

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20251586>

Case Series

The case series of Eisenmenger syndrome and its pregnancy outcome in tertiary care centres of South India

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Received: 22 March 2025

Revised: 04 May 2025

Accepted: 05 May 2025

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ABSTRACT

The incidence of the Eisenmenger syndrome (ES) is very rare in the pregnant women, but it has significant association with materno-fetal morbidity and mortality. The prognosis of ES in terms of materno fetal outcomes and neonatal outcomes in the pregnant women is unclear. The main aim of this study is to evaluate the materno-foetal outcome of pregnancy with ES in a tertiary care centre. The case series had been observed in retrospective aspect at 2 tertiary care centres of South India, Government Thiruvavur Medical College and Hospital, Government Villupuram Medical College and Hospital, Tamil Nadu, India over a period of 1 year from 2023-2024. This study analysed the occurrence of ES in the pregnant women with cardiac disease and their materno-foetal outcomes in tertiary care centres of South India. In our study period, 41,718 cases were delivered, in which 6515 cases had cardiac disease, 1105 cases had congenital heart disease. Of these, 6 cases had ES during pregnancy. In our study, ES was noted in 1: 6953 pregnant women, 1:1086 pregnant women with cardiac disease, 1:184 pregnant women with congenital cardiac disease. The mean age was 23.4 ± 0.52 and mean gestational age at delivery was 34 ± 1.25 weeks. The mean pulmonary arterial pressure was 73 mmHg. In our study, 3 cases had preterm deliveries and 1 case had term delivery, 2 cases delivered vaginally, 2 cases had caesarean section and 2 cases had abortions. As per our study, nil maternal mortality reported. For achieving optimum outcomes in the pregnant women with ES, the well-equipped obstetric critical care unit with multidisciplinary approach must be ensured in a tertiary care centre.

Keywords: Cyanotic heart disease, Pulmonary hypertension, Eisenmenger syndrome, Systemic vascular resistance, Atrial septal defect, Ventricular septal defect, Reduced end diastolic flow

INTRODUCTION

Eisenmenger syndrome (ES) has a very rare occurrence in pregnancy with the reported incidence of 3% in pregnant women with Congenital heart defects.¹ The reported incidence of maternal mortality due to ES was 30-50% but in the pregnant women who had undergone caesarean section it was 65%.² Pregnancy is the absolute contraindication for a woman with ES because of high maternal mortality rate and perinatal morbidities.

ES is defined as the process of long-standing left to right shunting associated with congenital heart disease (CHD)

which causes pulmonary vascular remodelling which leads to the development of pulmonary arterial hypertension with shunt reversal or bidirectional shunt. ES develops more commonly in CHD with non-restrictive communication at the levels of aortopulmonary, ventricular or atria.

The pathophysiology of ES was due to increased shear stress on the pulmonary endothelium triggers pulmonary vascular remodelling eventually which leads to irreversible changes in pulmonary vascularity resulting in pulmonary artery hypertension (PAH). The most devastating and refractory disease in pregnancy was PAH.

According to Banerjee et al, the multisystemic involvement of ES includes changes at cardiovascular, haematological, renal, neurological, immune levels. Chronic hypoxemia is related to its clinical manifestations. However, the long-term prognosis of ES in pregnant women depends on sub optimal sensitivity. Patients with isolated ES had better survival rate than patients with idiopathic PAH, also with favourable haemodynamics, attributes to persistent left to right shunt which allows relief of pressure overload on right ventricle by preserving systemic perfusion at the expense of systemic desaturation.³

According to Pandey et al, the pathophysiology of ES during pregnancy is mainly related to its cardiovascular changes, which includes SVR reduction leads to increased right to left shunt causing pulmonary perfusion reduction. In these conditions, systemic hypotension causes decreased right ventricular filling pressure which is insufficient to perfuse pulmonary arterial bed. This insufficient perfusion of pulmonary arterial bed will be exaggerated in conditions such as fasting, dehydration, hypovolemia due to haemorrhage, conduction anaesthesia in pregnancy. Hence, the features of decreased pulmonary perfusion as well as reduced right ventricular filling pressure eventually results in hypoxemia, which causes polycythaemia or secondary erythrocytosis, hypercoagulability and thromboembolism. Hence adverse materno-fetal outcomes occur in ES complicated pregnancy due to syncope and sudden death.⁴

