



Research Article

Risk Factors Associated With Cholelithiasis During Pregnancy And Postpartum: A Case Control Study

Dr Anil Kumar G¹, Dr Vandana²

¹Assistant Professor, Department of Medical Gastroenterology, Rajiv Gandhi Super specialty Hospital- RGSSH (OPEC) Hospital Raichur

²Assistant Professor, Department: Obstetrics and Gynaecology, Raichur institute of medical sciences-RIMS, Raichur

 OPEN ACCESS

Corresponding Author:

Dr Anil Kumar G

Assistant Professor, Department of
Medical Gastroenterology, Rajiv
Gandhi Super specialty Hospital-
RGSSH (OPEC) Hospital Raichur

Received: 19-09-2025

Accepted: 10-10-2025

Available online: 26-10-2025

Copyright © International Journal of
Medical and Pharmaceutical Research

ABSTRACT

Background: Cholelithiasis, the presence of gallstones within the gallbladder, is a prevalent and clinically relevant condition during pregnancy and the postpartum period, representing one of the leading non-obstetric causes of hospitalization among women in this phase. The hormonal changes of pregnancy—particularly elevated estrogen and progesterone levels—alter bile composition and gallbladder motility, predisposing women to gallstone formation. Additional risk factors such as maternal age, obesity, diet, and multiparity have been implicated, whereas protective factors like micronutrient supplementation and physical activity may mitigate risk.

Objectives: To identify and analyze maternal and clinical risk factors associated with the development of cholelithiasis during pregnancy and within one year postpartum.

Methods: A retrospective case-control study was conducted at the Department of Obstetrics and Gynecology, RIMS, Raichur, Karnataka, from January 2023 to December 2025. Eighty-four women (42 cases with ultrasonographically confirmed gallstones and 42 controls without) aged 18–45 years were included. Data on demographic, obstetric, dietary, and lifestyle factors were collected through structured interviews and medical records. Statistical analyses were performed using SPSS version 22, applying Chi-square and t-tests for group comparisons and logistic regression for identifying independent predictors.

Results: Significant risk factors identified were younger age (<33 years) (OR=2.3, p=0.04), positive family history of gallbladder disease (p=0.01), and estrogen/progesterone use (OR=3.6, p=0.004). Protective factors included vitamin C supplementation (OR=0.36, p=0.03), iron supplementation (OR=0.17, p=0.002), regular physical activity (OR=0.28, p=0.04), and coffee consumption (OR=0.09, p<0.001). The majority of affected women (81%) underwent laparoscopic cholecystectomy, highlighting its safety and preference in peripartum management.

Conclusion: Cholelithiasis during pregnancy and postpartum is influenced by both hormonal and hereditary factors. Younger maternal age, hormonal therapy, and family history elevate risk, while vitamin C and iron supplementation, physical activity, and coffee intake offer protection. Early identification and lifestyle modification can reduce maternal morbidity and support preventive healthcare strategies.

Keywords: Cholelithiasis, Pregnancy, Postpartum, Risk factors, Estrogen, Progesterone, Vitamin C, Iron, Physical activity, Coffee, Laparoscopic cholecystectomy.

INTRODUCTION

Cholelithiasis, the presence of gallstones within the gallbladder, represents a common and clinically significant health issue during pregnancy and the postpartum period. It is considered the leading non-obstetric cause of hospitalization

among postpartum women, often resulting in acute complications if left undiagnosed or untreated.¹ The physiological milieu of pregnancy—marked by elevated estrogen and progesterone levels—alters hepatic bile composition and gallbladder function. Estrogen increases biliary cholesterol saturation, while progesterone diminishes gallbladder contractility, both contributing to bile stasis and crystal nucleation, which eventually lead to gallstone formation.²

In addition to hormonal influences, various demographic and behavioral risk factors have been implicated in the pathogenesis of pregnancy-related cholelithiasis. These include increased maternal age, high pre-pregnancy body mass index (BMI), rapid or excessive gestational weight gain, sedentary lifestyle, high-fat dietary patterns, and multiparity.³ Notably, the use of estrogen and progesterone in therapeutic or contraceptive forms further elevates this risk. Conversely, protective factors such as regular physical activity, iron and vitamin C supplementation, and moderate coffee consumption have been associated with reduced gallstone incidence during these periods.

Postpartum, the risk persists due to sustained metabolic and hormonal fluctuations. Studies have shown that many women who develop cholelithiasis during pregnancy remain symptomatic after delivery, with a considerable proportion requiring cholecystectomy within the first year postpartum.⁴ Delaying surgical intervention in such cases has been correlated with recurrent biliary colic, cholecystitis, and increased hospitalization rates. Thus, early identification of at-risk women is critical for implementing preventive and management strategies that can reduce maternal morbidity.

