



## Original Research

# Management of Gallstone-Induced Acute Pancreatitis in Pregnancy: A Tertiary-Center Experience

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### Abstract

**Objectives:** Gallbladder stones are the most frequently reported etiology of acute pancreatitis in pregnancy and are often diagnosed in the third trimester. This condition is associated with both mother and infant morbidity and mortality, and its treatment remains controversial.

**Methods:** Relevant patient data between September 2010 and April 2017 from the Kanuni Sultan Suleyman Training and Research Hospital were analyzed regarding etiology (of gallstone pancreatitis), trimester of pregnancy, diagnostic tools, pancreatitis stage, clinical status, medical treatment, surgical interventions, and pregnancy status.

**Results:** We included 68 patients recorded with acute pancreatitis due to biliary gallstones. Pancreatitis symptoms developed in most (n=38) (55.8%) patients during the third trimester. Of 24 patients who had their first episode of pancreatitis in the first trimester of pregnancy, 12 (50%) were readmitted due to recurrence. Seven (11.3%) patients whose Ranson scale score was 3 underwent computed tomography evaluation. The number of patients with acute cholecystitis with pancreatitis was 5 (7.3%), whereas the number of patients with choledocholithiasis was 4 (5.8%). Sphincterotomy with endoscopic retrograde cholangiopancreatography was performed in 2 (2.9%) patients. Laparoscopic cholecystectomy was performed in 9 (13.2%) patients during pregnancy. No fetal and maternal morbidity and mortality was found in all periods.

**Conclusion:** Developments in supportive care, wide-spread use of imaging methods, and a multidisciplinary approach with better antenatal care of pregnant patients with acute pancreatitis can help prevent fetal and maternal morbidity and mortality in such cases. Early laparoscopic cholecystectomy should be considered especially in pregnant patients with acute pancreatitis due to gallstones in the first trimester.

**Keywords:** Acute pancreatitis; laparoscopic cholecystectomy; pregnancy.

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Acute pancreatitis in pregnancy is a relatively common problem. The incidence is almost 1/1000–10.000 pregnancies.<sup>[1, 2]</sup> It can be caused by gallstones, idiopathic hyperlipidemia, alcohol abuse, and, less commonly by, hyperparathyroidism, trauma, and medications.<sup>[1-3]</sup> Gallbladder stones are the most frequently reported etiology and are often diagnosed in the third trimester.<sup>[1-3]</sup>

Acute pancreatitis is classified into mild, moderate, and

severe forms. Mild and moderate forms are the most common presentations, and the established guidelines recommend cholecystectomy during the same admission in non-pregnant patients with gallstone-induced pancreatitis.<sup>[4]</sup> However, for patients who develop severe acute biliary pancreatitis, especially with necrotizing pancreatitis, the decision regarding the timing of cholecystectomy is a complex one and prolongs the treatment process. On

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the other hand, management of gallstone-induced pancreatitis in pregnant patients is controversial and requires a more careful consideration compared with that in non-pregnant patients due to the fatal effects associated with varying severity of pancreatitis on both the mother and fetus.

In order to explain how clinicians can easily understand and manage this condition, we aimed to identify the epidemiology, diagnosis, treatment, and outcomes along with maternal and fetal morbidity and mortality associated with gallstone-induced acute pancreatitis at a high-volume referral hospital with the highest number of obstetric surgeries in our country.

## Methods

Using hospital database, patient data between September 2010 and April 2017 was retrospectively analyzed using key terms “pregnancy” and “pancreatitis” with high amylase and lipase levels and ultrasonography findings. Patients with pancreatitis due to idiopathic hyperlipidemia, alcohol abuse, hyperparathyroidism, trauma, and medications were excluded from the study. Data were analyzed regarding etiology (gallstone-induced pancreatitis), trimester of pregnancy, diagnostic tools, pancreatitis stage, clinical status, medical treatment, surgical interventions, and pregnancy status. Ranson used at admission (leukocyte count >16.000/mL; glucose >200 mg/dL; age >55 years; LDH >350 IU/mL; aspartate aminotransferase >250 IU/mL) and Balthazar scores were evaluated in terms of the clinical status, laboratory parameters, and radiological findings of pregnant patients at the time of diagnosis. Revised Atlanta classifications were used for severity categorization. Mild pancreatitis was defined as the absence of organ failure complications. Moderate pancreatitis was defined as the presence of local complications with or without transient organ failure (<48 h), and severe pancreatitis was defined as persistent organ failure (>48 h).<sup>[5]</sup>

## Statistical Analysis

Statistical analyses were performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL). Continuous data were expressed as mean ( $\pm$ SD). Number of patients and percentages in brackets were used for categorical data.

