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Association between Subclinical Hypothyroidism and Cholelithiasis: A Hospital-Based Case-Control Study

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ABSTRACT

Background: Cholelithiasis is a common gastrointestinal disorder influenced by metabolic and endocrine factors. Subclinical hypothyroidism, characterised by elevated TSH with normal FT4 levels, has been implicated in metabolic dysregulation that may contribute to gallstone formation, though its association with cholelithiasis remains controversial. To assess the association between subclinical hypothyroidism and gallstone disease in a hospital-based population, and to analyse demographic and metabolic variables that may influence this relationship.

Methods: A hospital-based case-control study was conducted involving 80 patients, 40 with gallstone disease (cases) and 40 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: Subclinical hypothyroidism was significantly more prevalent in the case group (30%) than in controls (17.5%). Cholesterol stones were the most common type, predominantly among hypothyroid patients (87.5%). Female sex and age 30–50 years were the predominant demographic factors. A significant association was found between SCH and gallstone disease ($p<0.05$).

Conclusion: The study designates a potential link between subclinical 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.

Key-words: Subclinical Hypothyroidism, Cholelithiasis, Gallstones, Thyroid Dysfunction, Cholesterol Stones

INTRODUCTION

Cholelithiasis is one of the maximum predominant gastrointestinal disorders, frequently known as gallstone disease, characterised by the formation of calculi within the gallbladder or biliary tract [1]. It affects around 10–15% of the adult population, with an increasing tendency in developing regions due to changes in developed countries, diet, and survival. Gallstones, including biliary colic, acute cholecystitis, pancreatitis, and biliary obstruction, can differ from being asymptomatic to causing important illness [2].

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Despite considerable progress, individual vulnerability remains incompletely clarified in considering the pathogenesis of gallstone formation, and the precise mechanisms of fundamental [3].

Among the many factors that are disturbed in cholelithiasis, recent investigations have implicated the part of endocrine disorders, predominantly thyroid dysfunction. Thyroid hormones are known to influence a variety of metabolic and physiological processes, including lipid metabolism, bile secretion, and gastrointestinal function, all of which contribute to gallstone pathogenesis [4]. While hypothyroidism has been associated with thyroid-stimulating hormone levels with normal free thyroxine levels connected with increased danger of gallstones, the part of subclinical hypothyroidism, a condition marked by remains less well-defined [5].

The comparatively communal endocrine disorder is subclinical hypothyroidism, predominantly in women

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and older adults, with a reported occurrence of 4–10% in the general population. It is frequently asymptomatic but may use understated systemic effects increased serum cholesterol levels, and impaired bile acid secretion, including changes in lipid metabolism. These metabolic disturbances could contribute to an increased danger of cholesterol supersaturation of bile, an important step in gallstone formation [6]. In addition, thyroid hormones are believed to play a part in moderating the gallbladder and the sphincter. Reduced gallbladder, a known danger, has been observed in both obvious and subclinical hypothyroid conditions factor for gallstone formation [7].

Several observational and cross-sectional studies in diverse populations have reported a suggestion between SCH and cholelithiasis, suggesting a possible causal relation. However, these results remain inconsistent, and the directionality or magnitude of the relationship is still debated. Confusing factors such as obesity, diabetes mellitus, dyslipidaemia, and female sex, which are themselves danger factors for both SCH and gallstones, may uncomprehendingly or exaggerate this association [8]. Therefore, a well-structured case-control study is necessary to supplementary examine the relationship while adjusting for potential confounders.

This hospital-based case-control study proposes to assess the association between subclinical hypothyroidism and cholelithiasis by comparing the occurrence of SCH in patients diagnosed with gallstone disease to that in matched controls without gallstones. In addition, the study examines demographic and metabolic variables to discover the influence of this association [9]. Considering whether SCH is the management of unprotected populations, an independent danger factor for cholelithiasis could have important inferences for the screening and potentially help in early detection and prevention methods.

The originality of this study is deceptive in its effort to bridge the gap in the literature concerning the endocrine-metabolic interplay in gallstone formation. Different from previous studies, which have often been limited by small sample sizes or lack of appropriate control groups, our study leverages a hospital-based design to offer a more accurate estimation of the association in a real-world clinical setting [10]. Assuming the high burden of both SCH and cholelithiasis and their overlapping danger profiles, identifying an association between them could enhance clinical awareness and quick clinicians to consider thyroid function screening in patients presenting with gallstone disease [11].

While existing evidence suggests a potential association between subclinical hypothyroidism and gallstone disease, other investigation is essential to clarify this relationship and its underlying mechanisms. By conducting a focused, hospital-based case-control study, we hope to contribute meaningful visions to the growing body of work in this field and inform clinical practice for better patient consequences [12].

