Case Report

Hypertriglyceridemia - Induced Acute Pancreatitis in Pregnancy

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Abstract

Objective: To describe the prompt and successful treatment of an hypertriglyceridemia-induced acute prancreatitis in pregnancy complicated by severe preeclampsia case in a tertiary-level hospital in Indonesia.

Methods: A Case report. A 33-year-old woman, G3P2A0 at 32/33 weeks of gestation, presented with shortness of breath following severe heartburn, nausea, and fever. She had been experiencing constant thirst and frequent urination. Her level of consciousness was decreased (GCS E2V3M4), and she exhibited high blood pressure and tachycardia. There was no history of high blood pressure during her routine antenatal care. Laboratory tests revealed a leukocyte count of 22,670/µL, a random blood sugar level of 713 mg/dL, severe metabolic acidosis on blood gas analysis, an amylase level of 1,004.8 U/L, a lipase level of 899.4 U/L, and triglycerides at 789 mg/dL. An abdominal CT scan with contrast confirmed acute pancreatitis. Given her poor general condition, she was sedated and intubated. The termination of her pregnancy was postponed to focus on stabilizing her condition in intensive care.

Discussion: In pregnant patients presenting with severe heartburn and no prior history of hypertension, acute pancreatitis should be considered as a potential diagnosis. In the absence of alcohol abuse risk factors, hypertriglyceridemia should be investigated as a probable cause.

Conclusion: Pregnant patients presenting with symptoms of shortness of breath, severe heartburn, along with hypertriglyceridemia should be considered for acute pancreatitis as a differential diagnosis.

Keywords: Acute Pancreatitis, Hypertriglyceridemia, Pregnancy, Preeclampsia.

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INTRODUCTION

Pregnancy is characterized by the anticipation of a new life while also harboring concerns for its subsequent growth. It is a well-established fact that delaying the age at which women decide to have children has significant repercussions for both the mother and the baby[1].The pancreas is an elongated and planar gland situated in the upper abdominal region. The pancreas synthesizes enzymes and hormones that facilitate digestion and control glucose metabolism[2]. Pancreatitis refers to a condition characterized by inflammation of the pancreas. This inflammation can manifest as either acute, characterized by a quick start, or chronic, stemming from a previous bout of pancreatic inflammation that ultimately leads to pancreatic dysfunction[3]. Acute pancreatitis is an inflammatory condition that mostly affects the exocrine portion of the pancreas. It is characterized by severe stomach pain and the malfunction of several organs, leading to pancreatic necrosis and prolonged organ failure. The death incidence ranges from 1% to 5%. The illness has a worldwide prevalence of 30–40 cases per 100,000 individuals annually[4].

Acute pancreatitis in pregnancy (APIP) is a rare case, with an estimated incidence between 1/1000 and 1/10,000 of the pregnancies[5]. Most cases of APIP occur in the third trimester (50-52%) of pregnancy or early after delivery (38%)[6]. The incidence of pancreatic illness during pregnancy has increased significantly in the past 2–3 decades[1]. APIP has a sudden and severe beginning and typically poses challenges in terms of diagnosis and treatment. Based on a research analysis, APIP is more hazardous for the fetus compared to the mother. The incidence of maternal death caused by pancreatitis is documented at 37%, while the fetal mortality rate can reach up to 60%. However, recent advancements in diagnostic and treatment options have led to a decrease in maternal and fetal mortality[3,6,7]. Hypertriglyceridemia (4%-10%) is known as the third most common cause of acute pancreatitis after gallstones (66%) and alcohol abuse (12%)[8]. In one study it was reported that hypertriglyceridemia-induced pancreatitis (HTGP) reached up to 56% of APIP cases[9]. Preeclampsia/eclampsia that occurs with or aggravated by acute pancreatitis is a rare case and there are no more than two cases in any reported cases[10]. This case report is to describe the prompt and successful treatment of an hypertriglyceridemia-induced acute prancreatitis in pregnancy complicated by severe preeclampsia case in a tertiary-level hospital in Indonesia. Where this case report of severe preeclampsia is a complication of acute pancreatitis in pregnancy, which is different from most previously published journals.

