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ORIGINAL ARTICLE

Identifying risk factors for gallstones in postpartum women: A case–control study from a tertiary care setting of Peshawar

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ABSTRACT

Background: Cholelithiasis is common in women of reproductive age, and the postpartum period is associated with physiological changes that may increase gallstone risk. This study aimed to identify factors associated with cholelithiasis in postpartum women.

Methods: A case–control study was carried out from March 2024 to April 2025. One hundred and four postpartum women (52 ultrasonographically diagnosed cases of cholelithiasis and 52 controls with no gallstones) were recruited from Northwest General Hospital and Mercy Teaching Hospital. Demographic, obstetric, medical, lifestyle and biochemical data was collected using a structured proforma. Group comparisons used independent t-tests and chi-square tests; variables with $p < 0.20$ in univariate analysis were entered into multivariable logistic regression. Analyses were performed with SPSS v27.

Results: Mean age was higher in cases than controls ($p = 0.046$). Mean BMI was greater in cases (0.001). Multiparity ($p = 0.008$), diabetes mellitus ($p = 0.033$), positive family history ($p = 0.004$), elevated ALP ($p = 0.001$) and total bilirubin ($p < 0.001$) were more frequent in cases. Sedentary lifestyle was significant on univariate analysis but not after adjustment. On multivariable analysis, independent predictors were higher ($p = 0.003$), multiparity ($p = 0.029$), diabetes ($p = 0.049$), positive family history ($p = 0.022$) and bilirubin ($p = 0.001$).

Conclusion: In this postpartum study, metabolic (BMI, diabetes), obstetric (multiparity) and hereditary (family history) factors and raised bilirubin were independently associated with cholelithiasis. Targeted screening and preventive measures for high-risk postpartum women are warranted.

Keywords: Body Mass Index, Cholelithiasis, Complications, Postpartum Period, Parity, Risk Factors

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Introduction

Cholelithiasis, formation of gallstones in gallbladder, represents a significant gastrointestinal health problem worldwide. Women are disproportionately affected by gallstone disease, especially during pregnancy and the postpartum period, due largely to hormonal changes, altered bile composition, and gallbladder stasis (1). The postpartum period is particularly vulnerable as physiological changes reverse slowly and often in the context of weight fluctuations, breastfeeding, and metabolic stress (2). Globally, studies report variable prevalence of gallstones during and after pregnancy. A retrospective observational study in Baja California Sur found that among 137 women (104 in postpartum), overweight or obesity were present in ~66% of postpartum patients with cholelithiasis, highlighting the strong association of BMI with gallstone disease in this period (3). Similarly, in Saudi Arabia, research following bariatric surgery, which induces rapid weight changes, showed increased incidence of gallstones in those with higher postoperative weight loss and adiposity (4). Though not restricted to postpartum, these studies underscore that high BMI and weight changes are consistent risk factors. Dietary factors also play a key role, a recent study finds that certain diets consumed in the aftermath of childbirth correlate with gallbladder changes, possibly reflecting increased cholesterol absorption and biliary stasis in women with high-fat diets or irregular meal patterns (2). Other lifestyle factors such as physical inactivity have also been implicated in gallstone formation both in pregnancy and postpartum (5). Reproductive history, including parity, mode of delivery, breastfeeding duration—and family history are also established contributors. A study in Lahore, Pakistan, reported that approximately 32.4% of participants with cholelithiasis had at least one first-degree relative with gallstones, demonstrating a pronounced genetic or familial predisposition (6). Internationally, a large population-based study in Shanghai (7) found that positive family history increased risk of gallstones with an adjusted OR of ~2.8, after adjusting for age, gender, BMI, and other covariates, while regional cross-sectional work uses ultrasonography and report ~36% family prevalence among gallstone patients (8). Other medical comorbidities such as diabetes mellitus and hyperlipidemia have also been associated with gallstone disease. For instance, a study conducted in the Baja California noted that overweight and obesity, often coupled with metabolic derangements, were highly prevalent in postpartum women presenting with gallstones (3). Similarly, another cross-sectional work has shown that insulin resistance and dyslipidemia confer higher odds of gallstone formation (5).

