjuvant RT reduced the yearly risk of death by 40% after adjustment for chemotherapy use (HR 0.60, 95% CI 0.40–0.92;  $p = 0.02$ ). No survival benefit was observed for other traditional high-risk features. The authors concluded that adjuvant RT should be considered in multidisciplinary planning for patients with margin-positive ACC, although its utilisation in the U.S. remains limited.<sup>20</sup>

At the University of Michigan Endocrine Oncology Program, Gharzai *et al.* performed a retrospective, propensity-matched cohort study to evaluate the impact of adjuvant RT following adrenalectomy for ACC. Of 424 patients screened, 78 were included — 39 who received RT and 39 matched controls — matched by age, tumour stage, grade, surgical margin status, and adjuvant mitotane use. RT targeted the tumour bed with or without regional lymph nodes, with a median dose of 55 Gy (range 45–60 Gy). Adjuvant RT was associated with significantly improved LRFS ( $p = 0.002$ ), DFS ( $p = 0.0035$ ), and OS ( $p = 0.0024$ ) compared with matched controls. The authors emphasised that RT should be considered within a multidisciplinary

framework, particularly for patients with high-risk pathological features, incomplete resection margins, or large primary tumours.<sup>21</sup>

Wu and colleagues performed a retrospective single-centre study of 105 patients with localised ACC treated from 2015 to 2021; 46 patients (43.8%) received adjuvant RT within three months of surgery, and 59 underwent surgery alone. Median follow-up was 36.5 months (interquartile range [IQR] 19.7–51.8). RT was delivered with intensity-modulated techniques to the tumour bed (median dose 45.0 Gy, range 30.0–50.4 Gy), and patients were matched on margin status and stage for comparisons. At 3 years, OS was higher in the RT group (87.9% vs 79.5%; log-rank  $p = 0.039$ ), and median DFS increased from 16.5 months (no RT) to 34.6 months (RT) (log-rank  $p = 0.033$ ). Recurrence rates were lower with RT (50.0% vs 78.0%;  $p = 0.003$ ), and fewer deaths occurred in the RT arm (5 vs 20;  $p = 0.006$ ). On multivariable Cox modelling (adjusting for ENSAT stage and Ki-67), adjuvant RT remained independently associated with improved OS (adjusted HR 0.293, 95% CI 0.107–0.798;  $p = 0.016$ ) but did not show an independent benefit for DFS after adjustment ( $p = 0.164$ ). Toxicities were mostly mild–moderate (Radiation Therapy Oncology Group [RTOG]/ Common Terminology Criteria for Adverse Events [CTCAE]), with six grade-3 events documented (one grade-3 intestinal event and five grade-3 leucopenias). Subgroup analyses suggested the

survival and DFS benefit was particularly evident in patients with ENSAT I–II disease. The authors concluded that adjuvant RT was associated with better survival and longer DFS in their cohort and was generally well tolerated.<sup>22</sup>

Tsuboi and colleagues conducted a systematic review and meta-analysis to clarify the role of RT in patients with ACC following surgery. A total of seven retrospective studies were included, encompassing 1,249 patients, of whom 277 received adjuvant RT. Across the pooled data, adjuvant RT was associated with a significant improvement in locoregional RFS (HR 0.34, 95% CI 0.23–0.51,  $p < 0.001$ ) and OS (HR 0.60, 95% CI 0.45–0.81,  $p = 0.001$ ) compared to surgery alone. The benefit in DFS did not reach statistical significance in the overall cohort (HR 0.78, 95% CI 0.57–1.06,  $p = 0.11$ ). Subgroup analyses indicated the greatest OS benefit in patients with positive margins or advanced-stage disease. The authors acknowledged the limitations of relying solely on retrospective data, including potential selection bias, heterogeneity in RT doses and techniques, and variable use of concurrent/adjuvant mitotane. Nonetheless, they concluded that adjuvant RT appears to offer meaningful LC and survival advantages in selected high-risk ACC patients.<sup>23</sup>

A summary of key studies evaluating the impact of adjuvant radiotherapy in ACC is presented in Table 1.

Study	Design and population	Intervention	Key results	Conclusion
Habra <i>et al.</i> <sup>18</sup> MD Anderson (1998–2011)	Retrospective, 48 patients	RT vs no RT post-surgery	Local recurrence: RT 44% vs No RT 31%; no OS/RFS benefit	RT did not improve outcomes significantly
Sabolch <i>et al.</i> <sup>19</sup> University of Michigan (1991–2011)	Retrospective matched cohort (n=40)	RT (median 55 Gy) vs no RT	Local recurrence: RT 1/20 vs no RT 12/20 ( $p = 0.0005$ ); OS/RFS not significantly different	RT improves local control
Nelson <i>et al.</i> <sup>20</sup> NCDB analysis	Registry-based, 1184 patients	Surgery ± RT (stratified by margin)	OS benefit in R1 subgroup (HR 0.60); no benefit in R0	RT may benefit R1 resection only
Gharzai <i>et al.</i> <sup>21</sup> University of Michigan propensity-matched (2019)	Retrospective (n=78), matched for GRAS	RT (median 55 Gy) vs matched controls	3-yr OS: 78% (RT) vs 49% (no RT), $p = 0.002$ ; improved RFS	RT improves OS/RFS in matched cohort
Wu <i>et al.</i> <sup>22</sup> 2025 Single center study (2015–2021)	Retrospective (n=105); 46 received RT	RT median 45 Gy	3-yr OS: 87.9% (RT) vs 79.5%; DFS: 34.6 mo vs 16.5 mo	RT improved both OS and DFS; mild toxicity
Tsuboi <i>et al.</i> <sup>23</sup> meta-analysis (2025)	Meta-analysis, 12 studies, n=4606	Mitotane and/or RT	RT: OS HR 0.69; Mitotane: RFS HR 0.63; combo: local control	RT improves OS in high risk; Mitotane improves OS and RFS in margin negative; Combination beneficial in R1/high-risk

**Table 1:** Evidence base for the role of adjuvant radiotherapy in adrenocortical carcinoma.

**Abbreviations:** DFS: Disease-Free Survival; GRAS: Grade, Resection Status, Age, and Symptoms; HR: Hazard Ratio; mo: Months; NCDB: National Cancer Data Base; OS: Overall Survival; RFS: Recurrence-Free Survival; RT: Radiotherapy; yr: Year.

## Evolving Perspectives

The management of ACC has witnessed a gradual but meaningful shift over the past two decades. While surgical resection remains the cornerstone of treatment for localised disease, the high recurrence rates — especially in patients with adverse prognostic features — have prompted increasing interest in multimodality strategies. Historically, adjuvant mitotane was the main systemic option, despite limited prospective data and challenges related to its narrow therapeutic window, toxicity profile, and prolonged time to achieve effective plasma concentrations. The recent ADIUVO trial refined its role by showing no survival advantage in low- to intermediate-risk patients, thereby underscoring the need for patient selection and reserving mitotane monotherapy for higher-risk cohorts as per ENSAT and National Comprehensive Cancer Network (NCCN) recommendations.

Parallel to systemic therapy, adjuvant RT has emerged from a controversial adjunct to a more widely discussed component of multidisciplinary care. Early single-institution series suggested improved LC in high-risk patients, but concerns about retrospective bias and heterogeneity in technique limited broader adoption. In recent years, multi-institutional studies, propensity-matched analyses, and pooled meta-analyses have provided stronger evidence supporting RT's role, particularly in patients with positive surgical margins, large tumours, or high-grade histology. Improved RT technology, including conformal planning and image-guided delivery, has mitigated some of the toxicity concerns historically associated with adrenal bed irradiation. Consequently, contemporary perspectives increasingly view RT as a tailored option for selected high-risk patients rather than as a blanket recommendation.

Another evolving area is the integration of combined adjuvant modalities. Data remain sparse on the synergistic or additive effects of mitotane and RT, but ongoing studies — such as ADIUVO-2 — are expected to clarify whether concurrent or sequential use can improve outcomes in patients at higher risk of recurrence. Molecular profiling and biomarkers may further refine adjuvant treatment strategies in the future, enabling risk-adapted therapy that balances efficacy with quality of life.

## Recommendations as per Guidelines

Adjuvant RT plays a selective but important role in the management of ACC. According to expert consensus and institutional practice, RT is considered in cases where surgical resection is incomplete — either microscopically (R1) or macroscopically (R2) — as well as in the postoperative setting after local recurrence has been re-resected. RT is also preferred in patients with localised disease, restricted spread, or tumour capsule rupture, particularly when re-operation would be technically challenging or not feasible. However, RT is typically avoided in the presence of widespread metastatic disease due to limited therapeutic benefit in that context.

The NCCN Guidelines (Version 2.2025) recommend considering external beam radiation therapy (EBRT) to the tumour bed in patients at high risk for local recurrence. High-risk features include positive surgical margins, Ki-67 proliferation index greater than 10%, tumour rupture, large tumour size, and high-grade histology. In such patients, RT may serve as an important adjuvant modality to reduce the likelihood of local recurrence, although its use should be individualised based on patient factors and institutional expertise.

Mitotane is another adjuvant therapy option in ACC, especially for patients at high risk of recurrence. The NCCN guidelines recommend considering adjuvant mitotane therapy as a Category 3 recommendation in these settings. Mitotane therapy requires close monitoring, as therapeutic levels (typically 14–20 mcg/mL) may take several months to achieve, and its use is associated with significant adrenal suppression. Therefore, patients on mitotane usually require lifelong hormone replacement with hydrocortisone and/or fludrocortisone. While mitotane may offer greater benefit in controlling hormone-related symptoms, its role in directly controlling tumour progression remains uncertain, and its use is often guided by institutional experience and patient tolerance.

### Declaration of the use of artificial intelligence (AI) in the writing process

During the preparation of this work, the authors used AI tools only for language editing and grammar refinement. No generative AI was employed to create, analyse, or

interpret the scientific content. The authors reviewed and verified all text to ensure accuracy and integrity, and take full responsibility for the final content of the manuscript.

### Conclusion

ACC remains a rare but aggressive malignancy with a persistently high risk of recurrence despite optimal surgery. Adjuvant therapy plays a pivotal role in improving outcomes for patients with high-risk features. Current evidence supports the selective use of mitotane in patients with adverse prognostic indicators, guided by ENSAT and NCCN recommendations, while the role of adjuvant RT is increasingly supported by retrospective and pooled analyses, particularly in margin-positive or locally advanced cases. The heterogeneity of available data, coupled with the rarity of the disease, highlights the ongoing need for collaborative multicentre efforts, prospective trials, and standardised treatment protocols.

As the therapeutic landscape evolves, the emphasis is shifting toward personalised adjuvant strategies — matching treatment intensity to recurrence risk, optimising tolerability, and integrating advances in systemic therapy, radiotherapy, and molecular oncology. Until robust prospective evidence becomes available, clinical decision-making should remain multidisciplinary, incorporating surgical, medical oncology, and radiation oncology expertise to individualise adjuvant treatment for each patient with ACC.

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# From Bench to Bedside: Monoclonal Antibodies as Next-Generation Antimicrobials

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**Abstract:**

Monoclonal antibodies (mAbs) represent the future of infectious disease management amid rising antimicrobial resistance and emerging pathogens. Evolving from early serum therapies, mAbs now offer targeted and highly specific immune responses through multiple mechanisms, including neutralisation, complement, and cellular cytotoxicity. Several mAbs are approved for infections, including Coronavirus Disease 2019 (COVID-19), respiratory syncytial virus (RSV), Ebola, human immunodeficiency virus (HIV), and anthrax, with many more in various phases of development. This review explores the structure, types, and clinical applications of mAbs, including newer formats like bispecific antibodies, mimetics, and antibody-drug conjugates. mAbs also show promise in travel medicine and vaccine development. Their rapid deployment during the COVID-19 pandemic underscores their potential in responding to future public health emergencies.

**Key words:** Monoclonal Antibodies, Antimicrobial Resistance, Passive Immunotherapy, Infectious Diseases, COVID-19, Ebola, RSV, Bi-Specific Antibodies, Antibody Mimetics, Antibody-Drug Conjugates, Vaccine Development, Travel Medicine, Emerging Pathogens.

**Historical Perspective<sup>1</sup>**

Antibodies were first used in the late 19<sup>th</sup> century to treat toxin-producing bacterial infections such as diphtheria and tetanus. Von Behring won the Nobel Prize in medicine for his revolutionary work in diphtheria treatment. This ushered the beginning of the serum therapy era, where animal sera were used against other organisms like *Neisseria meningitidis* and Group A *Streptococcus*, though this often resulted in serum sickness. Human sera offered some improvement, but impurities still caused immune complex-mediated fever, rash, and hypotension.

In 1891, Klemperer demonstrated the benefits of serum therapy for *Streptococcus pneumoniae* when properly administered. However, because the bacterium had multiple serotypes, trials showed that mixing sera targeting various serotypes was better, and this became

the standard therapy for pneumonia. However, serum therapy failed during the meningitis outbreaks in the United States of America (USA) and Europe.

The discovery of penicillin by Alexander Fleming in 1928 marked the beginning of the antibiotic era for fighting infections, leading to the abandonment of serum therapy. Nevertheless, sera continued to be used for specific indications, such as snake bites. However, the indiscriminate use of antibiotics opened the Pandora's box, resulting in the emergence of multi-drug-resistant (MDR) organisms such as Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant *Enterococcus* (VRE). As per the World Health Organisation (WHO) and Centres for Disease Control and Prevention (CDC), antibiotic-resistant infections are estimated to cause 10 million

deaths annually by 2050, along with a 2%–3.5% reduction in global gross domestic product (GDP). An additional challenge is the emergence of new pathogens such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), along with the re-emergence of others like Ebola. Ebola has a mortality rate exceeding 50%, with no successful treatment options or vaccines. Antibody-based therapies have remained largely experimental, although convalescent sera and monoclonal antibodies (mAbs) were used during the Coronavirus Disease 2019 (COVID-19) pandemic under emergency use approvals. These recent outbreaks of Ebola and COVID-19, together with the grim scenario of antibiotic resistance, have catalysed renewed interest in mAbs as the next generation of antimicrobial agents. were used during the COVID-19 pandemic under emergency use approvals. These recent outbreaks of Ebola and COVID-19, together with the grim scenario of antibiotic resistance, have catalysed renewed interest in mAbs as the next generation of antimicrobial agents.

Today, antibody treatments are used for diseases like hepatitis B, rabies, respiratory syncytial virus (RSV) infection, tetanus, botulism, vaccinia virus infection, and certain enteroviral infections. These therapies generally involve pooled immunoglobulin (intravenous immunoglobulin, [IVIG] from multiple donors, leading to batch-to-batch variability, the need for large quantities due to low specificity, and limited supply dependent on donor availability. The potential of antibodies to treat infections like *Plasmodium falciparum*, *Pseudomonas aeruginosa*, *Mycobacterium tuberculosis*, and *Staphylococcus aureus* has been under-explored, under-estimated, and under-appreciated.<sup>2</sup>

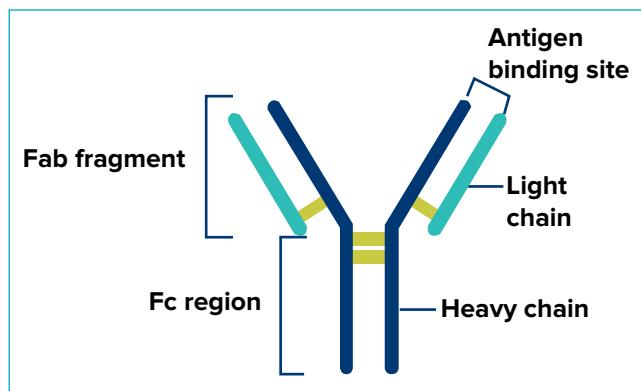
In 1975, Cesar Milstein and Georges Köhler developed the first mAbs via fusion of B lymphocytes (B cells) with immortal myeloma cells, an innovation that earned them the Nobel Prize in 1984.

### Introduction to Antibodies<sup>3,4</sup>

Antibodies, or immunoglobulins (Ig), are produced by B cells and play a crucial role in adaptive immunity by neutralising toxins and eliminating pathogens. Ig are found in blood, plasma, and other extracellular fluids (historically called "humors"); hence, their action is referred to as the 'humoral' immune response.

An antibody is a Y-shaped molecule, composed of 2 pairs of polypeptide chains: two heavy chains and two light chains. Each chain has a variable region

and a constant region. The variable regions of the heavy and light chains together form the antigen-binding site, which determines the antibody specificity. The constant regions are linked by disulfide bonds, providing structural stability to the molecule. The lower part of the Y, known as the fragment crystallisable (Fc) region, consists of constant segments of the heavy chains (Figure 1).



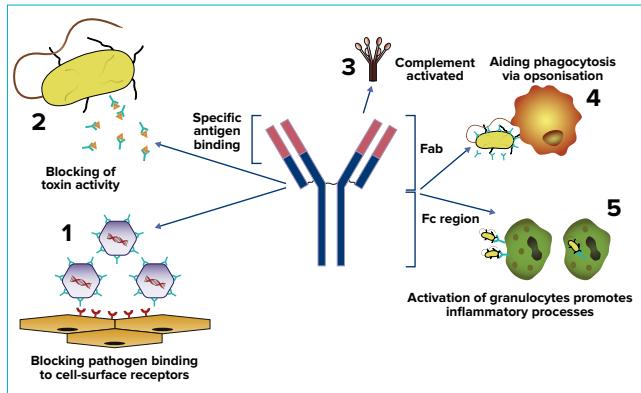
**Figure 1:** Structure of an antibody.<sup>3</sup> The heavy chains (blue), the light chains (green), the disulfide bonds (yellow).

**Abbreviations:** Fab: Fragment Antigen Binding; Fc: Fragment Crystallisable.

### Function of antibodies

- Neutralising function of antibodies:** The antigen-binding site binds to bacterial toxins or viruses, preventing their attachment to and entry into host cells, thereby neutralising the toxins and their harmful effects.
- Effector functions of antibodies:** Effector functions are triggered when the Fc region of an antibody binds to Fc receptors on immune cells after the antibody has attached to an infectious agent or an infected cell. The major effector functions include:
  - Complement activation:** Activation of the complement system leads to the lysis of pathogens, a process referred to as complement-dependent cellular cytotoxicity (CDC).
  - Phagocytosis:** Antibodies bound to pathogens enhance their uptake and destruction by phagocytic cells through Fc receptor interactions.
  - ADCC:** Antibodies recruit immune cells like macrophages, eosinophils, neutrophils, and natural killer (NK) cells to destroy infected cells via Fc receptor binding.

The various mechanisms through which antibodies exert their effects are summarised in Figure 2.



**Figure 2:** Functions of antibodies.<sup>5</sup>

**Abbreviations:** Fab: Fragment Antigen Binding; Fc: Fragment Crystallisable.

### Monoclonal Antibodies (mAbs)

Definition: highly purified antibodies produced from a single parent cell, ensuring specificity to one particular target for a disease.

#### Types of mAbs in clinical use

These antibody types differ in structure and function (Table 1). Over time, the human protein percentage has increased (Table 2).

Stage	Description	Example
Murine antibodies	Entirely mouse-derived immunoglobulin G (IgG)	OKT3 (Muramab-CD3, 1986)
Chimeric antibodies	Human constant regions + murine variable regions	Rituxan (rituximab)
Humanised antibodies	Human antibody structure with only murine antigen-binding complementarity-determining regions (CDRs)	Xolair (omalizumab)
Fully human antibodies	100% human sequence	Humira (adalimumab, 2002)

**Table 1:** Types of monoclonal antibodies in use.

Type	Composition	Human protein %
Murine	100% mouse protein	0%
Chimeric	Human constant + mouse variable regions	~65%
Humanised	Mostly human with mouse complementarity-determining regions (CDRs)	~95%
Fully human	100% human protein	100%

**Table 2:** Evolution of monoclonal antibodies to fully humanised form.

#### Nomenclature of mAbs

##### Pre-2021

Prior to 2021, all mAb names ended with the stem-mab. This naming scheme was replaced in 2021 by the World Health Organisation (WHO) International Nonproprietary Names (INN) nomenclature system, which classifies antibodies based on their structure and target. Examples of pre-2021 nomenclature: Altumomab: "-al-" (prefix) + "-tum-" (tumour target) + "-o-" (mouse origin) + "-mab" (suffix) (Table 3).

-mAb	Monoclonal antibody
-mo-mab	Mouse mab
-xi-mab	Chimeric mab
-zu-mab	Humanised mab
-mu-mab	Human mab
-tu-xx-mab	Tumour-directed xx mab
-II-xx-mab	Immune-directed xx mab
-ci-xx-mab	Cardiovascular-directed xx mab
-vi-xx-mab	Virus-directed xx mab

**Table 3:** Nomenclature of monoclonal antibodies (pre-2021).

## Post-2021<sup>6</sup>

The INN nomenclature for mAbs is a combination of a unique prefix, one or more infixes (sub-stems), and a suffix.

- **Prefix:** The prefix is random and decided by the manufacturer to ensure distinctiveness.
- **Infix(es):** One or more infixes or sub-stems indicate the target and source or purpose.
  - **Target (Infix A):** Indicates disease or target system.
  - **Source/Type (Infix B):** Previously indicated the origin (e.g., -o- for mouse) but is largely being phased out to avoid confusion with the new suffix system.
  - **Veterinary use:** The pre-substem "-vet-" can be used for veterinary products.
- **Suffix:** A new suffix system has replaced the outdated '-mab stem'. As per the 2021 WHO recommendations, the new suffixes for monospecific Ig are as follows:
  - -tug (anti-tumour)
  - -bart (anti-tumour)
  - -mig (multi-specific immunoglobulins)
  - -ment (anti-target for infectious diseases)

Thus, under the new system, the suffix indicates the drug's target or function, while the infixes specify the target class (e.g., -ta- for tumour) and where relevant the source of the antibody (e.g., -xi- for chimeric, -zu- for humanised).

### Example of post-2021 nomenclature for mAbs

Rituximab is a chimeric mAb targeting tumours. Chimeric is denoted by -xi- in the name. If this drug were to be renamed as per INN nomenclature, it would not have -xi-, nor -mab. Also -tu- is no longer used to indicate the target tumour and has been replaced by -ta-. So, ri-tu-xi-mab would be renamed Ri-ta-tug (Ritatug) if it had been named after 2021.

### Therapeutic applications of mAbs<sup>7</sup>

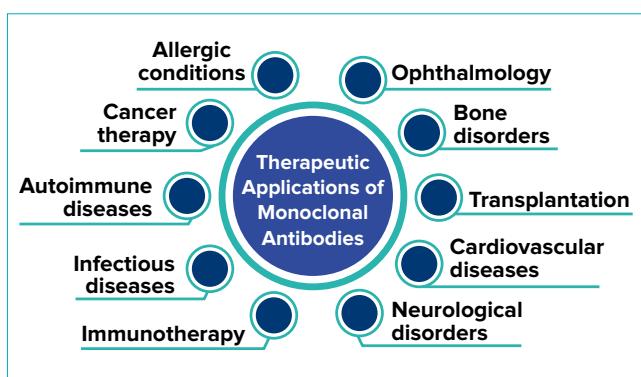
mAbs have both diagnostic as well as therapeutic indications. Diagnostic role includes immunoassays, cancer and disease detection, tissue typing and radio-

labelling for imaging purposes. The therapeutic uses are vast and some of these are listed below (Table 4) (Figure 3).

Therapy area	Mechanism of action	Examples and key indications
Oncology	Targeted therapy by attaching to tumour cells, enhancing destruction	Trastuzumab (Herceptin): Blocks human epidermal growth factor receptor 2 (HER2) protein in breast and stomach cancer Rituximab: Binds to the cluster of differentiation 20 (CD20) protein on B-cells, in lymphomas and leukaemias
Oncology	Targeting tumour microenvironment and vascular supply	Bevacizumab (Avastin): Blocks vascular endothelial growth factor (VEGF) to inhibit neo-vascularisation
Oncology	Conjugated mAbs 'smart bombs' for delivering cytotoxic drugs and radioisotopes	Brentuximab vedotin (Adcetris): antibody-drug conjugate (ADC) linking antibody targeting the cluster of differentiation 30 (CD30) antigen to a chemotherapy drug for Hodgkin lymphoma
Oncology	Immune check point inhibitors block immune checkpoint proteins (like PD-1 or CTLA-4) that help cancer cells to hide from the immune attack. This "releases the brakes" permitting immune response	Pembrolizumab (Keytruda) and nivolumab (Opdivo): Target PD-1 to boost the T-cell immune response in melanoma and lung cancer
Oncology	Bispecific antibodies to bind to two different targets simultaneously, bringing a cancer cell and an immune cell closer to trigger an attack	Blinatumomab (Blinacyto): Connects leukaemia cells expressing cluster of differentiation 19 (CD19) to T-cells expressing cluster of differentiation 3 (CD3), triggering the T-cells to kill the mitotic cells

Therapy area	Mechanism of action	Examples and key indications
Autoimmune disorders	Cytokine or tumour necrosis factor- $\alpha$ (TNF- $\alpha$ ) inhibitors reduce inflammation	Adalimumab (Humira), infliximab (Remicade): rheumatoid arthritis (RA), Crohn's disease
Autoimmune disorders	Targeting specific immune cells. mAbs can target and depleting specific immune cells	Rituximab (Rituxan): Depletes B-cells in RA, multiple sclerosis
Autoimmune disorders	Immuno-modulators for signalling pathways	Belimumab (Benlysta): Inhibits B-cell activating factor (BAFF or BlyS) to reduce harmful B-cells in systemic lupus erythematosus (SLE)
Infectious diseases	Neutralising viruses, binding to viral proteins, preventing host cell entry	Several mAbs used in COVID-19 treatment
Infectious diseases	Passive immunity	Palivizumab (Synagis): as prevention of serious respiratory syncytial virus (RSV) in infants.
Infectious diseases	Neutralise bacterial toxins	Sepsis treatment for diseases like anthrax (e.g., Raxibacumab).
Cardiovascular disease	Lowering low-density lipoprotein cholesterol (LDL-C) levels	Evolocumab and alirocumab.

**Table 4:** Therapeutic applications of monoclonal antibodies (mAbs).



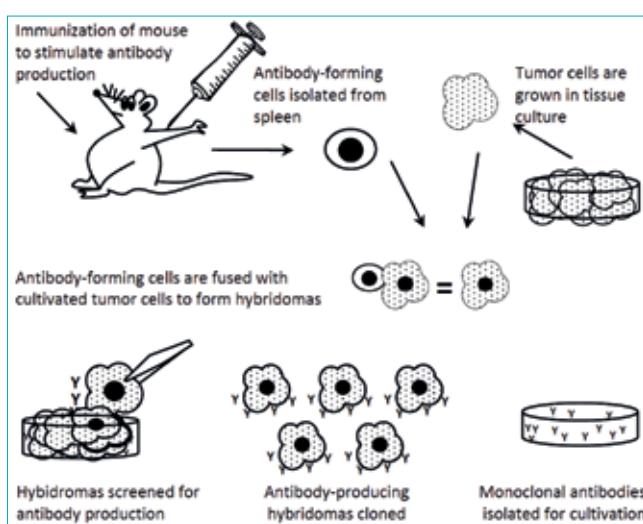
**Figure 3:** Therapeutic applications of monoclonal antibodies.<sup>8</sup>

## Production of mAbs

### Hybridoma technique

In this technique, specific mAbs are produced by fusing antibody-producing B-cells with immortal myeloma cells to create hybridomas, which can continuously secrete large quantities of highly specific identical, highly specific mAbs. The steps in the hybridoma technique include (Figure 4):

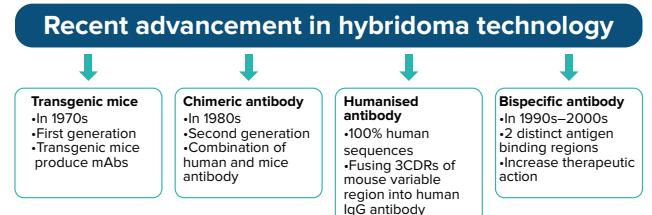
- **Step 1** - A mouse is immunised with a specific antigen to elicit an immune response
- **Step 2** - Antibody-producing B cells are harvested from the mouse spleen
- **Step 3** - Harvested B cells are fused with immortal myeloma cells (cancerous B cells) using chemical or electrical techniques
- **Step 4** - Fused cell hybridomas combine B cell's capacity for specified antibody production with the immortality of myeloma cells
- **Step 5** - Selection of hybridomas and culture to produce massive quantities of a specific mAb



**Figure 4:** Monoclonal antibody production with hybridoma technology.<sup>9</sup>

Some of the recent advances in hybridoma technology include the development of technologies for humanised antibody and bispecific antibody production (Figure 5); the use of genetically engineered yeast and mammalian cell lines for large-scale fermentation (up to 5,000 Litres); and improved cell line design and fermentation processes, which have improved specificity and reduced impurities. Additionally, the upscaling production has reduced mAb costs. Currently,

mAbs represent the fastest growing segment in the biopharma sector (> 100 billion dollars annually). Moreover, focus has expanded beyond cancer and autoimmune disorders to include infectious diseases.<sup>2,11,12</sup>



**Figure 5:** Advances in hybridoma technology.<sup>10</sup>

**Abbreviations:** mAbs: Monoclonal Antibodies; CDR: Complementarity-Determining Region.

### Advantages of mAbs over traditional anti-microbial therapy

With the emergence of MDR bacteria, mAbs are going to play a crucial role in the fight against infections in the near future (Table 5).

Feature	Serum therapy	Antibiotics	mAbs
Source	Animal or human sera	Chemical processes/fermentation	Tissue culture, hybridomas
Variation in each lot	Significant	Low	Low
Disease specificity	Narrow spectrum	Broad spectrum	Narrow spectrum
Side-effects	Poor tolerance, newer immunoglobulins safer	Low toxicity	Low toxicity
Pharmacokinetics	Variable	Consistent	Consistent
Route of administration	SC, IM or IV	Oral, IM, IV	SC, IM, IV

**Table 5:** Comparison of serum therapy, antibiotics, and monoclonal antibodies (mAbs) as anti-microbial therapy.

**Abbreviations:** IM: Intramuscular; IV: Intravenous; SC: Subcutaneous.

### Role of mAbs in viral infections (Table 6)

**RSV:** mAbs including nirsevimab and palivizumab offer key advantages over vaccines by providing immediate, long-lasting passive immunisation and preventing severe RSV infection in infants and vulnerable young children. Both target the fusion 'F' protein of the virus. Nirsevimab, with its extended half-life offers protection for an entire RSV season, whereas palivizumab requires monthly injections. Notably, plant-based expression platforms have been successfully used for production of recombinant RSV mAbs, which will reduce manufacturing costs compared to traditional mammalian platforms.<sup>13</sup>

**Human immunodeficiency virus (HIV):** mAbs can be potentially used in prophylaxis and treatment of multidrug-resistant (MDR) HIV in treatment-experienced patients. Ibalizumab has received approval for resistant HIV infection, while broadly neutralising antibodies (bNAbs) such as VRC01 are being tested for long acting pre-exposure prophylaxis (PrEP) and for immune enhancement in long-term treatment. The fact that HIV mutates rapidly remains a challenge.<sup>14,15</sup>

**Rabies:** Conventional post-exposure prophylaxis using equine or human rabies immunoglobulin (HRIG) faces limitations due to cost, availability and potential side-effects. mAbs produced by recombinant DNA technology, now offer a safer and more accessible alternative for immediate passive immunity after a potential exposure to the virus following an animal bite. Rabishield and Twinrab are approved for use and are administered by infiltration majorly around the wound site, with the remainder given intramuscularly.<sup>16</sup>

	Action	Effect/ Efficacy	Indications	Dose	Half-life ( $t_{1/2}$ )	Cost	Potential use
<b>RSV prevention</b>							
Palivizumab (RSV prevention)	Humanised mAB  Target RSV F protein site II	45.82% against RSV related hospitalisation in high-risk infants	Infants < 29 weeks of gestational age; chronic lung disease of prematurity; haemodynamically significant congenital heart defect; select cases of pulmonary abnormalities, neuromuscular disorders, and severe immunodeficiency	15 mg/kg administered monthly up to a maximum of 5 doses during RSV season	Short half-life of approximately 17–26 days	Expensive	Recommended in high-risk population only
Nirsevimab (RSV prevention)	Humanised mAB  Target RSV prefusion F protein site	Preterms: 70.1% reduction on RSV associated MALRTIs, 2.6% vs 9.5% on RSV disease compared to placebo	Universal indication (potential) on infants	Single dose 50 mg IM in infants weighing < 5 kg and 100 mg IM in those weighing > 5 kg	Long half-life of approximately 150 days due to modified Fc region	Relatively better cost to effectiveness ratio	Universal prophylaxis in children against RSV
<b>HIV therapy</b>							
Ibalizumab	Humanised mAB  Target CD4 T cell extracellular domain 1 and 2	In vitro neutralising activity against approximately 90% of a diverse panel of HIV strains  Rapid reduction of HIV-ribonucleic acid (RNA) levels, 43% of participants achieve HIV RNA suppression after 24 weeks therapy	Used in combination therapy in heavily treatment experienced MDR HIV-1 patients unresponsive to the current antiretroviral regimen	Initial dose: 2000 mg IV and maintenance dose 800 mg every fortnight	Extended $t_{1/2}$ with high dose due to saturable elimination	Very expensive	Only in patients with MDR HIV.
<b>Rabies prevention</b>							
Rabies Human mAb (rDNA)  Rabishield	Target a conformational epitope of the rabies G protein	It is as effective as serum derived hyper-immune IgG  It can fail against virus variants that circulate in Africa and North America	It must be given together with vaccine within 7 days after a bite for rabies post-exposure prophylaxis	3.33 IU/kg body weight		Cheaper than hyper-immune rabies IgG	Largely replaced by two mABs combination below
Miromavimab plus docaravimab (Twinrab)	Target the antigenic sites I and III of the rabies G protein	Combination is as effective as serum derived hyperimmune IgG	It must be given together with vaccine within 7 days after a bite	40 IU/kg body weight		Cheaper than hyper-immune rabies IgG	Highly recommended

**Table 6:** Currently approved mABs for RSV, HIV and Rabies virus.<sup>17</sup>

**Abbreviations:** Fc: Fragment Crystallisable; HIV: Human Immunodeficiency Virus; HRIG: Human Rabies Immunoglobulin; IgG: Immunoglobulin G; IM: Intramuscular; IV: Intravenous; MALRTI: Medically Attended Lower Respiratory Tract Infection; MDR: Multidrug-Resistant; mAb: Monoclonal Antibody; rDNA: Recombinant Deoxyribonucleic Acid; RSV: Respiratory Syncytial Virus;  $t_{1/2}$ : Half-Life.

**Ebola virus (Table 7):** The WHO has approved two mAbs as approved therapies for the treatment of infections caused by the Zaire strain of the Ebola virus. Inmazeb (REGN-EB3) is a cocktail of three mAbs — atoltivimab, mafivimab, and odesivimab — that bind to different, non-overlapping parts of the Ebola virus glycoprotein. Ebanga (mAb114), also known as ansuvimab is a single humanised mAb. These antibodies neutralise the virus by binding to its surface glycoprotein and prevent

its entry into host cells. In randomised clinical trials conducted during the 2018–2020 Ebola outbreak in the Democratic Republic of the Congo (PALM Trial), both mAbs demonstrated significant efficacy when administered early in the course of infection. These mAbs are not effective against the Sudan strain of the Ebola virus. Furthermore, they cannot be administered along with the live Ebola vaccine, as it reduces the vaccine's efficacy.<sup>18,19</sup>

Drug (Brand name; Company)	Target	Format	Technology	Indication	Year of FDA approval
Ansuvimab (Ebanga)	Ebola glycoprotein	Human IgG1	Human	Prevention and treatment of Ebola	2020
Atoltivimab, mafivimab and odesivimab (Inmazeb)	Ebola glycoprotein	Human IgG1	Transgenic mice	Prevention and treatment of Ebola	2020

▼  
**Table 7:** Monoclonal antibodies for Ebola.

**Abbreviations:** FDA: Food and Drug Administration; IgG1: Immunoglobulin G1.

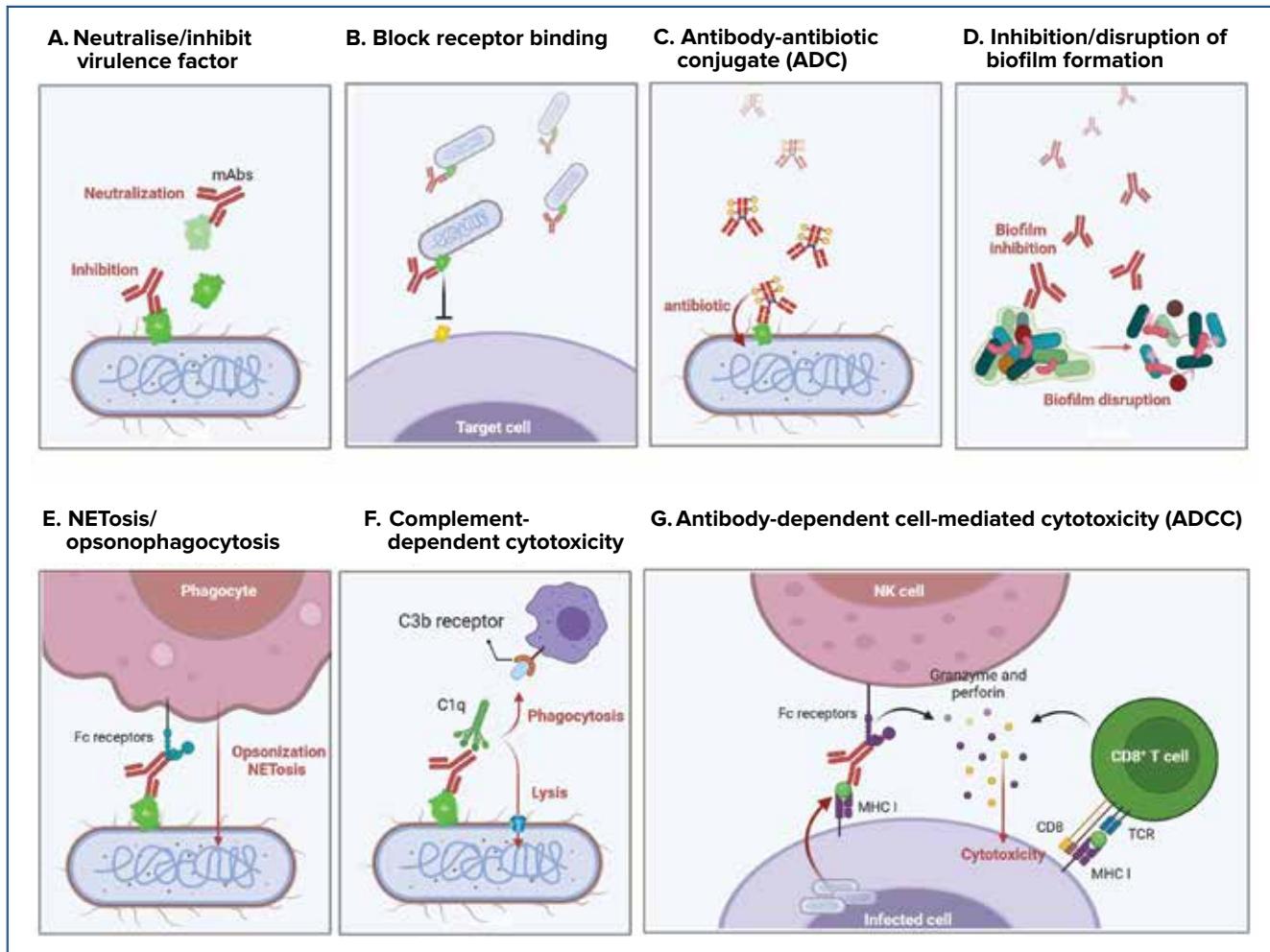
**COVID-19 infection:** mAbs were developed on a war-footing during the COVID-19 pandemic for the treatment of the SARS-CoV-2 infection. Examples include REGEN-COV (combination of casirivimab and imdevimab) targeting the virus spike protein, approved by the United States Food and Drug Administration (US FDA) and the European Union (EU) for both treatment and prevention. Other mAbs included bamlanivimab and etesevimab, tixagevimab and cilgavimab, bebtelovimab, and sotrovimab. However, the emergence of new SARS-CoV-2 variants posed a major challenge, limiting the continued usefulness of these antibody cocktails. Moreover, multiple studies including a randomised control trial comparing COVID-19 convalescent plasma with mAbs found no difference in efficacy in preventing the need for hospitalisation.<sup>20</sup>

#### Role of mAbs in bacterial infections<sup>21</sup>

With the emergence of MDR pathogens and indiscriminate use of antibiotics, extensive research is underway to explore the use mAbs as anti-microbials. This approach offers greater specificity towards individual targets, unlike broad-spectrum antibiotics,

thereby reducing the likelihood of developing antimicrobial resistance. The proposed mechanisms of action of mAbs against bacteria include the following (Figure 6):

- **Neutralisation of bacterial toxins** — e.g., bezlotoxumab for *Clostridium difficile*
- **Inhibition of bacterial adhesion to host cells** — e.g., mAbs targeting the Type III secretion system (TTSS) of *Pseudomonas aeruginosa*
- **Interference with bacterial communication system (quorum sensing)** — by blocking quorum sensing (QS) molecules, thereby reducing bacterial virulence
- **Opsono-phagocytosis** — by functioning as opsonins, to mark pathogens for enhanced destruction by macrophages and neutrophils
- **Complement-dependent cytotoxicity** — by activating the complement cascade
- **Disruption of biofilm** — by binding to the scaffolding matrix proteins within the biofilm



**Figure 6:** Mechanisms of monoclonal antibodies against bacterial infections.<sup>21</sup>

**Abbreviation:** NET: Neutrophil Extracellular Trap.

#### US FDA-approved antibacterial mAbs<sup>18,19</sup>

To date, only three antibacterial mAbs had received FDA approval, as follows:

1. **Bezlotoxumab (Zinplava®):** For adults at high risk of recurrent of *Clostridium difficile* infection. It works by binding to and neutralising the *C. difficile* toxin B.
2. **Raxibacumab (Abthrax®):** For the treatment and prophylaxis of inhalational anthrax caused by *Bacillus anthracis*. It works by neutralising the protective antigen (PA) component of the anthrax toxin.
3. **Obiltoxaximab (Anthim®):** For inhalational anthrax. Similar to raxibacumab, it also targets and neutralises the PA component of the anthrax toxin.

#### Challenges in development of anti-bacterial mAbs:

1. **Pathogen diversity:** Unlike viruses, bacteria possess hundreds of potential surface antigens and multiple serotypes. Consequently, a single mAb

may not provide broad protection, necessitating the development of antibody cocktails targeting multiple epitopes.

2. **Target accessibility:** A potential target may be masked by the polysaccharide capsule, making it difficult for mAb to bind.
3. **Clinical trial failures:** Many candidate mAbs have failed in human trials after being found useful in animal models. Moreover, co-administration with antibiotics during studies can confound results.
4. **Cost and market size:** The research and development of mAbs is very expensive, and the relatively small market size can limit commercial viability.
5. **Dependence on rapid diagnostics:** As mAbs are highly specific, effective treatment may depend on rapid and accurate diagnosis of the infective pathogen.

The key viral and bacterial targets currently under investigation for mAb development are summarised in Table 8.

