Cardiology in the Young

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Pregnancy in Eisenmenger syndrome: a case series from a tertiary care hospital of Northern India

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Abstract

Background: Despite advances in medical care, we still come across pregnancy in Eisenmenger syndrome. Eisenmenger syndrome represents the severe end of the spectrum for disease in pulmonary artery hypertension associated with CHD. Due to very high maternal and perinatal morbidity and mortality, pregnancy is contraindicated among these women. Current guidelines also recommend that the women who become pregnant should opt for early termination of pregnancy. Here, we present a case series of 11 women of Eisenmenger syndrome and their pregnancy outcome. *Methods:* It was a retrospective analysis of 12 pregnancies among 11 women with Eisenmenger syndrome who were managed in a tertiary care referral centre of Northern India. *Results:* The mean age of these women was 28 ± 4 years (range 22 to 36 years). Almost 80% of them (9/11) were diagnosed with Eisenmenger syndrome during pregnancy. The commonest cardiac lesion was Ventricular Septal defect (54.5%) followed by Atrial Septal defect (27.3%) and Patent Ductus arteriosus (9.1%). Only three women opted for medical termination of pregnancy, rest eight continued the pregnancy or presented late. Pregnancy complications found include pre-eclampsia (50%), abruption (22%), and fetal growth retardation (62.5%). There were three maternal deaths (mortality rate 27%) in postpartum period. *Conclusion:* This case series highlights the delay in diagnosis and treatment of CHD despite improvement in medical care. Women with Eisenmenger syndrome require effective contraception, preconceptional counselling, early termination of pregnancy, and multidisciplinary care.

Eisenmenger syndrome refers to any untreated congenital cardiac defect with intracardiac or extracardiac communication that leads to pulmonary hypertension, reversal of flow, and cyanosis.[1,2] It is a pathophysiological condition due to pulmonary vascular obstructive disease in an underlying CHD. Various congenital intracardiac or extracardiac defects can lead to Eisenmenger syndrome. The defects commonly seen are ventricular septal defect, atrioventricular septal defect, and patent ductus arteriosus.[3] With large shunts, pulmonary vascular resistance develops quickly and usually manifests in the first 2 years of life. Otherwise, Eisenmenger syndrome progresses slowly and is usually diagnosed later in life.[3]

Despite improvement in medical care, CHDs are often missed and diagnosed during pregnancy or child-bearing age in low- and middle-income countries.[4] Women with Eisenmenger syndrome are categorised under WHO pregnancy risk class IV.[5] Pregnancy is contraindicated in this group; still we come across women who not only are diagnosed during pregnancy but also elect to continue the pregnancy in spite of knowing the high risk.[4] The mortality in Eisenmenger syndrome ranges between 30 and 50%, and the leading causes of mortality are right ventricular failure, pulmonary hypertension, arrhythmia, and stroke.[6,7] Here, we report a case series of 11 women with Eisenmenger syndrome who had 12 pregnancies.

Methodology

This is a retrospective data collected from a tertiary care referral institute of Northern India. We have a dedicated cardio-obstetric unit to manage all the pregnancies complicated by heart disease. The maternal demographics and clinical details like age, parity, NYHA status at admission, and treatment taken were noted. The underlying cardiac lesion, size, ejection fraction, and reversed or bidirectional shunt at atrioventricular or aortopulmonary levels were also collected from the echocardiography reports. Arterial oxygen saturation and haemoglobin at admission

were also noted. The complete information of perinatal outcomes included the pregnancy outcome (abortion/live birth/stillbirth), mode of delivery, and intrapartum complications. Neonatal details like birth weight, sex, Appearance, pulse, Grimace, activity and respiration score, and presence of congenital malformations were also included. A note was made of neonatal admission in the intensive care/nursery and the status at the time of discharge.

Results

The records of a total of 11 women with 12 pregnancies were reviewed. The demographical and clinical characteristics have been summarised in Table 1. Out of the 11 women, 9 were diagnosed with Eisenmenger syndrome during pregnancy and the mean gestation at the time of diagnosis was 25^{+5} weeks, ranging from 8 to 35 weeks. Only three women opted for the termination of pregnancy, while rest all either elected to continue the pregnancy or were already beyond the window period for the termination of pregnancy when they reported. One woman (case 11) was admitted with heart failure, and rest all were having slight to marked limitation of functional status (NYHA class II/III).

