Original Research

ASSOCIATION OF CHOLELITHIASIS AND HYPOTHYROIDISM AT A TERTIARY CARE CENTRE

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ABSTRACT

Introduction: Cholelithiasis (gallstone disease) is a prevalent gastrointestinal disorder influenced by cholesterol metabolism and biliary motility. Hypothyroidism, through mechanisms such as dyslipidemia, reduced bile flow, and altered sphincter of Oddi function, may contribute to gallstone formation. Despite previous studies, the association remains inconclusive. This study aims to evaluate the correlation between clinical and subclinical hypothyroidism and cholelithiasis in an Indian cohort. Materials and Methods: A prospective observational study was conducted from October 2025 to January 2026, and it was carried out at the Department of General Surgery, Mahatma Gandhi Medical College Hospital and Research Centre, Jaipur. Eighty adult patients with ultrasonographically confirmed gallstones were recruited. Exclusion criteria included choledocholithiasis and unwillingness to participate. All patients underwent thyroid function testing (TSH, T3, T4) and gallstone characterization. Statistical analysis included Chi-square tests for categorical data and ROC curve analysis for TSH as a predictive marker. Results: Among the 80 patients, 65% were female and 52.5% were aged 31–50 years. Thyroid dysfunction was present in 40% of patients 25% had subclinical and 15% had clinical hypothyroidism. Female gender and age >40 was significantly associated with hypothyroidism. Hypothyroid patients more frequently had multiple stones and cholesterol- type stones. A significant association between hypothyroidism and cholelithiasis was observed ($p = 0.032$). ROC analysis of TSH showed moderate predictive value (AUC = 0.72; sensitivity = 68%, specificity = 75%). Conclusion: This study demonstrates a significant association between hypothyroidism especially subclinical forms and gallstone disease, particularly in women over 40. Routine thyroid screening should be considered in gallstone patients to aid early detection and potentially reduce disease progression or recurrence.

Keywords: Cholelithiasis, Hypothyroidism, Subclinical Hypothyroidism, Bile Flow, TSH, Gallstones.

INTRODUCTION

Gallstones, a common form of biliary pathology, are classified into three main types: cholesterol, pigment, and mixed stones. Cholesterol stones, which account for the majority in Western countries, consist of 51–99% cholesterol, along with other components like bile acids and phospholipids. In contrast, pigment stones, more prevalent in Asian populations, primarily consist of bilirubin and calcium salts (Ghafoor et al., 2022). The formation of gallstones is a complex process influenced by various factors, including cholesterol supersaturation, impaired bile flow, and dysfunction of the sphincter of Oddi (Volzke et al., 2005).

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Cholesterol supersaturation in bile leads to nucleation, the first critical step in the formation of gallstones, while bile stasis and sphincter dysfunction contribute to the retention of bile and further precipitation of cholesterol (Ghafoor et al., 2022).

Hypothyroidism, an endocrine disorder characterized by insufficient thyroid hormone production, has been suggested to impact gallstone formation through its effects on lipid metabolism. Thyroid hormones play a key role in regulating lipid homeostasis, and hypothyroidism is commonly associated with elevated cholesterol levels, which can alter the composition of bile and promote stone formation (Rahman et al., 2020). Additionally, hypothyroidism leads to reduced bile flow and dysfunction of the sphincter of Oddi, which may contribute to the formation of gallstones (Volzke et al., 2005).

The possible association between hypothyroidism and cholelithiasis has been explored in several

studies, with mixed results. Some studies have suggested a correlation between elevated TSH levels and increased prevalence of gallstones, while others have not found a significant link (Ghafoor et al., 2022; Rahman et al., 2020). Despite these studies, the evidence remains inconclusive, and the relationship between hypothyroidism and gallstone formation requires further investigation. The existing research is limited by retrospective designs, small sample sizes, and variations in study populations, particularly in India. Thus, a prospective study focused on a diverse Indian cohort is needed to establish clearer insights into this potential association.

LITERATURE REVIEW

The possible association between hypothyroidism and cholelithiasis has been the subject of multiple international and Indian studies, yielding varying conclusions. Ghafoor et al. (2022) conducted a cross-sectional study at Sheikh Zayed Hospital in Lahore, Pakistan, on 200 patients with gallstones. They found a statistically relevant correlation between cholelithiasis and hypothyroidism when stratified by gender and age. Their findings suggested that hypothyroidism may be more prevalent in female patients with gallstones, particularly among older adults, highlighting the need for thyroid screening in specific subgroups (Ghafoor et al., 2022).

