CASE REPORT ASIAN JOURNAL OF MEDICAL SCIENCES

Pancreatitis in pregnancy: The complex interplay with triglycerides and diabetes

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Submission: 19-12-2023 Revision: 03-03-2024 Publication: 01-04-2024

ABSTRACT

A rare and complex condition, severe gestational hypertriglyceridemia with acute pancreatitis in a primigravida poses a significant therapeutic challenge due to the absence of established guidelines. Many patients with hypertriglyceridemia exhibit concomitant insulin resistance, obesity, and fasting hyperchylomicronemia. This case report explores the successful management of a 20-year-old primigravida at 7 months of pregnancy presenting with severe gestational hypertriglyceridemia, diabetic ketoacidosis, and acute pancreatitis. Despite a lack of prior complications, the patient exhibited metabolic acidosis, hyperglycemia, hypertriglyceridemia, and acute kidney injury. A multifaceted approach involving insulin, statins, fenofibrate, antibiotics, and supportive measures resulted in improved lipid profiles and blood glucose levels. With induced labor and vaginal delivery, the intrauterine fetal death was addressed. The importance of routine lipid profile screening in high-risk pregnancies is underscored, emphasizing the need for early recognition and aggressive multidisciplinary management of severe metabolic complications in pregnant individuals with acute pancreatitis. This case stresses the critical role of a comprehensive approach for a successful outcome in such cases.

Key words: Hypertriglyceridemia; Pregnancy; Acute pancreatitis, Diabetes; Familial hyperchylomicronemia

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i4.60814

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

In this case report, we present a compelling case involving severe gestational hypertriglyceridemia and concurrent diabetes, resulting in acute pancreatitis and its associated complications. This case study aims to underscore the crucial role of monitoring lipid profiles in high-risk pregnancies. By doing so, we intend to emphasize the significance of proactive measures in mitigating and preventing the mortality and morbidity linked to pancreatitis and hypertriglyceridemia during pregnancy. Severe gestational hypertriglyceridemia is defined as plasma triglycerides (TGs) >1000 mg/dL. Maternal mortality is usually predicted at 20%, and fetal mortality at 50% with acute pancreatitis secondary to severe hypertriglyceridemia.[1]

CASE REPORT

A 20-year-old primigravida female with 7 months amenorrhea, on regular follow-up, having no previous complications came to OPD with chief complaints of severe generalized abdominal pain which was increasing in intensity and vomiting 3–4 episodes - nonbilious, non-projectile, non-blood containing, not relieved by anti-spasmodic and anti-emetics in the past 3 days. However, she did not complain of fever, diarrhea, headache, rashes, per vaginal bleeding, edema, and steatorrhea.

She had insignificant personal history, drug history, or obstetric history. Her father is a known case of Type 2 diabetes mellitus. The patient was tachypnoeic (RR-26/min), tachycardic (P-120/min), and normotensive (BP-124/84 mm Hg). Systemic examination showed

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severe epigastric tenderness with guarding and rigidity. However, there was no icterus, pallor, or any stigmata of hypertriglyceridemia.

Her initial laboratory investigations showed severe metabolic acidosis (pH-7.1; bicarb - 3) with a random blood sugar of 698 (RBS in 2nd trimester - 98 mg/dL) and acetone- 80 mg/dL, lipid profile showed hypertriglyceridemia (Total cholesterol [TC]-238 mg/dL; TGs-1116 mg/dL; high-density lipoprotein [HDL]-41 mg/dL; low-density lipoprotein [LDL]-59 mg/dL; very low-density lipoprotein [VLDL]-228 mg/dL), amylase - 395, lipase-568, HbA1c- 14.3% (Table 1 and Figure 1). She had dyselectrolytemia (Ca2+- 7.3 meq/L; K+ - 5.42 meq/L; Na+ - 127 meq/L). The urine routine showed glycosuria and ketonuria. She developed acute kidney injury with creatinine (1.74 mg/dL) and oliguria. Her APACHE II score was placed at 9 and BISAP score at 3, predicting maternal mortality from acute pancreatitis at 15%. Her C-peptide levels were 0.3 (0.7–5.19). GAD antibody (ELISA) -1.06 (>1.05-positive). Whole blood count, liver function test, coagulation profile, inflammatory markers (CRP, PCT), and viral markers were normal. Radiological investigations USG whole abdomen were suggestive of acute edematous interstitial pancreatitis with minimal retroperitoneal fluid collection and no organomegaly, no pancreatic mass. It showed intrauterine fetal death.

