# Pregnancy and Hemolysis, Elevated Liver Enzymes and Low Platelet Count Syndrome in Patients With Eisenmenger's Syndrome

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**Abstract:** Eisenmenger's syndrome is characterized by a right-to-left or bidirectional shunt in congenital heart diseases. Hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome, commonly occurring during pregnancy, includes hemolysis, elevated liver enzymes and low platelet counts. HELLP syndrome and pregnancy are extremely rare in patients with Eisenmenger's syndrome. The authors report 4 cases of pregnancy complicated by the HELLP and Eisenmenger's syndrome and describe their initial intervention and the in-hospital outcomes of these cases. Special emphasis is given to elaborate about the hemodynamic monitoring, magnesium sulphate for convulsions, corticosteroid treatment, anticoagulation therapy, management of pulmonary hypertension, the timing of delivery, and blood product transfusion.

**Key Indexing Terms:** Pregnancy; HELLP syndrome; Eisenmenger's syndrome. **[Am J Med Sci 2013;346(5):385–389.]**

Eisenmenger's syndrome is defined as the process in which an uncorrected left-to-right shunt caused by a congenital heart defect is associated with long-term elevated blood flow through the pulmonary vasculature, causing irreversible pulmonary hypertension and increasing pulmonary vascular resistance. In turn, this resistance meets or exceeds systemic pressures and causes reversal of the shunt into a right-to-left or bidirectional shunt. Patients with Eisenmenger's syndrome commonly present with chronic cyanosis and progressive exercise intolerance. The cyanosis is because of a decrease in oxygenated blood throughout the systemic circulation, which results in end organ damage because of lack of oxygen. Decreased exercise tolerance is because of an inability to increase pulmonary blood flow and limitation of oxygen uptake. Other symptoms include subtle neurological abnormalities, such as headache, dizziness, or visual disturbance because of erythrocytosis and hyperviscosity. Cardiac arrhythmias are common and may lead to sudden death. Cerebrovascular accidents may occur as a result of paradoxical embolization, venous thrombosis of cerebral vessels or intracranial hemorrhage. Increased pulmonary vascular resistance in Eisenmenger's syndrome carries a grave prognosis during pregnancy. The fall in systemic vascular resistance during gestation increases the right-to-left shunt and reduces pulmonary blood perfusion, leading to maternal and fetal hypoxemia and cyanosis. In addition, the reduction in systemic vascular resistance decreases filling pressure of the right heart. The consequent insufficient perfusion to the pulmonary arterial vasculature can lead to sudden profound hypoxemia and death. Mortality rates of the mother in pregnancies associated with Eisenmenger's syndrome are reported to be as high as 30% to 50% with cesarean section.[1] Overall fetal death and neonatal complications are reported in up to 30% of cases.[2] Eisenmenger's syndrome is an absolute contraindication to pregnancy.

Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome is a serious complication of pregnancy characterized by hemolysis, elevated liver enzymes and low platelet counts. HELLP occurs in 0.5% to 0.9% of all pregnancies and in 10% to 20% of cases with severe preeclampsia.[3] Weinstein[4] suggested that the signs and symptoms constituted an entity separate to severe preeclampsia and first described HELLP syndrome in 1982. Approximately 70% of cases develop before delivery, the majority between the 27th and 37th gestational week and the remainder within 48 hours of delivery. The presence of HELLP syndrome is associated with an increased risk of maternal death (1%–30%) and increased rates of maternal morbidities, such as eclampsia, abruptio placentae, disseminated intravascular coagulopathy, acute renal failure, pulmonary edema, pleural effusions, ascites and hematomas of the liver.[5,6] Pregnancies complicated by HELLP syndrome are also associated with increased rates of wound hematomas and the need for transfusion with blood and blood products.[5,6] The reported perinatal death rate ranges from 7.4% to 20.4%.[7] These infants have a high rate of acute neonatal complications, including respiratory distress syndrome, bronchopulmonary dysplasia, intracerebral hemorrhage and necrotizing enterocolitis.[7,8]

There are few published reports in recent literature that describe pregnancy and HELLP syndrome in patients with Eisenmenger's syndrome. There is no consensus on clinical features, treatment and prognosis of these extremely rare and severe diseases. We present 4 cases of pregnancy complicated by the HELLP syndrome in patients with Eisenmenger's syndrome, and we report our initial experience and the in-hospital outcomes of these unusual cases. The clinical management of such patients was conducted according to accumulated experience and principles of treatment on the HELLP or Eisenmenger's syndrome alone, during pregnancy.

