

Emergency cesarean section in pregnant women with severe pulmonary hypertension: the potential role of extracorporeal life support

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ABSTRACT

BACKGROUND: The aim of this study was to present our institutional experience with periprocedural management of emergency cesarean section (CS) operations and maternal and fetal cardiac complications in pregnant women with pulmonary hypertension (PH).

METHODS: Thirteen patients who were diagnosed with PH during pregnancy and/or prior to pregnancy according to European Society of Cardiology (ESC) criteria, and who were referred to our hospital with a decision for emergency CS from an external center, were included in the study. For patients who underwent urgent surgery, the following data were recorded: demographic characteristics, time of diagnosis, treatments for pulmonary hypertension used before pregnancy, during pregnancy, and/or after CS, arterial blood gas values, pulmonary and systemic pressure values after induction and at the 12th postoperative hour, extracorporeal membrane oxygenation (ECMO) requirements, time to extubation, length of intensive care stay, and mortality rates.

RESULTS: Eight of the 13 patients were diagnosed with idiopathic pulmonary arterial hypertension (IPAH). The mean systolic systemic arterial pressure (BPs), systolic pulmonary arterial pressure (PAPs), and mean pulmonary arterial pressure were 130 ± 14.2 mmHg, 93 ± 28 mmHg, and 52 ± 17 mmHg, respectively. Six of the 13 patients required ECMO support. The one-month mortality rate was 46%.

CONCLUSION: Pregnancy in women with PH is associated with significant maternal morbidity and mortality. If the underlying etiology is IPAH, the risk of mortality is higher than in other forms of PH. Mechanical circulatory support devices, including ECMO, may serve as a temporary bridge to lung transplantation in selected cases. Therefore, early diagnosis of IPAH, timely referral of patients to specialized centers, and planning of these operations by a multidisciplinary team consisting of cardiologists, gynecologists, and cardiac anesthesiologists are necessary.

Keywords: Extracorporeal membrane oxygenation (ECMO) support; emergency cesarean section; pulmonary hypertension.

INTRODUCTION

According to the 2022 European Society of Cardiology (ESC)/European Respiratory Society (ERS) guidelines, pulmonary hypertension (PH) is defined as an increase in mean pulmonary arterial pressure (PAPm) ≥ 20 mmHg at rest, as assessed by

right heart catheterization (RHC). Pulmonary arterial hypertension (PAH) refers to pre-capillary PH and is characterized by a pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg and a pulmonary vascular resistance (PVR) > 2 Wood units (WU). Idiopathic pulmonary arterial hypertension (IPAH) is included in this category. Post-capillary PH is defined by a

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PAPm ≥ 20 mmHg and a PAWP > 15 mmHg.^[1,2]

Pregnancy induces significant physiological changes, including increased blood volume, stroke volume, and cardiac output, along with decreased hemoglobin levels and total PVR.^[3,4] Although these physiological changes typically revert to pregestational levels within six months postpartum, they impose substantial cardiovascular stress.^[3,5] Pregnant women with PH, particularly those with IPAH, are at high risk of cardiac failure due to increased cardiac output (CO) and pulmonary arterial pressure (PAP), which may lead to right ventricular failure. Severe complications such as refractory hypoxia, hemodynamic instability, and right ventricular failure can occur, especially in patients undergoing emergency cesarean section (CS).^[6]

The World Health Organization (WHO) classifies pregnancy in women with PH as a Class IV risk condition and strongly recommends pregnancy avoidance in such cases.^[1] Despite these substantial risks, some women with PH choose to proceed with pregnancy. Therefore, the importance of early diagnosis and PH-specific treatment is emphasized for pregnant women with PH.^[6]

Over the past decade, advancements in PAH-targeted therapies have improved the quality of life and prognosis of affected patients.^[6] However, it remains uncertain whether these improvements have translated into reduced maternal mortality. In cases of perioperative right ventricular failure or respiratory failure unresponsive to medical therapy and mechanical ventilatory support, extracorporeal life support (ECMO) should be considered. High-risk CS procedures should be performed in specialized centers with multidisciplinary teams comprising cardiologists, pulmonologists, obstetricians, and cardiac anesthesiologists.^[6-8]

This study aims to present our institutional experience in the periprocedural management of emergency CS in pregnant women with PH, with a particular focus on maternal and fetal cardiac complications.

