# Pregnancies Complicated by Familial Hypertriglyceridemia: A Case Report

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## Abstract

**Background** Although rare, familial hypertriglyceridemia can cause acute and life-threatening complications in pregnancy.

**Cases** The first patient's pregnancy was complicated by multiple admissions for pancreatitis due to hypertriglyceridemia and noncompliance with gemfibrozil. In her second pregnancy, she was compliant with gemfibrozil and only experienced pancreatitis episodes toward the end of pregnancy. The second patient had diabetes mellitus and familial hypertriglyceridemia. She required multiple hospitalizations for diabetic ketoacidosis secondary to insulin noncompliance. In both pregnancies, she was compliant with gemfibrozil and had no complications related to hypertriglyceridemia.

**Conclusion** Treatment with gemfibrozil in pregnancies complicated by hypertriglyceridemia may prevent complications without adverse maternal or fetal effects and could be considered in treating pregnant patients with severe hypertriglyceridemia. These cases also demonstrate the importance of medication compliance in the prevention of poor outcomes.

**Keywords**
- familial hypertriglyceridemia
- pancreatitis
- gemfibrozil
- preterm delivery
- fetal demise

There are few cases of familial hypertriglyceridemia, and its management during pregnancy reported in the literature.[1,2] Familial hypertriglyceridemia is an autosomal dominant disorder associated with moderate elevations in the serum triglyceride concentration (200–500 mg/dL). Patients are heterozygous for inactivating mutations of the lipoprotein lipase gene. They are at a risk of pathological levels of triglycerides (>1,000 mg/dL) when they are exposed to exacerbating conditions such as pregnancy, hormone replacement therapy, and uncontrolled diabetes. During pregnancy, there is an increase in triglyceride and total cholesterol levels, which are mediated by estrogen, progesterone, and human placental lactogen.[3] The risk of pancreatitis is increased when triglyceride levels are above 500 mg/dL.[4] Triglycerides break down into free fatty acids by pancreatic lipase and can lead to lipotoxicity and acute pancreatitis. Hypertriglyceridemia during pregnancy may be responsible for 56% of the pancreatitis cases in contrast with 1–4% in the nonpregnant state.[5]

Acute pancreatitis is associated with poor pregnancy outcomes including preterm delivery, fetal distress, fetal demise, pancreatic necrosis, and electrolyte abnormalities.[6–8] Other maternal complications of hypertriglyceridemia include hyperviscosity syndrome, preeclampsia, and an increased likelihood of the development of hyperlipoproteinemia in the future.[9–11] Fetal effects include macrosomia and pancreatitis-related complications such as preterm delivery and demise.[12]

We report four pregnancies between two patients complicated by familial hypertriglyceridemia.

## Case Presentation

### Case 1

The patient is a 21-year-old G2P0Ab1 with a history of four prior hospital admissions for pancreatitis prior to this pregnancy. The patient presented at $13^{6/7}$ weeks-gestation with upper abdominal pain. Laboratory values demonstrated a lipase of 744U/L

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and triglycerides of 2,281 mg/dL, and she was admitted for acute pancreatitis. Her treatment was managed by a multidisciplinary team consisting of obstetricians, maternal fetal medicine specialists, internal medicine specialists, and a registered dietician. The patient was hospitalized for 5 days, and recovered with supportive care and was discharged with fish oil. At $18^{2/7}$ weeks, she was readmitted for acute pancreatitis with a lipase of 197U/L and triglycerides of 4,206 mg/dL. She admitted to noncompliance with her prescribed medication. The patient was admitted to the intensive care unit for possible hemorrhagic and/or necrotic pancreatitis. The patient was treated conservatively and recovered with fish oil, gemfibrozil 600 mg orally twice a day, and supportive care. She was readmitted at $26^{1/7}$ weeks for acute pancreatitis with a lipase of 731U/L and triglycerides of 2,633 mg/dL, underwent similar treatment, and again was noted to be noncompliant with medications. She then presented at $30^{5/7}$ weeks in preterm labor with a cervical dilation of 4 cm. The patient's preterm labor eventually arrested and she was subsequently discharged home. She returned at $32^{5/7}$ weeks with preterm premature rupture of membranes and delivered vaginally a male infant weighing 2,190 g with Apgar scores of 7 and 9 at 1 and 5 minutes, respectively. The patient self-discontinued her gemfibrozil after delivery.

The following year, the patient became pregnant again. She had prenatal care elsewhere but was admitted to our hospital for acute pancreatitis at 13 weeks of gestation with a lipase of 298U/L and triglycerides of 2,616 mg/dL and was restarted on gemfibrozil 600 mg orally twice a day. She was readmitted again at 16 weeks of gestation for recurrent pancreatitis, and again noted she did not take the gemfibrozil as prescribed. Following this hospital discharge, she was compliant with her gemfibrozil and did not have another episode of pancreatitis until 32 weeks of gestation. She was subsequently admitted again at 33 and 35 weeks for pancreatitis and intractable abdominal pain. Delivery at 35 weeks was recommended due to her intractable pain from recurrent pancreatitis. She underwent induction of labor and delivered vaginally a male infant weighing 2,530 g with Apgar scores of 7 and 8 at 1 and 5 minutes, respectively. The patient was seen for a postpartum visit and was lost to follow-up thereafter.

