

Management of Gallstone Induced Acute Pancreatitis in Pregnancy: a Tertiary Center Experience

Inanc Samil Sarici¹, Mustafa Uygur Kalayci¹

ABSTRACT:

Management of gallstone induced acute pancreatitis in pregnancy: a tertiary center experience

Objective: Acute pancreatitis due to gallbladder stones is the most frequent etiology in pregnancy period and often diagnosed in third trimester. Disease have a morbidity and mortality on both mother and infant, and treatment is still controversial.

Methods: Data was analysed from September 2010 to April 2017 in Kanuni Sultan Süleyman training and research hospital, etiology (gallstone pancreatitis), trimester of pregnancy, diagnostic tools, pancreatitis stage, clinical status, medical treatment, surgical interventions and pregnancy status.

Results: 68 patients were recorded with acute pancreatitis due to biliary gallstones. Pancreatitis symptoms occurred mostly (n=38) (55.8%) during the third trimester. 12 (50%) of patients readmitted with recurrence pancreatitis who had first episode in the first trimester of pregnancy. Seven (11.3%) patients whom Ranson scale was 3 underwent CT evaluation. Acute cholecystitis cases with pancreatitis was 5 (7.3%) while the number of cases with choledocholithiasis was 4 (5.8%). Sphincterotomy was performed with ERCP in 2 (2.9%) cases. Laparoscopic cholecystectomy performed in 9 (13.2%) patients during the pregnancy. No fetal and maternal morbidity and mortality was shown in all periods.

Conclusion: Developments in supportive care, wide spread use of imaging methods and multidisciplinary approach with better antenatal care of acute pancreatitis in pregnancy can be controlled without any fetal and maternal morbidity and mortality. Early laparoscopic cholecystectomy in pregnancy should be considered especially in cases with acute pancreatitis due to gallstones in the first trimester.

Keywords: Acute pancreatitis, laparoscopic cholecystectomy, pregnancy

ÖZET:

Gebelikte safra taşı nedenli akut pankreatit yönetimi: Üçüncü basamak merkez deneyimi

Amaç: Gebelik döneminde akut pankreatit etyolojisi en sık safra kesesi taşlarına bağlı olmaktadır ve hastalık sıklıkla gebeliğin üçüncü trimesterinde görülmektedir. Gebelikte pankreatit hem anne hem de fetüs için morbidite ve mortaliteyi arttırmakla birlikte teşhis ve tedavi günümüzde halen tartışmalıdır.

Yöntemler: Eylül 2010-Nisan 2017 tarihleri arasında Kanuni Sultan Süleyman eğitim ve araştırma hastanesi'nde, safra kesesi taşlarına bağlı pankreatit geçiren gebe hastaların teşhis anındaki trimester dönemleri, tanı yöntemleri, pankreatitin şiddeti, klinik takipleri, girişimsel işlem ve cerrahi sonuçları ve hamilelik durumu dahil olmak üzere retrospektif olarak analiz edildi.

Bulgular: 68 gebe hasta da safra taşlarına bağlı pankreatit saptandı. İlk pankreatit semptomları çoğunlukla (n=38) (%55.8) üçüncü trimester de tespit edildi. Gebeliğin ilk trimesterinde ilk atağı saptanan hastaların 12 'sinde (%50) gebelik dönemi içerisinde rekürren pankreatit tespit edildi. Orta derecede pankreatit tespit edilen ve Ranson 3 olan 7 (%11.3) hastada BT değerlendirmesi de yapıldı. 5 (%7.3) hastada pankreatitle birlikte akut kolesistit teşhisi, 4 (%5.8) hastada da koledokolitiazis teşhisi de konuldu. ERCP ile sfinkterotomi 2 (%2.9) olguda yapıldı. 9 (%13.2) hastada gebelik sırasında laparoskopik kolesistektomi yapıldı. Fetal ve maternal morbidite ve mortalite görülmedi.

Sonuç: Multidisipliner yaklaşım, görüntüleme yöntemlerinin etkin kullanımı ve gebelik dönemindeki takiplerin düzenli yapılması akut pankreatit teşhisinde hem fetal ve hem de maternal morbidite ve mortaliteyi ciddi oranda azaltır. Özellikle birinci trimesterdeki safra taşı nedeniyle akut pankreatit teşhisi konulan hastalarda rekürren pankreatit gelişimini engellemek için erken dönemde laparoskopik kolesistektomi önerilebilir.