METHODS

A 33-year-old woman, G3P2A0 at 32/33 weeks of gestation, was referred from a hospital with complaints of shortness of breath for six hours before admission. Prior to the shortness of breath, the patient experienced severe heartburn radiating to the back, which did not improve with self-medication at home, and was accompanied by nausea and fever since the previous day. The patient did not experience vomiting. According to family information, the patient had been constantly thirsty and frequently waking up to urinate since the previous day. The patient had a history of asthma (last recurrence in 2012) and was given salbutamol nebulization at the hospital, which did not improve her condition and instead worsened it. Due to the need for further treatment, the patient was referred. Upon admission, the patient had a GCS score of 456, which later decreased to GCS E2V3M4. She appeared short of breath with a respiratory rate of 36-44 breaths per minute, blood pressure of 170/110 mmHg, pulse rate of 134-140 beats per minute, temperature of 38.4°C, and SpO2 of 100% (with O2 NRM 10 L/min). No additional breath sounds were detected in the heart or lung fields. The patient had no history of high blood pressure during routine pregnancy check-ups. High blood pressure was only discovered when the patient began to complain of shortness of breath. From the patient's obstetric status, the height of the uterine fundus was 26 cm, with head presentation, no contractions, and a fetal heart rate (FHR) of 110-115 beats per minute. Laboratory results showed leukocytes at 22,670/µL, random blood sugar at 713 mg/dL, and severe metabolic acidosis (pH 6.944, pO2 148, pCO2 9.3, HCO3 5.5, BE -28.5, SO2 97%) on blood gas analysis. Previous hospital laboratory results indicated proteinuria and bacteria (+) in the urine. During antenatal care (ANC), the patient never had her blood sugar checked, but according to her husband, she had her blood sugar checked in 2020, before becoming pregnant, due to complaints of weakness. The results showed a random blood sugar level of >200 mg/dL. However, the patient only reduced her intake of sweets and did not pursue further examination at a health facility.

CASE

In this case, the patient presented in poor general condition with respiratory failure, loss of consciousness (GCS E2A3M4), and severe metabolic acidosis. She was sedated and intubated by the Emergency Medicine team. The termination of the pregnancy was postponed to prioritize stabilizing the mother's condition. The patient received fluid rehydration therapy, a sodium bicarbonate infusion, antibiotics, and insulin therapy via an insulin pump. She was treated in the ICU.

By the following morning, the patient was conscious and no longer sedated, had been extubated since dawn, with a blood pressure of 188/94 mmHg and a respiratory rate of 22 breaths per minute. Obstetric status revealed a good fetal heart rate (FHR) of 153-155 beats per minute. Further laboratory examination in the ICU showed a random blood sugar level of 319 mg/dL, elevated pancreatic enzymes with amylase at 1,004.8 U/L and lipase at 899.4 U/L, and elevated

triglycerides at 789 mg/dL. Suspecting acute pancreatitis, an upper and lower abdominal ultrasound or a CT scan with contrast was planned post-delivery.

With the patient's general condition improved and the fetus stable, we proceeded with a caesarean section to terminate the pregnancy. After the delivery, a contrast-enhanced abdominal CT scan confirmed acute pancreatitis. Postpartum, the patient continued on insulin pump therapy and antibiotics. During her 11-day hospital stay, the patient's condition gradually improved. Final laboratory results showed pancreatic amylase at 42.6 U/L and lipase at 105 U/L. The patient was discharged without complaints, along with a healthy baby.

