Case Report

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Anaesthesia Section

Segmental Spinal Anaesthesia Combined with TAP Block for Caesarean Section in a Patient with Eisenmenger Syndrome: A Case Report

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ABSTRACT

Pregnancy in patients with Eisenmenger Syndrome (ES) is associated with extremely high maternal and foetal morbidity and mortality, and anaesthetic management for caesarean section is particularly challenging because of fixed pulmonary hypertension, right-to-left shunting, and limited cardiovascular reserve. Present case report is of a 35-year-old gravida 3 with two previous abortions, diagnosed with ES, who presented at 35 weeks of gestation for elective caesarean section due to severe oligohydramnios and intrauterine growth restriction. Cardiac evaluation revealed a large Ventricular Septal Defect (VSD) with Patent Ductus Arteriosus (PDA) and bidirectional shunting, moderate-to-severe Tricuspid Regurgitation (TR), left ventricular systolic dysfunction with an ejection fraction of 45%, secondary polycythaemia, thrombocytopenia, and baseline oxygen saturation of 84% on room air. Following detailed multidisciplinary planning, segmental spinal anaesthesia was administered using low-dose isobaric ropivacaine with fentanyl under invasive haemodynamic monitoring. A prophylactic noradrenaline infusion was commenced to maintain Systemic Vascular Resistance (SVR) and prevent hypotension. Caesarean delivery was completed uneventfully with stable maternal haemodynamic throughout the procedure. A low-birth-weight neonate was delivered and managed in the Neonatal Intensive Care Unit (NICU). Postoperative analgesia was provided using bilateral Transversus Abdominis Plane (TAP) block, allowing effective pain control without significant haemodynamic compromise. The patient was monitored in a cardiac intensive care unit and had an uneventful postoperative course before discharge in stable condition. This case demonstrates that with meticulous multidisciplinary planning, invasive monitoring, judicious fluid administration, early vasopressor support, and low-dose segmental spinal anaesthesia, caesarean section can be safely accomplished in carefully selected patients with ES. However, pregnancy in ES remains extremely high risk and should to be strongly discouraged.

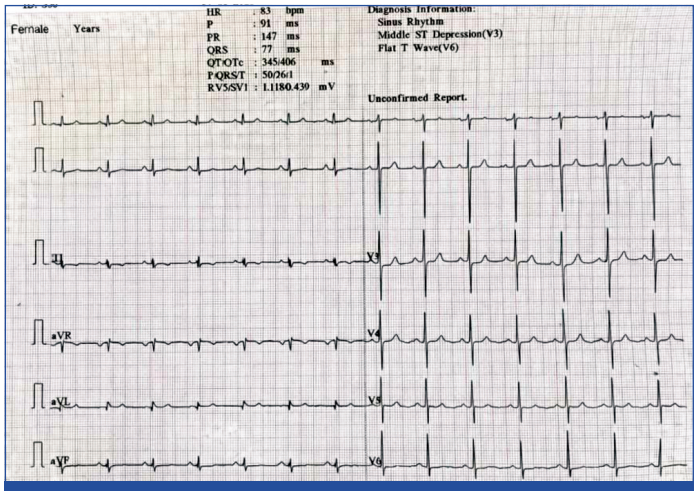
Keywords: Congenital heart disease, Maternal and foetal mortality, Pregnancy, Regional anaesthesia

CASE REPORT

A 35-year-old pregnant female, weighing 50 kg and measuring five feet four inches in height (Gravida 3, Abortion 2), classified as American Society of Anaesthesiologists (ASA) Physical Status IV was admitted to a tertiary care centre at 35 weeks of gestation for an elective caesarean section in view of severe oligohydramnios, severe intrauterine growth restriction, and colour Doppler showing absent diastolic flow. Four years ago, the patient had presented with haemoptysis and subsequently underwent routine investigations. Her haemoglobin was found to be 18 g/dL, prompting a cardiac work-up. She was then diagnosed for the first time with ES (2D Echocardiography: large perimembranous VSD of 19 mm with bidirectional shunt, large PDA bidirectional, dilated right atrium and ventricle, and moderate pulmonary hypertension). Based on these findings, the patient was categorised as World Health Organisation (WHO) pregnancy risk class IV [1]. She conceived subsequently and suffered two missed abortions, occurring subsequently three and two years, respectively before the present pregnancy. She was advised not to conceive and was prescribed Tab Tide Plus once daily (OD), Tab Ambrisentan OD, and Cap Autrin OD, with instructions for regular follow-up. However, she presented again with pregnancy, refused termination, and opted to continue. She was advised to discontinue her previous medication and instead start Tab Sildenafil 25 mg three times daily (TDS) and Tab Labetalol 100 mg TDS from the second trimester.

