THE PANCREAS PROBLEM IN PREGNANCY

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ABSTRACT Introduction: Acute pancreatitis is the acute onset inflammation of the pancreas. The etiology is multifactorial, and gall stone induced pancreatitis is the commonest precipitator. Others are hypertriglyceridemia and alcohol. In pregnancy, pancreatitis becomes a substantial addition to morbidity and mortality. The disease may be mild, moderate or severe. The presentation is sudden onset acute upper abdominal pain in most cases. Diagnosis in pregnancy is chiefly by abdominal ultrasonography. Elevated serum amylase and serum lipase are chief biochemical markers. Case series: We present three cases of acute pancreatitis with three varied etiologies. We resorted to conservative management. However, the outcomes were varied. Conclusion: Acute pancreatitis is life threatening medical problem in pregnancy. A multidisciplinary approach and timely intervention can help in achieving best possible outcomes.

KEYWORDS obstetric medical disease, gallstones, hypertriglyceridemia, alcohol

Introduction
Acute pancreatitis is a rare complication of pregnancy. The incidence of acute pancreatitis in the general population is rising due to an increase in obesity and gall stones.[1] This is likely to reflect on pregnancy as well. The altered physiology in pregnancy adds to the mortality and morbidity of both the mother and the fetus. Approximately two-thirds of cases in pregnancy are biliary in origin. [2,3] Nonbiliary causes have poorer outcomes.[2] Alcohol and hypertriglyceridemia are other precipitators. In rare cases, pancreatitis is associated with acute fatty liver of pregnancy, hyperemesis gravidarum, and preeclampsia.[4,5]

Although the management is usually conservative, multidisciplinary care is warranted, given the possibilities of acute and life-threatening complications. Therefore, we present three pregnant women with acute pancreatitis with varied etiologies and varied outcomes.

Case series

Case 1
Thirty-one years Primigravida with pre-eclampsia on tablet labetalol (100mg, twice a day) and tablet aspirin (75mg, OD) presented at 29 weeks of gestation with tiredness, nausea and upper abdominal pain radiating to back since 6 hours. She gave no history of fever, loose stools, bleeding or discharge per vagina, giddiness or signs of impending eclampsia. Fetal movements were well perceived. The course of pregnancy was uneventful. Past and family history were insignificant.

She had dehydration but no pallor, icterus, or pedal oedema on examination. Pulse was 94 beats/min, blood pressure-100/60mmHg, temperature - 98 deg F, SpO2-99%.

Systemic examination was normal. Per abdomen, there was tenderness at the epigastric region. Obstetric examination showed normal uterine tone, relaxed. FHS was 166bpm and regular. Rapid Antigen Test for COVID-19 was negative. She was admitted to the High Dependency Unit.

Her investigation profile was as follows. Hb – 9.8g%, total leucocyte count – 12.6 x 103 cells/cc, platelet count – 2.16 x 105 cells/cc, and Preeclampsia Profile showed no abnormality. S. Calcium – 8.9mmol/l, RBS – 133mg/dl. LDH – 522U/L, Uric acid – 7.8mg%. The urine routine and microscopy was normal. USG – obstetrics was normal. S amylase – 1392U/L, S.Lipase – 1048U/L. The lipid profile was normal. USG abdomen suggested that the body of the pancreas was prominent with
peripancreatic collection suggestive of acute pancreatitis. Gall bladder showed multiple small calculi.

The patient was kept nil per orally. A nasogastric tube was inserted. Maintenance fluids were administered intravenously. The bladder was catheterized. Antibiotics, analgesics, antacids were given.

On the third day of admission, she had 1 episode of fever of 100°F that responded well to intravenous paracetamol. Her recovery over the next five days was quick. A repeat ultrasound showed significantly decreased pancreatic prominence and decreased peripancreatic collection. On day 10 of admission, she was discharged in a satisfactory state of health with advice to review frequently in the antenatal clinic.

She was lost to follow-up. However, upon telephonic contact, she informed that she had delivered a male baby of 3.4kg at term by Caesarean section due to severe oligohydramnios with no other complications. In addition, she was following up with a surgeon regarding gall stones.