MATERIALS AND METHODS

This retrospective study included 13 pregnant women diagnosed with PH (either prior to pregnancy or during pregnancy) according to ESC criteria who underwent emergency CS between January 2013 and 2020 at our institution. All patients were referred from external centers; seven underwent CS due to fetal distress, and six due to severe maternal hypoxia. The study adhered to the principles of the Declaration of Helsinki, and ethics committee approval (No. 2021/7/497) was obtained. Informed consent was obtained from all participants.

Demographic data, PH treatment before pregnancy and after CS, arterial blood gas measurements, pulmonary and systemic arterial pressures, ECMO requirements, duration of intubation, intensive care unit (ICU) length of stay, and mortality rates were documented.

Continuous intraoperative monitoring included five-lead electrocardiography (ECG), pulse oximetry, invasive blood pressure measurement (radial/brachial artery), and urine output. General anesthesia (GA) was administered to all patients. Following standard sterile preparation and draping, induction was achieved using propofol (1-1.5 mg/kg) and rocuronium (0.6-0.8 mg/kg). After delivery, fentanyl (1.5 mcg/kg) was administered. Additionally, 20 IU of oxytocin (Synpitan®) was infused intravenously in 500 cc of 5% dextrose. Anesthesia maintenance was achieved with 3.0-6.0% desflurane without nitrous oxide. Mechanical ventilation settings included an FiO₂ of 100%, tidal volume of 6-8 mL/kg, respiratory rate of 16/min, and positive end-expiratory pressure (PEEP) of 3-5 cmH₂O, adjusted according to blood gas analysis.

Perioperative transesophageal echocardiography (TEE) was routinely performed to assess right ventricular volume, tricuspid annular plane systolic excursion (TAPSE), and overall cardiac function. Central venous catheterization (8.5 Fr; Arrow International Inc., PA, USA) via the right internal jugular vein was performed using the Seldinger technique, followed by pulmonary artery catheterization (7F Swan-Ganz; Edwards Lifesciences, USA) for continuous PAP monitoring. Hemodynamic parameters were recorded after delivery, when patients were most stable.

Intraoperative values were recorded during periods of maximal hemodynamic stability and included systolic systemic arterial pressure (BPs), diastolic systemic arterial pressure (BPd), mean pulmonary arterial pressure (PAPm), systolic pulmonary arterial pressure (PAPs), the PAPs/BPs ratio, and ECG findings. Blood gas parameters (pH, PaO₂, PaCO₂, and SaO₂) were measured following anesthesia induction. Postoperative hemodynamic and respiratory parameters were reassessed 12 hours after surgery.

Postoperatively, all patients were transferred to the ICU under orotracheal intubation. Hemodynamic and respiratory parameters were reassessed at 12 hours postoperatively. ECMO was instituted in patients experiencing severe right ventricular failure, using peripheral veno-arterial (V-A) or veno-venous (V-V) approaches based on hemodynamic status. ECMO was applied in six patients. Two of these patients experienced persistent hemodynamic and respiratory instability despite maximal medical therapy after surgery; therefore, V-A ECMO was preferred. The remaining four patients developed respiratory instability during their intensive care unit stay and were managed with V-V ECMO. The criteria for ECMO support were as follows: patients with hemodynamic instability (mean arterial pressure [MAP] < 50 mmHg) at any stage of the operation despite inotropic support received veno-arterial ECMO. Despite conventional mechanical ventilation strategies, patients with hypercarbia (partial pressure of carbon dioxide [PaCO₂] > 60 mmHg), hypoxemia (PaO₂ < 60 mmHg or oxygen saturation $< 80\%$), and a pH ≤ 7.2 on blood gas analysis received V-V ECMO if their hemodynamic status was stable.^[9]

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM, Chicago, IL, USA). Normality testing was applied to continuous variables, which were expressed as median (interquartile range [IQR]). Categorical variables were presented as frequencies and percentages.

