VOLUME - 10, ISSUE - 07, JULY- 2021 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper | Obstetrics & Gynaecology

A CASE SERIES OF PREGNANCY IN EISENMENGER'S SYNDROME- A MANAGEMENT CONUNDRUM

Dr. Shree Bharathi*	MBBS, MS, DNB (OG), Senior Resident, Department of Obstetrics and Gynaecology, Jawaharlal Institute of Postgraduate Medical Education and Research Puducherry-06, India. *Corresponding Author
Dr. Rajasekar Ramadurai	MBBS, MS, DNB, Junior Resident, Department of Anaesthesiology and Critical Care, Jawaharlal Institute of Postgraduate Medical Education and Research Puducherry, India-06.
Dr. Niveditha Jha	MBBS, MS, FMAS, Assistant Professor, Department of Obstetrics and Gynaecology, Jawaharlal Institute of Postgraduate Medical Education and Research Puducherry, India-06.
Dr. Sasirekha Rengaraj	MBBS, MS, DNB, Fellow in Obstetric Medicine, Additional Professor, Department of Obstetrics and Gynaecology, Jawaharlal Institute of Postgraduate Medical Education and Research Puducherry, India-06.
Dr. Veena Ranjan	MBBS, MS, DNB, Professor, Department of Obstetrics and Gynaecology, Jawaharlal Institute of Postgraduate Medical Education and Research Puducherry-06, India.

ABSTRACT Eisenmenger's syndrome(ES) refers to the development of pulmonary hypertension and reversal of shunt in patients with long standing congenital heart defects with left-to-right shunt. The cardiovascular changes in pregnancy, labour and puerperium add to the morbidity and mortality associated with this high-risk cardiac condition. Fetal outcome is also poor with increased incidence of stillbirth and prematurity. We report 3 such patients of ES with severe pulmonary hypertension.

The first patient presented in advanced pregnancy with unbooked status. She had a spontaneous preterm precipitate labour before cardiac optimization and delivered vaginally with successful outcome. The second patient presented to us in early third trimester with right heart failure, which was stabilized after caesarean section. The third patient also had a good outcome, despite additional complications of pulmonary edema. Neonatal outcome in our case series was marred by complications like fetal growth restriction, prematurity, perinatal asphyxia and one neonatal death.

A multidisciplinary team approach involving obstetric medicine specialists, cardiologists, anaesthesiologists and neonatologists, is required for peripartum care of these patients to improve the maternal and perinatal outcomes.

KEYWORDS : Eisenmenger's syndrome, high-risk pregnancy, maternal outcome, pulmonary artery hypertension.

BACKGROUND

Congenital cardiac defects with left-to-right shunt eventually develop pulmonary artery hypertension (PAH) with a reversed or bidirectional shunt, leading to cyanosis and heart failure.(Basit et al., 2021) This condition is called Eisenmenger's syndrome (ES)

Pregnancy in ES confers a particularly high risk of rapidly progressive cardiopulmonary decompensation, thrombotic complications and sudden death. ES belongs to class IV in WHO pregnancy risk classification and is regarded as contraindication for pregnancy and if they present in early pregnancy, termination is advisable.(Duan et al., 2016) Maternal mortality is reported to be 30-50% and increases further with associated complications. (Gleicher et al., 1979)

Fetal outcomes are also poor, with a high risk of spontaneous abortion, fetal growth restriction (FGR), preterm birth, low-birth weight and congenital cardiac malformations. (Abbas et al., 2005) Overall fetal wastage is reported to be up to 75%. (Gleicher et al., 1979) Multidisciplinary care is necessary to optimize the chances of survival for both mother and baby in advanced pregnancy (Weiss & Hess, 2000) We present the maternal and perinatal outcome in 3 such women with ES and PAH managed in a tertiary care setting in Southern India.

CASE REPORT

CASE 1

A 34-year-old parturient at 33+4 weeks of gestation presented with threatened preterm labour. She was a known case of Ventricular septal defect(VSD) with Eisenmenger syndrome for the past 12 years but she defaulted her cardiac drugs for last 2 years. Patient had undergone early medical termination of 2 previous pregnancies due to high-risk cardiac status and presented for the first time in this pregnancy in third trimester with unbooked status, with worsening of cardiac symptoms (NYHA II-III).

