

ORIGINAL ARTICLE

Association between Hypothyroidism and Gallstone Disease: A Tertiary Care Center Prospective Study

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ABSTRACT

Background: Cholelithiasis is a common gastrointestinal disorder influenced by metabolic and endocrine factors. Subclinical hypothyroidism, characterized by elevated TSH levels while FT4 levels remain normal, has been linked to metabolic dysregulation, which may indirectly contribute to gallstone formation. However, the exact association between subclinical hypothyroidism and cholelithiasis is still debated.

Aim: To assess the association between hypothyroidism and gallstone disease in a hospital-based population, and to analyze metabolic variables along with age that may influence this relationship.

Methods: A hospital-based Prospective study was conducted involving 46 patients, 28 with gallstone disease (cases) and 28 without gallstones (controls). Both groups underwent comprehensive clinical evaluation, laboratory testing, imaging, and gallstone analysis, where applicable. Data were analysed using appropriate tests to assess significance.

Results: Hypothyroidism was significantly more prevalent in the case group (46%) than in controls (12%). Cholesterol stones were the most common type, predominantly among hypothyroid patients (92.5%). Female sex and age 25–45 years were the predominant demographic factors. A significant association was found between Hypothyroidism and gallstone disease ($p<0.05$).

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Conclusion: The study designates a potential link between hypothyroidism and cholelithiasis, especially in middle-aged females with cholesterol-rich stones. Thyroid function screening in gallstone patients may aid in initial diagnosis and prevention. Supplementary longitudinal research is necessary to discover causality and therapeutic consequences.

KEYWORDS

- Hypothyroidism • Cholelithiasis • Metabolic Diseases • Thyroid Diseases
- Cholesterol Stones

INTRODUCTION

Gallstone disease (cholelithiasis) is a significant global health problem, affecting 10–20% of the adult population.¹ It constitutes one of the leading causes of hospital admissions for gastrointestinal diseases.² The pathogenesis of gallstones is multifactorial, involving genetic predisposition, environmental influences, dietary habits, obesity, dyslipidemia, and various endocrine factors.³ Among endocrine disorders, hypothyroidism has been suggested as a contributing factor to gallstone formation⁴. Thyroid hormones regulate several key processes relevant to biliary physiology, including hepatic cholesterol metabolism, bile acid synthesis, and gallbladder motility⁵. In hypothyroidism, reduced hepatic cholesterol clearance and impaired relaxation of the sphincter of Oddi may predispose to cholesterol supersaturation of bile, biliary stasis, and ultimately stone formation.⁶

Subclinical hypothyroidism, defined as elevated thyroid-stimulating hormone (TSH) with normal free thyroxine (FT4), is increasingly recognized in the general population⁷. Although often asymptomatic, it is associated with metabolic disturbances such as dyslipidemia, obesity, and insulin resistance all recognized risk factors for gallstones⁸. However, the relationship between hypothyroidism and gallstone disease remains controversial, with conflicting results from different studies.⁹

The present study was conducted to evaluate the association between hypothyroidism and gallstone disease in a hospital-based population, and to analyze metabolic and demographic variables particularly age and sex that may influence this relationship.

MATERIALS AND METHODS

Study Design

This was a prospective, hospital-based observational study conducted at a tertiary care center. The study spanned over a defined period and included both inpatient and outpatient populations.

Study Population

A total of 56 patients were initially screened. After applying inclusion and exclusion criteria, 46 patients were enrolled, of which:

- 28 patients formed the case group (with gallstones confirmed on ultrasonography).
- 18 patients served as controls (without gallstones on ultrasonography).

Inclusion Criteria

- Adults (>18 years of age).
- Both sexes included.
- Cases: Patients with ultrasonographically confirmed gallstones.
- Controls: Patients undergoing abdominal ultrasonography for other complaints, with no gallstones detected.

Exclusion Criteria

- Known history of chronic liver disease or hemolytic anemia.
- Patients who had undergone prior biliary surgery.
- Pregnant women.
- Patients on lipid-lowering drugs or thyroid replacement therapy.

Data Collection

All participants underwent:

- Clinical evaluation: Age, sex, presenting symptoms, family history.

- Laboratory tests: Serum TSH, FT4, fasting lipid profile, liver function tests.
- Imaging: Abdominal ultrasonography to detect presence and type of gallstones.
- Stone analysis (for operated cases): Chemical composition studied and classified into cholesterol, pigment, or mixed stones.