Infection	Target site
SARS-CoV2	S1 receptor binding domain (SBD) for binding spike protein S to ACE2
Influenza	Haemagglutinin (HA) and neuraminidase (NA) receptors
Ebola	Viral glycoprotein
Hepatitis C	E1-E2 complex
Zika and dengue	E protein
Bacterial infections	Toxin, lipopolysaccharide

▼  
**Table 8:** Targets for monoclonal antibodies (mAbs) against infectious diseases.

**Abbreviations:** ACE2: Angiotensin-Converting Enzyme 2; E: Envelope; E1-E2: Envelope Glycoprotein Complex; HA: Haemagglutinin; NA: Neuraminidase; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; SBD: Spike Binding Domain.

### Side-effects of mAbs

When evaluating mAb therapies, it is important to recognise that each mAb is a unique protein, and treatment involves administering a significant quantity of protein through IV, intramuscular, or subcutaneous routes. While mAbs generally have an excellent safety profile in both randomised controlled trials (RCTs) and observational studies, some have been linked to adverse events, which may be related to the specific characteristics of individual formulations. Side effects can include infusion-related reactions, fever, nausea, rash, diarrhoea, and hypotension. For instance, the combination of tixagevimab and cilgavimab was associated with a higher incidence of thromboembolic events compared with other mAbs, while the combination of casirivimab and imdevimab, and bamlanivimab alone, have shown a higher incidence of ischaemic heart disease events. Bevacizumab (Avastin), which targets a protein called vascular endothelial growth factor (VEGF), can cause hypertension, bleeding, thrombotic events, and kidney damage. Similarly, cetuximab (Erbitux), which targets the epidermal growth factor receptor (EGFR), may cause severe skin rashes in some people as EGFR is also present in normal skin cells.

### Application of mAbs in travel medicine<sup>22</sup>

**mAbs may be used in travel medicine in the following scenarios in the future:**

- **Pre-travel prophylaxis:** Passive immunisation using mAbs could prevent diseases such as malaria.
- **Post-exposure prophylaxis:** mAbs can prevent disease onset after exposure, as already demonstrated in rabies management.
- **Treatment of travel-acquired infections:** mAbs may be developed for infections like dengue fever and yellow fever.

Hypothetically, mAbs may offer advantages in certain situations over standard vaccines and prophylaxis methods. For example, using mAbs to prevent *Plasmodium falciparum* malaria could involve a single injectable dose administered before departure, providing protection without significant side effects, compared to daily or weekly oral anti-malarial prophylaxis. Other examples include single-dose mAb prophylaxis for hepatitis A or yellow fever in immunocompromised travellers who may not be able to produce a sufficient antibody response or where live attenuated vaccines, such as the yellow fever vaccine is contraindicated.

mAbs have also shown promise in treating diseases with high mortality, such as Ebola and yellow fever, and research is ongoing for diseases like rabies and dengue fever.

### Emerging mAbs against infectious diseases

**Nipah virus:** A human clinical trial to test the safety and efficacy of a novel monoclonal antibody, MBP1F5, is expected to begin in India and Bangladesh soon. Nipah virus has a high mortality rate (45%–75%), and currently lacks an approved vaccine.<sup>23,24</sup>

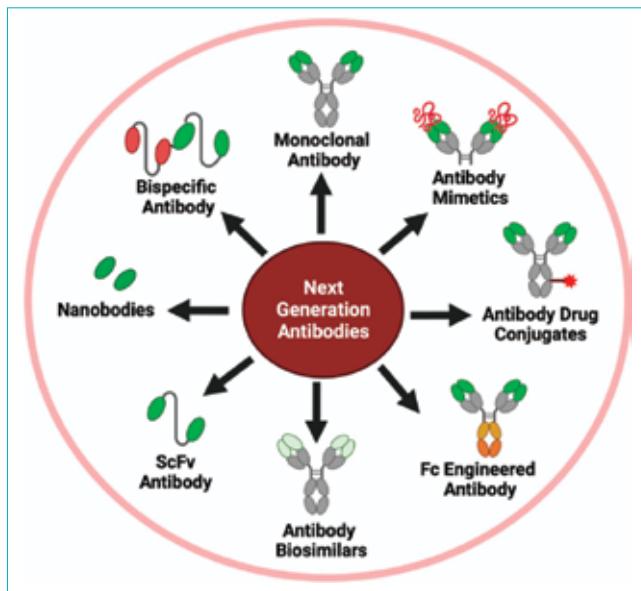
**Dengue:** Phase II clinical trials are underway for AV-1, an investigational human mAb developed by AbViro (USA), to mitigate clinical symptoms when administered before or after dengue infection.<sup>25</sup>

**Influenza:** mAbs in clinical development for influenza are aimed at treating active infections. Due to the annual variation in circulating strains, most mAbs under development target the highly conserved stem region of the haemagglutinin (HA) protein.

**Malaria:** Based on promising preclinical results from two mouse models of *Plasmodium falciparum* infection, the mAb CIS43LS is being developed as a long-acting immune prophylactic against malaria.

### Next generation antibodies<sup>26</sup>

The different formats and types of next-generation antibodies are illustrated in Figure 7.



**Figure 7:** Next generation antibodies.<sup>26</sup>

**Abbreviations:** Fc: Fragment Crystallisable; ScFv: Single-Chain Variable Fragment.

### Single-chain variable fragment (scFv) antibodies

mAbs have limitations in treating diseases because of their relatively large molecular size. To address this, smaller scFv recombinant antibodies have been developed. They consist of the variable heavy (VH) and variable light (VL) chains connected by a flexible poly-linker peptide (15–20 amino acids). The bacterial expression system, particularly *Escherichia coli*, is commonly used for scFv production. The size of scFvs (27 kDa) is roughly one-fifth that of a complete antibody, allowing easier penetration into tumours and accessibility to cryptic epitopes. Moreover, scFvs are cleared more easily from non-target healthy tissues causing lesser side-effects.

An scFv is thus a recombinant antibody format composed of a single polypeptide chain that retains the antigen-binding properties inherent in the intact antibody, while offering advantages in size, penetration, and manufacturability.

### Bispecific antibodies

mAbs have two arms that each recognises the same target antigen. Bispecific antibodies (bsAbs) have two unique binding domains simultaneously binding to two different antigens, offering an improved therapeutic approach. Early bsAbs were created by chemically combining two mAbs or fusing together two hybridoma cell lines, resulting in 'quadroma' cell lines. Recently, genetic engineering advancements have led to the development of more than 50 recombinant bsAbs. Removab (catumaxomab) and Blincyto (blinatumomab) were amongst the first clinically approved bsAbs, used for treating malignant ascites intraperitoneally and for relapsed or refractory B-cell acute lymphoblastic leukaemia (ALL) respectively.

### Antibody biosimilars

Antibody biosimilars are biologic drugs that closely resemble approved therapeutic mAbs (reference or originator mAbs) in structure, function, and efficacy. These have to replicate the safety, efficacy, and quality of the original mAbs, they are not identical to the originator molecule. Several biosimilars for including infliximab, rituximab, trastuzumab, and bevacizumab have been approved. These are more affordable although efficacy maybe lower.

### Antibody mimetics

Antibody mimetics, or "synthetic antibodies," are designed to mimic the functions of natural antibodies by replicating their antigen-binding segments, minus the Fc region and associated issues. These are more stable and cost-effective.

### Antibody drug conjugates (ADCs)

ADCs combine the specificity of mAbs with the potent cytotoxic effects of small-molecule drugs. ADCs selectively deliver powerful anticancer agents directly to tumour cells, minimising the systemic toxicity that typically accompanies chemotherapy eg. ado-trastuzumab emtansine (Kadcyla) for human epidermal growth factor receptor 2 (HER2) positive breast cancer. ADCs can be used in combination with other oncology treatments to enhance overall anti-tumour effects.

## mAbs as vaccines<sup>27</sup>

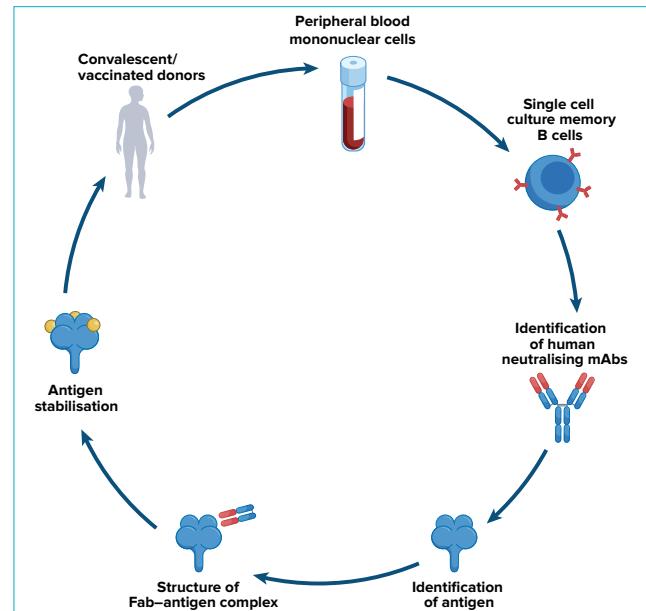
Although vaccines remain the most effective preventive measure against infections, effective vaccines have not yet been developed for pathogens such as HIV, RSV, Hepatitis C, and Ebola virus. For a vaccine to be effective, it must elicit a robust and durable antibody response. Identifying antibodies capable of effectively neutralising a pathogen is a key step in hastening vaccine development.

Pathogen-neutralising mAbs are used to identify antigenic structures on the pathogen's surface. These antigen-antibody complexes are then analysed to select antigenic structures suitable for vaccine design (Figure 8).

The concept of reverse vaccinology 2.0, also known as antibody-based vaccinology, aims to overcome the limitations of traditional vaccine development methods by creating novel vaccines through the use of structural information derived from mAb-antigen complexes. The process starts with single-cell cultures of plasma or memory B cells derived from convalescent patients or vaccinated donors. These cultures are screened to identify mAbs with neutralising activity against the target pathogen. The recombinant mAbs are then used to identify the antigen and analyse the three-dimensional (3D) structure of the antigen-mAb complex. This structural data is crucial for designing and optimising stabilised antigens for next-generation vaccine development.

### Roadmap for mAb use in infection outbreaks

Humanity has faced at least seven major viral outbreaks in the 21<sup>st</sup> century — SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV), influenza A (H1N1), Zika virus, Ebola virus, SARS-CoV-2,



**Figure 8:** Schematic representation of reverse vaccinology 2.0.<sup>27</sup>

and monkey pox (Mpox) — and must brace ourselves for further outbreaks. The war-paced development and deployment of mAbs for COVID-19 pandemic stands out as a scientific success story. This accomplishment saved countless lives and established a blueprint for contingency planning in future infectious disease emergencies. To further enhance mAb effectiveness, they could be combined with small-molecule antiviral drugs, which may lower viral loads and minimise the selection of mutant strains. Given the importance of early intervention, widespread use of mAbs will require the establishment of dedicated infusion centres and physician education, so that mAb therapy can be promptly administered to high-risk individuals during future outbreaks.

## Conclusion

mAbs have evolved from experimental immunotherapies to essential tools in infectious disease management. Their precision, adaptability, and safety make them promising alternatives to conventional antimicrobials, particularly in an era of rising MDR. Recent advances — including bispecific antibodies, antibody-drug conjugates, and mimetics — have expanded their clinical utility beyond oncology to encompass viral, bacterial, and parasitic infections. The rapid development of mAbs during the COVID-19 pandemic demonstrated their scalability and global relevance. Future priorities include cost-effective production, improved delivery systems, and equitable access to ensure mAbs become integral components of modern antimicrobial therapy.

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# The Future of Clinical Research: Navigating a New Era of Innovation, Efficiency, and Patient-Centricity

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## Abstract:

Clinical research stands at a critical juncture, facing persistent challenges of increasing complexity, high costs, and lengthy timelines. The traditional model, with its reliance on centralised, manual processes, is giving way to a new paradigm defined by the convergence of technology, a fundamental shift toward patient-centricity, and an evolving regulatory landscape. This report explores the interconnected megatrends reshaping the industry, the catalytic role of artificial intelligence (AI), the logistical and philosophical shift to decentralised and hybrid clinical trials (DCTs), the foundational reorientation around the patient experience, and the concurrent evolution of the regulatory and ethical framework. The analysis indicates that AI is not merely a tool for automation but has become a strategic partner capable of optimising trial design, predicting outcomes, and accelerating drug discovery. Meanwhile, DCTs, powered by digital health technologies such as wearables, are dismantling geographic and socioeconomic barriers, fostering greater diversity, and providing a continuous stream of high-quality, real-world data. This new, patient-centric philosophy is proving to be a cornerstone of success, leading to improved patient engagement and higher retention rates. However, these innovations are outpacing the current operational and regulatory infrastructure, creating significant challenges related to data privacy, algorithmic bias, and the need for new standards and greater collaboration. The future of clinical research is envisioned as an integrated ecosystem where technology, patient insights, and a harmonised regulatory framework converge. Success will depend on a proactive approach to collaboration, standardisation, and ethical governance, ensuring that the innovations of today lead to a more equitable, efficient, and ultimately more effective development pipeline for life-saving therapies.

**Key words:** Clinical Research, Clinical Trials, Drug Development, Patient-Centred Research, Regulatory and Ethical Frameworks, Operational Challenges in Clinical Trials, Artificial Intelligence, Machine Learning, Natural Language Processing, AI-Powered Predictive Analytics, Clinical Trial Simulation Tools.

## Introduction

The clinical research landscape is undergoing a profound transformation, compelled by the inherent inefficiencies of its traditional model.<sup>1</sup> The immense administrative complexity and high costs of bringing a new drug to market, with a staggering 70% of clinical sites reporting trials have become more challenging to manage in the last five years. This necessitates a fundamental change in approach.<sup>2</sup>

The stakes are extraordinarily high, as evidenced by a low average drug approval rate of 13.8% and an average duration of approximately 7.5 years from clinical testing to marketing approval.<sup>3</sup> This environment has created a powerful impetus for a new paradigm that prioritises efficiency, inclusivity, and adaptability.

The transformation is driven by three primary forces. First, technological innovation, particularly in artificial intelligence (AI), machine learning (ML), and digital health, is providing powerful new tools to address long-standing bottlenecks. Second, there is a philosophical shift to place the patient at the centre of the research process, redesigning trials to be more accessible, less burdensome, and more reflective of real-world experiences.<sup>4</sup> Finally, the confluence of these forces is exerting pressure on the regulatory framework, which must adapt to new methodologies and data sources while upholding the highest standards of safety and ethical conduct.<sup>5</sup>

This report is structured to provide a comprehensive analysis of this new era. It begins by examining the foundational technological trends, followed by an in-depth look at the patient-centric philosophy that unifies these trends. The report then addresses the significant operational, regulatory, and ethical challenges that must be navigated, concluding with a forward-looking vision and actionable recommendations for stakeholders to prepare for a more integrated and successful future.

### **The Rise of Technological Catalysts: Artificial Intelligence and Beyond**

#### **Precision in trial design and optimisation**

One of the most promising applications of AI is in the design of clinical protocols. By analysing vast amounts of historical data — including previous trial outcomes and medical data — AI can identify patterns and correlations at a scale unattainable by human researchers.<sup>6,20</sup> This capability enables the creation of more effective and safer protocols by refining participant selection criteria, optimising dosing schedules, and more accurately determining endpoints.<sup>7,8</sup> Machine learning models can simulate different trial designs to predict potential outcomes, allowing researchers to select the most efficient and robust protocols before a study even begins.<sup>9,10</sup> An example of this is the development of a clinical trial simulation (CTS) tool for Alzheimer's disease, which was endorsed by regulatory bodies to model disease progression and optimise trial parameters by integrating diverse datasets.<sup>11,12</sup>

#### **Accelerating patient recruitment and selection**

Patient recruitment and retention remain significant challenges, with high dropout rates contributing to costly delays.<sup>13</sup> AI-powered predictive analytics are addressing this by sifting through real-world data, such as electronic health records (EHRs), medical histories, and other relevant information, to find potential participants who meet trial criteria.<sup>14</sup> This approach not only accelerates enrolment but also ensures a more precise match of patients to a study's requirements. For example, companies like IQVIA are leveraging machine learning to model patient data, enabling hyper-targeted outreach campaigns to identify eligible participants both within a site's known population and in the broader community.<sup>7</sup> The use of natural language processing (NLP), a subset of AI, further enhances this process by sifting through unstructured data in medical records to extract relevant information and identify eligible patients more efficiently.<sup>15,16</sup>

#### **Enhancing data management and analytics**

The volume and complexity of Data generated in modern clinical trials are immense, sourced from EHRs, wearable devices, and patient-reported outcomes.<sup>17</sup> AI-powered analytics platforms are uniquely equipped to handle this "Big Data," processing and analysing vast datasets far more quickly than traditional methods.<sup>18,19</sup> These models can identify intricate patterns and correlations that may be overlooked by human analysts, which reduces human error in data interpretation and provides more reliable insights. AI systems continuously monitor trial data in real-time, detecting anomalies and potential issues before they can impact the trial's results.<sup>20,21</sup> For instance, AstraZeneca has developed an AI and ML system called Automating Identification Detection Adjudication (AIDA) to accelerate the assessment of clinical events, which has proven to be highly consistent with human expert adjudication and can significantly shorten study timelines.<sup>22</sup>

## Disclosure

The authors declare that no conflicts of interest exist. 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

The future of clinical research is not a simple linear evolution but a fundamental and necessary transformation. The convergence of technological innovation, particularly AI and DCTs, with a patient- centric philosophy, is reshaping the entire ecosystem. While these trends promise to make research faster, more efficient, and more equitable, they also introduce complex operational, regulatory, and ethical challenges. The industry's ability to succeed will depend on its capacity to foster collaboration, embrace integrated technologies, and govern these innovations with a steadfast commitment to ethical standards and patient welfare. Ultimately, this new era is poised to deliver a clinical research ecosystem that is not only more effective in accelerating the development of life-saving therapies but also more accessible and beneficial to the diverse populations it serves. The future of clinical research is not merely a linear progression of existing practices, but a fundamental transformation driven by the synergy of technology and a renewed focus on the patient. The current fragmented ecosystem, with its silos of technology, people, and processes, will give way to a more integrated, collaborative, and efficient model. In this new era, data from a wide array of sources — including EHRs, wearables, and genomic information — will be seamlessly collected, analysed by AI, and used to inform trial designs that are more precise and patient-friendly. The logistical and philosophical shift to DCTs will continue to make trials more inclusive and accessible, providing a continuous stream of real-world data that enhances the relevance of study findings.

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# High Precision Stereotactic Body Radiotherapy for the Treatment of Malignant Tumours: An Overview

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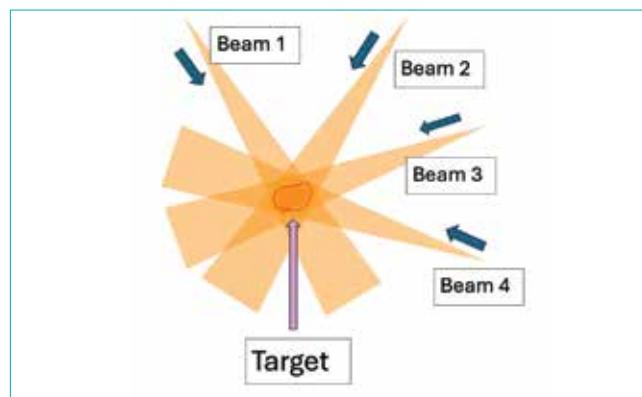
## Abstract:

Stereotactic body radiotherapy (SBRT) is an advanced form of cancer treatment that uses precisely targeted, high-dose radiation to destroy tumours while minimising damage to surrounding healthy tissue. It is commonly used to treat small tumours in organs such as the prostate, lung, and kidney, and serves as a non-surgical alternative for patients who may not be suitable for surgery. Unlike conventional radiation therapy, which can take several weeks, SBRT is typically completed in just one to five treatment sessions.

**Key words:** Stereotactic Body Radiotherapy (SBRT), Stereotactic Ablative Radiotherapy, Cancer Treatment, Radiotherapy, Metastatic Disease, Oligometastases, Precision Radiotherapy.

## Introduction

Stereotactic body radiotherapy (SBRT), also referred to as stereotactic ablative radiotherapy (SABR), is a high-precision radiation therapy technique.<sup>1</sup> This technique enables the delivery of large doses per fraction to small, well-defined extracranial targets over a limited number of treatment sessions.<sup>2</sup> Stereotactic radiotherapy was initially developed for treating intracranial conditions in a single or multiple sessions, which is known as stereotactic radiosurgery (SRS) or fractionated stereotactic radiotherapy (SRT). The integration of advanced imaging techniques for target localisation and tracking software, along with robust immobilisation devices and sophisticated delivery systems, allows SBRT to achieve steep dose gradients, effectively sparing adjacent normal tissues (organs at risk [OAR]) (Figure 1). This precision has expanded the curative potential of radiotherapy to clinical situations that were previously deemed inoperable.<sup>3,4</sup> With its outstanding results, SBRT has become a non-invasive and highly effective ablative treatment with little to no toxicity. Moreover, it can be repeated and sequentially combined with other systemic therapies.



**Figure 1:** Conceptual beams for a stereotactic body radiotherapy (SBRT) plan (multiple beams focusing on a target from different directions).

In the modern era, SBRT has become a cornerstone modality in managing early-stage non-small cell lung cancer (NSCLC), hepatocellular carcinoma (HCC), and pancreatic tumours. Furthermore, it is increasingly utilised for treating limited metastatic disease, known as metastasis-directed therapy, to delay systemic progression and improve survival outcomes.<sup>5</sup> Due to

its ability to achieve high local control with minimal toxicity, SBRT is now regarded as a vital component of modern precision radiotherapy.

### Radiobiological Rationale

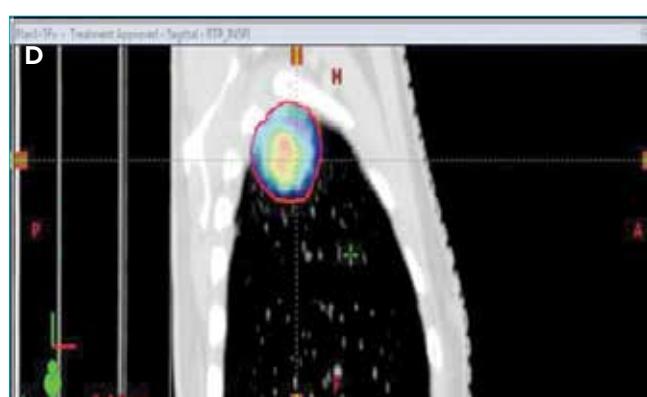
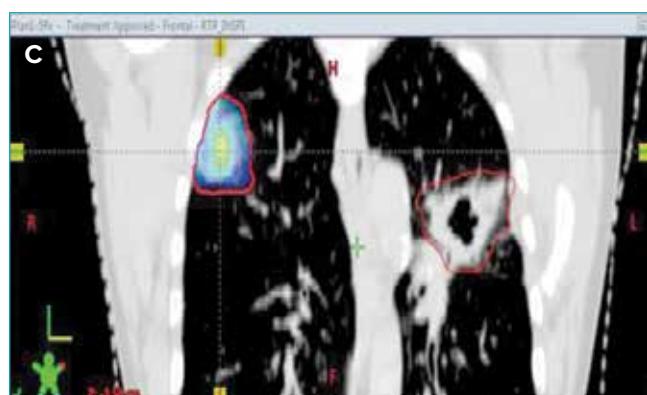
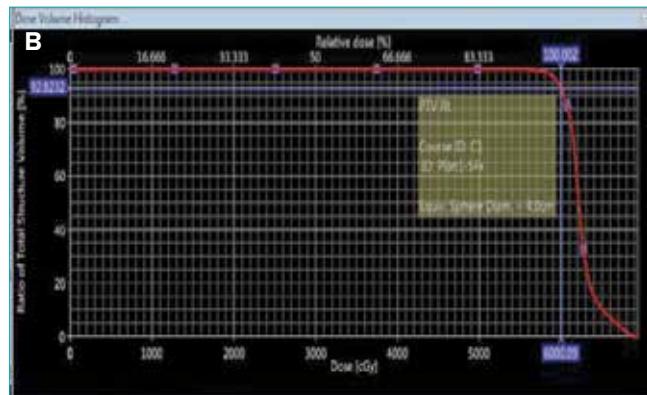
The biological effectiveness of SBRT stems from its ability to deliver high doses per fraction, resulting in a biologically effective dose (BED) substantially greater than that achieved with conventional fractionation.<sup>6</sup> The mechanisms of tumour eradication extend beyond direct deoxyribonucleic acid (DNA) double-strand breakage and include damage to the tumour vasculature and stimulation of antitumour immune responses. These processes involve endothelial apoptosis, vascular compromise, and induction of immunogenic cell death, which collectively enhance tumour control.<sup>7</sup>

### Clinical Applications

#### Early-stage non-small cell lung cancer (NSCLC) and lung metastasis

SBRT is established as the standard treatment for patients with medically inoperable, early-stage NSCLC. Prospective clinical trials have reported local control rates exceeding 90% at three years, with overall survival outcomes approaching those of surgical resection.<sup>8</sup> Standard dosing regimens commonly involve 48–60 Gy delivered over three to five fractions, providing both efficacy and safety in this patient group.

Similarly, lung metastasis has become an important indication for using SBRT (Figure 2).



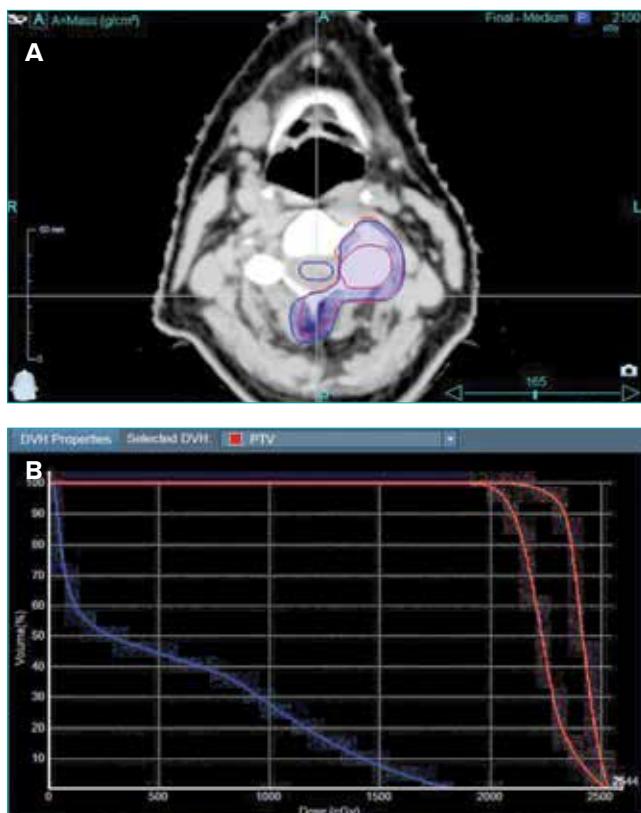
**Figure 2:** A 74-year-old male patient with metastatic carcinoma of the urinary bladder presented with progressive disease in both lungs after multiple lines of chemotherapy. He received stereotactic body radiotherapy (SBRT) to lesions in both lungs — right planning target volume (PTV) 60 Gy in 5 fractions and left PTV 40 Gy in 5 fractions — delivered using the deep inspiratory breath hold technique. The patient tolerated the treatment well and remains on regular follow-up. The multiple images show the dose wash of right-sided lesion in axial view (A), the dose volume histogram (B), coronal view (C), and sagittal view (D).

## Hepatocellular carcinoma (HCC)

For patients with primary liver tumours, SBRT provides excellent local control while maintaining hepatic function. Because the liver is sensitive to radiation, motion management and dose optimisation remain crucial for effective treatment. Reported two-year local control rates range between 70% and 90%, even among patients who are unsuitable for surgery or radiofrequency ablation (RFA).<sup>9</sup>

## Spinal lesions and bone metastasis

SBRT has emerged as a highly effective treatment for spinal and bone metastases, offering durable pain relief and local disease control. Standard protocols deliver 16–24 Gy in a single session or 27–30 Gy over three fractions (Figure 3). Image-guided delivery ensures sub-millimetre precision, minimising radiation exposure to the spinal cord.<sup>10</sup>



**Figure 3:** A 70-year-old female presented with C3 vertebral metastasis, having oligometastatic carcinoma of both breasts and a history of multiple lines of chemotherapy. She was planned for 21 Gy in 3 fractions to the planning target volume (PTV), with a simultaneous integrated boost of 24 Gy in 3 fractions to the gross tumour volume (GTV), achieving clear sparing of the spinal cord. The axial (A), sagittal (C) and coronal images (D) can be seen with dose wash, cleanly sparing the spinal cord. (B) shows the dose volume histogram of dose plan

## Pancreatic malignancies

In the management of locally advanced or unresectable pancreatic cancer, SBRT offers significant local control and palliation of symptoms. When combined with systemic therapy, it provides a feasible treatment option for patients who are not suitable candidates for surgical resection.

## Renal cancer

Surgery remains the standard of care for patients with primary renal cell carcinoma (RCC). However, SBRT is a novel alternative for patients who are medically inoperable, technically high-risk, or who decline surgery. Evidence supporting SBRT in primary RCC setting is growing. Optimal dose fractionation typically comprises 25–26 Gy in one fraction, or 42–48 Gy in three fractions for larger tumours. Routine post-treatment biopsy is not recommended, as it does not predict patient outcomes. Also, SBRT for primary RCC in a solitary kidney is safe and effective. Post-treatment follow-up guidelines include cross-axial imaging of the abdomen, including both kidneys and adrenals, along with chest surveillance initially every 6 months.

## Advantages and Limitations of SBRT

SBRT presents several advantages: it is non-invasive, completed within a short time frame (typically one to two weeks), and provides high local control rates comparable to those of surgery. The technique preserves organ function and the patient's quality of life. Moreover, SBRT has demonstrated efficacy in tumours traditionally considered radioresistant, such as melanoma and RCC and may enhance the effectiveness of immune-checkpoint blockade through immunomodulatory effects.<sup>11</sup>

Despite these benefits, several limitations exist. Motion management, particularly in thoracic and abdominal

sites, remains challenging. Dosimetric uncertainties can lead to toxicity if planning or dose constraints are inadequate. In addition, long-term outcome data are limited for specific tumour types and re-irradiation scenarios. The procedure requires specialised technology and a coordinated multidisciplinary team, which increases treatment costs and complexity.<sup>12</sup> Therefore, rigorous patient selection, meticulous planning, and quality assurance are essential for optimal outcomes.

## New Advancements in SBRT

Rapid technological and biological innovations are shaping the future of SBRT, with several emerging strategies designed to enhance precision and personalisation:

- 1. Radio genomics and biomarker-guided SBRT:** integrates genomic and imaging biomarkers to individualise fractionation and dosing strategies.
- 2. Combination with immunotherapy:** clinical trials are investigating SBRT in conjunction with programmed death-1/programmed death-ligand 1 (PD-1/PD-L1) inhibitors to augment systemic antitumour immune responses.<sup>13</sup>

These innovations collectively represent the next phase of biologically optimised, image-guided radiotherapy.

## Conclusion

One of the most significant barriers to successful cancer treatment is the failure to achieve adequate local control. SBRT exemplifies the synthesis of technological advancement and clinical efficacy in radiation oncology. By delivering ablative doses with microscopic precision, SBRT achieves durable tumour control while preserving normal organ function and minimising toxicity. Ongoing research into adaptive imaging, radiogenomic integration, and immunotherapeutic combinations is expected to refine its therapeutic potential further. As evidence continues to evolve, SBRT is positioned to remain a pivotal modality in both curative and metastasis-directed oncologic treatment paradigms.

Nidhi Sharma, Varshu Goel, Garima Singh, Khushboo Rastogi, Anusheel Munshi. High Precision Stereotactic Body Radiotherapy for Treatment of Malignant Tumours: An Overview. MMJ. 2025, December. Vol 2 (4).

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# From Likes to Lifestyle: How Social Media Shapes Modern Identity and Interaction

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## Abstract:

Social media has dramatically reshaped communication, identity formation, and everyday social life in the 21<sup>st</sup> century. What started as a tool for staying in touch has become a cultural force that influences self-image, relationships, and lifestyle decisions. This paper examines how online platforms impact modern identity and interaction, drawing on psychological theories, prior research, and global examples. It discusses how digital validation affects behaviour, how the line between online and offline identities has blurred, and how curated personas influence relationships and cultural trends. The findings highlight both benefits and risks of social media, emphasising the importance of digital literacy and conscious engagement.

**Key words:** Social Media, Digital Identity, Self-Presentation, Online Validation, Lifestyle Behaviour, Interpersonal Relationships.

## Introduction

Today, social media is woven into nearly every aspect of modern life. By 2025, more than 5.24 billion people worldwide use platforms such as Facebook, Instagram, TikTok, YouTube, and Twitter/X.<sup>1</sup> These platforms are no longer just communication tools, they are spaces where people shape identities, seek validation, and build lifestyles around digital expression.

Unlike traditional media, which provided limited ways to present oneself, social media offers endless opportunities to curate identity. Through carefully chosen posts, photos, and captions, people create an online version of themselves. Yet, this power also brings challenges: over-reliance on approval, anxiety about self-image, and pressure to conform to trending standards.

This paper explores three areas of influence:

1. How social media affects self-presentation and identity
2. How digital approval shapes lifestyle choices
3. How interpersonal relationships are transformed by digital interaction

## Literature review

Scholars often describe social media's role as paradoxical, offering both opportunities and challenges.

**Identity and self-presentation:** Classic theories like Goffman's *dramaturgy* remain relevant, as users manage digital impressions before multiple audiences. Recent studies show that online self-presentation is increasingly shaped by algorithmic visibility rather than direct social contexts.<sup>2</sup>

**Validation and well-being:** The system of likes and comments acts as a form of social capital. Recent studies report fluctuating self-esteem and even addictive behaviours driven by engagement-based feedback loops.<sup>3,4</sup>

**Relationships and society:** Digital connection is double-edged, promoting contact yet heightening emotional isolation.<sup>5</sup> However, it also supports “bridging capital” by maintaining extended networks online.<sup>6</sup>

Taken together, research shows that social media is neither fully positive nor negative; it is a dual force that empowers and pressures its users.

## Methods

This paper is based on a qualitative literature review. Academic research, survey reports, and case studies from different regions were analysed to understand social media’s impact. Sources include Pew Research Centre, United Nations Children’s Fund (UNICEF), and scholarly journals.

Three areas of influence guided the review:

- Identity formation and digital personas
- Lifestyle decisions - shaped by online approval
- The impact of online interaction on relationships

## Discussion

### 1. Social media and identity construction

**Digital self vs. real self:** Social media allows people to highlight selective parts of their lives, often creating an online version that looks more glamorous or ideal than reality. This gap can cause identity stress when one feels pressure to maintain a polished digital persona. According to the Pew Research Centre (2022), nearly six out of ten teenagers feel pressured to look attractive or popular online.<sup>7</sup>

**Case study – TikTok and youth identity:** TikTok has become central to how young people express themselves. Its algorithm promotes trends and challenges that encourage conformity, but it also creates spaces for marginalised groups, such as LGBTQ+ youth, to find support.<sup>8</sup>

### 2. From likes to lifestyle: digital validation as social currency

**Psychology of likes:** Research in neuroscience shows that likes trigger reward pathways in the brain.<sup>9</sup> This explains why users often plan posts to maximise attention, carefully selecting content that might gain higher engagement.

**Lifestyle influences:** Social media affects decisions in areas such as fashion, travel, and fitness.

**Fashion/beauty:** Influencers often shape consumer preferences by showcasing styles.

**Food/travel:** People increasingly seek “Instagram-worthy” meals or destinations; an Expedia (2023) report found that two-thirds of travellers chose destinations based on social media.<sup>10</sup>

**Health/fitness:** Movements like “#fitspiration” inspire exercise routines but also foster unhealthy body comparisons.

**Lifestyle branding:** Individuals increasingly turn themselves into brands, presenting daily routines in ways designed for audience engagement. For many, identity becomes inseparable from personal marketing.

### 3. Social media and interpersonal relationships

**Strengthening ties:** Social media helps maintain connections across distances. Even small gestures like likes, memes, and comments strengthen bonds.<sup>6</sup>

**Romantic relationships:** Online transparency complicates intimacy. Many couples report jealousy or mistrust due to constant access to a partner’s activity. An American Psychological Association (APA 2021) survey found that nearly half of couples experience social media-related conflicts.<sup>11</sup>

**Generational dynamics:** While young adults treat social media as an extension of life, older generations are more cautious. Yet, tools like WhatsApp have bridged family communication gaps, especially across borders.

### 4. The double-edged nature of influence

**Empowerment:** Social media has played a central role in movements like “#MeToo” and “#BlackLivesMatter”. During Coronavirus Disease 2019 (COVID-19), it also provided access to health information and community support.

**Risks:**

- **Misinformation:** False news during elections or health crises spreads rapidly
- **Cyberbullying:** UNICEF reports that one in three adolescents faces online harassment<sup>12</sup>

- **Echo Chambers:** Algorithms often reinforce existing opinions, fuelling polarisation

This dual role makes it clear that social media is both a tool of empowerment and a source of risks.

**Conclusion**

From likes to lifestyle, social media is deeply woven into how people form identities, make choices, and interact with others. It allows creativity, connectivity, and empowerment, but it also encourages dependence on validation and conformity to online trends.

The findings show that social media's effects depend on how it is used and how resilient individuals are. Promoting digital literacy and encouraging mindful use are essential for balancing the positives and negatives of online life.

Future studies should focus on long-term effects, especially on young people, and explore policies that balance freedom of expression with the need to prevent harm.

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# Glucagon-Like Peptide-1 Receptor Agonists and Aspiration Risk: A Perioperative Call to Action

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**Abstract:**

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are being widely prescribed for type 2 diabetes, obesity, polycystic ovary syndrome (PCOS), non-alcoholic fatty liver disease (NAFLD), and obstructive sleep apnoea (OSA). Their use for metabolic optimisation prior to surgery is rapidly increasing, yet their impact on gastric motility is an under-recognised anaesthetic challenge. We aim to highlight the aspiration risk associated with GLP-1 RAs in the perioperative period and during procedural sedation, and to offer perioperative strategies to mitigate this pharmacologically induced risk. This narrative commentary, informed by recent case reports, practice advisories, and international consensus statements, draws attention to a systems-level safety gap and emphasises the need for multidisciplinary awareness and action. Delayed gastric emptying caused by GLP-1 RAs may result in significant residual gastric contents, even after adherence to standard fasting guidelines. Reports from the Anaesthesia Patient Safety Foundation and others have documented aspiration and regurgitation events in fully fasted patients. Updated recommendations from the American Society of Anaesthesiologists (ASA), American Society for Metabolic and Bariatric Surgery (ASMBS), Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), Australian and New Zealand College of Anaesthetists (ANZCA), and American Diabetes Association (ADA) now emphasise individualised fasting, airway preparedness, and enhanced perioperative screening. GLP-1 RAs represent an invisible yet significant aspiration risk in the perioperative period. Surgeons, anaesthesiologists, endoscopists, and proceduralists must adapt by incorporating GLP-1 RA history into preoperative evaluation, extending fasting protocols where necessary, and employing airway protection strategies. This commentary advocates for institutional policy updates and interdisciplinary coordination to close this emerging safety gap.

**Key words:** GLP-1 Receptor Agonists, Aspiration Risk, Anaesthesia Safety, Perioperative Fasting, Delayed Gastric Emptying, Obesity, PCOS, NAFLD, Obstructive Sleep Apnoea, Surgical Risk Mitigation.

## Introduction

As anaesthesiologists, our role in safeguarding the perioperative period demands vigilance, precision, and anticipation of evolving risks. One such emerging concern is the growing impact of a new class of pharmacologic agents — glucagon-like peptide-1 receptor agonists (GLP-1 RAs) — on perioperative care and anaesthetic safety. Originally developed for glycaemic control in type 2 diabetes, these drugs are

now widely prescribed for chronic weight management, polycystic ovary syndrome (PCOS), non-alcoholic fatty liver disease (NAFLD), obstructive sleep apnoea (OSA) and metabolic optimisation prior to surgery.<sup>1,2</sup>

They act by delaying gastric emptying to prolong satiety, this mechanism has shifted the paradigm of fasting-based aspiration prevention. Increasing

evidence suggests that patients may arrive for anaesthesia or sedation while fully compliant with fasting instructions, yet harbour significant residual gastric contents. This creates a concealed aspiration risk that standard protocols may not address and significantly compromise patient safety.

Recent case reports and international advisories have raised awareness, prompting guideline updates from major anaesthesia and surgical societies. This commentary aims to alert all prescribing clinicians, anaesthesiologists, and perioperative teams to the implications of GLP-1 RAs and to outline practical steps for improving patient safety.<sup>2,3</sup>

### **A Whistleblower's Point of View: From Regular to Dangerous**

As anaesthesiologists, we are trained to anticipate aspiration risk. However, a new invisible threat has emerged — the pharmacologic full stomach caused by GLP-1 RAs. These agents are no longer confined to diabetes management; they are now widely used in patients with obesity, PCOS, NAFLD, OSA and for surgical weight optimisation.

Patients may present for routine endoscopy, interventional radiology, or dental procedures under sedation and appear fully fasted — yet retain gastric contents due to GLP-1-induced delayed emptying. This presents a serious systems-level gap: perioperative teams may be unaware of the patient's medication history, prescribers may not communicate usage, and sedation providers may not be prepared for sudden regurgitation.

This article is a call to action: it is time to update preoperative checklists, explicitly screen for GLP-1 RA use, and manage these patients as we would those with known gastroparesis. Until standardised pathways are widely adopted, vigilance and communication are our strongest safeguards.

### **Anaesthesia Patient Safety Foundation (APSF) Case Reports: Warning Signals**

The APSF highlighted a series of concerning cases in its 2023 newsletter, involving patients on GLP-1 RAs who experienced regurgitation or retained gastric contents despite standard fasting.

In one case, a gastric ultrasound prior to magnetic resonance imaging (MRI) under anaesthesia revealed solid food in the stomach 18 hours after fasting, leading to cancellation of the procedure. Another patient on semaglutide vomited undigested food from several days earlier during extubation; aspiration was avoided only because the endotracheal tube remained in place.<sup>2</sup>

A third patient undergoing sedation unexpectedly regurgitated mid-procedure, requiring emergency airway intervention.

