Original Article

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Cholecystectomy in Pregnant Women during Exacerbation of Calculous Cholecystitis

Hasanov Mushviq[1], Sevinç Qarayeva[2], Konul Qarayeva[2], Shamama Behzad[1], Erkut Attar[3]

[1]Azerbaijan Medical University Faculty of General Medicine, Department of General Surgery, Baku, Azerbaijan
[2] Ministry of Health of the Republic of Azerbaijan Research Institute, Department of Obstetrics and Gynecology, Baku, Azerbaijan
[3]Yeditepe University Hospital, Department of Obstetrics and Gynecology, İstanbul, Turkey

ABSTRACT

Purpose: Biliary tract disease is one of the most common non-obstetric surgical conditions during pregnancy, affecting up to 12% of pregnant women. Gallstone formation is driven by hormonal changes; estrogen increases hepatic cholesterol secretion into bile while progesterone reduces gallbladder contractility, creating optimal conditions for stone development. These mechanisms peak in the second trimester, establishing it as the period of highest lithogenic risk.

Methods: This retrospective observational case series from Azerbaijan Medical University included 25 pregnant women with chronic biliary pathology. Twenty-two patients were managed conservatively with dietary modification, antispasmodics, and ademetionine 800 mg/day. Three patients (12%) underwent urgent laparoscopic cholecystectomy for refractory biliary obstruction confirmed on ultrasound. Liver function tests [aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), bilirubin, cholesterol] were monitored serially each trimester.

Results: Exacerbations occurred predominantly in the second trimester (48%) and third trimester (52%). Biochemical markers showed the most pronounced elevations in the second trimester: AST +23%, ALT +24%, ALP +19%, cholesterol +18%, and total bilirubin +68% above trimester-specific reference values. Third trimester showed partial improvement in some markers, although AST and ALP remained elevated. All three surgical patients underwent laparoscopic cholecystectomy with CO_2 pneumoperitoneum at 10-14 mmHg, using modified positioning to minimize uterine compression. Mean operative time was 25 minutes with no conversions to open surgery. Clinical improvement occurred within 48 hours, with discharge by postoperative day 4. No perinatal complications or congenital anomalies were reported.

Conclusion: Findings support current SAGES guidelines recommending laparoscopic cholecystectomy as the preferred surgical approach when indicated during pregnancy. However, the study has significant limitations: small sample size (especially the surgical subgroup of three patients), retrospective design, incomplete parity data, absence of a control group, and lack of formal analysis of ademetionine efficacy. Results should be interpreted as preliminary observational data requiring confirmation in larger prospective studies.

Keywords: Pregnancy, biliary disease, cholelithiasis, liver function tests, laparoscopic cholecystectomy

INTRODUCTION

Biliary tract disease is one of the most common non-obstetric surgical conditions during pregnancy. Gallstone disease is the second most common non-gynecological condition requiring surgical intervention in pregnancy, affecting up to 12% of pregnant women,[1] with increasing incidence among younger women of reproductive age.[2,3]

Three clinical entities must be distinguished: cholelithiasis (presence of calculi within the gallbladder), cholecystitis (gallbladder wall inflammation, most commonly caused by cystic duct obstruction-calculous cholecystitis), and cholestasis of pregnancy (impaired bile flow with elevated serum bile acids and abnormal liver function tests, associated with adverse fetal outcomes.[4,5] These conditions share pathophysiological mechanisms but differ in clinical presentation and management.