Anahtar kelimeler: Akut pankreatit, laparoskopik kolesistektomi, gebelik

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¹Kanuni Sultan Süleyman Training and Research Hospital, Department of General Surgery, Istanbul - Turkey

Address reprint requests to / Yazışma Adresi: Inanc Samil Sarici, Kanuni Sultan Süleyman Training and Research Hospital, Department of General Surgery, Istanbul - Turkey

E-mail / E-posta: issarici2015@gmail.com

Phone / Telefon: +90-553-227-1140

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INTRODUCTION

Acute pancreatitis in pregnancy is relatively common problem. The incidence is almost 1/1000–10.000 pregnancies (1,2). It can be caused by gallstones, idiopathic hyperlipidaemia, alcohol abuse and, less commonly, hyperparathyroidism, trauma, and medications (1-3). Gallbladder stones are the most frequent etiology and often diagnosed in third trimester (1-3).

Acute pancreatitis is classified as mild, moderate, and severe form. Mild and moderate form is the most common presentation and guidelines recommended cholecystectomy during the same admission in non-pregnant condition for gallstone induced pancreatitis (4). However, for patients who develop severe acute biliary pancreatitis, especially with necrotising pancreatitis, a complex decision must be made regarding the timing of cholecystectomy and this process is prolonged. On the other hand, management of gallstone pancreatitis in pregnancy is controversial and it should be considered more carefully than the non-pregnant condition due to be fatal effect with varying severity of pancreatitis on both mother and the fetus.

In order to explain how clinicians can easily understand and manage this rarely condition we aimed to identify epidemiology, diagnosis, treatment and outcomes with maternal and fetal morbidity and mortality in high-volume referral hospital with the highest number of obstetric surgery in our country.

METHODS

Retrospective data of the patients was analysed from September 2010 to April 2017 with using hospital database in terms of 'pregnancy' and 'pancreatitis' with higher amylase, lipase levels and ultrasonography findings. Patients with pancreatitis according to idiopathic hyperlipidaemia, alcohol abuse, hyperparathyroidism, trauma, and medications excluded from the study. Data was analysed including, etiology(gallstone pancreatitis), trimester of pregnancy, diagnostic tools, pancreatitis stage, clinical status, medical treatment, surgical interventions and pregnancy status. Ranson used at

admission (leukocyte >16 000/mL; glucose >200 mg/dL; age >55; LDH >350IU/mL; AST >250 IU/mL), and Balthazar scores were evaluated in terms of patients clinical status, laboratory levels and radiological findings carried out on pregnant patients at the time of diagnosis. Revised Atlanta classifications used for severity categorisation. Mild pancreatitis defined as absence of organ failure complications. Moderate pancreatitis defined, local complications with or without transient organ failure(<48 hour) and severe pancreatitis , persistent organ failure (>48 hour) (5).

Statistical Analyses

Statistical analyses were performed using SPSS15.0 for Windows (SPSS Inc.,Chicago,IL). Continuous data were expressed as mean (\pm SD). Number of patients and percentages in brackets used for categorical data.

RESULTS

Patients Demographic

Total of 45.654 births from September 2010 to April 2017, 68 patients were recorded with acute pancreatitis due to biliary gallstones. Average age was 26.72 ± 7.25 (18-35) and none of patients had pancreatitis episode before pregnancy (Table-1). Pancreatitis symptoms occurred mostly (n=38) (55.8%) during the third trimester. 24 (35.3%) patients were in first trimester and 6 (8.9%) patients in second trimester. 12 (50%) of patients readmitted with recurrence pancreatitis who had first episode in the first trimester of pregnancy. Other trimester groups did not have recurrent pancreatitis (Table-1). The most important finding in the physical examination was upper and right abdominal pain, vomiting and abdominal distension. Mean hospitalization time is 8.45 ± 6.15 days.

Laboratory and Radiological findings

Laboratory and radiological findings was used for diagnosis of acute pancreatitis in all patients (Table-2).

