ORIGINAL ARTICLE

Management of acute cholecystitis during pregnancy: A single center experience

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ABSTRACT

BACKGROUND: The aim of the present study is to evaluate the results of two different approach; immediate surgery or delayed surgery following conservative management; in the management of acute cholecystitis during pregnancy.

METHODS: Twenty-pregnant women who were treated in our clinic for acute cholecystitis between 2010-2018 were included in the analysis for the study. Demographic characteristics, parameters related with acute cholecystitis (gall bladder wall thickness, laboratory data), duration of hospitalization, readmission rates and preterm labor rate were evaluated retrospectively.

RESULTS: Median age was 29.5 years (21-46y). Median gestational week was 20 (6-32w) weeks. Laparoscopic cholecystectomy was performed in 6 (30%) patients on admittance. Patients who received immediate surgery had higher gallbladder wall thickness, WBC count, CRP, ALT, AST, ALP, GGT levels when compared to the conservative management group ($p<0.05$). Furthermore, readmission rate and duration of hospitalization were lower in the patients who underwent immediate surgery ($p<0.05$). The preterm labor rate in conservative management and immediate surgery groups were 28.5% and 0% respectively ($p>0.05$).

CONCLUSION: In the present study the outcome of early surgery was better than conservative management even though these patients had thicker gall bladder wall and higher inflammatory markers suggesting severe inflammation. Although the characteristics of the conservative management group was more favorable complication rate seems high.

Keywords: Acute cholecystitis; choledocholithiasis; cholelithiasis; pregnancy.

INTRODUCTION

Gallstones can be detected in 1-3% of the pregnancies and the incidence of symptomatic biliary disease during this period ranges from 0.05 to 8%.[1,2] Gallstone formation in pregnancy is thought to be due to estrogen and progesterone mediated supersaturation of bile with cholesterol.[3] The most common cause of non-obstetric abdominal surgical pain during pregnancy is acute appendicitis and the second is acute cholecystitis.[4] Historical data related to biliary surgery during pregnancy describe a high fetal and maternal complication rate.[5] For this reason, traditionally a conservative approach has been advocated and surgical intervention was only used in the most severe cases or when conservative treatment failed.[6] However conservative treatment is not without risk for fetus and mother. Despite medical treatment there is a need for surgery in 27–36% of patients with symptomatic biliary disease. Another factor to consider is that the risk for recurrence of symptoms and readmission rate is reported to be between 38 and 69%.[7] Contrary to traditional medical treatment, more recent reports emphasize the safety of early laparoscopic cholecystectomy for symptomatic benign biliary diseases in pregnancy.[8] The aim of the present study is to evaluate the efficacy of laparoscopic surgery in different stages of pregnancies in gravid patients that were admitted with acute cholecystitis.

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MATERIALS AND METHODS

Allocation of The Patients and Definition of The Study Parameters

The study includes 20 pregnant patients with acute cholecystitis who were followed-up and treated at XXX University, Department of General Surgery between January 2010 and April 2018. We retrospectively evaluated the demographic data, gestational age, number of pregnancies, maternal and fetal complications, symptoms, physical examination, laboratory and radiological findings, diagnosis, treatment, number of hospital admissions and hospital length of stay of these patients.

The patients who received cholecystectomy in the index admission were grouped into Group A (Immediate Surgery Group; n=6). The patients who did not give consent for surgery and were conservatively managed and surgical therapy was performed in the postpartum period were grouped into Group B (Conservative Management and Delayed Surgery Group; n=14).

Demographic data included the patient age, gestational week, the trimester of the pregnancy and the number of gestations of the patient. Perioperative and intraoperative parameters included the mode of access to the abdomen, application of perioperative endoscopic retrograde choangiopancreaticoductography (ERCP).

Duration of hospitalization was defined as time starting from the admission till the discharge of the patient following surgery in Group A. In Group B, the duration of hospitalization was defined as the sum of index admission plus all the readmissions including the postpartum surgical therapy session.

Statistical Analysis

The sample size was limited and for this reason, continuous data were expressed as median (range [min-max]). Discrete variables are expressed as patient number and percentage of the study population. Mann-Whitney U test was used to test the relationship between dependent and independent variables and a p value less than 0.05 was considered as statistically significant. All the statistical analysis were performed on Statistical Program for Social Sciences software version 20 (SPSS v.20, IBM, USA).

RESULTS

The Demographic Characteristics of The Patients

In total, 20 pregnant women who had complicated gallstone disease such as acute cholecystitis, choledocholithiasis and cholangitis were included in the study. The demographic data of the patients according to the treatment groups are summarized in Table 1. Median age of the patients was 29.5 (21-46) years. Mean gestational week at the time of diagnosis was 20 (6-32) weeks and The distribution of the patients according to the trimester of pregnancy and the treatment groups is summarized in Table 1. Median number of pregnancies of the patients were 2 (1-4). All the demographic parameters of the patients were comparable except the number of pregnancies. The number of pregnancies in Group A was slightly (although significant) higher than Group B [3 (2-4) versus 2 (1-4); p=0.041].