The patient was kept nil by mouth. Parenteral fluids, higher antibiotics (Inj Meropenem, Inj Metronidazole) were started. Fetal induction was done by vaginal Misoprostol-Mifepristone followed by Drotaverine and Oxytocin in 36 h. Hyperglycemia and hypertriglyceridemia were managed with required high doses of intravenous (IV) regular insulin infusion for 72 h. High-dose statins (Tab Atorvastatin 80 mg) and Tab Fenofibrate were given. Repeat lipid profile after 24 h was TC -207 mg/dL, TG -884 mg/dL, HDL -34 mg/dL, LDL -71 mg/dL, VLDL -176 mg/dL. Subsequently, the lipid profile after 3 days (TC -171 mg/dL, TG -428 mg/dL, HDL -39 mg/ HDL LDL -90 mg/dL, VLDL -85 mg/dL) (Table 1 and Figure 1). Sugar readings were controlled. Renal failure improved with normal renal function. Oral feeding was started. Family screening of lipid profile was done. Her 18-year-old brother's lipid profile was (TC -173 mg/dL, TG - 74 mg/dL, HDL - 47 mg/dl, HDL LDL - 113 mg/dL, VLDL - 14 mg/dL). The patient was discharged asymptomatically with Atorvastatin 40 mg and insulin (basal-bolus regimen). Lipid profile in follow-up after 10 days was (TC -194 mg/dL, TG - 296 mg/dL, HDL - 63 mg/dL, LDL - 111 mg/dL, VLDL - 59 mg/dL). C-peptide level was repeated after 15 days which was 1.82 ng/mL (0.78–5.19).

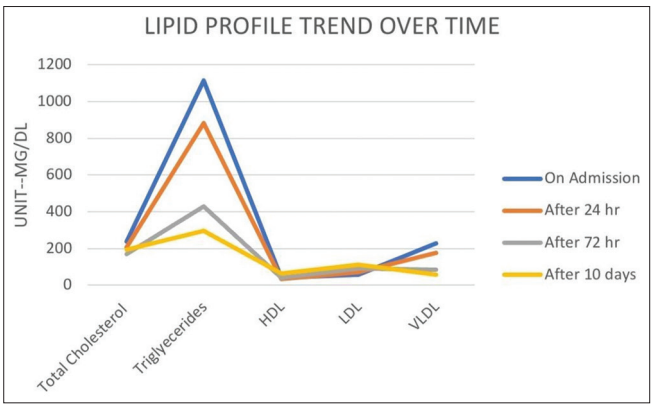

Figure 1: Graphical presentation of lipid profile trend

DISCUSSION

Pancreatitis during pregnancy is rare, with a prevalence estimated at 1 in 1000–10,000 pregnancies. Pancreatitis during pregnancy is more common in multiparous women, especially in the third trimester or early postpartum. Causes of pancreatitis in pregnancy can be biliary diseases, such as cholelithiasis with or without cholecystitis, metabolic conditions such as hyperlipidemia, hypertriglyceridemia, acute fatty liver, familial hypertriglyceridemia, hyperparathyroidism, and autoimmune factors. Ethnicity, drugs like tetracycline and thiazides, viral infections, and alcohol can also be contributing factors.

Hypertriglyceridemia is the second most common cause of acute pancreatitis in pregnancy. Jin et al., showed in a Chinese-based population study that for every increase in TGs of 88.5 mg/dL in the third trimester, there was an associated increased risk for gestational diabetes (odds ratio [OR], 1.37) and preeclampsia (OR, 1.50). Hypertriglyceridemia-induced pancreatitis in pregnancy

Table 1: Lipid profile trend of the patient with treatment

Lipid profile	On admission	After 24 h	After 72 h	After 10 days
Total cholesterol	238	207	171	194
Triglycerides	1116	884	428	296
HDL*	41	34	39	63
LDL+	59	71	90	111
VLDL++	228	176	85	59

HDL*: High-density lipoprotein, LDL+: Low-density lipoprotein, VLDL++: Very low-density lipoprotein

is associated with a maternal mortality rate as high as 20%.[2]

Pathophysiology

Elevation of TG levels of 2- to 4-fold by the third trimester of pregnancy is expected and well tolerated. TG levels usually remain below 250 mg/dL and rarely exceed 332 mg/dL (the 95th percentile value).[1]