On examination, the patient was noted to have cyanotic fingertips, grade 2 clubbing, and New York Heart Association (NYHA) grade II symptoms [2]. Her pulse rate was 104/min, blood pressure 144/92 mmHg, respiratory rate 22/min, and oxygen saturation 84% on room air. Airway and back and spine was normal in examination. On auscultation, a pansystolic murmur grade 3/6 with a loud P2 was present at the aortic and pulmonary area, with no added sounds in either lung. Electrocardiography (ECG) showed Right Bundle Branch Block (RBBB) in lead III and aVF and T wave inversion in lead III [Table/Fig-1].

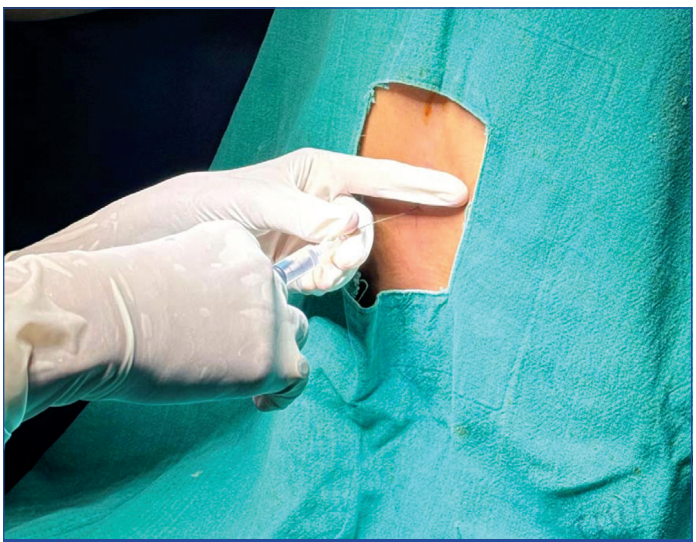
Two-dimensional echocardiography revealed a large VSD 16 mm (earlier records noted 19 mm, likely due to differences in imaging plane and interobserver variability), with bidirectional shunt, large PDA with bidirectional flow, mildly dilated right atrium and ventricle, moderate to



[Table/Fig-1]: Preoperative Electrocardiography (ECG) of the patient.

severe TR, left ventricular global hypokinesia, Left Ventricular Ejection Fraction (LVEF) 45%, and low systemic saturation. Her haemoglobin was 18.4 g/dL, with a haematocrit of 55.3% and platelet count of 80,000/mm^3. The remaining investigations were within normal limits. An elective caesarean section was scheduled after six hours of fasting in view of impending foetal distress, the mother's underlying cardiac disease, and the patient's refusal to consent for vaginal delivery after detailed counselling, to ensure timely and appropriate maternal and foetal management. Continuous maternal and foetal monitoring was maintained during the fasting period, with preparations in place to proceed as an emergency if required. High-risk written informed consent was obtained and explained to patient and her relative. The advantages of regional (segmental spinal) anaesthesia and the reasons for selecting this technique were explained to the patient, and her cooperation was requested. Platelet concentrates were arranged and made available prior to surgery. Inj. pipzo 1.5 gm i.v. (single dose) was administered to patient one hour prior to surgery for prophylaxis of infective endocarditis.

Intraoperative management: The patient was shifted to the operating room, and multiparameter monitors were attached and started oxygen at 4 litres per minute was started via facemask. One intravenous access was secured in right forearm with 18G cannula. She was premedicated with Inj. ondansetron 8 mg i.v. and Inj. Ranitidine 50 mg i.v. and started on a slow infusion of Ringer's lactate. Under aseptic precautions, a left radial arterial line was inserted under local anaesthesia for continuous invasive blood pressure monitoring. A right internal jugular central venous catheter was also placed under local anaesthesia for central venous pressure–guided fluid management, and a Foley urinary catheter was inserted for continuous urine output monitoring. Under aseptic precaution, segmental spinal anaesthesia was given in the sitting position with 27 G spinal needle in the midline at the T9-10 level. After free flow of clear Cerebrospinal Fluid (CSF), Inj. Ropivacaine isobaric 0.75% 1mL+Inj. fentanyl 0.2mL= total 1.2mL) was administered [Table/Fig-2].