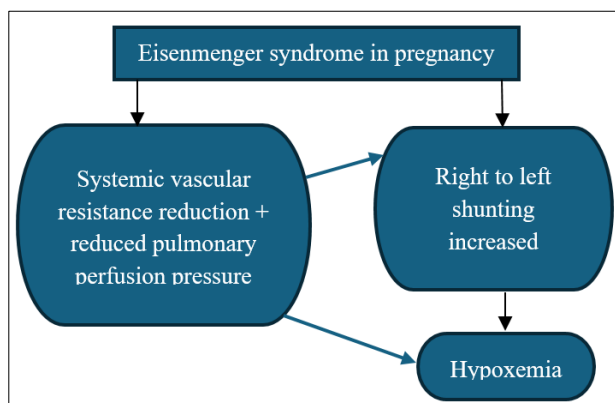


Figure 1: Pathophysiology of Eisenmenger syndrome in pregnancy.

According to Trojnaraska et al, the principal concern during intrapartum management of ES is to avoid hypotensive episodes which ultimately leads to cyanosis and low oxygen saturation due to hypoxemia, secondary erythrocytosis leading to polycythaemia and hyper viscosity with coagulation disturbances, heart failure and arrhythmia.⁵ The crucial period of ES in the pregnant women was the immediate postpartum period. The major risk factors causing maternal mortality includes congestive cardiac failure (CCF), anaemia, bleeding, haematocrit >60%, SpO₂ <80%, syncope due to sudden rise in pulmonary vascular resistance or reduced systemic

vascular resistance. The high-risk period of maternal mortality was peripartum period.⁶ But in our study population, postpartum period was uneventful. This study describes the clinical course of ES in the pregnant women and its maternofetal outcome in a tertiary care centre along with literature review of its management.

CASE SERIES

Case 1

A 24 years primigravida presented at 38 weeks with breathlessness and lower abdominal pain. On admission, her vitals were PR-112/min, BP-110/80 mmHg, SpO₂-82% with room air. On examination she had peripheral cyanosis, abdominal examination revealed single live fetus with term uterus, acting. Per vaginal examination revealed she was in active labour. She delivered an alive term girl baby of birth weight 2 kg after 6 hours of admission by normal vaginal delivery. Postnatally, she was stabilized, cardiology consultation was obtained. Chest X-ray-cardiomegaly. ECHO-atrioventricular defect 18 mm, atrioseptal defect 28 mm with bidirectional shunt, EF 50%, pulmonary arterial pressure-60 mmHg, her Hb 17 gm/dl, and Hct 50%. She was treated with oxygen therapy, infective endocarditis prophylaxis, thromboprophylaxis, sildenafil, diuretics, digoxin. She was discharged on postnatal day 14 with cardiac follow up.

Case 2

A 33 years G2P1L1/previous normal vaginal delivery presented at 9 weeks in view of medical termination of pregnancy. She had complaints of breathlessness on exertion. On examination her vitals were PR-108/min, BP 100/70 mmHg, SpO₂- 91% with room air. Her Hb-16 gm/dl, and Hct-66%. Chest X-ray-dilated central pulmonary arteries with pruning of peripheral pulmonary arteries. ECHO-ASD with 15 mm, perimembranous VSD, right to left shunt, severe pulmonary arterial hypertension (70 mmHg) due to ES. She underwent induced abortion uneventfully by medical method. She was treated with thromboprophylaxis, Infective endocarditis prophylaxis, oxygen therapy, diuretics, sildenafil. She was discharged on 14th post-abortion day with advice of regular cardiac follow up.

Case 3

A 27 years primigravida presented at 22 weeks + 3 days, complaints of leaking per vaginum, breathlessness, palpitation, headache, fatigue. On examination she had cyanosis, clubbing, PR-124/min, BP- 130/80 mmHg, SpO₂-86% with pan systolic murmur heard over lower left sternum. Abdominal examination- uterus corresponds to 22 weeks, relaxed. Per speculum- minimal clear liquor draining noted. Chest X-ray-cardiomegaly, increased pulmonary vascular markings. ECHO- large sub aortic VSD, biventricular hypertrophy, moderate AR, EF-43%, right to left shunt, severe pulmonary arterial hypertension

(76 mmHg) with ES. Her Hb 15.6 gm/dl, and Hct 58%. She delivered a still born girl baby of birth weight 480 gms after 36 hours of admission. She was treated with oxygen therapy, thromboprophylaxis, infective endocarditis prophylaxis, sildenafil, diuretics, digoxin, metoprolol. She was discharged on post-abortion day 14 with advice of regular cardiac follow up.