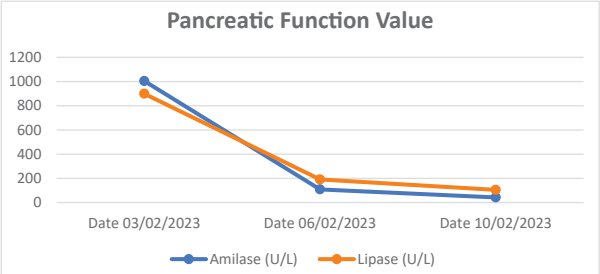

Figure 1. Changes in pancreatic function values patients during hospitalized

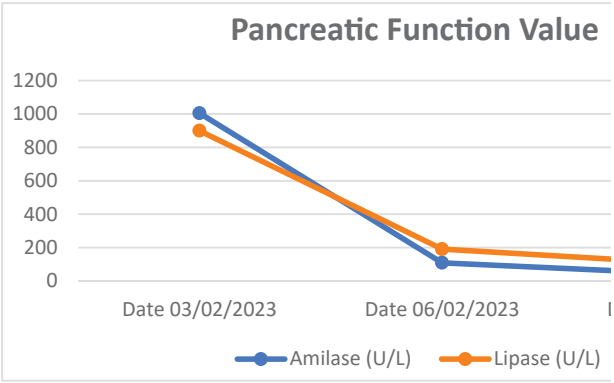

Figure 2. The results of abdominal CT Scan with contrast are consistent with acute pancreatitis

DISCUSSION

Acute pancreatitis during pregnancy is an uncommon occurrence. While uncommon, it is important to acknowledge that the likelihood of problems is twice as high in pregnant women compared to non-pregnant women. Pancreatitis during pregnancy can manifest in any trimester, but it is uncommon in the first 6 months (12%). It predominantly occurs in the third trimester (50–52%) or shortly after birth (38%)[11,12]. This aligns with the events of the case, which took place during the third trimester at around 32–33 weeks of gestation.

According to the updated Atlanta's categorization of acute pancreatitis, the diagnosis of acute pancreatitis necessitates the presence of at least two out of the following three characteristics; The abdominal discomfort is indicative of acute pancreatitis, characterized by continuous, intense pain in the upper abdomen that commonly spreads to the back; the activity of serum lipase (or amylase) is elevated to at least three times the normal limit; and acute pancreatitis characteristics identified using an abdominal CT scan, abdominal MRI, or abdominal ultrasound examination[13]. Although lipase and amylase tests are valuable for detecting acute pancreatitis, repeatedly measuring them in individuals with the condition is not helpful for forecasting the prognosis and severity of the disease. The rise in lipase levels has a more prolonged duration in comparison to the increase in serum amylase levels. Consequently, lipase is highly beneficial in patients who seek medical attention more than 24 hours after the start of discomfort[2]. Mild acute pancreatitis is defined by the absence of organ dysfunction and the absence of both local and systemic consequences. Patients experiencing organ failure that lasts less than 48 hours and/or consequences that affect a specific area or the entire body but do not result in ongoing organ failure are categorized as having moderately severe pancreatitis. Patients who have had organ failure for more than 48 hours are classified as having severe pancreatitis. Organ failure was categorized based on the modified Marshall score method for assessing organ dysfunction[2,13,14]. The patient mentioned can be definitively diagnosed with acute pancreatitis. This conclusion is based on several factors: the patient has been experiencing severe heartburn since the day before being referred; a sudden increase in blood sugar is found as a sign of pancreatic organ failure, there is an elevation in serum amylase and lipase activity (specifically, amylase values of 1,004.8 U/L and lipase values of 899.4 U/L); and the results of the abdominal CT scan reveal the presence of characteristics consistent with acute pancreatitis. This patient may be classified as having moderate-to-severe acute pancreatitis based on the severity. The PaO2/fiO2 ratio, which measures the oxygen levels in the blood, yielded a result of 185.