## CASE DESCRIPTION

### Case 1

A 32-year-old woman with an 18-year history of patent ductus arteriosus presented to our department at 33 weeks of gestation. She had never undergone intracardiac repair of the cardiac malformation and was diagnosed with Eisenmenger's syndrome 2 years earlier. The patient was cyanotic and presented with progressive exertional dyspnea accompanied by syncope over 2 weeks. Laboratory tests revealed the presence of 3+ proteinuria; hemoglobin, 169 g/L; hematocrit, 52.3%; platelet count, $52.4 \times 10^9$/L; lactate dehydrogenase (LDH), 376 μmol/L; alanine aminotransferase (ALT), 36 IU/L; aspartate transaminase (AST), 46 IU/L and uric acid (UA), 582.2 μmol/L. Hemodynamic data consisted of a blood pressure (BP) of 180–155/120–90 mm Hg; heart rate (HR), 86 beats per minute (bpm) and oxygen saturation ($SpO_2$), 74%. Blood gas tests revealed an arterial partial pressure of oxygen ($PaO_2$) of 53 mm Hg. On admission, the patient

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received oxygen through a face mask, magnesium sulphate to prevent convulsions, and dexamethasone to induce fetal lung maturity. Invasive monitoring with a Swan-Ganz catheter using the thermodilution method revealed a pulmonary arterial pressure (PAP) of 172/102 mm Hg and an ejection fraction of 55%. At 13 hours after admission, a Cesarean delivery was urgently performed under mechanical ventilation and general anesthesia. During surgery, the patient had a BP of 180–150/110–90 mm Hg and a PAP of 172–150/100–90 mm Hg. The surgical procedure was uneventful and a male infant weighing 1765 g with Apgar scores of 7-9-9 was delivered. Intraoperative blood loss was 400 mL. After delivery, the patient was mechanically ventilated and had a BP similar to the PAP, with a HR of 113–138 bpm and a $SpO_2$ of 90%. Intravenous dobutamine and alprostadil were initiated at a dose of 10 μg/kg per minute and 7 ng/kg per minute, respectively. At 5 hours postsurgery, the BP and PAP gradually reduced to 130–120/95–70 and to 140–113/98–61 mm Hg, respectively. Simultaneously, the HR reduced to 110 to 120 bpm, and the $SpO_2$ decreased to 85%. The patient received transfusions of concentrated platelets, red cell suspensions and fresh frozen plasma. The blood loss was calculated to be 800 mL postoperatively. At 3 days postpartum, the patient suffered from a pulmonary infection. At 4 days postpartum, mechanical ventilation was successfully discontinued, with oxygen delivered by mask and nasal catheter, at a flow of 5 L/min. At 5 days postpartum, the Swan-Ganz catheter was removed and deep vein thrombosis was detected in the vein sinuses of the calf muscles in the left lower extremities. At 10 days postpartum, the patient had a persistent high fever of 38.7°C. At 17 days postpartum, the patient suddenly became unconsciousness, hypotensive and hypoxemic. Cardiopulmonary resuscitation failed and the patient died.

## Case 2

A 21-year-old woman had been dyspneic on physical exertion since childhood and a patent ductus arteriosus was diagnosed. At 30 weeks gestation, she presented with shortness of breath and chest tightness after minimal exertion, which progressed rapidly to orthopnea. Laboratory tests revealed the presence of 4+ proteinuria; hemoglobin, 160 g/L, hematocrit, 46.7%; platelet count, 38.4 × $10^9$/L; LDH, 329 μmol/L; ALT, 4 IU/L; AST, 27 IU/L and UA, 684.5 μmol/L. Hemodynamic data indicated a BP of 130/90 mm Hg; HR, 90 bpm; $SpO_2$, 56% and PAP, 170 mm Hg. Blood gas tests revealed a $PaO_2$ of 29.6 mm Hg. On admission, the patient underwent continuous oxygen inhalation, electrocardiographic monitoring, diuretic therapy and treatment with magnesium sulphate and dexamethasone. Micropump intravenous alprostadil was administered at a dose of 7 ng/kg per minute. The patient was sedated with an intramuscular injection of pethidine (50 mg) and phenergan (25 mg). Five hours postadmission, the patient complained of epigastric pain and had thin yellow stools. Her BP was 151/100 mm Hg; HR, 147 bpm; respiratory rate, 46 breaths per minute and $SpO_2$, 35%. Physical examination revealed a clear outline of the uterine wall, no evidence of uterine contractions and a fetal HR of 130 bpm. Ultrasound examination revealed an umbilical arterial blood flow systolic to diastolic ratio value of 3.3, a fetal HR of 125 bpm and no abnormalities in the placenta. Epigastric pain and dyspnea progressively deteriorated with irregular fetal heart rhythms ranging from 80 to 100 bpm. Cardiac and respiratory arrest occurred 10 minutes after the onset of epigastric pain. Cardiopulmonary resuscitation failed and the patient died. No induction of labour was performed because of the spontaneous intrauterine death of a fetus based on the fact that no fetal heartbeat was felt.