Table-1: Severity of disease, treatment and follow-up of acute pancreatitis pregnant patients

Parameters	Patients n (%)
Acute pancreatitis (initial)	
Before pregnancy	None (0)
1. trimester	24 (35.3)
2. trimester	6 (8.9)
3. trimester	38 (55.8)
Re-admission*	12 (17.6)
Ranson scale	
1	50 (73.5)
2	11 (16.2)
3	7 (11.3)
4	None
5	None
Revised Atlanta Classification	
Mild	61 (89.7)
Moderate	7 (11.3)
Severe	None
Accompanying	5 (7.3)
Acute Cholecystitis	
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	8.45±6.15 days
Required ICU	None
Preterm fetal morbidity/mortality	None

ERCP: Endoscopic retrograde colangiopancreatography, ICU: Intensive care unit
 *All patients who had readmitted for pancreatitis episode in the first trimester of pregnancy

The mean serum amylase at diagnosis was 608.43±380.32 IU/l (normal range: 0-100 IU/l). Leukocyte levels increase in all patients with a mean number of 14.24±3.15×10⁹/L and a percentage of neutrophil percentage 81.17±5.12%. The Ranson scale was used at admission to classify the acute pancreatitis. 61 (89.7%) patients were Ranson 1 and 2 and 7 (11.3%) patients were Ranson 3. Radiologic

tools used for the diagnosis and additional requirements. Ultrasonography is the first preferred imaging method in all patients. MRCP and CT used to determine the severity of the disease in complicated situations. Peripancreatic area, gall bladder, and intra- extra hepatic bile ducts were evaluated with US. Seven (11.3%) patients whom Ranson scale was 3 underwent CT evaluation for exclude differential diagnoses. This cases were in the third trimester of pregnancy, and patients with the 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 one patient. These data are shown in Table-3. Acute cholecystitis cases with pancreatitis was 5 (7.3%) while the number of cases with choledocholithiasis was 4 (5.8%). Choledocholithiasis was detected by MRCP due to high levels of cholestasis enzyme with hyperbilirubinemia and sphincterotomy was performed with ERCP in 2 (2.9%) cases without any complications.

Treatment, Follow-up and Timing of Cholecystectomy

Conservative treatment started all pancreatitis patients includes pain control, spasmolysis, fluid resuscitation. After initial treatment in mild pancreatitis enteral nutrition started due to avoids complications associated with parental therapy. Symptoms were improved in 58 (85.2%) patients within 48 hours after treatment with enteral nutrition. Patients with mild pancreatitis and no evidence of infection no antibiotics were given. Antibiotics (cephalosporin) were given to patients with moderate

Table-2: Initial laboratory parameters of patients according to ranson scale and other disease-related values

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

AST: aspartate aminotranferase, 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

pancreatitis with resistance choledocholithiasis or patients who required interventional (ERCP, sphincterotomy) or surgical procedures. Fetal movements, heart rates and uterine contractions were closely followed. Serious complications as cholangitis, infected necrosis, sepsis and preterm labor were not detected in any patients. Laparoscopic cholecystectomy performed in 9 (13.2%) patients (5 patients in third and 4 patients in second trimester) diversion to open cholecystectomy in two patient due to adhesions of cholecystitis (Table-1). No postoperative complications occurred who underwent surgery and none of the patient required intensive care unit. Fifty nine patient underwent cholecystectomy in the postpartum period and all surgical procedure completed laparoscopically. No fetal and maternal morbidity and mortality was shown in all periods. Sixty two (80%) of pregnant women had normal deliveries and 6 patients required cesarean at the end of their pregnancy.