### Case 2

The patient is a 22-year-old G3P0Ab2 with familial hypertriglyceridemia and diabetes mellitus since childhood. She was previously on niacin and gemfibrozil but self-discontinued prior to pregnancy. She had prenatal care elsewhere but was admitted to our hospital at $28^{0/7}$ weeks gestation due to diabetic ketoacidosis (DKA) from insulin noncompliance. Her hemoglobin A1C was noted to be 7.6%. Her treatment was managed with a multidisciplinary team (obstetricians, maternal fetal medicine, internal medicine, and a registered dietician). Her insulin regimen was adjusted and she was started on gemfibrozil 600 mg orally twice a day. She left against medical advice but reported compliance with all medications at scheduled outpatient visits. She then presented at $35^{2/7}$ weeks complaining of decreased fetal movement and had a biophysical profile of 2. The patient delivered through cesarean section a male infant weighing 2,995 g with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. Patient had an uncomplicated postoperative course and was discharged home with insulin and gemfibrozil. However, she failed to follow up postpartum.

Seven months later, the patient presented in DKA and was found to be $15^{2/7}$ weeks pregnant. Her hemoglobin A1C was 8.3% on admission. She was on insulin and niacin, which was being managed by her primary care provider. During her admission, the niacin was discontinued and she was prescribed gemfibrozil 600 mg orally twice a day. She presented again at 27 weeks gestation in DKA triggered by a viral upper respiratory infection. Laboratory studies demonstrated a triglyceride level of 1,422 mg/dL and a normal lipase. At 29 weeks of gestation, the fetus was found to have mild ascites and a complex congenital heart anomaly on ultrasound (interrupted aortic arch), and she received fetal lung maturity steroids. At 34 weeks of gestation, she presented with possible preterm premature rupture of membranes and was transferred to another facility capable of fetal cardiothoracic intervention. She suffered a fetal demise within 3 days due to the complex congenital heart anomaly. She stated medication compliance throughout her entire pregnancy.

## Discussion

This case report is significant because it demonstrates that compliance with gemfibrozil decreased the frequency of acute pancreatitis. Prevention of pancreatitis in hypertriglyceridemia is critical because it is associated with decreased placental perfusion, fetal distress, and contractions, leading to significant morbidity. Historically, pancreatitis was associated with significant maternal and fetal mortality, up to 20% for both. However, this has improved with improved diagnosis and early intervention.[13,14]

There are no practice guidelines for the treatment of hypertriglyceridemia during pregnancy, with most recommendations coming from case reports. Wong et al proposed a hierarchical management strategy that includes a multidisciplinary team management and a low-fat and low-glycemic carbohydrate diet with nutritional support (replacement of omega 3 fatty acids and midchain triglycerides as needed), with care to avoid essential fatty acid deficiency. If patients are still refractory, consider hospitalization for parenteral nutrition or intravenous insulin therapy, fibrate use after the first trimester, and plasmapheresis.[12]

Triglyceride-lowering medication such as niacin and gemfibrozil are often discontinued since their safety during pregnancy has not been established. Niacin supplementation is present in prenatal vitamins and has not been associated with adverse effects.[15] However, the use of niacin in lipid-lowering doses has not been studied. Gemfibrozil has been evaluated in rats and rabbits for effects on the various phases of the reproductive process. Rats and rabbits received dosages up to 200 mg/kg during organogenesis without any reported teratogenic effects.[16] Several case reports demonstrate the successful use of gemfibrozil during pregnancy without any fetal harm.[9] To date, there are no epidemiology studies published on the congenital effects in infants whose mothers were treated with

gemfibrozil during pregnancy. In the preceding cases, the fetal heart anomaly was likely associated with the patient's diabetes. All the other fetuses demonstrated no anomalies on ultrasound or on physical examination after delivery.

In the four pregnancies presented, there were significant complications. The first patient was noncompliant with gemfibrozil and required hospitalizations throughout her first pregnancy. However, when she was compliant during her second pregnancy, she experienced clusters of admissions at the beginning of the pregnancy when she was restarting her medication and toward the end of her pregnancy, late preterm. This highlights how pregnancy can exacerbate triglyceride levels. The second patient was noncompliant with her insulin and was admitted for DKA on several occasions during her first pregnancy. She was compliant during her second pregnancy and only experienced DKA early on and during a viral infection. She remained compliant with her gemfibrozil and did not experience any episodes of acute pancreatitis during either pregnancy. These examples stress the importance of medication compliance in the prevention of complications associated with hypertriglyceridemia, especially during pregnancy due to the increased morbidity and mortality for both mother and fetus.

The four presented cases contribute to the scant literature on hypertriglyceridemia and pregnancy. Treatment with gemfibrozil in pregnancies complicated by hypertriglyceridemia may prevent complications without adverse maternal or fetal effects, contributing to the paucity of safety literature. Therefore, it is reasonable to recommend diet and lipid-lowering medication as a first-line treatment for hypertriglyceridemia during pregnancy. These cases highlight the importance of patient education and compliance in the prevention of maternal and fetal complications and poor outcomes.

### Conflicts of Interest

The authors declare no conflict of interest regarding the publication of this article.

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