Case 4

A 22 years old G2A1 at 35 weeks came with complaints of fatigue, breathlessness, headache, chest pain. On examination she had cyanosis, clubbing, PR- 116/min, BP-100/60mmHg, SpO₂- 90% with room air, abdominal examination-uterus 32 weeks, relaxed, and fetal heart sounds present. Chest X-ray-cardiomegaly, prominent main pulmonary artery segment. ECHO- large ASD (31 mm) moderate TR, severe PS, mild PR, right atrium and right ventricle dilated, severe PAH (76 mmHg), bidirectional shunt, EF 60%, and D shaped left ventricle. Her Hb was 16.2 gm/dl, and Hct 64%. She was treated with steroids for fetal lung maturity, diuretics, digoxin, sildenafil, infective endocarditis and thromboprophylaxis. She delivered an alive preterm boy baby of birth weight 1.6 kg with APGAR 7/10, 9/10 after 3 days of admission by normal vaginal delivery under epidural anaesthesia. Baby was admitted in NICU for low birth weight. She was discharged along with baby on postnatal day 18 with advice of cardiac follow up.

Case 5

A 24 years old primigravida presented at 20 weeks with cardiac screening revealed ventricular septal defect. She had complaints of fatigue, breathlessness on exertion, occasional palpitations SpO₂-97%. On examination, her PR-120/min, BP120/80 mmHg, SpO₂-97%, pansystolic murmur at left parasternal area. ECHO- large perimembranous VSD with severe PAH and left to right shunt. Her Hb 15.8 gm/dl, and Hct-50%. Despite of explaining risk, patient still wanted to continue the pregnancy. She was treated by cardiologist with sildenafil, thromboprophylaxis. She was on regular follow up and serial monitoring of fetal growth was done. At 34 weeks she developed breathlessness with ECHO revealing severe PAH (60 mmHg) and right to left shunt. Fetal growth restriction with reversal of end diastolic flow noted. Infective endocarditis prophylaxis was given. She underwent elective caesarean section under epidural anaesthesia to deliver an alive boy baby of birth weight 1.2 kg with APGAR 4/10,6/10. She was on continuous monitoring in obstetric ICU care with postpartum thromboprophylaxis, sildenafil. Both mother and baby discharged on postoperative day 18.

Case 6

A 20 years old primigravida presented at 27+4 weeks as a known case of Ebstein's anomaly. She underwent Blalock Taussig procedure (between right pulmonary artery and

subclavian artery) during her childhood. On examination she had stable vitals, with normal fetal growth. ECHO-typical Ebstein anomaly, situs solitus, severe dysplastic tricuspid valve, atrialized right ventricle, ASD (15 mm), mild RV dysfunction, EF 64%, and no PAH. Risk regarding the pregnancy was explained. She was put on thromboprophylaxis, beta blockers and on regular follow up. She developed breathlessness, palpitation, cyanosis on 33 weeks of gestational age with PR 126/min, BP-110/70 mmHg, SpO₂- 90% with room air. ECHO revealed same above findings with severe PAH (80 mmHg) with right to left shunt due to ES. Hb 17 gm/dl, and Hct- 55%. She underwent elective caesarean section due to fetal distress under epidural and general anaesthesia to deliver an alive boy baby of birth weight 1.9 kg with APGAR 8/10, 9/10. She was further treated with infective endocarditis prophylaxis, postpartum thromboprophylaxis, sildenafil, diuretics. She was discharged on postoperative day 42 along with her baby and advised for further follow up in cardiology.

DISCUSSION

In our study, the total number of antenatal cases who delivered at our tertiary centres over 1 year was 41,718. Out of 41,718 cases, 6515 antenatal cases had cardiac disease. Of these 6515 cases, 1105 cases had Congenital heart defects (CHD), 3909 cases had rheumatic heart disease (RHD) and other cardiac disease was 1501 cases. The higher incidence of cardiac disease in our tertiary centres, was due to effective ECHO screening of all pregnant women and scrutinization of all high-risk pregnant women. Out of 1105 cases in CHD group, 6 cases had ES. ES was seen in 1:6953 pregnant women, 1:1086 pregnant women with cardiac disease and 1:184 pregnant women with CHD. The mean age of these pregnant women was 23.4±0.52 years.