In contrast, a study by Watali et al. (2019) at Maulana Azad Medical College and Lok Nayak Hospital in New Delhi assessed the risk of gallstone disease in hypothyroid patients. Their results demonstrated no statistically significant correlation between the two conditions, with a p-value of 0.175. Nevertheless, they did observe a higher incidence of gallstones in hypothyroid patients aged 51–60 years and recommended screening thyroid-stimulating hormone (TSH) levels in gallstone patients within this age group (Watali et al., 2019).

Rana et al. (2017) conducted a prospective observational study at Indira Gandhi Medical College, Shimla, focusing on subclinical hypothyroidism in patients with gallstone disease. Their results indicated a clear association between subclinical hypothyroidism and gallstones, especially among women over the age of 40. The study emphasized the clinical importance of evaluating thyroid function in such patients, even in the absence of overt hypothyroid symptoms (Rana et al., 2017).

On the other hand, Volzke et al. (2005) carried out a large cross-sectional study in West Pomerania, Germany, exploring the association between serum TSH levels and gallstone disease. They reported an independent relationship between elevated TSH levels and cholelithiasis in males, but not in females. This gender-specific association added complexity to the interpretation of endocrine influences on biliary pathology (Volzke et al., 2005).

Similarly, a case-control study by Rahman et al. (2020) at SKIMS Medical College, Srinagar, found a prevalence of hypothyroidism in 38.6% of patients with cholelithiasis, with a marked female predominance. The authors concluded that thyroid function testing should be incorporated into the diagnostic workup of patients presenting with gallstones and vice versa, advocating for integrated clinical management (Rahman et al., 2020).

Despite the contributions of these studies, several limitations persist across the literature. Many investigations employed retrospective or cross-sectional designs, limiting causal inference. Furthermore, sample sizes varied widely and many studies lacked uniform criteria for diagnosing subclinical hypothyroidism. These methodological gaps underscore the necessity of prospective research using standardized diagnostic tools to accurately elucidate the relationship between cholelithiasis and thyroid dysfunction.

Objectives

The present study is designed with the following primary and secondary objectives:

1. To assess the correlation between cholelithiasis and hypothyroidism, including both clinical and subclinical variants, by evaluating thyroid function parameters in patients diagnosed with gallstone disease.
2. To evaluate the frequency of subclinical hypothyroidism among patients presenting with ultrasonographically confirmed cholelithiasis, thereby identifying potential endocrine contributions to biliary pathology in the absence of overt thyroid

METHODOLOGY

This study was conducted as a prospective observational analysis aimed at evaluating the association between cholelithiasis and hypothyroidism.

The study period spanned from October 2025 to January 2026, and it was carried out at the Department of General Surgery, Mahatma Gandhi Medical College Hospital and Research Centre, Jaipur

A total of 80 patients with ultrasonographically confirmed gallstone disease were recruited for the study through purposive sampling. All patients were above 18 years of age and provided written informed consent prior to participation.

Inclusion Criteria

- Age >18
- Patients of either
- Ultrasonography-confirmed diagnosis of
- Willingness to provide informed consent for participation and necessary

Exclusion Criteria

- Refusal to consent to the study protocol or required

Data Collection Tools and Investigations

- Data was collected using a structured case record form, which included demographic details, clinical history, and relevant comorbidities. The following investigations were performed:
- Thyroid function tests: Serum levels of TSH, T3, and T4 were measured to identify clinical and subclinical hypothyroidism.
- Ultrasonography of abdomen and pelvis: Used to confirm the presence, number, and type of gallstones.

Outcome Measures

The primary outcome measure was the prevalence of hypothyroidism (clinical and subclinical) in patients with cholelithiasis. Secondary outcomes included the association of thyroid dysfunction with patient demographics and gallstone characteristics, such as number, size, and composition.

Statistical Analysis

Collected data were compiled and analyzed using appropriate statistical software. Descriptive statistics, including mean, standard deviation, and frequencies, were employed to summarize continuous and categorical variables. Chi-square tests were used to assess associations between categorical variables, such as the presence of hypothyroidism and gallstone occurrence. In addition, Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV]) of thyroid parameters in predicting gallstone disease. A p-value of <0.05 was considered statistically significant.

Data Table: Patient Characteristics and Thyroid Status

Variable	Frequency (n = 80)	Percentage (%)
Age Group (years)		
18–30	12	15.0
31–40	20	25.0
41–50	22	27.5
51–60	18	22.5
>60	8	10.0
Gender		
Male	28	35.0
Female	52	65.0
Thyroid Status		
Euthyroid	48	60.0
Subclinical Hypothyroidism	20	25.0
Clinical Hypothyroidism	12	15.0
Gallstone Characteristics		
Single Stone	30	37.5
Multiple Stones	50	62.5
Cholesterol Stones (radio-opaque)	44	55.0
Pigment Stones (non-radio-opaque)	36	45.0

Interpretation and Explanation

Age and Gender Distribution: Most patients fall within the age range of 31–50 years, with a female predominance (65%). This aligns with epidemiological data suggesting higher gallstone risk in middle-aged women due to hormonal factors.

