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Recurrent acute pancreatitis in pregnancy

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Abstract
Adverse maternal and fetal outcomes occur due to pancreatitis. Acute biliary pancreatitis which recurs in subsequent pregnancies is rare and early recognition and management is essential. A 30 year old G2P1L1 at 33+5 weeks with symptoms of vomiting and pain abdomen was diagnosed to have mild acute pancreatitis (MAP). She suffered from acute pancreatitis during third trimester of her previous pregnancy and was conservatively managed. However, the cause was not elucidated. In this pregnancy there was sludge in gallbladder on USG abdomen. She was treated conservatively till her symptoms subsided and was on oral Urosodeoxycholic acid. She underwent emergency caesarean section at 37 weeks for fetal distress. On postnatal day 3 the gall bladder did not show any sludge. Recurrent pancreatitis during pregnancy is most commonly due to biliary cause. Early diagnosis of pancreatitis in pregnancy, prompt treatment prevents progression to severe disease and its complications.

Keywords: Acute pancreatitis, recurrent pancreatitis, pregnancy, biliary pancreatitis, recurrent gallstone pancreatitis, biliary sludge

1. Introduction
Acute pancreatitis (AP) affects 1 in 1000 to 1 in 10,000 pregnancies globally [1]. It is rare in the first and second trimester. It is most commonly (50%) seen in the third trimester followed by postpartum period [2]. The common causes of pancreatitis during pregnancy are cholelithiasis and hypertriglyceridemia. Acute biliary pancreatitis related to pregnancy (ABPP) has a high recurrence rate of 70% in subsequent pregnancies compared to general population [3]. Adverse maternal and fetal outcomes are reported in literature and their occurrence depends on early diagnosis and optimal management. We report maternal and fetal outcome of case of recurrent pancreatitis due to cholelithiasis during third trimester of pregnancy.

2. Case
A 30 year G2P1L1 Rh incompatible presented to our emergency services at 33+5 weeks of gestation with complaints of 5 episodes of vomiting and pain abdomen of one week duration. Vomiting was non- projectile, greenish, bilious, non – blood stained, non-foul smelling. Pain abdomen was continuous, moderate aching type of pain over the epigastric region radiating to back, increased on lying down and reduced on sitting. There was no history of diarrohea, constipation, fever, yellowish discolouration of urine, headache and burning micturition. She had regular antenatal care elsewhere and her first and second trimesters were uneventful.
She delivered her first child 3 years ago at our hospital. She was diagnosed to have acute pancreatitis at 9 months of gestation and was conservatively managed and delivered vaginally a term male baby of 3 kg. The baby was O Rh positive and she received anti D injection. Her postnatal period was uneventful.
On admission she was conscious oriented had mild pallor, dehydration and there was no icterus. Her pulse rate was 90/min and BP was 122/78 mmHg. Her BMI was 26 kg/m^2 which was in the mild obese range. Her cardiovascular and respiratory system examination was normal. Per abdominal examination showed uterine size of 34 weeks cephalic presentation with increased liquor an estimated fetal weight of 2.5 kg and good fetal heart sounds. Per speculum cervix and vagina showed curdy white discharge. Her non stress test was reactive. USG findings showed a single live intrauterine gestation, cephalic presentation with an estimated fetal weight of 2.43 kg, posterior location of placenta and an AFI of 25 cms, Umbilical artery Doppler Pulsatality index (PI) 0.7. Her urine ketones were positive. She was admitted to Obstetric ICU and was managed conservatively. Her investigations at admission were shown in table 1.