Out of 6 cases, 2 cases had ASD, while other 2 cases had VSD, 1 case had atrioventricular defect with ASD, 1 case had Ebstein anomaly. The mean pulmonary arterial pressure 73 mmHg. In our study, 2 cases had normal vaginal delivery, 2 cases had caesarean section, 2 cases had abortion. The mean gestational age at delivery was 34±1.25 weeks. Out of 6 cases, 33.3% (2/6) had vaginal deliveries, 33.3% (2/6) had caesarean section and 33.3% (2/6) had abortions. In our study 2 cases had caesarean section and the indications were fetal alarming signal and fetal Doppler changes -REDF. Out of 2 cases of abortions, one case undergone Therapeutic abortion at GA 9 weeks and another case had PPROM and spontaneously expelled at GA 22 weeks 5 days. In our study, observed maternal mortality was nil during our study period.

In 1897, ES was first described. In patients with CHD, the approximate reported incidence of ES was 3%. In association with VSD (ES+VSD) the reported maternal mortality rate of ES is 60% which was higher than ASD or PDA association due to hypovolemia, preeclampsia and thromboembolism.⁷ CHD in pregnant women such as

VSD, ASD and PDA causes pulmonary vascular remodelling, which eventually leads to ES. The clinical manifestations of ES in pregnant women includes dyspnoea, cyanosis or differential cyanosis, clubbing of fingers, fatigue, dizziness and right heart failure.⁸ Haemorrhagic manifestations such as haemoptysis, epistaxis has also been reported.⁹ On clinical examination, inspiratory crepitations, loud P2, systolic murmur at pulmonary area, elevated JVP, and pedal oedema may also be seen.¹⁰

Table 1: Parameters used to evaluate maternal-fetal outcomes of Eisenmenger syndrome in tertiary care centres.

S. no.	Evaluated parameters	Value
1	Occurrence of ES among antenatal women	1:6953
2	Occurrence of ES among antenatal women with cardiac disease	1:1086
3	Occurrence of ES among antenatal women with congenital cardiac disease	1:184
4	Mean age (years)	23.4±0.52
5	Mean gestational age at presentation (weeks)	24.4±0.6
6	Mean gestational age at delivery (weeks)	34±1.25
7	Mean pulmonary arterial pressure (mm Hg)	73
8	Maternal mortality (%) (0/6)	0
9	Preterm delivery (%) (3/6)	49.9
10	Vaginal delivery (%) (2/6)	33.3
11	Caesarean delivery (%) (2/6)	33.3
12	Fetal growth retardation (%) (4/4)	100
13	Fetal survival (%) (4/4)	100
14	Abortions (2/6)	33.3

Clinically patient have low oxygen saturation, polycythaemia but the machinery murmur in ES might be inaudible and associated PDA might be misdiagnosed.¹¹ Cardiomegaly and bilateral pulmonary congestion will be revealed in chest X-ray.¹⁰ ECG shows right ventricular hypertrophy sometimes left ventricular hypertrophy also noted. Cardiac catheterization was done to locate the defect in ES and also to detect pulmonary artery pressure.¹² ES in pregnant women causes severe complications such as heart failure, thromboembolic phenomenon, infective endocarditis and sudden death in postpartum period.¹³ Hence, the multidisciplinary approach care from a high-risk obstetrician, critical obstetrics care unit, cardiologist and anaesthetist will improve the materno-foetal outcome in ES complicated pregnancy.

Pregnancy is the absolute contraindication for ES. Hence these pregnant women were advised for termination of pregnancy in early weeks of gestation. So, antepartum foetal surveillance in this group of pregnant women

includes serial monitoring of haemoglobin and haematocrit. Hence to avoid relative anaemia in ES, iron supplementation should be advised. As per Kansaria et al study, pregnant women with hematocrit >65% had poor pregnancy outcomes.¹⁴ In our study, haematocrit values were raised for all cases, with mean value of >55%. The delayed diagnosis, delayed presentation, and severity of PAH are risk factors influences pregnancy outcome. Since hypotension exacerbates right-to-left shunt, hypovolemia must be avoided in ES. Hence, in antepartum period, heavy exercise, dehydration, haemorrhage, fasting, high altitude and air travel should be avoided.¹⁵ Maternal mortality rate in ES in pregnancy was 50%, whereas foetal mortality rate was 25%.¹⁶ In our study, foetal mortality rate was 33.3% and there was no maternal mortality rate.

