Acute pancreatitis in pregnancy: 5-year experience from a multidisciplinary centre

Saranya Srikumar, Sobha S. Nair*, Reshma Reghunath, Saranya Raj, Radhamany K.

ABSTRACT

Background: Acute pancreatitis is rare in pregnancy, but it is associated with increased incidence of maternal and fetal mortality. It should be one of the differential diagnosis of upper abdominal pain with or without nausea or vomiting. S. amylase, lipase and ultrasound abdomen were the diagnostic methods. Conservative management is the main stay in mild cases. Severe cases have multiorgan involvement and need multidisciplinary approach. The objectives of this study were to study the maternal and fetal outcome in pregnant women diagnosed with acute pancreatitis and to identify the risk factors for acute pancreatitis in pregnancy.

Methods: Retrospective descriptive study of pregnant women diagnosed with acute pancreatitis in Amrita Institute of Medical Sciences, Kochi during the period of 5 years from January 2011 to December 2016. A proforma having patients age, parity index, gestational age, symptoms with duration, blood investigations, ultrasonography, interventions done, mode of delivery, supportive treatment, complications were developed. Fetal weight, Apgar score, fetal complications were also noted.

Results: The mean gestational age of presentation was 30 weeks of pregnancy. Upper abdominal pain radiating to back, vomiting, fever was the commonest clinical presentation in majority of cases. The diagnostic methods were S.Amylase , Lipase and Ultrasound abdomen. The mean age of the patients were 26 years and 66.7% were primigravidas in the present study. There were 4 patients in SAP and 5 in MAP groups. Complications in SAP group were ARF, ARDS, DIC, MODS, metabolic acidosis etc. SAP group had 3 maternal and 3 fetal loss.

Conclusions: Severe acute pancreatitis has adverse maternal and fetal outcome due to multi organ failure and sepsis.

Keywords: Acute pancreatitis (AP), Acute pancreatitis in pregnancy (APIP), Acute renal failure (ARF), Adult respiratory distress syndrome (ARDS), Amylase, Epigastric pain, Intrauterine death (IUD), Mild acute pancreatitis (MAP), Multiorgan dysfunction (MODS), Severe acute pancreatitis (SAP)

INTRODUCTION

Acute pancreatitis (AP) during pregnancy is a rare event with wide variation in the incidence, ranging from 1:1000 to 1:10000.1 Biliary tract diseases are the most common cause of acute pancreatitis in pregnancy, with gallstone disease being responsible for more than 70% of cases.2 The susceptibility of gallstone formation during pregnancy is attributed to the lithogenic effect of gestation through estrogen and progesterone. More than 50% of cases in pregnancy are diagnosed in third trimester demonstrating that acute pancreatitis is more common with advancing gestational age, paralleling the frequency of gallstones in pregnancy.1
Abdominal pain (acute onset of a persistent, severe, epigastric pain often radiating to back), serum lipase or amylase activity at least three times greater than the upper limit of the reference interval and imaging (USG, CT, MRI) are used for the diagnosis of AP. Ultrasound is the imaging technique of choice for pregnant women because it can distinguish a normal appearing pancreas from one, i.e., enlarged, and it can also identify gallstones. In addition, ultrasound is safer than computed tomography (CT) scan in pregnancy.

Abdominal ultrasound, CT, endoscopic ultrasound, and magnetic resonance cholangiopancreatography (MRCP) are available for diagnosing a biliary etiology for acute pancreatitis.

**METHODS**

We conducted a retrospective descriptive study of pregnant women diagnosed with acute pancreatitis in Amrita Institute of Medical Sciences, Kochi during the period of 5 years from January 2011 to December 2016. A proforma having patients age, parity index, gestational age, symptoms with duration, blood investigations, ultrasonography, any interventions done, mode of delivery, supportive treatment, complications were developed. Fetal weight, Apgar score, fetal complications were also noted.

The diagnosis of acute pancreatitis in pregnancy according to the revised Atlanta classification requires two of the three following features:

- Abdominal pain consistent with acute pancreatitis
- Serum lipase and amylase activity increased at least three times the higher normal serum levels
- Characteristic imaging findings of acute pancreatitis on U/S, MRI or CT.

**Statistical analysis**

Numerical variables were expressed as mean and standard deviation and categorical variables were expressed as frequency and percentages. To obtain association between the categorical variables and groups, Chi-square test was applied.

To obtain the mean comparison of numerical variables between groups, independent two sample t-test was applied.