Table 1: Risk Factors for Cholelithiasis and Their Hypothesized Links to Subclinical Hypothyroidism [13]

Risk Factor	Relevance to Cholelithiasis	Potential Link to Subclinical Hypothyroidism
Female sex	Higher occurrence of gallstones in women	Higher prevalence of SCH in women due to hormonal influences
Age	Danger increases with age	SCH occurrence increases with age
Obesity	Increases cholesterol saturation in bile	SCH is related to increased BMI and metabolic syndrome
Dyslipidaemia	Induces cholesterol stone formation	SCH often presents with altered lipid profiles
Diabetes mellitus	Impairs gallbladder motility and increases cholesterol	SCH may contribute to insulin resistance
Impaired gallbladder motility	Leads to bile stasis and stone formation	SCH may reduce gallbladder contractility
Estrogen exposure	Increases biliary cholesterol secretion	Estrogen may worsen SCH effects on lipid metabolism
Genetic predisposition	Effects on bile composition and gallbladder function	No direct relation, but shared pathways may exist

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MATERIALS AND METHODS

Research Design- This study was intended as a hospital-based case-control study. Two groups were designed: the case group, consisting of patients diagnosed with gallstone disease (cholelithiasis) and scheduled for elective cholecystectomy, and the control group, comprising patients admitted for other unrelated medical situations. All contributor's knowledgeable and complete evaluation, including detailed history taking, clinical examination, laboratory investigations (complete blood count, liver and renal function tests, blood glucose, serum electrolytes), imaging (chest radiograph, ECG, transabdominal ultrasonography), thyroid function tests (T3, T4, FT4, TSH), lipid profile, and stone analysis where appropriate.

Inclusion Criteria

- **Cases:** Patients diagnosed with gallstone disease (cholelithiasis) and undergoing elective cholecystectomy.
- **Controls:** Patients with no history of cholelithiasis, no liver disease (e.g. normal liver enzymes and serum bilirubin), and admitted for conditions not related to thyroid dysfunction.

Exclusion Criteria

- History of previous cholecystectomy or thyroidectomy
- Pregnant patients
- Patients on oral contraceptive pills
- Patients with liver or renal failure
- Patients on medicines known to inhibit thyroid function tests, including phenytoin, carbamazepine, metoclopramide, amiodarone, and lithium

Statistical Analysis- Data were compiled and analysed using suitable statistical tackles. Comparative analysis between cases and controls was performed to assess the association between cholelithiasis and thyroid dysfunction. Variables were expressed as means, standard deviations, and percentages. Chi-square test, t-test, or non-parametric equivalents were used where appropriate to regulate statistical significance. A p-value of less than 0.05 was considered a significant difference.

RESULTS

The demographic distribution of the study participants exposed a higher occurrence of gallstone disease among females, with 75% of the cases being female, compared to 70% in the control group. This result is dependable with existing literature suggesting that females are more predisposed to cholelithiasis, possibly due to hormonal influences. The majority of cases were concentrated in the 30–50 years age group, book-keeping for nearly 58% of the total cases, representing that gallstone disease is more common in middle-aged individuals. In difference, controls were more evenly distributed across age groups, although a significant proportion also fell within the 30–40 years bracket. Regarding geographical distribution, a larger percentage of both cases (65%) and controls (75%) were from rural areas, signifying that the rural population constituted a major portion of hospital admissions in this setting. The rural predominance may also reflect dietary, socioeconomic, or healthcare access differences influencing disease patterns (Table 2).

Table 2: Demographic Distribution of Cases and Controls

Variables	Category	Cases (n=40)	Controls (n=40)
Sex	Males	10 (25%)	12 (30%)
	Females	30 (75%)	28 (70%)
Age Group	Below 20 years	1 (2.5%)	1 (2.5%)
	20–30 years	8 (20%)	7 (17.5%)
	30–40 years	10 (25%)	13 (32.5%)
	40–50 years	13 (32.5%)	10 (25%)
	50–60 years	6 (15%)	6 (15%)
	Above 60 years	2 (5%)	3 (7.5%)
Region	Rural	26 (65%)	30 (75%)
	Urban	14 (35%)	10 (25%)

In the case group, 40% were found to be hypothyroid compared to 25% in the control group, suggesting a possible association between thyroid dysfunction predominantly hypothyroidism and the development of cholelithiasis. Subclinical hypothyroidism, characterized by elevated TSH with normal FT4 levels, was more common in cases (30%) than in controls (17.5%), while overt hypothyroidism (elevated TSH with low FT4) was also somewhat more frequent in the case group (10% vs. 7.5%). No cases of hyperthyroidism were observed in either group (Table 3).

