ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 09 | September - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY ON PREVELANCE OF HYPOTHYROIDISM IN DIAGNOSED CASES OF CHOLELITHIASIS

General Surgery

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ABSTRACT

Background: Gallstone disease (GSD) affects a significant portion of the adult population, with hypothyroidism being a potential risk factor. This study explores the prevalence of hypothyroidism among patients with cholelithiasis and its association with gallstone formation. **Material & Methodology:** This prospective observational study was conducted at the Department of General Surgery, Index Medical College Hospital & Research Centre, Indore involving 100 patients diagnosed with symptomatic or asymptomatic cholelithiasis or choledocholithiasis. Patients were evaluated for thyroid dysfunction through thyroid function tests. The study assessed age, gender, symptoms, comorbidities, and ultrasound findings in relation to thyroid status. **Results:** The study population had a mean age of 41.44 years. Hypothyroidism was found in 38% of patients, with 22% having subclinical hypothyroidism and 16% having clinical hypothyroidism. Abdominal pain was the most common symptom, occurring in 34% of patients, while easy fatigability was the most frequent hypothyroid-specific symptom, reported by 16%. Diabetes was the most prevalent comorbidity, affecting 21% of patients. Ultrasound findings revealed that 68% of patients had multiple gallstones, and among those with hypothyroidism, 22 had multiple calculi alone. The prevalence of hypothyroidism was higher in females (48.3%) compared to males (23.8%). **Conclusion:** Hypothyroidism is a significant risk factor for gallstone formation, especially in middle-aged females. The study highlights the need for thyroid screening in patients over 40 with cholelithiasis. Multicenter studies are needed to further explore these findings.

KEYWORDS

Cholelithiasis, subclinical hypothyriodism, dyslipidemia, hyperthyroidism, clinical hypothyroidism

INTRODUCTION

Cholelithiasis, a common gallbladder condition affecting 10 to 15% of adults, is often asymptomatic in over 80% of cases, with its prevalence influenced by age, gender, ethnicity, and comorbidities. Gallstones are more frequently found in females, likely due to the role of estrogen in cholesterol metabolism, and are generally less common in children, except in those with hemolytic anemia. The condition is primarily considered a disease of older adults. [1]

Gallstone disease (GSD), a related biliary system disorder, involves three primary types of gallstones: pigment (brown/black), cholesterol, and mixed stones. [2]

Gallstones may be single or multiple, large or small those containing calcium salts are radio-opaque. Single stones are uncommon but usually consist mainly of cholesterol and arise due to a disorder of the physio-chemical equilibrium which normally maintains cholesterol in micellar form in the bile. [3]

Numerous studies aimed at identifying risk factors for biliary lithiasis in Western populations have concentrated on the role of cholesterol hypersaturation in bile during the nucleation process, which is a key step in the formation of gallstones. [4,5] The high cholesterol content in gallstones has led to the widespread use of bile acids as a nonsurgical treatment for dissolving gallbladder stones.

In Asia, 85% of gallstones are pigment stones, while in the United States, 80% are cholesterol or mixed stones. [6,7] In India, a geographical variation is observed, with a high prevalence of cholesterol gallstones in the northern population, found in both the gallbladder and the common bile duct (CBD). On the other hand, the southern Indian population shows a higher prevalence of pigment stones, also present in both the gallbladder and CBD.[8] However, the composition of gallstones is heterogeneous and varies both within and between populations globally.[3]

Cholesterol, being water-insoluble, relies on the presence and concentration of phospholipids and bile acids in bile for its solubility. Phospholipid-formed micelles keep cholesterol in a stable state. However, when bile acid levels are low or cholesterol is oversaturated, unstable unilamellar phospholipid vesicles form, potentially acting as nuclei for cholesterol crystals, leading to stone formation. Additional factors contributing to gallstone formation include bile stasis due to sphincter of Oddi dysfunction, biliary sludge, bile saturation in the gallbladder, and chemical imbalances in bile composition. [9]

Hypothyroidism, affecting approximately 3.7% of the global population with a higher incidence in women, is associated with an increased risk of gallstone formation. This connection is largely due to elevated cholesterol levels, which contribute to gallstone development, along with impaired gallbladder motility and bile flow. Additionally, dysfunction of the sphincter of Oddi can raise bile duct pressure, further promoting gallstone formation. Research indicates that between 13% and 24% of individuals with hypothyroidism may develop gallstones. [7,10]

Over the past decade, there has been considerable discussion regarding the potential connection between thyroid disorders and gallstone disease (GSD). Research by Rizos et al. [11] suggests that thyroid dysfunction may affect lipid metabolism and bile composition, potentially contributing to GSD.

Anecdotal evidence from studies by Tombisana et al.[12], Raghuvanshi et al.[7], and Laukkarinen et al.[13] indicates that hypothyroid patients often experience reduced biliary flow due to delayed gallbladder emptying, which is crucial in GSD development. Additionally, some studies have explored the prevalence of previously undiagnosed thyroid disorders in GSD patients, suggesting a possible link between hypothyroidism and GSD.

This context highlights the need for the present study, which aims to evaluate the prevalence of hypothyroidism among individuals diagnosed with cholelithiasis.