[Table/Fig-2]: The patient underwent segmental spinal anaesthesia.

The patient was positioned supine after spinal anaesthesia. After a careful risk-benefit assessment and haematology consultation, the patient with thrombocytopenia (platelet count 80,000/mm^3) received one unit (~65 mL) of platelet concentrate intraoperatively after confirmation of spinal anaesthesia effect and haemodynamic stability, the transfusion was uneventful. The level of anaesthesia achieved was between T6 and L1. Regular beat to beat invasive blood pressure and ECG monitoring was done. Although there was no episode of severe hypotension but prophylactic infusion of Inj. noradrenaline was started at 8 ug/minute to keep Mean Arterial Pressure (MAP) 55-60 mm Hg. Heart rate remained stable between beats 70-100 per minute without any arrhythmias [Table/Fig-3].

A single live female infant weighing 900 gram was delivered but did not cry immediately after birth. The newborn was intubated and shifted to the NICU for further resuscitation. Inj. oxytocin i.v. 20 unit was given slowly after delivery of baby while carefully monitoring blood pressure and heart rate. Total intraoperative input was 200 mL ringer lactate and 100 mL dextrose normal saline along with 65 mL, platelet concentrate with 100 mL urine output. Total duration of surgery was 45 minutes.

At the end of the surgery, a bilateral landmark-guided Transverse Abdominis Plane (TAP) block was performed for postoperative analgesia after regression of the spinal sensory block to the T10 dermatome, ensuring accurate identification of tissue planes and avoiding interference from residual spinal anaesthesia. With the patient in the supine position and under strict aseptic precautions, the lumbar triangle of Petit was identified. The needle insertion point was located at the mid-axillary line between the lower costal margin and the iliac crest. A 23-gauge, 1.5-inch blunt-tipped needle was advanced perpendicular to the skin using the loss-of-resistance technique. Two distinct "pops," corresponding to penetration of the external and internal oblique muscles, confirmed correct needle placement within the TAP plane. After negative aspiration, 20 mL of 0.75% isobaric ropivacaine was administered on each side. The procedure was well tolerated, with no immediate complications [Table/Fig-4].

The noradrenaline infusion was tapered and then stopped and blood pressure was monitored for any incidences of hypotension. Patient was shifted to Intensive Cardiac Care Unit (ICCU) for observation, the effect of TAP block was assessed and arterial line was removed carefully after few hours.

As per the cardiologist's opinion, her cardiac medications were resumed once oral intake was initiated, and postoperative analgesia was maintained with oral paracetamol 500 mg TDS after regression of the TAP block effect, which lasted approximately eight hours. The mother remained haemodynamically stable and was shifted to the ward on the third postpartum day; however, on the third postoperative day, the patient's neonate succumbed despite intensive supportive care. The patient was discharged on the fifth postoperative day and subsequently returned to her native place, after which she did not report for further follow-up, limiting the availability of long-term maternal outcome data.