RESULTS

Demographic Profile

Table 1: Demographic Profile of Study Population

Variable	Cases (Gallstones, n=28)	Controls (n=18)	Total (%)	Mean	SD	P-value	(N = 46)
Sex							
Female	24 (85.7%)	8 (44.4%)	32 (68%)				
Male	4 (14.3%)	10 (55.6%)	14 (32%)	11.5	8.70	0.008 (Sig)	
Age Group							
25–45 years	22 (78.6%)	6 (33.3%)	28 (59%)				
46–60 years	5 (17.9%)	8 (44.4%)	13 (27%)				
>60 years	1 (3.5%)	4 (22.3%)	5 (14%)	7.67	7.39	0.007 (Sig)	

- A total of 46 patients were included: 28 cases with gallstones and 18 controls.
- Females formed the majority (85.7%), while males constituted 14.3%.
- The age distribution showed that most patients belonged to the 25–45-year age group (78.6%), followed by 46–60 years (17.9%) and >60 years (1%).
- Female predominance was observed in both cases and controls but was more pronounced in the gallstone group.

Prevalence of Hypothyroidism

Table 2: Prevalence of Hypothyroidism in Study Groups

Thyroid Status	Cases (n=28)	Controls (n=18)	p-value
Hypothyroid	13 (46%)	2 (12%)	<0.05 (Significant)
Euthyroid	15 (54%)	16 (88%)	—

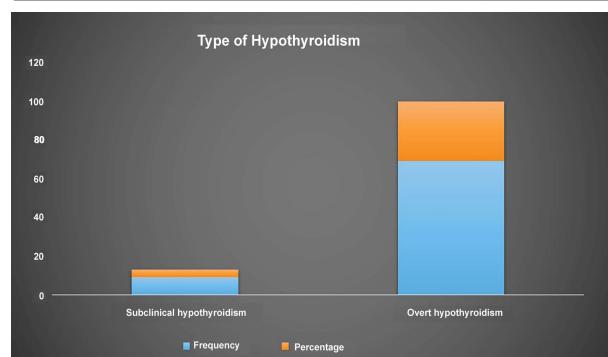
- Hypothyroidism was present in 13 out of 28 gallstone patients (46%), compared to only 2 out of 18 controls (12%).
- The difference was statistically significant ($p < 0.05$).

Statistical Analysis

Data were analyzed and descriptive statistics were applied for demographic variables. Chi-square test and Fisher's exact test were used for categorical variables, while Student's t-test was used for continuous variables. A p-value of <0.05 was considered statistically significant.

Table 3: Pattern of Hypothyroidism Among Gallstone Patients (n = 13)

Type of Hypothyroidism	Frequency	Percentage
Subclinical hypothyroidism	9	69.2
Overt hypothyroidism	4	30.8

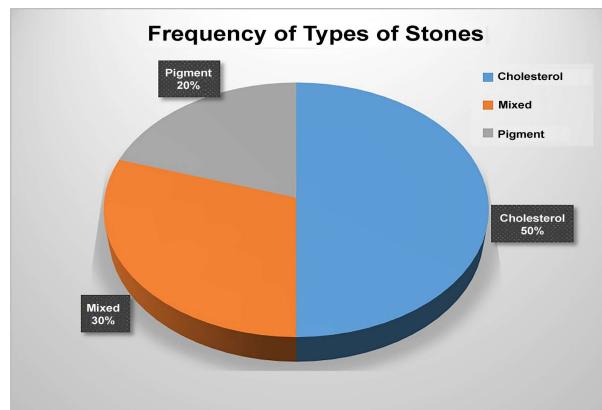


- Among hypothyroid cases, subclinical hypothyroidism accounted for the majority (69%), while overt hypothyroidism was found in 31%.
- Controls largely maintained normal thyroid function profiles.

Gallstone Composition

Table 4: Gallstone Composition ($n = 40$ stones analyzed)

Type of Stone	Frequency	Percentage
Cholesterol	20	50%
Mixed	12	30%
Pigment	8	20%
Mean		13.3
SD		6.11
P value		0.018 (Significant)



- Of the gallstones analyzed, **cholesterol stones accounted for 92.5%**, followed by mixed stones (5%) and pigment stones (2.5%).
- The majority of cholesterol stones were found in patients with hypothyroidism, highlighting the metabolic link.

Age and Sex Distribution

Table 5: Age and Sex Distribution of Hypothyroid Gallstone Patients ($n = 13$)

Variable	Frequency	Percentage
Sex		
Female	10	78%
Male	3	22%
Age Group		
25–45 years	8	62%
46–60 years	3	23%
>60 years	2	15%

- Female patients accounted for **78% of hypothyroid gallstone cases**, with the highest incidence in the **25–45-year age group**.

- Male patients represented a smaller fraction but still demonstrated an association between hypothyroidism and gallstone formation.

DISCUSSION

The present hospital-based prospective study demonstrates a significant association between hypothyroidism and gallstone disease. Nearly half of the gallstone patients (46%) were hypothyroid compared to only 12% in the control group, a difference that reached statistical significance ($p < 0.05$). Moreover, the majority of stones in hypothyroid patients were cholesterol stones, and the demographic analysis showed a clear predominance among middle-aged females (25–45 years).