Intraoperative and Perioperative Characteristics of The Patients

The Eighteen (90%) of 20 patients were diagnosed with acute cholecystitis and two (10%) with acute cholecystitis and choledocholithiasis. All diagnoses were made with a combination of medical history, physical examination, laboratory tests and imaging techniques such as ultrasonography (USG) and magnetic resonance cholangiopancreatography (MRCP). USG was performed in all patients for diagnosis. In 2 (10%) patients MRCP was performed for diagnosis of choledocholithiasis. detected with elevated serum amylase and lipase levels and ultrasonographic signs of pancreatic inflammation. Eighteen patients had right upper quadrant pain, nausea and vomiting. Two patients with acute cholecystitis and choledocholithiasis had cholangitis symptoms. Endoscopic retrograde cholangiopancreatography (ERCP) was performed in these two patients. In one patient, biliary stone extraction and stent placement was performed and in the other one only biliary stone extraction was performed. Murphy's sign was positive in all patients. Laparoscopic cholecystectomy was performed in 6 (30%) patients during pregnancy. Four patients were at the second trimester and two were at the third trimester in this group. In two patients who had choledocholithiasis and acute cholecystitis, laparoscopic cholecystectomy was performed after ERCP application. An open laparoscopic approach with the Hasson trocar rather than the Veress needle was utilized in each case. Pneumoperitoneum at 10–12 mmHg was used in laparoscopic procedures. Fourteen (70%) patients were treated medically. One patient did not continue follow-up after medical treatment. Medical treatment included cessation of oral intake, intravenous fluid replacement, intravenous antibiotic and analgesic therapy. For five (25%) patients (all of them were at the second trimester of pregnancy), operation was recommended but none of them accepted it. In 11 (84.6%) of 13 patients (one patient did not continue follow-up) who were treated medically, acute cholecystitis developed again in antepartum (n:8) or postpartum (n:3) period. Eight patients that developed acute cholecystitis in antepartum period were treated medically again.. In 13 patients that treated medically in pregnancy, laparoscopic cholecystectomy was performed in postpartum period. The median duration to postpartum laparoscopic cholecystectomy was 6 (4-6) months in these patients.

Laboratory and Radiologic Characteristics of The Study Groups

The laboratory and radiologic data related with acute chole-

Table 1. Summary of the demographic and laboratory data of the patients in the study

	Immediate surgery (Group A; n=6)	Conservative management and delayed surgery (Group B; n=14)	p*
Age	29.5 (25–33)	29.5 (21–46)	0.96
Gestational week	22 (19–31)	19.5 (6–32)	0.31
1st trimester	0 (0%)	5 (36%)	0.24
2nd trimester	4 (67%)	6 (43%)	
3rd trimester	2(33%)	3 (21%)	
Number of pregnancies	3 (2–4)	2 (1–4)	0.041
Gallbladder wall thickness (mm)	4.65 (4.6–5)	4.5 (4.1–7)	0.009
White blood cells	16.1 (15.4–19)	11.9 (9.6–16.8)	0.026
C-reactive protein	5.55 (4.9–8.6)	2.8 (0.6–4.1)	<0.001
Aspartate aminotransferase	87.5 (65–101)	55.5 (23–99)	0.002
Alanine aminotransferase	94 (77–101)	53.5 (36–87)	<0.001
T. Bilirubin	0.95 (0.6–5)	0.85 (0.4–1)	0.6
Alkaline phosphatase	101 (94–365)	60.5 (24–99)	<0.001
Gamma glutamyl transferase	111.5 (87–467)	62.5 (24–88)	<0.001
Amylase	42 (29–55)	43 (23–52)	0.84
Lipase	31 (21–55)	45 (23–66)	0.11
Readmission rate (%)	- (0%)	11 (78.50%)	0.007
Duration of hospitalization (days)	3 (2–4)	11 (5–13)	<0.001
Preterm labor rate (%)	- (0%)	4 (28.50%)	0.323

*Mann-Whitney U test.

cystitis are summarized in Table 1. The gall bladder wall thickness in Group A and Group B was 4.65 (4.6-5) mm and 4.5 (4.1-7) mm; respectively (p=0.009). The median leukocyte count was higher in Group A ($16.1x10^3$ versus $11.9x10^3$; p=0.026). Median CRP level in Group A was 5.55(4.9-8.6) mg/dl while it was 2.8 (0.6-4.1) mg/dl in Group B (p<0.001). Mean AST levels in group A and B were 87.5 (65-101) and 55.5 (23-99) IU/ml; respectively (p=0.002). Median ALT levels were higher in Group A (94 IU/ml versus 53.5 IU/ml; p<0.001). Median ALP levels in Group A was 101 (94-365) IU/ml where as it was 62.5 (24-99) IU/ml in Group B (p<0.001). Median GGT level was higher in Group A when compared to Group B (111.5 IU/ml versus 62.5IU/ml; p=0.007). Median amylase, lipase and total bilirubin levels did not significantly change among the study groups (Table 1).