RESULTS

Demographic characteristics are detailed in Table 1. The median (IQR) age was 26 (25-28) years. Of the 13 patients, eight

had IPAH, and five received PAH-specific therapy (bosentan, sildenafil) before pregnancy and after CS.

Intraoperative and postoperative hemodynamic and blood gas parameters are presented in Table 2. The duration of intubation, requirements for mechanical support, ICU and hospital length of stay, and mortality rates are summarized in Table 3. The 30-day postpartum maternal mortality rate was 46%, with deaths occurring between postpartum days 13 and 18. ECMO was required in six patients; two received perioperative V-A ECMO following intraoperative cardiac arrest, while four received postoperative V-V ECMO.

Table 1. Demographic characteristics of the patients

P	Age	Etiology	G/P	NYHA	Time to diagnosis	Pre-pregnancy treatment	C/S timing (weeks+days)
1	25	IPAH	1/1	IV	Pregestational	Bosentan	36
2	24	IPAH	2/1	IV	Gestational	-	35+1
3	40	MS	1/1	III	Pregestational	-	38+4
4	27	IPAH	1/1	IV	Gestational	-	36+4
5	25	IPAH	1/1	IV	Gestational	-	37
6	29	VSD	1/1	III	Pregestational	-	38+4
7	21	MS	1/1	III	Pregestational	-	39
8	30	ASD	2/1	III	Pregestational	-	37
9	32	IPAH	1/1	IV	Gestational	-	37+1
10	26	IPAH	1/1	IV	Pregestational	Sildenafil+iilioprost	36
11	28	IPAH	1/1	IV	Pregestational	Sildenafil+bosentan	39
12	27	IPAH	1/1	IV	Pregestational	Sildenafil	34
13	25	VSD/Eisenmenger	1/1	IV	Pregestational	Sildenafil	35+6

P: Patient; G/P: Gravida/para; NYHA: New York Hearth Association; IPAH: Idiopathic pulmonary arterial hypertension; C/S: Cesarean section; MS: Mitral stenosis; ASD: Atrial septal defect; VSD: Ventricular septal defect.

Table 2. Respiratory and hemodynamic parameters of the patients

	Intraoperative Period Median (IQR)	Postoperative Period Median (IQR)
pH	7.39 (7.37-7.42)	7.35 (7.25-7.39)
SaO ₂	100 (96-100)	98 (95-98)
PaCO ₂	36 (33-40)	40 (37-42.5)
PaO ₂	102 (97-106.5)	128 (123-133)
BPs (mmHg)	100 (100-110)	90 (90-97.5)
BPd (mmHg)	80 (74-85)	72 (67-76.5)
PAPs (mmHg)	58 (47.5-133)	55 (45-129)
PAPm (mmHg)	50 (29-72)	48 (32.5-70)
PAPs/BPs	0.55 (0.5-1.19)	0.61 (0.49-1.26)

SaO₂: Arterial oxygen saturation; PaCO₂: Partial pressure of arterial carbon dioxide; PaO₂: Partial pressure of arterial oxygen; BPs: Systolic systemic arterial pressure; dBP: Diastolic systemic arterial pressure; PAPs: Systolic pulmonary arterial pressure; PAPm: Mean pulmonary arterial pressure.