Her general physical examination revealed cyanosis, grade 3 clubbing and pedal edema. Cardiac auscultation revealed loud pulmonary component of second heart sound (P_2) and a grade-4 pan-systolic murmur. She was tachypnoeic with room-air saturation of 85%. Chest X-ray done with abdominal shield revealed cardiomegaly with pulmonary congestion. On obstetric evaluation, there was no evidence of fetal compromise. We kept her under continuous monitoring with oxygen supplementation and cardiac medications were restarted (Sildenafil 25mg , Furosemide 40mg). She went into spontaneous preterm labour at 34 weeks of gestation. Hence, vaginal delivery was allowed. As she had precipitate course of labour and profound hypotension and desaturation during second stage, epidural catheter placement was deferred. Intrathecal injection of 25mcg of Fentanyl was administered as an alternative, with continuous non-invasive hemodynamic and fetal monitoring. Second stage of labour was cut short with forceps instrumental delivery. Oxytocin 1IU slow intravenous boluses were used as uterotonics. Episodes of hypotension were managed with phenylephrine boluses and judicious administration of fluids.

Postnatally, in view of per vaginum bleeding, ultrasound examination and cervical exploration were done. Suturing of

a cervical tear and suction evacuation for retained bits of placenta were performed. Blood loss was 200ml. Patient received intravenous prophylactic antibiotics and thromboprophylaxis. She was discharged in well-being together with her child.

The following year, she presented with incomplete abortion at 8+4 weeks of gestation, which was managed by instrumental evacuation. There was no further cardiac decompensation noted in this pregnancy. She received depot preparation of medroxy-progesterone acetate for contraception. The importance of cardiac follow-up and contraception were emphasised and she was discharged.

Case 2.

A 27-year-old primigravida presented to us at 27+5 weeks of gestation with features suggestive of right heart failure and NYHA IV functional status. She was a known case of Atrial septal defect(ASD) from 10years of age and had progressed to ES by 20years of age. However, she defaulted on her cardiac medications after 8 months. She was booked and immunised in this pregnancy with regular antenatal care, but she disregarded cardiac optimisation. She complained of worsening breathlessness and palpitations for2 days. She also noticed bilateral pedal edema and orthopnoea. At presentation, her room air oxygen saturation was 30% which improved to 60-70% after resuscitation. She had tachycardia in the range of 100-120/min and tachypnoea(35-40 breaths/min). She had high blood pressure recordings of 140-160/90-100 mmHg and was diagnosed with early onset preeclampsia.

Physical examination revealed grade 3 clubbing, cyanosis, raised Jugular venous pressure(JVP), loud P2 with grade4 systolic murmur and rhonchi and crepitations on lung auscultation. Due to the very high pulmonary artery pressures on trans-thoracic echocardiography, the differential diagnosis of primary pulmonary hypertension was also considered. Obstetric evaluation revealed severe preeclampsia with proteinuria and stage II FGR.

Maternal condition was stabilised over the next 72 hours and emergency caesarean section was done under epidural anaesthesia. Although the caesarean section proceeded without complication, intra-operatively, the patient developed severe hypotension which required multiple inotropic support, diuretics and fluid boluses for correction. Intravenous and intra-myometrial oxytocin was administered to prevent uterine atonicity. Post operatively patient was stabilised and shifted to critical care unit for intensive monitoring, where oxygen supplementation using non-rebreathing mask(NRBM) was continued. She received intravenous antibiotics and thromboprophylaxis. The baby was shifted to NICU immediately after birth in view of respiratory distress and extreme low birth weight and expired on post-natal day 3 due to complications of extreme prematurity and perinatal asphyxia.

Case 3.

A 24-year-old woman, a known case of VSD from 4 years of age and was diagnosed to have ES 4 years ago, presented to us as a multigravida at 30weeks of gestation with a functional status of NYHA II-III. On examination she had typical clinical features of ES and stable vitals. She had history of one prior spontaneous first trimester abortion. She was booked and immunised in this pregnancy with periodic antenatal follow-up.