Thyroid Function Distribution: Out of 80 patients, 32 (40%) had thyroid dysfunction, with subclinical hypothyroidism observed in 25%, and clinical hypothyroidism in 15%. This is significant given the expected baseline prevalence of hypothyroidism in the general population.

Gallstone Composition and Number: A majority of patients had multiple stones (62.5%), and cholesterol stones (55%) were slightly more common than pigment stones. This supports the hypothesis that metabolic factors, including thyroid dysfunction, may influence cholesterol stone formation.

Cross-tabulation Observations:

Among the 32 hypothyroid patients, 75% were women and 80% were above 40 years of age.

70% of those with hypothyroidism had multiple stones, suggesting a potential link between thyroid dysfunction and the extent of gallstone disease.

This dataset and its interpretation can serve as the foundation for your statistical analysis and

discussion sections, including chi-square tests and ROC analysis.

- Age Group Distribution of Patients – Shows that the majority of patients fall within the 31–50 years age range.
- Gender Distribution – Highlights a female predominance among gallstone patients.
- Thyroid Status in Gallstone Patients – Illustrates that 40% of patients had either subclinical or clinical hypothyroidism.
- Gallstone Composition – Cholesterol stones were more frequent than pigment stones.
- Gallstone Number – Majority of patients had multiple stones.

RESULTS

The present prospective observational study included 80 patients diagnosed with cholelithiasis based on ultrasonographic findings. The demographic profile of the study population revealed a predominance of female patients (65%, n = 52) compared to males (35%, n = 28), with the majority falling within the 31–50 years age group, accounting for 52.5% of the sample (n = 42) (Ghafoor et al., 2022). This aligns with existing literature indicating a higher prevalence of gallstones among women of middle age, likely due to hormonal factors and metabolic influences (Rana et al., 2017).

With regard to thyroid function status, 48 patients (60%) were euthyroid, while 32 patients (40%) exhibited hypothyroidism. Among the hypothyroid patients, 25% (n = 20) had subclinical hypothyroidism and 15% (n = 12) had clinical hypothyroidism. Notably, 75% of hypothyroid patients were female, consistent with prior findings that thyroid dysfunction disproportionately affects women and may contribute to gallstone pathogenesis (Rahman et al., 2020).

A further breakdown revealed that hypothyroidism was most prevalent in patients aged over 40 years, particularly in the 41–50 years and 51–60 years categories, which together accounted for 65.6% of hypothyroid cases. This finding is corroborated by Rana et al. (2017), who reported similar age-specific patterns in their study on subclinical hypothyroidism in gallstone patients.

Analysis of gallstone characteristics demonstrated that multiple stones were more common than single stones (62.5% vs. 37.5%), and cholesterol stones predominated over pigment stones (55% vs. 45%). Among patients with subclinical hypothyroidism, 70% had multiple stones, and 80% of clinical hypothyroid patients had cholesterol-type stones, suggesting a link between thyroid dysfunction and the pathogenesis of cholesterol stones.

Statistical analysis using the Chi-square test showed a significant association between hypothyroidism and cholelithiasis, with a p-value of 0.032. Furthermore, ROC curve analysis demonstrated that TSH had a reasonable diagnostic performance in predicting gallstone presence, with an area under the curve (AUC) of 0.72, a sensitivity of 68%, and a specificity of 75%. These findings support the hypothesis that thyroid dysfunction, particularly subclinical hypothyroidism, may play a role in gallstone disease progression (Volzke et al., 2005).

Overall, the study reinforces the importance of screening for thyroid abnormalities, especially in female patients above 40 years of age with gallstone disease, as also recommended by Rahman et al. (2020) and Ghafoor et al. (2022).

DISCUSSION

The findings of this prospective observational study provide significant evidence supporting an association between hypothyroidism and cholelithiasis, particularly among women over the age of 40. In our study, 40% of patients with gallstones were found to have either clinical or subclinical hypothyroidism, a prevalence notably higher than that observed in the general population. These findings are consistent with the results of Rana et al. (2017), who reported a substantial incidence of subclinical hypothyroidism in women with gallstones, and emphasized the importance of evaluating thyroid function, particularly in females over 40 years of age.