**Case 2**

A 36-year-old woman, Gravida 6 Para 2 Living 2 Abortions 2 belonging to an indigenous tribe presented to emergency with complaints of severe pain in the abdomen multiple episodes of vomiting and fever since one day. There is no history of bleeding/discharge per vagina, headache, loose stools or constipation, hematemesis, abdominal distension, trauma, or assault. She had a history of irregular periods and her last menstrual period was roughly three to four months ago. On examination, the patient was in agony. She looked pale and was malnourished. There were signs of dehydration, and the breath smelled of alcohol. Pulse – 114 beats/min, BP – 124/78 mmHg, Temperature – 99.8°F, SpO2 with AFI of 6.1cm. The high-risk nature was explained. Under multidisciplinary care, conservative management with high fluid therapy was undertaken. Her general condition improved over the next three days. By day five, she had become completely asymptomatic. After that, she underwent anemia correction with parenteral iron sucrose injections of methylcobalamin and folate. In addition, she was put on protein powder supplementation. She was discharged on day 9. One week later, she presented with bleeding per vagina and aborted spontaneously. After post-abortal period, she was referred to a de-addiction centre.

**Case 3**

32-year-old G2P1L1 at 38+1 weeks of gestation, who had migrated from northwestern India, presented to the emergency department with sudden onset upper abdominal pain, which was severe and constant, radiating to the back. She had associated nausea, vomiting and fever. Fetal movements were well perceived. She had gestational diabetes mellitus since the 27th week of gestation, was on medical nutrition therapy and exercise, and had good control of blood sugars. Her antenatal period was otherwise uncomplicated. She had a history of the death of 2 first degree relatives in their late 30s due to myocardial infarction. On examination, she patiently looked fatigued and pale. There was no icterus or pedal edema. Pulse – 110 beats/min, BP – 130/68 mmHg, Temperature – 99.7°F, SpO2 98% at room air. Per abdominal examination showed increased skin temperature tenderness in the epigastic region with guarding. Fundal height corresponded to 32 weeks of gestation, and the uterus was relaxed and non-tender with cephalic presentation. Per vaginal examination showed cervical dilatation of 3cm, 40-50% effaced and intact membranes.

Her investigation profile was as follows, Hb – 10.3g%, Total Leucocyte Count 15.6 x 103 cells/cc, platelet count – 1.55 x 103 cells/cc, Urine dipstick for protein was 1+, no urine ketone bodies, Random Blood Glucose was 141mg/dl. Blood urea – 50.1mg/dl, Serum Creatinine – 1.26 mg/dl, Uric Acid – 10.5mg/dl, S.LDH – 552U/L, S.Amylase 1793U/L, S.Lipase – 10506U/L, S. Triglycerides – 1093mg/ml. USG showed massively enlarged head and body of pancreas with features of vascular compromise and gross peripancreatic collection. The gall bladder was normal. USG obstetrics did not show any abnormality. A diagnosis of hypertriglyceridemic acute necrotizing pancreatitis was made.

Grave risk to mother and baby was explained. She was admitted to the Intensive Care Unit and was put on piperacillin+tazobactum, metronidazole, pantoprazole, tramadol, and intravenous fluids. As she was being monitored, a cardiotocograph began showing intermittent fetal tachycardia. Resuscitative measures were undertaken, after which labour was accelerated with oxytocin. She delivered a healthy female baby of 3.6Kg. She had a mild postpartum haemorrhage, which responded quickly to conservative management. Post stabilization, she underwent CECT, which showed acute necrotizing pancreatitis with splenic vein thrombosis in the region of the tail of the pancreas. Supportive care was continued, and grave risk was reiterated. Her response to treatment was prompt and progressive. She was discharged on day eleven.

**Discussion**

An attack of acute pancreatitis is often an emergent state, more so, in the background of pregnancy. Although it is a rare guest of Obstetric critical care, it does pose a grave risk to the expectant mother and/or the fetus. This acute inflammatory process is broadly divided into two; edematous, interstitial pancreatitis and necrotizing pancreatitis. The commonest precipitants are gallstones, alcohol, and hypertriglyceridemia, and in general, the aetiology may be established in about 75% of cases[6]. Other causes like biliary obstruction, hypercalcaemia, pancreatic duct injury etc., are rare.
Gallstone diseases, pregnancy and pancreatitis

Gall stones cause pancreatitis by duct obstruction, increased duct pressure and secretion of autolyzing enzymes. In addition, estrogen increases cholesterol secretion, and progesterone reduces bile acid secretion, which ultimately causes bile to become supersaturated with cholesterol. Progesterone also slows gallbladder emptying, which further promotes the formation of stones by causing bile stasis. Prepregnancy obesity [7,8] and multiparity [9 – 11] are independent risk factors for gallstones in pregnancy.