Cardiac characteristics

The cardiac findings of echocardiography are shown in Table 2. The commonest cardiac lesion was ventricular septal defect (54.5%) followed by ASD (27.3%) and patent ductus arteriosus (9.1%). Case 7 had inlet ventricular septal defect (18–20 mm) and patent ductus arteriosus (8 mm) both with bidirectional shunt, who presented with abnormal behaviour and later found to have thalamic abscess along with Eisenmenger syndrome. The size of lesion ranged between 8 mm to 35 mm. All these women were having severe pulmonary artery hypertension with right ventricular systolic pressure of more than 50 mmHg. The functional class of these women remained almost same during pregnancy except one who presented with heart failure. However, periodic echocardiography was not performed to assess the changes during pregnancy. All these women were given sildenafil [phosphodiesterase inhibitor] 20 mg ter die sumendus (translates as 'to be taken three times a day) after the diagnosis and continued throughout the pregnancy. They were also provided intermittent oxygen therapy and rest during hospital stay. The oxygen saturation at room air ranged between 74 and 95%. The mean haemoglobin was 14.5 g, and one-third of them were having thrombocytopenia (platelet count less than 1 lac per/microlitre).

Pregnancy outcome

Table 2 also elaborates the details of pregnancy, perinatal outcome, and the complications. Total 12 pregnancies were reviewed, one patient (case 10 and case 12) first presented in year 2020 with heart failure at 21 weeks of gestation, and after stabilisation was advised medical termination of pregnancy. However, she opted to continue the pregnancy and aborted spontaneously at 22 weeks. She again conceived within a year and delivered a live born at 34 weeks.

Out of these 11 cases, 3 women opted for medical termination of pregnancy, and 1 had spontaneous abortion at 22 weeks. Rest eight of them continued or presented late. The average gestational age at the time of delivery was 34^{+3} weeks (ranging from 31 to 36 weeks). In antenatal period, 50% of them developed pre-eclampsia and 62.5% had fetal growth retardation. Two women delivered vaginally, and rest underwent cesarean section (two elective and four emergency cesareans) for obstetric indications.

Table 1. Demographic and clinical characteristics.

Variables	Number (proportion)	Variables	Number (proportion)
Age (mean ± SD)	28 ± 4 years	Cardiac lesion (n = 11)	
		VSD	7 (64)
		ASD	2 (18)
		PDA	1 (9)
Parity		Others (PDA and VSD)	1 (9)
Nullipara	10 (91)		
Para 1	1 (9)		
Education			
Matric	10 (91)		
Graduation	1 (9)	Pregnancy outcome (n = 12)	
		MTP	3 (25)
		Abortion	1 (8)
Diagnosed (n = 11)		Live birth	8 (67)
Before pregnancy	2 (18)		
During pregnancy	9 (82)	Abortion/MTP (n = 4)	
		Suction and Evacuation	2 (50)
		Foleys and dinoprostone gel	1 (25)
During pregnancy (n = 9)		Spontaneous abortion	1 (25)
First trimester	2 (22)		
Second (13–28 weeks)	3 (33)		
Third (>28 weeks)	4 (45)	Mode of delivery (n = 8)	
		Elective cesarean	2 (25)
		Emergency cesarean	4 (50)
NYHA class at presentation		Vaginal delivery	2 (25)
NYHA I	2 (18)		
NYHA II-III	8 (73)		
NYHA IV	1 (9)	Maternal outcome (n = 11)	
		Survived	8 (73)
		Died	3 (27)

ASD = Atrial septal defect; MTP = Medical termination of pregnancy; PDA = Patent ductus arteriosus; VSD = Ventricular septal defect.

Two of them had intrapartum abruption; one delivered vaginally and other had emergency cesarean section. Most of these neonates (75%) has low birth weight, required intensive neonatal care, and survived. None of the babies was found to have CHD or any other malformation.

We lost three mothers in postpartum period (days 3, 5, and 8): case 2 had massive intrapartum abruption, case 6 developed

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Table 2. Echocardiography findings and investigations and pregnancy outcomes.