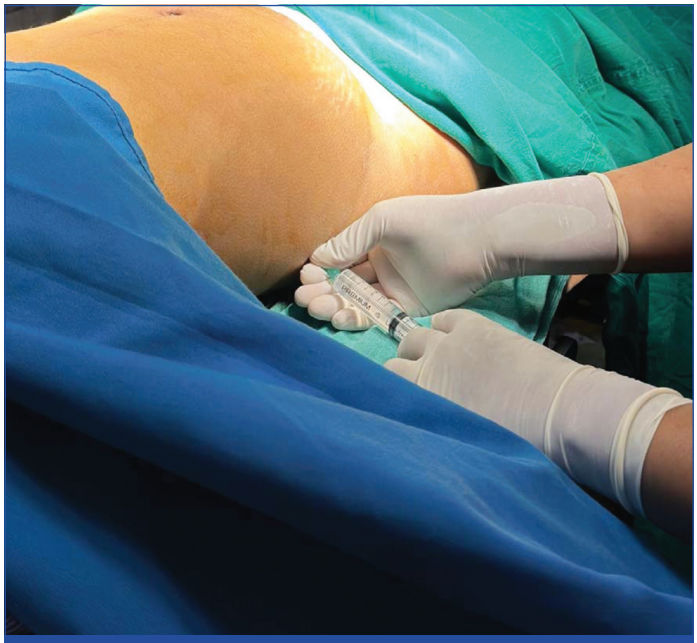
DISCUSSION

The ES is characterised by markedly elevated pulmonary vascular resistance with consequent reversal of shunt flow, resulting in right-to-left shunting through a systemic-to-pulmonary circulation connection [3]. The underlying pathophysiology involves a chronic right-to-left shunt through a large systemic-to-pulmonary communication-most commonly a VSD or PDA -leading to progressive pulmonary vascular remodelling, fixed pulmonary hypertension, and sustained elevation of pulmonary vascular resistance [3]. In 1897, Victor Eisenmenger first described this condition in a 32-year-old man with a large VSD and advanced pulmonary vascular disease, after which the syndrome was eponymously named [4].

Pregnancy in women with ES remains a formidable clinical challenge, associated with substantial maternal and foetal morbidity and mortality. Published series report maternal mortality rates ranging from 30-50%, with mortality increasing to 50-65% among those undergoing caesarean section [4]. The profound haemodynamic adaptations of normal pregnancy-including expansion of plasma volume, increased cardiac output, reduction in SVR, and the abrupt circulatory changes occurring at delivery due to uterine autotransfusion and shifts in preload and afterload-can exacerbate right-to-left shunting, worsen hypoxaemia, precipitate right ventricular failure, and provoke life-threatening arrhythmias. Additionally, the chronic hypoxaemia-induced polycythaemia commonly observed in ES increases blood viscosity, thereby predisposing patients to thromboembolism and end-organ dysfunction [4,5].

Haemodynamic parameters	Before surgery in preop area	Before segmental spinal anaesthesia	After segmental spinal anaesthesia	After baby delivery	After closure of uterus	End of the surgery	After TAP block	Shifted to ICCU	After 24 h
IBP (mmHg)	155/101	150/89	143/84	110/74	100/70	110/76	112/73	118/78	128/85
HR (beats/min)	90	95	88	84	82	80	77	85	80
SpO_2 (%)	82 (on Room Air)	91 (with O_2)	90 (with O_2)	90 (with O_2)	88 (with O_2)	90 (with O_2)	88 (with O_2)	89 (with O_2)	85 (with O_2)
RR (breaths/ min)	22	22	20	20	20	18	18	20	18
CVP (cmH_2O)	10	10	9	9	9	8	9	10	9
Urine output (mL)	-	30	40	65	88	100	110	130	700

[Table/Fig-3]: Haemodynamic parameters of patient.
IBP: Invasive blood pressure; HR: Heart rate; SpO_2: Peripheral capillary oxygen saturation; RR: Respiratory rate; CVP: Central venous pressure; O_2: oxygen; TAP block: Transversus abdominis plane block; ICCU: Intensive cardiac care unit; mL: millilitres; hrs: hours
Urine output was recorded at predefined intraoperative and postoperative time points after insertion of a Foley urinary catheter. Data for the preoperative time point are not available as catheterisation was not performed in the preoperative area.



[Table/Fig-4]: Postoperative analgesia was provided using a bilateral TAP block.

From a foetal perspective, ES is associated with high rates of prematurity, intrauterine growth restriction, low birth weight, and increased neonatal morbidity and mortality [4,6]. Owing to these substantial risks, most authorities strongly recommend effective contraception and advise against pregnancy in women with ES, with early termination often advocated when pregnancy occurs. In a retrospective case series from West China, only one of eleven pregnancies progressed to term; maternal mortality reached 36%, and foetal complications-including preterm delivery, small-for-gestational-age infants, and foetal or neonatal death-were frequent [6]. Nevertheless, isolated reports describe successful pregnancies and deliveries when managed with meticulous, multidisciplinary planning and close monitoring [3,7].