Given the considerable burden of cholelithiasis in postpartum women and the diverse risk factors suggested by recent research, this study aims to identify what risk factors are most strongly associated with cholelithiasis during the postpartum period in the context of Peshawar, Pakistan.

Methods

This study was designed as a hospital-based case–control study and was conducted at the General Surgery departments of Northwest General Hospital & Research Center (NWGH & RC), and Mercy Teaching Hospital Peshawar, Pakistan, from 1st March 2024 to 30th April 2025. This tertiary care hospital serves both urban and rural populations, ensuring access to a broad spectrum of patients. Ethical approval was obtained from the Institutional Review Board and Ethical Committee of Northwest General Hospital, Peshawar *(Approval No: IRB&EC/ 2024-GH/0305) (Date: 20-02-2024)*. All participants were provided with informed written consent after a clear explanation of study objectives, and confidentiality of data was maintained throughout the study. The study population comprised postpartum women, defined as females within one year after delivery. Two distinct groups were identified; Cases were defined as postpartum women with ultrasonographically confirmed gallstones. Gallstones were diagnosed when echogenic intraluminal foci with posterior acoustic shadowing and/or mobility were detected within the gallbladder using standard abdominal ultrasonography performed by a consultant radiologist. Only newly diagnosed patients during the postpartum period were included to avoid bias from pre-existing gallstone disease, while Controls were defined as postpartum women, also within one year after delivery, who underwent abdominal ultrasonography during the same period and were found to have no evidence of gallstones. These women were recruited from the same hospital and were selected from those attending for routine postpartum follow-up visits or minor complaints not related to gallbladder disease. The sample size was calculated using the OpenEpi sample size calculator (Unmatched Case–Control study, Version 3.01). The following parameters were entered: 95% confidence level, 80% power, and a 1:1 case-to-control ratio. Based on published literature, the estimated prevalence of positive family history of gallstones among cases was set at 32%, derived from a Pakistani study (6) that demonstrated approximately one-third of gallstone patients reported family history. For controls, the prevalence was set at 9.5%, as reported in a population-based study (7) from Shanghai. These values correspond to an estimated odds ratio of ~4.48. Kelsey's method, used in OpenEpi calculated a minimum sample size of 52 cases and 52 controls making a total of 104 participants. A non-probability consecutive sampling technique was employed. All postpartum women meeting the inclusion criteria were approached consecutively in surgical outpatient clinics, inpatient wards, and emergency admissions until the target sample size was achieved. This method minimized selection bias within the constraints of a hospital-based design.

Specific inclusion criteria for participation were applied, women aged 18–45 who had given birth within the last 12 months and were willing and able to provide written informed consent. Exclusion criteria were applied stringently i.e., women with a history of cholecystectomy, chronic liver disease, hemolytic anemia, malignancy or on medications affecting bile composition such as ceftriaxone or octreotide. All participants underwent clinical assessments and interviews. For collection of data, a structured proforma was formulated through a critical review of current literature of gallstone disease and subsequently reviewed by experts. Sociodemographic variables were determined by a questionnaire that also assessed anthropometric indices (such as body mass index-BMI), obstetric variables (such as parity, manner of delivery, accumulated duration of breastfeeding, and post-delivery duration), and medical comorbid disorders (such as high blood pressure and diabetes mellitus). Data regarding family history of gallstones in first-degree relatives were recorded. Lifestyle factors such as exercise status, oral contraceptive use, and dietary fat intake, were also assessed. For cases and controls, biochemical markers including alkaline phosphatase (ALP) (U/L; units per liter), total bilirubin (obstetric cholestasis) (mg/dl; mg per liter), and serum alanine transaminase (ALT) (U/L; units per liter) were taken, to assess whether impaired hepatobiliary function may play a role in gallstone formation. Cases and controls also underwent abdominal ultrasound scans performed by a consultant radiologist according to a standardized protocol for abdominal ultrasound scanning for gallstones. For surgical candidates, laparoscopic cholecystectomy was performed utilizing the traditional four-port technique, confirmed with a critical view of safety prior to cystic duct and artery ligation. (9) In the case of technical difficulties or uncertain anatomy, cholecystectomy was converted to an open procedure, as per the SAGES guidelines. (10) Postoperative care was standard hospital care including multimodal analgesia, early mobilization, and close monitoring for complications.