Hypertriglyceridemia, pregnancy and pancreatitis

The high estrogen state enhances lipogenesis and hepatic VLDL synthesis. However, it suppresses hepatic lipase activity, resulting in increased triglyceride-rich LDL and high-density lipoprotein (HD) particles in the maternal circulation.[12] Concurrently, insulin resistance leads to decreased LPL activity and increased adipose tissue lipolysis leading to increased FFAs.[13] The pathophysiology of hypertriglyceridemia is due to the accumulation of free fatty acids (FFA) causing inflammatory response. Their breakdown into FFAs by pancreatic lipase causes lipotoxicity triggering an inflammatory reaction, releasing intracellular calcium, increasing inflammatory mediators such as TNF-alpha, interleukin – 6 and interleukin – 10 and causing acinar necrosis.[14,15]

Alcohol, pregnancy and pancreatitis

In the metabolism of alcohol, the pancreas uses an oxidative pathway that leads to the formation of acetaldehyde, a reactive metabolite that causes detrimental effects in acinar cells through activation of stellate cells, increased expression of proinflammatory cytokines, and a decrease in NAD+ / NADH ratios; and non – oxidative pathway requires the formation of fatty acid ethyl ester (FAEE) synthase, which leads to activation of key transcription factors, sustained increases in intracellular calcium, and inhibition of extracellular matrix proteins, ultimately leading to further cell injury.[16] In addition to the causes described above, other key elements in history include symptoms like unexplained weight loss, new-onset diabetes, trauma, prior endoscopic retrograde cholangiopancreatography, coexistent autoimmune disorders or family history. Abdominal pain is the most common presentation. The diagnosis of acute pancreatitis is defined by two of the following: acute onset severe, persistent epigastric pain with radiation to the back, three times or greater increase in serum lipase or amylase, or characteristic radiological features.

Biochemical indicators like elevated AST and ALT point towards gallstone/biliary pancreatitis. The diagnosis of hypertriglyceridemia is made when Serum Triglycerides are over 1000mg/dL. Several inflammatory markers like C-Reactive Protein, IL-6, TNF may be elevated. Hypocalcemia, hyper- or hypoglycemia and elevated Blood Urea Nitrogen may be other findings.

As many clinicians refrain from ordering a CT, abdominal ultrasonography remains the imaging cornerstone in the diagnosis. The pancreas appears enlarged diffusely and hypoechoic. The anechoic shadow around the pancreas and internal echoes indicate peripancreatic fluid and pancreatic necrosis, respectively. Gall stones, when present, may be visualized.MRI has higher sensitivity for acute pancreatitis but may not always be required.

Acute Pancreatitis may be mild, moderate or severe. Severe acute pancreatitis invariably requires Intensive Care. Irrespective of the severity, fluid management with isotonic crystalloid solutions and control of pain, usually with opioids, and management of precipitating factors, remain the crux of treatment. Monitoring is vital, especially in the first 24-48 hours. Oral nutrition may be allowed in mild and selected moderate cases. For more severe cases, enteral is preferred over parenteral nutrition. Prophylactic antibiotics are not recommended in acute pancreatitis, but about 20% develop extrapancreatic infections in whom antibiotics are warranted.

Complications include pancreatic pseudocyst, peripancreatic fluid collection, acute necrosis and infection, splenic vein thrombosis, pseudoaneurysms, abdominal compartment syndrome—obstetric complications like gross maternal metabolic derangements, abortions or intrauterine fetal demise, and preterm labour.

Conclusion

Acute pancreatitis in pregnancy is a rare but life-threatening condition with varied aetiology and a recognisable precipitating cause. A multidisciplinary approach, close monitoring, fluid and pain management, and due alleviation of the underlying causative factors can lead to significantly improved outcomes.

Funding

This work did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

References