Postoperative Follow-up

The postoperative period was analyzed in terms of readmission rates, duration of hospitalization and development of early preterm labor. All data are summarized in Table 1. In 4 (28.5%) of the 14 patients who were treated medically, preterm labor (before 37th week) occurred; fortunately no fetal complication had been observed. On the other hand no fetal complication such as abortion or preterm labor occurred in Group A. The difference in the preterm labor rate was not significant for the sample size was very low (p=0.323).

The readmission rate in group B was significantly higher than in Group A (78.5% versus 0%; p=0.007). Median duration of hospitalization in group A and B were 3 (2-4) days and 11(5-13)days; respectively (p<0.001).

DISCUSSION

The symptomatology of acute cholecystitis is much the same in pregnant and nonpregnant women. Nausea, vomiting, dyspepsia, intolerance of fatty foods, and an acute onset of a colicky or stabbing pain that begins over the mid-epigastrium or right upper abdominal quadrant and radiates to the back are typical. Murphy's sign can be detected less commonly in majority of the pregnant women with acute cholecystitis.[9] In our study, in accordance with the literature all patients had the same symptoms but Murphy's sign was positive in all patients.

Ultrasound is the diagnostic procedure of choice in pregnancy because it is non-invasive, speed, and accuracy of approximately 95–98% in detecting gallstones. If there are classic findings of acute cholecystitis such as, gallbladder calculi, wall thickening (>3 mm), pericholecystic fluid, and the sonographic Murphy's sign (focal tenderness under the ultrasound transducer positioned over the gallbladder) the diagnosis can be detected by USG easily.[10] In this study, USG was used in all patients as a radiological imaging for diagnosis mostly be-

cause the patients were pregnant and also the diagnosis was accurately performed by USG.

Magnetic resonance is an imaging modality that can be relied upon to diagnose different etiologies of abdominal pain in any stage of pregnancy.[11] Contrary to traditional fears, in some recent reports, safety of MRCP in pregnancy was approved.[12,13] Symptomatic common bile duct stones during pregnancy may require ERCP with biliary sphincterotomy, biliary stone extraction, or stent placement for symptom relief as well as prevention of complications. However, ERCP infrequently could be complicated with post-ERCP pancreatitis, hemorrhage or perforation. Although there are limited data available regarding the safety of ERCP in pregnancy, it is being applied safely in recent years.[14] In this study, MRCP and ERCP was performed in two patients for diagnosis and treatment of choledocholithiasis. In these patients biliary sphincterotomy, biliary stone extraction and stent placement was applied by ERCP without any maternal and fetal complications.

Treatment of complicated gallstone disease in pregnancy is still controversial. Traditionally, the management of complicated biliary disease during pregnancy has often been non-surgical to avoid fetal and maternal harm.[15] However, non-operative treatment of complicated gallbladder diseases in pregnancy results high symptom recurrence rates and multiple hospital admissions in antepartum or postpartum period.[16] In their study Dixon et al. reported that, 44 pregnant patients were managed conservatively due to acute cholecystitis and 58% of those had recurrent symptoms. Twenty-seven percent of these women were rehospitalized two or more times during their pregnancy. The average hospital stay for these women was 14 days as opposed to 6 days for the group with surgical intervention.[17] Cosenza et al. published a retrospective study in 1999. In their study, 69 pregnant women were treated medically due to complicated gallbladder diseases but in 32 cases (46%) surgical treatment required because of persistent symptoms and multiple readmission to hospital.[18] Jelin et al. reported an increased risk of fetal death when episodes were managed conservatively compared to women undergoing LC.[19] In the other study, Dhupar R. et al. defined that patients who were treated medically in their pregnancy had higer rates of obstetric complications rates (36%) than cholecystectomy group (18%).[20] Development in surgical, anesthesiologic and obstetrical techniques and strategies has lowered the risks of intervention and it is now considered both safe and feasible with early intervention in all trimesters, with laparoscopic cholecystectomy as the treatment of choice.[21,22] According to Society of American Gastrointestinal Endoscopic Surgeons (SAGES) guidelines laparoscopic cholecystectomy can be performed safely in pregnant patients during any trimester. The argument for the early surgical management of symptomatic biliary disease in pregnancy is further supported by the fact that non-operative management is associated with high rates of symptom recurrence, hospital admission and complicated disease, and thus increased risk of preterm labor, spontaneous abortions and maternal morbidity and mortality. Symptom recurrence rates are as high as 92% when the initial presentation is in the 1st trimester, 64% in the 2nd trimester and 44% in the 3rd trimester.[23] In our study, 11 (84.6%) of 13 patients that treated conservatively admitted hospital for recurrence symptoms in antepartum or postpartum period. Also, in four patients preterm labor occurred. In a study from Australia, Paramanathan A. et al. reported that, they performed laparoscopic cholecystectomy in 22 pregnant patients due to complicated gallstone diseases with no operative mortality or recorded fetal loss for the duration of pregnancy.[24] In our study, laparoscopic cholecystectomy was performed in six patients with no fetal and maternal complications. Similarly, we have found higher readmission and preterm labor rates and longer duration of hospitalization in 14 patients (one was lost to follow-up) that were conservatively managed. Fortunately, no fetal loss was encountered in the present study.

The results of the present study suggest that, the severity of the disease in patients with immediate surgery was more than the patients who received conservative management as shown by the differences in gall bladder wall thickness, liver function and cholestasis tests and furthermore the inflammatory markers were higher in the immediate surgery. However, the duration of hospitalization and preterm labor rate was lowest in this group. Furthermore, although more favorable laboratory and radiologic were present for conservative management group, they experienced longer duration of hospitalizations, higher readmissions and preterm labor rate. This in fact, suggests the safety of laparoscopic cholecystectomy during pregnancy and in all trimesters. One important finding in the present study is that more severe disease was observed in multiparous women (in Group A) when compared to lower number of births observed in Group B. In fact, Basso et al.[25] have found that symptomatic cholelithiasis was more common among multiparous women. Other studies have also suggested the role of parity in development of symptomatic gall stones.[26,27]

As a result, the management of complicated gallstone diseases in pregnancy is a difficult subject because of high fetal and maternal complication rates. Conservative treatment may lead to recurrences, multiple admissions to hospital and fetal complications such as preterm labor, miscarriage. Laparoscopic cholecystectomy can safely be performed in pregnancy with lower fetal and maternal complications rates.

Conflict of interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZET*

Gebe hastalarda akut kolesist tedavisi: Tek merkez deneyimi

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AMAÇ: Gebe hastalarda akut kolesistit tedavisi zordur. Bu çalışmanın amacı merkezimizde akut kolesistit nedeniyle opere edilen gebe hastalarda laparoskopik kolesistektominin etkinliğinin araştırılmasıdır.
GEREÇ VE YÖNTEM: 2010 ve 2018 yılları arasında merkezimizde akut kolesistit nedeniyle tedavi edilen 20 hasta değerlendirmeye alınmıştır. Bu hastalardan sadece bir tanesi merkezimizde takiplerine gelmemiş kalan hastalar çalışmaya dahil edilmiştir. Hastaların demografik özellikleri, akut kolesistit ile ilişkili radyolojik ve laboratuvar parametreleri, hastanede kalış, tekrar başvuru oranları ve erken eylem oranları retrospektif olarak analiz edilmiştir.
BULGULAR: Ortanca yaş 29.5 (21-46) yıldı. Ortanca gebelik haftası 20(6-32) hafta idi. Altı (30%) hastaya indeks yatışta laparoskopik kolesistektomi gerçekleştirildi. Erken kolesistektomi yapılan hastalarda safra kesesi duvar kalınlığı, lökosit sayısı, CRP, ALT, AST, ALP, GGT konzervatif izlenen hastalara göre daha fazla idi ($p<0.05$). Bunun yanında erken cerrahi uygulana grupta tekrar başvuru ve hastanede yatış süresi daha az olarak gözlendi ($p<0.05$). Preterm eylem erken kolesistektomi ve konzervatif izlem grubunda sırasıyla %0 ve %28.5 olarak bulundu ($p>0.05$).
TARTIŞMA: Erken cerrahi uygulanan hastaların karaciğer fonksiyon ve kolestatik testleri daha fazla olmasına ve inflamatuvar belirteçleri daha yüksek olmasına rağmen kolesistektomi güvenle gerçekleştirilmiştir. Konzervatif izlem grubunda daha uzun hastanede yatış ve daha fazla preterm eylem oranı gözlenmiştir. Dolayısı ile gebelerde akut kolesistitte tedavide cerrahi güvenli ve etkindir.
Anahtar sözcükler: Akut kolesistit; gebelik; koledokolitiazis; kolelitiazis.

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