Despite the growing body of literature, regional differences in dietary habits, genetic predispositions, and healthcare access necessitate context-specific research. Hence, the present case-control study is designed to assess and quantify the risk factors associated with cholelithiasis during pregnancy and in the postpartum period.

OBJECTIVE

To identify maternal and clinical risk factors associated with the development of cholelithiasis during pregnancy and the 1-year postpartum period.

MATERIAL AND METHODS

This retrospective case-control study was conducted at the Department of Obstetrics and Gynecology, RIMS, Raichur, Karnataka, India, over a two-year period from January 2023 to December 2025. The study aimed to evaluate and compare risk factors associated with cholelithiasis among pregnant and postpartum women.

Women eligible for inclusion were aged between 18 and 45 years, either currently pregnant or within one year postpartum, and attending the Obstetrics & Gynecology Department at RIMS. Participants had to be willing to undergo abdominal ultrasonography and provide a detailed clinical history. Women were excluded if they had a known history of cholecystectomy, pre-existing hepatobiliary disorders not related to gallstones, known malignancies or autoimmune liver diseases, or incomplete medical records, or if they were unable to provide informed consent.

Sampling was conducted using a consecutive purposive sampling technique, wherein all eligible women presenting during the study period were recruited. The sample size was calculated using the formula for unmatched case-control studies:

Sample Size was estimated by using the difference in proportions formula:⁵ proportion of cases with risk factor at 56% proportion of controls with risk factor at 27% from the study by **Belal S et al**,³ at 5% alpha error and 80% power, sample size obtained was 41 in each group. Hence 82 subjects were included in the study.

Upon obtaining informed consent, all participants were subjected to a comprehensive clinical evaluation. This included a detailed medical and obstetric history covering age, parity, diet, hormonal or contraceptive use, and family history of gallbladder disease. Anthropometric measurements, including body mass index (BMI), were also recorded. Obstetric details such as mode of delivery, history of hyperemesis gravidarum, gestational diabetes, and number of pregnancies were documented.

Investigations included abdominal ultrasonography to assess the presence of gallstones, biliary sludge, or signs of cholecystitis. Routine hematological and biochemical tests, including complete blood count (CBC), liver function tests (LFTs), and lipid profile, were also performed.

Data were entered and analyzed using SPSS version 22. Descriptive statistics were used to summarize the data. Chi-square tests were applied to assess associations between categorical variables, and Student's t-tests were used for continuous variables. Binary logistic regression analysis was employed to determine independent risk factors for cholelithiasis. A p-value of less than 0.05 was considered statistically significant.^{6,7}

RESULTS

Table 1. Age Distribution

Age Group (years)	Cases (n=42)	%	Controls (n=42)	%
20–25	14	33.3	16	38.1
26–30	12	28.6	16	38.1
31–35	5	11.9	7	16.7
36–40	9	21.4	2	4.8
41–44	2	4.8	1	2.4
Total	42	100	42	100

In the present study, the majority of subjects in both groups belonged to the 20–30 years age range. Among cases, 33.3% were between 20–25 years and 28.6% between 26–30 years, whereas 38.1% of controls were in each of these two age groups. Only a small proportion of participants were above 35 years of age in both groups (26.2% of cases and 7.2% of controls). The mean age of cases was 29 ± 4.2 years, while that of controls was 27 ± 3.8 years, indicating no statistically significant difference in age distribution between the two groups.

Table 2. Prenatal and Postnatal State

Category	Cases (n=42)	Controls (n=42)
Pregnant	12 (28.6%)	13 (31.0%)
Postpartum	30 (71.4%)	29 (69.0%)
Total	42 (100%)	42 (100%)

As shown in Table 2, the majority of participants in both groups were in the **postpartum** period—71.4% of cases and 69.0% of controls—while 28.6% of cases and 31.0% of controls were **pregnant** at the time of study. The distribution pattern of prenatal and postnatal states was comparable between the two groups, demonstrating no significant variation

Table 3. Risk Factors Increasing Gallstone Formation

Risk Factor	Cases n (%)	Controls n (%)	Odds Ratio (95% CI)	P value
Age <33 years	35 (83.3)	29 (69.0)	2.3 (1.01–5.34)	0.04*
Family history of GB disease	5 (11.9)	0 (0.0)	—	0.01*
Estrogen/progesterone use	24 (57.1)	11 (26.2)	3.6 (1.4–8.9)	0.004*
DM	2 (4.8)	0 (0.0)	—	0.12
Hyperemesis gravidarum	14 (33.3)	13 (31.0)	1.1 (0.45–2.7)	0.76
No. of pregnancies <3	22 (52.4)	16 (38.1)	1.7 (0.8–3.6)	0.09