Address for Correspondence: Shamama Behzad, MD, Azerbaijan Medical University Faculty of General Medicine, Department of General Surgery, Baku, Azerbaijan
E-mail: shamama.behzad@gmail.com **ORCID ID:** orcid.org/0009-0007-4553-5665
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Gallstone formation during pregnancy is driven by the hormonal changes of gestation. Elevated estrogen promotes hepatic cholesterol secretion into bile, raising its saturation index, while simultaneously impairing gallbladder contractility.[6,7] Progesterone further reduces gallbladder emptying, causing bile stasis and prolonging exposure of bile to lithogenic conditions.[6] As a result, biliary cholesterol saturation increases progressively across trimesters, with the greatest rise observed in the second trimester.[7,8]

When conservative management fails, surgical intervention is indicated. Current SAGES guidelines establish laparoscopic cholecystectomy as the treatment of choice for symptomatic gallbladder disease during pregnancy, regardless of trimester, with CO_2 pneumoperitoneum of 10-15 mmHg considered safe.[9] Anesthetic risk, preterm labor, and gestational age remain important perioperative considerations requiring multidisciplinary coordination.[9]

The present study describes trimester-related clinical and biochemical patterns of biliary pathology in pregnant women and reports outcomes of conservative and surgical management in this cohort.

METHODS

This study was conducted as a retrospective observational case series at the Department of General Surgery and Research Center of Azerbaijan Medical University, in collaboration with the Research Institute of Obstetrics and Gynecology of the Ministry of Health of the Azerbaijan Republic, Baku. The study was conducted in accordance with the Declaration of Helsinki. This study received approval from the of Azerbaijan Medical University Ethics Committee (approval number: 38, date: 17.09.2024). Medical records of pregnant women with chronic biliary system pathology were reviewed. A total of 25 patients were included: 22 were managed conservatively and 3 underwent urgent surgical intervention.

Inclusion criteria were: Gestational age ≥8 weeks, reproductive age (≥18 years), and a documented history of chronic biliary system pathology confirmed prior to pregnancy.

Exclusion criteria were: Gestational age <8 weeks, decompensated systemic organ disease, and chronic liver disease of infectious or autoimmune origin (including Wilson's disease and primary biliary cirrhosis).

Diagnostic criteria were standardized as follows: Biliary pathology was confirmed by clinical presentation (right upper quadrant pain, nausea/vomiting), serial laboratory assessment, and ultrasonographic findings each trimester. Biliary obstruction was defined as ultrasonographic evidence of ductal dilatation with persistent symptoms refractory to conservative management.

Liver function was monitored by serial measurement of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin, and total cholesterol throughout all trimesters. Ultrasonographic examination was performed each trimester to evaluate the gallbladder, liver, and fetal development.

Conservative management included dietary modification, antispasmodic therapy when required, and ademetionine 1,4-butanedisulfonate 800 mg/day orally for two months, administered as part of routine hepatoprotective care. Patients with persistent or recurrent symptoms and ultrasonographic evidence of biliary obstruction despite conservative treatment underwent urgent laparoscopic cholecystectomy under general anesthesia. Patients were positioned in a semi-sitting anti-Trendelenburg position with left lateral tilt to minimize uterine compression. CO_2 pneumoperitoneum was maintained at 10-14 mmHg, consistent with SAGES recommendations.[9] Trocar placement was adapted according to gestational age and uterine size. Fetal well-being was assessed before and after surgery in collaboration with the obstetric team.

All patients were followed throughout the perinatal, intranatal, and postnatal periods. Obstetric outcomes recorded included gestational age at delivery, mode of delivery, and neonatal status.

Statistical Analysis

Statistical analysis was performed using SPSS, version 22 (IBM Inc., Armonk, NY, USA). Quantitative variables were compared between trimesters using the Mann-Whitney U test, with trimester I values serving as the reference group for pairwise comparisons against trimesters II and III. A p value of <0.05 was considered statistically significant.

RESULTS

Twenty-five pregnant women with biliary system pathology were included. Age distribution was: 18-21 years: 3/25 (12%); 22-25 years: 5/25 (20%); 26-30 years: 4/25 (16%); 31-35 years: 8/25 (32%); >35 years: 5/25 (20%). Parity data were available for a subgroup of 15 patients based on detailed clinical history; of these, 11/15 (74%) were in their third pregnancy. In this subgroup, clinical manifestations were reported as more pronounced compared with women in their first pregnancy but this observation should be interpreted with caution, given the incomplete parity data for the full cohort.

