

## CASE REPORT

# Hypertriglyceridemia-Induced Acute Pancreatitis in Pregnancy

Mindaugas Serpytis<sup>1,4</sup>, Vytautas Karosas<sup>4</sup>, Rokas Tamosauskas<sup>6</sup>,  
Jurate Dementaviciene<sup>2</sup>, Kestutis Strupas<sup>3,5</sup>, Audrius Sileikis<sup>3,5</sup>, Jurate Sipylaite<sup>1,4</sup>

<sup>1</sup>Clinic of Anesthesiology and Intensive Care, <sup>2</sup>Department of Radiology, Nuclear Medicine and Medicine Physics, and <sup>3</sup>Clinic of Gastroenterology, Nephrourology and Surgery, Faculty of Medicine, Vilnius University; <sup>4</sup>Centre of Anesthesiology, Intensive Therapy and Pain Management, and <sup>5</sup>Centre of Abdominal Surgery, Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania. <sup>6</sup>Department of Anaesthesia, Addenbrooke's Hospital, Cambridge University Hospitals NHS Trust, Cambridge, United Kingdom

### ABSTRACT

**Context** Hypertriglyceridemia is a well known phenomenon of pregnancy occurring due to physiologic changes in sex hormone levels. Occasionally, it could lead to development of acute pancreatitis. Gestational hypertriglyceridemia-induced acute pancreatitis occurs in pregnant women usually with preexisting abnormalities of the lipid metabolism and is associated with additional diagnostic and therapeutic challenges related to hypertriglyceridemia and pregnancy. **Case report** We present a case of hypertriglyceridemia-induced acute pancreatitis in pregnant woman with no previous history of lipid abnormality and pregnancy as the only known triggering factor for hypertriglyceridemia. **Conclusions** Hypertriglyceridemia-induced acute pancreatitis is a rare complication of pregnancy; however, it should be suspected in all pregnant patients admitted for non-obstetric abdominal pain.

### INTRODUCTION

Acute pancreatitis is a rare complication of pregnancy. It is diagnosed approximately in a range from 1 out of 1,000 to 1 out of 10,000 pregnancies with gallstone pancreatitis accounting for 70% of all cases [1]. Hypertriglyceridemia is recognized as the third most common cause of gestational acute pancreatitis after gallstones and alcohol and occurs in about 4% of all cases [2]. An increase in plasma lipid level during pregnancy has been well documented. It is thought to represent a physiologic response to the hormonal changes; however, not sufficient to cause acute pancreatitis. Gestational pancreatitis due to hypertriglyceridemia usually occurs in pregnant women with preexisting abnormalities of the lipid metabolism. We report a case of hypertriglyceridemia-induced acute pancreatitis in a previously healthy pregnant woman and emphasize diagnostic and treatment challenges associated with this condition.

### CASE REPORT

A 31-year-old female with past history of miscarriage (gravida 2, para 0) was admitted to a district general hospital at the 33<sup>rd</sup> gestational week complaining of upper abdominal pain and nausea. At the time of admission her vital signs were stable. Gynecological examination showed no evidence of premature labor: uterus tone was normal and cervix was closed. Her WBC were 15,000 mm<sup>-3</sup> (reference range: 4,000-9,000 mm<sup>-3</sup>), CRP 65 mg/L (reference range: 0-5 mg/L). On the second day the symptoms of peritonitis developed; acute appendicitis was suspected and the patient underwent emergency laparotomy. Chylous ascites was drained; however, no cause of peritonitis was found intraoperatively. A normal appendix was removed. Post-operative blood tests were non evaluable due to high lipemia. On the third day of admission, she was transferred to a tertiary university hospital, where blood analysis showed increased level of triglyceride 87.5 mmol/L (reference range: 0-1.8 mmol/L), CRP 418 mg/L (reference range: 0-5 mg/L), procalcitonin 1.19 µg/L (reference range: 0-0.05 µg/L), lactate 5.78 mmol/L (reference range: 0.63-2.44 mmol/L), lipase activity 1,176 IU/L (reference range: 8-78 IU/L), and WBC 13,470 mm<sup>-3</sup> (reference range: 4,000-9,000 mm<sup>-3</sup>), neutrophils 92% (reference range: 50-72%). The hematocrit was 36.2% (reference range: 36-42%). Electrophoretic pattern of lipoprotein was consistent