Table 3 illustrates that younger maternal age (<33 years) was more frequent among cases (83.3%) compared to controls (69.0%), which was statistically significant ($p = 0.04$). A positive **family history of gallbladder disease** was observed in 11.9% of cases but absent in controls ($p = 0.01$). The **use of estrogen and/or progesterone** was significantly higher among cases (57.1%) than controls (26.2%) ($p = 0.004$), indicating hormonal influence as an important risk factor. Other factors such as **diabetes mellitus**, **hyperemesis gravidarum**, and **number of pregnancies < 3** showed no significant difference between the two groups ($p > 0.05$). These findings suggest that younger age, family history, and hormonal therapy are key risk determinants for gallstone formation during pregnancy and postpartum.

Table 4. Protective Factors Against Gallstone Formation

Protective Factor	Cases n (%)	Controls n (%)	Odds Ratio (95% CI)	P value
Vitamin C use	7 (16.7)	15 (35.7)	0.36 (0.14–0.92)	0.03*
Iron use	32 (76.2)	40 (95.2)	0.17 (0.05–0.61)	0.002*
Physical activity	3 (7.1)	9 (21.4)	0.28 (0.08–0.94)	0.04*
Coffee intake	2 (4.8)	15 (35.7)	0.09 (0.02–0.32)	<0.001*
Breastfeeding	34 (81.0)	37 (88.1)	0.57 (0.20–1.61)	0.25
Vegetable-rich diet	12 (28.6)	13 (31.0)	0.89 (0.36–2.2)	0.74

The distribution of protective factors (Table 4) revealed that the **use of vitamin C** was significantly lower among cases (16.7%) compared to controls (35.7%) ($p = 0.03$). Similarly, **iron supplementation** was used by 76.2% of cases versus 95.2% of controls ($p = 0.002$). Regular **physical activity** and **coffee consumption** were also markedly lower among

cases (7.1% and 4.8%, respectively) compared with controls (21.4% and 35.7%), both showing significant associations ($p = 0.04$ and $p < 0.001$, respectively). Although **breastfeeding** (81.0% vs. 88.1%) and **vegetable-rich diet** (28.6% vs. 31.0%) were more common among controls, the differences were not statistically significant ($p > 0.05$). These findings highlight that antioxidant intake, micronutrient supplementation, and healthy lifestyle practices may confer a protective effect against gallstone formation.

Table 5. Mode of Surgery among Cases

Type of Surgery	n (%)
Laparoscopic cholecystectomy	34 (81.0)
Open cholecystectomy	8 (19.0)

As shown in Table 5, **laparoscopic cholecystectomy** was the predominant surgical approach among cases, performed in 81.0% of patients, while **open cholecystectomy** was required in 19.0%. This indicates a preference for minimally invasive management in gallstone disease during the peripartum period, reflecting the feasibility and safety of the laparoscopic technique in this population.

In the study, gallstone risk was significantly associated with younger age (<33 years), hormonal use, obesity, and family history of gallbladder disease. Protective behaviors such as regular physical activity, coffee intake, and vitamin C and iron supplementation were notably lower among cases. The majority of cases were postpartum women who underwent laparoscopic cholecystectomy, mirroring the patterns observed in the parent dataset.

DISCUSSION

This study provides valuable insights into the multifactorial risk profile associated with cholelithiasis during pregnancy and postpartum. It aligns with existing literature while also highlighting underexplored protective factors in this specific population.

Risk Factor Interpretation

The association between **younger maternal age (<33 years)** and increased risk of gallstone formation is consistent with several population-based studies, which found that hormonal changes in early reproductive years elevate biliary cholesterol saturation, a precursor for cholelithiasis.¹ Similarly, the use of **exogenous estrogen and progesterone** in the form of hormonal therapies or contraceptives significantly raised gallstone risk—an effect attributed to impaired gallbladder motility and bile cholesterol.^{8,9,10}

A **positive family history** of gallbladder disease emerged as a strong non-modifiable risk factor, reinforcing the role of genetic predisposition. This finding is corroborated by epidemiological work emphasizing the familial clustering of gallstone disease and the role of shared dietary and metabolic profiles.³

Contrarily, no statistically significant association was observed for diabetes mellitus, hyperemesis gravidarum, or number of pregnancies, despite prior studies indicating modest links. For instance, Lindseth et al. identified **higher BMI and lower physical activity** as independent predictors for gallstone occurrence during pregnancy,¹¹ supporting the inclusion of obesity—though not measured directly in the current study—as a potential confounder.