Table 3. Perioperative data of the patients

P	Inotropic agents	Pulmonary therapy	ECMO	ECMO initiation (day)	Extubation time (day)	ICU stay (days)	Hospital stay (days)	Cause of mortality	Mortality
1	ADR, DBX	Tad+Mac+iNO	+	7	13	13	13	Sepsis	+
2	ADR, DBX	Tad+Mac+iNO	+	End of surgery	14	14	14	MOF	+
3	-	-	-		1	3	5		-
4	ADR, DBX	Tad+Mac+iNO	+	End of surgery	1	15	15	MOF	+
5	-	Mac	-		5	10	15		-
6	-		-		0	2	6		-
7	-		-		0	2	5		-
8	-		-		0	2	7		-
9	ADR, DBX	Tad+Mas+llo+iNO	+	6	20	20	20	CVD	+
10	ADR, DBX	Mac+Sil+llo+iNO	+	4	18	18	18	Sepsis	+
11	ADR, DBX	Bos+Sil+iNO	+	3	12	12	12	Sepsis	+
12	-	Sil+Mac	-		5	15	25		-
13	-	llo+Mac	-		3	10	20		-

P: Patient; ECMO: Extracorporeal membrane oxygenation; ICU: Intensive care unit; ADR: Adrenaline; DBX: Dobutamine; Tad: Tadalafil; Mac: Macitentan; llo: Iloprost; iNO: Inhaled nitric oxide; Bos: Bosentan; Sil: Sildenafil; MOF: Multiorgan failure; CVD: Cerebrovascular disease.

Five of the six patients who died were diagnosed with IPAH. No neonatal complications were observed.

DISCUSSION

In our series of pregnant women with different forms of severe pulmonary hypertension, cesarean section was the standard mode of delivery. Various proactive post-delivery management strategies, including prolonged mechanical ventilation, parenteral iloprost, inhaled nitric oxide (10-20 ppm), inotropic agents, and extracorporeal membrane oxygenation, were implemented. PH during pregnancy carries a greater risk of clinical deterioration when the underlying etiology is idiopathic pulmonary arterial hypertension compared to other forms of PH. This increased risk is attributed to delayed diagnosis, severe hypoxia, right ventricular failure, fetal developmental anomalies, and higher maternal mortality rates.^[10] Because the patient population in our study was rare and included only patients who underwent surgery under emergency conditions, we did not have the opportunity to perform a statistical comparison between the IPAH and non-IPAH groups. Nevertheless, our clinical experience suggests that mortality and morbidity are higher in patients with IPAH, which is consistent with relevant data reported in the literature.

Additionally, delayed hospitalization, administration of general anesthesia, and the severity of PH have been identified as significant risk factors for maternal mortality in pregnant women with PH.^[11-13] Early diagnosis and treatment with PH-targeted therapies may help reduce maternal morbidity and mortality in this population.^[1]

Maternal mortality in pregnant women with PH has been reported to range from 17% to 56% in the literature.^[1,6,7,10,11,14] In our study, the maternal mortality rate was 46%, with no additional deaths occurring within the first year postpartum. A PH crisis is defined as a sudden increase in pulmonary arterial pressure, with a systolic pulmonary arterial pressure-to-systemic systolic blood pressure (sPAP/BPs) ratio exceeding 0.8.^[15] In our cohort, a PH crisis was documented in 8 of 13 patients (61%). The median (IQR) PAPm value among our patients was 50 (29-72) mmHg, consistent with the definition of severe PH. A major contributing factor to the high mortality rate was the elevated PAPs/BPs ratio (>0.8) observed in eight patients who underwent emergency CS, fulfilling the criteria for a PH crisis. Additionally, 61% of our study population had IPAH, and only five of these patients had been diagnosed prior to pregnancy and were receiving PAH-targeted therapies. These clinical characteristics may have contributed to an increased risk of clinical deterioration following emergency CS.^[10]

The most commonly reported form of PH during pregnancy is group II (post-capillary PH), which is frequently associated with mitral valve disease or other left heart pathologies. Data from the multicenter Registry of Pregnancy and Cardiac Disease (ROPAC) suggest that postpartum maternal mortality is higher in women with IPAH compared to those with group II PH.^[16] Consistent with these findings, mortality in our cohort occurred exclusively in the postpartum period.