**RESULTS**

The mean age of presentation was 26 years and the gestational age was 30 weeks. We had 66.6% of primigravidas in the study group (Figure 1). Among the 9 cases, 6 were referred to us. 7 (77.8%) had pancreatitis in third trimester and 1 (11.1%) each in first and second trimesters. Epigastric pain radiating to back was present in all patients (100%).

The other symptoms were nausea/vomiting in 5 (55.6), fever in 3 (33.3%), diarrhoea in 2 (22.2%), decreased fetal movement in 3 (33.3%), jaundice, hypotension and tachycardia in 1 (11.1%) (Figure 2). There was flare up of SLE in 1 case. 3 of our patients had pregnancy induced hypertension (PIH) (Figure 3).
alone. CT scan was done in 2 cases of SAP where ultrasound was inconclusive (Figure 4).

Figure 4: CT scan-bulky pancreas with peripancreatic fluid.

We grouped patients into two as SAP and MAP, based on the severity of the disease as per revised Atlanta classification. There were 4 (44.4%) in SAP and 5 (55.6%) in MAP groups (Table 1). The mean CRP in SAP group was 211.5 mg/dl and in MAP group it was 83.71 mg/dl.

Table 1: SAP versus MAP outcome.

<table>
<thead>
<tr>
<th>Variables</th>
<th>SAP group</th>
<th>MAP group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Complications (ARF, ARDS, septic shock, pneumonia, metabolic acidosis, MODS, etc)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>CRP (mean in mg/dl)</td>
<td>211.5</td>
<td>83.7</td>
</tr>
<tr>
<td>Maternal death</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Fetal loss</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

Conservative management was the initial treatment given to MAP group while SAP had undergone treatment for the complications that had occurred. 1 patient underwent laparotomy and the finding was an extensive saponification of fat.

The complications were ARF in 4, sepsis in 3, ARDS in 2, MODS in 1, metabolic acidosis in 2, septic shock in 1, DIC in 1, encephalitis in 1, pneumonia in 1 and pleural effusion in 2 (Figure 5).

3 (33.3%) patients underwent haemodialysis. Ventilator with ionotropic supports were given to 4 (44.4%) patients. Antibiotics were given to 3 (33.3%) in SAP group. We had 3 maternal death, all were in SAP group and none in MAP group (Figure 6).

Figure 6: Maternal and fetal mortality in SAP/MAP.

There were 8 preterm deliveries and 1 term delivery in the present study. 3 patients had spontaneous onset of labour pains. 4 had vaginal deliveries and 5 had caesarean section. Indication for caesarean section was 1 with non-progression of labour, 1 with growth restriction and Doppler abnormality (which was the patient who had pancreatitis at 11 weeks), 1 term previous caesarean section, 1 abruptio placentae and 1 fetal distress with SAP. Among the 3 decreased fetal movements, 2 were intrauterine deaths and 1 neonatal death 12 hours after birth. The average birth weight in live birth group was 1816 grams. The average duration of hospital stay was 17.67 days.

DISCUSSION

The mean age of the patients was 26 years. There were 6 primigravida in the present study. APIP was more in the third (77.8%) trimesters as compared to first (11.1%) and second trimesters, which is consistent with the finding that the frequency of APIP increases as pregnancy progresses. Acute pancreatitis (AP) in pregnancy is most often associated with gallstone disease or hypertriglyceridemia. Gallstones are the most common cause of acute pancreatitis during pregnancy, accounting for more than 70% of cases. Acute gallstone pancreatitis is caused by a stone passing through the ampulla of Vater, and is associated with maternal mortality if not recognized and treated appropriate. Up to 10% of patients develop stones or sludge (muddy sediment, precursor to gallstone formation) over the course of each pregnancy, obesity and increased leptin being risk factors. Pregnancy itself can be a cause due to
the physiological changes such as increasing weight, increased triglycerides, and increased levels of oestrogen. Risk of acute pancreatitis from hypertriglyceridaemia in pregnancy also seems to be the highest in third trimester and tends to be a more severe form of pancreatitis than that due to gallstones.\textsuperscript{8} Drug such as Metformin and Diabetes mellitus type 2 is associated with 2.8-fold higher risk.\textsuperscript{9,10} Hyperthyroidism, connective tissue diseases, infections and trauma: both iatrogenic and accidental are other rare causes of acute pancreatitis. However, primary diseases were absent in most cases (57.89%).\textsuperscript{11}

One patient had sludge (11.1%), 1 (11.1%) SLE with PIH, 2 (22.2%) PIH and remaining 5 (55.6%) idiopathic causes in the present study.