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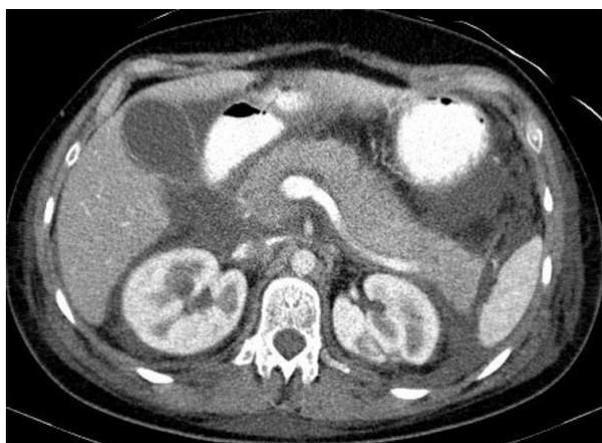
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**Correspondence** Mindaugas Serpytis  
Clinic of Anesthesiology and Intensive Care; Faculty of Medicine  
Vilnius University; Siltnamiu 29, LT-04130; Vilnius; Lithuania  
Phone: +3706-864.79.23; Fax: +3705-236.52.35  
E-mail: mindaugas.serpytis@santa.lt

with type V hyperlipoproteinemia. High concentrations of amylase (3,520 IU/L) and lipase (39,160 IU/L) were found in drainage fluid. Abdominal US revealed hypoechoic structure and blurred edge of the pancreas. Due to impending signs of fetal hypoxia an emergency Caesarean section was performed on the fourth day of hospitalization and healthy newborn female was delivered. Exploratory laparotomy revealed fat necrosis in the peripancreatic retroperitoneal space, omentum, and mesenteric root. Abdominal CT confirmed the diagnosis of acute pancreatitis (Figure 1). After delivery, triglyceride remained high (43.76 mmol/L) despite conservative hypertriglyceridemia treatment with heparin and insulin. Three sessions of plasmapheresis were performed with the aim of reducing hypertriglyceridemia. She was discharged at the 30<sup>th</sup> hospitalization day with triglyceride concentration of 4.75 mmol/L and cholesterol of 6.07 mmol/L (reference range: 0-5.2 mmol/L).

## DISCUSSION

We report a case of the hypertriglyceridemia-induced acute pancreatitis in pregnant patient with no previous history of abnormal lipid metabolism. In this case, pregnancy was considered to be the obvious factor for the development of hypertriglyceridemia. To our knowledge, there is a single published report describing such complication of pregnancy where even higher concentration of triglyceride (115 mmol/L) has been reported [3]. An association between hypertriglyceridemia and acute pancreatitis is well established. However, mild-to-moderate elevations of triglyceride are seen in up to 50% of all-cause acute pancreatitis and are generally regarded an epiphenomenon rather than a cause. Current consensus suggested that serum triglyceride concentration higher than 11.3 mmol/L is essential for acute pancreatitis to develop [1, 4]. During pregnancy, there is a physiologic estrogen-induced increase in triglyceride-rich lipoprotein production and decrease in clearance of triglyceride due to suppression of lipoprotein lipase



**Figure 1.** CT image shows a diffusely enhancing and enlarged pancreas with hypodense foci in the pancreatic head; increased density of the peripancreatic tissue and a large amount of fluid in abdominal cavity.

activity in the liver and adipose tissue. The highest concentration of triglyceride is observed in the third trimester and may rise up to 2-4 times above normal, yet it rarely exceeds 11 mmol/L. An increase in cholesterol concentration usually follows similar pattern [3, 5, 6]. Although exact pathogenesis of hypertriglyceridemia-induced acute pancreatitis is not yet fully elucidated, two plausible mechanisms have been implicated. Hydrolysis of the excessive amount of triglyceride in the pancreas results in local release of highly concentrated free fatty acids, which could exert their cytotoxic effect on acinar cells and vascular endothelium. Another theory postulated that high concentrations of chylomicrons could increase blood viscosity and even precipitate capillary obstruction in the pancreas, leading to local pancreatic ischemia, acidosis, and activation of trypsinogen [4, 7].

There are numerous diagnostic challenges and treatment controversies of acute pancreatitis associated with pregnancy and hypertriglyceridemia described in literature. Most symptoms, which are common in acute pancreatitis such as nausea, vomiting, abdominal discomfort, or pain, are frequently reported in pregnancy. Moreover, clinical evaluation of acute abdomen in pregnancy can be confusing, due to anatomical displacement of abdominal organs by the gravid uterus. The classic signs and symptoms of peritonitis may be less prominent than those in non-pregnant patients because of the stretching and lifting of the anterior abdominal wall away from the area of inflammation. The underlying inflammation has limited contact with the parietal peritoneum, which precludes abdominal muscular response. Furthermore, the uterus hampered the movement of the omentum to an area of inflammation. Such alterations distort the clinical picture of acute abdomen and can lead to misdiagnosis or unnecessary non-obstetric surgical interventions which are associated with a higher premature labor rate [8]. Leukocytosis due to an increase in neutrophils count represents normal physiological response to pregnancy, yet elevated white cell count is common in acute pancreatitis [9]. Hemoconcentration due to fluid redistribution is one of the laboratory features of acute pancreatitis. However, hematocrit in pregnancy is decreased, particularly in the last trimester. This occurs not only due to iron-deficiency anemia, but also due to a dilution effect secondary to an increased in plasma volume up to 50% above baseline. The lower reference value for hematocrit may be as low as 31% in normal pregnancy [10]. Lipemia may affect an automated analysis of electrolytes, glucose, liver enzymes, urea, creatinine, total bilirubin, etc. by altering light scattering, increasing the non-aqueous phase, and partitioning between the polar and non-polar phases [11]. Elevated amylase and/or lipase are the diagnostic hallmarks of acute pancreatitis; yet, in hypertriglyceridemia-induced acute pancreatitis, amylase levels may be reported as normal or even low in more than 50% patients. This phenomenon has been attributed to an interference of