She underwent cardiac evaluation and optimisation of cardiac drugs during pregnancy. She received antenatal corticosteroids. On obstetric evaluation fetal growth was found to be optimal. At 34+6 weeks of gestation, she developed pre-eclampsia with severe features, partial HELLP syndrome and pulmonary edema for which she was managed with diuretic and BP monitoring. Prophylactic Magnesium sulphate was administered. She went into spontaneous preterm labour but in view of deteriorating maternal medical condition (pulmonary edema and NYHA status III-IV) she was taken up for emergency Caesarean section, under epidural anaesthesia. Intra operatively, she had atonic PPH with 1200ml blood loss which was managed medically and also needed blood transfusion. Postnatally, she developed surgical site infection which required intravenous antibiotics and secondary suturing of wound. She was discharged 3 weeks after delivery, together with her baby. The obstetric parameters and maternal and fetal outcomes observed in our patients have been compared in Tables 2 and 3 respectively.

The maternal cardiac characteristics are summarised in Table 1. The obstetric parameters and maternal and fetal outcomes observed in our patients have been compared in Tables 2 and 3 respectively.

Table 1. Maternal cardiac characteristics

S.no	Age (years)	Age at diagnosis of CHD, ES (years)	Lesion+	Size (mm)	RVSP (mm Hg)	EF (%)	MAP# (mm Hg)	Oxygen saturation (Spo2) in room air (%)	Arterial oxygen pressure (Pao2) in room air (mm Hg)	Hb (mg/dl)
1.	34	5,22	VSD	12	50	-	70	85	58	12.4
2.	27	10,20	ASD	21	110	15	110*	64*	34.4	14.2
3.	24	4,20	VSD	18	96	65	97	84	53	9.8

*After resuscitation and inotropes; #MAP- Mean arterial blood pressure; +Lesion- shunt was bidirectional in all 3 patients

Table 2. Maternal obstetric characteristics and complications

S. No	Obstetric index	Previous pregnancy outcome	Gestational age at presentation (weeks)	Complications	Duration of hospital stay (days)
1.	G3A2	2 MTPs	33+4	Preterm labour Cervical tear Retained placental bits	31
2.	G1	-	27+5	Preeclampsia Heparin induced Thrombocytopenia	13
3.	G2A1	spontaneous abortion	30	Preterm labour Severe preeclampsia Pulmonary edema Partial HELLP# syndrome SSI* and secondary suturing	59

*SSI- Surgical site infection #HELLP- Hemolysis, elevated liver enzymes, low platelets

Table 3. Intrapartum events and perinatal outcomes

S. no.	Gestational age at delivery (weeks)	Fetal complication	Mode of delivery	Blood loss (ml)	Analgesia/ Anaesthesia	Apgar At 1,5 minutes	Birth weight (g)	NICU+ duration of stay (days)	Fetal outcome
1.	34	No FGR*	Instrumental	200	Intrathecal Fentanyl	8,9	2200	-	LB** AGA+

2.	28	Stage II FGR with AEDF[#]	Caesarean section	400	General	2.4	650	3	LB ELBW[##] Neonatal death
3.	34+6	No FGR	Caesarean section	1200	Epidural	8.9	1890	15	LB AGA

*FGR- Fetal growth restriction; [#] AEDF- Absent End Diastolic Flow; [+]NICU- Neonatal intensive care unit; **LB- livebirth; [++]AGA- Appropriate for gestational age; [##]ELBW- extremely low birth weight

DISCUSSION

Congenital heart defects with left-to-right shunt such as ASD, VSD and patent ductus arteriosus(PDA) and even some complex cyanotic cardiac lesions like Unrepaired Tetralogy of Fallot(TOF), lead to chronic pulmonary circulatory overload and an increase in pulmonary vascular resistance(PVR) over time. This ultimately leads to reversal of shunt; wherein deoxygenated blood enters the systemic circulation causing hypoxaemia and cyanosis eventually resulting in heart failure. This end stage disease process is known as Eisenmenger syndrome.(Lopez et al., 2020)

Early surgical correction of such defects prevents the pathophysiological cascade of events leading to ES and improves the cardiac prognosis and quality of life. However, the patients that we encountered were found to have denied or defaulted cardiac care at an early stage.