## Results

### Patient Demographics

Among a total of 45.654 births from September 2010 to April 2017, 68 patients were recorded to have acute pancreatitis due to biliary gallstones. The average patient age

was  $26.72\pm 7.25$  (18–35) years, and none of the patients had a pancreatitis episode before pregnancy (Table 1). Pancreatitis symptoms developed in most (n=38) (55.8%) patients during the third trimester. Of all, 24 (35.3%) patients were in first trimester, and 6 (8.9%) patients were in second trimester. Of the 24 patients with the first episode of pancreatitis in the first trimester, 12 (50%) were readmitted due to recurrence of pancreatitis. Other trimester groups did not experience recurrent pancreatitis (Table 1). The most important finding on physical examination was upper and right abdominal pain, vomiting, and abdominal distension. The mean hospitalization time was  $8.45\pm 6.15$  days.

## Laboratory and Radiological Findings

Laboratory and radiological findings were used for diagnosis of acute pancreatitis in all the patients (Table 2). The mean serum amylase level at diagnosis was  $608.43\pm 380.32$  IU/L (normal range: 0–100 IU/L). Leukocyte count increased in all the patients, with a mean of  $14.24\pm 3.15\times 10^9/L$  and a

**Table 1.** Severity of disease, treatment, and follow-up of pregnant patients with acute pancreatitis

Parameters	Patients n (%)
Acute pancreatitis (initial)	
Before pregnancy	— (0)
1 <sup>st</sup> trimester	24 (35.3)
2 <sup>nd</sup> trimester	6 (8.9)
3 <sup>rd</sup> trimester	38 (55.8)
Re-admission*	12 (17.6)
Ranson scale	
1	50 (73.5)
2	11 (16.2)
3	7 (11.3)
4	—
5	—
Revised atlanta classification	
Mild	61 (89.7)
Moderate	7 (11.3)
Severe	—
Accompanying Acute Cholecystitis	5 (7.3)
ERCP(Sphincterotomy)	2 (2.9)
Cholecystectomy during pregnancy	9 (13.2)
Laparoscopic	7 (10.2)
Open	2 (3)
Cholecystectomy after pregnancy	59 (86.8)
Mean hospital stay (days)	$8.45\pm 6.15$
Required ICU	—
Preterm fetal morbidity/mortality	—

ERCP: endoscopic retrograde cholangiopancreatography; ICU: intensive care unit. \*All patients who were readmitted for pancreatitis episode after the first trimester of pregnancy.

neutrophil percentage of  $81.17 \pm 5.12\%$ . The Ranson scale was used at admission to classify acute pancreatitis. Of all the patients, 61 (89.7%) had Ranson scores 1 and 2 and 7 (11.3%) had Ranson score 3. Radiologic tools were used for the diagnosis and additional requirements. Ultrasonography (US) is the first preferred imaging method in all patients. Magnetic resonance cholangiopancreatography (MRCP) and computed tomography (CT) are used to determine the severity of the disease in complicated cases. Peripancreatic area, gall bladder, and intra- and extra-hepatic bile ducts were evaluated using US. Seven (11.3%) patients whose Ranson score was 3 underwent CT evaluation for differential diagnosis. These patients were in the third trimester of pregnancy, and patients with moderate acute pancreatitis according to revised Atlanta classification. No severe pancreatitis was seen in all periods. Baltazar grade C was reported in 6 patients and grade D (pancreatic collection) in 1 patient. These data are shown in Table 3. The number of patients having acute cholecystitis with pancreatitis was 5 (7.3%), while the number of patients with choledocholithiasis was 4 (5.8%). Choledocholithiasis was detected using MRCP due to high levels of cholestasis enzyme with hyperbilirubinemia; sphincterotomy was performed with endoscopic retrograde cholangiopancreatography (ERCP) in 2 (2.9%) patients without any complications.