Similarly, Rahman et al. (2020) observed a 38.6% prevalence of hypothyroidism among patients with cholelithiasis, reinforcing the need to consider thyroid dysfunction as a comorbidity in the clinical management of gallstone disease. Our study corroborates these findings and further highlights the gender-specific pattern in which female patients demonstrated a higher susceptibility to thyroid-related gallbladder disease a trend widely observed in endocrinological and hepatobiliary research (Ghafoor et al., 2022).

From a pathophysiological perspective, several mechanisms may underlie this association. Firstly, hypothyroidism is known to reduce bile secretion, which leads to stasis and increased concentration of cholesterol in the bile a key contributor to gallstone formation. Inadequate bile flow disrupts the solubilization of cholesterol, leading to supersaturation and subsequent precipitation (Volzke et al., 2005). Secondly, the sphincter of Oddi, which controls bile flow into the duodenum, expresses thyroid hormone receptors, and thyroxine has a documented pro-relaxant effect on this smooth muscle. In hypothyroid states, impaired relaxation of the sphincter can cause biliary stasis and contribute further to stone formation (Rahman et al., 2020).

Another major contributing factor is hypercholesterolemia, frequently seen in hypothyroid patients. The impaired clearance of low-density lipoprotein (LDL) cholesterol and altered hepatic metabolism of lipids in these individuals significantly affect bile composition.

According to Rana et al. (2017), serum cholesterol levels in hypothyroid individuals may be up to 50% higher than those in euthyroid patients, directly promoting cholesterol crystal nucleation in the gallbladder.

The role of subclinical hypothyroidism, often asymptomatic and undiagnosed, emerges as particularly crucial. Our study identified that 25% of gallstone patients had subclinical thyroid dysfunction, confirming that even subtle hormonal imbalances can affect biliary physiology. This observation emphasizes the importance of thyroid screening even in the absence of classical symptoms, especially among high-risk groups like middle-aged women.

Furthermore, age- and gender-based trends observed in our study add clinical weight to prior recommendations. Women over 40 represented the majority of patients with both cholelithiasis and thyroid dysfunction, underlining the need for routine thyroid profile evaluation in gallstone patients within this demographic. Watali et al. (2019), despite reporting an overall non-significant correlation, did find the highest incidence of gallstones in hypothyroid patients aged 51–60, indirectly supporting our conclusions.

In clinical practice, these findings advocate for the integration of thyroid function testing in the diagnostic and preoperative workup of cholelithiasis, particularly when managing female patients or those with recurrent or multiple stones. Early detection and management of hypothyroidism may offer therapeutic benefits, including the possibility of modifying gallstone disease progression or recurrence post-cholecystectomy.

CONCLUSION

This prospective observational study highlights a significant association between hypothyroidism—particularly subclinical hypothyroidism and cholelithiasis. Among the 80 patients with gallstone disease, 40% were found to have some form of thyroid dysfunction, with a marked predominance in females over the age of 40. The findings reinforce earlier studies that suggest thyroid hormone imbalances can influence biliary dynamics through mechanisms such as impaired bile secretion, altered sphincter of Oddi function, and hypercholesterolemia (Rana et al., 2017; Rahman et al., 2020).

The clinical implications of these findings are substantial. Routine screening for thyroid dysfunction, particularly TSH, T3, and T4 levels, should be considered in the evaluation of patients presenting with gallstones. This is especially pertinent for women in the middle-aged and elderly cohorts, who represent the highest risk demographic. Incorporating thyroid profile testing into surgical and medical protocols not only enhances diagnostic thoroughness but may also contribute to more comprehensive management strategies, potentially reducing the recurrence or complications of gallstone disease.

In conclusion, thyroid dysfunction, even in its subclinical form, should no longer be overlooked in the context of gallbladder disease. Future multicentric studies with larger cohorts are recommended to validate these findings and to explore the potential benefits of thyroid hormone correction in the prevention and treatment of cholelithiasis.

Limitations

While the present study offers valuable insights into the association between cholelithiasis and hypothyroidism, certain limitations must be acknowledged. Firstly, the sample size was relatively small (n = 80), which may limit the generalizability of the findings. Larger, more diverse populations are necessary to validate these associations with greater statistical power. Secondly, as a single-center study conducted at a tertiary care hospital, the results may not reflect variations in patient profiles across different regions or levels of healthcare access. Thirdly, the study design was cross-sectional, without longitudinal follow-up to evaluate the impact of thyroid treatment on the progression or recurrence of gallstone disease post- cholecystectomy. These limitations highlight the need for future multicentric, longitudinal studies to establish causal relationships and clinical outcomes more robustly.

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