Regional anaesthesia may result in a reduction in SVR, which can aggravate right-to-left shunting and thereby worsen hypoxaemia. Lumbar neuraxial techniques carry a potential risk of spinal haematoma, particularly in patients with altered coagulation profiles. Epidural anaesthesia, when carefully titrated, has no specific additional risks declared in this context. General anaesthesia is associated with multiple haemodynamic and respiratory concerns, including decreased venous return and cardiac output, reduced SVR, exacerbation of right-to-left shunting, deterioration in oxygen saturation, and the potential for difficult extubation in the postoperative period. In contrast, segmental spinal anaesthesia, when carefully titrated, has no specific additional risks declared in this context [4].

Published reports on anaesthetic management of parturient with congenital heart disease complicated by severe pulmonary hypertension or Eisenmenger physiology reveal heterogeneity in practice, reflecting the delicate balance required between maternal haemodynamic stability and adequate surgical anaesthesia [Table/Fig-5] [3,7-12]. Earlier studies often favoured general anaesthesia, particularly in patients with severe hypoxaemia or advanced symptoms, as reported by Fang G et al., and Hong S et al., [8,12]. Regional anaesthetic techniques- particularly graded epidural anaesthesia- have been increasingly reported in parturients with ES, as demonstrated by Rathod S and Samal SK, Fang G et al., and Zhang Y et al., [7,8,11]. Given the competing risks of haemodynamic instability, several authors advocate the use of slow, incremental, low-dose neuraxial techniques, including graded spinal anaesthesia, and Combined Spinal-Epidural (CSE), performed under invasive haemodynamic monitoring with careful fluid titration and readiness to support systemic blood pressure using vasopressors [3,9,10]. Gehlot RK et al., reported the successful use of low-dose sequential CSE anaesthesia for caesarean delivery in a parturient with ES, achieving minimal haemodynamic disturbance and a favourable foetal outcome [3]. Similarly, Tanuwijaya TM and Aryasa T, described successful low-dose spinal anaesthesia with bupivacaine and fentanyl, supplemented by a norepinephrine infusion, in a 25-week pregnant patient with ES [9]. More recently, segmental spinal anaesthesia has emerged as an alternative regional technique; YanYangste SN and Kalyanasundram K, reported the use of thoracic segmental spinal anaesthesia in a patient with a large VSD and severe pulmonary hypertension [10].

Anaesthetic management of parturients with ES undergoing caesarean section poses a significant clinical challenge, as both general and regional anaesthetic techniques are associated with substantial risks. General anaesthesia avoids abrupt sympathetic blockade and sudden reductions in SVR; however, positive-pressure ventilation may impair venous return, reduce cardiac output, and exacerbate right-to-left shunting. In addition, laryngoscopy and tracheal intubation can trigger catecholamine surges, further contributing to haemodynamic instability [8]. Conversely, neuraxial techniques such as spinal or epidural anaesthesia carry the risk of rapid sympathetic blockade, leading to a decrease in SVR, increased shunt fraction, and worsening hypoxaemia [4]. These risks are further amplified by pregnancy-related physiological changes, which can exacerbate pulmonary hypertension and ventricular dysfunction in patients with ES.

In view of these considerations, segmental thoracic spinal anaesthesia was selected as it permits a precise and limited neuraxial block with superior haemodynamic control. In the present case, a low volume of 0.75% isobaric ropivacaine combined with 10 µg fentanyl was administered at the lower thoracic level. The use of an isobaric local anaesthetic ensures that drug spread remains largely independent of patient positioning, while ropivacaine is associated with greater cardiovascular stability compared with bupivacaine. Administration of 1.2 mL of isobaric ropivacaine with fentanyl resulted in a confined sensory block extending approximately three to four dermatomes above and below the injection site, with relative sparing of the lumbosacral segments. This targeted sympathetic blockade minimises venous pooling in the lower limbs, preserves