Comparison with Previous Studies

Our findings are consistent with several published reports. Inkinen *et al.* (2007) observed a higher prevalence of subclinical hypothyroidism among patients with common bile duct stones, suggesting a link between thyroid dysfunction and choledocholithiasis.² Similarly, Eshraghian & Eshraghian (2011) reviewed mechanisms such as cholesterol supersaturation and impaired sphincter of Oddi relaxation.³ Similarly, Volzke *et al.* (2005) reported that thyroid function, particularly subclinical hypothyroidism, was associated with an increased risk of gallstones in a population-based study¹. More recent reviews Ravi *et al.*, (2023)⁴, Han & Zhu, (2025)⁵ further reinforce the notion that thyroid dysfunction both overt and subclinical may act as a metabolic risk factor for cholelithiasis.

However, not all studies are in agreement. Certain cross-sectional analyses have failed to establish a statistically significant correlation between hypothyroidism and gallstones. Variations in study design, sample size, population genetics, iodine status, and diagnostic thresholds for subclinical hypothyroidism may explain these discrepancies. Nevertheless, the overall trend across multiple studies including ours leans towards a positive association.¹⁰

Pathophysiological Mechanisms⁷⁻⁹

The pathogenesis of gallstone formation in hypothyroid patients appears multifactorial:

1. Altered Cholesterol Metabolism

- Hypothyroidism reduces hepatic LDL receptor activity and decreases clearance of plasma cholesterol, resulting in cholesterol-rich bile.
- This supersaturation predisposes to cholesterol crystallization and gallstone formation.

2. Bile Acid Metabolism

- Thyroid hormones stimulate cholesterol 7-alpha-hydroxylase, the rate-limiting enzyme in bile acid synthesis.
- Hypothyroidism reduces bile acid production, leading to impaired cholesterol solubilization in bile.

3. Gallbladder Motility

- Hypothyroidism is associated with reduced gallbladder contractility, leading to biliary stasis.
- Biliary stasis allows cholesterol crystals to accumulate and grow into stones.

4. Sphincter of Oddi Dysfunction

- Experimental data suggest hypothyroidism may impair relaxation of the sphincter of Oddi, impeding bile flow and promoting stasis.

These mechanisms explain the predominance of cholesterol stones among hypothyroid patients observed in our study (92.5%).

Demographic Correlation

The female preponderance and the peak age group of 25–45 years are well established risk factors for gallstone disease. Estrogen increases biliary cholesterol secretion, and when combined with hypothyroidism-induced bile stasis, the risk of cholesterol gallstones is magnified. Our study highlights this additive risk, underscoring the importance of evaluating thyroid status particularly in women of reproductive and middle age.

Clinical Implications

The findings of this study carry several clinical implications:

- **Screening:** Routine thyroid function testing in gallstone patients may help detect undiagnosed subclinical hypothyroidism.

- **Prevention:** Early diagnosis and treatment of hypothyroidism may reduce the risk of gallstone formation, although prospective interventional studies are needed to confirm this.
- **Holistic Management:** For patients with gallstones and coexistent hypothyroidism, a multidisciplinary approach involving endocrinologists and surgeons may improve outcomes.

Limitations of the Study

Despite the significant findings, the study has limitations:

- Small sample size, which may limit the generalizability of results.
- Hospital-based design, possibly introducing selection bias.
- Lack of longitudinal follow-up, which prevents establishing a causal relationship between hypothyroidism and gallstone disease.
- No assessment of dietary, genetic, or lifestyle factors, which are known contributors to gallstone formation.

Future Directions

To establish causality, larger multicentric longitudinal studies are needed. In addition, interventional studies evaluating whether thyroid hormone replacement in subclinical hypothyroidism reduces gallstone incidence would be of immense clinical value. Molecular studies examining thyroid hormone effects on bile composition and gallbladder motility could further elucidate the mechanisms underlying this association.

CONCLUSION

This prospective hospital-based study highlights a significant association between hypothyroidism and gallstone disease, with hypothyroidism observed nearly four times more frequently among gallstone patients compared to controls. Cholesterol stones predominated, particularly among hypothyroid individuals, and middle-aged females represented the most affected group. These findings suggest that thyroid dysfunction contributes to gallstone pathogenesis through metabolic and motility-related mechanisms. Routine thyroid function screening in patients with gallstones may aid in early detection of

subclinical hypothyroidism and guide holistic management. Larger longitudinal studies are warranted to clarify causality and evaluate the potential preventive role of thyroid hormone replacement in gallstone disease.

Key Points

- Hypothyroidism was significantly more prevalent among gallstone patients (46%) compared to controls (12%).
- Cholesterol stones were the predominant type (92.5%), especially in hypothyroid patients.
- Female sex and age group 25–45 years were major demographic risk factors.
- Thyroid dysfunction screening in gallstone patients may have diagnostic and preventive value.

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