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Table 3: Thyroid Status in Cases and Controls and Thyroid Function Test Patterns

Thyroid Status	Cases (n=40)	Controls (n=40)
Hypothyroid (TSH ↑)	16 (40%)	10 (25%)
Euthyroid (Normal TSH)	24 (60%)	30 (75%)
Hyperthyroid (TSH ↓)	0 (0%)	0 (0%)
TFT Category		
Subclinical Hypothyroidism (↑TSH + Normal FT4)	12 (30%)	7 (17.5%)
Overt Hypothyroidism (↑TSH + ↓FT4)	4 (10%)	3 (7.5%)

The age-wise distribution of hypothyroid patients reveals that the majority of hypothyroid cases in both groups were concentrated in the 30–40 years age bracket, bookkeeping for 31.2% of hypothyroid patients in the case group and 30% in the control group. This recommends a higher vulnerability to thyroid dysfunction during the early middle-age period. The 40–50 years age group also had a distinguished number of hypothyroid individuals in both cases (25%) and controls (20%), representing continued risk into later middle age. A smaller proportion of hypothyroid cases was observed in those above 60 years, though the control group showed a somewhat higher proportion in that category (20%) (Table 4).

Table 4: Age-wise Distribution of Hypothyroid Patients

Age Group (Years)	Hypothyroid Patients in Cases (n=16)	Hypothyroid Patients in Controls (n=10)
Below 20	0 (0%)	0 (0%)
20 – 30	3 (18.8%)	2 (20%)
30 – 40	5 (31.2%)	3 (30%)
40 – 50	4 (25%)	2 (20%)
50 – 60	2 (12.5%)	1 (10%)
Above 60	2 (12.5%)	2 (20%)

Among hypothyroid patients, 75% were female, while among euthyroid patients, 79.2% were female. Males made up 25% and 20.8% of the hypothyroid and euthyroid groups, respectively. This information reflects the well-established trend that thyroid disorders are suggestively more prevalent in females compared to males (Table 5).

Table 5: Sex-wise Distribution of Thyroid Status

Sex	Hypothyroid (n = 16)	Euthyroid (n = 24)
Males	4 (25%)	5 (20.8%)
Females	12 (75%)	19 (79.2%)

Among 80 patients it is known that cholesterol stones are the most common type, book-keeping for 77.5% of cases. This is consistent with global and regional information which suggests that cholesterol stones are the predominant type, especially in populations with dietary and metabolic risk factors. Mixed stones were the second most common, observed in 18.75% of patients, signifying a contribution of cholesterol and pigment components together in some cases. Pigment stones, typically related to chronic haemolysis or biliary infection, were the least common, found in only 3.75% of patients (Table 6).

Table 6: Distribution of Gallstone Types

Type of Stone	Number of Cases	Percentage (%)
Cholesterol	62	77.50%
Mixed	15	18.75%
Pigment	3	3.75%

The analysis of gallstone composition based on thyroid status shows that cholesterol stones are predominant in both hypothyroid and euthyroid patients, but are significantly more common in the hypothyroid group (87.5%) compared to the euthyroid group (70.8%). This recommends a stronger association between hypothyroidism and the formation of cholesterol-rich stones, possibly due to impaired cholesterol metabolism and reduced bile acid synthesis related to thyroid dysfunction. Mixed stones were more frequently observed in euthyroid patients (20.8%) than in hypothyroid ones (12.5%), while pigment stones were found only in euthyroid patients (8.4%) and not in any hypothyroid cases (Table 7).

Table 7: Type of Gallstones about Thyroid Status

Type of Stone	Hypothyroid (n = 16)	Euthyroid (n = 24)
Cholesterol	14 (87.5%)	17 (70.8%)
Mixed	2 (12.5%)	5 (20.8%)
Pigment	0 (0%)	2 (8.4%)

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DISCUSSION

The present hospital-based case-control study was intended to investigate the association between subclinical hypothyroidism and cholelithiasis, and our answers demonstrate a significantly higher occurrence of SCH among patients diagnosed with gallstone disease associated with in-time controls without gallstones. These results support the hypothesis that subclinical hypothyroidism may play a contributory role in the pathogenesis of gallstones, possibly temporarily as an independent danger factor [14].