Table 1: Investigations on the day of admission

Hematological tests Hemoglobin –11.6 g/dl Total count-12440 cells/µL Differential count- N_{85} $L_{12}M_2$ Platelet count-1.4 Lakh/L HIV-Non-Reactive HB_SAg- Non-Reactive VDRL-Non-Reactive	*Pancreatic enzymes* Amylase-773 U/L Lipase-1043 U/L *Lipid profile* Total cholesterol (TC) - 182 mg/dl Triglyceride (TG) – 255 mg/dl HDL- 33 mg/dl LDL- 139 mg/dl VLDL- 51 mg/dl
Renal function tests Urea-11 mg/dl Creatinine-0.5 mg/dl Na^{2+}-135 mEq/L K^{+}-4.4 mEq/L Ca^{2+}-10 mEq/L	Glucose challenge test (GCT) -103 mg/dl TSH – 2 IU/L Urine culture – sterile Stool ova/cyst - nil
Liver function tests Total bilirubin –0.21 mg/dl Direct bilirubin-0.08 mg/dl Total protein –5.8 mg/dl Albumin-2.9 mg/dl AST-20 U/L ALT-10 U/L	Serum PTH- 27.6 pg/ml Vitamin D – 8.89 ng/ml

Laboratory reports showed elevated serum amylase and serum lipase more than three times the normal. USG Abdomen showed bulky pancreas with signs of peri-pancreatic inflammation. Surgery opinion was taken and a provisional diagnosis of mild acute pancreatitis (MAP) was made. Conservative management included intravenous fluid therapy and nasogastric aspiration. She received prophylactic intravenous antibiotic therapy which included third generation cephalosporins.

In view of past history of pancreatitis during her last pregnancy an MRCP was done which showed bulky, oedematous pancreas with a rim of per pancreatic fluid with normal main pancreatic duct, common bile duct and gall bladder. Ryle's tube aspirate was bilious and in decreasing trend. Her pain abdomen reduced and bilious aspirate reduced to 100 ml/ day and hence conservative management was stopped after 10 days and she was put on fat free diet. Her investigations during this period were shown in Table 2.

Table 2: Investigations during the hospital stay

Investigation	Date	1/6/21	2/6/21	4/6/21	7/6/21	26/6/21 (Readmission)
Complete Haemogram	Hb gm/dl	11.6	10.3	10.2	11.2	10.6
	Total Count cells/µL	12,440	12,690	11,130	6870	9,140
	Differential Count	N-51; L12	N-83; L-11	N-79; L-13	N-70; L-6	N-72; L-22
	Platelet count Lakh/L	1.4	1.7	1.6	1.72	1.31
Renal Function tests	Urea mg/dl	11	13	19	11	8
	S. Creatinine mg/dl	0.5	0.46	0.5	0.50	0.5
Liver Function tests	Total Bilirubin/Direct Bilirubin mg/dl	0.4/0.07	-	0.58/0.23	0.59/0.15	0.5/0.67
	AST/ALT-(IU/L)	20/10	-	18/9	20/12	20/10
	Total Protein/Albumin gm/dl	5.8/2.9	5.5/2.9	/2.7	5.6/3	5.7/3
	S. Amylase(IU/L)	773	364	142	183	228
	S. Lipase (IU/L)	1043	620	90	159	343
Lipid Profile mg/dl	Total Cholesterol	182	173	-	220	175
	Triglycerides	255	195	-	255	185
	HDL	33	35	-	38	32
	LDL	139	138	-	147	120
	VLDL	51	39	-	51	37
Serum electrolytes meq/L	Na+	135	136	137	136	136
	K+	4.2	4.3	3.5	3.4	4
S. Calcium mg/dl		10.2	10.2	10	10.5	10.2

Fetal monitoring was done by daily fetal kick count and alternate day NST. Antenatal cortico-steroids were given for fetal lung maturity. Repeat USG abdomen showed distended gall bladder with biliary sludge (Fig. 1). Hence the cause was ascertained as acute biliary pancreatitis

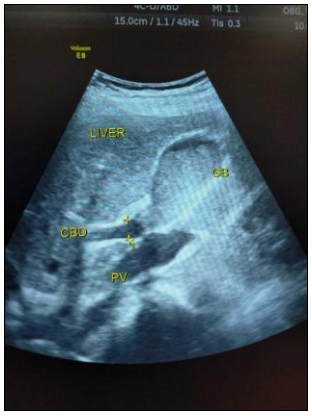

Fig 1: USG abdomen showing biliary sludge in the gall bladder

She was started on ursodeoxycholic acid and erythromycin and a discussion with surgical gastroenterologist for ERCP (Endoscopic retrograde cholangiopancreatography) and sphincterotomy was deferred. She was discharged home at request at 36 weeks.