DISCUSSION

Acute pancreatitis in pregnancy is not an uncommon problem. The incidence of acute pancreatitis in general population 6 in 10000 (6). However in pregnancy, it changes and is approximately 0.2 to 1 in 10,000 pregnant (7,8). Etiology is commonly associated with gallstone disease, alcoholism and hypertriglyceridemia and bile stones bring up to 70% of cases (9,10). In our study according to our medical records we found 68 patients with acute pancreatitis due to gallstones in 45654 pregnancy. Many causes are involved in pathogenesis; especially in the last trimester with increasing cholesterol secretion more than bile acids that leads to formation of cholesterol crystals and

calcification (11). Along with this, progesterone causes relaxation of the gallbladder's smooth muscle, increasing biliary stasis and gallstone formation. Although diseases related to biliary stones are common in the population in Turkey, cholecystectomy is performed in the last treatment of symptomatic patients regardless of their pathogenesis. However, especially the timing of diagnosis, follow-up and cholecystectomy can be different in different clinics. In addition to the diagnosis of pancreatitis, the management of the disease can also become a complex step if the patient is pregnant.

Diagnosis of acute pancreatitis included the same criteria as well as pregnancy by clinical presentation (epigastric pain and vomiting), increasing lipase or amylase values and imaging methods. Imaging through abdominal US confers no risk of radiation to the fetus and can identify gallstones in cases of 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 (12). CT used to determine the severity of the disease in complicated situations. We preferred CT according to the clinical grade of the patient. Ranson 3 with thought of complicated disease in 7 (11.3%) patients we used CT. No fetal problem related to the use of CT was seen postpartum period. MRCP which has 92% sensitivity without exposing radiation to the mother and fetus (13). 4 (5.8%) patient imaging with MRCP due to resistant cholestasis enzyme elevation and hyperbilirubinemia. ERCP is indicated in severe biliary pancreatitis with cholangitis and/or with evidence of common bile duct obstruction and also safe procedure for pregnant women (14). In our data, sphincterotomy was performed with ERCP in 2 (2.9%) cases without any complications.

Another alternative imaging is endoscopic ultrasound has higher sensitivity in both choledoch lesions and determining surrounding tissues and involves no radiation risk and is sensitive for diagnosis (13). However, it can be performed with experienced physicians in experienced centers it is difficult to reach this tool in all centers.

Ranson scale and revised Atlanta scoring which are often used scales in acute pancreatitis to predict morbidity and mortality risk and guide to clinicians

how to manage with the patients (15). Mild acute pancreatitis (without local complications and organ failure), which is the most common form treated with conservatively. However, severe acute pancreatitis required complex management with high maternal and fetal morbidity required intensive care. In our study 61 (89.7%) patients were Ranson 1 and 2 and 7 (11.3%) patients were Ranson 3 and no severe pancreatitis was seen in groups. According to our results due to be a gynecological referral center, rapid and intense multidisciplinary networks with emergency department, gynecology and radiology as a result of early diagnosis and treatment of acute pancreatitis in pregnant prevented the seriousness of the cases. One of the controversial in acute pancreatitis is using antibiotics. Guidelines do not recommend use of prophylactic antibiotics in pancreatitis and there is no role for antibiotics in mild form. Additionally, prophylactic use of antibiotics in acute pancreatitis is controversial. However, in severe acute pancreatitis some studies in the literature recommended prophylactic antibiotics but some studies have shown that there is no benefit (16,17). In our study, we did not use antibiotics in mild pancreatitis. However, we used antibiotics in patients with complicated pancreatitis, accompanying cholecystitis, sphincterotomy with ERCP, and required surgical intervention.

The timing of cholecystectomy in acute biliary pancreatitis during pregnancy remains controversial. Indications for surgery in pregnancy are severe symptoms, obstructive jaundice, acute cholecystitis resistance to medical treatment, and peritonitis (18). It is generally accepted that laparoscopy is safe 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 periods of pregnancy (19). It is important to note that the recurrence risk of pancreatitis due to gallstones in pregnancies is significant in our study. According to the results of our study, patients in the first trimester had a recurrence rate of 50% during the onset of pregnancy. 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 decreasing for patients due to better supportive care of pancreatitis with improvements in antenatal care and wide spread use of US, MRCP, EUS and ERCP as well as laparoscopy with multidisciplinary approach in experienced centers have definitely contributed to better maternal and fetal outcomes. According to our results with no fetal and maternal morbidity and mortality, our opinion is that follow-up and treatment of these patients with a multidisciplinary scale especially in centers where general surgery (experienced endoscopist), gynecology, intensive care unit and radiology departments work in coordination.

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ISS and MUK: Project development, Data Collection, Manuscript writing

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