These cases, published by APSF in 2023, reinforced that patients on GLP-1 RAs can have significant residual gastric content despite prolonged fasting, and may appear asymptomatic. APSF called for increased vigilance, preoperative disclosure, and consideration of extended fasting or gastric ultrasound in high-risk patients.<sup>2,3</sup>

### **Expanding Indications**

The perioperative relevance of GLP-1 RAs has grown considerably due to their expanding therapeutic indications across multiple disciplines, thereby increasing the likelihood of encountering these agents in surgical candidates. In PCOS, they improve insulin sensitivity, weight loss, and menstrual cyclicity. In NAFLD and non-alcoholic steatohepatitis (NASH), GLP-1 RAs reduce hepatic steatosis and inflammation, with evidence from trials like ESSENCE demonstrating histological improvements, including NASH resolution and fibrosis regression. The recent Food and Drug Administration (FDA) approval of semaglutide for NASH and its endorsement in international PCOS guidelines indicate these medications will become increasingly prevalent in perioperative care.<sup>4-7</sup>

### **OSA: An Emerging Therapeutic Frontier**

GLP-1 RAs are gaining recognition for their role in mitigating OSA, a major perioperative risk in patients with obesity. By inducing significant weight loss, they reduce apnoea-hypopnoea index (AHI) and improve airway stability. The 2024 SURMOUNT-OSA trials showed that tirzepatide reduced AHI by up to 25 events/hour, leading to FDA approval as the first pharmacological treatment for OSA. While semaglutide and liraglutide are not yet approved for this indication, their metabolic effects may similarly benefit undiagnosed

or high-risk patients. As these agents become more widespread, anaesthesiologists must recognise their expanding respiratory implications — not only for aspiration risk, but also for OSA modulation.<sup>8-10</sup>

### Evolving Guidelines and the Aspiration Risk Spectrum

GLP-1 RAs delay gastric emptying via central and peripheral mechanisms. This disrupts the reliability of standard fasting intervals. The American Society of Anaesthesiologists (ASA) initially recommended holding daily GLP-1 RAs on the day of surgery and weekly agents for seven days. However, following these recommendations, stopping GLP-1 RAs before procedures, many centres reported unexpected cancellations and disruptions to surgical schedules. Recognising this unintended impact on patient care, experts revisited the guidance — focusing instead on tailoring fasting protocols and perioperative plans based on individual risk, rather than applying a one-size-fits-all approach (Table 1).<sup>11,12</sup>

In 2024, a joint consensus statement from ASA, American Society for Metabolic and Bariatric Surgery (ASMBS), Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), and American Gastroenterological Association (AGA) emphasised individualised risk assessment. They proposed continuing GLP-1 RAs in asymptomatic patients, provided a 24-hour clear liquid fast is observed. Patients with recent initiation, high-dose escalation, or gastrointestinal symptoms should be considered full-stomach and elective procedures may need to be deferred.<sup>12</sup>

In the United Kingdom, the Centre for Perioperative Care (CPOC) and in Australia, the Australian and New Zealand College of Anaesthetists (ANZCA) and the Australian Diabetes Society (ADS) echoed this risk-adapted approach. Their guidance emphasises continuation of GLP-1 RAs with a 24-hour clear fluid fast, preoperative risk screening, and the use of gastric ultrasound, prokinetics, or rapid sequence induction (RSI) where indicated.<sup>13,14</sup>

Organisation	Year	Recommendation
ASA (USA)	2023	Hold daily GLP-1 RA on the day of surgery; hold weekly agents 7 days prior.
ASA/ASMBS/ SAGES/AGA Consensus	2024	Continue if asymptomatic; enforce 24-h clear liquid fast; assess symptoms.
CPOC (UK)	2023	Continue; 24-h clear fluids; assess for symptoms and use gastric ultrasound if needed.
ANZCA/ADS (Australia)	2025	Continue; apply 24-h clear fluid fast; consider RSI and risk stratification.

**Table 1:** Summary of recent international guidelines related to preoperative GLP-1 RAs.

**Abbreviations:** ADS: Australian Diabetes Society; AGA: American Gastroenterological Association; ANZCA: Australian and New Zealand College of Anaesthetists; ASA: American Society of Anaesthesiologists; ASMBS: American Society for Metabolic and Bariatric Surgery; CPOC: Centre for Perioperative Care; GLP-1 RA: Glucagon-Like Peptide-1 Receptor Agonist; RSI: Rapid Sequence Induction; SAGES: Society of American Gastrointestinal and Endoscopic Surgeons; UK: United Kingdom; USA: United States of America.

### Risk Mitigation Strategies

- Enforce 24-hour clear fluid fasting in all GLP-1 RA-treated patients.
- Incorporate GLP-1 RA use in preoperative screening and anaesthesia checklists.
- Use point-of-care gastric ultrasound for high-risk or uncertain cases.
- Consider erythromycin preoperatively in symptomatic patients.
- Employ RSI and secured airway techniques for recent initiators or symptomatic individuals.

GLP-1 RAs are a burden in perioperative period that is often overlooked. Their delayed gastric emptying effects may quietly undermine preoperative fasting measures, which could raise the risk of regurgitation, aspiration, or airway compromise without any obvious signs. If not recognised, they could lead

to complications that could have been avoided and make surgical outcomes worse. As their use becomes widespread, it is important to recognise their hidden effects and actively include ways to lessen them in perioperative workflows.

## Conclusion

GLP-1 RAs represent a novel and under-recognised aspiration risk in the perioperative landscape. As their indications expand across endocrinology, hepatology, and preventive medicine, clinicians must develop pathways to identify and manage patients on these agents. Discontinuation alone is insufficient. A combination of screening, fasting modification, airway management, and inter-speciality communication is required. This commentary serves as a clinical whistleblower's alert: GLP-1 RA awareness should be embedded into every pre-anaesthesia protocol, sedation checklist, and procedural plan.

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# Anaesthesia for Mediastinal Masses: A Retrospective Review

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**Abstract:**

Perioperative management of patients undergoing resection of mediastinal masses can be challenging due to the potential for airway compromise, cardiovascular collapse, major blood loss and neurological compromise in myasthenic patients. This article aims to highlight the wide variety in pathologies, surgical and anaesthetic approaches, intraoperative and postoperative events encompassed by the term 'surgery for mediastinal mass'. This was a retrospective, observational, descriptive study in which records of 31 patients who underwent resection of mediastinal masses were analysed. Wide variation in symptomatology, surgical approach, structures resected, intraoperative blood loss and duration of surgery was noted. Thymectomy was the most common surgery performed, accounting for a little over 50% of cases. Breathlessness was the most common presenting symptom. Additional lung resection was required in 32.25% of patients, and 35.48% required major vascular or pericardial resection. Blood loss ranged from less than 100 mL to 15 L, and the average duration of surgery was 6.09 hours. All patients except one were extubated on the table. There is no single formula for providing anaesthesia to patients with mediastinal masses. Anticipation of challenges and individualised management are key to positive outcomes.

**Key words:** Mediastinal Mass, Thymectomy, Major Blood Loss.

**Introduction**

The mediastinum is a cavity within the thorax between the two pleural sacs. It lies in the midline behind the sternum and anterior to the thoracic vertebral column, and contains the heart, great vessels, hollow viscera such as the trachea and oesophagus, the splanchnic and sympathetic chains, and the thymus. In addition, it contains mediastinal lymphatics, lymph nodes and connective tissue. While any of these organs or tissues can enlarge pathologically, thymomas, lymphomas, enlarged thyroid, neurogenic tumours and germ cell tumours are the most common causes of mediastinal masses. Due to close proximity to vital vascular structures and the airway, anaesthetic and surgical management of these tumours is challenging. Vascular compression, vascular infiltration or airway compression may necessitate the use of cardiopulmonary bypass

(CPB). Resection around the heart and great vessels increases the possibility of major blood loss. The asymptomatic nature of these tumours allows them to grow to a large size before causing compressive symptoms, unless they are incidentally diagnosed at an earlier stage.

Despite the multiple challenges involved, surgical treatment is worthwhile, as achieving complete surgical resection (R0) improves the prognosis of most mediastinal masses.<sup>1,2</sup> In this case series, we retrospectively analysed 31 surgical patients in terms of the preoperative symptoms, intraoperative surgical and anaesthetic approaches, and the postoperative hospital course.

## Materials and Methods (Including Statistical Analysis)

Institutional review board approval was obtained, and data were collected retrospectively from records of 31 patients who underwent surgery for excision of mediastinal masses. Notes were made of the patients' preoperative symptoms, pre-existing comorbidities, preoperative work-up, the surgery performed, and the anaesthetic plan, including the technique of induction, intraoperative blood loss, duration of anaesthesia, whether CPB was used or kept ready, the method of postoperative analgesia and the need for postoperative ventilation. The data was tabulated in Microsoft Excel and interpreted as percentages.

## Results

Out of the 31 patients with mediastinal masses, 16 (51.61%) underwent thymectomy. Of these, 11 were operated robotically, 3 via midline sternotomy, and 2 via video-assisted thoracoscopic surgery (VATS), of which 1 was converted to median sternotomy (Table 1).

Type of surgery	Number of patients (%)
Total thymectomies	16/31 (51.61%)
• Robotic thymectomy	11/16 (68.75%)
• VATS thymectomy	1/16 (6.25%)
• Open thymectomy	4/16 (25.00%)

**Table 1:** Thymectomy approaches.

**Abbreviation:** VATS: Video-Assisted Thoracoscopic Surgery.

Ten out of the 31 patients (32.25%) required additional lung resections in the form of wedge resection, lobectomy or segmentectomy. Eleven patients (35.48%) had pericardial, atrial or great vessel involvement requiring resection and repair (Table 2).

Surgical approach/intervention	Number of patients (%)
Sternotomy	14/31 (45.16%)
Clamshell thoracotomy	1/31 (3.22%)
Pericardium/great vessels resected	11/31 (35.48%)
Lung resected	10/31 (32.25%)
CPB on standby	6/31 (19.35%)
CPB used	2/31 (6.45%)

**Table 2:** Surgical approach and resection characteristics.

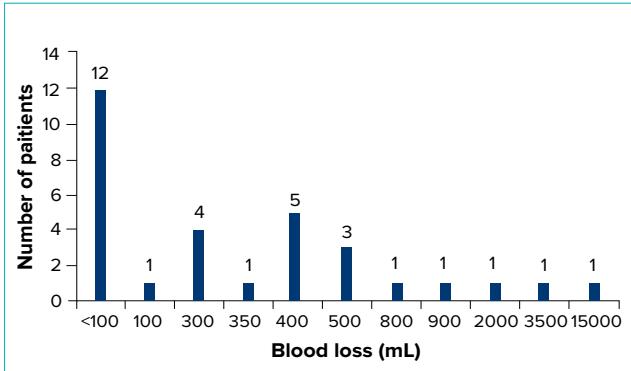
**Abbreviation:** CPB: Cardiopulmonary Bypass.

Twelve patients presented with breathlessness, 8 had motor weakness due to myasthenia gravis, and 6 were incidentally diagnosed (Table 3). Four of the myasthenic patients received intravenous immunoglobulin (IVIg) treatment preoperatively, and one of them also underwent plasma exchange due to myasthenic crisis.

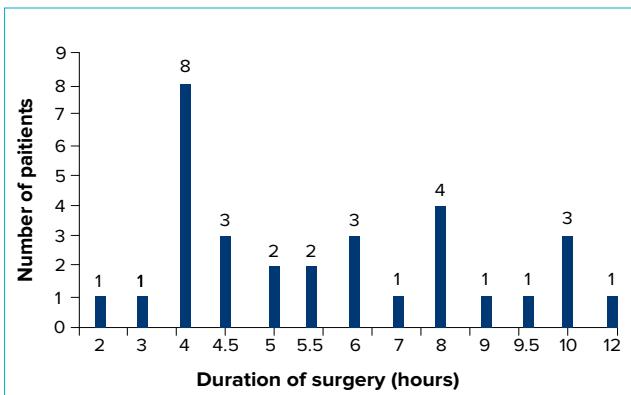
Symptom at presentation	Number of patients (%)
Breathlessness	12/31 (38.70%)
Chest pain	5/31 (16.12%)
Incidental	6/31 (19.35%)
Myasthenia	8/31 (25.8%)

**Table 3:** Symptoms at presentation.

There was a wide range of intraoperative blood loss and total duration of surgery. The average blood loss was 882 mL (interquartile range [IQR]), and the average duration of surgery was 6.09 hours (IQR). The maximum blood loss encountered was 15 L in one patient, while 12 patients had less than 100 mL blood loss. In total, 8 out of 31 had  $\geq 500$  mL loss (Figure 1). The duration of surgery ranged from 2 to 12 hours (Figure 2). Only one patient required postoperative ventilation, while the rest of them were extubated on table.



**Figure 1:** Patient distribution by intraoperative blood loss.



**Figure 2:** Patient distribution by surgery duration.

All patients received multi-modal analgesia postoperatively with intravenous (IV) paracetamol and non-steroidal anti-inflammatory drugs (NSAIDS). In addition, nearly half of the patients received IV patient-controlled analgesia (PCA) fentanyl, and 9 out of 31 (29.03%) received epidural analgesia (Table 4).

Analgesia method	Number of patients (%)
Intravenous PCA fentanyl	13/31 (41.93%)
Intravenous analgesics	9/31 (29.03%)
Epidural analgesia	9/31 (29.03%)

**Table 4:** Postoperative pain management.

**Abbreviation:** PCA: Patient-Controlled Analgesia.

All patients were discharged home in 3–4 days after intercostal drain (ICD) removal, and there was no in-hospital mortality.

## Discussion

Mediastinal masses are uncommon tumours to encounter. Just like the many organs and tissues that occupy the mediastinal cavity, mediastinal masses include a varied group of benign and malignant growths that can arise in one of the four compartments. Anterior mediastinal masses are the most common, with thymomas, lymphomas, and germ cell tumours being the most frequent pathologies in adults.<sup>3</sup> Among the 31 patients operated on at our centre over 2 years, a large majority (29) had anterior mediastinal masses.

The anterior mediastinum allows these tumours to grow significantly before any obvious signs and symptoms appear.<sup>4</sup> Compression of the large airways can cause breathlessness or a persistent cough. Worsening of symptoms in the supine position may be observed. This is of particular importance to the anaesthesiologist as it indicates the possibility of critical compression of the airway during induction of anaesthesia. A vague chest pain or heaviness is often reported by patients. Metabolic disturbance may occur due to thyroid or thymus involvement. Myasthenia gravis, presenting with muscular and generalised weakness, difficulty in breathing and swallowing, and dystonia, is typical of thymomas. Incidental diagnosis of the mass is possible, especially in case of previously operated patients on regular follow-up. However, about 60% patients show some clinical symptoms prompting investigation.<sup>4,5</sup> Mediastinal syndrome refers to respiratory or haemodynamic compromise due to a mediastinal mass causing compression of surrounding structures like the trachea, heart, and great vessels. There is often a positional component, with worsening of symptoms in the supine position. Induction of general anaesthesia carries the risk of complete decompensation in these patients. While the majority of our patients presented with symptoms of breathlessness, muscular weakness or chest pain, none of them had positional symptoms of airway or haemodynamic compromise.

The preferred anaesthetic plan for surgical resection is general anaesthesia, often with invasive lines for advanced haemodynamic monitoring. Since resection occurs close to the heart and great vessels, beat-to-beat blood pressure monitoring is essential. An arterial line also allows intermittent sampling to assess acid-base status, hydration and haemoglobin levels in case of massive blood loss. We secured large-bore IV access in the lower limb for selected patients. This can be lifesaving, especially when resection involves

or is in the proximity of the aorta and superior vena cava (SVC). If central venous access is required, the femoral veins are cannulated in cases with cardiac or SVC involvement. Depending on the surgical approach, lung isolation using a double-lumen tube or bronchial blocker may be needed. Minimally invasive techniques like robotic or thoracoscopic surgery require the ability to selectively ventilate the lungs. In our series, 25 out of 31 patients were intubated with double-lumen tubes, allowing selective ventilation during surgery if required. This included all robotic and thoracoscopic procedures, as well as some open procedures where one-lung ventilation might have been required to facilitate easier resection.

Induction of general anaesthesia in an asymptomatic patient is generally straightforward using intravenous induction and muscle paralysis. Mask ventilation and intubation follows as per usual protocol. However, patients with respiratory symptoms in any position pose a significant challenge to the anaesthesiologist. It is important to carefully assess radiological scans to note the tumour size, extent, and involvement of surrounding structures while planning the anaesthesia management. Airway narrowing, vascular involvement and proximity can be appreciated in these. Traditional teaching advocates IV induction for the asymptomatic patients and inhalational induction while maintaining spontaneous respiration for those with respiratory symptoms.<sup>6</sup> The rationale is that the administration of anaesthetic agents alone can cause loss of tone in the pharyngolaryngeal musculature causing the mediastinal mass to further obstruct the airway. This is expected to worsen with muscle paralysis. Inhalational induction can theoretically be more gradual and allows the patient to maintain spontaneous respiration.<sup>7</sup> However, in practice, it is seldom possible to achieve the depth of anaesthesia required for laryngoscopy and intubation while preserving respiratory drive. In a spontaneously breathing patient with a partially obstructed airway, the depth of anaesthesia achieved with inhalational agents alone is often unpredictable. It may be insufficient to allow airway manipulation and yet still cause partial obstruction due to a large mediastinal mass. The safest approach when airway obstruction is anticipated is to perform an awake fibreoptic intubation, after topicalising the airway, and in the position the patient finds most comfortable.<sup>7,8</sup> Once the tube is passed beyond the level of obstruction, a muscle relaxant can be given. A rigid bronchoscope and an experienced operator must be present in the theatre at the time of

induction to rescue and stent the airway if needed. Haemodynamic collapse due to compressive effects of a large mass may also occur post-induction of anaesthesia. If either airway or haemodynamic collapse is expected to occur under anaesthesia, readiness for CPB by cannulating the femoral vessels is a safe option. Although rarely used, cannulation must be done pre-emptively as CPB cannot serve as a rescue technique due to the time required to cannulate the vessels and go on pump.<sup>7,8</sup>

A special work-up is required for patients with thymomas as they may have raised acetylcholine receptor antibodies (AchR Ab), with or without overt muscular weakness. Neuromuscular testing with repeated nerve stimulation and electromyography maybe needed to establish the diagnosis in patients who test negative for antibodies.<sup>9</sup> Optimisation of respiratory reserve and muscle strength by instituting right treatment in the form of cholinergic drugs, steroids and if required immunoglobulins or plasmapheresis is essential for reducing perioperative morbidity. Anaesthesia planning must include additional monitoring like neuromuscular transmission monitor and depth of anaesthesia monitor. It is wise to avoid the use of neuromuscular blockers or at least use them sparingly while monitoring train-of-four (TOF) response intraoperatively to prevent excessive muscle weakness and postoperative respiratory compromise. The combination of rocuronium and sugammadex avoids the use of neostigmine and may provide a more reliable reversal of neuromuscular blockade when muscle relaxants cannot be avoided.<sup>10</sup> We used TOF monitors for all thymomas and avoided infusions or timed doses of muscle relaxant, which we normally use in robotic surgeries. Instead, small boluses of atracurium were administered as and when needed, guided by TOF response. In our experience, equally important was the preoperative optimisation of muscle strength and prompt re-institution of cholinergic drugs and steroids post-surgery. Gradual tapering of treatment as tolerated by patients helps avoid precipitating myasthenic crisis. All our myasthenic patients could be extubated on table and were observed in high-dependency units for a minimum of 24 hours. Surprisingly, a previously asymptomatic patient experienced an episode of muscular weakness and respiratory distress after discharge home and required ventilatory support for five days on readmission. The patient responded well to steroids and cholinergic drugs and was discharged home after two weeks.

In mediastinal mass, whether thymoma or otherwise, involvement of cardiac chambers or aorta or SVC due to tumour infiltration might necessitate the use of CPB intraoperatively to allow tumour resection. In such cases, anticoagulation with heparin is required. This must be anticipated, and anaesthetic planning should reflect this possibility by avoiding neuraxial techniques, particularly epidural catheter placement, in patients who may require full heparinisation. These patients also tend to have higher intraoperative blood loss and may require blood transfusion due to the resection of vascular structures. Even when full-dose heparinisation is not required, such as in pericardial or SVC resection without CPB, patients often receive heparin at a dose of 100 units/kg at regular intervals to maintain an activated clotting time (ACT) of around 200 seconds.

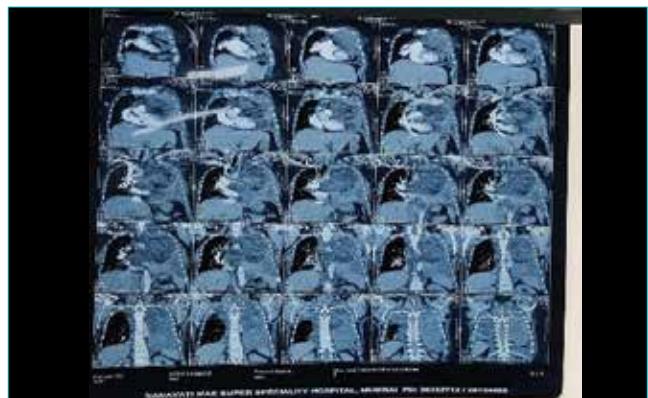
Concomitant excision of lung tissue might be needed depending on the extent of the mass. Therefore, a preoperative assessment of the patient's suitability through evaluation of cardiopulmonary reserve and lung function testing is essential.

Optimal postoperative analgesia is essential for early mobilisation and compliance with respiratory physiotherapy. Available options include epidural catheter, paravertebral block (with or without a catheter), erector spinae block or IV PCA with opioids. Paracetamol and NSAIDS should be used in all patients to reduce the requirement of opioids and catheter-based infusions.

In our practice, all patients received multimodal analgesia with paracetamol, NSAIDS and either local infiltration of the incision site or intercostal block administered by surgeons. We avoided using epidural analgesia in patients with a high likelihood of requiring CPB. Most of these patients received IV PCA fentanyl and remained reasonably comfortable. Epidurals were placed in open procedures without cardiac or major vascular involvement, as well as in minimally invasive surgeries with a high possibility of conversion to an open approach. IV PCA was given after minimally invasive surgeries when round-the-clock paracetamol and NSAIDS alone were insufficient to control pain and facilitate mobilisation and effective physiotherapy.

We encountered a wide spectrum of pathologies from mediastinal cysts requiring marsupialisation to infiltrative masses involving the heart and lungs. Overall, thymectomies were the most predictable surgeries in terms of minimal blood loss involved, feasibility of

robotic approach, and low likelihood of requiring CPB. Two of our patients underwent redo surgeries, one for recurrence and the other for residual disease, as part of a planned staged procedure. The highest blood loss occurred in a patient with a mediastinal paratracheal mass that had expanded to fill the entire hemithorax (Figures 3 and 4).



▼ **Figure 3:** Imaging of a giant mediastinal mass.



▼ **Figure 4:** Excised giant mediastinal mass.

This patient underwent a 10-hour surgery and experienced blood loss of more than 10 L, necessitating a massive transfusion protocol that included 22 units of packed red cells, 8 units of fresh frozen plasma, 6 units of cryoprecipitate and 5 units of platelets. This was an eventful surgery that demonstrated excellent teamwork from anaesthesia, surgical, transfusion medicine and critical care teams. Another patient with a posterior mediastinal mass required a clamshell thoracotomy incision, which is unusual in adults (Figure 5). However, access to the posterior attachments of the tumour would have been impossible without this approach. There were concerns about postoperative analgesia in this young adult, but a thoracic epidural at the T7–T8 level was effective throughout the 4-day recovery period.



**Figure 5:** Clamshell thoracotomy incision.

Multi-disciplinary meetings involving the thoracic surgeon, anaesthesia team, neurologist, cardiologist and chest physician were organised to discuss key concerns and formulate plans for preoperative optimisation, intraoperative equipment and personnel arrangements, and postoperative care. Co-ordination with the blood bank was vital in cases with potential for major blood loss. We found that pre-emptive communication with the transfusion team before induction, dedicating a single liaison person, and having designated staff and runners in place during massive transfusion cases facilitated a faster and more efficient response.

## Conclusion

This article highlights the wide variety in pathologies, surgical and anaesthetic approaches, and intraoperative and postoperative events that fall under the umbrella of 'surgery for mediastinal mass'. There is no single formula for providing anaesthesia to patients with mediastinal masses. Key considerations include signs of mediastinal syndrome, metabolic conditions such as myasthenia, involvement of major vessels, heart or large airways requiring resection, the possibility of major blood loss, the need for CPB, and prolonged operative duration. Thoughtful planning for each of these factors contributes to safe intraoperative anaesthetic management, smooth and pain-free recovery, and an uneventful discharge home.

Aditi Tilak, Shalini Saksena. Anaesthesia for Mediastinal Masses: A Retrospective Review. MMJ. 2025, December. Vol 2 (4).

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# Silent Saboteurs: Anxiety in Parkinson's Disease

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## Abstract:

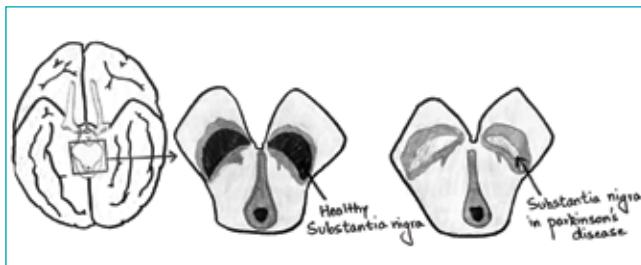
Anxiety represents a prevalent yet under-recognised, non-motor manifestation of Parkinson's disease (PD), affecting approximately one-third of patients globally while remaining substantially underdiagnosed, with detection rates of only 50%. This comprehensive review synthesises current evidence on anxiety in PD, emphasising regional Indian data and emerging therapeutic interventions. Epidemiological studies reveal marked geographical disparities, with Indian prevalence ranging from 14.1 per 100,000 in rural Kashmir to 328.3 per 100,000 in Mumbai, and projections indicating 2.8 million cases by 2050. The pathophysiology involves progressive degeneration of dopaminergic, noradrenergic, and serotonergic circuits within frontal-basal ganglia networks, with early raphe nucleus and locus coeruleus involvement often preceding motor symptoms. Electrophysiological investigations demonstrate significant correlations between theta wave activity (4-8 hertz [Hz]) in basal ganglia structures and anxiety severity, providing novel therapeutic targets. Current assessment relies on gold-standard instruments including the Movement Disorder Society–Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and Parkinson's Anxiety Scale (PAS), though systematic screening remains inadequately implemented. Therapeutic approaches encompass selective serotonin reuptake inhibitors as first-line pharmacological agents, cognitive behavioural therapy, and lifestyle modifications, though PD-specific evidence remains limited. Emerging adaptive deep brain stimulation technologies represent a paradigmatic shift toward precision neuromodulation, utilising closed-loop systems that monitor anxiety-specific neural oscillations and adjust stimulation parameters in real-time. Future directions include large-scale epidemiological investigations, biomarker development, culturally sensitive treatment approaches, and integrated care models combining neurological, psychiatric, and rehabilitation services. This review emphasises the urgent need for improved recognition and evidence-based management while highlighting the transformative potential of precision medicine approaches incorporating genetic profiling and artificial intelligence-driven optimisation.

**Key words:** Parkinson's Disease, Anxiety, Non-Motor Symptoms, Deep Brain Stimulation, Epidemiology, Neuromodulation, Precision Medicine, Biomarkers.

## Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterised by selective degeneration of dopaminergic neurons in the substantia nigra pars compacta, manifesting clinically as the cardinal motor symptoms of bradykinesia, rigidity,

tremor, and postural instability.<sup>1</sup> However, the clinical spectrum extends beyond motor dysfunction to encompass a constellation of non-motor symptoms, among which anxiety represents a particularly prevalent and disabling manifestation (Figure 1).<sup>2</sup>



**Figure 1:** Site of involvement of Parkinson's disease.  
**Source:** Conceived and guided by Dr. (Prof) Man Mohan Mehndiratta, hand-drawn by Dr. Navya Jaitly.

Anxiety in PD is defined as excessive and ongoing worry or fear that can manifest as panic disorder, social phobia, generalised anxiety disorder (GAD), or non-specific anxiety symptoms. It severely impairs patients' quality of life and ability to function, with a prevalence of 25%.<sup>3</sup> It is caused by PD's effect on the brain's chemical mediators like dopamine, serotonin, and gamma-aminobutyric acid (GABA), and can be termed as a "pre-motor" symptom before the motor challenges appear. Despite its clinical significance, anxiety in PD remains under-recognised and undertreated, with diagnostic rates approximating only 50% of actual prevalence.<sup>4</sup> This comprehensive review synthesises current evidence regarding the epidemiology, pathophysiology, assessment, and management of anxiety in PD, with particular emphasis on regional data from India and emerging therapeutic interventions, including adaptive neuromodulation techniques.

## Epidemiological Landscape

### Global perspectives

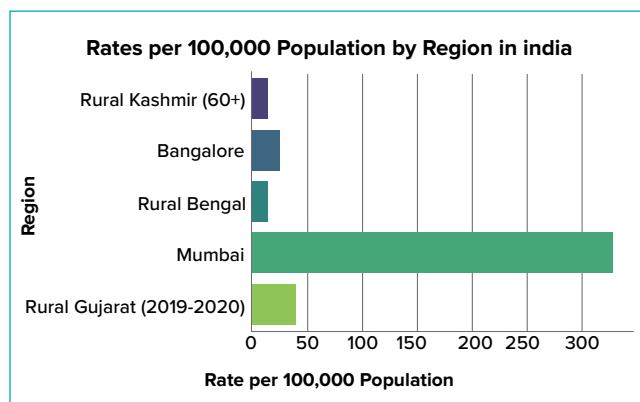
The global burden of PD is projected to reach unprecedented levels, with epidemiological projections indicating a doubling of cases by 2040. Anxiety comorbidity affects approximately 25%–40% of PD patients across different populations, though prevalence estimates vary considerably based on diagnostic criteria and assessment methodologies.<sup>5</sup> The anxiety syndromes in PD are believed to be associated with the underlying brain disease, as evidenced by the presence of noradrenergic dysfunction.<sup>6</sup>

### Indian epidemiological data

India faces a substantial and growing PD burden, with projections indicating approximately 2.8 million cases

by 2050, representing 10% of the global PD population. Anxiety may manifest as a standalone symptom or as a component of depressive disorders; nevertheless, clinically significant anxiety syndromes are observed in up to 40% of people with PD. These syndromes may precede or accompany a major depressive illness and should be considered distinct from anxiety, which is a rational psychological reaction to motor disability or other personal issues.<sup>7</sup> Regional prevalence studies demonstrate marked geographical heterogeneity (Figure 2):<sup>8</sup>

- **Rural Kashmir:** 14.1 per 100,000 (age > 60 years)
- **Bangalore:** 27 per 100,000
- **Rural Bengal:** 16.1 per 100,000
- **Mumbai:** 328.3 per 100,000
- **Rural Gujarat (2019-2020):** 42.3 per 100,000 overall prevalence



**Figure 2:** Regional prevalence map of Parkinson's disease in India showing geographical variations.

Neuropsychiatric comorbidities, including anxiety and depression, affect approximately one-third of Indian PD patients, with tertiary care settings reporting a high prevalence of anxiety, depression, irritability, and apathy.<sup>8</sup>

### Impact of Anxiety in PD

Individuals with PD experience anxiety during their "off" period. Symptoms will be alleviated when an individual consumes their medication. However, these symptoms may occasionally recur prior to the anticipated expiration of a medication dose or prior to the subsequent one. This results in fluctuations in an individual's condition

and is referred to as "wearing off." For instance, the individual may experience a sudden inability to continue walking while on a walk or may be unable to rise from a seated position to answer the door. PD is distinguished by the presence of discrete anxiety disturbances at specific periods of the day, such as in the late afternoon or early evening. These episodes, to elaborate, have been identified as being associated with fluctuations in motor function and levodopa levels, with the majority of them occurring during "off" periods.<sup>9</sup> The symptoms of anxiety are precisely observed because of the loss of serotonergic neurons, out of which, the particular 5-hydroxytryptamine receptor 1A (5-HT1A) receptor modulates the release of GABA, glutamate, and dopamine, and its modulation can lead to neuropsychiatric complications in the progression of PD. Therefore, the prominent role of the serotonergic degeneration rather than just dopaminergic degeneration in the pathogenesis of the non-motor triad (apathy, depression and anxiety) has also been an established pathway during recent years. Anxiety in PD is linked directly to the increased mortality rate. In order to improve the quality of living, there is an urgent need to treat anxiety in PD. Some patients experience anxiety disorders as a "reactive" response preceding their PD diagnosis. In other cases, it may be secondary to the impairment and limitation caused by motor symptoms. Anti-Parkinsonian medications (e.g., levodopa, pergolide) may also contribute to anxiety in patients with PD.

## Aetiopathogenesis

### 1. Genetic determinants

Most PD cases demonstrate genetic underpinnings involving multiple susceptibility loci. Key genetic determinants include:<sup>10</sup>

- $\alpha$ -synuclein gene (SNCA): Point mutations and duplications/ triplications
- Leucine-rich repeat kinase 2 (LRRK2): Most common genetic cause of familial PD
- PRKN parkin RBR E3 ubiquitin protein ligase (Parkin), PTEN-induced kinase 1 (PINK1), Parkinson disease protein 7 (DJ-1): Associated with early-onset autosomal recessive forms

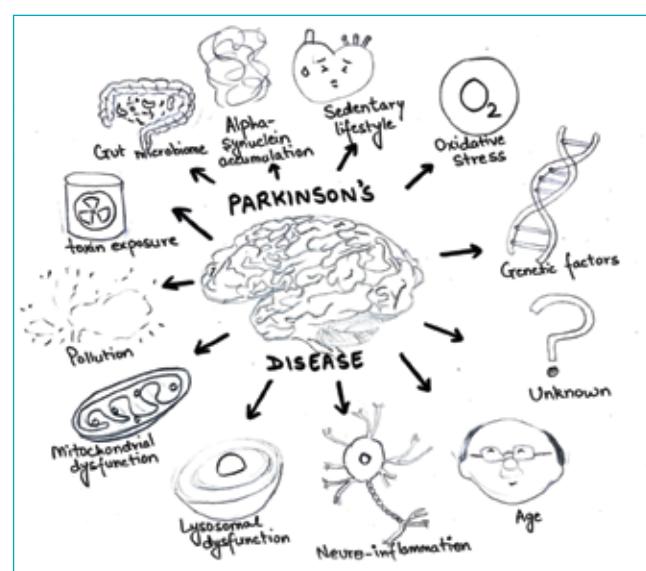
- Vacuolar protein sorting 35 (VPS35), glucocerebrosidase (GBA): Contributing to sporadic PD risk

### 2. Environmental factors

Environmental exposures significantly contribute to PD pathogenesis, including industrial pollution, heavy metal exposure, agricultural pesticide exposure through contaminated water sources, occupational toxin exposure, and rural-urban environmental gradients.<sup>11</sup>

### 3. Anxiety-specific mechanisms

Anxiety in PD originates from complex interactions between neurodegeneration (progressive loss of serotonergic and noradrenergic brainstem nuclei), stress response dysregulation (altered hypothalamic-pituitary-adrenal axis with elevated cortisol levels), oxidative stress (enhanced inflammatory cascades and mitochondrial dysfunction), and psychosocial factors (disease-related stigma and adaptive challenges)<sup>12</sup> (Figure 3).



**Figure 3:** Comprehensive aetiological diagram showing genetic, environmental, and age-related factors in Parkinson's disease development.

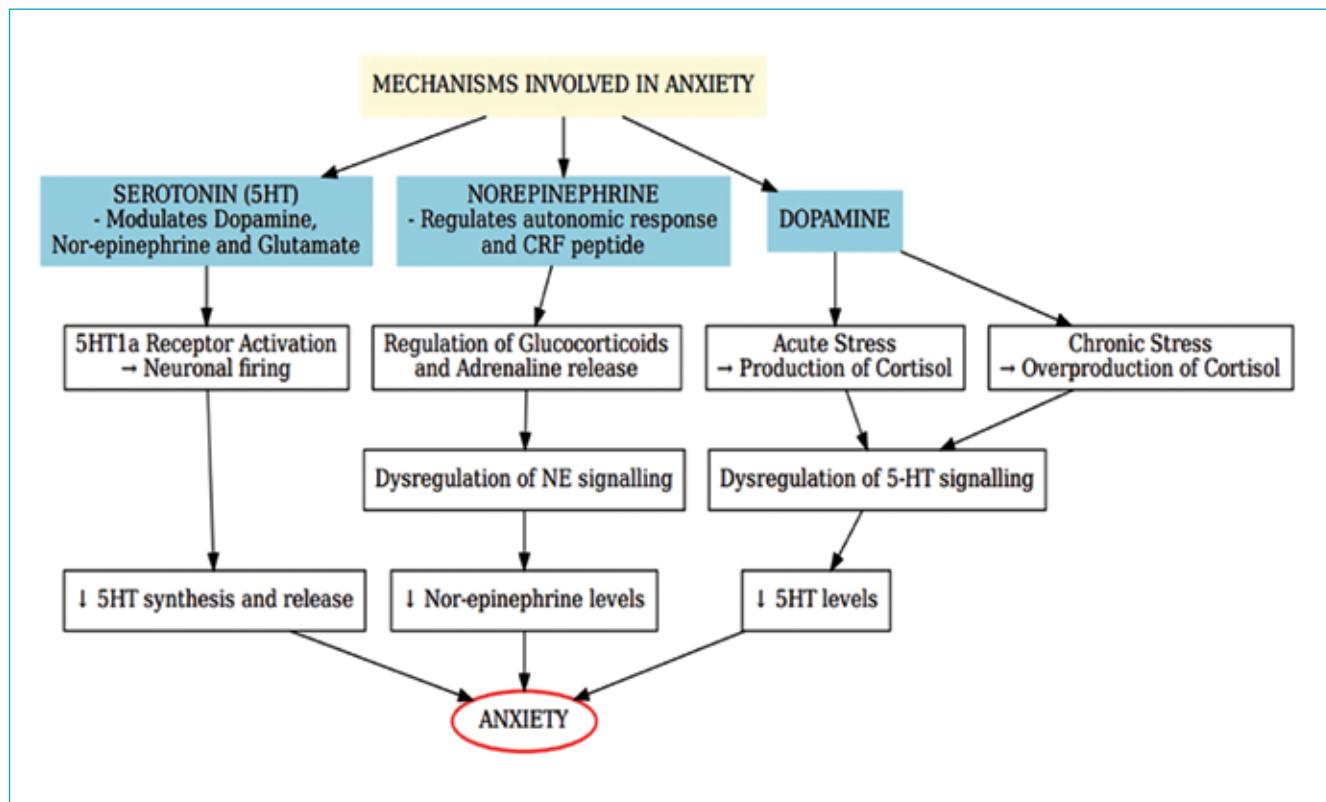
**Source:** Conceived and guided by Dr. Abhishek Dixit, hand-drawn by Dr. Navya Jaitly.

## Pathophysiological Mechanisms

### Neural circuit dysfunction

Anxiety symptomatology in PD results from progressive degeneration of interconnected subcortical and cortical circuits involving dopaminergic, serotonergic, and noradrenergic neurotransmitter systems.<sup>13</sup> The pathophysiological substrate encompasses frontal-basal ganglia circuits with dopaminergic pathways

(nigrostriatal and mesocortical circuit dysfunction), serotonergic systems (raphe nucleus degeneration affecting mood regulation), and noradrenergic networks (locus coeruleus pathology contributing to anxiety manifestations) (Figure 4).



**Figure 4:** Pathophysiological schematic showing neural circuits involved in anxiety manifestation in Parkinson's disease.

### Temporal progression

Early involvement of the raphe nucleus (serotonin) and locus coeruleus (norepinephrine) frequently precedes motor symptom onset, suggesting anxiety as a potential prodromal marker.<sup>13</sup>

### Electrophysiological correlates

Neuroimaging and electrophysiological investigations demonstrate significant correlations between theta wave activity (4–8 Hz) in basal ganglia structures and anxiety severity, providing novel targets for neuromodulation interventions.<sup>14</sup>

### Assessment and Diagnostic Approaches

The non-motor symptoms of PD are frequently disregarded. The following possibilities were cited as the basis for this investigation:<sup>14</sup>

- Constrained consultation time
- The patient and their attendant believe that their symptoms are unrelated to the disease (e.g., visual hallucinations or diplopia)
- The physician's lack of awareness, as they may only address the motor symptoms of PD
- The anticipated management of non-motor symptoms in the community, typically by the family doctor or community health nurse

Identifying non-motor symptoms is easier when supported by quantitative, validated assessment tools. These include the Epworth sleepiness scale for sleep-related issues; the hospital anxiety and depression scale (HADS), Hamilton depression rating scale (HDRS), and Beck depression inventory (BDI) for mood disorders; as well as the PD quality of life questionnaire, the Parkinson's disease non-motor symptoms questionnaire (NMSQuest), the revised unified Parkinson's disease rating scale (UPDRS), and others.

## Gold-Standard Instruments

### Primary assessment tools

- **Movement Disorder Society-unified PD rating scale (MDS-UPDRS):** Comprehensive evaluation including motor and non-motor domains<sup>15</sup>
- **International Parkinson's and Movement Disorder Society non-motor rating scale:** Systematic assessment of anxiety frequency and severity alongside other non-motor symptoms
- **Structured clinical interviews:** Gold standard for diagnostic and statistical manual of mental disorders-5 (DSM-5)-defined anxiety disorder diagnosis<sup>16</sup>

### Specialised anxiety scales

- **Parkinson's anxiety scale (PAS):** Disease-specific instrument for anxiety assessment
- **Geriatric anxiety inventory:** Age-appropriate anxiety evaluation
- **Beck anxiety inventory:** Validated anxiety severity measurement

### Diagnostic challenges

Current evidence indicates substantial underdiagnosis of anxiety in PD, with detection rates approximating 50% of actual prevalence. Contributing factors include symptom overlap with motor fluctuations, healthcare provider unfamiliarity with non-motor symptoms, patient reluctance to report psychiatric symptoms, and absence of routine screening protocols.

## Therapeutic Interventions

### Pharmacological management

#### First-line agents

Selective serotonin reuptake inhibitors (SSRIs) are preferred agents due to favourable side effect profiles and minimal interference with dopaminergic therapy, though evidence base is primarily derived from general elderly populations. Buspirone, a serotonin 5-HT1A partial agonist, offers reduced sedation compared to benzodiazepines with favourable drug interaction profiles.<sup>17</sup>

#### Second-line options

Benzodiazepines have limited use due to cognitive impairment risk and dependency potential. Tricyclic antidepressants are reserved for refractory cases. Medication timing and dosing require careful optimisation due to motor fluctuation interactions, polypharmacy concerns, and age-related pharmacokinetic changes.<sup>18</sup>

### Non-pharmacological interventions

#### Psychological therapies

Cognitive behavioural therapy (CBT) serves as an evidence-based first-line psychological intervention. Acceptance and commitment therapy represents an emerging therapeutic approach, while mindfulness-based interventions provide stress reduction and anxiety management.

#### Physical interventions

Exercise therapy demonstrates neuroprotective effects and anxiety reduction. Yoga and tai chi serve as mind-body interventions with demonstrated efficacy. Physiotherapy and occupational therapy provide comprehensive rehabilitation approaches.

#### Lifestyle modifications

These include sleep hygiene optimisation, nutritional counselling, social support enhancement, and stress management techniques.

## Emerging therapeutic frontiers

### Adaptive deep brain stimulation (aDBS)

Recent technological advances have enabled the development of closed-loop deep-brain stimulation (DBS) systems capable of real-time parameter adjustment based on biomarker feedback.<sup>19</sup> Key developments include target identification through theta wave activity (4–8 Hz) in basal ganglia correlating with anxiety severity, adaptive algorithms using machine learning-based stimulation parameter optimisation, and biomarker integration through local field potential (LFP) monitoring for feedback control.

### Clinical applications

Clinical applications include subthalamic nucleus (STN) targeting for traditional motor symptom management with anxiety modulation potential, globus pallidus internus (GPI) stimulation as an alternative target with mood stabilisation effects, and novel targets including pedunculopontine nucleus and other anxiety-specific regions under investigation.

### Safety and efficacy

Preliminary studies demonstrate superior safety profiles compared to conventional DBS, with enhanced therapeutic precision and reduced adverse effects.<sup>19</sup>

### Future technological developments

#### Closed-loop systems

These systems feature biomarker-driven stimulation with real-time adjustment based on multiple physiological parameters, artificial intelligence (AI) integration with predictive algorithms for optimal therapeutic outcomes, and miniaturisation advances for improved device tolerability and longevity.