She got re-admitted at 37 weeks with pain abdomen again and she underwent induction of labour for oligohydramnios. Her biochemical investigations are shown in Table 2. An emergency caesarean was done in view of intrapartum fetal distress in first stage of labour and an alive term male baby weighing 3.4 kg was born. Baby blood group was O positive and she received anti D injection. Postoperatively she was started on fat free diet. Her repeat USG of abdomen on postnatal day 3 was normal and there was no gall bladder sludge (Fig. 2). Both mother and baby were discharged in a stable condition on postoperative day 5.

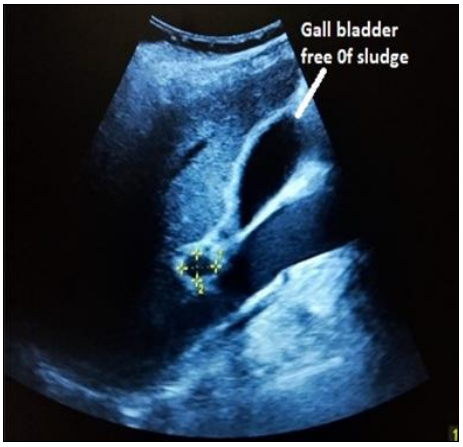

Fig 2: USG Liver on 3 rd post-natal day

3. Discussion

The physiological changes in pregnancy can mislead the diagnosis of acute pancreatitis [3]. The presenting symptoms such as anorexia, pain abdomen, Vomiting and low grade fever can also be seen in other medical conditions such as appendicitis, cholelithiasis, renal colic, peritonitis, peptic ulcer disease as well as obstetric conditions such as ectopic pregnancy, threatened abortion, hyperemesis, torsion of uterus or adnexa and in women with concealed abruption [1].

Pregnancy perse does not predispose to acute pancreatitis [4]. During pregnancy there is an increase in gallbladder volume, decrease in the flow of bile and biliary stasis which occurs due to increased estrogen and bile cholesterol. Progesterone causes gallbladder smooth muscle relaxation and enhances the stasis which causes gallstones formation. Gallstones migrate in the main pancreatic duct causing obstruction and activation of digestive enzymes of the pancreas leading to pancreatitis [2]. Pregnancy also increases the release of estrogen induced triglycerides due to decreased lipoprotein lipase activity [1]. This causes hydrolysis of triglycerides leading to release of free fatty acids which are toxic to the acinar cells of pancreas. Increased concentrations of chylomicrons rises the blood viscosity obstructing the pancreatic capillaries causing ischemia, acidosis and necrosis of the pancreas. Obesity, oral contraceptive usage and mutiparity also increase the risk of acute pancreatitis by the above mechanisms [3, 5]. The common aetiology of acute pancreatitis in pregnancy are biliary (gallstones or sludge), hyperlipidaemia, alcohol intake and in few cases it is idiopathic.

Biliary cause is the commonest accounting to 66% cases in pregnancy [4]. The other causes include hyperparathyroidism, hereditary, post-ERCP (endoscopic retrograde cholangiopancreatography), acute fatty liver of pregnancy, pre-eclampsia and drug-induced such as thiazide diuretics [6]. In the current women who is pregnant gallbladder sludge was the predisposing factor and it was mild pancreatitis which did not progress to severe disease.

There are no standard diagnostic and management criteria for acute pancreatitis in pregnancy [4]. Those which are used in non-pregnant patients are used to guide the diagnosis and management in pregnancy. Pregnancy linked hematological and biochemical alterations have an impact on the diagnosis. An elevated serum amylase and lipase three times the normal has good positive predictive value for the diagnosis of acute pancreatitis in pregnancy [4, 7]. The serum lipase level has a better sensitivity and specificity than serum amylase level to diagnose acute pancreatitis as serum lipase remains elevated up to two weeks [7]. Initial assessment includes history taking for alcohol consumption and drug intake. Haematological tests for liver enzymes, electrolytes and lipid profile to be done to rule out possible etiology.

