

# Pregnancy in the Patient with Eisenmenger's Syndrome

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## Abstract

Eisenmenger's syndrome occurs when a large congenital or surgically created shunt between the left and right sides of the heart causes an increase in pulmonary vascular resistance that equals or surpasses systemic resistance, resulting in a reversal of the shunt from a left-to-right shunt to a right-to-left or bi-directional shunt. The maternal mortality rate of pregnancy in the presence of Eisenmenger's syndrome is reported to be as high as 50–65% with cesarean section. We present the case of a 32-year-old woman with Eisenmenger's syndrome who gave birth at 29 weeks of gestation via C-section to a healthy baby boy, and we review the literature regarding the management of such patients.

**Key Words:** Eisenmenger's syndrome, pregnancy, congenital heart disease.

## Introduction

IN PATIENTS with a congenital left-to-right shunt, a progressive increase in pulmonary vascular resistance may lead to shunt reversal or bi-directional shunting, resulting in Eisenmenger's syndrome. It occurs in these patients secondary to irreversible damage to the pulmonary vasculature from prolonged exposure to systemic pressures due to the left-to-right shunting. When right-sided pressures meet or exceed systemic pressures, a reversal occurs in the shunt, leading to the morbidity and mortality associated with this condition. These hemodynamic changes may lead to thromboembolic events, cerebrovascular complications, or the hyperviscosity syndrome. Pregnancy or noncardiac surgery is associated with a high mortality rate in patients with this syndrome. Most patients with the syndrome survive for only 20–30 years (1–4).

The increased pulmonary resistance that occurs in Eisenmenger's syndrome carries a serious prognosis during pregnancy. During the antepartum period, the decreased systemic vascular resis-

tance associated with pregnancy increases the likelihood and the degree of right-to-left shunting, and therefore cyanosis to both the mother and the fetus may ensue. The maternal mortality rate of pregnancy in the presence of Eisenmenger's syndrome is reported to be as high as 50–65% with cesarean section. Overall fetal wastage is reported to be up to 75%. Medical termination of pregnancy is the preferred management for women with Eisenmenger's syndrome who present early in pregnancy (5, 6). We present the case of a 32-year-old woman with Eisenmenger's syndrome who gave birth at 29 weeks of gestation to a healthy baby boy, and we review the literature regarding the management of such patients.

## Case Summary

A 32-year-old African American woman with a history of congenital cyanotic heart disease with tricuspid atresia, transposition of the great vessels, irreversible pulmonary hypertension, double outlet left ventricle, patent ductus arteriosus (PDA), and patent foramen ovale (PFO) presented to our cardiology clinic during her third month of pregnancy. She had never undergone surgery to correct her cardiac defects. This was the patient's first pregnancy, and she was referred to our clinic from her pediatric cardiologist.

The patient related progressive cyanosis and dyspnea on exertion over the prior several years. Her medical regimen included digoxin and

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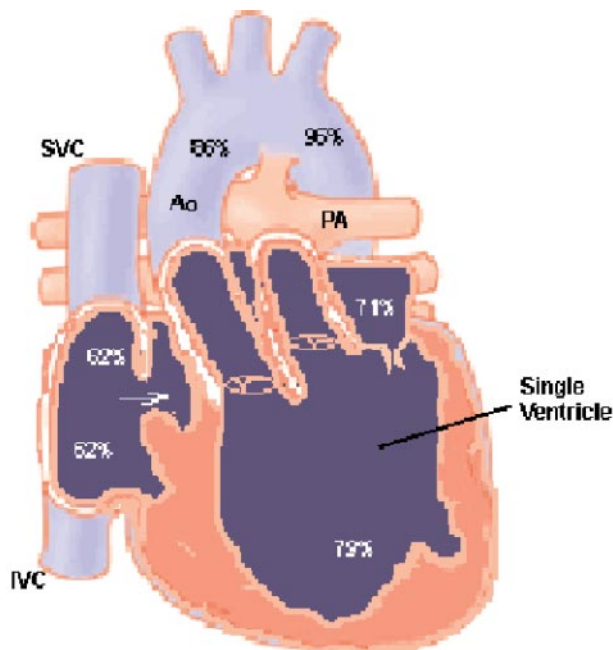
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furosemide daily. On physical examination, the patient's blood pressure was 145/85 mm Hg, her pulse was 80/min, and oxygen saturation was 80–88%. Her lungs were clear to auscultation, and cardiac exam showed regular rate and rhythm with a preserved S1 and S2, but revealed a palpable thrill over the right sternal border and a III/VI continuous murmur at the right upper sternal border and the mid-scapular area. A ventricular heave with a bounding apical impulse was also noted. No peripheral edema was observed. Her ECG revealed sinus rhythm at a rate of 80 beats/min with significant voltage, indicating ventricular hypertrophy.