#### Precision medicine approaches

These approaches incorporate genetic profiling for personalised therapy selection based on genetic susceptibility patterns, neuroimaging biomarkers for structural and functional magnetic resonance imaging (MRI)-guided treatment decisions, and pharmacogenomics for individualised medication selection and dosing.

## Surgical Interventions

### Deep brain stimulation

#### Current standards

DBS remains the gold standard surgical intervention for advanced PD motor symptoms, with typical candidacy assessment occurring 10–13 years post-diagnosis. Established outcomes include 50%–60% reduction in MDS-UPDRS Part II/III scores for motor improvement, significant levodopa dose reduction and dyskinesia improvement for medication management and sustained functional improvements for quality-of-life enhancement.

#### Non-motor applications

Emerging evidence supports DBS efficacy for non-motor symptoms, including urinary dysfunction, sleep disturbances, and anxiety and mood disorders. Investigation of anxiety-specific DBS protocols represents an active area of clinical research.<sup>20</sup>

## Future Research Directions

### Clinical research priorities

- Large-scale epidemiological studies involving multi-ethnic population investigations to establish global anxiety prevalence patterns
- Biomarker development for early detection and risk stratification markers for anxiety in PD
- Therapeutic trials through randomised controlled studies of anxiety-specific interventions
- Cultural adaptation through development of culturally sensitive assessment and treatment approaches

### Technological innovation

- Advanced neuromodulation through refinement of closed-loop DBS systems with anxiety-specific biomarkers
- Digital therapeutics via smartphone and wearable device-based intervention platforms
- Telemedicine integration through remote monitoring and treatment delivery systems
- AI applications for personalised treatment optimisation

## Healthcare system integration

- Integrated care models combining neurology, psychiatry, rehabilitation, and caregiver support
- Screening protocols for systematic anxiety assessment in routine PD care
- Healthcare provider education through training programs for non-motor symptom recognition and management
- Policy development for healthcare system reforms to support comprehensive PD care

## Limitations

This review acknowledges several limitations, including the heterogeneity of anxiety assessment tools across studies, the limited availability of PD-specific anxiety treatment data, potential publication bias toward positive results, and varying diagnostic criteria for anxiety disorders across different healthcare systems. Additionally, most of the therapeutic evidence derives from general psychiatric populations rather than PD-specific cohorts.

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## Conflicts of interest

The authors declare no conflicts of interest related to this work.

## Author contributions

All authors contributed to the conception, literature review, drafting, and revision of this manuscript. All authors approved the final version for submission.

## Conclusion

Anxiety represents a prevalent and clinically significant manifestation of PD that remains substantially under-recognised despite its profound impact on patient quality of life and functional outcomes. The pathophysiological substrate involves complex interactions between neurodegenerative processes affecting multiple neurotransmitter systems, psychosocial factors, and individual susceptibility patterns.

Current therapeutic approaches encompass pharmacological interventions, psychological therapies, and lifestyle modifications, though evidence specifically derived from PD populations remains limited. Emerging technologies, particularly adaptive deep brain stimulation targeting anxiety-specific neural oscillations, offer unprecedented opportunities for precision neuromodulation interventions.

Future research priorities include large-scale epidemiological investigations, biomarker development for early detection and risk stratification, and implementation of integrated care models addressing the complex multidimensional needs of PD patients. The development of culturally sensitive assessment and treatment approaches, particularly relevant for diverse populations such as those in India, is a critical area requiring immediate attention.

The continued evolution of precision medicine approaches, incorporating genetic profiling, neuroimaging biomarkers, and artificial intelligence-driven treatment optimisation, holds substantial promise for transforming anxiety management in PD from a standardised approach to truly personalised therapeutic interventions.

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# Chronic Inflammatory Demyelinating Polyradiculoneuropathy as the First Manifestation of Systemic Lupus Erythematosus in an Elderly Male

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## Abstract:

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a rare neurological manifestation of systemic lupus erythematosus (SLE), particularly uncommon as an initial presentation. A 61-year-old man presented with progressive symmetric paraparesis, sensory ataxia, and areflexia. Neurophysiology showed demyelinating sensorimotor polyneuropathy; cerebrospinal fluid (CSF) demonstrated albuminocytologic dissociation. He improved with corticosteroids but relapsed after two months with quadriplegia and severe sensory ataxia. Repeating studies supported CIDP. Subsequent workup revealed features consistent with SLE. He responded to intravenous immunoglobulin (IVIG) and tapering oral steroids, regaining functional ambulation. CIDP can be an initial manifestation of SLE even in elderly males. Early recognition and immunomodulatory therapy are critical for recovery.

**Key words:** Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP), Systemic Lupus Erythematosus (SLE), Neuro-Lupus, CNS Involvement in SLE.

## Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease with diverse neuropsychiatric involvement.<sup>1</sup> Peripheral neuropathy occurs in approximately 10%–20% of SLE patients; however, chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is rare, estimated in about 0.2% of cases.<sup>2</sup> Distinguishing CIDP from acute demyelinating neuropathies such as Guillain-Barré syndrome (GBS) is crucial, as CIDP evolves over eight weeks or more and typically requires sustained immunomodulation. The pathogenesis of SLE-associated CIDP likely involves humoral and cellular immune mechanisms,<sup>2</sup> including immune-complex mediated microvascular injury and

autoantibody-mediated demyelination. We report a case of CIDP as the first manifestation of SLE in a 61-year-old male, highlighting diagnostic challenges and therapeutic response.

## Case Report

A 61-year-old man with hypertension, chronic smoking, and alcohol use presented with one month of progressive, symmetric weakness of the lower limbs, sensory disturbances, moderate back pain, and headache.

### Examination revealed:

- **Lower limbs:** Proximal power 4–, distal power 4+, areflexia, graded sensory loss, absent joint position and vibration sense, positive Romberg's sign.
- **Upper limbs:** Reduced grip strength and areflexia.
- **Higher mental functions and cranial nerves:** Normal.

Nerve conduction studies (NCS) demonstrated bilateral symmetric sensorimotor demyelinating polyneuropathy, more pronounced in the lower limbs. Cerebrospinal fluid (CSF) analysis showed elevated opening pressure with albuminocytologic dissociation (protein 100, cells 2) and oligoclonal bands. Magnetic resonance imaging (MRI) of the brain and spine were unremarkable. Initial autoimmune panel, including anti-nuclear antibodies (ANA), and serum protein electrophoresis, were negative. He received intravenous corticosteroids followed by tapering oral steroids, with improvement over 3–4 weeks. His motor strength improved, reflexes returned, and ataxia resolved.

After two months of remission, he developed an abrupt headache, back pain, and rapidly progressive symmetric paraparesis with ataxia over three days. Examination showed greater severity in quadriplegia compared to prior tests: power 2/5 in lower limbs, 4/5 in upper limbs, generalised areflexia, loss of proprioception, and sensory ataxia. Repeat CSF analysis showed albuminocytologic dissociation, and NCS reconfirmed demyelinating sensorimotor polyneuropathy, predominantly in lower limbs. A diagnosis of CIDP was made. Subsequent evaluation identified features consistent with SLE. He was treated with intravenous immunoglobulin

(IVIG), with marked improvement in motor power, independent ambulation and discharged on tapering oral corticosteroids.

### Discussion

CIDP is an uncommon but important peripheral nervous system manifestation of SLE. In contrast to GBS, CIDP evolves over at least eight weeks and often relapses, requiring ongoing immunomodulatory therapy. The clinical phenotype typically includes symmetric sensorimotor deficits, proprioceptive loss, and areflexia affecting both upper and lower limbs.<sup>3</sup> Diagnostic hallmarks include demyelinating features on NCS (slowed conduction velocities, conduction block, prolonged F-waves) and albuminocytologic dissociation on CSF analysis. MRI is often unremarkable. While autoimmune serologies in SLE-associated CIDP may show ANA, anti-double-stranded DNA (anti-dsDNA), anti-Smith (anti-Sm), anti-SSA/Ro, and low complement levels, serological activity can be variable, and initial tests may be negative early in the disease.<sup>4</sup>

Proposed mechanisms include immune-complex deposition, microvascular injury resembling vasculitis, and autoantibody-mediated demyelination at the nodes of Ranvier. Anti-ganglioside antibodies have been reported in a subset of SLE patients with neuropathy, but associations with CIDP are inconsistent. Treatment typically involves high-dose corticosteroids,<sup>5</sup> IVIG, or plasmapheresis, alone or in combination. In SLE-associated cases, early recognition and prompt immunotherapy are associated with favourable outcomes; some patients respond well to steroids alone, while others require IVIG, particularly with systemic activity or relapse.

### Conclusion

CIDP may be the first manifestation of SLE, even in older males. Neurophysiology and CSF studies are pivotal for diagnosis when imaging is unrevealing. Relapse after steroid response should prompt reassessment for underlying systemic autoimmunity. IVIG can be effective in steroid-responsive but relapsing disease, supporting combined immunomodulatory strategies.

Pallavi Walunj, Hitisha Aggarwal, Nikhil Dongre. Chronic Inflammatory Demyelinating Polyradiculoneuropathy as the First Manifestation of Systemic Lupus Erythematosus in an Elderly Male. MMJ. 2025, December. Vol 2 (4).

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# "A Girl of Twelve, Bravery True – She Gave Her Liver, Gave Life Anew."

## Can a Paediatric Deceased Donor Liver be Transplanted to an Adult Patient?

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### Abstract:

Despite the growing volume of liver transplantation (LT) over the past decade, there remains a shortage of donor livers. In addition to the increased use of expanded-criteria donors, an alternative option is the use of paediatric-donor livers. Although paediatric grafts should ideally be used for paediatric recipients, they may be allocated to adult recipients in certain situations when declined by the paediatric recipient pool. Paediatric-to-adult deceased donor LT involves the use of liver grafts taken from paediatric donors (typically children under 12 years) and transplanted into adult recipients. Although this practice is relatively rare, it is increasingly considered due to the ongoing shortage of donor organs. Paediatric-to-adult deceased donor LT is a valuable strategy in selected adult recipients with appropriate size and clinical matching. When conducted with careful donor-recipient selection and technical expertise, outcomes are comparable to standard adult-to-adult transplants. As there is limited evidence regarding the effectiveness of paediatric liver grafts in adult recipients, more data is needed to understand the outcomes of paediatric-to-adult LT. We report a successful case of deceased donor liver transplant from a 12-year-old girl to a 70-year-old female suffering from decompensated chronic liver disease.

**Key words:** Liver Transplant, Paediatric Donor, Hepatic Artery Thrombosis.

### Introduction

Transplanting organs from paediatric donors to adults is uncommon. It is a technically challenging procedure as the paediatric vessels are small in size. Successful outcomes require centres with substantial experience in paediatric liver transplantation (LT) to minimise the risk of major vascular complications.<sup>1</sup>

Outcomes of paediatric-to-adult deceased donor liver transplants show comparable graft and patient survival rates to those receiving grafts from adult donors, particularly when appropriate recipient selection and careful surgical management are ensured.<sup>1,2</sup>

Multiple studies demonstrate equivalent patient and graft survival rates at one, three and five years for adult recipients of paediatric donor livers compared with

matched adult donor livers.<sup>3</sup> The incidence of major complications, including vascular and biliary issues, is similar, with no significant differences in length of intensive care unit (ICU) and hospital stay, with good long-term outcomes.<sup>1,2,4</sup>

Patient selection remains the Achilles' heel in such clinical scenarios. Good outcomes are most consistently reported in smaller adult recipients (often females with lower body mass index [BMI]), as careful size matching minimises technical challenges and postoperative risks.<sup>3</sup> If the donor liver is too small with a graft-to-recipient weight ratio (GRWR) of less than 0.8, complications like early allograft dysfunction and small-for-size syndrome may occur.<sup>5</sup>

### Case Report

We report a case of a 70-year-old female who presented to us with jaundice, ascites, and altered liver function tests three years ago. She had been a known case of diabetes mellitus (DM) for the past 20 years. On further evaluation, she was diagnosed with decompensated liver disease secondary to non-alcoholic steatohepatitis (NASH). She had hepatorenal syndrome with a serum creatinine level of 3.64 mg/dL, which responded to medical management. Her model for end-stage liver disease (MELD) score was 26. She had multiple hospital admissions for large-volume paracentesis due to recurrent ascites, which was not responding to the maximum dose of diuretics. In view of refractory ascites, she underwent transjugular intrahepatic portosystemic shunt (TIPSS) in 2023. Due to the non-availability of a living donor in the family, she was registered with the zonal transplant coordination committee (ZTCC) and placed on the waiting list for a deceased donor liver transplant in January 2023. She was further evaluated by contrast computed tomography (CT) of the abdomen, which showed a shrunken liver with nodularity with no evidence of liver lesions, portal vein thrombosis or any major porto-systemic collaterals. She was kept under regular follow-up and medical management. After being on the waiting list for more than two years, she finally received a deceased donor liver allotted to her, but it was a 12-year-old paediatric brain-dead donor from Kolkata. Initially, the liver was allocated to a paediatric patient from Mumbai. However, the paediatric recipient tested positive for Coronavirus Disease 2019 (COVID 19) and was deemed unfit for surgery. There was no other paediatric recipient active on the list, due

to which the Regional Organ and Tissue Transplant Organisation (ROTO) and National Organ and Tissue Transplant Organisation (NOTTO) allotted the liver to the adult pool. After a multidisciplinary meeting, we decided to accept the liver for our adult recipient, as the recipient's BMI ( $22.4 \text{ kg/m}^2$ ) was matching with the paediatric donor's BMI ( $18 \text{ kg/m}^2$ ). The surgery was uneventful (Figure 1). The cold ischaemia time was 5 hours 45 minutes. Our recipient recovered well and was discharged in one week. She is currently under regular follow-up 3 months post-transplant and is leading a normal life.



**Figure 1:** Paediatric deceased donor healthy liver at the time of organ retrieval.

### Discussion

The outcomes of adult LT using grafts from deceased paediatric donors remain inadequately characterised. Given the ongoing organ shortage and the high mortality rates among patients on the liver transplant waiting list, transplant teams are compelled to explore alternative strategies to mitigate this supply–demand gap.<sup>6</sup> Utilising paediatric donor livers for adult recipients represents one such option, typically when these grafts are declined by paediatric candidates.<sup>7</sup> Nevertheless, recent data from the Organ Procurement and Transplantation Network (OPTN)/Scientific Registry of Transplant Recipients (SRTR) indicate a decline in the use of paediatric livers for adult transplants from 11.7% to 7.7% without a corresponding rise in their use within the paediatric population.<sup>8</sup>

Our donor was a 12-year-old female whose liver was initially allocated to a paediatric recipient. However, as the recipient tested positive for COVID-19 and was deemed unfit for surgery, the paediatric liver was then offered to our adult recipient. As it was a paediatric donor, we had

to be careful when selecting our recipient, who was lean and had a low BMI. The liver was offered to a female recipient with a BMI of 22.4 kg/m<sup>2</sup>, which was close to the paediatric donor BMI (18 kg/m<sup>2</sup>). Our patient had an uneventful recovery without any complications.

Previous studies in the literature have found comparable graft survival and overall complication rates between paediatric-to-adult and adult-to-adult LT.<sup>6-9</sup> However, paediatric-donor grafts have been associated with an increased risk of vascular complications, particularly hepatic artery thrombosis (HAT).<sup>8,9</sup> Paediatric grafts are thought to be associated with a higher risk of vascular complications due to various factors, including small vessel calibre and graft size.<sup>8</sup>

Of note, Croome *et al.* found no differences in graft survival at the same intervals but noted that 90-day graft survival was lower in the paediatric donor group.<sup>4</sup> In the same cohort, an additional subgroup analysis found that 90-day graft survival was significantly lower among patients with a GRWR less than 0.8% compared to those with a GRWR greater than or equal to 0.8%.<sup>4</sup> Similarly, patient survival, re-transplantation, and length of hospital

stay (LOS) were not significantly different between the paediatric- and adult-donor groups.<sup>4,8,9</sup> Nevertheless, achieving acceptable outcomes largely depends on an optimal recipient selection. In our practice, consideration to use paediatric ( $\leq 12$  years) grafts in adults is based on the absence of a suitable paediatric recipient, availability of well-selected recipients shown to be favourable to these types of grafts (smaller, leaner individuals with lower BMI and no previous abdominal surgery), and the surgeon's discernment.<sup>9</sup>

It is important to highlight that our centre has an established paediatric liver transplant programme, as well as an active living donor liver transplant programme. Therefore, beyond careful patient selection, our excellent results could be strongly related to the fact that having such programmes implies a certain degree of expertise and surgical proficiency with challenging procedures, with small vessels and management of associated complications.

## Conclusion

Hence, in properly selected patients, paediatric-to-adult cadaveric transplant can be successfully conducted at high volume centres with surgical expert.

Gaurav Chaubal, Aditya Nanavati, Hunaid Hatimi, Amith Kumar Pakkala, Amith Sreekant, Harshit Chaksota, Premal Narkhede, Blossom Dsouza, Uday Sanglodkar, Alisha Chaubal, Hardik Shah, Tejas Joshi, Radhika Ruhatiya, Abdul Ansari, Wasim Khot, Samir Shah. "A Girl of Twelve, Bravery True – She Gave Her Liver, Gave Life Anew." Can a Paediatric Deceased Donor Liver be Transplanted to an Adult Patient? MMJ. 2025, December. Vol 2 (4).

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# Robotic Sigmoid Neovaginoplasty in Mayer–Rokitansky–Küster–Hauser Syndrome: A Case Report of a Feasible and Safe Reconstructive Approach

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## Abstract:

Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome is a rare congenital disorder characterised by vaginal agenesis with normal ovarian function and karyotype. Neovaginoplasty remains the cornerstone of management for patients seeking functional sexual outcomes. While laparoscopic sigmoid vaginoplasty has been widely reported, the robotic approach offers enhanced precision, ergonomics, and three-dimensional (3D) visualisation. We present the case of a 21-year-old female diagnosed with MRKH syndrome who underwent robotic sigmoid neovaginoplasty. The procedure was successfully completed with an operative time of 5 hours and an estimated blood loss of less than 50 mL. Postoperative recovery was uneventful, and the patient was discharged on postoperative day 7. At 8 weeks of follow-up, the neovagina demonstrated satisfactory length, cosmetic appearance, and functional outcomes. This case highlights that robotic sigmoid neovaginoplasty is a safe and feasible technique for vaginal reconstruction in MRKH syndrome, combining the advantages of minimally invasive surgery with enhanced surgical dexterity.

**Key words:** Mayer–Rokitansky–Küster–Hauser (MRKH) Syndrome, Robotic Surgery, Sigmoid Neovaginoplasty, Colovaginoplasty.

## Introduction

Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome is a rare congenital malformation affecting approximately 1 in 4,500–5,000 female births. It is characterised by congenital absence or hypoplasia of the uterus and upper vagina in phenotypically normal females with a 46,XX karyotype and normal secondary sexual characteristics. The diagnosis is often made during adolescence when patients present with primary amenorrhoea despite normal pubertal development.

Reconstructive options include non-surgical dilation (Frank's method), McIndoe vaginoplasty, Davydov procedure, and intestinal (sigmoid or ileal) vaginoplasty. Among these, sigmoid vaginoplasty offers several

advantages: a well-vascularised mucosa, self-lubrication, and adequate vaginal length with long-term durability.

Traditionally performed via open or laparoscopic methods, sigmoid neovaginoplasty has evolved with the advent of robotic-assisted surgery. Robotic technology provides enhanced dexterity, tremor filtration, and superior visualisation in confined pelvic spaces, potentially improving outcomes in such complex reconstructive procedures.

Here, we report a case of robotic sigmoid neovaginoplasty in a patient with MRKH syndrome, highlighting the technical aspects, perioperative outcomes, and clinical implications.

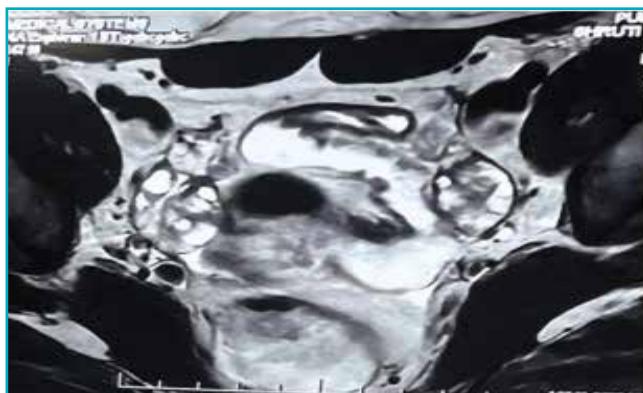
## Case Report

A 21-year-old female presented with primary amenorrhoea. She reported normal pubertal development and absence of cyclic abdominal pain. On examination, she was phenotypically normal with normal breast and pubic hair development. Examination of the external genitalia revealed normal labial development with an absent vaginal orifice, as shown in Figure 1.

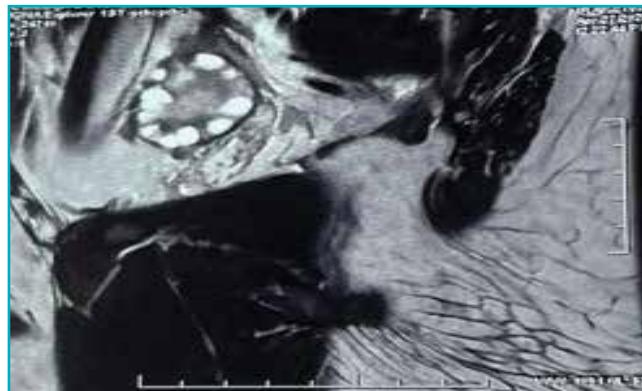


**Figure 1:** Examination of the external genital showing normal labial folds and vaginal dimple.

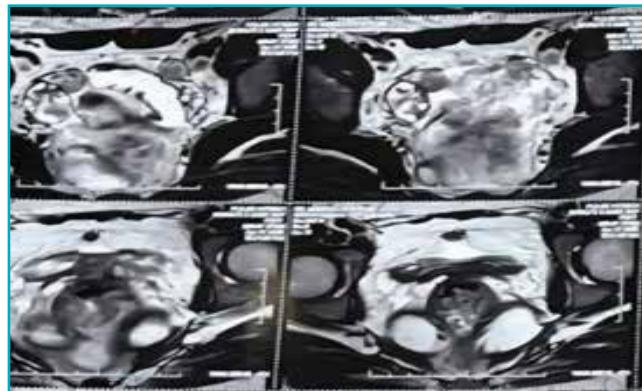
Ultrasonography and magnetic resonance imaging (MRI) revealed a non-functional hypoplastic uterus and absent vagina, with normal bilateral ovaries and kidneys, as shown in Figures 2A–C. Karyotyping confirmed 46,XX. A diagnosis of MRKH syndrome with a variation was established.



**Figure 2A:** View of bilateral polycystic ovaries (PCO).



**Figure 2B:** View of string of pearls — polycystic ovaries (PCO).



**Figure 2C:** View of rudimentary bicornuate uterine horns.

The patient was counselled regarding available options for vaginal reconstruction. Considering her preference for surgical creation of a neovagina, a robotic sigmoid neovaginoplasty was planned. Written informed consent was obtained from the patient.

## Surgical technique

Under general anaesthesia, the patient was positioned in lithotomy with a steep Trendelenburg tilt. A four-port robotic approach was employed using the da Vinci Xi system.

- 1. Port placement:** An 8-mm camera port was inserted at the umbilicus, with three 8-mm robotic ports and one assistant port placed under direct vision as shown in Figures 3A and 3B.



**Figure 3A:** Placements of the ports.



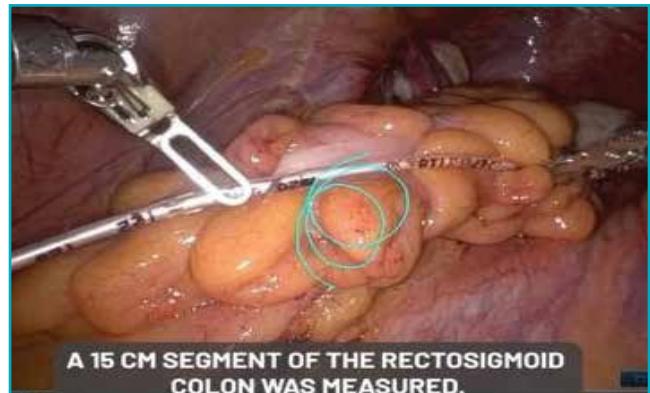
**Figure 3B:** Left lower docking.

**2. Neovaginal space creation:** A hysterectomy with bilateral salpingectomy was performed. A perineal incision was made, and blunt dissection was used to create a neovaginal canal between the bladder and rectum up to the peritoneum, as shown in Figure 4.



**Figure 4:** Rudimentary bicornuate hysterectomy specimen.

**3. Sigmoid segment mobilisation:** A 12–15 cm well-vascularised sigmoid segment, based on its mesenteric blood supply, was mobilised as shown in Figure 5.

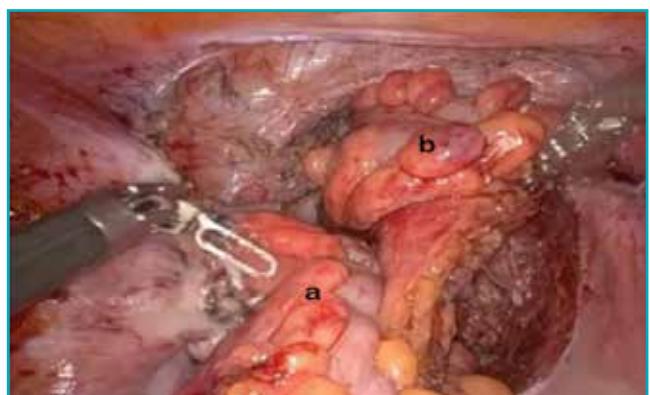


**Figure 5:** Mobilisation of the sigmoid segment.

**4. Anastomosis:** The distal end of the sigmoid pedicle was pulled down and sutured to the perineal skin at the neovaginal introitus, while the proximal end was closed using a SureForm stapler. End-to-end anastomosis was performed robotically with the help of a trans-anal circular stapler, allowing precise anastomosis as shown in Figures 6A–C.



**Figure 6A:** Application of SureForm stapler.



**Figure 6B:** **a.** Reanastomosed rectosigmoid, **b.** Right-sided vascular colo neovaginal pedicle.



**Figure 6C:** Colo labial anastomosis.

**5. Completion:** Haemostasis was secured; anastomosis and bowel integrity were checked using an Asepto syringe, and vascularity was checked with intravenous indocyanine green as shown in Figure 7.



**Figure 7:** Intraoperative assessment.

The operative time was 5 hours, with an estimated blood loss of less than 50 mL. There were no intraoperative complications.

### Postoperative course

The patient recovered uneventfully and was discharged on postoperative Day 7. No vaginal mould was placed intraoperatively. At the 5-week visit, mild stenosis was suspected due to upward traction of the pedicle; dilatation was performed under anaesthesia, and the patient was instructed on a self-dilatation protocol.

At 2-month follow-up, the neovagina was patent with a length of 12 cm. The mucosa appeared healthy with adequate lubrication. The patient reported no complications such as stenosis, fistula, or excessive mucus discharge.

### Discussion

The MRKH syndrome presents unique reconstructive challenges, requiring the creation of a functional neovagina that enables satisfactory sexual function and psychosocial well-being. Although non-surgical dilation remains the first-line management, a subset of patients either fail conservative therapy or prefer definitive surgical reconstruction for durable and physiological outcomes.<sup>1,2</sup> Among surgical techniques, sigmoid vaginoplasty remains the gold standard due to the segment's robust vascularity, mucosal lubrication, and tissue similarity to the native vagina. The sigmoid colon provides a well-vascularised, self-lubricating mucosa that minimises postoperative stenosis and ensures long-term patency.<sup>3</sup> The advent of minimally invasive techniques — particularly robotic-assisted surgery — has refined this approach, offering enhanced visualisation, precise dissection, and superior instrument control. Robotic-assisted surgery provides substantial ergonomic and technical advantages over laparoscopy, including three-dimensional (3D) magnified vision, tremor filtration, and enhanced dexterity with wristed instruments. These features are particularly valuable during deep pelvic dissection and anastomosis, reducing the risk of injury to adjacent organs and improving operative accuracy.<sup>4,5</sup> Multiple reports indicate that robotic sigmoid vaginoplasty achieves comparable or improved perioperative outcomes relative to conventional approaches. Beyond intraoperative precision, the success of neovaginoplasty depends on postoperative functionality. Studies demonstrate that a sigmoid neovagina provides excellent sexual satisfaction, adequate lubrication, and minimal long-term complications such as stenosis or mucous overproduction.<sup>3</sup> In our case, the patient achieved adequate vaginal length and calibre with satisfactory cosmetic and functional outcomes within two months postoperatively. The robotic platform likely contributed to reduced intraoperative complications. Psychosexual rehabilitation is integral to recovery and long-term patient satisfaction. Counselling, structured dilation programmes, and gradual resumption of sexual activity are essential to achieving optimal results.<sup>1</sup> The minimally invasive and precise nature of robotic surgery may positively influence body image, confidence, and psychological well-being, thereby enhancing overall quality of life in MRKH patients.

undergoing genital reconstruction. Despite its benefits, robotic sigmoid neovaginoplasty has limitations. The high cost, limited access to robotic platforms, and a significant learning curve remain barriers to widespread adoption.

Future multicentric prospective studies with larger sample sizes and long-term follow-ups are warranted to validate the superiority of robotic techniques in terms of anatomical, functional, and psychosocial outcomes.

### Conclusion

Robotic sigmoid neovaginoplasty represents a safe, precise, and functionally effective reconstructive technique for patients with MRKH syndrome. It merges the advantages of minimally invasive surgery with improved ergonomics and visualisation, offering excellent anatomical, functional, and psychosocial results when performed in experienced centres.

UddhavRaj Dudhedia, Manmohan Kamat, Anukrati Singh, Shreya Alluri, Akhil Kumar Mishra. Robotic Sigmoid Neovaginoplasty in Mayer–Rokitansky–Küster–Hauser Syndrome: A Case Report of a Feasible and Safe Reconstructive Approach. MMJ. 2025, December. Vol 2 (4).

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# Complex Case of Compromised Airway with Triple-Vessel Disease: An Innovative Approach

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**Abstract:**

Hoarseness and dyspnoea are common ear, nose and throat (ENT) symptoms that may occasionally coexist with systemic illnesses, thereby complicating management. Airway surgery in patients with significant cardiac comorbidities carries a higher anaesthetic risk, while untreated airway obstruction increases the risk of cardiac procedures requiring general anaesthesia. A 64-year-old male, a known case of carcinoma of the base of the tongue, post-chemoradiotherapy in 2016, presented with hoarseness of voice and shortness of breath for six months. Videolaryngoscopic evaluation revealed a large polypoidal growth arising from the right vocal cord, occluding approximately 70% of the glottic lumen. Pre-anaesthetic evaluation revealed a positive treadmill test (TMT), and coronary angiography showed triple-vessel disease (TVD). The case was jointly evaluated by ENT and cardiothoracic and vascular surgery (CTVS) teams. Instead of performing a tracheostomy followed by staged procedures, a combined approach was adopted. Under general anaesthesia, using a carbon dioxide (CO<sub>2</sub>) laser with a Linear AcuBlade (1 mm, 10 W), the vocal cord growth was excised through a laser-compatible endotracheal tube. The tube was then replaced with a conventional 8.0 mm tube, and off-pump coronary artery bypass grafting (CABG) using three grafts was successfully performed. The postoperative course was uneventful, with no airway compromise or bleeding. Videolaryngoscopy prior to extubation showed a patent airway, and the patient was extubated successfully with good voice quality. This case highlights the importance of multidisciplinary planning in managing patients with concurrent airway obstruction and severe coronary artery disease. Transoral CO<sub>2</sub> laser excision provides a safe, minimally invasive solution for securing the airway prior to cardiac surgery, avoiding tracheostomy-related morbidity. A coordinated approach between ENT and CTVS teams allowed for safe airway management and successful cardiac revascularisation without the morbidity associated with tracheostomy.

**Key words:** Hoarseness, CO<sub>2</sub> Laser Surgery, Vocal Cord Growth, Airway Obstruction, Coronary Artery Bypass Grafting, Multidisciplinary Approach, Laryngeal Surgery.

## Introduction

Hoarseness and shortness of breath are frequent complaints in otolaryngology and respiratory medicine. While most cases arise from benign or localised laryngeal pathology, in select patients, these symptoms may coincide with serious systemic diseases, including ischaemic heart disease (IHD), posing unique diagnostic

and therapeutic challenges complicating management. In patients with significant cardiac comorbidities, airway surgery carries a higher anaesthetic and perioperative risk. Conversely, untreated airway obstruction increases the risk during cardiac procedures requiring general anaesthesia.

In patients with coronary artery disease (CAD), airway surgery entails significant anaesthetic and perioperative risks, whereas untreated airway obstruction poses substantial hazards during cardiac surgery under general anaesthesia.<sup>1-3</sup> In such complex situations, a coordinated multidisciplinary strategy between ear, nose and throat (ENT), anaesthesia, and cardiothoracic teams is crucial for safe and successful outcomes.<sup>4,5</sup>

### Case Report

A 64-year-old male presented with a six-month history of progressive hoarseness and shortness of breath. He was a known case of carcinoma of the base of the tongue, post concurrent chemoradiotherapy (CCRT) in 2016. There was no history of dysphagia, weight loss, or chest pain.

Initial examination at an outside hospital revealed a polypoidal growth over the right vocal cord. During pre-anaesthetic evaluation, a treadmill test (TMT) was positive, and coronary angiography demonstrated triple-vessel disease. He was referred to the Cardiothoracic and Vascular Surgery (CTVS) Department at BLK-Max Super Speciality Hospital, New Delhi, for coronary artery bypass grafting (CABG) evaluation.

At our institution, videolaryngoscopy revealed a large, polypoidal growth arising from the right vocal cord, occluding nearly 70% of the glottic lumen, with restricted right cord mobility (Figure 1). Given the risk of airway compromise, a joint ENT–CTVS–anaesthesia discussion was held to determine the safest management plan.



**Figure 1A:** Preoperative picture of right vocal cord growth.



**Figure 1B:** Postoperative Day 7.

Two approaches were considered:

1. Tracheostomy under local anaesthesia, followed by CABG and later removal of the laryngeal growth.
2. Single-stage management with transoral carbon dioxide (CO<sub>2</sub>) laser excision of the growth using a laser-compatible tube, followed immediately by CABG.

The second option was preferred to avoid tracheostomy-related morbidity and prolonged recovery.

### Operative details

Under general anaesthesia, a size 6 laser-compatible endotracheal tube was inserted. Using a CO<sub>2</sub> laser with a Linear AcuBlade (1 mm spot, 10 W power), the entire polypoidal mass from the right vocal cord was excised in toto. Haemostasis was achieved, and the glottic airway was significantly widened.

Subsequently, the laser tube was replaced with a standard size 8 endotracheal tube, and CABG with three grafts on a beating heart was performed under appropriate heparinisation. The surgery and recovery were uneventful.

### Postoperative course

The patient was monitored in the intensive care unit. No airway bleeding or compromise was noted. Videolaryngoscopy performed the following day showed a well-healed right vocal cord and a patent glottic airway. He was successfully extubated with good phonation and oxygen saturation. The patient was discharged in stable condition, with improved cardiac function and normal voice quality.

## Discussion

The coexistence of airway obstruction and IHD presents unique perioperative challenges. Airway manipulation in such patients may precipitate haemodynamic instability, while cardiac revascularisation under airway compromise carries significant anaesthetic risk.<sup>4,6</sup>

Traditionally, tracheostomy under local anaesthesia is used to secure the airway before cardiac surgery; however, it is associated with morbidity, including infection, bleeding, delayed decannulation, and long-term voice changes.<sup>7</sup>

In this case, transoral CO<sub>2</sub> laser excision provided a precise, haemostatic, and minimally invasive method to restore airway patency.<sup>8,9</sup> The CO<sub>2</sub> laser's ability to achieve haemostasis and minimise thermal injury makes it an ideal tool for delicate laryngeal work, particularly in patients with cardiac risk where prolonged procedures and bleeding must be avoided.<sup>10,11</sup>

Performing both surgeries in a single sitting reduced total anaesthetic exposure, hospitalisation time, and postoperative morbidity. The favourable outcome underscores the importance of a multidisciplinary approach, emphasising preoperative coordination and intraoperative communication between ENT, anaesthesiology, and cardiac teams.<sup>4,5</sup>

## Acknowledgements

The authors acknowledge the contributions of the Departments of ENT and Cardiothoracic and Vascular Surgery, BLK-Max Super Speciality Hospital, New Delhi, for their teamwork and expertise in managing this complex case.

## Conflict of interest

None declared.

## Conclusion

This case illustrates that simultaneous transoral CO<sub>2</sub> laser excision of an obstructive vocal cord lesion followed by CABG is feasible and safe when planned collaboratively. Avoiding tracheostomy minimised morbidity and expedited recovery. Such multidisciplinary teamwork is essential in managing patients with concurrent airway and cardiac disease.

WVBS Ramalingam, Neha Sood, Pratibha Desai, Ramji Mehrotra, Shailender Nath Sahay. Complex Case of Compromised Airway with Triple-Vessel Disease: Innovative Approach. MMJ. 2025, December. Vol 2 (4).

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# Case of Fungal Pleural Effusion in an Immunocompetent Patient: A Case Report and Review of the Literature

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## Abstract:

Fungal pleural effusion (FPE) is an uncommon cause of pleural infection, accounting for only 1%–3% of all cases. It usually occurs in immunocompromised individuals, such as those with malignancy, diabetes, human immunodeficiency virus (HIV), or chronic steroid use. We report a rare case of left-sided *Candida*-associated pleural effusion in an 85-year-old man with no known comorbidities or immunosuppressive conditions. The patient presented with left-sided chest pain and weakness for two weeks. The pleural fluid analysis showed an exudative, lymphocyte-predominant effusion with low adenosine deaminase (ADA) levels. Medical thoracoscopy with pleural biopsy revealed fungal hyphae consistent with *Candida* species, confirming the diagnosis. The patient was treated with oral fluconazole 200 mg twice daily for eight weeks, showing marked clinical improvement and radiological resolution without the need for surgical intervention. This case highlights that FPE can occur even in immunocompetent individuals, emphasising the need for early pleural biopsy and timely antifungal therapy in undiagnosed exudative effusions.

**Key words:** Fungal Pleural Effusion, *Candida*, Immunocompetent, Pleural Biopsy, Fluconazole.

## Introduction

Fungal pleural effusion (FPE) is a rare cause of pleural infection, representing only a very small proportion of pleural effusions worldwide. It usually occurs when fungal organisms invade the pleural space, either directly or through adjacent pulmonary or surgical infection. Although bacteria remain the most frequent cause of pleural infections, fungi are occasionally isolated, most often *Candida* species and less commonly *Aspergillus*.<sup>1,2</sup>

Fungal infections of the pleura are typically seen in individuals with underlying illnesses such as diabetes mellitus, malignancy, human immunodeficiency virus (HIV) infection, organ transplantation, or prolonged use of corticosteroids.<sup>3,4</sup> They may also develop following chest surgery, trauma, or prolonged hospitalisation.

However, pleural infections caused by fungi in immunocompetent individuals are extremely uncommon. Such presentations may delay diagnosis because they are not usually suspected in patients without risk factors. Early use of diagnostic procedures such as medical thoracoscopy and pleural biopsy can be crucial in identifying the cause.

We describe a rare case of *Candida*-associated pleural effusion in an elderly but otherwise healthy patient, emphasising that fungal infection should not be excluded based on only immune status. This case also focuses on the role of direct pleural sampling in the diagnosis of unusual causes of pleural effusion.

## Case Report

An 85-year-old male, a non-smoker with no significant past medical history or immunosuppressive condition, presented to Max Super Speciality Hospital, Patparganj, with complaints of left-sided chest pain persisting for the past two weeks along with generalised weakness. The chest pain was significant enough to compel the patient to lie in the left lateral decubitus position for relief.

On examination, the patient had poor general condition. But he was conscious, oriented, haemodynamically stable, and maintaining oxygen saturation on room air. Respiratory examination revealed reduced air entry in the left infrascapular region.

Initial investigations included a chest X-ray (Figure 1), which showed blunting of the left costophrenic angle, suggestive of a moderate left-sided pleural effusion. Initial laboratory investigations were as follows:

- **Complete blood count (CBC):**

Total leucocyte count (TLC) –  $4.2 \times 10^9/L$ , haemoglobin – 8.3 g/dL, and platelets –  $177 \times 10^9/L$

- **Kidney function test (KFT):**

Creatinine – 1.2 mg/dL, sodium – 128.9 mmol/L, potassium – 4.31 mmol/L

- **Liver function test (LFT):**

Alkaline phosphatase (ALP) – 131.2 IU/L, albumin: globulin (A:G) ratio – 0.85

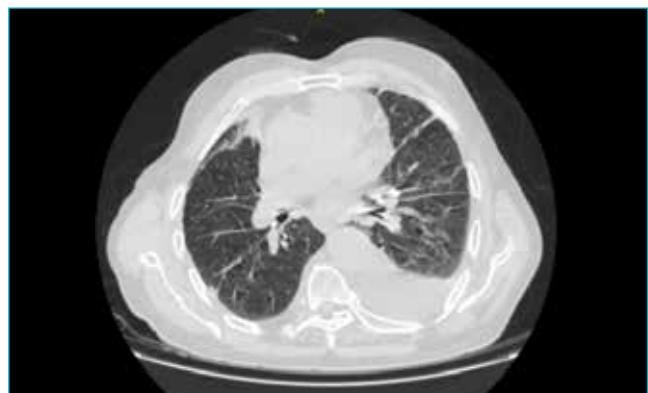


**Figure 1:** Chest X-ray-posteroanterior (CXR-PA) view, on presentation.

A high-resolution computed tomography (HRCT) chest (Figures 2 and 3) was done to rule out any lung parenchymal pathology and to look for any mediastinal lymph nodes. It showed a mild pleural effusion on left side with consequent atelectatic changes in left lower lobe, along with subcentimetric lymph nodes in the right paratracheal, aortopulmonary (AP) window and subcarinal regions.



**Figure 2:** High-resolution computed tomography (HRCT) chest (mediastinal window), on presentation.



**Figure 3:** High-resolution computed tomography (HRCT) chest, lung window, on presentation.

A diagnostic thoracentesis was performed, revealing slightly turbid pleural fluid that was exudative, lymphocyte predominant, with low adenosine deaminase (ADA) levels. The pleural fluid analysis showed: glucose 137 mg/dL, protein 94.1 g/dL, albumin 2.29 g/dL, TLC 1250 cells/mm<sup>3</sup> (neutrophils 10%, lymphocytes 90%, with a few macrophages and mesothelial cells), ADA 8.10 U/L, and negative malignant cytology.

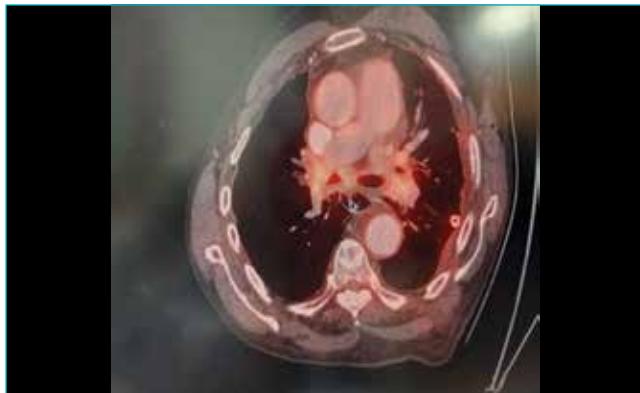
In view of low ADA levels with exudative, lymphocytic effusion, malignancy was suspected, and the patient

was taken up for medical thoracoscopy with pleural biopsy during which approximately 6500–7000 mL of straw-coloured pleural fluid was drained. The visceral pleura and parietal pleura were visualised. Multiple blackish to brownish discolourations were noted over the visceral pleura, from which targeted pleural biopsies were obtained. Post-thoracoscopy X-ray shows expansion of lung parenchyma (Figure 4).