Clinical Presentation and Timing of Exacerbations

Thirteen patients (52%) reported prolonged nausea and vomiting. The remaining patients predominantly presented with acute right upper quadrant pain radiating to the right shoulder or scapular region. Exacerbations occurred in the second trimester in 12/25 (48%) and in the third trimester in 13/25 (52%).

Biochemical Findings

Serial liver function assessment demonstrated trimester-related changes (Table 1). At the end of the first trimester, AST, ALT, and cholesterol were moderately elevated above the pregnancy-specific upper limits of normal, while ALP remained within the expected physiological range for the first trimester. Total bilirubin was approximately 25% above the pregnancy-specific reference value in the first trimester, with elevation attributable mainly to four patients in whom gallstone disease was confirmed ultrasonographically. In

Table 1. Dynamics of liver function biomarkers (mean ± SD) in pregnant women with biliary system pathology, with pregnancy-specific reference ranges

No	Trimester	AST (U/L)	ALT (U/L)	ALP (U/L)	Total Bilirubin (μmol/L)	Cholesterol (mg/dL)
1	I	32.36±0.9	36.41±0.9	272.8±17.2	1.37±0.08	229.7±5.3
2	II	38.0±1.2**	42.9±1.1**	355.7±8.9*	1.85±0.11**	260.2±5.4**
3	III	39.15±1.7**	40.2±1.1***	367.1±16.7**	1.84±0.15*	260.4±8.2**
Ref. range	I/II/III	3-23/3-33/4-32	3-30/2-33/2-25	17-88/25-126/38-229	1.7-6.8/1.7-13.7/1.7-18.8	<200/<200/<200

*p<0.01; **p<0.001; ***p<0.05 vs. Trimester I (Mann-Whitney U test)
ALP: Alkaline Phosphatase; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase

the second trimester, a more pronounced average rise was observed across all markers: AST +23%, ALT +24%, ALP +19%, cholesterol +18%, and total bilirubin +68% above trimester-specific reference values. In the third trimester, a partial reduction in average values of ALT, cholesterol, and total bilirubin was noted; however, AST and ALP remained elevated above pregnancy-specific reference ranges (Table 1). All comparisons were made against trimester I values as reference, using the Mann-Whitney U test; statistically significant differences are indicated in Table 1.

Surgical Outcomes

Despite conservative management, three patients (12%) had persistent symptoms with ultrasonographically confirmed biliary duct obstruction and underwent urgent laparoscopic cholecystectomy. Mean operative time was 25 minutes, with no conversions to open surgery. Clinical improvement was observed within 48 hours and all three patients were discharged by postoperative day 4 with ongoing antenatal follow-up. Across the full cohort, pregnancies proceeded without reported perinatal complications. Deliveries were described as physiologic, and no congenital anomalies were identified in the newborns.

DISCUSSION

This retrospective case series describes trimester-related clinical and biochemical patterns in pregnant women with biliary system pathology and reports outcomes largely of conservative management with a few patients experiencing surgical intervention. The main findings were: (i) exacerbations clustered in the second and third trimesters (48% and 52%, respectively); (ii) liver function biomarkers showed the most pronounced elevations in the second trimester, particularly total bilirubin and ALT; and (iii) three patients (12%) required urgent laparoscopic cholecystectomy due to refractory biliary obstruction, with favorable short-term maternal and fetal outcomes.

The predominance of exacerbations in the second and third trimesters is consistent with the known pathophysiology of pregnancy-related biliary disease. As described in the Introduction, estrogen-driven cholesterol hypersecretion and progesterone-mediated gallbladder hypomotility peak during mid-pregnancy, creating the most lithogenic biliary environment in the second trimester.[6,7] The partial biochemical improvement observed in some markers during the third trimester may reflect partial adaptation of hepatobiliary function, though AST and ALP remained elevated above pregnancy-specific reference ranges throughout, indicating general persistent hepatobiliary stress in this cohort.