Five years earlier, the patient had undergone cardiac catheterization (Figure). At that time her right atrial (RA) pressure was 16–18 mm Hg, and her pulmonary artery (PA) pressure was 106/46 mm Hg. Pulmonary capillary wedge pressure (PCWP) was 20 mm Hg and the left atrial (LA) pressure was 16–24 mm Hg. Left ventricular (LV) pressure was 106/14 mm Hg, and the ascending aorta pressure was 106/66 mm Hg. The shunt ratio (Qp:Qs) was 2.2:1. Echocardiography showed a dilated double-outlet left ventricle with unrestricted pulmonary blood flow and an ejection fraction of 33%. Severe pulmonary hypertension and tricuspid atresia were also noted.



**Figure.** Diagram detailing this patient's congenital anomaly. The percentages on the diagram are the oxygen saturations noted in these cardiac chambers at catheterization. The arrow reveals the defect in the atrial septum. (SVC=superior vena cava; IVC=inferior vena cava; Ao=aorta; PA=pulmonary artery; PDA=patent ductus arteriosus).

The patient had been told several times that she should undergo termination of her pregnancy, given the serious danger imposed on her and the fetus by her congenital anomaly. This recommendation was reiterated during our first encounter with her. However, she chose to continue her pregnancy.

Over the next few months, the patient underwent frequent close follow-up with both the cardiology clinic and the high-risk obstetrics clinic. At 27 weeks, she was admitted to the hospital in anticipation of labor induction and monitored on telemetry. Fetal monitoring was also undertaken. The patient was maintained on bed rest, supplemental oxygen, and heparin. Transthoracic echocardiography revealed pulmonary artery pressure of 95 mm Hg and a Qp:Qs ratio of 2:1. The issue of the optimal time of elective C-section to optimize fetal development while hoping to minimize maternal risk was considered. At 29 weeks, labor ensued and delivery of the baby via C-section was undertaken. At that time, the patient also had fallopian tubal ligation. Both she and the baby did well in the postpartum period. The patient was monitored after the C-section, and then discharged to home. She continues to follow up with us in cardiology clinic. She is maintained on home oxygen, digoxin, furosemide, and warfarin anticoagulation; and she continues to do well.

## Discussion

Congenital defects associated with Eisenmenger's syndrome include ventricular septal defect (VSD), atrial septal defect (ASD), atrioventricular defects, PDA, D-transposition of the great vessels, and surgically created aortopulmonary connections. Since the first description by Viktor Eisenmenger in 1897 (7), it has been noted that about 8% of all patients with congenital heart disease and about 11% of those with left-to-right cardiac shunting develop the Eisenmenger syndrome (1, 8). Approximately 50% of infants with a large, nonrestrictive VSD or PDA develop increased pulmonary resistance by early childhood, and 40% of patients with a VSD or PDA and transposition of the great arteries develop pulmonary hypertension within the first year of life. With a large secundum ASD, only 10% of cases progress to pulmonary hypertension, and they do so more slowly and usually not until after the third decade of life. In almost all patients with persistent truncus arteriosus and unrestricted pulmonary blood flow, and almost all patients with common atrioventricular canal, severe pulmonary resistance develops by the second year of life. With surgically created systemic-to-pulmonary shunts, the frequency of pulmonary hypertension varies depending on size and anatomy of the shunt (1, 2, 8–10).

Patients who develop Eisenmenger's syndrome generally present with impaired exercise tolerance due to an inability to increase pulmonary blood flow. This inability to increase pulmonary blood flow, limits oxygen uptake. Other symptoms include subtle neurologic abnormalities such as headache, dizziness, or visual disturbances due to erythrocytosis and hyperviscosity. In addition, arrhythmias are common, and may lead to sudden death. Hemoptysis may also occur, due to damage of the pulmonary vasculature. Cerebrovascular accidents may occur as a result of paradoxical embolization, venous thrombosis of cerebral vessels, or intracranial hemorrhage. In addition, patients may also develop a brain abscess (10).

The pathophysiology of Eisenmenger's syndrome consists of the initial morphologic alterations (medial hypertrophy of the pulmonary arterioles, intimal proliferation and fibrosis, and occlusion of the small vessels), which are potentially reversible. As the disease progresses, more advanced morphologic changes (plexiform lesions and necrotizing arteritis) are irreversible. The result is obliteration of much of the pulmonary vascular bed, leading to increased pulmonary vascular resistance and reversal of the shunt (11).