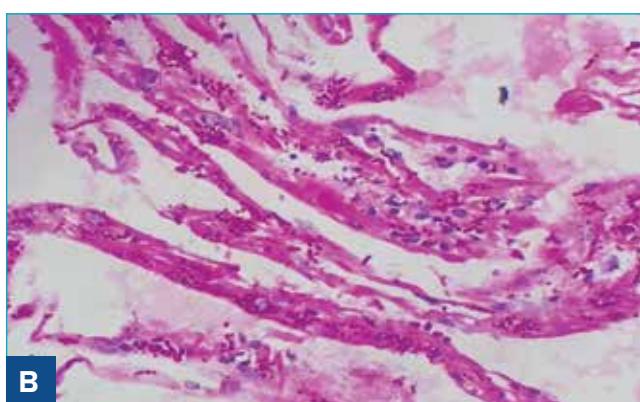
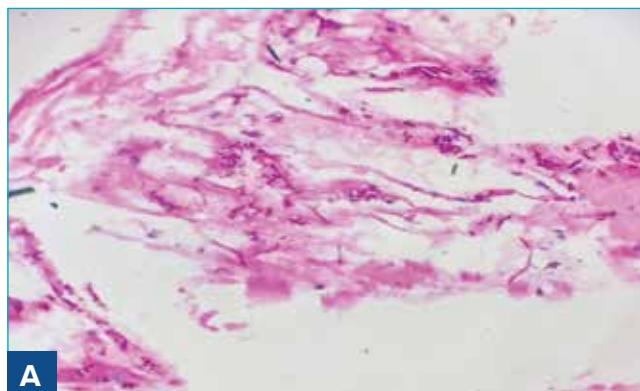
**Figure 4:** Chest X-ray-posteroanterior (CXR-PA) view, post medical thoracoscopy.

To further evaluate the cause, a whole-body  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography–computed tomography ( $^{18}\text{F}$ -FDG PET-CT) scan was conducted after thoracoscopy. Since the patient was initially unwilling to undergo PET imaging, we proceeded with medical thoracoscopy and pleural biopsy. The PET scan was performed later, once the patient subsequently consented. The scan showed (Figure 5) faint FDG-avid minimal left-sided pleural effusion with corresponding subsegmental collapse, along with necrotic mediastinal lymphadenopathy. Enlarged bilateral hilar, subcarinal, and parahilar lymph nodes were noted — the largest measuring  $1.8 \times 1.9$  cm in the subcarinal region,  $1.5 \times 1.8$  cm at the left hilum, and  $1.9 \times 1.7$  cm at the right hilum. No metabolically active mass or distant organ involvement was seen.



**Figure 5:** Positron emission tomography (PET) scan post medical thoracoscopy.

Histopathological examination (Figure 6) of the pleural biopsy revealed pleura with mononuclear cells and fungal hyphae consistent with *Candida* spp., with no granulomas or malignant cells. This confirmed the diagnosis of *Candida*-associated FPE.



**Figure 6:** Pleural biopsy showing tubular, filamentous hyphae consistent with *Candida* spp. under periodic acid-Schiff stain (PAS Stain) 400x magnification, A. Shows pseudohyphae and histiocytes, B. Presence of histiocytes more prominently seen.

In view of the rare findings on the pleural biopsy, the patient's attendants requested a second opinion on the pathology slides. The samples were reviewed at Lab Core Diagnostics, which reported the following:

- Block A: Histiocytes with yeast forms and pseudohyphae of fungus
- Block B: Fibrocollagenous tissue showing a few reactive mesothelial cells and histiocytes

The final diagnosis was the presence of fungal organisms, with morphology favouring *Candida*.

The patient was initiated on oral fluconazole at a dose of 200 mg twice daily (BD) for a total duration of eight weeks, following which he showed gradual symptomatic improvement, with resolution of cough and chest discomfort.

We reviewed 7 case reports on fungal pleurisy available on PubMed, and the clinical, diagnostic along with treatment outcomes are summarised in Table 1.

Article name	Age and sex	Risk factors	Pathogen isolated	Galactomannan test	(1→3)- $\beta$ -D-Glucan	Antifungal therapy	Surgical intervention	Outcome
Glendening & Koroscil, 2020 <sup>5</sup>	73/M	Post-COVID pneumonia	<i>Candida albicans</i>	Not done	Not reported	Fluconazole (intravenous)	Chest tube drainage	Recovered
Swaminathan et al., 2022 <sup>3</sup>	62/M	Post-COVID, uncontrolled DM	<i>Candida albicans</i>	Not done	Not reported	Fluconazole → voriconazole	Chest tube drainage	Improved
Jing et al., 2023 (16 cases total) <sup>4</sup>	Median: ~55 yrs	HIV, cancer, steroids	<i>Aspergillus</i> , <i>Candida</i> spp.	Done in most <i>Aspergillus</i> cases (positive)	Positive in some <i>Candida</i> cases	Voriconazole, amphotericin B, fluconazole	Most required drainage, few had surgery	10 improved, 2 deaths
Cheng et al., 2023 <sup>6</sup>	N/A (comparative study)	Mixed (bacterial/fungal empyema)	<i>Candida</i> spp., <i>Aspergillus</i> spp.	Partially available	Not detailed	Fluconazole, amphotericin B	Thoracoscopic decortication (VATS)	Comparable to bacterial group
Rakhecha et al., 2023 <sup>7</sup>	42/M	Chronic pancreatitis	<i>Candida albicans</i>	Not done	Not done	IV Fluconazole	Tube thoracostomy	Recovered
Solomon et al., 2023 <sup>8</sup>	40/M	None (Immunocompetent)	<i>Candida parapsilosis</i>	Not available	Not done	Fluconazole	Chest tube	Full recovery
Iqbal et al., 2024 (26 cases) <sup>2</sup>	Median: 43 yrs; 20M/6F	Cancer, diabetes, post-op, post-COVID	81% <i>Candida</i> , 27% <i>Aspergillus</i> (some co-infection)	Positive in most <i>Aspergillus</i> cases	Not always tested	Fluconazole, amphotericin B, voriconazole	Chest tube in all; decortication in 9	61.5% recovery, 38.5% mortality

**Table 1:** Summary of published case reports and case series of fungal pleural effusion — diagnosis and management.

**Abbreviations:** COVID: Corona Virus Disease 2019; DM: Diabetes Mellitus; F: Female; HIV: Human Immunodeficiency Virus; IV: Intravenous; M: Male; spp: Species; N/A: Not applicable; Post-op: Post-Operative; VATS: Video-Assisted Thoracoscopic Surgery.

## Discussion

FPE is rare but important to recognise because its diagnosis can be difficult. Although the overall incidence is low, these infections often present diagnostic and treatment challenges. According to the latest European Respiratory Society/European Society of Thoracic Surgeons (ERS/ESTS) guidelines (2023), fungal infections are responsible for only about 1.75% of community-acquired and 2.68% of hospital-acquired pleural infections.<sup>1</sup>

Most case series report *Candida albicans* as the most frequent organism, followed by non-albicans species such as *C. glabrata* and *C. parapsilosis*.<sup>2,5</sup> Earlier studies report that affected patients usually have identifiable risk factors, such as malignancy, recent thoracic surgery, or significant immunosuppression.<sup>6,7</sup>

Our patient had none of these typical risk factors, making this presentation unusual. This suggests that fungal pleural infections can sometimes occur even in people who are otherwise immunocompetent. Advanced age or subtle mucosal injury may play a role, although such contributing factors are not always obvious.

The pleural fluid pattern in our case also differed from the patterns usually described. Fungal empyema commonly produces a neutrophilic, purulent exudate

with a very low pH.<sup>2</sup> However, our patient had an exudative, lymphocyte-predominant effusion with low ADA. This may reflect a small fungal load limited mainly to the pleural tissue, causing a slower, cell-mediated inflammatory response rather than a frank empyema.

Diagnosing FPE requires a high level of suspicion. Pleural fluid cultures may be negative, and a pleural biopsy may be necessary to confirm the diagnosis. In this case, histopathology showing fungal hyphae compatible with *Candida* gave a definite diagnosis.

Management includes systemic antifungal therapy, drainage of the pleural space, and surgery in more severe cases. Fluconazole is effective for most *Candida* species, while azoles or amphotericin B are recommended for *Aspergillus* infections.<sup>9,10</sup> Our patient improved with oral fluconazole alone, without the need for surgery, highlighting the importance of early recognition and timely treatment.

Overall, this case adds to the limited body of evidence showing that FPE can occur even in patients without obvious risk factors. When pleural effusions remain unexplained and routine tests are inconclusive, fungal causes should be considered. Early thoracoscopy, pleural biopsy, and prompt antifungal therapy can significantly improve outcomes.

## Conclusion

FPE remains a rare and often overlooked diagnosis, particularly in individuals without obvious risk factors. This case highlights the need for clinicians to consider less common causes of pleural effusion, especially when the pleural fluid analysis is indeterminate. In such scenarios, early use of diagnostic tools like thoracoscopy and pleural biopsy is key to uncovering unusual pathogens such as fungi. Prompt initiation of appropriate antifungal treatment can lead to good recovery — even in the absence of surgical procedures. Recognising and treating such atypical presentations early can make a significant difference in patient outcomes.

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# Dexterity in Complexity: Case Series of Challenging Cervicothoracic Surgeries through Robotic Platforms

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**Abstract:**

Robotic-assisted surgery has revolutionised the landscape of minimally invasive surgical oncology by enabling enhanced precision, dexterity, and visualisation, especially in anatomically complex regions. The integration of robotic platforms into oncological surgery offers a distinct advantage in achieving oncological safety with minimal morbidity. This case series demonstrates the feasibility, safety, and adaptability of robotic techniques in challenging cervicothoracic and head-neck oncologic procedures. It includes three patients who underwent complex robotic surgeries: a robotic oesophagectomy in a frail patient with poor pulmonary function, salvage transoral robotic surgery (TORS) after dual radiation exposure, and a robotic thyroidectomy using the bilateral axillo-breast approach (BABA). Each case was planned and executed after multidisciplinary evaluation, with emphasis on patient selection, surgical planning, and intraoperative considerations. All procedures were successfully completed using robotic platforms without intraoperative complications. Patients demonstrated satisfactory postoperative recovery with minimal morbidity and excellent cosmetic and functional outcomes. Histopathological evaluation confirmed negative margins in all cases. Robotic-assisted surgery offers significant advantages in precision dissection, access to deep anatomical spaces, and improved postoperative recovery in carefully selected oncologic cases. This series highlights the versatility of robotic platforms in addressing surgical challenges across the cervicothoracic and head-neck regions. Further studies with larger cohorts and long-term follow-up are warranted to establish oncologic equivalence and cost-effectiveness.

**Key words:** Robotic Surgery, Surgical Oncology, Transoral Robotic Surgery (TORS), Robotic Oesophagectomy, Robotic Thyroidectomy, Bilateral Axillo-Breast Approach (BABA), Cervicothoracic Surgery, Minimally Invasive Surgery, Head and Neck Cancer, Oncologic Outcomes.

## Introduction

The term “robot” was coined in the beginning of the last century, coming originally from the Czech word “roboťa”, meaning “labour”.<sup>1</sup> The U.S. Department of Defence and National Aeronautics and Space Administration (NASA) partnered along with Stanford Research Institute to explore robotics for remote battlefield or space surgeries.

The aim was to allow expert surgeons to operate from afar via robotic arms. In early 2000, “da Vinci” became the first robotic system approved by the Food and Drug Administration (FDA) for general laparoscopic surgery — marking the true beginning of robotic-assisted surgery in clinical practice.<sup>2</sup> Table 1 summarises the timeline of major milestones in the evolution of robotic surgery.

Phase	Milestone
1990s	Early robotic prototypes (Automated Endoscopic System for Optimal Positioning [AESOP], Zeus Robotic Surgical System [ZEUS]) assist in laparoscopic surgery
2000	Food and Drug Administration (FDA) approval of da Vinci — beginning of true robotic-assisted minimally invasive surgery (MIS)
2001–2010	Rapid expansion into urology, gynaecology, and cardiac surgery
2010s	Mainstream adoption in general and colorectal surgery; training programmes evolved

**Table 1:** Timeline of major milestones in the evolution of robotic surgery.

### Cutting edge meets cancer care: What surgical oncology demands?

Surgical oncology demands precision, oncological safety, meticulous dissection, and adherence to sound anatomical and oncological principles such as achieving negative margins, appropriate lymphadenectomy, and minimising tumour handling. These goals often require complex dissections in confined anatomical spaces and careful preservation of critical structures. Robotic surgery, with its enhanced three-dimensional (3D) visualisation, wristed instruments, and improved dexterity, offers a powerful tool to fulfil these demands. It allows the surgeon to perform precise and controlled movements even in anatomically challenging areas, facilitating oncological resections with minimal morbidity. Furthermore, robotic platforms enable better access to deep pelvic, mediastinal, and retroperitoneal regions, making them highly suitable for complex cancer surgeries where conventional open or laparoscopic approaches may fall short. When used judiciously and with proper oncologic intent, robotic surgery serves as a valuable extension of the surgical oncologist's armamentarium.

### Case Report 1: Robotic Oesophagectomy in a Frail Patient

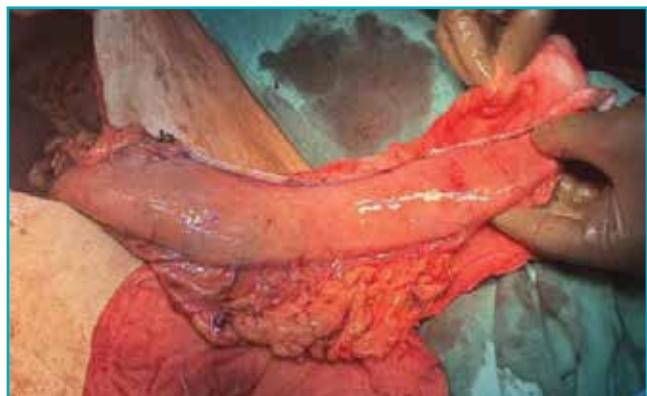
A 53-year-old male with an Eastern Cooperative Oncology Group (ECOG) score of 2, presented with complaints of dysphagia for solid food for 2 months duration associated with significant weight loss. Upon evaluation patient was found to have a circumferential growth in the lower third oesophagus, 34 cm from the incisor teeth. Positron emission tomography–computed tomography (PET–CT) scan revealed bulky lower third oesophageal growth with enlarged subcarinal nodes with no evidence of distant metastasis. There were features of chronic obstructive pulmonary disease (COPD) and aspiration pneumonitis in CT. Patient was advised four cycles of neoadjuvant fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) chemotherapy. After a shared decision in the multidisciplinary tumour board, we decided to go ahead with robotic oesophagostomy. Since the patient was a known case of COPD with a poor ECOG score, we felt that it was prudent to offer a robotic platform for this patient.



**Figure 1.1:** Camera port is placed about 2 intercostal spaces (ICS) below the tip of the right scapula. Robotic arm 1 (R1) is taken 7 cm from the midline, about 2–3 ICS above the camera port, lying parallel to the medial border of the scapula. Robotic arm 2 (R2) is taken about 2 ICS below the camera port, about 7 cm from the midline. The assistant port is triangulated between R2 and the camera.

The patient was placed in a prone position. Usually, a single-lung ventilation is initiated using a double-lumen endotracheal tube, but in this patient, we wanted to avoid single-lung ventilation owing to poor pulmonary functions. The ports were placed as described above (Figure 1.1). Circumferential dissection of the oesophagus from surrounding structures was carried out. The azygos

vein was clipped and divided to carry out the supra-azygos dissection. Enlarged subcarinal nodes were removed with precision (Figures 1.2A–B). This was followed by gastric conduit creation (Figures 1.3A–B) through mobilising the stomach.



**Figure 1.2A:** Enlarged subcarinal nodes were removed. The movements made by the robotic arms help in precise dissection at these crucial areas. This would have been difficult with the conventional laparoscopic techniques.



**Figure 1.2B:** Subcarinal region post-dissection showing complete clearance.



**Figure 1.3A:** Gastric conduit creation.



**Figure 1.3B:** Anastomosis between the gastric conduit and the cervical oesophagus made using the a small neck incision on the left side of neck 'Barcelona Technique' where a side-to-side anastomosis was made using a linear cutter stapler.

The patient was started on a liquid diet on postoperative Day 10 (POD 10) and was subsequently discharged. There were no major post operative events despite the poor general condition of the patient. The final histopathological examination (HPE) report revealed poorly differentiated adenocarcinoma; the resected margins were free. A total of 15 lymph nodes were retrieved. The subcarinal nodes and intrapulmonary nodes showed metastatic deposits. The patient was started on adjuvant chemotherapy after 3 weeks of surgery.

#### Key considerations:

- Preoperative optimisation in the form of nutritional support, spirometry, etc., plays a crucial role during early postoperative recovery.
- In frail patients with poor pulmonary function, it is better to avoid single-lung ventilation; instead, both lungs can be ventilated with low tidal volumes.
- Identify and preserve the thoracic duct to prevent chyle leak.
- The conduit viability can be assessed using intraoperative indocyanine green (ICG) dye.

#### Case Report 2: Pushing the Limits — “Salvage Transoral Robotic Surgery (TORS) after Dual Radiation Exposure”

A 74-year-old male was previously diagnosed in 2007 with squamous cell carcinoma of the right tonsil (cT4cNxMx) and treated with radical radiation therapy. After an 18-year disease-free interval, he developed a second primary

cancer in the soft palate, staged as cT1–2NOM0. He was planned for definitive radiation with concurrent chemotherapy, but chemotherapy was not given due to unfitness. He received intensity-modulated radiotherapy (IMRT) to the head and neck region from 21<sup>st</sup> February 2025 to 9<sup>th</sup> April 2025, delivered in 33 fractions with a total dose of 60–66 Gy. During follow-up, the patient had a residual lesion in the soft palate. PET–CT scan revealed a low-grade metabolism in the oropharynx. There were no significant fluorodeoxyglucose (FDG) avid neck nodes. A biopsy was done, which reported low-grade squamous cell carcinoma. After discussion in the tumour board, we decided to go ahead with salvage surgery. The lesion involved the soft palate, extending to the uvula medially and posteriorly to the posterior pharyngeal wall (Figures 2.1A–B).

### Discussion:

Surgical access to tumours in the oropharynx and base of the tongue has traditionally posed significant challenges due to the anatomic complexity and limited exposure of these regions.

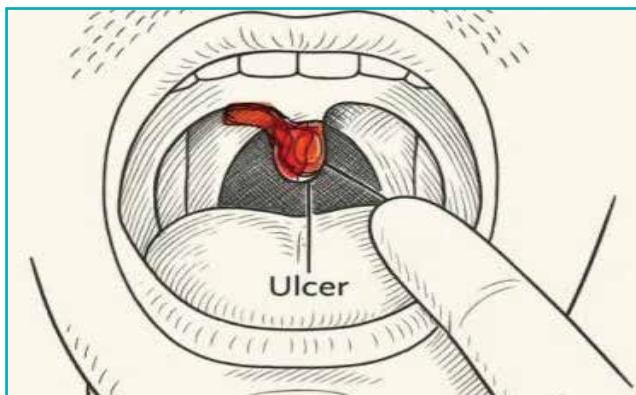
The conventional mandibular swing approach — an invasive technique involving osteotomy of the mandible — has long been used to achieve sufficient visualisation and access for tumour resection. While effective in terms of access, this method is associated with significant morbidity. Patients often endure complications such as malocclusion, non-union or malunion of the mandible, damage to the inferior alveolar nerve resulting in numbness, prolonged hospitalisation, and cosmetic deformity due to surgical scars.<sup>3</sup> The conventional mandibulotomy approach and extent of exposure achieved are illustrated in Figures 2.2A–C.



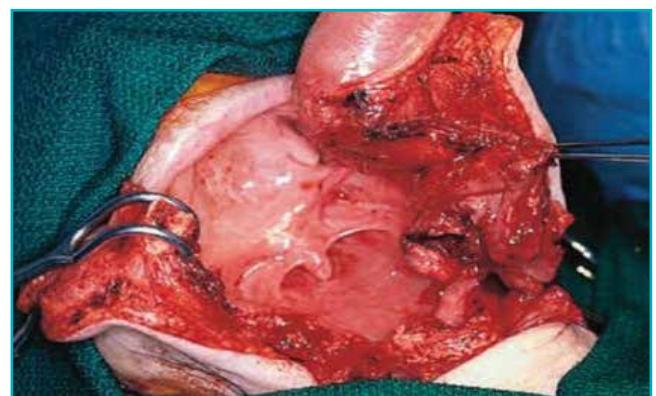
**Figure 2.1A:** Showing the lesion in the soft palate extending to the uvula medially and posteriorly extending to the posterior pharyngeal wall.



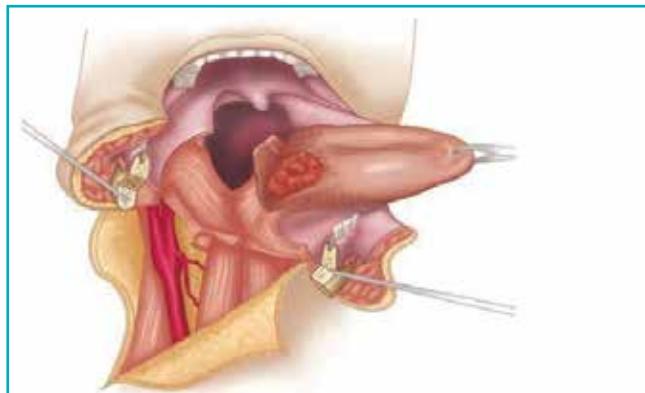
**Figure 2.2A:** The skin incision being outlined.  
**Source:** Jatin Shah textbook of Head and Neck Surgery.<sup>3</sup>



**Figure 2.1B:** Schematic diagram of the palatal lesion shown.



**Figure 2.2B:** Exposure of tumour through the mandibulotomy approach.  
**Source:** Jatin Shah textbook of Head and Neck Surgery.<sup>3</sup>



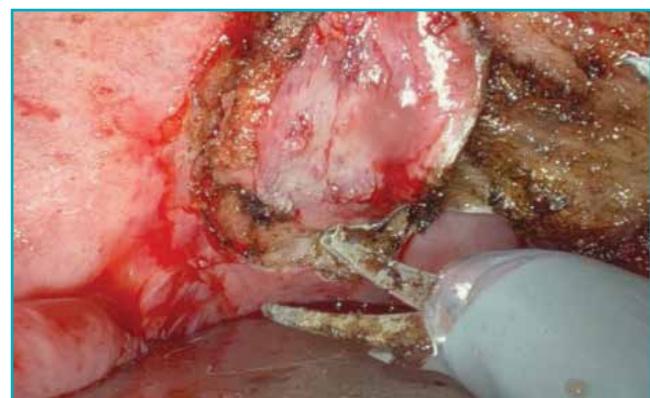
**Figure 2.2C:** Diagrammatic representation of the exposure obtained through a mandibulotomy.

**Source:** Jatin Shah textbook of Head and Neck Surgery.<sup>3</sup>

TORS represents a paradigm shift in the surgical management of oropharyngeal tumours (Figures 2.3A–C). Speech and swallowing functions are better preserved with TORS, reducing the need for long-term rehabilitation and improving overall quality of life. Patients undergoing TORS typically experience less postoperative pain, shorter hospital stays, and quicker return to oral intake. Tracheostomy and feeding tubes are often avoided or required only for short durations.



**Figure 2.3B:** The endoscope and the robotic arms being introduced in the oral cavity.



**Figure 2.3C:** The assistant retracts the tongue with a tongue depressor. Dissection over the posterior pharyngeal wall becomes easy with of monopolar scissors.



**Figure 2.3A:** Patient positioning and docking of robotic arms being done.

#### Key considerations:

- Conventional surgery in a previously irradiated neck would add to the morbidity of the patient. TORS would be ideal in these cases.
- Use an appropriate retractor system (example: Feyh–Kastenbauer [FK] retractor) to prevent pressure-related injury to the lips, teeth, or tongue.
- Monitor closely for delayed haemorrhage, which is most common during the first two weeks.

#### Case Report 3: Thyroid Surgery Re-Imagined — Robotic Techniques for a Scarless Neck

A 35-year-old female working in the information technology (IT) industry presented with complaints of swelling in the front of the neck for 1 month. Upon evaluation, she was found to have a solitary thyroid nodule with fine-needle aspiration cytology (FNAC) showing Bethesda III. She was advised to undergo

surgery. She was more concerned about her cosmesis and requested a scarless surgery. Hence, a robotic platform was chosen.

The trans axillary approach to the thyroid surgery was pioneered by the South Korean team from Seoul, led by Chung, in late 2007.<sup>4,5</sup> The robotic-assisted transaxillary thyroid surgery (RATS) approach was first described in North America by Kupersmith and Holsinger in 2011.<sup>6</sup> Since it was first introduced, more than 3,000 RATS procedures were performed in South Korea, and more than 6,000 worldwide.<sup>7</sup> Subsequent advances in robotic retraction and access systems have further improved visualisation and ergonomics for upper aerodigestive and thyroid procedures.<sup>8</sup> Patient positioning and port placement for the bilateral axillo-breast approach are shown in Figures 3.1 and 3.2.



**Figure 3.1:** This image depicts the patient positioning before docking the robotic arms. The patient lies in supine position with both arms abducted and raised up.



**Figure 3.2:** Image describes the port positioning. Bilateral axillary and bilateral circumareolar ports are placed.

We have described the steps of the bilateral axillo-breast approach robotic thyroidectomy (BABA-RT). The patient lies in the supine position, with the neck slightly extended.

Both arms are raised and fixed to expose the axilla. A 5–12 mm incision is made along the natural skin crease of each axilla. Two circumareolar ports are placed. Blunt dissection is done through the subcutaneous tissues to create a tunnel towards the neck. A working space is developed over the pectoralis major, clavicle, and up to the thyroid cartilage. Retractors or carbon dioxide (CO<sub>2</sub>) insufflation may be used to maintain space. The robotic arms of the da Vinci surgical system are docked. Instruments such as the endoscope (camera), force bipolar, monopolar scissors and prograsp forceps are inserted. The strap muscles are retracted laterally to expose the gland. Lateral dissection is carried out until the common carotid artery is visualised. Parathyroid and recurrent laryngeal nerve are safeguarded. After ligating the superior pedicle and inferior thyroid vessels, the gland is dissected off from the trachea. Key intraoperative steps, including identification of the external laryngeal nerve, gland dissection, and final specimen retrieval, are illustrated in Figures 3.3A–C.



**Figure 3.3A:** External laryngeal nerve identified and safeguarded before ligating the superior thyroid. The sternothyroid muscle was cut and retracted.



**Figure 3.3B:** Final dissection where the nodule is being dissected from the tracheal surface.



**Figure 3.4:** Two weeks after surgery, the patient was reviewed in follow-up and expressed satisfaction with the cosmetic result of her robotic thyroidectomy.

### Conclusion

Our case series demonstrates that robotic surgery is a safe and feasible approach in selected patients undergoing procedures in anatomically challenging regions. While the learning curve and cost remain important considerations, our experience highlights that with appropriate patient selection and surgical expertise, robotic-assisted techniques can be successfully integrated into head, neck, and upper gastrointestinal oncology practice. Larger prospective studies and longer follow-up will be essential to further validate the oncological safety, functional outcomes, and long-term benefits of this evolving surgical modality.

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# Simultaneous Pancreas and Kidney Transplant: From Insulin and Dialysis to Living Again – One Surgery, Two Miracles, Restoring Balance of Pancreas and Kidney Together

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## Abstract:

Type 1 diabetes mellitus (T1DM) is a major contributor to chronic kidney disease (CKD) and end-stage renal disease (ESRD). Despite significant advances in therapeutic strategies, managing T1DM remains challenging for clinicians worldwide — particularly when complicated by CKD or ESRD. The onset and progression of CKD in T1DM patients lead to considerable increases in morbidity, mortality, healthcare costs, and a diminished quality of life. Simultaneous pancreas–kidney transplantation (SPKT) offers a promising and potentially curative option for individuals with advanced CKD/ESRD secondary to T1DM, addressing both the underlying disease and its associated complications. The pancreas restores insulin production, and the kidney replaces dialysis, improving survival and quality of life. Nonetheless, limited organ availability, lifelong immunosuppressive therapy, the risks of peri- and postoperative complications, scarcity of expertise and resources in many centres, and substantial surgical and postoperative costs remain formidable challenges. The reported 5-year and 10-year patient survival range from 87%–93% and 70%–79% respectively. There are very few cases of SPKT reported from India. We report a case of a 25-year-old young adult with T1DM and ESRD who underwent a successful SPKT and is currently living an insulin and dialysis-free life.

**Key words:** Diabetes Mellitus, Pancreas Transplant, Kidney Transplant, Chronic Kidney Disease.

## Introduction

Simultaneous pancreas–kidney transplant (SPKT) is a surgical procedure offered primarily to patients with type 1 diabetes mellitus (T1DM) who have developed end-stage renal disease (ESRD) as a result of diabetic nephropathy.<sup>1,2</sup> In SPKT, both the pancreas and kidney are

transplanted at the same time, from the same deceased donor. This approach aims to restore insulin production and renal function, offering the potential for patients to be insulin-independent and free from dialysis.<sup>1,3,4</sup>

In India, cadaver donations have increased significantly from 340 in 2013 to 1,128 in 2024. The annual number of pancreas transplants alone (PTA) was around 44, and SPKT was 37 cases in 2024, with very few centres having dedicated pancreas transplant programs.<sup>5</sup> Our institute is one of those that developed a pancreas transplantation program.

There is only one study reported from India on outcomes of SPKT.<sup>6</sup> We would like to contribute to the Indian literature of SPKT by reporting a case of a 25-year-old male suffering from T1DM and ESRD who successfully underwent SPKT.

### Case Report

We report a case of a 25-year-old male patient with T1DM and chronic kidney disease (CKD) referred to us for consideration of a SPKT. He was diagnosed with T1DM at the age of 5 years and has been on insulin therapy since then. He was diagnosed with ESRD at the age of 19 years and was on haemodialysis three times a week. He was advised a SPKT and was listed under the Zonal Transplant Coordination Committee (ZTCC) and put on waiting list for the same in 2024. After a waiting period of one year, a cadaveric pancreas and kidney was allocated to him.

The deceased donor was a 41-year-old male with a body mass index (BMI) of 24 kg/m<sup>2</sup>. He was on minimal inotropic support. His haemoglobin A1c (HbA1c), fasting blood sugar, serum amylase, serum lipase, and serum creatinine were within normal range. He was a standard criteria donor. Once the quality of the pancreas and kidney was deemed healthy by the organ retrieval team, both organs were retrieved from the deceased donor. Both the kidney and pancreas were perfused with University of Wisconsin (UW) solution. Bench preparation of the pancreas with duodenum and kidney was done. A 'Y' graft was anastomosed to the splenic and superior mesenteric artery, following which the organs were transplanted with the duodenum anastomosed to the ileum. Postoperatively, hourly monitoring of blood glucose and urine output was done. The procedure and the postoperative course were uneventful. Our patient was off insulin and dialysis from postoperative Day (POD) 1. He was started on a normal diet since POD 3 and was discharged on POD 15. Presently, he is four months post-SPKT and is under regular follow-up every three months leading an insulin-free and dialysis-free life.

### Discussion

Patients considered for SPKT usually have to meet the following criteria:<sup>1,2,5</sup>

- Confirmed T1DM on insulin therapy with low or absent C-peptide.
- CKD stage 4/5 (creatinine clearance < 15mL/min) or already on dialysis.
- Good compliance with prior therapies and ability to tolerate surgery and immunosuppression.
- There is increasing evidence about the role of SPKT in patients with type 2 diabetes mellitus (T2DM) based on retrospective studies and transplant registry-based studies.
- Proposed indications of SPKT in T2DM include: age < 55 years, BMI < 30 kg/m<sup>2</sup>, insulin dependence, total insulin requirements < 1 U/kg of ideal bodyweight/day (IBW/d), presence of renal failure (dialysis-dependent or pre-dialysis advanced diabetic nephropathy with glomerular filtration rate [GFR] ≤ 20 mL/min/1.73 m<sup>2</sup>), fasting C-peptide < 10 ng/mL, low cardiac and vascular disease risk, and history of medical and dietary compliance.
- Patients with chronic pancreatitis, cystic fibrosis, benign pancreatic tumours, or patients with other exocrine disorders of the pancreas can also be candidates for a pancreas transplant in combination with a kidney, liver or lung or for a pancreas transplant alone.

### Contraindications

#### Absolute:

- Significant, non-correctable cardiovascular disease
- Active infection, malignancy, or sepsis
- Severe comorbidities making surgery or immunosuppression unsafe<sup>1,6</sup>

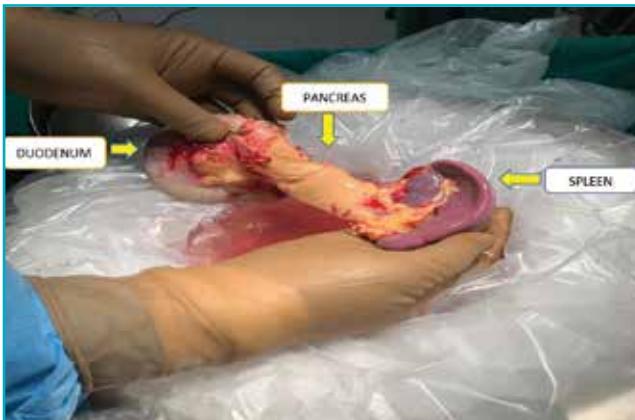
#### Relative:

- Age > 60 years, BMI > 30kg/m<sup>2</sup>
- History of stroke or severe vascular disease
- Persistent substance abuse

## Surgical procedure

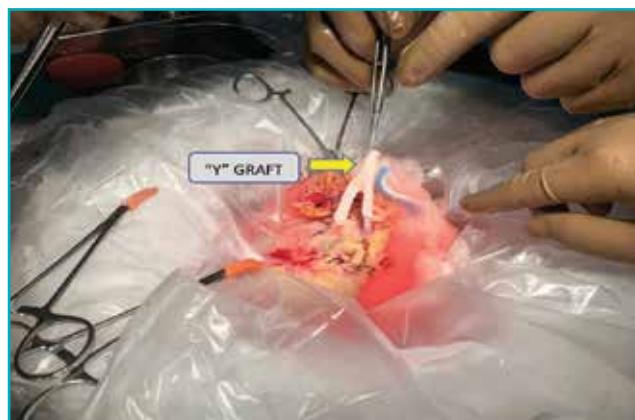
SPKT typically takes about 4–8 hours and usually involves two surgical teams:<sup>7,8</sup>

- **Organ retrieval:** The pancreas (with duodenum and often spleen) and kidney are harvested en bloc from a brain-dead donor (Figure 1).



▼  
**Figure 1:** The pancreas (with duodenum and often spleen) is harvested en bloc from a brain-dead donor.

- **Pancreas transplantation:** The pancreas is placed intra-abdominally, generally in the right iliac fossa. Its arteries are reconstructed using a 'Y' graft from the donor's iliac vessels and anastomosed to the recipient's iliac artery (Figure 2). The donor portal vein is connected to the recipient's iliac vein or inferior vena cava. The donor duodenum is attached to either the recipient's small bowel (enteric drainage) or bladder (bladder drainage).



▼  
**Figure 2:** Superior mesenteric artery and splenic arteries are reconstructed using a 'Y' graft from the donor's iliac vessels and anastomosed to the recipient's iliac artery.

- **Kidney transplantation:** The kidney is placed in the left iliac fossa, with its vessels and ureter attached to the recipient's vessels and bladder.
- The recipient's native pancreas and kidney are usually left in place.<sup>9,10</sup>
- Patients are put under general anaesthesia and monitored closely during and after surgery.

## Outcomes and benefits

- **Survival and graft function:** Five-year patient survival after SPKT is approximately 85%–88%; kidney graft survival 77%; pancreas graft survival 69%<sup>11-13</sup>
- **Complications:** Graft thrombosis, rejection, infection, delayed graft function, and surgical complications such as haemorrhage or leakage at anastomosis sites<sup>12,14</sup>
- **Benefits:**
  - Normalisation of blood glucose, eliminating the need for insulin injections
  - Prevention or stabilisation of diabetes-related complications (neuropathy, retinopathy, cardiovascular disease)
  - Improved quality of life and survival compared to dialysis or kidney transplant alone<sup>4,16</sup>

## Patient selection and pre-emptive transplant

- Careful patient selection is essential, as SPKT is a complex surgery requiring lifelong immunosuppression and compliance.
- Pre-emptive SPKT (before dialysis initiation) is associated with better outcomes, while prolonged time on dialysis prior to transplant may negatively impact results.<sup>1,17</sup>

## Conclusion

SPKT is considered the gold standard for patients with T1DM and ESRD. It offers significant improvements in glycaemic control and renal function, thereby reducing the risk and progression of diabetes-related complications. Due to its complexity and potential risks, careful evaluation by a multidisciplinary transplant team is essential to determine candidacy and ensure optimal outcomes.<sup>1,3,11</sup>

Gaurav Chaubal, Aditya Nanavati, Rashmi Algeri, Jatin Kothari, Hunaid Hatimi, Amith Kumar Pakkala, Amith Sreekant, Harshit Chaksota, Premal Narkhede, Blossom Dsouza, Radhika Ruhatiya, Abdul Ansari, Wasim Khot, Samir Shah. Simultaneous Pancreas and Kidney Transplant: From Insulin and Dialysis to Living Again – One Surgery, Two Miracles, Restoring Balance of Pancreas and Kidney Together. MMJ. 2025, December. Vol 2 (4).

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# The Backstabber: Pain That Hid a Deeper Threat

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## Abstract:

Back pain is a frequent complaint among young individuals and is often attributed to benign musculoskeletal causes. However, infectious aetiologies such as paravertebral abscess, though rare in this age group, must be considered, as delayed diagnosis can result in severe complications, including neurological deficits or sepsis. We report the case of a 13-year-old previously healthy female presenting with a two-day history of progressive lower back pain, intermittent fever, and mild restriction of movement. Initial evaluation suggested mechanical back strain, but the persistence of pain and elevated inflammatory markers, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), warranted further investigation. Magnetic resonance imaging (MRI) of the spine revealed multiple abscesses from C7–T4 and a small collection from T10–L1 levels, with surrounding soft-tissue inflammation. Blood cultures and abscess aspirate confirmed *Staphylococcus aureus* infection. The patient was treated with intravenous antibiotics followed by a course of oral therapy. Significant clinical improvement was observed, which prevented surgical drainage of the abscess, and follow-up imaging showed significant resolution. This case emphasises the diagnostic challenge of differentiating spinal infections from mechanical back pain in young patients. The absence of classic risk factors or systemic toxicity often contributes to a diagnostic delay. MRI remains the gold standard for early detection of spinal infections. Paravertebral abscess, though uncommon in young individuals, should be included in the differential diagnosis of persistent or atypical back pain. Early recognition and appropriate management are crucial to prevent morbidity and ensure favourable outcomes. A high index of suspicion, timely imaging, and multidisciplinary management are essential for optimal care.

**Key words:** Back Pain, Paravertebral Abscess, Spinal Infection, MRI, MRSA, Spinal Abscess.

## Introduction

Paravertebral abscesses — collections of pus in the soft tissues adjacent to the vertebrae — are rare but potentially life-threatening conditions in the paediatric population.<sup>1</sup> These abscesses can result from haematogenous spread, contiguous infections, or post-surgical complications. When symptoms of back pain persist or worsen, particularly in the absence of clear trauma, serious underlying pathologies should be considered. In young children, the presentation

of paravertebral abscesses is often non-specific and can be easily overlooked. Symptoms such as back pain, fever, irritability, and decreased mobility may be mistaken for more common musculoskeletal complaints or viral infections.<sup>2</sup> As a result, the diagnosis is frequently delayed, which can lead to severe complications, including vertebral osteomyelitis, spinal deformities, or even sepsis. Despite its rarity, the condition should be considered in any child with

unexplained or progressive back pain, particularly when accompanied by systemic signs such as fever or lethargy. Imaging, especially magnetic resonance imaging (MRI), plays a crucial role in confirming the diagnosis.<sup>3</sup> Early recognition and prompt treatment, including surgical drainage and antibiotic therapy, are essential for improving outcomes and preventing long-term sequelae.

### Case Report

A 13-year-old female presented to Max Super Speciality Hospital, Nagpur, with complaints of shortness of breath, fever, back pain, and lower limb pain for two days. She was referred from an outside hospital where she had been admitted one day earlier for the same complaints. She was initiated on non-invasive ventilation (NIV) support and referred.

Her significant outside reports were N-terminal pro-B-type natriuretic peptide (NT-proBNP): 6806 ng/L, D-dimer: 3.3 mg/L. Clinical evaluation showed her to be febrile with bilateral crepitations in the infra-axillary and subscapular areas, requiring  $\text{FiO}_2$  of 50% on NIV support. The initial laboratory investigations revealed C-reactive protein (CRP), 323 mg/L and procalcitonin of 22 ng/mL, with a normal total leukocyte count.

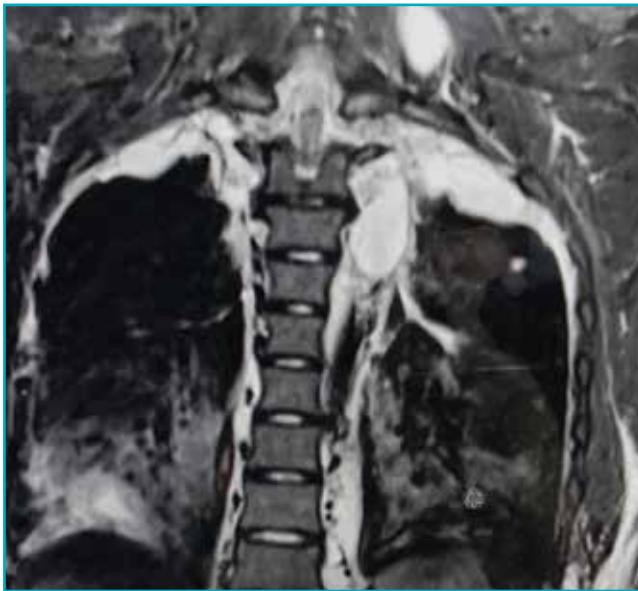
On imaging, computed tomography pulmonary angiography (CTPA) showed a few subpleural ground-glass nodular opacities in both lobes, indicating a septic emboli-like picture, with no evidence of pulmonary oedema or embolism. Echocardiography showed a normal ejection fraction with no evidence of right atrial or right ventricular dilatation. The flu panel was negative. Thus, workup for pulmonary embolism and viral pneumonia as a cause of acute respiratory distress with hypoxia was insignificant.

The patient was therefore started on potent antibiotics — meropenem and teicoplanin — in view of raised procalcitonin and CRP. The patient gradually responded to the line of treatment, with improvement in  $\text{O}_2$  saturation and CRP levels. She was gradually weaned off NIV support and shifted to nasal prongs. Blood culture revealed growth of methicillin-resistant *Staphylococcus aureus* (MRSA). The source of MRSA sepsis was still undiagnosed.