Pregnancy induced hypertension (PIH) also rarely causes acute pancreatitis due to the micro vascular abnormalities involving splanchic circulation which results in pancreatic ischemic changes.\textsuperscript{12} Pancreatitis in pregnancy may be associated with HELLP syndrome or preeclampsia leading to high fetal mortality or preterm delivery.\textsuperscript{9}

Clinical characteristics of acute pancreatitis in pregnancy do not differ from the non-pregnancy state. The usual symptoms are abdominal pain, anorexia, nausea, vomiting, dyspepsia, low-grade fever, tachycardia, fatty food intolerance.\textsuperscript{13} All our patients had epigastric pain radiating to back (100%), nausea/vomiting in 5 (55.6%), fever in 3 (33.3%) etc.

Serum amylase and lipase are important for diagnosing acute pancreatitis but are not clinical markers of severity. Moreover, these markers for forecasting severity within the first 24-72 hours are of limited value for predicting the development of pancreatic necrosis, persistent organ failure, or death. CRP is the most frequently used single biomarker for assessment of severity in AP today. A concentration of more than 150 mg/dL is often accepted as a predictor of severity in AP. At this cut-off level, CRP has a sensitivity of 80-86% and specificity of 61-84% for diagnosing necrotizing pancreatitis within first 48 hours of onset of symptoms.\textsuperscript{14} The mean S. amylase was 800 IU/L and S. lipase 1660 IU/L in the present study. Elevated WBC and CRP were also found in the study.

Ultrasonography is a reliable and safe method for identifying gallstones in pregnant women. Gallstones and sludge are easily visualized on ultrasound, with sensitivity and specificity approaching 100 percent.\textsuperscript{15} Transabdominal ultrasonography can provide visualization of the pancreas and some complications (e.g. edema, necrosis, or pseudocysts).\textsuperscript{16}

Ultrasound was done in all cases. Sludge in 1 case, bulky pancreas with peripancreatic collection in 2 cases and 1 with necrosis. 2 cases where ultrasound was inconclusive underwent CT scan (pregnancy was terminated and underwent CT scan in the immediate postpartum period) and for the diagnosis of pancreatitis.

CT scans can help to diagnose AP/IP and determine the scale and depth of invasion. This test is also indicated if a patient is experiencing abdominal pain or when ultrasonography fails to detect any lesions. The use of magnetic resonance imaging might also be considered. This technique has not been linked to fetal toxicity and it is an accurate method to identify the cause of acute abdominal and pelvic pain during pregnancy; however, magnetic resonance imaging should be used only when the ultrasonographic findings are indeterminate.\textsuperscript{16}

The course of pancreatitis during pregnancy is usually mild and self-limited but can be rapidly progressive and fulminant due to severe complications such as pancreatic necrosis, generalized peritonitis, acute respiratory distress syndrome (ARDS), disseminated intravascular coagulopathy (DIC) and multiple organ failure.\textsuperscript{17}

According to the Atlanta classification, severe AP is defined by the presence of local complications and/or organ failure (shock, pulmonary insufficiency, and renal failure Organ failure develops often early in the course of AP.\textsuperscript{18}

The revised Atlanta classification also outlines other important findings to be evaluated with imaging such as causes of pancreatitis, including cholecystolithiasis and cholecdocholithiasis, or complications related to acute pancreatitis, including extrahepatic biliary dilatation; splenic, portal, and mesenteric venous thrombosis, varices; arterial pseudoaneurysm; pleural effusion; and ascites.\textsuperscript{3}

The severity of acute pancreatitis is probably the most important issue that must be elucidated as early as possible since pancreatitis is an evolving disease. Mild acute pancreatitis (MAP), which is the most common form, has no organ failure or local or systemic complications and resolves in the first week. Severe acute pancreatitis (SAP) is defined by persistent organ failure, that is, organ failure for more than 48 hours. Local complications include peripancreatic fluid collection and peripancreatic or pancreatic necrosis.\textsuperscript{3} As per this classification, we had 4 patients in SAP and 5 in MAP group (Table 1). The complications in the present study are shown in Figure 5.

The respiratory system function is compromised during pancreatitis by pleural effusion, atelectasis, acute pulmonary oedema or ARDS resulting in hypoxemia and dyspnea.\textsuperscript{19,20}

The circulatory complications are characterized by shock due to hypovolemia and/ or hypotension. The main reasons are loss of fluids retroperitoneally or in the abdominal cavity and/or peripheral vasodilatation.\textsuperscript{20} There were 2 ARDS, 1 Pneumonia 1, 1 pleural effusion
The cardiac complications are characterized by manifestations of tachycardia and non-specific disturbances rather than depression of cardiac function due to the young age of the pregnant patient. One of the patient presented as tachycardia, hypotension, cough and reduced fetal movement. She expired within 72 hours.