Whatever the etiology of Eisenmenger's syndrome, increased pulmonary resistance carries a grave prognosis during pregnancy. During the antepartum period, the decreased systemic vascular resistance associated with pregnancy increases the likelihood and the degree of right-to-left shunting. The increase in right-to-left shunting decreases pulmonary perfusion. This decrease results in hypoxemia to both the mother and the fetus. In such a patient, systemic hypotension leads to a decreased right ventricular filling pressure, and in the presence of fixed pulmonary resistance, such decreased right heart pressure may be insufficient to perfuse the pulmonary arterial bed. This insufficiency may result in sudden profound hypoxemia and death. Maternal hypotension during pregnancy can result from hemorrhage or complications of anesthesia. This sequence of events is the principal clinical concern in the peripartum management of patients with increased pulmonary resistance (11–13).

The rate of survival among patients with Eisenmenger's syndrome is 80% ten years after diagnosis, 77% at 15 years, and 42% at 25 years (14, 15). Death usually occurs suddenly, presumably caused by arrhythmias, but some patients die of heart failure, hemoptysis, a brain abscess, or a stroke. A history of syncope, right ventricular systolic dysfunction, low cardiac output, and severe hypoxemia indicates a poor prognosis (1, 8).

The treatment of patients with Eisenmenger's syndrome is difficult. Intravascular volume depletion, heavy exertion, high altitude, and the use of vasodilators should be avoided. Because of high maternal and fetal morbidity and mortality, pregnancy should also be avoided. Although no therapy has been proven to reduce pulmonary vascular resistance, intravenous epoprostenol may be beneficial (16). Phlebotomy with isovolumic replacement should be performed in patients with symptoms of hyperviscosity (17). For patients who have markers of poor prognosis such as syncope, right heart failure and/or severe hypoxemia, lung transplantation with repair of the cardiac defect or combined heart-lung transplantation is an option (18). Because of the reasonably good likelihood of survival among patients treated medically and the limited success of transplantation, the latter should only be used as a last resort in carefully selected patients.

Eisenmenger's syndrome is an absolute contraindication to pregnancy and if a patient with this syndrome does become pregnant, early termination is highly recommended due to the maternal mortality (as high as 50%). Yentis et al. (19) examined the maternal mortality in a group of patents from 1990–1995 and found that, similar to initial reports from the 1950s, maternal mortality remains high—around 40%—and fetal loss about 8%. Only 15% of infants studied were born at term. Maternal mortality associated with Eisenmenger's syndrome therefore remains as high as it has been for the past 50 years (19).

Researchers have looked at methods to decrease maternal mortality in pregnancy with Eisenmenger's syndrome. Avila et al. (20) examined a group of 13 pregnancies among 12 patients. They found three spontaneous abortions, one premature labor at 23 weeks of gestation and two maternal deaths during the 23rd and 27th weeks of gestation. Seven of the 12 patients reached the end of the second trimester. This group was hospitalized until delivery and received heparin (20,000–40,000 units per day) and oxygen therapy. Cesarean section was performed on all patients as a result of worsening maternal or fetal clinical condition during the third trimester of gestation. All of the mothers were discharged from the hospital, but one of them died on the 30th post-partum day. These investigators concluded that although pregnancy should be discouraged in women with Eisenmenger's syndrome, it can be successful with prolonged bed rest and the use of heparin and oxygen therapy to improve maternal and infant outcomes (20). Other studies, however, have found a negative effect of heparin prophylaxis in these patients (21). Thus the role of anticoagulation in the

care of pregnant patients with Eisenmenger's syndrome remains controversial.

Inhaled nitric oxide is a potent and selective pulmonary vasodilator used in patients with pulmonary hypertension. It is thought that direct inhalation of nitric oxide may reduce pulmonary resistance and improve oxygenation because of optimization of ventilation-perfusion relations. There have been reports of nitric oxide use during pregnancy in patients with Eisenmenger's syndrome (22). Goodwin et al. (23) report the case of a 27-year-old woman treated with nitric oxide to correct the refractory hypoxemia of Eisenmenger's syndrome during the birth of her 36-week-old infant. Despite continued vasodilator therapy, however, the patient died on post-partum day 6. Another report by Lust et al. (24) cites the use of nitric oxide in the peripartum period of a 29-year-old primigravid female at 34 weeks' gestation. After giving birth, however, she died of worsening pulmonary hypertension and heart failure on post-partum day 21 (24).

### Conclusion

Patients with Eisenmenger's syndrome should be counseled against becoming pregnant. Eisenmenger's syndrome is an absolute contraindication to pregnancy, and if a patient with this syndrome does become pregnant, early termination is highly recommended due to high maternal mortality. Maternal mortality associated with Eisenmenger's syndrome, despite recent efforts at its mitigation, remains as prevalent as it has been for the past 50 years. We presented the case of a 32-year-old woman with Eisenmenger's syndrome who, despite medical advice, decided to continue her pregnancy and gave birth to a healthy baby at 29 weeks' gestation.

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