The patient complained of persistent back pain with mild bilateral lower limb weakness and myalgia (power 4/5). Therefore, creatine phosphokinase (CPK) levels were sent in view of possible viral myositis, which came out to be 515 U/L, indicating that it was not significant. Detailed history and evaluation of the back pain revealed that all the other presenting complaints had initially started with back pain. MRI of the whole spine with contrast (Figure 1) revealed multiple abscesses in the prevertebral region from C7-T4 and a small collection from the T10-L1 level (Figure 2). Multiple multiloculated, peripherally enhancing collections are scattered throughout the intermuscular planes and intramuscular tissues of the back, including the splenius cervicis and erector spinae muscles on either side, with pleural-based collections in the region of the bilateral upper lung fields along the mediastinal and pleural surfaces. Further image-guided aspiration of the abscess showed no evidence of tuberculosis (TB) but did demonstrate growth of *Staphylococcus aureus*.



**Figure 1:** T2-weighted magnetic resonance imaging (MRI) images showing paravertebral abscess.



**Figure 2:** T2-weighted magnetic resonance imaging (MRI) coronal images showing multiloculated enhancing abscesses along the intermuscular and intramuscular planes, along the mediastinal and pleural surfaces.

With the establishment of the source of infection, intravenous meropenem and teicoplanin were continued for treatment of multilevel paravertebral abscesses, as the culture reports were sensitive to the same. Intravenous methylprednisolone was started initially for respiratory failure. Glycosylated haemoglobin (HbA1c) and viral markers for hepatitis B, hepatitis C, and human immunodeficiency virus (HIV) were sent to rule out an immunocompromised status. The reports were negative. The patient was discharged on oral linezolid for 14 days. On follow-up, the patient was afebrile, asymptomatic, and a follow-up MRI of the spine (Figure 3) revealed complete resolution of the paravertebral abscesses.



**Figure 3:** Follow-up magnetic resonance imaging (MRI) showing significant resolution of the abscesses.

## Discussion

Paravertebral abscesses, although rare in paediatric populations, are serious infections that can lead to significant morbidity and mortality if not diagnosed and treated promptly.<sup>3</sup> *Staphylococcus aureus*, particularly MRSA, is the most common pathogen responsible for spinal infections, including paravertebral abscesses in children. Haematogenous spread from distant infection sites (such as the skin, bones, or joints), or contiguous spread from adjacent soft tissues, can lead to abscess formation in the paravertebral space.

In young children, risk factors for spinal infections may include recent trauma, surgeries, or systemic infections such as bacteraemia, particularly in the presence of an immunocompromised state.<sup>4</sup> However, in many cases like ours, there may be no clear antecedent event, making early diagnosis more difficult. Invasive procedures, such as lumbar puncture or intravenous catheter insertion, can also predispose children to bacteraemia and subsequent spinal infections. The clinical presentation of paravertebral abscesses in children is often insidious and can mimic other common paediatric conditions, such as musculoskeletal pain, or viral infections.<sup>5</sup> Fever and back pain, although common in paravertebral abscesses, are often non-specific. In our case, the child's symptoms of unexplained back pain and fever led to further investigation. Imaging, particularly MRI, is crucial for diagnosing paravertebral abscesses, as it provides detailed soft-tissue visualisation. Blood cultures are essential for identifying the causative organism, and *Staphylococcus aureus* — especially in cases complicated by sepsis — is frequently isolated.

The management of paravertebral abscesses involves a combination of surgical drainage and antibiotic therapy. In this case, the child was managed by targeted intravenous antibiotic therapy. The choice of antibiotics is often guided by culture results, with *Staphylococcus aureus* generally sensitive to beta-lactams or MRSA-directed therapy in resistant cases.<sup>6</sup> Empirical treatment should include broad-spectrum antibiotics, with later de-escalation based on microbiological findings. The clinical course following appropriate treatment, in our case, was favourable, and the child showed significant improvement without complications. Delay in treatment can result in the spread of infection to the vertebral bodies, leading to osteomyelitis, discitis, or even sepsis. Close follow-up is necessary to monitor for recurrence or complications.

## Conclusion

Our patient presented as a diagnostic challenge. The young age of the patient, along with the paucity of findings on physical examination, and the presenting features of acute-onset respiratory distress, made the diagnosis of paravertebral abscess as a source of sepsis obscure. The septic emboli-like picture on pulmonary angiography was initially confused clinically with pulmonary embolism and viral pneumonia. Persistent back pain in the young should not be overlooked or dismissed. While it may seem minor at first, untreated back pain can lead to significant long-term problems. Key risk factors for MRSA infections in the young include direct contact, skin breaks, poor hygiene, immunocompromised states, chronic conditions (e.g., eczema, asthma), and frequent or unnecessary use of antibiotics, which promote resistance.

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# Congenital Factor VII Deficiency in Pregnancy: A Multidisciplinary Management Approach

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## Abstract:

Congenital Factor VII (FVII) deficiency is a rare autosomal recessive bleeding disorder with an estimated incidence of approximately 1 in 500,000 individuals. Pregnancy in affected women presents significant challenges related to the risk of haemorrhage during labour, caesarean delivery, and the postpartum period. We report the case of a 28-year-old woman who is gravida 2, para 0, with no living children and one prior abortion (G2P0LOA1) with severe congenital FVII deficiency (<1% activity) who underwent a successful caesarean delivery through a multidisciplinary approach. Perioperative management involved recombinant activated Factor VII (rFVIIa), prothrombin complex concentrate (PCC), and fresh frozen plasma (FFP) to achieve haemostatic stability. An individualised plan, intensive monitoring, and coordination between obstetrics, haematology, anaesthesiology, and neonatology teams resulted in favourable maternal and neonatal outcomes. This case highlights the need for tailored haemostatic strategies and reinforces the importance of multidisciplinary management in such rare coagulation disorders during pregnancy.

**Key words:** Factor VII, Haemophilia, Pregnancy, Novoseven.

## Introduction

Congenital Factor VII (FVII) deficiency is among the rarest inherited coagulation disorders. It is characterised by variable bleeding severity that does not consistently correlate with plasma FVII activity levels.<sup>1</sup> Being an autosomal recessive condition caused by mutations in the F7 gene, clinical presentations range from mild mucosal bleeding to life-threatening haemorrhage during surgery or childbirth.<sup>2</sup>

Pregnancy in women with congenital FVII deficiency presents a high-risk condition that requires specialised multidisciplinary coordination. Although pregnancy induces physiological hypercoagulability, these changes may not fully compensate for severe deficiencies, leading to unpredictable haemostasis during labour or surgical interventions.<sup>3</sup> There are no standardised guidelines for managing such pregnancies, and

therapeutic strategies must be individualised depending on severity, clinical history, and available resources.<sup>4</sup>

This case report demonstrates successful multidisciplinary management of a pregnant woman with severe congenital FVII deficiency undergoing caesarean section, with emphasis on individualised haemostatic optimisation using recombinant activated Factor VII (rFVIIa), prothrombin complex concentrate (PCC), and fresh frozen plasma (FFP).<sup>1</sup>

## Case Report

A 28-year-old woman, who is gravida 2, para 0, with no living children and one prior abortion (G2P0LOA1), was admitted at 37 weeks' gestation for elective caesarean delivery at Nanavati Max Super Speciality Hospital,

Mumbai. She was a known case of severe congenital FVII deficiency, identified five years earlier during an open cholecystectomy at KEM Hospital, where she experienced excessive perioperative bleeding, necessitating two doses of rFVIIa and nine units of blood transfusion. She also had a history of abdominal tuberculosis, treated successfully, and a large incisional hernia post-cholecystectomy.

Her obstetric history included a prior spontaneous miscarriage treated by dilation and curettage, during which she did not experience abnormal bleeding. During the current pregnancy, she was closely co-managed by the obstetrics and haematology teams. Serial coagulation profiles showed persistently low FVII activity (<1%). She and her family were counselled about the significant risk of peripartum haemorrhage and the necessity for haemostatic support at delivery.

At 33 weeks, she developed preterm contractions, which were managed conservatively with tocolysis and corticosteroids. At 37 weeks, a multidisciplinary conference finalised the delivery plan: an elective lower segment caesarean section (LSCS) under general anaesthesia, with preoperative haemostatic correction using PCC, FFP, and rFVIIa.

Preoperative laboratory investigations showed haemoglobin level of 9.1 g/dL, platelet count of 220,000/ $\mu$ L, prolonged prothrombin time, and FVII activity <1%. One day before surgery, 500 IU PCC and six units of FFP raised FVII activity to approximately 35%. Just prior to skin incision, 2 mg intravenous rFVIIa (Novoseven) and 12 units of FFP were administered.

The caesarean section was performed via a transverse incision; intraoperative findings included mild peritoneal adhesions. A live female neonate weighing 2.77 kg was delivered with good Apgar scores and admitted to the neonatal intensive care unit (NICU) for observation.

Moderate intraoperative bleeding (~900 mL) consistent with postpartum haemorrhage was controlled successfully with vaginal misoprostol and intrauterine carboprost. Postoperatively, FVII activity increased to 182%.

On postoperative Day 1, FVII activity dropped to 1% and haemoglobin to 6.1 g/dL, necessitating transfusion of four units of FFP and two units of packed red cells. Analgesia was maintained with intravenous paracetamol; intramuscular injections were avoided to reduce haematoma risk. Antibiotic prophylaxis was continued, with no secondary haemorrhagic or thrombotic complications. The patient's postoperative course was otherwise uneventful, and both mother and baby were discharged in a stable condition on postoperative Day 4.

## Discussion

Congenital FVII deficiency poses significant challenges in obstetrics due to its unpredictable bleeding tendency and lack of standardised treatment protocols.<sup>1</sup> FVII plays a critical role in initiating the extrinsic coagulation pathway by activating Factor X; thus, even partial deficiency markedly impairs haemostasis.<sup>2</sup>

Though pregnancy induces mild physiological increase in procoagulant factors, these are insufficient to normalise FVII levels in severe deficiency.<sup>3</sup> Consequently, individualised replacement therapy is essential, aiming for FVII activity above 15%–20% for vaginal delivery and 30%–50% for caesarean section.<sup>5</sup>

As the cornerstone of therapy, rFVIIa offers rapid action and a favourable safety profile during pregnancy, although its short half-life and potential thrombotic risk demand close monitoring and repeated dosing.<sup>6</sup> In resource-limited scenarios, plasma-derived concentrates like PCC and FFP may be combined effectively, as illustrated in this case.<sup>1</sup>

Multidisciplinary coordination was pivotal for dosing and timing to maintain perioperative haemostasis, with vigilant postoperative surveillance due to rapid FVII level decline and risk of delayed bleeding.<sup>1</sup> Importantly, no thrombotic events occurred, likely due to careful dosing, concurrent FFP use, and avoidance of thrombogenic triggers.<sup>7</sup>

## Conclusion

Successful pregnancy outcomes in severe congenital FVII deficiency require early multidisciplinary planning, tailored haemostatic replacement strategies, and intensive monitoring. This case exemplifies that with judicious use of rFVIIa, PCC, and FFP, maternal and neonatal morbidity can be minimised even in severe deficiency.

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# Early-Onset Gitelman Syndrome Presenting with Recurrent Hypokalaemia and Tetany in an Eight-Year-Old Girl: A Case Report

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**Abstract:**

Gitelman syndrome (GS) is a rare autosomal recessive renal tubular disorder characterised by hypokalaemia, hypomagnesaemia, metabolic alkalosis, and hypocalciuria. It typically manifests during adolescence or adulthood, while paediatric presentations are uncommon and often misdiagnosed. We report the case of an eight-year-old girl presenting with recurrent episodes of severe hypokalaemia and muscle cramps triggered by acute gastroenteritis. Genetic testing identified two heterozygous pathogenic variants in the solute carrier family 12 member 3 (SLC12A3) gene, confirming GS.

**Key words:** Gitelman Syndrome, Metabolic Alkalosis, Hypokalaemia, Hypomagnesaemia, SLC12A3.

## Introduction

Gitelman syndrome (GS) is an autosomal recessive disorder affecting the thiazide-sensitive sodium-chloride cotransporter (NCC) in the distal convoluted tubule of the kidney, with an estimated incidence of one in 40,000 individuals.<sup>1</sup> The lack of function of the NCC increases the amount of sodium in the collecting duct, increasing urinary excretion of potassium and hydrogen, and promoting reabsorption of urinary calcium and excretion of magnesium. This is responsible for the metabolic abnormalities. GS typically presents during adolescence or early adulthood with symptoms ranging from muscle cramps and fatigue to tetany and cardiac arrhythmias. Paediatric presentations, particularly in early childhood, are rare and often challenging to diagnose due to overlapping symptoms with more common conditions such as gastroenteritis or neurological disorders.

We describe an unusual case of GS in an eight-year-old girl presenting with recurrent hypokalaemia and muscle stiffness after illness, emphasising the clinical and diagnostic approach and management considerations.

## Case Report

An eight-year-old girl presented to the emergency department with a two-day history of loose stools and vomiting, accompanied by severe abdominal pain and painful stiffness of both hands suggestive of tetany. The child was conscious but restless and hyperventilating. Examination revealed mild dehydration, carpopedal spasm, and periorbital twitching. There was no history of fever, seizures, or trauma.

The family reported a previous hospitalisation one year earlier following a diarrhoeal illness with similar symptoms, during which she was diagnosed with hypokalaemia. Due to her restlessness during that episode with abnormal stiffening of hands, a neurological exam and magnetic resonance imaging (MRI) were done, both of which were normal. There was no significant family history of renal or genetic disorders. The child had a history of easy fatigability, which the parents attributed to dietary issues.

Laboratory investigations on admission revealed a venous blood pH of 7.383 with markedly elevated lactate (11.9 mmol/L), hypokalaemia (3.14 mEq/L),

and hypomagnesaemia (1.4 mg/dL). Serum calcium was normal. Neurological evaluation, including electroencephalography (EEG), was normal. Dehydration was corrected with intravenous fluids, but persistent hypokalaemia (3 mEq/L) and metabolic alkalosis (pH of 7.483) were noted. Urinalysis demonstrated increased potassium excretion and decreased urinary calcium excretion. The child did not have hypertension, and the ultrasonography of the kidneys, ureters, and bladder (USG-KUB) was normal.

The patient's symptoms improved, and she was discharged with a recommendation for paediatric nephrology follow-up. Within two weeks, she presented again with similar complaints precipitated by vomiting. Repeat laboratory investigations confirmed metabolic alkalosis (pH of 7.53), hypokalaemia (2.8 mEq/L), hypomagnesaemia (1.4 mg/dL), and reduced urinary calcium excretion. Given the biochemical profile and clinical presentation, a diagnosis of GS was considered. As the child continued to experience tetany during the hospital stay, intravenous magnesium was administered for 24 hours until serum magnesium levels rose to 2.1 mg/dL and the symptoms resolved.

A paediatric nephrology consultation was obtained, and genetic testing for mutations in the solute carrier family 12 member 3 (SLC12A3) gene was performed. The patient was started on oral magnesium oxide supplementation, which was well tolerated. Magnesium oxide was continued on discharge. Genetic analysis identified two heterozygous pathogenic variants in SLC12A3, confirming autosomal recessive GS.

During subsequent follow-up visits, the child remained asymptomatic on maintenance therapy, with stable electrolytes and no further episodes of spasms or weakness.

## Discussion

GS is a rare, heterogeneous disease typically characterised by the presence of hypokalaemia, metabolic alkalosis, hyperreninemic hyperaldosteronism, hypomagnesaemia, and hypocalciuria, although variable clinical presentation and severity can occur.<sup>2</sup> Most patients are diagnosed during adolescence or adulthood, but neonatal presentation and diagnosis may also occur.<sup>3</sup> This phenotypic variability is associated not only with the SLC12A3 mutation identified but also with the presence of other modifier genes, the

co-existence of compensatory mechanisms, sex, diet and environmental factors.<sup>4</sup>

A range of symptoms may occur due to the underlying biochemical abnormalities seen in these patients. The most frequent complaints include cramps, muscle weakness, fatigue, and tetany.<sup>5,6</sup> Although thirst and salt cravings are frequent symptoms due to renal salt wasting and subsequent hypovolaemia,<sup>5,6</sup> these complaints were not reported by our patient. The child was also normotensive. Polyuria and nocturia are also frequently reported due to urinary salt and water wasting. Abnormal glucose metabolism is also common in GS.<sup>7</sup>

Though 24-hour urine samples may be more accurate, spot urine samples are usually adequate to evaluate the renal excretion of potassium, magnesium, calcium, sodium and chloride.<sup>8</sup> The classic biochemical hallmarks — hypokalaemia, hypomagnesaemia, metabolic alkalosis, and hypocalciuria — help distinguish GS from other tubulopathies like Bartter syndrome, which typically presents earlier and with hypercalciuria and more severe salt wasting.

Our patient's presentation with recurrent hypokalaemia episodes precipitated by gastroenteritis is typical of paediatric GS, which is often diagnosed during or after dehydration episodes, revealing the underlying defect. It was noted that the patient's symptoms did not correspond to the serum potassium levels, which were initially near normal, indicating a lack of correlation between the two. Initial symptoms such as muscle cramps and carpopedal spasm reflect neuromuscular irritability from electrolyte disturbances. Persistent hypokalaemia despite dehydration correction, coupled with decreased urinary calcium excretion, is highly suggestive of GS, warranting evaluation.

Management focuses on correcting hypokalaemia and hypomagnesaemia to reduce symptoms and prevent complications such as arrhythmias. Oral magnesium supplementation and potassium-sparing agents are mainstays, but clinical response and tolerance vary. Regular monitoring for growth and renal function is essential.

Advances in genetic testing allow early and definitive diagnosis, enhancing patient counselling and tailored therapy. This case reinforces the need for awareness among clinicians about paediatric presentations of GS to avoid misdiagnosis and unnecessary testing, such as neurological imaging or interventions.

Future directions include exploring gene therapy and novel pharmacological agents that improve tubular function, though evidence remains limited. Multidisciplinary care

involving nephrologists, paediatricians, and geneticists is optimal.

## Conclusion

This case report documents an early childhood presentation of genetically confirmed GS manifesting as recurrent electrolyte abnormalities and neuromuscular symptoms. It highlights the importance of considering inherited tubulopathies in children with refractory hypokalaemia, especially following dehydration. Early recognition and genetic confirmation allow precise diagnosis and effective management, improving clinical outcomes and quality of life. Increased clinical suspicion is vital to preventing complications and unnecessary investigations.

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# Ochronotic Arthropathy Effectively Treated with Staged Bilateral Total Hip and Knee Arthroplasty: A Case Report

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## Abstract:

Homogentisic acid deposition within connective tissues causes ochronotic arthropathy, a rare musculoskeletal consequence of alkaptonuria that causes progressive degenerative changes in the joints. Significant impairment and unique intraoperative challenges during surgical management may result from advanced involvement of weight-bearing joints. We present the case of a 53-year-old adult who arrived with radiating hip and knee pain, stiffness, and limited mobility. The patient's history of dark urine prompted a biochemical analysis that showed high levels of homogentisic acid. It's interesting to note that there were no traditional outward signs of ochronosis, such as bluish-black scleral discolouration (Osler's sign) or auricular cartilage pigmentation. Both the hip and knee joints showed significant degenerative changes on radiographs. A phased surgical approach was chosen due to the advanced arthropathy, starting with bilateral total hip replacement and progressing to bilateral total knee replacement. Pathognomonic symptoms of ochronotic arthropathy, i.e. diffuse blackish-brown pigmentation of the articular cartilage and subchondral bone, were observed during surgery. Following surgery, the patient experienced a smooth recovery and reported long-lasting pain relief along with a return to his normal level of mobility and independence. The Harris Hip Score (HHS) increased from 31 to 93, and the Knee Society Score (KSS) increased from 40 to 93 at the 12-month follow-up, indicating a notable improvement in functional assessment. The current case of ochronotic arthropathy demonstrated pain relief and functional restoration after the staged bilateral total hip and knee arthroplasty. Despite the intraoperative challenges posed by pigmented and friable tissues, the use of common modern implants produced stable fixation and facilitated a smooth recovery for the patient.

**Key words:** Ochronotic Arthropathy, Alkaptonuria, Total Knee Arthroplasty, Osteoarthritis.

## Introduction

Homogentisate 1,2-dioxygenase deficiency leads to alkaptonuria, a rare autosomal recessive condition that causes ochronosis and an accumulation of homogentisic acid.<sup>1</sup> Connective tissues gradually deteriorate due to ochronosis, or pigment deposition in alkaptonuria. Additionally, it increases the risk of two early degenerative joint diseases: osteoarthritis and arthritis.<sup>2</sup> Globally, the prevalence is thought to be between 1 in 250,000 and 1 in 1,000,000, with

higher clusters reported in Slovakia and the Dominican Republic.<sup>3</sup> Only isolated cases and a few small case series have been reported in the Indian population, indicating that the condition is not only rare but also probably underdiagnosed.<sup>4</sup>

Patients frequently experience early-onset osteoarthritis of the hips, knees, and spine, making musculoskeletal involvement the most incapacitating characteristic.

Conservative measures such as physiotherapy, analgesics, and lifestyle modification provide only temporary relief, while medical therapies like vitamin C or nitisinone have shown limited benefit in altering disease progression.<sup>5</sup> Once arthropathy advances, total joint arthroplasty is the definitive treatment.<sup>6</sup> Studies have confirmed that both total hip and total knee arthroplasty restore function and relieve pain, although intraoperative findings of pigmented, brittle tissues and altered bone quality pose unique surgical challenges.<sup>7,8</sup> Globally published literature describes single joint replacement, and reports of patients undergoing staged bilateral hip and knee arthroplasty are extremely limited.<sup>9</sup> Furthermore, cases without classical external signs are difficult to recognise, often delaying diagnosis.<sup>10</sup>

Given the limited literature on ochronotic arthropathy without classical external signs, this report helps fill an important gap by documenting favourable short-term outcomes following staged arthroplasty. It highlights the diagnostic challenges of atypical presentations and offers clinically relevant insights to guide surgical management in comparable cases.

### Case Report

A 53-year-old man arrived with a four-month history of bilateral hip and knee pain that had been getting worse over time, along with stiffness and irregularities in his gait. The pain significantly restricted patients' daily activities, and he required the use of a cane for ambulation. The patient also described dull, non-radiating lower back pain that had recurred intermittently for the past four years but had become disabling in recent months. The present case also summarises the history of urine discolouration, characterised by progressive dark brown pigmentation on standing, with no reported family history of comparable illness.

On examination, no external signs, like the scleral or auricular pigmentation, were observed. Internal and external rotation were painfully limited, and hip flexion was limited to 90°. The knees showed fixed flexion deformities of 5° on the right and 10° on the left, with further flexion possible to 120°. Lumbar spine mobility was preserved, and neurological examination was unremarkable.

Urinary homogentisic acid was elevated (2637.00 mg/24 hrs), confirming alkaptonuria with routine biochemical investigations within normal limits. Radiographs revealed significant degenerative changes in the knees and hips, as well as calcification of the pelvic tendon and intervertebral disc (Figure 1). Magnetic resonance imaging (MRI) revealed multiple-level cervical and lumbar disc herniations without canal compromise. A scanogram verified the abnormal alignment and narrowing of joint spaces in both lower limbs (Figure 2).

Differential diagnoses considered included primary osteoarthritis and spondyloarthropathy; these were excluded on the basis of biochemical confirmation of homogentisic aciduria and the characteristic intraoperative pigmentation subsequently observed. The final diagnosis was confirmed as ochronotic arthropathy secondary to alkaptonuria.



**Figure 1:** A. Pelvic radiograph (anteroposterior view) showing destruction of the femoral head bilaterally, B. Radiograph of the knee (anteroposterior standing and lateral view) showing severe osteoarthritis knee, C, D. Lumbar radiographs (anteroposterior and lateral views) and magnetic resonance imaging (MRI) screening of the whole spine showing multilevel narrowing of the thoracic and lumbar intervertebral spaces with osteophytosis, calcification, and subchondral osteosclerosis.



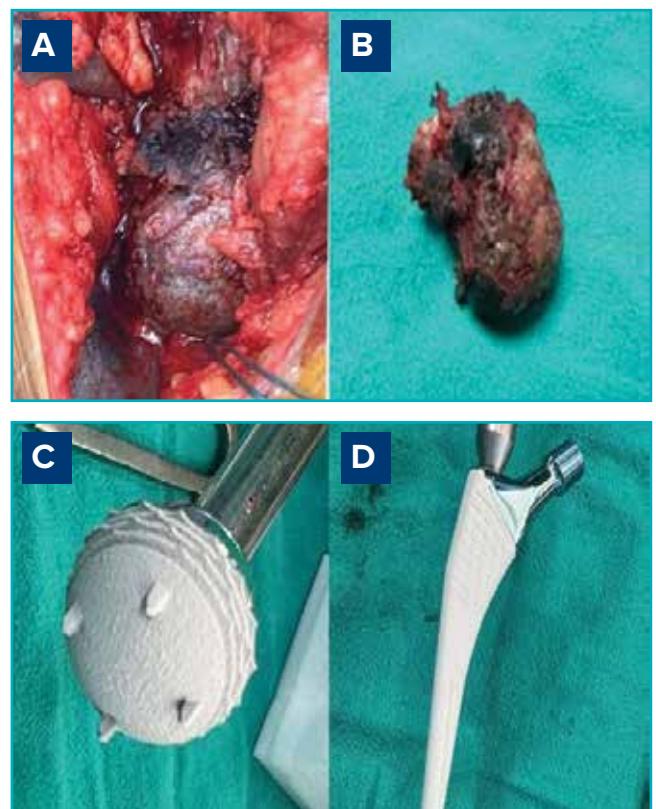
**Figure 2:** A. Scanogram of both lower limbs, B. Radiograph of the knee (anteroposterior standing and lateral view) showing a severe osteoarthritic knee, C. Six months follow-up of bilateral total hip replacement.

## Clinical Outcomes

### First surgery: Bilateral total hip arthroplasty (THA)

The patient was admitted with worsening hip pain and subsequently underwent staged bilateral THA using the posterolateral (Moore's) approach, performed 17 days apart. Intraoperatively, the femoral head, acetabulum, and articular cartilage exhibited pronounced ochronotic pigmentation varying from brown to black, whereas the subcutaneous tissue and tensor fascia lata appeared unremarkable. The femoral head was destroyed, with subchondral bone exposure in weight-bearing areas (Figure 3). Based on these findings, a macroscopic diagnosis of ochronosis was made. The pigmented cartilage, bone, and hypertrophied synovium were sent for histopathological evaluation. A hydroxyapatite-coated spiked titanium acetabular cup with a dual mobility liner and a porous-coated uncemented femoral stem was implanted for optimal osseointegration (Figure 3). The patient was mobilised on the first postoperative day with full weight-bearing and was

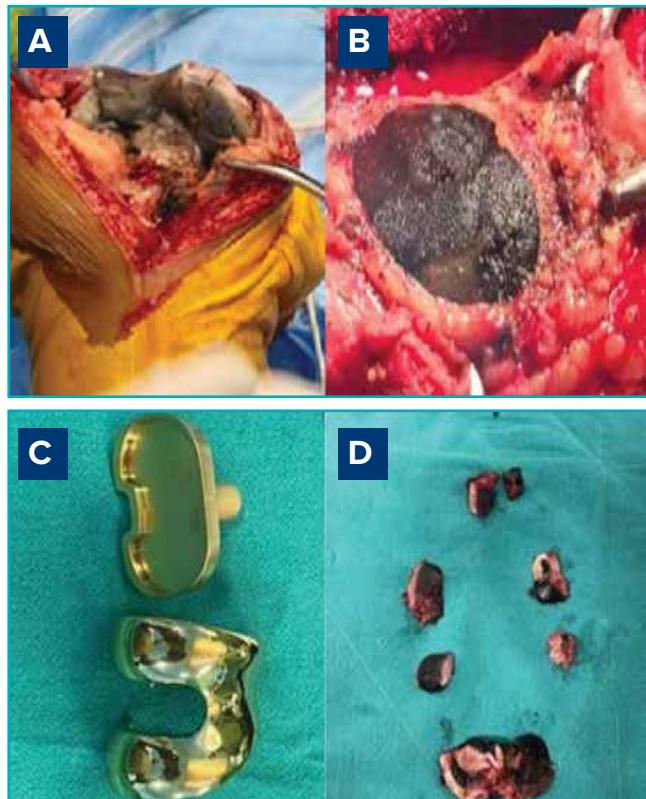
discharged on postoperative Day 3. According to the Harris Hip Score (HHS), there was a notable improvement in joint stability, mobility, and pain relief at the six-month follow-up.



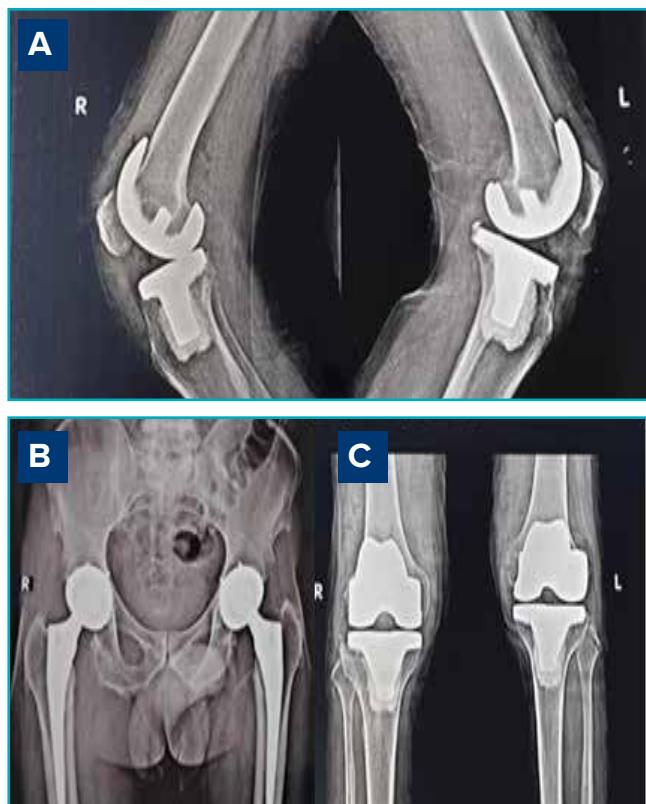
**Figure 3:** A, B. Intraoperative images showing severe destruction of the acetabular and femoral head cartilage with darkened subchondral bone, C, D. Porous-coated uncemented acetabular and femoral stem.

### Second surgery: Bilateral total knee arthroplasty (TKA)

Six months later, owing to persistent severe knee pain, the patient was readmitted and underwent bilateral TKA. The subvastus technique, spinal anaesthesia, an intraoperative ultrasound-guided adductor canal block, and no tourniquet were used during the procedure. Intraoperatively, the cartilage and synovium showed diffuse dark-brown pigmentation, similar to what was observed during THA. Closer evaluation revealed extensive destruction of the distal femoral cartilage and darkened subchondral bone in both femoral and tibial cuts, changes characteristic of ochronotic arthropathy (Figure 4). To maximise biocompatibility, longevity, and functional recovery following bony cuts, a bilateral cruciate-retaining gold knee prosthesis was implanted (Figure 5).



**Figure 4:** A, B, D. Intraoperative images showing severe destruction of the distal femoral cartilage with darkened subchondral bone in the femoral and tibial cut, C. Gold knee prosthesis.



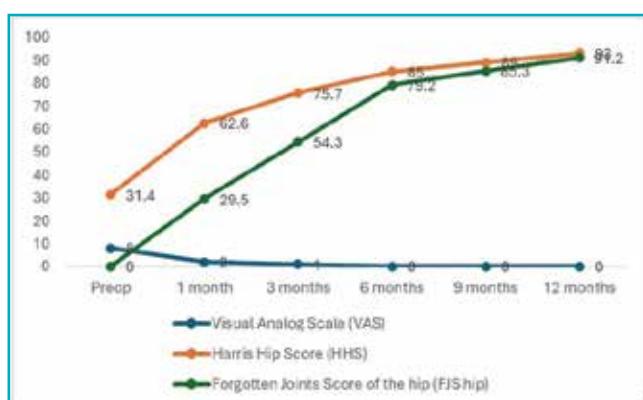
**Figure 5:** A, C. 6 months follow-up X-ray of total knee replacement lateral and anterolateral view, B. 12 months follow-up X-ray of total hip replacement anteroposterior view.

On the day of surgery, full weight-bearing mobilisation and postoperative quadriceps-strengthening exercises were initiated. By the third postoperative day, the patient was able to climb stairs and walk independently. Follow-up assessments over the next few months confirmed sustained functional recovery, which was characterised by improved mobility and a noticeable reduction in pain.

#### Postoperative functional outcomes after THA

Follow-up evaluations at 1, 3, 6, 9, and 12 months post-THA were conducted using the Visual Analogue Scale (VAS), Harris Hip Score (HHS), and Forgotten Joint Score-Hip (FJS-Hip). As per Nilsdotter *et al.* 2011, the VAS score improved from 8 preoperatively to 2 at 1 month, 1 at 3 months and remained at 0 thereafter.<sup>11</sup> The HHS increased from 31.4 preoperatively to 62.6, 75.7, 85.0, 89.0, and 93.0 at 1, 3, 6, 9, and 12 months postoperatively, respectively.

Additionally, the FJS-Hip improved from 0 preoperatively, to 29.5 at 1 month. The score continued to improve to 54.3, 79.2, 85.3, and 91.2 at 3, 6, 9, and 12 months, respectively (Figure 6).

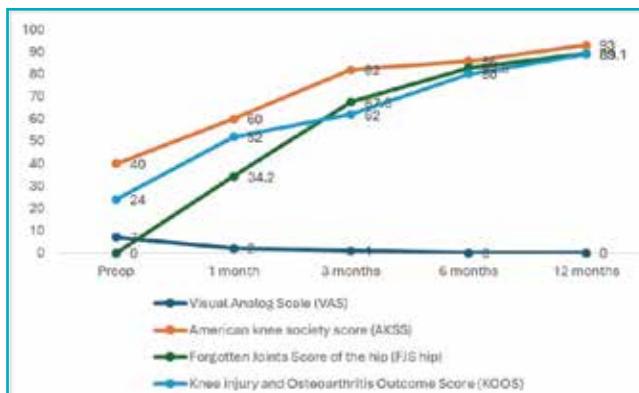


**Figure 6:** Trends in Visual Analogue Scale (VAS), Harris Hip Score (HHS), and Forgotten Joint Score-Hip (FJS-Hip) preoperatively and at 1, 3, 6, 9, and 12 months post-THA follow-up.

#### Postoperative functional outcomes after TKA

Postoperative recovery following bilateral TKA was evaluated at 1, 3, 6, and 12 months using the Visual Analogue Scale (VAS), the American Knee Society Score (AKSS), and the Forgotten Joint Score-Knee (FJS-Knee). The VAS score improved from 7 preoperatively to 2 at 1 month, 1 at 3 months, and 0 at both 6 and 12 months. After a baseline score of 40, the AKSS increased to 60 at 1 month, 82 at 3 months, 86 at 6 months, and

93 at 12 months. The FJS-Knee increased from 34.2 at 1 month to 67.5 at 3 months, 82.8 at 6 months, and 89.1 at 12 months. Given that the preoperative FJS-Knee score was 0, these postoperative values represent substantial improvement from baseline. These results show a steady and progressive functional recovery that leads to almost full joint function restoration and pain-free mobility within the first year following surgery (Figure 7).



**Figure 7:** Trends in Visual Analogue Scale (VAS), American Knee Society Score (AKSS), Forgotten Joint Score-Hip (FJS-Hip), and Knee Injury and Osteoarthritis Outcome Score (KOOS) preoperatively and at 1, 3, 6, and 12-months postoperative follow-up.

## Discussion

A rare musculoskeletal symptom of alkaptonuria, ochronotic arthropathy is typified by the progressive degeneration of large weight-bearing joints. Diagnosis is frequently delayed, particularly in the absence of classical external features such as scleral or auricular pigmentation, as observed in our patient.<sup>12</sup> At one year, the HHS improved from 31.4 preoperatively to 93, the

AKSS improved from 40 to 93, and both the hip and knee-FJS exceeded 90. These results demonstrate that mobility and quality of life were nearly fully restored within the first year following surgery.

When compared with larger series, our outcomes align closely. Pachore *et al.* 2019, reported 10 patients (12 hips) undergoing THA for ochronotic arthritis, with HHS improving from a preoperative mean of 36 to 88 at long-term follow-up (up to 24 years).<sup>13</sup> Compared to this, our patient achieved a slightly higher HHS at 12 months. The results of Rajkumar *et al.* (2020), who reported improvement in the KSS from 27.2 to 89.4 and the HHS from 17.8 to 78 across 27 arthroplasties, closely resemble the results we saw (HHS 93, KSS 93).<sup>14</sup>

According to a systematic review of TKA in ochronotic patients by Lee *et al.* (2019), pain alleviation and functional recovery were consistent across reported cases, irrespective of implant design.<sup>15</sup> By 6 months, our patients' knee pain VAS decreased from 7 to 0 and their KSS increased to 93. Durability was further supported by Spencer *et al.* (2004), who reported 11 joint replacements with outstanding function at 6–12 years.<sup>16</sup> The extent of improvement is in line with these long-term findings, despite the case's one-year follow-up.

A strength of this case is the detailed documentation of validated outcome measures over sequential follow-up visits, which allows direct benchmarking against existing literature. A limitation for this case study was the shorter follow-up with one patient, which restricts assessment of implant survival and generalisability.

## Conclusion

This case demonstrates that staged bilateral THA and TKA can be a viable treatment option for patients with ochronotic arthropathy even in the absence of classical external features, highlighting both the diagnostic challenges and the potential for favourable early surgical outcomes.

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# Sclerosing Encapsulating Peritonitis in an Extensively Drug-Resistant Tuberculosis Patient Presenting as Intestinal Obstruction – A Case Report

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## Abstract:

Sclerosing encapsulating peritonitis (SEP), also called abdominal cocoon syndrome, is a rare cause of intestinal obstruction. In 1907, Owtschinnikow first termed it as *peritonitis chronica fibrosa encapsulata*. It can be either idiopathic or secondary. Secondary cocoon syndrome may be due to medications, infections such as tuberculosis (TB) in endemic regions, cirrhosis, peritoneal dialysis and gynaecological malignancies.

A 37-year-old female diagnosed with abdominal TB, who had not complied with anti-tubercular therapy (ATT) for the last 5 years, presented with acute intestinal obstruction and a history of recurrent subacute intestinal obstruction. Computed tomography (CT) imaging of the abdomen showed dilated bowel loops with a transition point in the ileum, multiple large calcified mesenteric lymph nodes and ascites. Diagnostic laparoscopy revealed dense adhesions and a fibrocollagenous membrane encapsulating the intestine. It was converted to laparotomy, an abdominal cocoon was confirmed, and extensive adhesiolysis and ileocolic anastomosis were done. GeneXpert showed extensively drug-resistant tuberculosis (XDR-TB), and the patient was started on an XDR-TB regimen.

Abdominal cocoon syndrome secondary to TB, presenting as intestinal obstruction, is a rare but serious complication that requires surgical intervention. This case further highlights the importance of adherence to medication and the consideration of resistant forms of TB, such as XDR-TB, in patients with non-compliance with treatment. Surgical management, along with appropriate modification of ATT based on drug-resistance profiling, for patient recovery is essential.

**Key words:** Sclerosing Encapsulating Peritonitis, Abdominal Cocoon, Intestinal Obstruction, XDR-TB.

## Introduction

Sclerosing encapsulating peritonitis (SEP) is a rare disease that causes a thick fibrocollagenous membrane, partially or completely enveloping the small intestine. It was first termed in 1907 by Owtschinnikow as *peritonitis chronica fibrosa encapsulata*.<sup>1</sup> It may be either idiopathic or secondary. Secondary cocoon syndrome may be caused by medications, infections such as tuberculosis (TB) in endemic regions, cirrhosis, peritoneal dialysis

and gynaecological malignancies. The treatment of SEP includes identifying the cause and treating it.<sup>2</sup>

In TB-endemic areas, abdominal and peritoneal TB are still the leading causes of cocoon abdomen. Chronic peritoneal inflammation in TB can induce fibrotic reactions, leading to secondary abdominal cocoon syndrome.<sup>3</sup>

## Case Report

A 37-year-old female was admitted to the hospital with complaints of abdominal pain, distension, vomiting, and obstipation, with a history of multiple subacute intestinal obstruction episodes for one year. Diagnostic laparoscopy was done in 2019; following this, abdominal TB was diagnosed and anti-tubercular therapy (ATT) was started. She had been non-compliant with treatment for the last five years.

On examination, the patient was haemodynamically stable. The abdomen was distended with diffuse tenderness and sluggish bowel sounds. Laboratory investigations were unremarkable except for mild hypoalbuminaemia.

A contrast-enhanced computed tomography (CECT) scan of the abdomen showed proximal small bowel dilatation with a transition point in the ileum, collapse of distal loops, ascites, and multiple lobulated hyperdense foci in the mesentery — likely calcified lymph nodes — suspicious for chronic inflammatory pathologies, such as abdominal TB with possible cocoon formation (Figures 1A and 1B).



**Figure 1A:** Contrast-enhanced computed tomography of the abdomen showing dilated small bowel loops.



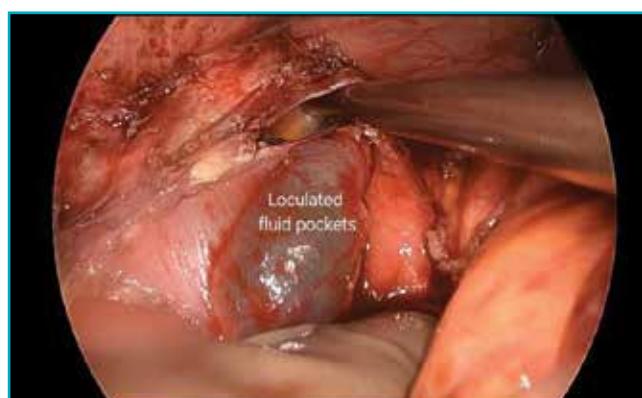
**Figure 1B:** Mesenteric lymphadenopathy with small bowel loops and ascites.

Given the clinical status and radiological findings, the patient was taken up for diagnostic laparoscopy, which revealed dense inter-bowel and omental adhesions forming a fibrous cocoon around the small bowel (Figure 2).

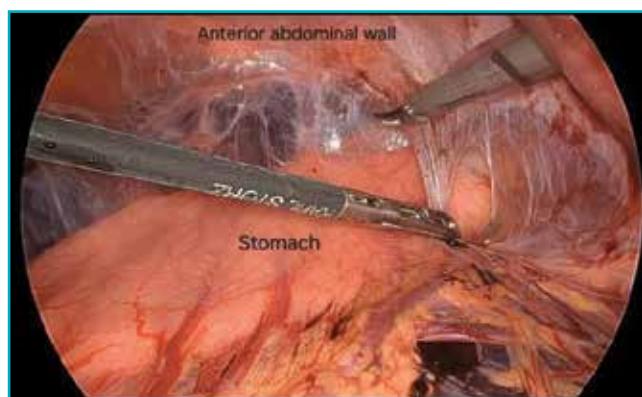


**Figure 2:** Diagnostic laparoscopy showing a fibrous cocoon around the intestine.

There were multiple loculated ascitic fluid collections (Figure 3), and the bowel loops were matted and adherent to the anterior abdominal wall, liver, and urinary bladder (Figure 4).