**Table 2.** Initial laboratory parameters of patients according to Ranson scale and other disease-related values

Parameters	Results	Normal Range
Leucocytes (mm <sup>3</sup> )	14.24±3.15	3.7–9.5×10 <sup>3</sup>
LDH (IU/L)	282.23±150.45	105-333
AST (IU/L)	34.21±30.32	10–40
Glucose(mg/dl)	83.45±22.4	70–100
Amylase (IU/L) blood	608.43±380.32	30–118
Lipase (U/L)	548.34±302.21	0–51
Total bilirubin (mg/dL)	2.1±1.3	0.3-1.9
Direct bilirubin (mg/dL)	0.8±0.5	0-0.3

AST: aspartate aminotransferase; LHD: lactate dehydrogenase.

**Table 3.** Radiological examinations used for the diagnosis of acute pancreatitis

Radiological Imaging	Patients n (%)
US	68 (100)
CT	
Balthazar grade C	6 (8.8)
Balthazar grade D	1 (2.5)
MRCP	4 (5.8)

US: ultrasonography; CT: computed tomography; MRCP: magnetic resonance cholangiography.

## Treatment, Follow-up, and Timing of Cholecystectomy

Conservative treatment was initiated for all pancreatitis patients and included pain control, spasmolysis, and fluid resuscitation. After initial treatment in patients with mild pancreatitis, enteral nutrition was initiated to avoid complications associated with parenteral therapy. Symptoms were improved in 58 (85.2%) patients within 48 h of initiation of enteral nutrition. No antibiotics were given to patients with mild pancreatitis and no evidence of infection. Antibiotics (cephalosporin) were given to patients with moderate pancreatitis with resistance choledocholithiasis or patients who required interventional (ERCP, sphincterotomy) or surgical procedures. Fetal movement, heart rate, and uterine contractions were closely followed. Serious complications such as cholangitis, infected necrosis, sepsis, and preterm labor were not detected in any patients.

Laparoscopic cholecystectomy was performed in 9 (13.2%) patients (5 patients in third and 4 in second trimester); there was conversion to open cholecystectomy in 2 patients due to adhesions of cholecystitis (Table 1). No postoperative complications were observed in patients who underwent surgery, and none of the patients was admitted to intensive care unit. Fifty-nine patients underwent cholecystectomy in the postpartum period, and all surgical procedures were laparoscopically completed. No fetal and maternal morbidity and mortality was observed in all periods. Sixty-two (80%) pregnant women had normal deliveries and 6 underwent cesarean delivery at term.

## Discussion

Acute pancreatitis in pregnancy is not an uncommon problem. The incidence of acute pancreatitis in general population is 6 in 10,000.<sup>[6]</sup> However, among pregnant females, the incidence changes and is approximately 0.2–1 in 10,000 pregnant females.<sup>[7, 8]</sup> Its etiology commonly includes gallstone disease, alcoholism, and hypertriglyceridemia, with bile stones accounting for up to 70% of cases.<sup>[9, 10]</sup> In our study, we found 68 patients with gallstone-induced acute pancreatitis among the hospital records of 45,654 pregnant patients. Several mechanisms are involved in the pathogenesis of acute pancreatitis; in the last trimester, cholesterol secretion exceeds the levels of bile acids, leading to the formation of cholesterol crystals and calcification.<sup>[11]</sup> Along with this, progesterone causes relaxation of the gallbladder smooth muscles, increasing biliary stasis and gallstone formation. Although diseases related to biliary stones are common among the population in Turkey, cholecystectomy is performed in the last treatment of symptomatic patients regardless of their pathogenesis. However, the tim-

ing of diagnosis, follow-up, and cholecystectomy can be different at different clinics. In addition to the diagnosis of pancreatitis, the management of the disease can become complicated if the patient is pregnant.