plasma lipids with the assay and/or to the presence of a circulating inhibitor of amylase in serum and urine [4, 12, 13]. In such cases, dilution or ultracentrifugation of the sample is recommended to ensure accurate analysis.

Imaging plays an important role in diagnosing of acute pancreatitis, in establishing underlying etiology and grading the severity of disease. Gallstones are responsible for 70% of all acute pancreatitis cases in pregnancy and should be excluded first. US is safe for fetus and is the initial imaging method of choice to identify gallstones and acute pancreatitis. However, often the pancreas may not be visible by US because of overlying bowel gas. EUS has proven to be very sensitive in diagnosing even very small gallstones and could be applicable in pregnancy with suspected choledocholithiasis. ERCP or CECT (a gold standard for diagnosing common bile duct stones and pancreatitis) could expose fetus to the ionizing radiation and should be performed only when benefit outweighs the risk. The diagnostic efficacy of MRI is comparable to that of CECT in helping assess the location and extent of peripancreatic inflammatory changes, fluid collections and the degree of pancreatic necrosis. There is growing body of evidence that MRI is safe in pregnancy. The American Association of Radiologists recommended using MRI in pregnant patients below 1.5 T, although recent publications advocate standard MRI pancreas protocol without contrast when investigating pregnant patient for acute pancreatitis. Potential hazards of MRI investigation to the fetus include teratogenic effects of intravenous gadolinium-based contrast and the effects of strong electromagnetic field. Gadolinium-based contrast agents are assigned to pregnancy category C by the Food and Drug Administration and should be given for pregnant patients only with well documented risk-benefit analysis. The heating effect of MRI on fetus and direct non-thermal interaction of the electromagnetic field with biological structures raise an additional concerns regarding teratogenicity and risk of miscarriage, especially in the first trimester of pregnancy. Despite these concerns MRI is the preferred imaging modality in pregnancy if US failed to find out a cause of an acute abdomen [14].

There are no well-defined management recommendations for hypertriglyceridemia-induced acute pancreatitis, especially in pregnant patient. One of the initial therapeutic goals should aim at lowering triglyceride levels. Low-fat diet is essential to decrease triglyceride input. Enteral nutrition should be tried first as it maintains gut integrity and attenuates the acute phase response. Long-term intake of diets rich in omega-3 fatty acids may reduce triglyceride levels significantly; however, the impact on lipid metabolism during acute illness is currently unknown. It has been postulated that supplementing enteral or parenteral nutrition with omega-3 fatty acids may influence the acute inflammatory response in critically ill patients, but published data remain equivocal [15]. When enteral

nutrition is not feasible, intravenous lipids should be considered only when triglyceride is less than 3-4 mmol/L. Insulin and heparin both increase lipoprotein lipase activity and thus facilitate triglyceride clearance [16]. Niacin, fibrates, and statins are widely used to treat dyslipidemia; however, it usually takes several weeks to reach the lipid-lowering goals with such agents, thus rendering them futile in acute pancreatitis. Moreover, niacin, fibrates, statins, and heparin were assigned to pregnancy category C by the Food and Drug Administration and should be only administered when there is no alternative and benefit outweighs the risk.

Triglyceride concentration should decline after delivery due to a rapid drop in estrogen levels. Termination of pregnancy is indicated only when the condition of the patient and/or fetus is progressively worsening. Our patient's results after delivery showed only slightly reduced levels of triglyceride; thus plasmapheresis was initiated. A single session of plasmapheresis could be expected to reduce triglyceride concentration by up to 70%. Plasmapheresis, as well as lipoprotein apheresis, appears to be useful in critical situations and safe in pregnancy [17, 18, 19].

## CONCLUSION

Hypertriglyceridemia is common in pregnancy due to physiological changes, and occasionally it could lead to development of acute pancreatitis. Although rare, acute pancreatitis should be suspected in all pregnant patients admitted for non-obstetric abdominal pain. Symptoms and laboratory findings may be distorted by pregnancy and hypertriglyceridemia; therefore, timely and accurate diagnosis of acute pancreatitis remains challenging in such setting.

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**Conflicts of interest** None of the authors have any potential conflicts of interest

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