Case no.	Current age (years)	Age (years.) at which diagnosed to have CHD	Heart lesion	Lesion diameter (mm)	Ejection fraction percentage %	Flow at shunt	Parity	Gestation at presentation (weeks)	Gestation at delivery or termination (weeks)	Mode of delivery/ termination	O_2 saturation on room air	Hb (g/dl)	Platelet count (platelets/µl)	Maternal outcome	Fetal outcome	Complication
1	27	27	PDA	12	60	Left to right shunt	PGR	22 + 6	31 + 3	Elective cesarean, breech with severe pre-eclampsia	75–80%	16.1	106,000	Alive and well	LB, 1.12 kg	FGR Severe pre-eclampsia HELLP
2	26	4	VSD	12 mm	50	Right to left shunt	G2P0010	23	35	Emergency cesarean for massive abruption	74%	12.6	180,000	Died on day 8 post-partum	LB, 1.8 kg	FGR Abruption, arrhythmia, and cardiogenic shock
3	36	30	VSD	17 mm	55	Left to right with gradient of 22 mmHg	G2P1001	15 + 5	16	MTP, cerviprime with foleys	92%	13.5	210,000	Alive and well	Abortus, 400 g	–
4	28	28	VSD	18 mm	60	Bidirectional	PGR	8 + 2	9	MTP suction evacuative	88%	14.9	175,000	Alive and well	–	–
5	23	22	VSD	N.A.	60	NA	PGR	10 + 3	11	MTP suction evacuative	93%	18.2	328,000	Alive and well	–	–
6	28	28	VSD	16.2 mm	60	Left to right with gradient of 30 mmHg	G3P0020	31	36	Vaginal delivery	80–85%	15.7	46,000	Died on day 5 postpartum	LB, girl, 1.6 kg	FGR Severe pre-eclampsia, cardiac arrhythmia, and cardiogenic shock
7	23	23	VSD PDA	18 mm 8 mm	35–40	Bidirectional	PGR	32 + 1	34 + 4	Emergency cesarean for thalamic pyogenic abscess in labour	95%	12.7	270,000	Alive and well	LB, boy, 2.1 kg	Thalamic pyogenic abscess
8	31	31	ASD	30	55%	Bidirectional	PGR	34	36 + 5	Emergency cesarean for severe pre-eclampsia with poor Bishop	85%	14.5	56,000	Alive and well	LB, girl, 1.88 kg	FGR Pre-eclampsia
9	30	30	VSD	29 mm	55%–60%	Bidirectional	G3P0020	33	34 + 5	Elective cesarean for pre-eclampsia with poor Bishop	82–85%	16.6	64,000	Alive and well	LB, girl, 1.28 kg	FGR Pre-eclampsia
10*	29	29	VSD	35 mm	55%	Bidirectional	PGR	20	22	Spontaneous abortion at 22 weeks	80–85%	14.6	130,000	Alive and well	Girl, 400 g	NYHA IV, heart failure
11	22	22	ASD	35 mm	40%–45%	Right to left	G2P1001	35	35	Emergency cesarean for maternal stabilisation	–	10.4	133,000	Died on day 3 postpartum	LB, boy, 2.15 kg	Biventricular failure
12*	30	29	VSD	35 mm	55%	Bidirectional	G2P0010	21 + 2	34 + 2	Vaginal delivery					LB, girl, 1.4 kg	FGR Intrapartum abruption, and postpartum hemorrhage

ASD = Atrial septal defect; LB = Live birth; MTP = Medical termination of pregnancy; PDA = Patent ductus arteriosus; PGR = Primi gravida; VSD = Ventricular septal defect
*Case 10 and case 12 are same case, presented in 2020 and 2021

cardiac arrythmias on day 5 postpartum, and case 11 was admitted with heart failure (NYHA IV).

Case 2 was 28 years old G2 P0010 who was diagnosed with CHD at the age of 4 years but was not on regular follow-up. She was booked in CO clinic at 22^{+6} weeks of gestation. Her underlying cardiac lesion was ventricular septal defect of 12 mm. At 32^{+3} weeks gestation, she was admitted with cold, cough, and tachypnoea. At 34^{+3} weeks, she went into spontaneous labour and had massive abruption. She underwent emergency cesarean section and was transfused 2 units of packed red blood cells. She remained stable for 5 days in critical cardiac unit; however, she again deteriorated on day 6 and expired.

Case 6 was 28 years old G3P0020 who had the history of infertility and conceived on ovulation induction drugs. At 28 weeks of gestation, she was diagnosed to have ventricular septal defect with severe pulmonary artery hypertension. She was referred to our institute at 36 weeks of gestation with increased blood pressure and thrombocytopenia in labour. She delivered vaginally and remained stable. On day 5, she developed arrhythmias and cardiogenic shock and could not be revived.

Case 11 was 22 years old, G2P1001 at 35^{+3} weeks of gestation admitted in emergency with heart failure. On evaluation diagnosed to have large ASD with Eisenmenger syndrome. She also went into spontaneous labour and was taken up for emergency cesarean section. She remained unstable throughout, did not improve even after delivery, and expired in ICU on day 4 postpartum.