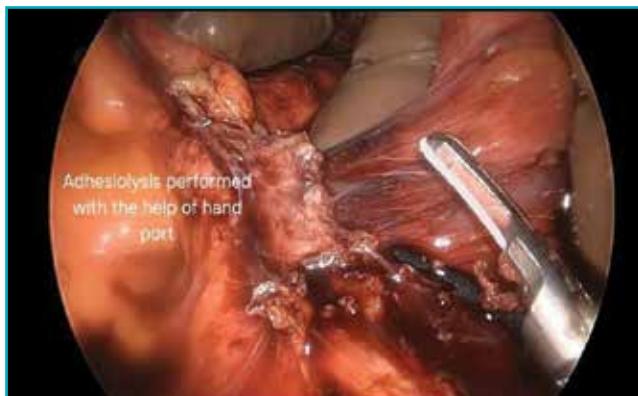


**Figure 3:** Multiple loculated ascitic fluid pockets.



**Figure 4:** Dense adhesion between bowel and anterior abdominal wall.

Multiple enteric fistulous openings with dense adhesions were noted at the distal ileum. Hand assisted laparoscopic surgery (HALS) was attempted to do extensive adhesiolysis through suprapubic incision (Figure 5).



**Figure 5:** Adhesiolysis performed through hand assisted laparoscopic surgery (HALS).

An exploratory laparotomy through a midline incision was performed because of dense adhesions and multiple enteric fistulae. Thorough peritoneal lavage was carried out. Primary closure of the ileal fistulae and ileocolic anastomosis was performed.

GeneXpert testing of tissue and ascitic fluid samples confirmed *Mycobacterium tuberculosis*, resistant to rifampicin, isoniazid, and fluoroquinolones (levofloxacin and moxifloxacin), indicating XDR-TB.

Postoperatively, the patient was initially managed with *nil per os* (NPO) and was started on total parenteral nutrition (TPN) and enteral feed. She was referred to a national TB centre for the initiation of XDR-TB-specific treatment. She was started on a linezolid, clofazimine, cycloserine and bedaquiline regimen. Her postoperative recovery was further complicated by low bilious output from the anastomotic drain, which prompted a follow-up CECT that excluded major anastomotic leaks or intra-abdominal collections. The pelvic drain was removed on postoperative Day 12, and the anastomotic drain was removed on postoperative Day 13. She is stable and tolerating the XDR-TB regimen at follow-up after 1 and 5 months.

## Discussion

Abdominal cocoon syndrome, also known as SEP, is a rare but important cause of intestinal obstruction due to chronic granulomatous inflammation that results in fibrosis, adhesions, and encapsulation of bowel loops in TB patients.<sup>4</sup>

This patient, being non-compliant with ATT and having recurrent episodes of subacute intestinal obstruction progressing to an acute presentation, raised concern for complications of TB, including fibrotic cocoon formation, fistula, or treatment failure due to drug resistance or non-compliance.

Imaging, particularly CECT, plays an important role in raising suspicion. Surgical exploration remains the definitive method for both diagnosis and treatment.

Even on ATT, abdominal TB can cause progressive fibro-inflammatory complications. SEP in TB patients should be suspected in chronic or recurrent bowel obstruction. Drug-resistance testing, such as GeneXpert, becomes very important in the persistence or atypical presentation of TB.<sup>5</sup> Surgical management, along with appropriate modification of ATT as necessary based on drug resistance profiling, will be key to the patient's recovery.

## Ethical approval

This case report has been reported in line with the SCARE criteria.

## Sources of funding

None.

## Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest regarding the content of this report.

## Conclusion

Secondary abdominal cocoon syndrome is an infrequent but serious complication of abdominal TB. The case also underlines the role of surgical management in an advanced disease and tissue testing in identifying drug resistance, thus allowing appropriate adjustment of ATT by a multidisciplinary team for optimal outcomes.

Vikas Panwar, D.V. Sneha, Vedant Rai. Sclerosing Encapsulating Peritonitis in an Extensively Drug-Resistant Tuberculosis Patient Presenting as Intestinal Obstruction – A Case Report. MMJ. 2025, December. Vol 2 (4).

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# Young Kidney Donor with Double Whammy: Nutcracker Syndrome with Early Branching Left Renal Artery

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## Abstract:

Nutcracker syndrome (NCS) is a rare renal vein compression disorder. In its classical presentation, the left renal vein is compressed between the aorta and the superior mesenteric artery. It may present with symptoms like haematuria, proteinuria, pain in the left lumbar or lower abdomen, or symptoms due to pelvic congestion, or be asymptomatic. In suspected cases, the diagnosis can be established by radiological imaging.

We report a 23-year-old female who presented as a live kidney donor and was diagnosed with NCS during preoperative evaluation. Our case is unique because the donor presented not only with NCS but also with a left-sided early-branching renal artery and a single right renal artery, creating a surgical dilemma in selecting the appropriate side for nephrectomy.

In NCS, surgical treatment is recommended for patients with serious symptoms. In our case, the donor had both left-sided NCS and an early-branching left renal artery, with a single right renal artery, and she was asymptomatic for NCS. Instead of choosing the right side that could have made the recipient surgery easier, we made the surgically difficult decision and chose the left donor kidney with practically two renal arteries to avoid future prospective complications to the donor. In this article, we highlight the right approach to select the side of kidney in such a living donor.

**Key words:** Nutcracker Syndrome, Kidney Donor, Transplantation.

## Introduction

Nutcracker syndrome (NCS) is a rare renal vein compression disorder. In its classical presentation, left renal vein is compressed between the aorta and the superior mesenteric artery (SMA).<sup>1,2</sup> NCS may be seen in all age groups, but its prevalence peaks during the 2<sup>nd</sup> and 3<sup>rd</sup> decades.<sup>2,3</sup> The compression over the renal vein may induce sufficient pressure in the affected kidney's venous system, leading to proteinuria, microscopic haematuria and progressive loss of renal function.<sup>4</sup> Patients with NCS usually seek medical attention with clinical symptoms such as pain in the left lumbar or lower

abdomen, orthostatic proteinuria, gross or microscopic haematuria, gynaecological symptoms due to pelvic congestion in females and varicocele in males.<sup>5</sup> Rarely, this can lead to renal vein thrombosis and pulmonary thromboembolism.<sup>6</sup> If NCS is suspected, the diagnosis can be made by Doppler ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI).<sup>7,8</sup>

Case of a prospective kidney donor with NCS has rarely been reported in literature.<sup>9</sup> Our case is further unique

because not only did the donor have NCS, but also had left-sided early-branching renal artery with right single artery causing a surgical dilemma to choose between the two sides.

### Case Report

A 23-year-old female underwent evaluation as a prospective kidney donor for her father. A detailed preoperative evaluation was performed. All the haematological, biochemical and immunological tests were within normal limits. Complement-dependent cytotoxicity (CDC) crossmatch tests were negative. The donor had no complaints or findings in her routine donor evaluation to suggest the NCS.

In the preoperative donor evaluation, there was no microscopic haematuria or proteinuria. The 24-hour urinary protein was 29 mg/day. The glomerular filtration rate (GFR) on diethylenetriaminepentaacetic acid (DTPA) renal scan was 116 mL/min, and both kidneys had equal differential renal function.

On CT renal angiography, both the right and left kidney size and parenchymal thickness were similar. However, there was an early branch arising from the upper border of the main renal artery and supplying the lower pole of the left kidney (Figure 1). In axial section images, it was determined that the left renal vein was compressed between the aorta and the SMA. The diameter of the left renal vein was 9.87 mm before the compression site, and 2.32 mm at the compressed region (Figure 2A). In sagittal plane images, the aortomesenteric angle (AMA) was measured as 14° (Figure 2B) and the distance between the aorta and the SMA was 3.1 mm.



**Figure 1:** Computed tomography (CT) renal angiography showing left early division renal artery.



**Figure 2A:** Compression of left renal vein between the superior mesenteric artery (SMA) and the aorta seen on axial section.



**Figure 2B:** Abdominal aortomesenteric angle (AMA) measurement on the sagittal plane.

Since there was early branching in renal artery, which would have become two arteries after harvesting, it required one additional anastomosis during transplantation. We still preferred to take the left side kidney, since there was significant renal vein compression by the SMA. The donor's family was counselled about future risk to the donor because of NCS and the need to proceed with left side kidney donation, requiring additional arterial anastomosis. After consent, the donor was planned for the left laparoscopic nephrectomy.

During the laparoscopic donor nephrectomy, mild dilatation was seen in the renal vein, left gonadal vein, left adrenal vein, and left lumbar vein. To avoid any harm to the kidney and the donor, the renal vein dissection towards the SMA was avoided. The kidney was harvested after securing the renal artery and renal vein and performing the transection of the renal vein proximal to the site of compression (Figure 3). The harvested left donor kidney was transplanted into the right iliac fossa of the recipient in the standard manner using the external iliac artery and

vein. As the inferior epigastric artery was of very narrow calibre, the additional lower pole renal artery anastomosis was also performed with the external iliac artery (Figure 4). Both recipient and donor surgeries were uneventful intraoperatively, and postoperative recovery was normal.



**Figure 3:** Laparoscopic view of early division of renal artery and renal vein.



**Figure 4:** Two arterial anastomoses with the external iliac artery in the recipient.

## Discussion

Most patients with NCS are asymptomatic. In symptomatic individuals, the most frequent finding is microscopic haematuria because of rupture of thin-walled varicose veins that develop in the collecting duct system because of high pressure in the renal vein.<sup>1-4</sup> Pain spreading from the left lumbar to the left inguinal region is another frequent finding. Patients may present with pain due to venous congestion, which is aggravated by walking, sitting, standing, and running.<sup>5</sup> Depending upon the degree of pelvic congestion, varicocele in males and

dyspareunia, dysuria, dysmenorrhea, and polycystic ovary in females can be detected.

The presence of proteinuria is another possible finding in NCS. The prevalence of proteinuria in NCS is 0.6%–10.7%.<sup>1</sup> This protein leak in the calyceal system is due to increased pressure, and the degree of proteinuria is affected by postural changes. In our case, the donor was asymptomatic, and a 24-hour urine collection revealed proteinuria of less than 29 mg/day with no microscopic haematuria.

Low body mass index (BMI) is also correlated with NCS. Previously, it has been reported that intense weight loss reduces retroperitoneal fat tissue, causing the AMA to become narrower and, as a result, NCS may occur.<sup>1</sup> In our case, the BMI of the donor was 21.6 kg/m<sup>2</sup>.

In NCS, the diagnosis is mainly established by imaging methods. Radiological findings should be supplemented by physiological flow information (ultrasound and/or catheter-based venography).<sup>2,7</sup> In Doppler US, flow patterns of the main renal vein and collateral veins, varicose formations, retrograde blood flows may be evaluated, and vein diameters measured.<sup>7</sup> In recent years, multi-detector CT angiography and MR angiography images have been reported to be highly efficient for diagnosis.<sup>8</sup> In axial sections of CT, when comparing proximal normal renal vein diameter with the diameter of the narrow part, if the ratio is over 4:1 and if the AMA measurement on sagittal planes is narrower than 50°, then the diagnosis can be established with the accompanying symptoms.<sup>10</sup> In the three-dimensional (3D) CT angiography, an AMA of 39.3 ± 4.3 degrees and a distance between the SMA and the aorta 3.1 ± 0.2 mm suggest NCS, while in normal individual, the AMA is 90 ± 10 degrees and the distance between the SMA and the aorta is 12 ± 1.8 mm.<sup>7</sup> In our donor, the AMA is 14°, and distance between the SMA and the aorta is 3.1 mm.

For symptomatic NCS patients, treatment is recommended. The aim is to correct renal vein blood flow, treatment modalities include intravascular stenting, left renal vein bypass, left renal vein transposition, superior mesenteric artery transposition, renal-to-inferior vena cava shunt and rarely autotransplantation.<sup>1,3,5</sup> After treatment, haematuria usually disappears within a few days.

A patient with NCS can also be a kidney donor as in this case,<sup>9</sup> where the left kidney was chosen as a graft. In a

routine donor, usually selection of kidney is based on simpler anatomy and differential function of both the kidneys. In this donor, both kidneys were equally functioning, but because of the right single renal artery and left early branching renal artery, the common selection would have been the right kidney. However, in view of the presence of NCS, we selected the left kidney, which needed one additional anastomosis with inferior epigastric artery. This avoided any future risk to the donor and risk of surgical correction later in life.

If the donor is symptomatic, most of the present symptoms will probably disappear after graft nephrectomy. Because the phenomenon does not cause a pathological problem at the glomerular and tubular level in the kidney, the graft function of the recipient will have an optimal outcome. In our case, postoperatively, GFR of the recipient remained at a fairly good level, and there was no proteinuria or microscopic haematuria.

### Conclusion

In NCS, surgical treatment is recommended for patients with serious symptoms. Surgical interventions and stenting are treatment modalities. In our case, the donor had both left NCS and an early-branching left renal artery; instead of going for the right kidney that could have made recipient surgery easier, we made the surgically difficult decision to choose left donor kidney with practically two renal arteries, to avoid future prospective complications to the donor. By reporting this case, we highlight the right approach to select the side of kidney in such donor.

Amit Kumar Devra, Lok Prakash Choudhary, Anuj Arora, Ravi Rai, CPS Chauhan, Anil Prasad Bhatt. Young Kidney Donor with Double Whammy: Nutcracker Syndrome with Early Branching Left Renal Artery. MMJ. 2025, December. Vol 2 (4).

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# Combined Complex Off-Pump Cardiac Surgery: Surgical Coronary Artery Revascularisation and Innominate–Right Atrial Appendage Bypass in a Patient with Chronic Total Superior Vena Cava Occlusion and Coronary Artery Disease — Our Experience

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## Abstract:

Chronic total occlusion (CTO) of the superior vena cava (SVC) is a recognised cause of venous hypertension, particularly among haemodialysis patients with repeated central venous catheterisations. Although endovascular therapy is the initial treatment of choice, long-segment fibrosis frequently results in failure, necessitating surgical reconstruction. Concomitant coronary artery disease (CAD) further complicates management. We report a 53-year-old, dialysis-dependent female with symptomatic SVC CTO and triple-vessel CAD. After failed endovascular recanalisation, she underwent simultaneous off-pump coronary artery bypass grafting (OPCAB) and innominate vein–right atrial appendage (RAA) bypass. A 13-mm autologous pericardial tube graft was created intraoperatively and used as the venous conduit. OPCAB $\times$ 3 and innominate–RAA bypass were performed successfully. Dense fibrosis at the SVC–right atrium (RA) junction confirmed chronicity and explained the prior endovascular failure. Postoperatively, the patient showed rapid improvement in facial and upper-limb oedema, effective venous drainage, and stable graft flows. Recovery was uneventful, and follow-up imaging demonstrated sustained patency of the coronary grafts and the pericardial venous conduit. Autologous pericardial tube grafting provides a durable, infection-resistant option for central venous reconstruction, particularly valuable in dialysis-dependent patients. Combining this approach with OPCAB minimises inflammatory and coagulopathic risk, avoids prosthetic complications, and enables effective treatment of complex chronic pathology. This case highlights the importance of individualised off-pump strategies using autologous tissue to achieve safe and durable outcomes.

**Key words:** Chronic SVC Occlusion, Innominate Vein Bypass, Autologous Pericardium, Complex Cardiac Surgery.

## Introduction

Chronic total occlusion (CTO) of the superior vena cava (SVC) is increasingly encountered, especially in haemodialysis patients with long-term central venous

catheterisation. The reported prevalence of central venous stenosis ranges from 4.3% to 41% depending on catheter duration and modality of imaging.<sup>1,3</sup> Endovascular

therapy is typically the first-line treatment, but long-segment fibrotic CTOs frequently fail and require surgical bypass.<sup>4,5</sup>

Multiple graft materials have been used for central venous reconstruction (Table 1), including expanded polytetrafluoroethylene (ePTFE) prosthetic grafts, bovine pericardial tubes, spiral saphenous vein grafts, vascular allografts, and autologous pericardium.<sup>6-11</sup> Autologous pericardium offers excellent biocompatibility and a low infection and thrombosis risk, making it especially suitable for dialysis-dependent patients.

The presence of coexistent coronary artery disease (CAD) complicates the operative strategy. Off-pump coronary artery bypass grafting (OPCAB) avoids cardiopulmonary bypass-induced inflammation, coagulopathy, and the need for additional venous cannulation — beneficial in patients with compromised venous access.<sup>12,13</sup>

This case highlights the combined use of autologous pericardial tube grafting and OPCAB to treat simultaneous SVC CTO and multivessel CAD.

Graft type	Advantages	Limitations/Risks	Reported outcomes	References
Expanded polytetrafluoroethylene (ePTFE, Gore-Tex, synthetic)	Readily available, easy to size, proven surgical use	Thrombosis risk, infection risk if contaminated, may require anticoagulation	Good immediate flow and symptom relief; mid-term patency, but possible late occlusion	5, 12
Autologous pericardium tube graft	Biocompatible, low infection risk, prosthetic material avoided	Requires additional time to construct, limited size	Good early and mid-term patency, preferred for infected/thrombogenic fields	10, 11
Bovine pericardium (stapled tube)	Off-the-shelf biologic, low thrombogenicity	Potential for degeneration (calcification) over time	Acceptable mid-term patency in cardiac literature	9
Vascular homograft/Allograft	Good biological properties, infection-resistant	Limited availability, potential immune response	Reported success in selected cases of infected mediastinitis	7

**Table 1:** Surgical options and outcomes with different graft materials.

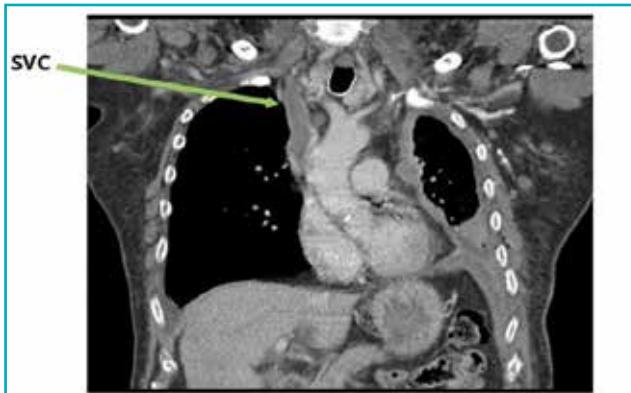
## Case Report

A 53-year-old female on long-term haemodialysis presented with progressive upper-body venous congestion. Repeated vascular access procedures suggested catheter-related fibrosis as the aetiology.<sup>1,2</sup> Computed tomography (CT) venography revealed long-segment SVC occlusion with extensive azygos and hemiazygos collateralisation (Figure 1A). Endovascular attempts failed as guidewires were unable to cross the densely fibrotic obstruction, consistent with CTO.<sup>3,4</sup> Coronary angiography confirmed triple-vessel CAD.

Surgical techniques used included OPCAB and innominate–right atrial appendage (RAA) bypass. To

avoid cardiopulmonary bypass–related complications, OPCAB was performed using reverse saphenous vein grafts to the left anterior descending (LAD), obtuse marginal (OM), and posterior descending artery (PDA).<sup>12</sup>

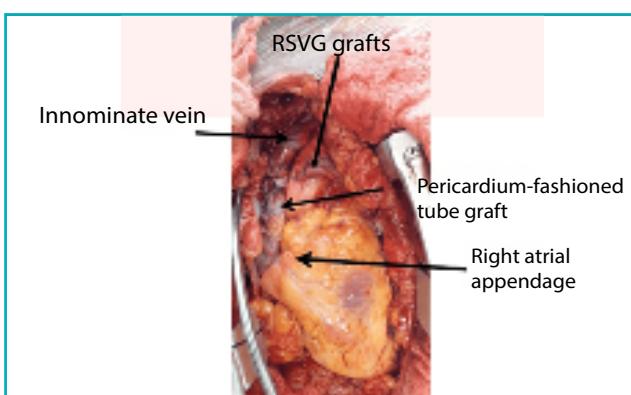
The innominate–RAA bypass was performed using an autologous pericardial tube graft (Figures 1B and 1C). Given the thrombosis and infection risks of prosthetic grafts, and the risk of calcification in bovine pericardium,<sup>8,9</sup> a 13-mm autologous pericardial tube graft was constructed over a Hegar dilator following established techniques.<sup>10,11</sup> The graft was anastomosed end-to-side from the innominate vein to the RAA.



**Figure 1A:** Venogram showing superior vena cava (SVC) stenosis.



**Figure 1B:** Pericardium tube graft creation.



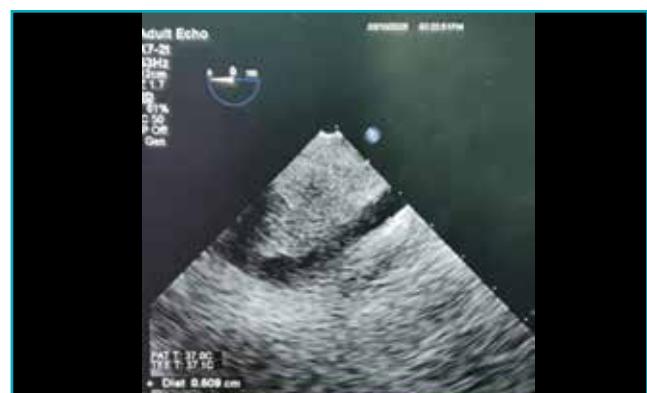
**Figure 1C:** Intraoperative image showing the grafts: Reverse saphenous vein graft (RSVG) and pericardium-fashioned tube graft.

## Results

**Intraoperative findings:** Dense fibrosis involving the innominate vein and SVC-RA junction confirmed a chronic, non-crossable obstruction, consistent with endovascular failure patterns.<sup>4</sup> All coronary targets were adequate for grafting.

**Postoperative course:** Venous congestion improved significantly within 48 hours. The autologous pericardial conduit demonstrated excellent flow dynamics and handling properties, consistent with previously reported patency profiles.<sup>10,11</sup>

**Follow-up:** Serial imaging confirmed sustained patency of both venous (Figure 1D) grafts. The patient remained asymptomatic with resolution of SVC syndrome.



**Figure 1D:** Postoperative 2D echo showing patent pericardium-fashioned tube graft.

## Discussion

Autologous pericardial grafts offer superior durability and resistance to infection compared with synthetic grafts, making them ideal for central venous reconstruction in dialysis-dependent patients.<sup>6,8,10,11</sup>

Prosthetic grafts such as ePTFE are convenient but associated with higher thrombosis and infection, while bovine pericardial grafts may calcify over time.<sup>9</sup> Allografts are effective but limited by availability.<sup>7</sup>

OPCAB offers additional benefits by avoiding cardiopulmonary bypass, reducing inflammation, minimising coagulation disturbances, and eliminating the need for venous cannulation — advantages particularly significant in patients with SVC pathology.<sup>12,13</sup> Simultaneous central venous bypass and OPCAB is feasible and effective in experienced centres.<sup>10-13</sup>

## Conclusion

The simultaneous management of CAD and chronic SVC occlusion requires meticulous planning and a tailored surgical strategy. The successful use of an autologous pericardial tube graft and OPCAB in this patient highlights the versatility of biologic conduits and the safety of avoiding cardiopulmonary bypass in high-risk populations. This combined approach offers effective restoration of venous drainage and myocardial perfusion with favourable early outcomes.

Nukala Rao Mallikarjuna, Debashish Panigrahi, Shobhit Saurav, Pankaj Kumar Gupta, Rahul Dutta, Adarsh Subrahmanyam Koppula, Rajneesh Malhotra. Combined Complex Off-Pump Cardiac Surgery: Surgical Coronary Artery Revascularisation and Innominate–Right Atrial Appendage Bypass in a Patient with Chronic Total Superior Vena Cava Occlusion and Coronary Artery Disease — Our Experience. MMJ. 2025, December. Vol 2 (4).

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# THE IMAGES

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Peripheral Squamous Cell Carcinoma of the Lung in a Smoker: A Radiological Case Report

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# Peripheral Squamous Cell Carcinoma of the Lung in a Smoker: A Radiological Case Report and Literature Review

**Sylvia Bedas Nsato<sup>1</sup>, Eeta Jain<sup>2</sup>, Flora Lwakatare<sup>2</sup>, Richa Bansal<sup>2</sup>, Bharat Aggarwal<sup>2</sup>**

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## Abstract:

Squamous cell carcinoma (SCC) of the lung most often arises in the central bronchi and is strongly associated with tobacco exposure. However, peripheral squamous cell carcinoma (pSCC) is increasingly recognised as a distinct variant, often radiologically resembling adenocarcinoma and posing diagnostic difficulties, particularly in smokers with emphysema. A 76-year-old chronic smoker presented with persistent cough and weight loss. Chest X-ray revealed an ill-defined opacity in the right perihilar region, with a few thin atelectatic linear bands in the lower zones. Contrast-enhanced computed tomography (CT) of the chest showed an irregular, spiculated soft-tissue mass measuring approximately  $4.4 \times 3.7$  cm in the superior segment of the right lower lobe, with multiple smaller spiculated nodules in the right upper and middle lobes on a background of centrilobular emphysema. Mildly enlarged right pre-paratracheal and subcarinal lymph nodes were also noted. CT-guided biopsy revealed SCC. Histopathology showed well-differentiated SCC with keratin pearls and intercellular bridges. Immunohistochemistry was positive for p40 and cytokeratin 5/6 (CK5/6) and negative for thyroid transcription factor-1 (TTF-1) and Napsin A. Peripheral squamous cell carcinoma, though less common than central SCC, should be considered in smokers presenting with spiculated peripheral pulmonary nodules. These lesions can mimic adenocarcinoma radiologically, may invade the pleura, and often require CT-guided biopsy or surgical resection for definitive diagnosis. Awareness of this variant is important to avoid misclassification and guide appropriate management.

**Key words:** Peripheral Lung Carcinoma, Squamous Cell Carcinoma, Smoking, CT Chest, Radiology, Case Report.

## Introduction

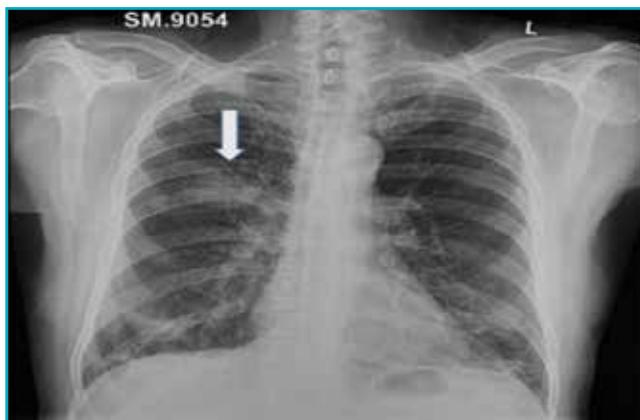
Lung cancer remains the leading cause of cancer-related mortality worldwide. Squamous cell carcinoma (SCC) traditionally arises from the central bronchi and is strongly linked to long-term smoking.<sup>1</sup> However, an increasing number of SCCs are being identified peripherally within the lung parenchyma, a phenomenon attributed to changes in smoking habits and improved imaging detection.<sup>1-3</sup> Peripheral squamous cell carcinoma (pSCC) can closely mimic adenocarcinoma on imaging due to its peripheral location and spiculated appearance.<sup>4,5</sup> Recognition of this subtype is important, as it exhibits

different histopathological characteristics, biological behaviour, and therapeutic implications.<sup>6,7</sup>

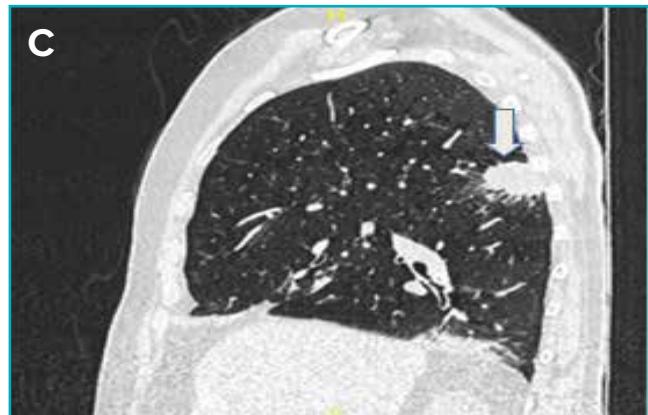
## Case Report

A 76-year-old male chronic smoker presented with chronic cough, dyspnoea, and unintentional weight loss. Chest X-ray (posteroanterior view) revealed an ill-defined opacity in the right perihilar region, with thin atelectatic bands in both lower zones (Figure 1). Contrast-enhanced computed tomography (CT) of the chest showed an

irregular, spiculated soft-tissue mass measuring  $4.4 \times 3.7$  cm in the superior segment of the right lower lobe, along with multiple smaller spiculated nodules in the right upper and middle lobes on a background of centrilobular emphysema (Figure 2A–C). Mild right pre-paratracheal and subcarinal lymphadenopathy was noted, with no evidence of pleural effusion or chest wall invasion.



**Figure 1:** Chest X-ray (anteroposterior view) showing an ill-defined opacity in the right perihilar region, with thin atelectatic linear bands in the lower zones of the right lung (white arrow).



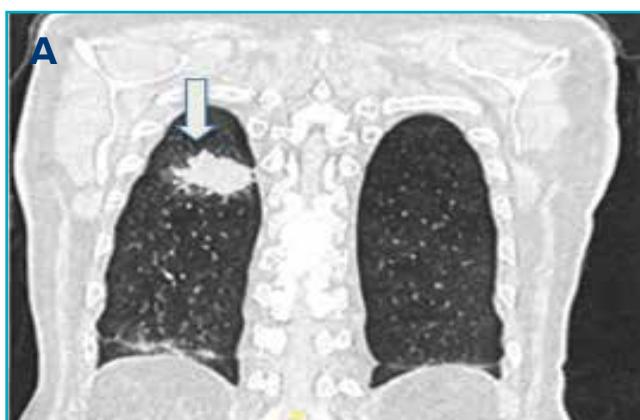
**Figure 2A–C:** High-resolution computed tomography (HRCT) images — coronal, axial (A and B), and sagittal (C) views — showing a spiculated soft-tissue mass in the superior segment of the right lower lobe, with background centrilobular emphysema (white arrows).

#### Histopathology findings:

CT-guided biopsy revealed SCC characterised by keratin pearls and intercellular bridges. The degree of differentiation was consistent with well to moderately well-differentiated SCC. Immunohistochemistry showed positivity for p40 and cytokeratin 5/6 (CK5/6) and negativity for thyroid transcription factor-1 (TTF-1) and Napsin A, confirming squamous differentiation.

#### Discussion

pSCC is an uncommon subtype of pulmonary SCC that arises from smaller bronchi or alveolar epithelium, unlike the more typical central SCC.<sup>3,4</sup> Although most SCCs are centrally located, peripheral SCC should be considered in smokers presenting with spiculated peripheral pulmonary lesions, as failure to recognise this variant may delay accurate diagnosis and management. Radiologically, pSCC appears as a spiculated or lobulated peripheral mass, occasionally with cavitation or adjacent emphysema.<sup>5,6</sup> Distinguishing pSCC from adenocarcinoma based solely on imaging is challenging.<sup>7</sup> Histopathologically, pSCC demonstrates keratinisation and intercellular bridges, with immunohistochemistry (p40+, CK5/6+, TTF-1-, Napsin A-) being crucial for confirming squamous differentiation.<sup>8</sup> Several studies and case series, including the one by Watanabe *et al.*, have characterised the clinicopathologic and radiologic features of pSCC,<sup>3,4</sup> highlighting the importance of awareness and accurate diagnosis to guide management and prognostication.



## Declarations

- **Ethics approval and consent to participate:** Not required, as this report describes anonymised radiological data.
- **Consent for publication:** Not applicable, as no identifiable patient information is included.
- **Competing interests:** The authors declare no competing interests.

- **Funding:** None.

- **Authors' contributions:** Dr. Sylvia Bedas Nsato conceived the case, performed imaging analysis, conducted the literature review, and drafted the manuscript. Supervisors and co-authors contributed to imaging interpretation, critical revision, and manuscript approval. All authors reviewed and approved the final manuscript.

## Conclusion

pSCC is a less frequent but increasingly recognised variant of pulmonary SCC. It should be actively considered in the differential diagnosis of spiculated peripheral lung masses in smokers, as imaging alone is non-specific. Histopathological and immunohistochemical confirmation are essential for accurate diagnosis, appropriate treatment planning, and prognostication.

Sylvia Bedas Nsato, Eeta Jain, Flora A. Lwakatare, Richa Bansal, Bharat Aggarwal. Peripheral Squamous Cell Carcinoma of the Lung in a Smoker: A Radiological Case Report and Literature Review. MMJ. 2025,

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# Complete Gut Malrotation Incidentally Discovered in an Adult: A Radiological Case Report

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**Abstract:**

Intestinal malrotation is a rare congenital anomaly resulting from abnormal rotation and fixation of the midgut during embryogenesis. While commonly diagnosed in infancy, adult presentation is rare and often incidental. This report describes an incidentally discovered complete gut malrotation in an elderly patient who was evaluated for bilateral ureteric calculi. A 68-year-old male with a history of hypertension and diabetes underwent a non-contrast computed tomography of the kidney, ureters, and bladder (CT KUB) to investigate flank pain. Imaging revealed bilateral moderate hydronephrosis secondary to ureteric calculi with an incidental finding of complete intestinal malrotation. The duodenojejunal (DJ) flexure and jejunal loops were located on the right side, while the cecum, ileocecal junction, and ascending colon were positioned on the left. The relationship between the superior mesenteric artery (SMA) and the superior mesenteric vein (SMV) was reversed, confirming the diagnosis of malrotation. There was no evidence of bowel obstruction or volvulus. Although rare in adults, intestinal malrotation may be incidentally identified during imaging for unrelated clinical conditions. Recognising key CT features, including reversed SMA–SMV orientation and abnormal bowel positioning, is essential for accurate diagnosis and appropriate surgical planning.

**Key words:** Intestinal Malrotation, CT Abdomen, SMA–SMV Relationship, Intestinal Malrotation, Radiology.

**Introduction**

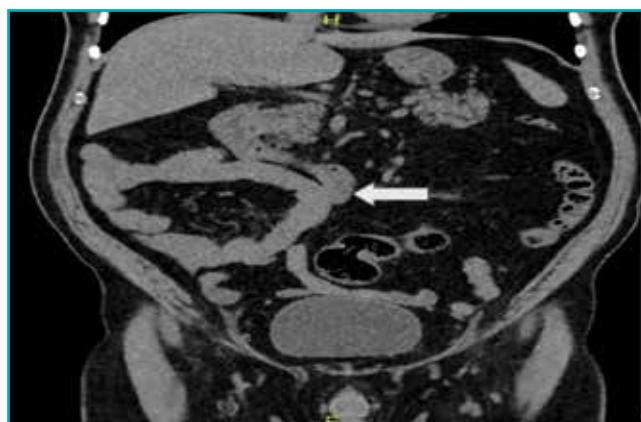
Intestinal malrotation arises from incomplete rotation of the midgut around the superior mesenteric artery (SMA) during embryonic development. Although its estimated incidence is approximately 1 in 500 live births, detection in adulthood is exceedingly rare and typically occurs incidentally or during assessment for non-specific abdominal complaints.<sup>1,2</sup> Adult presentations of malrotation present diagnostic challenges, and radiologists must be aware of its characteristic imaging features to prevent misdiagnosis.<sup>3</sup>

**Case Report**

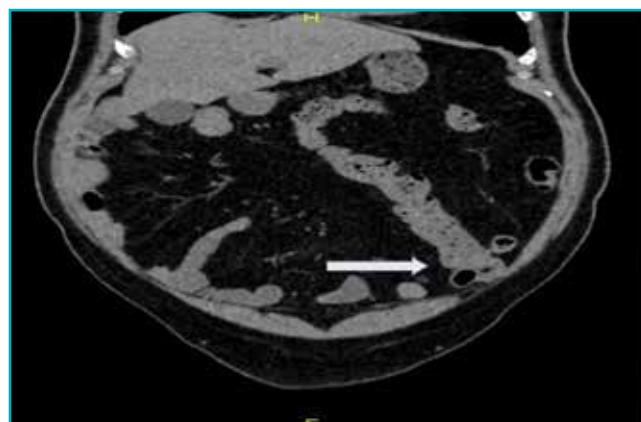
A 68-year-old male with a known history of hypertension and type II diabetes mellitus presented for routine follow-up. He reported mild flank discomfort but denied vomiting, abdominal pain, or bowel disturbance. Non-contrast computed tomography of the kidney, ureters, and bladder (CT KUB) was performed to evaluate for renal calculi.

The scan incidentally revealed features consistent with complete intestinal malrotation (Figures 1–3). The duodenojejunal (DJ) flexure and jejunal loops were located on the right side, while the cecum, ileocecal junction, and ascending colon were positioned on the left (Figures 1 and 2). The relationship between the SMA and superior mesenteric vein (SMV) was reversed, with

the SMA situated to the right of the SMV (Figure 3). No evidence of obstruction, volvulus, or ischaemia was identified.



**Figure 1:** Plain coronal computed tomography (CT) image showing complete malrotation of the bowel. Jejunal loops are located on the right side of the abdomen (white arrow), while both the ascending and descending colon lie on the left.



**Figure 2:** Plain coronal computed tomography (CT) image demonstrating a malpositioned cecum in the left iliac fossa with the ileocecal junction and ascending colon seen in the left half of the abdomen (white arrow).



**Figure 3:** Axial computed tomography (CT) image showing reversed superior mesenteric artery–superior mesenteric vein (SMA–SMV) relationship with the superior mesenteric artery lying to the right of the vein (white arrow).

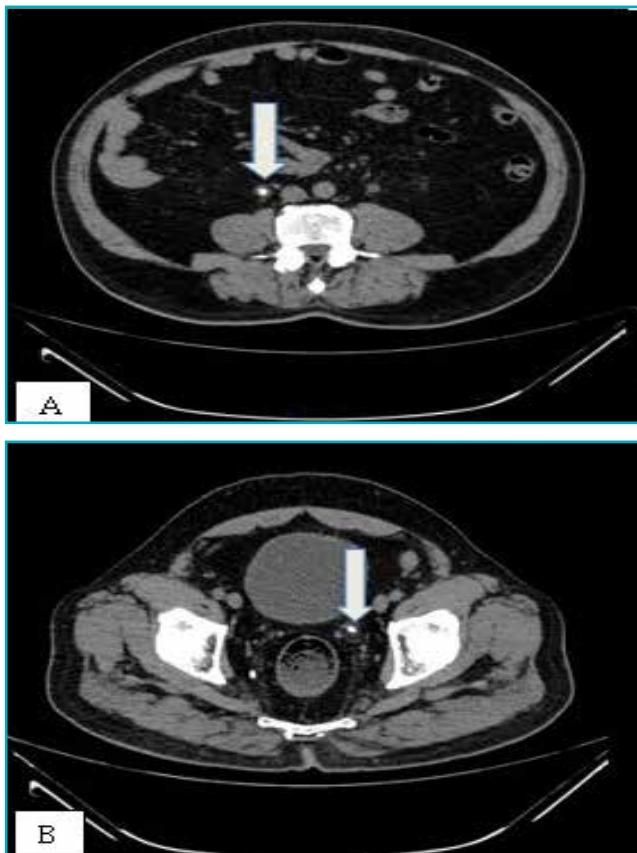
Further evaluation in imaging revealed both kidneys to be normal in size and position, with bilateral mild perinephric fat stranding and moderate hydronephrosis (Figure 4). A  $6 \times 4$  mm calculus was seen in the right upper ureter at the level of L4 (Figures 5 and 6A), and an  $8.6 \times 6.6$  mm calculus with a density of 1000 Hounsfield units (HU) was located in the left lower ureter just proximal to the ureterovesical junction (Figure 6B).



**Figure 4:** Coronal computed tomography of kidney, ureters, and bladder (CT KUB) image showing bilateral moderate hydronephrosis with mild perinephric fat stranding.



**Figure 5:** Coronal computed tomography of kidney, ureters, and bladder (CT KUB) image demonstrating a  $6 \times 4$  mm ureteric calculus in the right upper ureter at the level of the upper border of L4 vertebral body (white arrow) with associated perinephric fat stranding.



**Figure 6:** A. Axial computed tomography of kidney, ureters, and bladder (CT KUB) image showing a  $6 \times 4$  mm calculus in the right upper ureter (white arrow), which was seen at the level of the upper border of L4. B. Axial CT KUB image showing an  $8.6 \times 6.6$  mm calculus (1000 HU) in the left lower ureter just proximal to the ureterovesical junction (white arrow).

## Imaging findings

Non-contrast CT KUB revealed characteristic features of complete intestinal malrotation:

- Jejunal loops located on the right side of the abdomen (Figure 1)
- Cecum and ascending colon lying in the left abdomen (Figure 2)
- Reversed SMA–SMV relationship (SMA on the right side of SMV) (Figure 3)
- No evidence of midgut volvulus, Ladd's bands, or bowel obstruction
- Bilateral moderate hydronephrosis with ureteric calculi (Figures 4–6)
- Additional findings included hepatic steatosis

## Discussion

Adult intestinal malrotation is a rare congenital anomaly caused by incomplete rotation and fixation of the midgut during embryologic development, with an estimated incidence of less than 0.2% in adults.<sup>4,5</sup> Most adult cases remain asymptomatic and are often identified incidentally during imaging for unrelated conditions.

In this case, the anomaly was incidentally detected on a non-contrast CT KUB, performed to evaluate ureteric calculi. Although contrast-enhanced CT or CT angiography is considered the standard imaging modality for assessing mesenteric vascular orientation and related complications,<sup>6,7</sup> careful evaluation of bowel and vascular landmarks on plain CT can still reveal characteristic features of malrotation.

The hallmark findings include failure of the DJ flexure to cross the midline, small bowel loops predominantly on the right, colon positioned on the left, and reversal of the SMA–SMV relationship.<sup>8,9</sup> In the present case, all these features were appreciable despite the absence of intravenous contrast, underscoring the importance of maintaining a high index of suspicion even on routine KUB scans.

CT remains the imaging modality of choice for diagnosing intestinal malrotation, as it enables identification of both abnormal vascular orientation and potential complications such as volvulus or ischaemia.<sup>9</sup> However, in asymptomatic or incidentally discovered cases, as in this patient,

conservative management with documentation is typically appropriate.<sup>10</sup>

This case emphasises that meticulous assessment of non-contrast CT images can occasionally reveal significant congenital anomalies. Awareness of these findings prevents misinterpretation as postsurgical changes or internal hernia, ensuring accurate reporting and clinical correlation.

### Teaching Points

1. Adult intestinal malrotation is a rare but noteworthy incidental finding on CT.
2. Recognition of reversed SMA–SMV relationship and abnormal bowel positioning is diagnostic.
3. Awareness of this anomaly prevents misinterpretation as postsurgical anatomy or internal hernia.
4. Asymptomatic incidental malrotation typically requires no surgical intervention but should be documented clearly.

### Declarations

- **Ethics approval and consent to participate:** Not required; this report describes anonymised radiological data.
- **Consent for publication:** Not applicable; no identifiable patient information is included.
- **Competing interests:** The authors declare no competing interests.
- **Funding:** None.
- **Authors' contributions:** Dr. Sylvia Bedas Nsato conceived the case, performed imaging analysis, conducted literature review, and drafted the manuscript. Supervisors and co-authors contributed to imaging interpretation, critical revision, and manuscript approval. All authors reviewed and approved the final manuscript.