Data was entered and analyzed using SPSS version 27.0 (IBM). Descriptive statistics for continuous variables included the means and standard deviations, while for categorical variables, frequencies with percentages. Group comparisons between controls and cases were made using the independent-sample t-test for continuous variables like time since delivery, and biochemical parameters, and chi-square test for categorical variables like parity, diabetes, hypertension, family history, contraceptive use, and lifestyle factors. Where counts of expected cells were below five, Fisher's exact test was used. To determine independent predictors of gallstone disease, multivariable logistic regression analysis was conducted using variables with univariate p-value of less than 0.20. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and statistical significance was set at $p < 0.05$.

Results

A total of 104 postpartum women were included, comprising52caseswithultrasono Graphically confirmed cholelithiasis and 52 controls without cholelithiasis. The mean age of overall participants was 31.3 ± 5.6 years. The mean age of cases was higher than controls (32.4 ± 5.8 vs. 30.1 ± 5.2 years). Similarly, cases had a higher mean BMI compared to controls (28.3 ± 3.7 vs. 25.9 ± 3.2 kg/m²). Multiparity (≥3 births) was significantly more common among cases (57.7% vs. 32.7%; $\chi^2 = 7.10$, $p = 0.008$). Cesarean delivery was slightly higher among cases (40.4% vs. 34.6%) but not significant ($\chi^2 = 0.40$, $p = 0.53$). Breastfeeding for >6 months was more frequent in controls (78.8% vs. 67.3%), though not statistically significant ($\chi^2 = 1.65$, $p = 0.20$). The mean time since delivery was slightly shorter among cases (5.8 ± 3.1 vs. 6.4 ± 3.4 months), but difference was not significant ($t = -0.88$, $p = 0.38$). Diabetes mellitus was significantly more prevalent among cases (23.1% vs. 7.7%; $\chi^2 = 4.53$, $p = 0.033$). Hypertension was similar in both groups (19.2% vs. 15.4%; $\chi^2 = 0.23$, $p = 0.63$), indicating no significant association. A positive family history was reported in 32.7% of cases vs. 9.6% of controls, a highly significant difference ($\chi^2 = 8.10$, $p = 0.004$). Sedentary lifestyle was significantly associated with gallstones (51.9% vs. 28.8%; $\chi^2 = 6.43$, $p = 0.011$). A high-fat diet was more frequent in cases (55.8% vs. 48.1%), but the association was not significant ($\chi^2 = 0.64$, $p = 0.42$). Oral contraceptive use was slightly higher among cases (21.2% vs. 15.4%), but without statistical significance ($\chi^2 = 0.52$, $p = 0.47$) (Table 1).

Table 1. Comparison of Age, BMI, Obstetric Characteristics, Medical Comorbidities, Family History and Lifestyle Characteristics between the 2 groups.

Variable	Cases group (n=52)	Controls group (n=52)	
Age (years, mean ± SD)	32.4 ± 5.8	30.1 ± 5.2	
BMI (kg/m², mean ± SD)	28.3 ± 3.7	25.9 ± 3.2	
Variable	**Cases group (n=52)**	**Controls group (n=52)**	**χ² (p-value)**
Multiparity (≥3 births)	30 (57.7%)	17 (32.7%)	$\chi^2 = 7.10$, $p = 0.008$
Cesarean delivery	21 (40.4%)	18 (34.6%)	$\chi^2 = 0.40$, $p = 0.53$
Breastfeeding >6 months	35 (67.3%)	41 (78.8%)	$\chi^2 = 1.65$, $p = 0.20$
Time since delivery (months, mean ± SD)	5.8 ± 3.1	6.4 ± 3.4	$t = -0.88$, $p = 0.38$
Diabetes mellitus	12 (23.1%)	4 (7.7%)	$\chi^2 = 4.53$, $p = 0.033$
Hypertension	10 (19.2%)	8 (15.4%)	$\chi^2 = 0.23$, $p = 0.63$
Positive family history	17 (32.7%)	5 (9.6%)	$\chi^2 = 8.10$, $p = 0.004$
Sedentary lifestyle	27 (51.9%)	15 (28.8%)	$\chi^2 = 6.43$, $p = 0.011$
High-fat diet (self-reported)	29 (55.8%)	25 (48.1%)	$\chi^2 = 0.64$, $p = 0.42$
Oral contraceptive use	11 (21.2%)	8 (15.4%)	$\chi^2 = 0.52$, $p = 0.47$