Author	Anomaly	Age (years)	Gestational age	Symptoms	Anaesthetic management
Gehlot RK et al., 2021 [3]	Non restrictive perimembranous Ventricular Septal Defect (VSD) with a size of 32 mm with bidirectional shunt, severe MR, severe TR, and moderate PR	24	30th week	Sporadic history of dyspnoea, and it progressively increased in the last 15 days	Combined spinal and epidural anaesthesia with invasive arterial pressure monitoring and central pressure monitoring.
Rathod S and Samal SK, 2014 [7]	Biventricular hypertrophy and echocardiography reported large perimembranous VSD with severe Pulmonary Artery Hypertension, Tricuspid Regurgitation (TR) and bidirectional shunt with ejection fraction 40%	27	34th week 4th day	Pedal oedema of one month duration and history of breathlessness on exertion for past three years	Epidural anaesthesia with central pressure monitoring.
Fang G et al., 2011 [8]	1) 13 mm VSD with prominent right-to-left shunt, dilated right atrium (55 mm) and right ventricle (48 mm), right ventricular hypertrophy (12 mm), moderate-to-severe Tricuspid Regurgitation (TR), estimated systolic pulmonary artery pressure of 107 mmHg, and an estimated Left Ventricular Ejection Fraction (EF) of 74%	19	33 weeks	Severe fatigue, progressive cough, and shortness of breath nine days prior to admission	General anaesthesia.
	2) 20 mm VSD with bidirectional blood flow at rest, enlarged left ventricle (54 mm), mild dilation of the right atrium, hypertrophy of the right ventricle, mild tricuspid regurgitation, estimated systolic pulmonary artery pressure of 166 mmHg, mild pericardial effusion, and an estimated left ventricular EF of 61%	30	33 weeks	Asymptomatic	Epidural anaesthesia with CVP monitoring
Tanuwijaya TM and Aryasa T, 2024 [9]	Dilated RA-RV, LV concentric remodelling, EF BP 85%, TAPSE 1.9 cm; D-shaped LV, severe TR with high probability of pulmonary hypertension, moderate pulmonal regurgitation, mPAP 48 mmHg, eRAP 3 mmHg, ASD secundum R-L shunt measuring 2.2 cm with a diagnosis of Eisenmenger Syndrome (ES)	25	34 weeks	Shortness of breath since three months of gestation	Low dose of lumbar spinal anaesthesia
YanYangste SN and Kalyanasundram K, 2022 [10]	Echo showed a large perimembranous VSD, bidirectional shunt, adequate left ventricular function, severe pulmonary hypertension (RVSP-73 mmhg), RARVdilated, valves normal, no clot.	22	34-35 week	Patient had exertional dyspnoea from 24th week of pregnancy but otherwise able to take care of her daily activities	Thoracic segmental spinal anaesthesia.
Zhang Y et al., 2023 [11]	Transthoracic echocardiography (TTE) revealed the occlusion (manifesting as a stronger echo) between the descending aorta and pulmonary artery	38	22 weeks	Asymptomatic	Epidural anaesthesia with CVP monitoring.
Hong S et al., 2023 [12]	Echocardiogram showed a large ASD measuring 30 mm with bidirectional and mainly right-to-left shunt, severe pulmonary hypertension with a systolic pressure of 135 mmHg, moderate TR, and LVEF of 67%.	32	36 weeks	Hypoxic with an oxygen saturation (SpO_2) of 72% on ambient air and digital clubbing.	General anaesthesia.

[Table/Fig-5]: Published case reports describing anaesthetic management of parturients with congenital cardiac defects complicated by pulmonary hypertension or Eisenmenger physiology [3,7-12].
ASD: Atrial septal defect; VSD: Ventricular septal defect; MR: Mitral regurgitation; TR: Tricuspid regurgitation; PR: Pulmonary regurgitation; RA: Right atrium; RV:Right ventricle; LV: Left ventricle; EF:Ejection fraction; LVEF:Left ventricular ejection fraction; PAH:Pulmonary arterial hypertension; sPAP:, Systolic pulmonary artery pressure; mPAP: Mean pulmonary artery pressure; RVSP: Right ventricular systolic pressure; CVP:Central venous pressure; TTE:Transthoracic echocardiography; TAPSE: Tricuspid annular plane systolic excursion; SpO_2: Peripheral oxygen saturation; R-L:Right-to-Left.

venous return, and reduces the risk of hypotension. Consequently, segmental thoracic spinal anaesthesia was considered the most appropriate technique to provide adequate surgical anaesthesia while maintaining haemodynamic stability in this high-risk cardiac patient [9,10].