## Case 3

A 20-year-old woman had cyanosis of the lip and nail bed and limitations of activity over the preceding 9 years. The patient had not previously been to hospital for examination or treatment. At 34 weeks gestation, the patient complained of dyspnea on minimal exertion and sudden onset syncope 4 days earlier. A diagnosis of pregnancy complicated by ventricle septal defect (VSD) and pulmonary hypertension was made. Laboratory tests revealed the presence of 4+ proteinuria; hemoglobin, 114 g/L; hematocrit, 37.2%; platelet count; 65 × $10^9$/L; LDH, 609 μmol/L; ALT, 18 IU/L; AST, 37 IU/L and UA, 566.4 μmol/L. Hemodynamic data indicated a BP of 172–150/110–100 mm Hg; HR, 82 bpm; $SpO_2$, 76.6% and PAP, 170/113 mm Hg. Blood gas analysis revealed a $PaO_2$ of 41 mm Hg. On admission, the patient received continuous low-dose oxygen inhalation, magnesium sulphate and dexamethasone treatment and transfusions of red cell suspensions. Two days postadmission, a Cesarean delivery was performed under mechanical ventilation and general anesthesia. Invasive monitoring with a Swan-Ganz catheter using the thermodilution method revealed a BP of 170–160/110–90 mm Hg; PAP, 160–130/100–86 mm Hg; HR, 108 to 88 bpm and $SpO_2$, 70%. Crystalloids were restricted to 1 L to avoid pulmonary congestion. Urine volume and blood loss were 150 and 200 mL, respectively. The surgical procedure was uneventful, and a male infant of 1830 g with Apgar scores of 0-6-8 was delivered with an amniotic fluid volume of 500 mL. The infant had multiple malformations, including fetal sacrococcygeal meningocele, VSD and congenital valgus foot. Tracheal intubation was conducted for mechanical ventilation because of severe respiratory distress. Cardiopulmonary resuscitation failed and the baby died.

After delivery, the patient was mechanically ventilated with a central vein pressure of 9 cm $H_2O$. Intravenous dobutamine and alprostadil were initiated at a dose of 10 μg/kg per minute and 7 ng/kg per minute, respectively. The patient received transfusions of concentrated platelets, red cell suspensions, fresh frozen plasma and albumin. At 20 hours postpartum, the HR gradually increased to 120 bpm. At 32 hours postpartum, the BP suddenly reduced to 30/10 mm Hg. Cardiopulmonary resuscitation failed, and the patient died.

## Case 4

A 30-year-old woman presented with exertional dyspnea over the preceding 12 years. A VSD was diagnosed at the age of 18 years. Ten years later, Eisenmenger's syndrome was diagnosed, which was secondary to the persistent uncorrected defect. At 34 weeks gestation, the patient complained of a cough productive of yellow sputum and edema of the lower extremities. Laboratory tests revealed the presence of 1+ proteinuria; hemoglobin, 156 g/L; hematocrit, 46.3%; platelet count, 74 × $10^9$/L; LDH, 298 μmol/L; ALT, 87 IU/L; AST, 88 IU/L and UA, 298 μmol/L. Hemodynamic data indicated a BP of 147/90 mm Hg; HR, 78 bpm; $SpO_2$, 70.9% and PAP, 134/74 mm Hg. Blood gas test revealed a $PaO_2$ of 37.5 mm Hg. On admission, the patient received continuous oxygen inhalation, antibiotics to control the infection, magnesium sulphate to prevent convulsions, and dexamethasone to accelerate fetal lung maturation. One day postadmission, cesarean delivery was performed under epidural anesthesia. Invasive monitoring with a Swan-Ganz catheter using the thermodilution method revealed a BP of 160–170/110–90 mm Hg; PAP, 140–130/90–70 mm Hg; HR, 70 bpm and $SpO_2$, 78%. The surgical procedure was uneventful, and a male infant weighing 1660 g with Apgar scores of 9-9-9 was delivered. Intraoperative blood loss was 300 mL. Sildenafil was administered orally at