The diagnostic criteria of acute pancreatitis are the same in non-pregnant and pregnant patients and include clinical symptoms (epigastric pain and vomiting), increased lipase and amylase levels, and imaging methods. Imaging through abdominal US confers no risk of radiation to the fetus and can identify gallstones in patients with gallstone pancreatitis. We started with US as the first diagnostic tool in our clinical practice. On the other hand, CT, MRCP, and ERCP should be used with caution.<sup>[12]</sup> CT is used to determine the severity of the disease in complicated cases. We prefer CT depending on the clinical grade of the patient. In 7 (11.3%) patients with Ranson score 3, which indicates a complicated disease, we used CT. No fetal complication related to the use of CT was seen in the postpartum period. MRCP has 92% sensitivity, and it does not expose the mother and fetus to radiation.<sup>[13]</sup> In 4 (5.8%) patients, imaging was performed using MRCP due to resistant cholestasis enzyme elevation and hyperbilirubinemia. ERCP is indicated in patients with severe biliary pancreatitis with cholangitis and/or with evidence of common bile duct obstruction and is a safe procedure for pregnant women.<sup>[14]</sup> In our study population, sphincterotomy was performed with ERCP in 2 (2.9%) patients without any complications. Another alternative imaging modality is endoscopic ultrasound that has a high sensitivity for both choledoch lesions and surrounding tissues and involves no radiation risk and is sensitive for diagnosis.<sup>[13]</sup> However, it can only be performed by experienced physicians at advanced centers, and it is difficult to make this tool available at all centers.

Ranson scale and revised Atlanta scoring are the commonly used scales in acute pancreatitis patients for predicting morbidity and mortality risk and guiding clinicians how to manage the patients.<sup>[15]</sup> Mild acute pancreatitis (without local complications and organ failure) is the most common form treated conservatively. However, severe acute pancreatitis requires complex management and intensive care due to high maternal and fetal morbidity. In our study, 61 (89.7%) patients had Ranson scores 1 and 2 and 7 (11.3%) patients had Ranson score 3; severe pancreatitis was not observed in any of the groups. Presumably, due to our hospital being a gynecological referral center, rapid and intense multidisciplinary networking with emergency, gynecology, and radiology departments, leading to an early diagnosis and treatment of acute pancreatitis in pregnant patients, prevented the seriousness of the cases. One of the controversies in acute pancreatitis treatment is use of antibiotics. Guidelines do not recommend the use of prophylactic anti-

biotics in patients with pancreatitis, and there is no role for antibiotics in its mild form. Additionally, prophylactic use of antibiotics in acute pancreatitis is controversial. Some studies have recommended the use of prophylactic antibiotics in severe acute pancreatitis, whereas some have reported no benefits with their use.<sup>[16, 17]</sup> In our study, antibiotics were not used in patients with mild pancreatitis. However, antibiotics were used in patients with complicated pancreatitis, accompanying cholecystitis, and sphincterotomy with ERCP and those requiring surgical intervention.

The timing of cholecystectomy in pregnant patients with acute biliary pancreatitis remains controversial. Indications for surgery in such cases are severe symptoms, obstructive jaundice, acute cholecystitis resistance to medical treatment, and peritonitis.<sup>[18]</sup> Laparoscopy has been accepted as a safe method for both mother and fetus in the second trimester. However, with recent developments in surgery, it has been shown that laparoscopic surgery can be performed safely in all the trimesters of pregnancy.<sup>[19]</sup> Notably, the recurrence risk of pancreatitis due to gallstones in pregnancy is significant in our study. In our study, patients in the first trimester had a recurrence rate of 50% for pancreatitis. This increases hospital costs and reduces the quality of life of patients. In this case, especially considering this situation, the cholecystectomy procedure can be recommended at any stage of the pregnancy. Additionally, it is important to highlight that preferably a laparoscopy should have been performed rather than a laparotomy.

## Conclusion

In conclusion, acute pancreatitis in pregnancy can have a lethal effect up to 20% on both the mother and the fetus. However, recently this risk has been decreasing due to better supportive care of patients with pancreatitis, with improvements in antenatal care and wide-spread use of US, MRCP, EUS, and ERCP as well as laparoscopy. Furthermore, a multidisciplinary approach at advanced centers has definitely contributed to better maternal and fetal outcomes. According to our results showing no fetal and maternal morbidity and mortality, we recommend treatment and follow-up of such patients with a multidisciplinary approach especially at centers where general surgery (with experienced endoscopist), gynecology, intensive care unit, and radiology departments work in coordination.

## Disclosures

**Ethics Committee Approval:** All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and in compliance with the 1964 Helsinki declaration

and its later amendments or comparable ethical standards.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

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