### Conclusion

This case highlights an incidental detection of intestinal malrotation on a non-contrast CT KUB, illustrating that careful scrutiny of even limited-field, non-enhanced scans can reveal important congenital anomalies. While contrast-enhanced CT or CT angiography remains the gold standard for vascular assessment, awareness of the characteristic anatomic landmarks allows radiologists to recognize malrotation in unexpected contexts and guide appropriate management.

Sylvia Bedas Nsato, Karthikeya Jain, Flora A. Lwakatare, Vandana, Amit Kumar Sahu. Complete Gut Malrotation Incidentally Discovered in an Adult: A Radiological Case Report. MMJ. 2025, December.

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# Imaging Pitfalls: A Case of Fat Necrosis Masquerading as Recurrent Breast Carcinoma.

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## Abstract:

Fat necrosis is a non-malignant breast condition that can closely mimic cancer recurrence on imaging, especially in individuals with a prior history of breast cancer and reconstructive procedures. We report the case of a 34-year-old woman with a history of left breast cancer who developed a new palpable breast mass after undergoing mastectomy and reconstruction. Multimodal imaging — including mammography, ultrasound, magnetic resonance imaging (MRI) and positron emission tomography (PET)/computed tomography (CT) — demonstrated features that raised concern for possible malignancy. A definitive diagnosis of fat necrosis was confirmed through histopathological analysis of a biopsy sample.

This case underscores the importance of correlating imaging findings with tissue diagnosis to accurately differentiate benign post-surgical changes from true cancer recurrence, thereby avoiding unnecessary treatments or procedures.

**Key words:** Fat Necrosis, Recurrent Breast Carcinoma, Breast Imaging, Post-Surgical Changes.

## Introduction

Fat necrosis is a benign, non-suppurative inflammatory process of adipose tissue. Accurate recognition is important, as its imaging characteristics can closely resemble those of breast carcinoma.<sup>1</sup>

Fat necrosis of the breast most commonly occurs following trauma, surgery, or radiotherapy. Less common causes include anticoagulation, infection, or idiopathic origin. Other rare causes include polyarteritis nodosa, Weber-Christian disease, and granulomatous angiopanniculitis. In some patients, the cause of fat necrosis remains unknown.<sup>1,3</sup>

The imaging manifestations of fat necrosis on mammography, ultrasonography, and magnetic resonance imaging (MRI) vary depending on the stage of evolution, which has important clinical implications as certain

appearances can be virtually indistinguishable from malignancy, often necessitating biopsy for definitive diagnosis.<sup>1,4</sup>

Furthermore, fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) can misinterpret fat necrosis as malignancy due to its metabolic activity, resulting in false-positive findings and physicians must be aware of this as a potential pitfall.<sup>5,6</sup>

In this report, we present a case of a 34-year-old female with a history of breast cancer who underwent mastectomy and reconstruction surgery and subsequently presented with a breast lump, raising concern for recurrence. In this case, ultrasound, mammography, and PET/CT demonstrated features that were suspicious of malignancy.

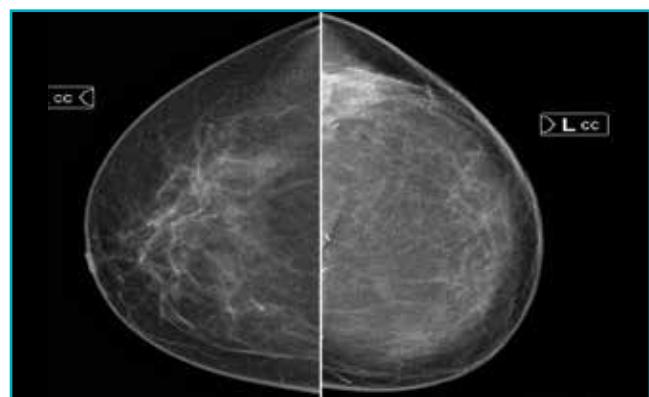
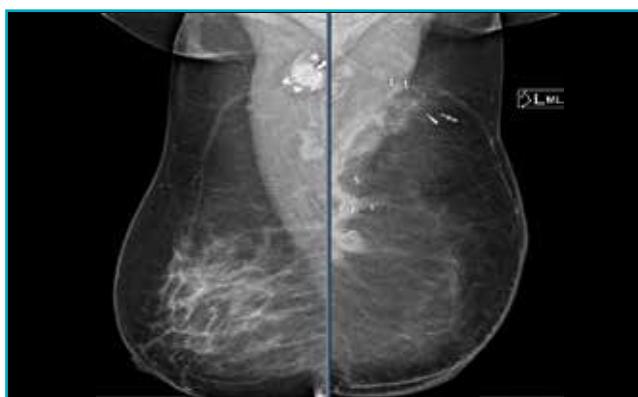
## Case Report

A 34-year-old female presented with a new, painless lump in the left breast. She had a history of left breast cancer (invasive ductal carcinoma [IDC], grade 2 with extensive ductal carcinoma in situ [DCIS], hormone receptor [HR] negative, and human epidermal growth factor receptor 2 [HER-2] positive) — eight months prior to this presentation. She had undergone left mastectomy and sentinel lymph node biopsy (SLNB) and was managed with chemotherapy (paclitaxel) and HER2-targeted therapy (trastuzumab).

She subsequently underwent deep inferior epigastric perforator (DIEP) breast reconstruction.

On examination, there was irregular thickening at 12 to 1 o'clock. No palpable axillary lymph nodes were noted.

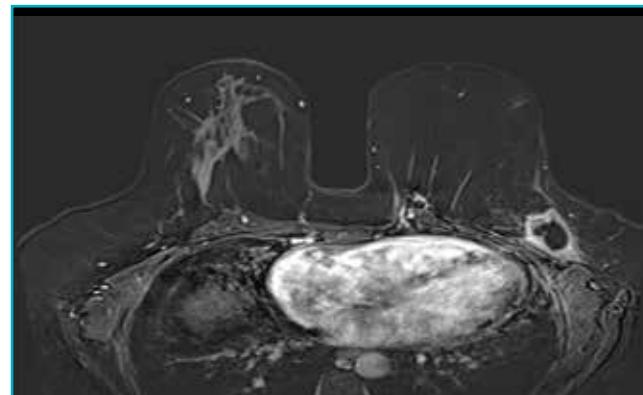
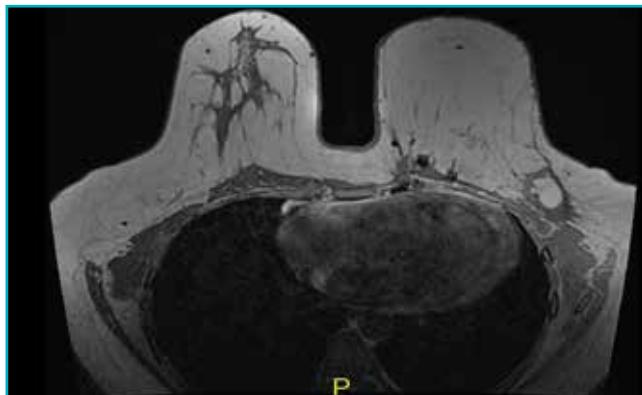
She underwent several imaging investigations, including mammography, ultrasound, MRI and PET/CT examinations, which are described below (Figure 1–4).



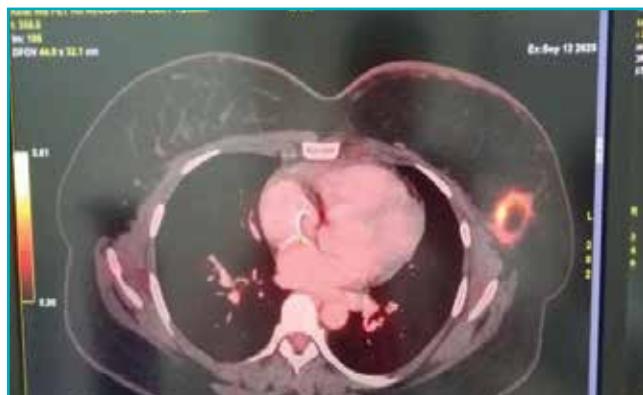
**Figure 1:** Mediolateral oblique (MLO) and craniocaudal mammographic images of both breasts demonstrate a reconstructed left breast with irregular isodense areas and dystrophic calcifications seen superolaterally along the flap. Surgical clips are noted.



**Figure 2:** Ultrasound images show multiple heteroechoic areas, some demonstrating posterior shadowing, along the lateral and superior margin of the flap in the reconstructed left breast. The largest lesion measures approximately 2.8 cm x 2.2 cm.



**Figure 3:** Magnetic resonance imaging (MRI) images showing multiple coalescent lesions with central fat signal intensity and a thick, irregular peripheral rim enhancement seen along the posterolateral margin of the flap in the reconstructed left breast, the largest measuring approximately 30 mm x 27 mm. Mild surrounding parenchymal oedema pattern, skin thickening, and architectural distortion are also noted.



**Figure 4:** Positron emission tomography/computed tomography (PET/CT) images show metabolically active, multiple coalescent and discrete nodular enhancing soft-tissue lesions along the lateral and superior margins of the flap, with areas of fat density within the reconstructed left breast. The largest lesion measures approximately 3.1 cm x 2.5 cm, suggestive of inflammation versus tumour recurrence. Clinical and histopathological evaluation was advised. Low-grade metabolically active and inactive, left level I axillary lymph nodes are also seen, the largest measuring approximately 9 mm x 7 mm, likely inflammatory in nature. No other significant metabolically active lesion was identified in the body surveyed.

Core needle biopsy of the left breast lesion was performed. Histopathology findings revealed fat necrosis. Core needle biopsy of the left axillary node revealed benign lymphoid tissue.

## Discussion

Fat necrosis often presents as a palpable mass and can raise suspicion for breast carcinoma, especially in patients with a history of breast cancer or surgery.<sup>7</sup> Our patient had a history of mastectomy and reconstructive surgery following breast cancer diagnosis and presented with a palpable mass, which raised suspicions for recurrence.

Ultrasound findings in fat necrosis are variable and depend on the stage of the lesion. In the early phase, fat necrosis may appear as a hypoechoic or complex cystic mass with indistinct margins and posterior acoustic

shadowing. These features have been reported in association with breast cancer and were also observed in our case.<sup>8</sup>

On mammography, fat necrosis can present with a wide spectrum of appearances, ranging from benign-appearing oil cysts with or without rim calcifications to suspicious spiculated masses or focal asymmetries. In the early stages, the small foci of calcification in the wall of an oil cyst appear similar to fine microcalcifications and need differentiation from the disease process.<sup>4</sup>

In our patient, the mammographic findings included a high-density, irregular mass with architectural distortion — features that closely mimic invasive carcinoma. This underscores the well-documented potential of fat necrosis to imitate malignancy on conventional imaging, particularly

when classical features such as rim calcifications or fat lucencies are absent.

Fat necrosis produces a wide spectrum of findings on MRI. The MRI appearance of fat necrosis may be indistinguishable from that of malignancy and can mimic tumour recurrence after breast conservation therapy.<sup>4</sup>

MRI can offer valuable diagnostic information in complex or equivocal cases, particularly when conventional imaging raises suspicion for malignancy. In our case, MRI of the left breast revealed a reconstructed flap with multiple coalescent lesions along the posterolateral margin. These lesions demonstrated central fat signal intensity with thick, irregular peripheral rim enhancement, associated with mild surrounding parenchymal oedema, skin thickening, and architectural distortion. These findings closely mimicked a malignant process, particularly due to the irregular rim enhancement and surrounding tissue changes. However, the presence of a central fat signal

was an important clue pointing toward a benign aetiology, such as fat necrosis.

PET/ CT is commonly employed in the surveillance of breast cancer patients, particularly post-surgical or post-reconstructive cases, to evaluate for recurrence or metastatic disease. However, fat necrosis can exhibit increased FDG uptake, especially when associated with active inflammation, further complicating differentiation from malignancy.<sup>6</sup>

In our case, PET/CT showed metabolically active nodular soft tissue lesions along the lateral and superior margins of the reconstructed left breast flap, raising the possibility of either an inflammatory process or recurrent malignancy. The FDG avidity, combined with the morphological features on mammography and ultrasound, heightened clinical concern for tumour recurrence, especially in a post-surgical breast where architectural distortion is common, therefore necessitating a histological diagnosis.

## Conclusion

Fat necrosis of the breast is a benign condition that can mimic malignancy across all imaging modalities, especially in post-surgical or reconstructed breasts. This case underscores the need for a broad differential diagnosis, clinical correlation, and, when imaging is inconclusive, timely histopathologic confirmation to guide appropriate management and avoid unnecessary interventions.

Flora A. Lwakatare, Eeta Jain, Sylvia Bedas Nsato, Richa Bansal, Bharat Aggarwal. Imaging Pitfalls: A Case of Fat Necrosis Masquerading as Recurrent Breast Carcinoma. MMJ. 2025, December. Vol 2 (4).

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# STUDENTS' CORNER

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# Research Methodology and Biostatistics

## Series VIII – Statistical Relationship Versus Cause–Effect Relationship Between Medical Factors

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### Abstract:

A statistical relationship refers merely to a change in one factor accompanied by the change in one or more of the others. A relationship between two or more factors can be considered cause-effect when it is statistically significant to begin with and satisfies most of the following criteria: (i) biological plausibility, (ii) experimental evidence, (iii) dose-response relationship, (iv) consistency across time and space, (v) specificity, and, (vi) statistical significance, as mentioned earlier. These criteria are hard to achieve; hence, establishing a cause-effect relationship is challenging. This article provides a brief overview of the distinction between a cause-effect relationship and a statistical relationship.

**Key words:** Statistical Relation, Cause-Effect, Regression, Spurious Correlation.

### Introduction

A statistical relationship refers to the change in one factor accompanied by an increase or decrease in one or more of the others. Although modern medical science divides the human body into tissues, organs, and systems, these systems function in tandem with one another with intricate dependence. The body also interacts with the environmental factors such as microbes, dietary intake, and physical activity. Psychological factors such as tension, stress, family support, and appreciation or criticism, also make a substantial contribution to medical parameters. With such a large number of factors at work, it is natural to investigate how and to what extent these factors affect health parameters, and how various health parameters interact with one another. Statistically, these relationships are studied through their structure and strength, and more exactly by ascertaining the cause–effect mechanisms involved.

### Statistical Relationships

A statistical relationship between two or more factors is studied in two dimensions: the structure of the relationship and the strength of the relationship.

The statistical study of relationships requires identifying one or more variables as dependent and others as independents. The dependents may represent the outcome, response, or consequence, whereas the independents may be the risk factors, antecedents, or predictors that are anticipated to determine the outcome. In a statistical relationship, the independents are known as regressors and the structure of the relationship is described by regression. The dependent may be qualitative, such as survival or death; however, for ease of understanding, we will consider only quantitative dependents for the moment. For example, Skovlund<sup>1</sup> discussed the following regression between C-reactive protein (CRP) concentration and quality of life scores (QoL) in patients with metastatic bowel cancer:

$$\text{QoL} = 75.6 - 0.177 \times \text{CRP}$$

This is an example of a simple regression with one dependent variable (QoL) and one independent variable (CRP). The QoL on the left side in a regression is not the value of an individual but the average QoL among subjects with a specific CRP level — a fact often overlooked in research. This example is linear, as it can be plotted as a straight line, but relationships can also be curvilinear or even multidimensional surfaces when several independents are involved. A regression can include not only multiple independents but, in rare cases, multiple dependent variables as well.

Regression is obtained as the 'best fit' to the data, although this best fit may still be poor. The adequacy of fit for quantitative variables is measured by the Pearson correlation coefficient. This ranges from -1 to +1, with 0 indicating no correlation. When one dependent variable is related to several independents, the multiple correlation coefficient is used. A correlation exceeding 0.8 in either direction is considered strong. However, a big limitation of the Pearson correlation is that it measures only a linear relationship. Two variables may have a strong non-linear (curved) relationship, yet still produce a low correlation coefficient. For example, lung function shows a curvilinear relationship with age — it increases from childhood to adulthood and decreases in old age. It is not linear. To assess non-linear relationships, the coefficient of determination is used instead of the multiple correlation coefficient. Nevertheless, even these measures may be spurious, as discussed later in this communication.

When a qualitative variable, such as disease severity (none, mild, moderate, serious, critical), is investigated for its dependence on various laboratory or radiological parameters, the regression is termed logistic regression. The strength of the relationship in this case is measured mostly by Nagelkerke  $R^2$ , which is similar to the square of the multiple correlation coefficient.

When the variable of interest is a duration, such as survival time in cancer patients or hospitalisation duration in liver transplant recipients, a Cox regression is used. This approach accounts for the generally highly skewed distribution of durations and the presence of censored observations due to limited follow-up.

### Cause-Effect Relationships

The relationships presented in the previous section are statistical in nature and they can sometimes be

spurious. For example, the incidence of cardiovascular disease (CVD) in India has been increasing, while the birth rate has been declining over the past 50 years. These two variables show a strong negative relationship, with a correlation coefficient of nearly -0.7. The relationship exists statistically, but does it have any medical significance? Clearly not, it is spurious, fostered by factors such as increasing life expectancy and sedentary lifestyle in the case of CVD, and greater awareness of the disadvantages of large families in the case of birth rates. Both trends are part of the same development process.

Correlation does not imply causation — increasing the birth rate will not reduce the incidence of CVD. Louizi *et al.*<sup>2</sup> discussed the role of carotid stenosis as a possible explanation for a spurious correlation between white matter hyperintensities and coronary artery disease.

Cause is a strong term. Although its usage varies, it generally refers to a factor directly responsible for an outcome, which precedes the effect. For instance, smoking can be considered a cause of lung cancer, although the mechanism is mediated through cotinine, which has the potential to alter cell structure. A similar situation exists between obesity and diabetes — the association appears direct but works through metabolic mediators.

It is sometimes argued that a factor qualifies as a cause if it is both necessary and sufficient for the effect to appear. However, this is an overly strict condition in medical contexts. Obesity is neither necessary nor sufficient to cause diabetes, yet it is still considered as a causal factor. Thus, most medical relationships fall at least partly within the statistical domain. If the presence of a factor increases the chances of an outcome and its absence reduces the likelihood, the factor can reasonably be considered a cause, although this could be one of several possible causes. This aspect is often overlooked, despite its relevance to interpreting medical outcomes.

'Just how much evidence is enough to conclude a cause-effect relationship?' is a crucial question that does not have a clear answer. Nonetheless, the following set of criteria is often used to infer a cause-effect relationship:

- (i) **Biological plausibility** — The strongest evidence for a cause-effect relationship arises from a biological explanation of how the presence of a factor triggers a biological response that produces the effect. This mechanism may be obscure in some

cases until it is fully explored, and the epistemic uncertainties due to incomplete knowledge may also be a limiting factor. Bellavite and Imbriano<sup>3</sup> described the biological mechanism underlying the protective effects of hesperidin, reinforcing the causal relationship between skin aging and hesperidin.

(ii) **Experimental evidence** – A clinical trial with pre-defined inclusion and exclusion criteria, and features such as randomisation and blinding, provides controlled conditions that attribute the observed effect almost exclusively to the intervention. Since clinical trials cannot ethically be conducted for factors with unknown or harmful effects, the other criteria in this list are often relied upon to infer cause-effect relationship in such cases.

(iii) **Dose-response relationship** – A cause-effect relationship is supported when a factor of greater magnitude produces a greater effect. For example, blood pressure (BP) levels and coronary events exhibit a dose-response relationship. Liu and Qiao<sup>4</sup> studied a similar relationship between sleep duration and the mediation of phenotypic age acceleration.

(iv) **Consistency** – This criterion has several facets: (a) the effect must occur across different populations where the cause exists; (b) the relationship should persist across different time periods; and most importantly; (c) under identical conditions, a specific magnitude of the cause should consistently produce a similar effect. For instance, the relationship between homocysteine levels and coronary disease was found to lack consistency and was therefore discarded as a cause (Unadkat *et al*).<sup>5</sup>

(v) **Specificity** – For a true cause-effect relationship, the absence of the factor should be associated with a reduced magnitude of the outcome, if not its complete absence. This can be viewed as extension of the dose-response concept, though the emphasis here is on absence. For example, if anaemia is absent in pregnant women, can that reasonably ensure normal birth weight?

(vi) **Statistical significance** – Empiricism is the backbone of medical research; conclusions are drawn from data-based evidence. However, all empirical studies rely on samples, as future cases cannot be included. Sampling fluctuations mean we can never be completely certain, and Type-I and Type-II errors are unavoidable. Statistical significance and adequate study power are therefore the best safeguards for keeping these errors within acceptable limits and ensuring confidence that the observed effect is real. Thus, a relationship must be statistically significant to support the conclusion that it exists.

None of these criteria alone is sufficient to conclude a cause-effect relationship. The starting point in empirical research should be the statistical significance of a correlation, association, regression, or difference between the groups. If this significance is lacking, there is no reasonable assurance that the relationship exists, and further exploration is futile. When statistical significance is achieved, one should examine alternative explanations such as bias, inappropriate study design, or confounding factors. If no alternative explanation is available, and at least four of the six criteria above are fulfilled, a cause-effect relationship may be reasonably concluded.

**Conflicts of interest:** None.

**Funding:** None.

## Conclusion

A relationship between medical factors is statistical when the change in one is accompanied by change in one or more of the others. This relationship can be spurious when it arises due to a third intervening factor. Cause-effect relationship can be concluded when it satisfies most of the criteria listed in this paper.

Abhaya Indrayan. Research Methodology and Biostatistics Series VIII – Statistical Relationship Versus Cause-Effect Relationship Between Medical Factors. MMJ. 2025, December. Vol 2 (4).

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# Expert Interview: The Future of Indian Healthcare and Medical Education

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## 1. Need for More Young Doctors and Unmet Medical Needs in India

### 1.1. India still faces a significant shortfall in doctor-patient ratios despite producing thousands of graduates each year. What are the main barriers preventing adequate doctor deployment where they're needed most?

India's doctor-patient distribution remains uneven because many young doctors choose urban centres where infrastructure, mentorship, and career growth are more robust. Rural and remote regions still have limited facilities, insufficient diagnostic support, and safety concerns, which discourage long-term postings. Additionally, limited opportunities in remote areas further contribute to the shortfall in these areas.

### 1.2. How does the NMC plan to bridge the gap between medical education output and public health needs, especially in underserved regions?

The NMC is strengthening district hospitals as teaching platforms, expanding medical seats responsibly, and aligning the curriculum with India's

epidemiological profile. By promoting primary care, community-based postings, and competency-driven learning, NMC seeks to ensure that the growing number of medical graduates is directly aligned with national health priorities, particularly in underserved regions. The NMC has introduced the District Residency Programme, wherein junior doctors must serve in district hospitals, in addition to their originally allotted postgraduate (PG) training institutions.

### 1.3. What structural reforms are being considered to ensure young doctors are not just well-trained but also motivated to serve within India's healthcare system?

Reforms focus on improving training quality through competency-based education, mentorship frameworks, structured assessments, and wellness support. We also need to create strong career opportunities for family physicians, community-care physicians, and emergency-medicine doctors to serve at Community Health Centres (CHCs) and Primary Health Centres (PHCs) level. The number of PG seats is increasing, which provides the opportunity to young doctors to be trained within the country rather than going offshore. Moreover, doctors working in government hospitals are given preference during counselling for admission to PG courses.

## 2. Doctor Training and Medical Education Reform

### 2.1. With the new competency-based curriculum, how is the NMC ensuring that graduates are not only academically competent but also clinically confident and ethically grounded?

Students get early clinical exposure and are also exposed to simulation labs. They receive training in communication skills, and ethics modules teach them professional responsibility. Through all this,

the NMC helps students gain both knowledge and practical skills as well as professionalism skills. The goal is to create confident and ethical doctors who are ready to face real medical challenges from the very beginning of their careers.

### **2.2. How can PG training programs be better aligned with the real-world healthcare challenges of India, especially in primary and family care?**

Reforms emphasise a stronger grounding in primary care, community health, emergency medicine, family medicine, and the disease patterns most prevalent in India. By integrating rotations in district hospitals and rural facilities, the NMC ensures that PG doctors gain the practical experience needed to tackle India's real epidemiological burden. Simultaneously, state governments need to create more job opportunities for them.

### **2.3. What steps is the NMC taking to reduce burnout and improve mentorship for residents and young doctors in training?**

The NMC promotes balanced residency training by regulating duty hours, encouraging wellness initiatives, strengthening grievance redressal systems, and developing faculty as mentors. The NMC has also worked to create mental health support guidelines and a framework, anti-ragging regulations to help medical students. This ensures residents receive not only technical training but also emotional and academic support throughout their demanding years of service. There is a policy for stipends to be paid to resident doctors, and NMC is very strict in ensuring compliance by medical colleges. Mental health and mentorship of resident doctors are at the top of the NMC's agenda.

## **3. Rural–Urban Divide in Healthcare**

### **3.1. Despite policy incentives, rural healthcare infrastructure still lags urban centres. What strategies can realistically attract doctors to rural service?**

Effective rural service requires a combination of robust infrastructure, better working conditions, and attractive incentives. The NMC supports policies that provide financial benefits, academic credits, career acceleration, and safe living environments to make rural postings a viable and appealing choice for young doctors. Doctors in government hospitals

serving rural postings are given credits at the time of counselling for admission to PG courses.

### **3.2. Can telemedicine and digital health be effectively leveraged to minimise this rural–urban divide without compromising quality of care?**

Telemedicine enables specialist consultations, second opinions, and continuous care delivery to remote regions. The NMC's focus is on standard protocols, digital training, and quality monitoring so that telemedicine supplements on-ground care effectively without compromising patient safety. A lot must be done in the field of telemedicine considering the recent technological advances.

### **3.3. Would the NMC support integrating rural health rotations as mandatory, meaningful training components for all medical graduates?**

The District Residency Programme is a compulsory part of PG medical training. Every MD/MS student must spend at least three months working in a district hospital during their residency. The district hospitals serve as referral centres for the rural areas. These experiences ensure every graduate understands rural health challenges and develops confidence in delivering care in diverse environments.

## **4. Expectations from Doctors in the Changing Healthcare Landscape**

### **4.1. Society today expects doctors to be not only healers but also communicators, leaders, and advocates. How should medical education evolve to prepare doctors for these multidimensional roles?**

Medical education is evolving to include leadership skills, communication training, teamwork, digital literacy, and public health awareness so that future doctors can function as clinicians, communicators, and leaders. This holistic approach prepares doctors to serve patients more effectively while contributing to healthcare system strengthening. The competency-based curriculum, and its successful implementation, will be the road map for preparing doctors for tomorrow, who will have multidimensional capabilities.

### **4.2. How can institutions strike a balance between patient satisfaction metrics and evidence-based medical decision-making?**

The NMC encourages doctors to make decisions together with their patients. It also highlights the

need for clear and honest communication. Doctors should think carefully about what is right and fair. They must consider what patients want, but they should always follow scientific evidence and good medical practice when making decisions.

## 5. Medical Ethics and Professionalism

### 5.1. In an era of commercialisation and social media influence, how can young doctors uphold medical ethics while navigating modern-day pressures?

The NMC stresses that young doctors must adhere to ethical principles, maintain professional boundaries online, and prioritise patient welfare over commercial or social pressures. Ethical awareness is embedded throughout medical training. The NMC has zero tolerance towards the use of any unethical means reported to it against medical professionals.

### 5.2. What role should the NMC play in promoting ethical behaviour and preventing professional misconduct beyond punitive measures?

The NMC promotes ethical conduct in the medical profession by focusing on training, awareness, and strong support systems. Medical students receive structured teaching on ethical values, patient rights, confidentiality, consent, and respectful behaviour. These lessons continue throughout their education so that ethics becomes a natural part of their daily practice. Continuous professional development is equally important. Doctors are expected to update their knowledge, improve their skills, and stay aware of new ethical challenges in modern medicine. Through these combined efforts, the NMC works to build a culture of trust, integrity, and lifelong professionalism across the medical community.

## 6. Scope of Artificial Intelligence (AI), Family Medicine, and Primary Care

### 6.1. How does the NMC view the integration of AI into medical training and clinical decision-making?

The NMC views AI as a helpful tool that can strengthen diagnostics, clinical decision-making, and medical learning. AI can support doctors by improving accuracy, speeding up analysis, and offering useful insights during patient care. However, the NMC emphasises that AI should only assist — not replace — the clinician. The core principle remains that human decision-making must always guide patient care, with AI serving only as a supportive aid.

### 6.2. Family Medicine is gaining global importance as the backbone of healthcare systems. How does NMC plan to strengthen and popularise this discipline in India?

Family Medicine plays a key role in India's primary healthcare system, as it focuses on continuous, comprehensive, and person-centred care. Recognising this, the NMC has taken several steps to strengthen the specialty. It is increasing PG seats in Family Medicine to ensure more trained specialists are available across urban and rural areas. Efforts are being made to promote Family Medicine as a respected and vital specialty that offers broad clinical skills and serves as the foundation of an effective healthcare system.

### 6.3. Can AI and Family Medicine complement each other to improve continuity of care and population health outcomes?

AI has the potential to greatly strengthen the work of family physicians by improving how they manage chronic diseases, deliver preventive care, and monitor community health trends. With AI-based tools, doctors can track patient data more accurately, identify early warning signs, and customise treatment plans based on each patient's needs. However, a lot remains to be done in this field.

## 7. Job Opportunities and Reverse Brain Drain

### 7.1. With many Indian doctors working abroad, what measures can encourage the reverse migration of skilled professionals back to India?

India is improving its medical system by upgrading hospitals, building more medical colleges, and increasing facilities so that doctors have better places to work. The country is also creating more chances for medical research in areas like technology, public health, and new treatments. The corporate hospitals are providing an excellent career pathway to doctors returning back to India. To make it easier for Indian doctors abroad to return, the rules for registration and practice are being made simpler. NMC is committed to building an environment where returning doctors feel welcome, supported, and able to grow in their careers.

### 7.2. How can the healthcare ecosystem create meaningful job opportunities and career growth for young doctors, especially beyond tertiary care hospitals?

New fields like digital health, public health, emergency medicine, and medical research are creating many different career paths for young doctors in India. These areas offer exciting opportunities to work with new technologies, improve community health, respond to emergencies, and contribute to scientific discoveries.

## 8. Message to the Future Generation of Doctors

### 8.1. What message would you like to share with young medical students and residents who are passionate but often disillusioned by systemic challenges?

The NMC encourages young doctors to stay kind, honest, and committed to learning throughout their careers. Medicine is challenging, and doctors often face long hours, tough decisions, and high expectations. But even with these difficulties, young doctors are essential to building a stronger and healthier India. Their skills, compassion, and dedication directly shape the future of the country's healthcare system. The NMC is committed to supporting them by improving training, creating better opportunities, and ensuring they have the guidance they need. The goal is to help every young doctor grow with confidence and contribute positively to patients and society.

### 8.2. How can the next generation of doctors contribute to rebuilding public trust in the medical profession?

Trust between doctors and patients grows when doctors explain things clearly, act honestly, and always put the patient's well-being first. Good communication helps patients feel safe, while ethical behaviour strengthens their confidence in medical care. The NMC encourages future doctors to stay transparent in their decisions, treat every patient with compassion, and maintain high professional standards.

## 9. Medico-Legal Challenges (with Professional Perspective)

### 9.1. Medico-legal cases have become a major concern for doctors, often leading to defensive medicine. What reforms do you think are needed to protect both patients and doctors?

The NMC believes that clear and uniform medico-legal rules are essential to protect both doctors and patients. Better documentation helps ensure transparency and accuracy in medical decisions. The NMC also supports stronger safety and protection measures for doctors so they can work without fear of violence or unfair blame. These steps aim to reduce defensive medicine, improve trust, and make the system fairer for everyone involved.

### 9.2. How can NMC and the legal system collaborate to ensure fair investigation processes and clear medical jurisprudence standards?

The NMC believes that medico-legal cases must be handled in a fair, timely, and transparent way across the entire country. To achieve this, the NMC advocates common training programs where doctors, police, and legal professionals learn the same guidelines and procedures. This helps everyone understand their roles clearly and reduces confusion. The NMC also promotes uniform forensic standards so that post-mortems, medical reports, and evidence collection follow the same quality everywhere.

### 9.3. Would you support a national mechanism for medico-legal mediation to reduce unnecessary litigation and restore doctor-patient trust?

The NMC supports creating a national system for medico-legal mediation so that disputes between doctors and patients can be resolved quickly and fairly. Instead of going straight to court, mediation allows both sides to talk openly, understand each other's concerns, and reach an agreeable solution with the help of a trained mediator. This reduces unnecessary lawsuits, saves time and stress, and keeps the focus on healing relationships rather than conflict.

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# Max Institute of Medical Education Announcements

December – 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 each medical, nursing, and paramedical professionals gain the confidence to use their skills with practised ease, maintaining the highest standards in an environment that is also safe for the patients.

## CREATING THE NEXT GENERATION OF LEADERS IN HEALTHCARE

**10,000**

Students Trained Annually

**800**

Faculty Members

**150**

Courses, including Offline and Online

## CORE ELEMENTS OF OUR TRAINING



Extensive Practical Training



World-Class Faculty



Customised Training



Online Library - Elsevier Clinical Key



Simulation Lab



Learning Management System

# DELIVERING UNPARALLELED QUALITY IN MEDICAL EDUCATION

## DIPLOMATE OF NATIONAL BOARD (DNB)

Max Healthcare Institute Ltd. is recognised by the National Board of Examinations to permit practical training for students undergoing courses of DNB broad and super-specialities in India in over 40 disciplines. At present, we have 618 DNB residents in our group of network hospitals.

## INTERNATIONAL AFFILIATED PROGRAMMES



### INTERNAL MEDICINE TRAINING – IMT (MRCP-UK)

A 3-year full-time post-graduate 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.

#### TRAINING LOCATION:

- Max Super Specialty Hospitals – Delhi and Mumbai

**ADMISSION IS OPEN FOR THE NEW SESSION FY 2025**



### 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, membership of the RCOG (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.

**KEY HIGHLIGHTS:** We have launched RCOG-MHC Obstetrics & Gynaecology Programme (RCOG) at Max Super Speciality Hospital, Lucknow, UP.

#### TRAINING LOCATION:

- Max Super Specialty Hospitals – Delhi and Lucknow

**ADMISSION IS OPEN FOR THE NEW SESSION FY 2025**



### 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 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.

## 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 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 & Robotic Surgery
- Women's Imaging and more

## Open Fellowships

Location	Department	Doctors
Max Super Speciality Hospital, Nagpur	Arthroplasty, Arthroscopy and Complex - Trauma	Dr. Manoj Pahukar
Max Super Speciality Hospital, Patparganj	Interventional Radiology	Dr. Jitender Singh
Max Super Speciality Hospital, Lucknow	Advanced Laparoscopic & Robotic GI Surgery	Dr. Ajay Kumar Yadav
Max Super Speciality Hospital, Patparganj	Medical Oncology	Dr. Meenu Walia
Max Hospital, Gurugram	Endoscopic Sinus, Microscopic Ear & Sleep Surgery	Dr. Ravinder Gera
Max Super Speciality Hospital, Vaishali	Musculoskeletal Imaging	Dr. Anuradha Sural
Max Super Speciality Hospital, Vaishali	Onco & Robotic Anaesthesia	Dr. Arun Puri
Max Super Speciality Hospital, Saket	Neuro Critical Care Medicine	Dr. Omender Singh
Max Smart Super Speciality Hospital, Saket	Robotics Urology & Renal Transplant	Dr. PP Singh
Max Super Speciality Hospital, Mohali	Joint Replacement Surgery	Dr. Jatinder Singla
Max Super Speciality Hospital, Shalimar Bagh	Minimal Invasive & Robotic Surgery	Dr. KK Trehan
Max Smart Super Speciality Hospital, Saket	Minimally Invasive Laparoscopic & Robotic Gynaecological Surgery	Dr. Usha M Kumar
Max Super Speciality Hospital, Vaishali	Head & Neck Onco-Surgery	Dr. Pawan Gupta
Max Super Speciality Hospital, Shalimar Bagh	Endo-Urology & Renal Transplant	Dr. Waheed Zzaman
Max Super Speciality Hospital, Patparganj	Respiratory Critical Care	Dr. Praveen Kumar Pandey
Max Super Speciality Hospital, Saket	Emergency Medicine	Dr. Anupam Ranjan
Max Smart Super Speciality Hospital, Saket	Endo-Urology & Renal Transplant	Dr. PP Singh
Max Super Speciality Hospital, Lucknow	Robotic Endo-Urology & Renal Transplant	Dr. Rahul Yadav
Max Super Speciality Hospital, Vaishali	Musculoskeletal Oncology	Dr. Vivek Verma
Max Super Speciality Hospital, Patparganj	Endo-Urology & Robotic Urology	Dr. Pawan Kesarwani
Max MedCentre, Lajpat Nagar	Medical Oncology	Dr. Pramod Kumar
Max Super Speciality Hospital, Saket	Onco & Robotic Anaesthesia	Dr. Raj Tobin
Nanavati Max Super Speciality Hospital, Mumbai	Neuro Imaging	Dr. Deepak Patkar
Nanavati Max Super Speciality Hospital, Mumbai	Musculoskeletal Imaging	Dr. Deepak Patkar
Max Hospital, Gurugram	Medical Oncology	Dr. Bhuvan Chugh
Max Super Speciality Hospital, Saket	Breast Onco-Surgery	Dr. Aditi Chaturvedi
Max Super Speciality Hospital, Vaishali	Interventional Radiology	Dr. Ritu Verma

Location	Department	Doctors
Max Super Speciality Hospital, Mohali	Joint Replacement	Dr. Jatinder Singla
Max Super Speciality Hospital, Patparganj	Maxillofacial Trauma	Dr. Manoj Johar
Max Super Speciality Hospital, Vaishali	Onco & Robotic Anaesthesia	Dr. Arun Puri
Max Super Speciality Hospital, Noida 128	Joint Replacement - Arthroplasty	Dr. Gaurav Rathore
Max Super Speciality Hospital, Noida 128	Joint Replacement - Arthroplasty	Dr. Sumit Bhushan Sharma
Max Super Speciality Hospital, Noida 128	Joint Replacement - Arthroplasty	Dr. B S Murthy
Max Super Speciality Hospital, Dwarka	Neuro Imaging	Dr. Kanika Sethi
Max Super Speciality Hospital, Dwarka	Interventional Radiology	Dr. Prashant Garg
Max Super Speciality Hospital, Dehradun	Cardiac Sciences	Dr. Preeti Sharma
Max Super Speciality Hospital, Dehradun	Joint Replacement, Arthroscopy, & Sports Injury	Dr. Vineet Tyagi
Max Super Speciality Hospital, Dehradun	Radiology	Dr. Mohammed Kashif/ Dr. Pradeep Kumar Roul

## Doctor of Philosophy (Ph.D.)

MIME, affiliated to the Academy of Scientific and Innovative Research (AcSIR) (An Institution of National Importance established by an Act of Parliament, Govt. of India) announces Ph.D. Admissions – January 2026.

Shape the future of healthcare with Max Healthcare's sponsored Ph.D. Research Program in Medical Research, Public Health, and Biological Sciences.

## Post-Graduate (PG) Diploma & Master of Science (M.Sc.) Course

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:

- **PG Diploma & Master of Public Health** certified by the Academy of Scientific and Innovative Research (AcSIR).
- **PG Diploma & Master of Healthcare Quality Management** certified by AcSIR.
- **PG Diploma in Clinical Research** certified by the Regional Centre for Biotechnology (RCB).
- **PG Diploma in AI in Healthcare** in collaboration with Bennet University.

**Minimum Eligibility:** Bachelor's degree/Graduation in science.

**Duration:** 1 year for PG Diploma & 2 years for M.Sc.

## 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 the criteria set by the department. Observerships are customised training programs designed to develop the skills and knowledge of medical graduates, allowing them to learn as an observer.

## Internships

Internships are provided to expose the students to the industry and give them 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: Dec 2025

#### • **Max Super Speciality Hospital, Saket**

1<sup>st</sup> Dec: BLS Provider  
2<sup>nd</sup>/3<sup>rd</sup> Dec: ACLS Provider (Traditional)  
18<sup>th</sup> Dec: BLS Instructor  
19<sup>th</sup> Dec: ACLS Instructor  
22<sup>nd</sup> Dec: BLS Provider  
22<sup>nd</sup>/23<sup>rd</sup> Dec: ACLS Provider

#### • **Max Super Speciality Hospital, Nagpur**

2<sup>nd</sup> Nov: BLS Provider  
8<sup>th</sup> Nov: BLS Provider  
9<sup>th</sup>/10<sup>th</sup> Nov: ACLS Provider (Traditional)  
18<sup>th</sup> Nov: BLS Provider  
22<sup>nd</sup> Nov: BLS Provider  
23<sup>rd</sup>/24<sup>th</sup> Nov: ACLS Provider (Traditional)  
26<sup>th</sup> Aug: BLS Provider

## Bespoke/Certificate Courses

MIME provides upskilling for physicians and other healthcare professionals through various short-term courses. All our workshops and courses are conducted by experienced and knowledgeable faculty. We have a well-equipped high-fidelity simulation lab with state-of-the-art training manikins to help conduct these courses.

List of short-term training schedules in Dec 2025:

Name of the Course	Duration	Eligibility
<b>Certificate Course in Essentials of Cardiac Nursing</b>	3 months online; 1 day in-person	General nursing and midwifery (GNM)/B.Sc. Nursing/M.Sc. Nursing with clinical experience. Nurses posted in cardiac intensive care unit (ICU), coronary care unit (CCU), catheterisation laboratory (cath lab), and cardiology wards.
<b>Certificate Course in Echocardiography</b>	3 months online; 1 day in-person	Medical professionals such as cardiac sonographers and other healthcare practitioners, with an appropriate B.Sc. or Diploma, are eligible to apply. Final year students in MBBS and International medical students may also apply.
<b>Paediatric Cardiac CT</b>	8 weeks	Doctor of medicine (MD)/DNB/Diploma in medical radiodiagnosis (DMRD).
<b>Mammography Reporting</b>	8 weeks	MD/DNB/DMRD in Radiodiagnosis.
<b>Liver Transplant Donor Evaluation Imaging</b>	3 days	MD/DNB/DMRD in Radiodiagnosis.
<b>Advanced Course in Endoscopic Gynaecological Surgery</b>	3 days	MD, MRCOG, or DNB qualification, along with mandatory DMC registration.

# Foreign Medical Graduate (FMG) Clinical Skills Courses

These courses enable the 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. It has been our experience that sufficient hands-on training and clinical exposure can lead to success in the Foreign Medical Graduate Examination (FMGE). 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:** FMG

**Duration:**

- **Basic** – 15 Days
- **Advanced** – 20 Days
- **Batch Commencement** – Jan 2026

## MIME Online Courses

MIME brings online training courses for healthcare professionals – 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    Online Certificate Courses

<ul style="list-style-type: none"> <li>● Diabetes Management</li> <li>● Infectious Disease</li> <li>● Emergency Medicine</li> <li>● Critical Care</li> <li>● Clinical Cardiology</li> <li>● Bariatric Anaesthesia</li> <li>● Management of Liver Disorder</li> </ul>	<ul style="list-style-type: none"> <li>● Aesthetic Medicine and Surgery</li> <li>● Healthcare Quality Management</li> <li>● Public Health</li> <li>● Clinical Research</li> <li>● Bariatric Nutrition</li> <li>● Acute Liver Failure (ALF)</li> <li>● Geriatrics Care</li> <li>● Difficult Airway Management</li> </ul>
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## 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 Speciality 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.  
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