The anesthetic management of pregnant women with PH undergoing emergency CS presents specific challenges that require proactive strategies distinct from those used in elective

CS cases.^[17,18] The risk of PH worsening during pregnancy is significant. Given the physiological and hemodynamic changes that occur during pregnancy and immediately after CS, key anesthetic goals include maintaining sinus rhythm, optimizing right ventricular preload, ensuring systemic vasoconstriction, enhancing right ventricular contractility, and reducing pulmonary vascular resistance. Impairment of atrial contraction can exacerbate right ventricular failure. Right ventricular volume status should be carefully regulated using transesophageal echocardiography and central venous pressure (CVP) monitoring. In cases of decreased preload, right ventricular contractility is impaired, whereas excessive preload can worsen tricuspid regurgitation, leading to interventricular septal deviation and further deterioration of right ventricular wall tension. Maintaining systemic vascular resistance is crucial for adequate coronary perfusion.^[19-21]

Pulmonary artery catheterization (PAC) and TEE play vital roles in ensuring hemodynamic stability. PAC is essential for assessing and managing cardiac output (CO), PAP, PVR, mixed venous oxygen saturation, cardiac preload, and right ventricular function, all of which are critical for maintaining hemodynamic stability.^[9] Intraoperative TEE allows real-time assessment of right and left ventricular function. Additionally, the evaluation of regional wall motion abnormalities can help identify the underlying causes of hemodynamic instability, assess intravascular volume status, and detect congenital anomalies such as a patent foramen ovale (PFO) or intracardiac thrombus, thereby guiding anesthetic management.^[9] The combined use of TEE and PAC measurements after anesthetic induction may enable more precise and controlled perioperative management.

Pharmacological interventions to maintain hemodynamic stability include inotropic agents (epinephrine, norepinephrine, and dobutamine), phosphodiesterase III inhibitors (milrinone), and the selective pulmonary vasodilator inhaled nitric oxide (iNO). Adequate diuresis should be maintained, and hypoxia and hypercarbia must be avoided.^[19-21,22,23] Preventing right ventricular failure and mitigating increases in PVR are key objectives in anesthetic management. The use of veno-arterial ECMO should be considered in selected patients with severe PAH, Eisenmenger's syndrome, left systemic ventricular dysfunction and/or right ventricular dysfunction.^[10,24] In our study, ECMO support was provided to patients who did not respond to medical therapy or mechanical ventilation. Six patients required inotropic support at the end of surgery, with epinephrine and dobutamine being the preferred agents. Two patients with refractory hemodynamic instability received perioperative veno-arterial ECMO support, while four hemodynamically stable patients were managed postoperatively with veno-venous ECMO in the intensive care unit.

Lung transplantation remains a critical option for patients with severe PH. However, delays in referral, prolonged waiting times, and organ donor shortages contribute to increased mortality and worsening clinical severity among patients

awaiting transplantation.^[10] Unfortunately, in our cohort, none of the patients requiring ECMO could be successfully bridged to transplantation, and those who could not be weaned from ECMO support ultimately succumbed to their illness.

Currently, there are no randomized controlled trials comparing general anesthesia (GA) and regional anesthesia (RA) for emergency CS in pregnant women with PH.^[17,21] However, retrospective case series published between 1997 and 2007 indicate that GA is associated with a fourfold higher mortality risk compared to RA. Epidural anesthesia, when carefully titrated, is often considered the preferred technique because it provides adequate anesthesia while minimizing hemodynamic instability.^[6,14,17,25-27] In our study, GA was administered to all patients due to the urgency of the CS procedures and the patients' inability to tolerate the delayed onset of epidural anesthesia. Additionally, GA was favored because of the unknown preoperative medical treatment status of the patients, the potential need for mechanical support during surgery, and the high pulmonary pressures observed in these critically ill patients. GA also allowed optimal anesthetic management, including maintenance of systemic vascular resistance, monitoring of right ventricular function, control of pulmonary pressure, respiratory support, and TEE-guided assessments.