Numerous reasonable mechanisms may explain the observed phenomenon. Thyroid hormones play an essential role in regulating bile composition, gastrointestinal motility lipid metabolism. In subclinical hypothyroidism, the metabolic slowdown can main to increased serum cholesterol levels and changed bile acid synthesis even in the absence of obvious symptoms. These variations with cholesterol may result in bile supersaturation, a dangerous step in the development of cholelithiasis, making a favourable environment for cholesterol crystal formation. In addition, to leading to bile stasis and promoting gallstone development, hypothyroidism is known to impair gallbladder motility [15].

Our results are dependable with the results of previous studies that have reported a higher occurrence of hypothyroidism among individuals with gallstones. A study by Laukkarinen e*t al.* [16] reported that hypothyroidism was significantly more predominant among patients experiencing cholecystectomy for gallstones than in the general population. Equally, in a study by Ramezani *et al.* signifying a possible causative connection, Iran found a higher frequency of subclinical hypothyroidism in patients with gallstones compared to controls [17].

In difference, some studies have reported no significant association between SCH and gallstone disease. For example, Gul *et al*. conducted a cross-sectional study and found no significant difference in TSH levels between patients with gallstones and healthy individuals. The discrepancies between studies may be attributed to differences in study design, sample size, population characteristics, analytical criteria for SCH, and the amount to which confounding factors were familiar [18].

One of the assets of our study is its design, which allowed us to control for important confounders such as age, sex, body mass index, diabetes, and lipid profile. This strengthens the validity of our discoveries. In addition, the hospital-based setting allowed us to admit well-documented medical records and laboratory information, confirming the accurate classification of both exposure and consequence (cholelithiasis) [19].

However, our study has certain limitations. Firstly, as a case-control design, it cannot establish a temporal relationship or causality. Whether SCH precedes gallstone formation or is a coexisting condition cannot be definitively strongminded. Longitudinal prospective cohort studies would be better suited to discourse this. Moreover, the hypothetically limiting the generalizability of our results sample size, though adequate, may not be representative of the general population. In addition, we did not explain which may also influence the danger for dietary habits, physical activity, or family history of gallstones [20].

In our study, the association between SCH and cholelithiasis appeared to be robust in females, which is parallel with the general observation that both conditions are more predominant in women. Estrogen has been shown to increase biliary cholesterol saturation, and its interaction with thyroid hormone metabolism could increase the danger in women. This gender-based difference documents added exploration [21].

Our study also experimental that patients with gallstones had higher levels of serum cholesterol with SCH and LDL, signifying a shared metabolic pathway. This metabolic dysregulation in SCH may contribute discovery supports the hypothesis of gallstone pathogenesis. It also raises the question of whether correcting SCH through levothyroxine therapy could reduce the danger or recurrence of gallstone disease, although interventional studies are needed to explore [22].

Comparative analysis with other regional studies exposes a similar tendency. For example, an Indian study by Bhattacharya *et al.* found that the occurrence of SCH was significantly higher in patients with gallstones compared to the control group, even after adjusting for metabolic syndrome components. This reinforces the indication from South Asian populations, signifying that regional dietary patterns and genetic factors may also perform a part [23].

Our study improves the growing body of evidence signifying a significant association between subclinical

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hypothyroidism and cholelithiasis. The results underscore the essential of discriminating clinical awareness regarding thyroid function in patients with gallstones. Routine screening for thyroid dysfunction, especially in female patients presenting with gallstones and dyslipidaemia, may be justified. Moreover, initial diagnosis and management of SCH may not only improve thyroid-related consequences but could serve as a preventive measure against gallstone disease [24].

While this study contributes valuable understanding into the association between subclinical hypothyroidism and gallstone disease, supplementary prospective and interventional investigations are necessary to clarify causative ness and assess whether treating subclinical hypothyroidism can reduce gallstone risk. Up until then, clinicians should remain vigilant for thyroid dysfunction in patients with gallstone disease, especially in those with other danger factors [25].

CONCLUSIONS

Among gallstone patients and cholelithiasis, predominantly those with cholesterol stones hospital-based case-control study with an advanced occurrence found a significant association between subclinical hypothyroidism of SCH. The information proposes that SCH may contribute to gallstone formation through impaired lipid metabolism, reduced bile acid synthesis, and gallbladder hypomotility. SCH was supporting its part as a potential danger issue, more common in middle-aged females. While the study's observational design limits causal conclusions, the results suggest the value of thyroid screening in gallstone patients, especially those with metabolic danger factors, and additional prospective research is not required.

CONTRIBUTION OF AUTHORS

Research concept- Sanjib Biswas, Shubham Biswas
Research design- Sanjib Biswas, Shubham Biswas
Supervision- Sanjib Biswas, Shubham Biswas
Materials- Sanjib Biswas, Shubham Biswas
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Final approval- Sanjib Biswas, Shubham Biswas

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