Coagulation disturbances and especially DIC (Disseminated Intravascular Coagulation) are very important during pregnancy since they are accompanied by multiple organ failure and result in high rate of fetal and maternal death. One of our patient who had extensive saponification of fat on laparotomy went into DIC, encephalitis, MODS and death.

Renal function is easily impaired during severe acute pancreatitis resulting in uremia and oliguria either through prerenal azotemia or acute tubular necrosis. Of our patients had acute renal failure, of which 3 had haemodialysis. Metabolic complications comprise hypocalcaemia, hyperglycaemia, hypertriglyceridaemia, hypoglycaemia and acid-base disturbances. Metabolic disturbances were present in 2 of our patients.

In the presence of a single organ failure, mortality is less than 10%, whereas in multiorgan failure the mortality rate is 35-50%. Mortality in acute pancreatitis is usually due to systemic inflammatory response syndrome and organ failure in the first two-week period, while after two weeks it is usually due to sepsis and its complications Sepsis related multiorgan failure and infected pancreatic necrosis account for about 40-50% of all mortality in acute pancreatitis. We had 1 case of septic shock. Maternal mortality was 3 (33.3%) in the present study.

Conservative medical management of pancreatitis includes intravenous fluids, nasogastric suctioning, bowel rest, use of analgesics and antispasmodics, fat restriction with parenteral nutrition and antibiotics. There is no role for antibiotics in mild acute pancreatitis (MAP) but in severe acute pancreatitis (SAP) its role remains controversial. However, the indications for therapeutic antibiotic use are extrapancreatic infection (such as cholangitis, catheter-acquired infections, bacteremia, urinary tract infections, pneumonia) and infected necrosis. A systematic review and meta-analysis show antibiotic prophylaxis does not reduce mortality or protect against infected necrosis and frequency of surgical intervention. In the present study conservative management was the main stay in MAP group, while in SAP group interventions pertaining to the system involved were done. Antibiotics were given to 3 patients in SAP group, but had maternal loss.

For APIP, most scholars advocate non-surgical treatment except when there is i) pancreatic abscess or infected effusion; ii) an association with other serious complications such as gastrointestinal perforation; or iii) a deterioration after active treatment for 2 to 3 days.

For one of our patient arterial insult was suspected and underwent laparotomy. There was an extensive saponification of fat suggestive of pancreatitis.

Indications for pregnancy termination include full-term gestation, deteriorated condition after 24-48 hours of treatment, no improvement of paralytic ileus, stillbirth, fetal malformation, and severe pancreatitis. We did termination of pregnancy in 6 cases. There were 8 preterm and 1 term delivery in present study. 3 patients had spontaneous onset of preterm labour pains. Decision for termination of pregnancy was taken in 6 patients in view of maternal and fetal status.

4 had vaginal deliveries (2 intra uterine deaths in the SAP group, 1 with multiorgan failure in SAP group, 1 PPROM with in MAP group) in present study. 5 patients under went caesarean sections. Indication for caesarean section were 1 with non-progression of labour, 1 term previous caesarean section, 1 with multiorgan failure, 1 abruptio placentae (which was the patient who had pancreatitis at 11 week) and 1 fetal distress.

Despite the maternal danger during severe acute pancreatitis it is important to evaluate the fetal distress and morbidity during the exacerbation of systemic complication of pancreatitis in pregnancy. The most prominent consideration is that the incidence of preterm delivery and perinatal morbidity is higher in moderately severe and severe acute pancreatitis than mild acute pancreatitis because of lower supportive efficiency of the maternal-fetal interface which increases the fetal distress. Hypovolemic shock, hypercoagulable state and inflammation due to pancreatitis can cause a significant decline in placental perfusion leading to fetal distress. The maternal acid-base disturbances affect the fetal acid base status which activates the fetal mechanisms of homeostasis as in the cases of fetal hypoxemia which results in redistribution of fetal blood to support the vital organs. Additionally, the uterus could prematurely contract because of the diffuse peritonitis. Therefore, prematurity and mortality of the foetus could be associated with the severity of the disease. Among the 3 with decreased fetal movements (SAP group), 2 were intra uterine deaths and 1 neonatal death 12 hours after birth. The average birth weight in live birth group was 1816 grams.

**CONCLUSION**

Severe acute pancreatitis (SAP) in pregnancy was associated with adverse maternal and fetal outcome. Early diagnosis, classifying the severity of disease and treatment with multidisciplinary approach is the gold standard treatment.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES
