ORIGINAL ARTICLE

Management of acute cholecystitis during pregnancy: A single-center experience

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ABSTRACT

BACKGROUND: This study aimed to present to evaluate the results of two different approaches in the management of acute cholecystitis during pregnancy: immediate surgery and delayed surgery following conservative management.

METHODS: In this study, 20 pregnant women who were treated in our clinic for acute cholecystitis between 2010 and 2018 were included in the analysis. Demographic characteristics, parameters related with acute cholecystitis (gallbladder wall thickness, laboratory data), duration of hospitalization, readmission rates, and preterm labor rate were retrospectively evaluated.

RESULTS: The median age was 29.5 years. The median gestational week was 20 (6–32) weeks. Laparoscopic cholecystectomy was performed in 6 (30%) patients on admittance. When compared with the conservative management group, patients who received immediate surgery had higher gallbladder wall thickness. WBC count, and CRP, ALT, AST, ALP, and GGT levels ($p<0.05$). 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 this study, even though these patients had thicker gallbladder wall and higher inflammatory markers suggesting severe inflammation, the outcome of early surgery was better than conservative management. Although the characteristics of the conservative management group was more favorable, complication rate seemed to be high.

Keywords: Acute cholecystitis; choledocholithiasis; cholelithiasis; pregnancy.

INTRODUCTION

Gallstones can be detected in 1%–3% of the pregnancies; and during this period the incidence of symptomatic biliary disease ranges from 0.05% to 8%.[1,2] Gallstone formation in pregnancy is considered to be caused by estrogen and progesterone mediated supersaturation of bile with cholesterol.[3] During pregnancy, the most common cause of non-obstetric abdominal surgical pain is acute appendicitis, and the second most common is acute cholecystitis.[4] Historical data related to biliary surgery during pregnancy describe a high fetal and maternal complication rate.[5] Therefore, traditionally a conservative approach was advocated, and surgical intervention was only used in the most severe cases or when conservative treatment failed.[6] However, conservative treatment has risks for fetus and mother. Despite medical treatment, surgery is needed in 27%–36% of patients with symptomatic biliary disease. It should be considered 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 on the safety of early laparoscopic cholecystectomy for symptomatic benign biliary diseases in pregnancy.[8] This study aimed to evaluate the efficacy of laparoscopic surgery in different stages of pregnancies in gravid patients who 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 Department of General Surgery, Inonu University 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).

The 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 and application of perioperative endoscopic retrograde choangiopancreatico-ductography (ERCP).

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

Statistical Analysis

The sample size was limited; and hence, continuous data were expressed as median (range [min–max]). Discrete variables are expressed as patient number and percentage of the study population. The 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 with the Statistical Program for the Social Sciences software version 20 (SPSS v.20, IBM, USA).

RESULTS

The Demographic Characteristics of the Patients

In total, 20 pregnant women with 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. The median age of the patients was 29.5 (21–46) years. The mean gestational period 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. The median number of pregnancies of the patients was 2 (1–4). All the demographic parameters, except the number of pregnancies, of the patients were comparable. The number of pregnancies in Group A was slightly (although significant) higher than that in Group B [3 (2–4) versus 2 (1–4); p=0.041].

Intraoperative and Perioperative Characteristics of the Patients

Of 20 patients, 18 (90%) were diagnosed with acute cholecystitis, and 2 (10%) were diagnosed 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). In all patients, USG was performed 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 symptoms of cholangitis. 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. In all patients, Murphy's sign was positive. Laparoscopic cholecystectomy was performed in 6 (30%) patients during pregnancy. In this group, four patients were at the second trimester and two were at the third trimester. 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. Of all the patients, 14 (70%) were medically treated. One patient did not continue follow-up after medical treatment. Medical treatment included cessation of oral intake, intravenous fluid replacement, and intravenous antibiotic and analgesic therapy. Operation was recommended to 5 (25%) patients (all of them were at the second trimester of pregnancy), but none of them accepted it. In 11 of 13 (84.6%) patients (one patient did not continue follow-up) who were medically treated, acute cholecystitis developed again in antepartum (n=8) or postpartum (n=3) period. Eight patients who developed acute cholecystitis in antepartum period were treated medically again. In 13 patients who were treated medically during 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, n (%)	0 (0)	5 (36)	0.24
2nd trimester, n (%)	4 (67)	6 (43)	
3rd trimester, n (%)	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, n (%)	0 (0)	11 (78.50)	0.007
Duration of hospitalization (days)	3 (2–4)	11 (5–13)	<0.001
Preterm labor rate, n (%)	0 (0)	4 (28.50)	0.323

*Mann-Whitney U test.

cystitis are summarized in Table 1. The gallbladder 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 (16.1×103 versus 11.9×103; p=0.026). The 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). The mean AST levels in Groups A and B were 87.5 (65–101) and 55.5 (23–99) IU/ml, respectively (p=0.002). The median ALT levels were higher in Group A (94 IU/ml versus 53.5 IU/ml; p<0.001). The median ALP level in Group A was 101 (94–365) IU/ml where it was 62.5 (24–99) IU/ml in Group B (p<0.001). The median GGT level was higher in Group A when compared with Group B (111.5 IU/ml versus 62.5 IU/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 medically treated, 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; it 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). The median duration of hospitalization in Groups 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 non-pregnant 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, fast, and has 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 easily detected by USG.[10] In this study, USG was used in all patients as a radiological imaging for diagnosis

mostly because the patients were pregnant and 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 safely applied in recent years.[14] In this study, MRCP and ERCP were 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 nonsurgical to avoid fetal and maternal harm.[15] However, nonoperative 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.[17] reported that 44 pregnant patients were conservatively managed because of 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. In 1999, Cosenza et al.[18] published a retrospective study. In their study, 69 pregnant women were medically treated because of complicated gallbladder diseases, but in 32 cases (46%) surgical treatment was required because of persistent symptoms and multiple readmissions to hospital. Jelin et al.[8] reported an increased risk of fetal death when episodes were conservatively managed compared with women undergoing LC. In the other study, Dhupar et al.[19] defined that patients who were medically treated in their pregnancy had higher rates of obstetric complications rates (36%) than the patients in the cholecystectomy group (18%). 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.[20,21] According to Society of American Gastrointestinal Endoscopic Surgeons guidelines, laparoscopic cholecystectomy can be safely performed 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 first trimester, 64% in the second trimester, and 44% in the third trimester.[22] In our study, 11 (84.6%) of 13 patients who were conservatively treated and admitted in the hospital for recurrence symptoms in antepartum or postpartum period. Also, preterm labor occurred in four patients. In a study from Australia, Paramanathan et al.[23] reported that they performed laparoscopic cholecystectomy in 22 pregnant patients because of complicated gallstone diseases with no operative mortality or recorded fetal loss for the duration of pregnancy. 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) who were conservatively managed. Fortunately, no fetal loss was encountered in this study.

The results of this 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 gallbladder 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 this study is that more severe disease was observed in multiparous women (in Group A) when compared with lower number of births observed in Group B. In fact, Basso et al.[24] have found that symptomatic cholelithiasis was more common among multiparous women. Other studies have also suggested the role of parity in development of symptomatic gallstones.[25,26]

Hence, because of high fetal and maternal complication rates, the management of complicated gallstone diseases in pregnancy is a difficult subject. Conservative treatment may lead to recurrences, multiple admissions to hospital, and fetal complications such as preterm labor, miscarriage. Laparoscopic cholecystectomy can be safely 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 ameliyat edilen gebe hastalarda laparoskopik kolesistektominin etkinliğinin araştırılmasıdır.
GEREÇ VE YÖNTEM: 2010 ve 2018 yılları arasında merkezimizde akut kolesistit nedeniyle tedavi edilen 20 hasta değerlendirmeye alındı. Bu hastalardan sadece bir tanesi merkezimizde takiplerine gelmedi, kalan hastalar çalışmaya alındı. Hastaların demografik özellikleri, akut kolesistit ile ilişkili radyolojik ve laboratuvar parametreleri, hastanede kalış, tekrar başvuru oranları ve erken eylem oranları geriye dönük olarak analiz edildi.
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 enflamatuvar 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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