Cases had significantly higher mean serum alkaline phosphatase (142.6 ± 38.4 vs. 118.9 ± 29.3 U/L; $t = 3.47$, $p = 0.001$) and total bilirubin (1.4 ± 0.5 vs. 0.9 ± 0.3 mg/dL; $t = 6.01$, $p < 0.001$). ALT levels were slightly higher in cases (34.8 ± 11.2 vs. 32.9 ± 10.5 U/L) but did not reach statistical significance ($t = 0.87$, $p = 0.39$) (Table 2).

Table 2. Biochemical Parameters of both groups.

Variable	Cases group (n=52)	Controls group (n=52)	t-test (p-value)
ALT (U/L, mean ± SD)	34.8 ± 11.2	32.9 ± 10.5	$t = 0.87$, $p = 0.39$
ALP (U/L, mean ± SD)	142.6 ± 38.4	118.9 ± 29.3	$t = 3.47$, $p = 0.001$
Total Bilirubin (mg/dL, mean ± SD)	1.4 ± 0.5	0.9 ± 0.3	$t = 6.01$, $p < 0.001$

When entered logistic regression, higher BMI, multiparity, diabetes, family history, and elevated bilirubin remained independent predictors of cholelithiasis. Sedentary lifestyle lost its significance after adjustment (Table 3).

Table 3. Multivariable Logistic Regression Analysis between Cases and Controls groups.

Variable	Adjusted OR	95% CI	p-value
BMI (per unit increase)	1.15	1.05–1.27	0.003
Multiparity	2.51	1.09–5.78	0.029
Diabetes mellitus	3.45	1.00–11.85	0.049
Family history	3.89	1.21–12.47	0.022
Bilirubin (per mg/dL rise)	2.02	1.32–3.10	0.001
Sedentary lifestyle	1.60	0.70–3.65	0.26

Discussion

Women are disproportionately affected by gallstone disease, especially during pregnancy and the postpartum period, due largely to hormonal changes, altered bile composition, and gallbladder stasis (1). In our case–control of 104 postpartum women (52 cases, 52 controls), the mean age among cases was 32.4 ± 5.8 years versus 30.1 ± 5.2 years among controls. Body mass index (BMI) differed significantly in our sample. Age as a factor is supported by a study conducted by Xiao et al., reported a weighted prevalence of gallstones of 10.4% with clear increases with advancing age, and showing older age groups having higher odds of gallstone disease (11). Wang et al. reported a positive association between adiposity indices and gallstones with adjusted ORs in the range of 1.2–1.6 per adiposity increment depending on metric; similarly, the triglyceride-glucose index and related metabolic indices studies report ORs for elevated indices near 1.3–1.8 for gallstone presence (12). Thus numerically, our mean BMI difference (~2.4 kg/m^2) corresponds to a clinically meaningful increase compatible with the magnitudes reported in these studies, supporting the interpretation that higher adiposity in postpartum women increases gallstone risk.