Abdominal USG is safe and sensitive than CT for diagnosis of gall stones during pregnancy. MRCP (Magnetic resonance cholangiopancreatography) has 90% sensitivity [7] and can be used as an alternative when USG findings are indeterminate and to assess severity without exposing the mother and fetus to non-ionizing radiation. In the present case the initial USG abdomen showed bulky pancreas with peripancreatic inflammation with no stones in the gallbladder and MRCP showed no stones in the main pancreatic duct with no mention about gall bladder sludge. In addition the serum triglyceride levels was less than 1000 mg/dl [8] ruling out the possible hyperlipidemia or gallstone induced pancreatitis.

There was no history of alcoholism, surgeries in the past, prolonged intake of any drugs, Family history of hyperlipidemia or pancreatic diseases and hence the etiology was considered to be idiopathic initially. Acute biliary pancreatitis related to pregnancy (ABPP) has a high recurrence rate of 70% [3] in subsequent pregnancies compared to general population. The frequency of pregnancy, multiparity and obesity increases the risk of biliary stasis and thereby gall stone formation. In addition the gravid uterus in the third trimester increases the intra-abdominal pressure on the biliary tree increases [1] the risk of acute pancreatitis.

The current lady was multiparous whose repeat USG abdomen by a different investigator showed biliary sludge in the gall bladder. She also has history of acute pancreatitis in third trimester of her previous pregnancy which was managed conservatively explaining the possible etiology being biliary. As microliths are frequent during pregnancy only endoscopic ultrasound [4] has higher sensitivity than MRCP for diagnosis of

choledocholithiasis. The severity was assessed using Ranson's score which was less than 3 showing 2% [4] chance of mortality. Acute Pancreatitis is associated with high risk of pregnancy complications such as preterm labour, prematurity and intrauterine fetal demise hence early diagnosis and appropriate management is essential to prevent the same.

Management includes analgesics, fluid therapy, probiotics and cessation of oral feeding to prevent auto digestion of pancreas [7]. Early enteral feeding is recommended to prevent bacterial translocation and to maintain the immunity of gut flora. Antibiotic therapy is needed only in presence of biliary infection and necrotizing pancreatitis [8]. Management is similar in idiopathic acute pancreatitis also and this resulted in good maternal and fetal outcome [8]. A case of recurrent gallstone induced pancreatitis at 26 weeks which was managed conservatively and presented again at 28 weeks was treated with endoscopic retrograde cholangiopancreatography (ERCP) followed by laparoscopic cholecystectomy during pregnancy was reported to have had good maternal and perinatal outcome [9]. As ABPP has high chances of recurrence a consensual strategy [4] can be adopted according to severity and gestational age. In the first trimester and second trimester conservative treatment and laparoscopic cholecystectomy can be done. In the third trimester conservative management or ERCP with endoscopic sphincterotomy followed by laparoscopic cholecystectomy in the early postpartum is the treatment of choice.

Ursodeoxycholic acid (UDCA) is a class B drug that can be safely used in pregnancy during second trimester for symptomatic relief and to prevent complications due to pregnancy-induced gall bladder sludge [10]. It acts by cholelitholytic mechanism and favours formation of vesicles composed of phospholipids in bile which favours dissolution of gallstones [11]. It also improves the gall bladder contractility and reduces oxidative stress. However the maximum dose and its safety in other trimesters warrant further clinical studies [10]. Dietary factors such as consumption of vegetarian diet, vitamin C, soy lecithin and iron help in prevention of gallstones. A Mixture of plant terpenes (Rowchal) has been used to dissolve radiolucent gallstones. There is some scientific evidence that gallbladder flush which is a folk remedy to promote the passage of gallstones can be beneficial in some people [12].

4. Conclusion

Obstetric conditions may mimic symptoms of acute pancreatitis in pregnancy. Acute biliary pancreatitis during pregnancy has a high recurrence rate in subsequent pregnancies. Screening for cholelithiasis (gall bladder sludge) and adopting strategies for dissolution of sludge and gallstones is important to prevent the complication of pancreatitis during pregnancy. Conservative management in early stages of mild pancreatitis prevents progression to severe pancreatitis and results in good maternal and fetal outcome.

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