Table 1. Modified Marshall Scoring System for Organ Failure[14]

Organ System	Score				
Respiratory (PaO_2/FiO_2)	**0** >400	**1** 301-400	**2** 201-300	**3** 101-200	**4** ≤101
Rena l* (serum creatinine, µmol/l)	≤134	134-169	170-310	311-439	>439
(serum creatinine, mg/dl)	<1.4	1.4-1.8	1.9-3.6	3.6-4.9	>4.9
Cardiovascular (systolic blood pressure, mmHg)†	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH <7.3	<90, pH <7.2
For non-ventilated patient, the FiO2 can be estimated from below :					
Supplemental oxygen (l/min)	FiO_2 (%)				
Room Air	21				
2	25				
4	30				
6-8	40				
9-10	50				

A score of 2 or more in any sytem defines the precense of organ failure
*A score for patients with pre-existing chronic renal failure depends on the further deterioration of baseline renal function. No formal correction exists for a baseline serum creatine ≥ 134 µmol/l or ≥ 1.4 mg/dl
† off inotropic support

Hypertriglyceridemia is defined as a fasting serum triglyceride levels above 150 mg/dL (1.7 mmol/L)[9]. In a typical pregnancy, there are specific adjustments in the way lipids are processed. This involves an increase in the production of lipoproteins, which is caused by higher levels of estrogen. Additionally, there is a decrease in the activity of lipoprotein lipase owing to increased insulin resistance. The purpose of these modifications is to guarantee the placenta's requirements and the glucose and lipid demands of the developing fetus. This involves enhancing glucose production, synthesis progesterone, and promoting lipogenesis while simultaneously decreasing lipolysis. The elevation in estrogen levels and subsequent enhancement of lipoprotein production contribute to an elevation in triglyceride levels. Additionally, the decrease in lipoprotein lipase activity hinders the removal of triglycerides, leading to elevated triglyceride levels in the bloodstream[6,11,15–17]. Triglyceride levels reach their highest point during the third trimester of pregnancy, often increasing to 2-4 times higher than normal values. However, this rise very rarely goes over 300 mg/dL (16.7 mmol/L), which is not enough to trigger severe pancreatitis. Acute pancreatitis is more likely to develop when triglyceride levels are above 500 mg/dL; however, it most commonly happens when triglyceride levels surpass 1000 mg/dL[1,6]. The incidence of hypertriglyceridemia-induced pancreatitis (HTGP) has been documented to be as high as 22 percent; however, it is often believed to account for 5% of all instances of acute pancreatitis and up to 56% of cases of acute pancreatitis during pregnancy[9]. One of the complications of hypertiglyceridemia in pregnancy is hyper-viscosity syndrome, which is preeclampsia and an increased risk of hyperlipoproteinemia later in life. Hypertriglyceridemia has a significant impact on the pathogenesis of pregnancy-induced preeclampsia and is associated with an increase in lipid peroxidation products that act as a dysfunction of endothelial oxidative stress.[16-18]. In this instance, there was no record of alcohol misuse. The CT scan results revealed no abnormalities in the gallbladder or its ducts. The patient's triglyceride level was measured at 789 mg/dL, which the author considers to be a significant contributing factor in the development of acute pancreatitis in this case.

Severe preeclampsia can exacerbate the onset of acute pancreatitis. Severe preeclampsia is linked to microvascular alterations, such as arteriole spasms, microthrombosis, DIC (disseminated intravascular coagulation), and vasculitis, which impair the functioning of several organs, including the pancreas. The presence of microvascular abnormalities in pregnant women with eclampsia is believed to be a contributing