Endogenous or exogenous estrogen is an infrequent cause of severe hypertriglyceridemia by inhibiting lipoprotein lipase (LPL). Physiologic alterations occur during pregnancy to ensure sufficient nutrition for the fetus. During pregnancy, estrogen and human placental lactogen rise in the late second and third trimesters. Elevated estrogen levels cause enhancement of lipogenesis, hepatic VLDL synthesis, and suppression of hepatic lipase activity. As a result, levels of HDL and LDL rich in TGs rise. Elevated human placental lactogen causes insulin resistance, leading to a decrease in LPL activity and increased lipolysis in adipose tissue. Due to an increase in free fatty acids in the circulation, there is now increased substrate for hepatic TG synthesis. As a result, there is an increase in the production of VLDL. Diet and environmental factors also play a crucial role in modulating TG production.[1]

The pathophysiology of the relationship between hyperchylomicronemia and pancreatitis is unknown. One theory is that the lipid-rich blood sludges, leading to pancreatic ischemia. Another theory is that the small amount of lipases that normally leak from the acinar cells lead to exuberant local lipolysis leading to the formation of free fatty acids and lysolecithin, a toxic lipid produced by lipase hydrolysis of phosphatidylcholine, and further acinar cell damage to adjacent cells.[3] Nikolova et al., demonstrated another mechanism in which altered liver X receptor signaling played an important role in early pregnancy lipogenesis in animal studies.[4]

The trigger level of TGs leading to pancreatitis is variable, with some patients having TGs more than 10,000 mg/dL with no symptoms, whereas others develop pancreatitis at much lower levels, yet usually more than 1000–2000 mg/dL.[3] Mutations in the APOA5, LPL, APOE, APOC2, and GP1HBP1 genes have all been implicated in severe gestational hypertriglyceridemia.[2] Fasting hyperchylomicronemia in adults is frequently associated with comorbidities, with uncontrolled diabetes and a family history of low HDL being common. These factors can significantly increase the risk of acute pancreatitis during pregnancy.

The concomitant insulin resistance, obesity, and/or overt diabetes in many hypertriglyceridemic patients often make it difficult to isolate one specific cause of this metabolic disturbance. In contrast, it has been suggested that isolated TG elevation does not lead to more vascular disease. In the presence of dysmetabolic syndrome, TG elevation probably predisposes vascular diseases through unclear mechanisms.[3]

Management

Treatment for severe gestational hypertriglyceridemia should be initiated immediately and aggressively to avoid risk to the mother and infant. Due to a lack of studies, there are no guidelines available for the management of hypertriglyceridemia in pregnancy. We believe that it should be managed with a multidisciplinary team. The choice of therapy will depend on the patient's clinical status and other comorbidities. Therapy includes diet modifications and various medications such as niacin, fibrates, statin, IV heparin, insulin, and apheresis. The importance of screening of dyslipidemia in pregnancy cannot be more emphasized. Early diagnosis of hypercholesterolemia can prevent serious and fatal complications in pregnancy. This can be achieved by initiating a strict low-fat, low-calorie diet and nutritional support with medium chain TGs as well as omega-3 fatty acids. Fasting lipid profiles should be monitored intensely, and one or more lipid-lowering medications such as fibrates, statins, niacin, and gemfibrozil can be added when high levels are noted.

CONCLUSION

We strongly emphasize the importance of proactively screening lipid profiles in pregnant women exhibiting altered metabolic parameters. Such screening efforts have the potential to prevent serious complications for both mother and child, including fetal and maternal death. We also want to emphasize that the interplay of metabolic factors contributing to acute pancreatitis in pregnancy, coupled with the absence of standardized guidelines, creates significant challenges for both the diagnosis and management of these patients.

ACKNOWLEDGMENT

I would like to thank professor Dr. Suthar Sir for his expert advice and encouragement throughout this manuscript writing. Special thanks to professor Dr. Sneha Shah, professor Dr. Mayuri Singh for guiding patient care. There were no grants supporting the writing of this manuscript.

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Authors Contribution:
PB- First draft manuscript, editing, literature survey, clinical care; **HS-** Review manuscript, preparation of figure, submission of article, clinical care; **NS-** Review manuscript, literature survey, clinical care; **AB-** Review manuscript and editing.

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Source of Support: Nil, **Conflicts of Interest:** None declared.