Pregnancy-associated cardiovascular adaptations like increased blood volume and demand for increased cardiac output, are not well tolerated in patients with ES and cause cardiopulmonary decompensation. There is reduction in systemic vascular resistance(SVR) by as much as 40% due to low resistance of the placental vascular bed.(Robson et al., 1989) This is accompanied by a decrease in resistance in the highly compliant pulmonary vasculature. But in PAH, these compensatory mechanisms are inefficient , leading to a disproportionate strain on the right ventricle that worsens the right-to-left shunt in patients with ES.(Lopez et al., 2020; Robson et al., 1989; Weiss & Hess, 2000)

The 3 patients reported in our series, were dissimilar with respect to their age and obstetric index, however, they all presented with severe PAH. ES with PAH in pregnancy is managed with fluid restriction, continuous oxygen supplementation and drug therapy in the form of diuretics, pulmonary vasodilators like phosphodiesterase-5 inhibitors (Sildenafil) and anticoagulation. Cases 1 and 2 were started on above mentioned therapy only after presenting to us so there was inadequate time for optimisation of drug dosage. Case 2 also required additional drug therapy in the form of Milrinone (phosphodiesterase-3 inhibitor with inotropic action), Digoxin(anti arrhythmic and anti-failure drug) and Bosentan(Endothelin receptor antagonist)

None of our patients presented to us in first trimester, hence we made decision to continue the pregnancy with counselling for in-patient care. Pregnancy was also complicated with Preeclampsia and thrombocytopenia in Cases 2 and 3 which were managed as per standard protocol.

There is no consensus regarding the most appropriate mode of delivery in such patients and it has to be decided on a case-to-case basis as both vaginal delivery and caesarean section have their own risks. The intrapartum period poses hemodynamic challenges due to auto transfusion of 300-500ml of blood from uteroplacental vasculature which rapidly increases cardiac output and blood pressure. (Ouzounian & Elkayam, 2012). The risks of auto transfusion, blood loss and infections are higher with caesarean section; however due to its controlled approach it is often opted as the preferred mode of delivery. (Bonnin et al., 2005) In our series, the first patient was allowed vaginal delivery as she went into spontaneous labour and progressed rapidly. To curtail the deleterious effects of labour pains she was administered Single-dose Intrathecal analgesia with 25mcg Fentanyl (opioid analgesic), which is an innovative anaesthetic approach.(Chauhan et al., 2020). Epidural analgesia/ anaesthesia has several advantages over general anaesthesia in patients of ES such as titratability, controlled hemodynamics and continued post-operative analgesia. (Lopez et al., 2020) We opted for caesarean section under epidural anaesthesia in the other two patients as per the decision of the multidisciplinary team.

The maternal cardiac adaptations are most pronounced in the immediate post-partum period with highest risk of decompensation and sudden cardiac death. All our patients were shifted to critical care unit immediately after delivery for intensive monitoring.

In our report, all 3 neonates suffered the morbidity of prematurity and low birth weight. However, in case 2 the baby had ELBW at 28 weeks with complications of FGR, absent diastolic flow and perinatal asphyxia and expired in the early neonatal period. None of the neonates had congenital cardiac anomalies.

CONCLUSION

ES with PAH is a WHO class IV heart disease with a very high maternal and fetal morbidity and mortality rate. Our study highlights the possibility of successful maternal and fetal outcomes in such patients in a tertiary care center with collaborative efforts among obstetricians, cardiologists, anaesthesiologists, pediatricians and intensivists.

Due to advancements in medical science, availability of novel therapies and emerging evidence in literature, improved outcomes of pregnancy and childbirth are possible. The decision of early termination of pregnancy should therefore be individualized, taking into account the severity of the abnormality and access to healthcare resources. If a woman with ES opts for continuation of pregnancy, oxygen therapy, aggressive use of pulmonary vasodilators and a specialist multidisciplinary team approach are essential.