factor to the development of acute pancreatitis. In addition, severe preeclampsia is linked to higher levels of inflammatory mediators or a higher sensitivity to these mediators. These can potentially cause or start inflammation of the pancreatic gland tissue, which can lead to acute pancreatitis or its worsening. The presence of simultaneous hyperlipidemia, cholestitis, or cholelithiasis increases the likelihood of developing acute pancreatitis[10]. After doing an examination, we found that the individual had high blood pressure readings of 170/110, and protein was detected in a thorough urine analysis. Nevertheless, there was no documentation of elevated blood pressure throughout prenatal care. The patient initially had dyspnea, which was then accompanied by intense heartburn, nausea, and a variable body temperature, leading to the detection of hypertension. During the patient's hospitalization, there is a gradual decline in blood pressure, which corresponds to a drop in amylase levels or an improvement in acute pancreatitis. Hence, it may be inferred that the acute pancreatitis in this patient led to the onset of severe preeclampsia, which was a result of hypertriglyceridemia. The patients recovery from acute pancreatitis and a decline in blood pressure were indicators of this. This demonstrates that the sequence in this case differs from most others, with acute preeclampsia occurring after acute pancreatitis, while in the case series, acute pancreatitis was a complication that resulted from preeclampsia.

Hypertriglyceridemia-induced acute pancreatitis during pregnancy is a rare illness, and there is less scientific evidence available to inform its treatment. Efficient management depends on a varied care team of professionals with proficiency in other fields, in addition to the physicians' competence[19]. In this instance, the author engaged a multidisciplinary team consisting of the author as an obstetrics specialist, along with colleagues specialising in endocrinology, anesthesia, and stomach surgery.

The initial management of acute pancreatitis during pregnancy does not significantly differ from the management of acute pancreatitis in non-pregnant individuals. The primary therapeutic measures include administering oxygen, restoring fluid levels, managing discomfort, and discontinuing oral intake (bowel rest) to inhibit the exocrine activity of the pancreas, thereby averting self-digestion by the pancreas. Upon the identification of hypertriglyceridemia, treatment should be initiated with the objective of decreasing triglyceride levels[11,19]. The main therapy used in this case is fluid rehydration with normal saline (NS) and insulin pump, which is adjusted to the patient's sugar level. Elevated blood glucose in acute pancreatitis is an indication of more severe acute pancreatitis. This can occur due to a complex endocrine insufficiency. This can lead to a decrease in insulin production, a rise in insulin resistance, or a mix of both[3,4].

Insulin increases lipoprotein lipase activity, thereby decreasing the production of Very Low Density Lipoprotein (VLDL) and also reducing serum triglycerides. There is little evidence that insulin is superior to the NPO diet (nil per os/ nothing by mouth) in reducing serum triglycerides in the treatment of hypertriglyceridemia-induced acute pancreatitis[19]. In this scenario, insulin is administered at an initial rate of 5 U/hour, with the possibility of adjusting the dosage up or down based on the patient's blood glucose level. Regrettably, we failed to verify the serum triglyceride levels again after correcting them with insulin in this particular instance.

The case studies have examined the conservative strategy of using a low-lipid diet together with omega-3 fatty acid supplementation. Omega-3 fatty acids are recognized for their ability to decrease the secretion of triglycerides in the liver and enhance the activity of lipoprotein lipase. Omega-3 fatty acids have fewer negative effects compared to other medications that decrease triglyceride levels, such as fibrates, statins, and nicotinic acid. This makes omega-3 fatty acids the preferable therapeutic choice for managing hypertriglyceridemia during pregnancy. There have been no documented adverse effects associated with the use of Supplement (this patient has omacor), which contains omega-3 fatty acids. However, there is one case study that described instances of diarrhea and respiratory distress syndrome in neonates. Another study found no correlation between preterm birth and the administration of omega-3 fatty acids during pregnancy[8]. Nevertheless, the patients we now serve have not been offered this therapeutic alternative. However, in the future, using this therapy as a potential strategy for treating acute pancreatitis in pregnancy due to hypertriglyceridemia might be considered.

CONCLUSION

Pregnant patients presenting with symptoms of shortness of breath, severe heartburn not relieved by treatment, a history of fever, a sudden increase in blood sugar, and hypertriglyceridemia should be considered for acute pancreatitis as a differential diagnosis. Rapid identification and appropriate treatment can reduce maternal and fetal mortality.

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