The lowest gestational age at delivery among our patients was 34 weeks. Although IPAH has been associated with a higher risk of neonatal growth restriction compared to other forms of PAH during pregnancy, no neonatal complications were observed in our study.^[10]

This study has several limitations. First, the sample size was small. Second, the retrospective design limited the ability to control for confounding variables. Third, preoperative clinical data were incomplete because many patients were referred from external centers, making it difficult to assess their management before admission. Additionally, newborn follow-up data were unavailable, as neonatal care was provided at different institutions.

CONCLUSION

Pregnancy in women with PH, particularly those with IPAH, is associated with significant maternal morbidity and mortality. The anesthetic management of CS in these patients is critical and must be tailored to address the underlying pathophysiology. Early diagnosis, timely referral to specialized centers, and multidisciplinary perioperative planning involving cardiologists, obstetricians, and cardiac anesthesiologists are essential for improving outcomes. When the underlying etiology is IPAH, the risk of mortality is higher than in other forms of PH. Mechanical circulatory support devices, including ECMO, may serve as a temporary bridge to lung transplantation in selected cases.

Ethics Committee Approval: This study was approved by the Kartal Kosuyolu Yuksek İhtisas Training and Research

Hospital Ethics Committee (Date: 13.07.2021, Decision No: 2021/7/497).

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ORİJİNAL ÇALIŞMA - ÖZ

Ciddi pulmoner hipertansiyonlu gebelerde acil sezaryen seksiyon ameliyatı – Olası Extracorporeal yaşam desteği

AMAÇ: Bu çalışmadaki amacımız, pulmoner hipertansiyonlu (PH) gebelerde acil sezaryen (CS) operasyonlarının periprocedürel yönetimi ve maternal ve fetal kardiyak komplikasyonlar konusundaki klinik deneyimimizi sunmaktır.

GEREÇ VE YÖNTEM: Avrupa Kardiyoloji Derneği (ESC) kriterlerine göre gebelik ve/veya gebelik öncesi PH tanısı konulan ve dış merkezde acil CS kararı ile hastanemize sevk edilen 13 hasta çalışmaya dahil edildi. Acil olarak operasyona alınan hastaların demografik verileri, tanı zamanı, gebelik öncesi, gebelik ve/veya CS sonrası kullanılan pulmoner hipertansiyon tedavileri, arteriyel kan gazları, indüksiyon sonrası ve postoperatif 12. saat pulmoner basınç ve sistemik basınç değerleri, ekstrakorporeal membran oksijenatör (ECMO) gereksinimleri, ekstübasyon ve yoğun bakım süresi ve mortalite oranları kaydedildi.

BULGULAR: 13 hastanın sekizine idiyopatik pulmoner arteriyel hipertansiyon (İPAH) tanısı kondu. Ortalama sistolik sistemik arter basıncı (KB), PAB ve ortalama pulmoner arter basıncı sırasıyla 130 ± 14.2 mmHg, 93 ± 28 ve 52 ± 17 olarak bulundu. 13 hastadan 6'sının ECMO desteğine ihtiyacı oldu. 1 aylık mortalite oranı %46 idi.

SONUÇ: PH'lu kadınlarda gebelik, önemli derecede anne morbiditesi ve mortalitesi ile ilişkilidir. Altta yatan etiyoloji İPAH ise mortalite riski diğer PH türlerine göre daha yüksektir. ECMO dahil mekanik dolaşım destek cihazları, seçilmiş vakalarda akciğer transplantasyonuna geçici bir köprü görevi görebilir. Bu nedenle İPAH'nın erken teşhisi, hastaların merkezlere zamanında yönlendirilmesi ve bu operasyonların kardiyoloji, jinekoloji ve kardiyak anestezi uzmanından oluşan multidisipliner bir ekiple planlanması gerekmektedir.

Anahtar sözcükler: Acil sezaryen seksiyon; ECMO desteği; pulmoner hipertansiyon.

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