In conjunction with invasive arterial and central venous pressure monitoring, cautious fluid administration, and prophylactic noradrenaline infusion to maintain MAP, this strategy was consistent with established haemodynamic principles. The technique provided stable intraoperative haemodynamics, maintained acceptable oxygen saturation (SpO_2 approximately 88-91%), and facilitated timely delivery with minimal blood loss and limited fluid shifts-factors that are critical in preventing an increase in right-to-left shunt and avoiding cardiovascular decompensation [11].

Furthermore, postoperative analgesia achieved with a bilateral TAP block likely contributed to effective pain control without the need for high-dose systemic opioids or repeated sympathetic stimulation, thereby minimising fluctuations in systemic and pulmonary vascular resistance during the vulnerable postpartum period [13]. Several authors, including Kim GS et al., have emphasised that optimal postoperative analgesia, early mobilisation, and vigilant monitoring in an intensive care unit setting are essential to reduce the risk of delayed complications such as heart failure, thromboembolism, and arrhythmias [14].

Present case represented an exceptionally high-risk scenario, as the patient had a large VSD and PDA with bidirectional shunting, severe polycythaemia (haematocrit 55%), thrombocytopenia (platelet count 80,000/mm^3), and low baseline oxygen saturation (84% on room air), along with significant obstetric complications including oligohydramnios, severe intrauterine growth restriction, and absent end-diastolic flow on Doppler assessment. The decision to proceed with an elective caesarean section at 35 weeks' gestation was driven by impending foetal compromise in the setting of a precarious maternal condition. Despite optimal management, the neonate was extremely low birth weight (900 g) and required neonatal intensive care, a finding consistent with the high incidence of prematurity, low birth weight, and neonatal morbidity reported in pregnancies complicated by ES, as described by Dachlan EG et al., [15].

Nevertheless, maternal survival and a relatively stable postoperative course in index patient support the view that, with meticulous multidisciplinary planning and individualised perioperative management, successful delivery may be achieved even in very high-risk cases of ES [12,16].

This case highlights several important considerations in the management of pregnancy complicated by ES. Pregnancy in women with ES should ideally be avoided, and if pregnancy occurs, early counselling regarding termination should be offered. However, when pregnancy continues-particularly in the presence of strong maternal preference-a carefully individualised, multidisciplinary management strategy becomes essential. Such an approach should focus on optimisation of cardiopulmonary status, advance planning for invasive haemodynamic monitoring, ensuring the availability of blood products, provision of intensive care support, and coordination with appropriate neonatal services. With regard to anaesthetic management, low-dose neuraxial techniques, including segmental spinal anaesthesia, incremental spinal dosing, or CSE

anaesthesia, appear to be reasonable and potentially preferable alternatives to single-shot spinal or general anaesthesia. These techniques should be undertaken only with preparedness for prompt treatment of hypotension using vasopressors and careful maintenance of adequate preload. Meticulous perioperative haemodynamic management is paramount and should include judicious fluid administration, avoidance of large fluid shifts, appropriate use of vasopressors, and effective pain control, with regional analgesic techniques such as TAP blocks playing an important role in minimising haemodynamic fluctuations during and after surgery. Postoperatively, close monitoring in an intensive care setting is mandatory, with consideration of thromboprophylaxis where not contraindicated, alongside early mobilisation and vigilant surveillance for complications including heart failure, arrhythmias, and thromboembolic events. Despite optimal maternal management, neonatal outcomes remain unpredictable, with a high incidence of prematurity, intrauterine growth restriction, low birth weight, and the need for neonatal intensive care, and parents should therefore be counselled regarding these risks early in the course of pregnancy [6,12,13,16].

CONCLUSION(S)

Although pregnancy in ES is associated with exceptionally high maternal and foetal morbidity and mortality, carefully individualised, multidisciplinary perioperative planning- including low-dose neuraxial anaesthesia, invasive haemodynamic monitoring, restrictive fluid management with judicious vasopressor support, and vigilant postoperative care may permit successful maternal and neonatal outcomes even in very high-risk cases. Nevertheless, such favourable outcomes should not be interpreted as evidence of overall safety. Pregnancy in ES should remain strongly discouraged, and pre-pregnancy counselling with effective contraception continues to be the cornerstone of management.

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