The important predictor of fetal outcome was the degree of maternal hypoxemia due to hypoxia, arterial oxygen desaturation and polycythaemia. CHD is the underlying cause for ES in pregnancy, hence the risk for developing CHD in offspring ES complicated pregnancy was 10%. In order to prevent CHD occurrence in offspring, Fetal ECHO is recommended between 18-22 weeks of gestation for these pregnant women.¹⁷ In ES complicated pregnancies, there is a chance for FGR by 30%, so it should be included in antepartum foetal surveillance.¹⁸ As maternal hypoxemia increases the incidence of spontaneous abortions, FGR, low birth weight (LBW) and preterm birth in ES complicated pregnancies, maternal arterial oxygen saturation pressure should be maintained at a level ≥ 70 mmHg to avoid those complications.¹⁹

As per Bedard et al study, 24% of the pregnant women with ES had FGR and 86% had preterm birth.²⁰ Brach-Prever et al, study showed 54.9% of preterm birth in ES complicated pregnancy.¹⁸ In our study, 2 cases had delayed manifestations but multidisciplinary approach helped in salvaging the mother as well as fetuses. One foetus who succumbed for spontaneous expulsion by 22 weeks due to maternal hypoxemia. In our study, out of 6 cases with ES complicated pregnancy, 4 cases were delivered, out of which 75% had preterm birth and 100% had FGR.

As per Brazilian study suggested that case series of 13 pregnancies showed improved maternal mortality rate with treatment of oxygen administration, pulmonary vasodilators (category B drugs) and prophylactic anticoagulation.²¹ According to Pitts et al study, 5 cases were died due to secondary haemorrhage.¹⁹ In our study, postpartum thromboprophylaxis was given to all 6 cases with nil maternal mortality. As per case report study of Mukhopadhyav, conservative management of ES complicated pregnancy with oxygen, IE prophylaxis, diuretics in a tertiary care centre had successful pregnancy outcome.⁹ Lacassie et al study reported that management of PAH in pregnancy with sildenafil and L-arginine had successful maternal outcomes.²² Cartago et al study showed that monotherapy treatment with sildenafil in ES complicated pregnancies leads to maternal stabilization

and optimum maternal outcome.²³ In our study, sildenafil with supportive measures improved pregnancy outcomes.

Mode of delivery in ES complicated pregnancy is still a debatable one. Hence, the aim during labour is to maintain oxygen saturation, pain relief, fluid balance to avoid hypotension, BP control since it determines the extent of right to left shunt. Epidural and incremental spinal anaesthesia are the preferred mode for caesarean section for ES in view of reduction in SVR in general anaesthesia, which lowers right to left shunting resulting difficult intubation.⁶ Gleicher et al study reported that 34% mortality as compared to 75% mortality with caesarean section.¹⁷ In our study, nil maternal mortality reported in Caesarean section because of strict BP control, intrapartum fluid balance, oxygen saturation maintenance. According to Canobbio et al, optimizing BP monitoring during intrapartum period is very critical to maintain a balance between systemic and pulmonary blood flow as decreased SVR or increased PVR, results in increased right to left shunting which ultimately increases hypoxemia and increased foeto-maternal maternal death risk. IE prophylaxis should be advised. Vaginal delivery is considered to be safer, because of average blood loss, but it is associated with increased maternal effort so advised to cut short the second stage of labour.²⁴ As we have already discussed, in our study caesarean section done for 2 cases in view of obstetric indication only and 2 cases were delivered vaginally.

Deep vein thrombosis (DVT) preventive measures should be taken in ES complicated pregnancy as these patients have hyper viscosity. In postpartum period early ambulation, use of elastic stockings, use of anticoagulants reduces the risk for DVT. Since ES complicated pregnancy is the absolute contraindication, Tubal ligation is strongly recommended. Progesterone only contraceptive pills, progesterone implants and depot preparations can be used as these medications are safe in pregnancy, due to its low risk for thrombotic tendency. Since copper T intrauterine devices causes menorrhagia there will be increased risk for infective endocarditis hence it is not recommended for ES complicated pregnancy. So, levonorgestrel intrauterine contraceptive device is considered to be safer.²⁴ To achieve satisfactory maternal and perinatal outcomes bed rest, oxygen therapy, heparin use is generally advisable.

CONCLUSION

The outcome of ES in pregnancy has been improved due to combined management of modern cardiological and obstetrical practices. During preconceptional counselling, the severity of heart failure and higher chances of prematurity and FGR should be considered and advised to opt for termination of pregnancy. Due to heterogeneity of underlying cardiac lesion in pregnancy and its variable clinical presentations of ES during pregnancy, to achieve a satisfactory pregnancy outcome, optimised multi-disciplinary approach should be ensured in all tertiary care centres.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Nathan JM, Thirupathi K. The case series of eisenmenger syndrome and its pregnancy outcome in tertiary care centres of South India. *Int J Reprod Contracept Obstet Gynecol* 2025;14:1940-5.