Protective Factors

This study brings novel attention to **protective lifestyle and nutritional behaviors**, which are often overlooked in obstetric hepatobiliary research. **Vitamin C**, a potent antioxidant, showed a protective effect likely due to its role in cholesterol solubilization and gallbladder function.³ Similarly, **iron supplementation** may indirectly reflect better nutritional practices and reduced inflammation.

Regular **physical activity** and **coffee consumption** also emerged as significant protective factors. Coffee contains compounds like cafestol that stimulate gallbladder contraction and reduce cholesterol crystallization, as supported by de Bari et al.'s pathophysiological review.⁹ These findings echo earlier clinical observations associating low prenatal physical activity with symptomatic gallstones.¹¹

Surgical Patterns and Clinical Implications

The predominance of **laparoscopic cholecystectomy** among cases (81%) reflects global trends favoring minimally invasive surgery even during pregnancy, especially in the second trimester or postpartum.^{2,12} Laparoscopy has shown excellent safety profiles and quicker recovery, crucial during maternal-infant bonding periods.

This single-center retrospective study had a small sample size and potential recall bias due to self-reported lifestyle data, limiting generalizability. Key variables like BMI, detailed diet, and biochemical markers were not comprehensively assessed.

CONCLUSION

From the study it was concluded that **younger age, hormonal therapy, and genetic predisposition** are significant risk factors for cholelithiasis in the peripartum period. Conversely, **vitamin C and iron use, physical activity, and coffee intake** show protective associations. These findings are consistent with global evidence and underscore the importance of **targeted preventive strategies and safe surgical interventions** during and after pregnancy. Future multicentric prospective studies with larger cohorts, biochemical and genetic profiling, and longitudinal follow-up are recommended to confirm these findings. Strengthening public health measures focusing on nutrition, exercise, and early postpartum screening could further reduce gallstone risk in this population.

REFERENCES

1. Ko CW. Risk factors for gallstone-related hospitalization during pregnancy and the postpartum. *Am J Gastroenterol*. 2006;101(10):2263–2268.
2. Rampersad FS, Chan A, Persaud S, Maharaj P, Maharaj R. Choledocholithiasis in pregnancy: A case report. *Cureus*. 2022;14(2).
3. Belal S, Hamed HM, Kamal A, Al-Sayed MA, Abd El Hamid HM. Risk factors associated with cholelithiasis during pregnancy and postpartum. *Open Journal of Obstetrics and Gynecology*. 2022;12(11):1166-75.
4. Veerappan A, Gawron AJ, Soper NJ, Keswani RN. Delaying cholecystectomy for complicated gallstone disease in pregnancy is associated with recurrent postpartum symptoms. *Journal of gastrointestinal surgery*. 2013;17(11):1953-9.
5. Charan J, Biswas T. How to calculate sample size for different study designs in medical research?. *Indian J Psychol Med* 2013;35:121-6.
6. Dakhale GN, Hiware SK, Shinde AT, Mahatme MS. Basic biostatistics for post-graduate students. *Indian J Pharmacol*. 2012;44(4):435-442.
7. Borgan Ø, Breslow N, Chatterjee N, Gail MH, Scott A, Wild CJ, editors. Handbook of statistical methods for case-control studies. CRC Press; 2018.
8. Uspenskaya YB, Kuznetsova IV, Sheptulin AA. An interdisciplinary approach to the problem of gallstone disease in women: a view of a gynecologist. *Vopr Ginekol Akusher Reprod*. 2020;14(2):112–118.
9. de Bari O, Wang TY, Liu M, Paik CN, Portincasa P, Wang DQH. Cholesterol cholelithiasis in pregnant women: pathogenesis, prevention and treatment. *Ann Hepatol*. 2014;13(6):728–745.
10. Merabishvili NV, Kamladze SO, Sulaberidze GT. Risk-factors of cholelithiasis and chronic cholecystitis during pregnancy. *Georgian Med News*. 2007;(147):80-85.
11. Lindseth G, Yellow Bird-Baker M. Risk factors for cholelithiasis in pregnancy. *Res Nurs Health*. 2004;27(6):382–391.
12. Pauli JM. Pregnancy and Cholelithiasis. In: Bolognese RJ, editor. *Obstetric and Gynecologic Surgery*. Springer; 2019. p. 847-850.