Multiparity was more common among cases in our series and remained an independent predictor. A systematic review/meta-analysis focused on pregnancy and gallstones reported pooled increased odds for multiparous women (pooled ORs typically between 1.4–2.5) depending on parity thresholds; thus, our adjusted OR of ~2.5 sits at the higher end of pooled estimates and is consistent with parity being a meaningful obstetric risk in postpartum women (13). Diabetes mellitus in our study was significantly more frequent in cases (23.1% vs 7.7%; χ^2 = 4.53; p = 0.033) and was independently associated (adjusted OR 3.45; 95% CI 1.00–11.85; p = 0.049). In Wang et al. study (12) the triglyceride-glucose index and other insulin-resistance proxies have been associated with gallstone presence with ORs typically between 1.5–3.0 for the highest vs lowest categories; reporting elevated triglyceride-glucose index associated with higher prevalence and earlier onset of gallstones, i.e., our observed adjusted OR of ~3.5 is within the range reported in the mentioned insulin-resistance-focused study, supporting that diabetes (or related metabolic derangements) is an important risk factor in postpartum women as well.

Costa and colleagues' 2024 review of genetics of gallstone disease reported clinical studies from 2021–2024 (14) stating family-history ORs generally in the 2–4 range, i.e., our adjusted OR ≈ 3.9 aligns well numerically with these contemporary reports, reinforcing a strong hereditary component in our postpartum sample. Biochemically, cases had higher mean ALP and total bilirubin. Aly et al., a case–control biochemical study, reported similar directional differences with higher ALP and bilirubin in gallstone/acute biliary disease cases; mean ALP elevations in their cases were on the order of ~25–40 U/L higher than controls, comparable to our observed difference (~24 U/L) (15). This numerical concordance suggests that even in a postpartum group, biochemical markers reflect biliary stasis and can correlate with ultrasonographic disease. Regarding lifestyle and diet, sedentary behavior was more frequent among cases but lost significance in multivariable analysis (adjusted OR 1.60; p = 0.26). Xiao et al. found improved lifestyle/LE8 scores reduced gallstone odds substantially (adjusted ORs often <1 for better scores) (11), while the BMC fiber study (2023) reported an inverse association (fiber intake lowering odds; ORs in protective range ~0.6–0.8) (16). Our loss of independent effect for sedentary lifestyle after adjustment likely reflects the stronger influence of metabolic variables (BMI, diabetes) and family history captured in the model—consistent with these population-level analyses.

When comparing effect sizes, our independent predictors adjusted ORs (BMI per unit adjusted OR 1.15; multiparity adjusted OR ~2.5; diabetes adjusted OR ~3.45; family history adjusted OR ~3.9; bilirubin per mg/dL adjusted OR 2.02) are broadly comparable to the magnitudes reported in contemporary studies of metabolic, familial, and biochemical predictors, which commonly report ORs between 1.1–4.0 depending on exposure definition and population. (11) For instance, lipid-index studies report adjusted ORs per index quintile in the 1.2–2.0 range, (12) while family-history studies report ORs between 2–4 (14), consistent with the range of our results.

Study Strengths & Limitations

Strengths of the study include being among the first to address postpartum gallstones in Pakistan, the use of ultrasonographic confirmation of cases, matched postpartum controls, and comprehensive assessment of multiple risk factors analyzed through multivariable regression, enhancing the reliability of the findings. The study was limited by its modest sample size, single-center design, and reliance on self-reported variables for diet and lifestyle, which may have introduced recall bias. As a case–control study, causality could not be established, and biochemical parameters such as lipid profiles were not included.

Future Recommendations

Larger multicenter and prospective studies are recommended to validate these findings and establish causal pathways. Broader biochemical profiling and genetic studies should be incorporated, while preventive strategies focusing on weight control, diabetes management, and postpartum follow-up may help reduce gallstone risk in high-risk women.

Conclusion

This study found that postpartum women with cholelithiasis were more likely to have higher age, BMI, multiparity, diabetes, positive family history, and elevated bilirubin compared to controls. Sedentary lifestyle showed significance in univariate analysis but lost significance after adjustment. Cesarean delivery, breastfeeding duration, hypertension, high-fat diet, and contraceptive use were not significantly associated. The findings highlight metabolic, hereditary, and obstetric factors as key determinants of gallstone formation in postpartum women. These results underscores need for targeted preventive and screening strategies in high-risk groups.

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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.	