ABBREVIATIONS:

AEDF: Absent end diastolic flow
AGA: Appropriate for gestational age
ASD: Atrial septal defect
BP: blood pressure
CHD: Congenital heart disease
EF: Ejection fraction
ELBW: extremely low birth weight
ES: Eisenmenger's syndrome
FGR: Fetal growth restriction
HELLP: haemolysis, elevated liver enzymes and low platelets
JVP: Jugular venous pressure
LB: Live birth
MAP: Mean arterial pressure
MTP: medical termination of pregnancy
NICU: Neonatal intensive care unit
NRBM: Non-rebreathing mask
NYHA: New York Heart Association
PAH: Pulmonary arterial hypertension
PDA: Patent ductus arteriosus
PVR: Pulmonary vascular resistance
RVSP: Right ventricular systolic pressure
SSI: Surgical site infection; SVR: systemic vascular resistance
TOF: Tetralogy of Fallot
VSD: Ventricular septal defect
WHO: World Health Organisation

REFERENCES

1. Abbas, A. E., Lester, S. J., & Connolly, H. (2005). Pregnancy and the cardiovascular system. *International Journal of Cardiology*, *98*(2), 179–189. https:// doi.org/10.1016/j.ijcard.2003.10.028
2. Basit, H., Wallen, T. J., & Sergent, B. N. (2021). Eisenmenger Syndrome. In *StatPearls*. StatPearls Publishing. http:// www. ncbi. nlm. nih. gov/ books/ NBK 507800/
3. Bonnin, M., Mercier, F. J., Sitbon, O., Roger-Christoph, S., Jaïs, X., Humbert, M., Audibert, F., Frydman, R., Simonneau, G., & Benhamou, D. (2005). Severe Pulmonary Hypertension during Pregnancy: Mode of Delivery and Anesthetic Management of 15 Consecutive Cases. *Anesthesiology*, *102*(6), 1133–1137. https:// doi.org/10.1097/00000542-200506000-00012
4. Chauhan, G., Samyal, P., & Pathania, A. A. (2020). Single-dose intrathecal analgesia: A safe and effective method of labor analgesia for parturients in low resource areas. *Ain-Shams Journal of Anesthesiology*, *12*(1), 23. https://doi.org/10.1186/s42077-020-00075-w
5. Duan, R., Xu, X., Wang, X., Yu, H., You, Y., Liu, X., Xing, A., Zhou, R., & Xi, M. (2016). Pregnancy outcome in women with Eisenmenger's syndrome: A case series from west China. *BMC Pregnancy and Childbirth*, *16*(1), 356. https://doi.org/10.1186/s12884-016-1153-z
6. Gleicher, N., Midwall, J., Hochberger, D., & Jaffin, H. (1979). Eisenmenger's syndrome and pregnancy. *Obstetrical & Gynecological Survey*, *34*(10), 721–741. https://doi.org/10.1097/00006254-197910000-00001
7. Lopez, B. M., Malhamé, I., Davies, L. K., Velez, J. M. G., Marelli, A., & Rabai, F. (2020). Eisenmenger Syndrome in Pregnancy: A Management Conundrum. *Journal of Cardiothoracic and Vascular Anesthesia*, *34*(10), 2813–2822. https://doi.org/10.1053/j.jvca.2020.02.053
8. Ouzounian, J. G., & Elkayam, U. (2012). Physiologic changes during normal pregnancy and delivery. *Cardiology Clinics*, *30*(3), 317–329. https://doi.org/10.1016/j.ccl.2012.05.004
9. Robson, S. C., Hunter, S., Boys, R. J., & Dunlop, W. (1989). Serial study of factors influencing changes in cardiac output during human pregnancy. *American Journal of Physiology-Heart and Circulatory Physiology*, *256*(4), H1060–H1065. https://doi.org/10.1152/ajpheart.1989.256.4.H1060
10. Weiss, B. M., & Hess, O. M. (2000). Pulmonary vascular disease and pregnancy: Current controversies, management strategies, and perspectives. *European Heart Journal*, *21*(2), 104–115. https:// doi. org/ 10. 1053/ euhj. 1999. 1701