The observed cluster of exacerbations in multiparous women, although based on incomplete parity data (15/25 patients), is consistent with the established association between higher parity and increased gallstone risk, as parity is among the strongest independent risk factors for gallstone disease in women of reproductive age.[1,8] This observation should be interpreted with caution given the incomplete parity data available for the full cohort, and no formal statistical comparison between parity groups was performed.

Regarding surgical management, the good outcomes observed in our three surgically treated patients are consistent with published data on laparoscopic cholecystectomy in pregnancy. A systematic review of 590 patients reported an intraoperative complication rate of 3.5%, a conversion rate of 2.2%, and a fetal loss rate of 0.4%, with the majority of procedures performed in the second trimester.[10] A more recent meta-analysis of 45,883 pregnant women demonstrated that operative treatment significantly reduced the composite of adverse pregnancy outcomes compared to nonoperative management (odds ratio: 0.60; 95% confidence interval: 0.42-0.87).[11] Furthermore, laparoscopic cholecystectomy compared to open cholecystectomy was associated with significantly lower fetal, maternal, and surgical complication rates,[12] supporting the laparoscopic approach as the preferred surgical option when intervention is required. These findings also align with the 2024 updated SAGES guidelines, which conditionally recommend laparoscopic cholecystectomy over nonoperative treatment for biliary disease in pregnancy.[9]

Ademetionine (Heptral) was utilized in this cohort as part of routine hepatoprotective conservative management, in accordance with local clinical practice. However, no control group was included in this study, and no formal comparison of outcomes between treated and untreated patients was performed. Therefore, no conclusions regarding the efficacy or necessity of ademetionine can be drawn from these data. Its use in pregnancy requires further evaluation in controlled studies before any recommendations can be made.

Study Limitations

This study has several important limitations that must be acknowledged. First, the retrospective observational design limits the ability to establish causality. Second, the small sample size and in particular the surgical subgroup of only three

patients, markedly restricts the generalizability of the findings. Third, parity data were available for only 15 (60%) patients, limiting the validity of parity-related observations. Fourth, the absence of a control group precludes any comparative analysis of treatment outcomes. Fifth, exact *p* values were not available for all comparisons due to the method of original data recording. Future prospective studies with larger cohorts and standardized data collection are needed to better characterize biliary disease patterns and optimal management strategies in pregnancy.

CONCLUSION

In this retrospective case series, exacerbations of biliary system pathology occurred predominantly in the second and third trimesters, accompanied by measurable and trimester-dependent changes in liver function biomarkers. When conservative management failed and biliary obstruction was confirmed ultrasonographically, urgent laparoscopic cholecystectomy was feasible and was associated with favorable short-term maternal and fetal outcomes in a small selected subset of patients. These findings are consistent with current international guidelines supporting laparoscopic cholecystectomy as the preferred surgical approach in pregnancy when clinically indicated.[9] Given the limitations of this study, the results should be interpreted as preliminary observational data requiring confirmation in larger prospective studies.

Ethics

Ethics Committee Approval: This study received approval from the of Azerbaijan Medical University Ethics Committee (approval number: 38, date: 17.09.2024).

Informed Consent: This study was conducted as a retrospective observational case series.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.M., Concept: H.M., E.A., Design: H.M., K.Q., Data Collection or Processing: H.M., S.Q., K.Q., Analysis or Interpretation: K.Q.,S.B., Literature Search: S.Q., S.B., Writing: S.Q., S.B., E.A.

Conflict of Interest: One author of this article, Erkut Attar, is a member of the Editorial Board of the Anatolian Journal of Obstetrics and Gynecology Research. However, he did not involved in any stage of the editorial decision of the manuscript.

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