Discussion

The pregnancy in women with Eisenmenger's syndrome poses an additional stress to an already compromised cardiovascular function. In pregnancy, there is gradual increase in blood volume (30–50%) and cardiac output.[8] This leads to a gradual remodelling of heart, increase in ventricular volume and wall thickness. There is physiological reduction in systemic vascular resistance and decrease in resistance of pulmonary vasculature. But in Eisenmenger syndrome due to pulmonary arterial hypertension, the pulmonary vasculature does not compensate and puts additional strain on right ventricle, which further worsens the right to left shunt.[9] As pregnancy is poorly tolerated by women with Eisenmenger syndrome, prevention or early termination of pregnancy is the recommended as the standard of care.[10] However, in this study, not even a single woman had any preconception checkup or counselling before planning the pregnancy. Out of 11 women, 9 were diagnosed during pregnancy and 3 (27.3%) presented in early pregnancy and opted for medical termination of pregnancy.

Regarding the outcome of pregnancy in Eisenmenger syndrome, in our study, 72.7% of women were discharged in stable condition and 62.5% (five out of eight) tolerated the pregnancy well and went home with their babies. These women are also at increased risk of adverse perinatal outcome which include abortions, small-for-gestational-age (SGA) babies, and pre-term deliveries.[11] In our case series, all had pre-term delivery, mean gestation at the time delivery was 34^{+3}weeks, and most of the babies were small for gestational age. Almost half of our cases develop pre-eclampsia in third trimester. In such cases, there is no association of pre-eclampsia and Eisenmenger syndrome, but extremely high mortality has been reported in the pregnancy of Eisenmenger syndrome which were complicated by severe pre-eclampsia.[12]

Katsurahgi et al have mentioned three factors for favourable outcome in pregnancy complicated with Eisenmenger syndrome which include early hospitalisation, introduction of newer drugs, and improved anesthetic management.[13] The gestation age for early hospitalisation depends on the symptoms like worsening of oxygen saturation and the functional class. In index study, the women who were diagnosed in second trimester were followed up in outpatient department. In addition to routine obstetric care, oxygen saturation and NYHA functional class was assessed at each visit. Women were hospitalised at around 30–32 weeks of gestation for safe confinement. They were managed with adequate bed rest, and oxygen therapy and phosphodiesterase inhibitors were also initiated after the diagnosis.

Regarding the mode of delivery in women with Eisenmenger syndrome, there is no consensus or specific recommendations in the literature.[9,10] In our study, women who presented in spontaneous labour were allowed to deliver under vigilant monitoring and cesarean was performed for obstetric indication only. In a case series by Ruiqi Duan et al, they preferred cesarean section over vaginal delivery and found greater stability and control over the haemodynamics.[14] Valsalva of labour seems to be better tolerated in Eisenmenger syndrome as compared to primary pulmonary hypertension due to the presence of shunt. In our study, 75% (6/8) of women underwent cesarean and all were done under general anaesthesia. In literature, some have preferred epidural anaesthesia or combined epidural anesthesia, whereas few supported general anaesthesia over regional.[15–17] It has been mentioned that general anaesthesia could allow better placement of oesophageal ultrasound probe during surgery and early initiation of thromboprophylaxis. A very high morbidity and mortality have been reported in women with Eisenmenger syndrome in pregnancy; therefore, pregnancy is an absolute contraindication.[9] In our study, the mortality rate was 27.3%, and we lost all these mothers in postpartum period.

There are several limitations in this study: it was a retrospective study, the number of subjects was very small, and the further correlation of cardiac findings with perinatal outcome was not possible. The factors which led to late diagnosis or diagnosis during pregnancy were not reviewed. Although pulmonary artery hypertension targeted drug, that is, sildenafil was given to most of our patients, the effect of drug on pregnancy could not be assessed.

Conclusion

Our study highlights the delay in diagnosis and treatment of CHD. Early diagnosis and treatment could have played an important role in maternal and perinatal outcome of all these women. Women with Eisenmenger syndrome require an effective preconceptional counselling and early termination of pregnancy. Women who elect to continue the pregnancy require multidisciplinary care by obstetricians, cardiologists, anesthesiologists, and neonatologists. In our setting, we need to have more studies to assure the safety of drugs and outcome of these pregnancies.

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Conflicts of interest. None.

Ethical standards. The study was approved by the Departmental review board (OBGYN/EC/119on 23.05.2022).

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