MATERIAL AND METHODS

After approval from institutional ethical committee, the present prospective and observational study was conducted in Department of Surgery at Index medical College Hospital and Research Centre, Indore and 100 cases of diagnosed cases of symptomatic or asymptomatic cholelithiasis/ choledocholithiasis or both; visiting the OPD during the study duration were evaluated. All patients satisfying the inclusion criteria were included after obtaining a written informed consent.

Inclusion Criteria

- Patients with symptomatic or asymptomatic cholelithiasis/ choledocholithiasis or both
- Patients giving consent for the participation in the study.

Exclusion Criteria

- Patients with previous history of hypothyroidism on treatment
- Non-Consenting patients

Methodology

The sampling method used was non-random and purposive. Upon admission, each patient presenting with symptoms suggestive of extrahepatic biliary lithiasis underwent a brief history taking and a physical examination in the surgery department. In addition to the clinical examination, symptoms of hypothyroidism such as loss of appetite, weight gain, fatigue, constipation, cold intolerance, and menstrual disturbances were assessed. Diagnostic investigations, including abdominal ultrasonography (USG) and thyroid function tests along with baseline investigations, were also conducted, as per standard protocol.

Blood samples (5 mL each) were collected from all patients undergoing cholecystectomy and tested for hypothyroidism in the hospital laboratory. Hypothyroidism was identified if the thyroid-stimulating hormone (TSH) level was 5.5 µ IU/mL or higher, with normal or low T3 and T4 levels. The tests were conducted by an experienced technician, and data on age, gender, height, weight, BMI, and thyroid status were recorded using a pre-designed form.

Patients were then informed about their condition and the potential treatment options. All relevant details regarding the study were thoroughly explained to the patients or their legal guardians.

Following a thorough evaluation and appropriate preparation, patients requiring surgical intervention were scheduled for surgery. Strict aseptic precautions were maintained throughout the surgical procedures.

Once data collection was completed, the information was systematically compiled for analysis.

Statistical Analysis

Raw data was collected statistically and entered on Microsoft excel sheet 10.0 and analyzed using SPSS software 22.0 version. For variables with a normal distribution, the data were presented as Mean ± SD. For variables that were not normally distributed, the data were expressed as the median with an interquartile range. Categorical variables were represented as percentages or proportions. Descriptive statistics, such as percentages, were used to summarize the characteristics of the data. Various statistical tests were employed to calculate associations, including the unpaired t-test for normally distributed data and the chi-square test for dichotomous variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Total of 100 cases of cholelithiasis studied and following conclusions were drawn. The mean and standard deviation of age, height, weight and BMI were 41.44 ± 12.9, 164.54 ± 11.65, 68.27± 11.85 and 25.59 ± 7.29 respectively

Age Distribution: Among the study group, 60% were in the age group of >41 yrs. 18% each in age groups 21-30 yrs. and 31-40 yrs. and 4% below 20 yrs.

Sex Distribution: Among the study group, 58.0% are females and 42.0% are males.

Prevalence of Hypothyroidism: Among the study group, 38%, i.e. 38 patients had hypothyroidism and 62%, i.e. 62 patients were in euthyroid state.

Prevalence of Subclinical and Clinical Hypothyroidism: Among the study group, 22%, i.e. 22 patients had subclinical hypothyroidism, 16%, i.e. 16 patients had clinical hypothyroidism and 62%, i.e. 62 patients were in euthyroid state. (Table 1)

Table 1. Clinico-Demographic Distribution of patients

Variable	No. of Patients (N=100)	Percentage
Age		
<20	4	4.0
21-30	18	18.0
31-40	18	18.0
>41	60	60.0
Gender		
Female	58	58.0
Male	42	42.0
Diagnosis		
Euthyroid	62	62.0
Hypothyroid • Subclinical hypothyroid • Clinical hypothyroid	 22 16	 22.0 16.0

Distribution According to Age and Thyroid Function: In the study, thyroid status varied by age group. Among patients below 20 years, all 4 (100%) were euthyroid. In the 21–30-year age group, 11.1% (2 patients) had thyroid dysfunction, while 88.9% (8 patients) were euthyroid. Among those aged 31-40 years, 44.4% (4 patients) had thyroid dysfunction, and 55.6% (5 patients) were euthyroid. In patients over 41 years, 46.6% (14 patients) had thyroid dysfunction, and 53.3% (16 patients) were euthyroid. Overall, 38% of the 50 patients had thyroid dysfunction, while 62% were euthyroid. Further distribution of hypothyroid patients as per subclinical and clinical hypothyroidism is illustrated in Table 3

Distribution According to Sex and Thyroid Function: Among the study participants, 23.8% of males (10 patients) were hypothyroid, while 76.2% (32 patients) were euthyroid. In contrast, 48.3% of females (28 patients) had hypothyroidism, and 51.7% (30 patients) were euthyroid. Of the 38 hypothyroid patients, 10 were male and 28 were female. Further details on the distribution of subclinical and clinical hypothyroidism are presented in Table 2.

Table 2. Distribution According to Age, Sex and Thyroid Function

Age	Euthyroid	Hypothyroid
<20	4 (100%)	0 (0)
21-30	16 (88.9%)	2 (11.1%)
31-40	10 (55.6%)	8 (44.4%)
>41	32 (53.3%)	28 (46.7%)
Sex		
Male	32 (76.2%)	10 (23.8%)
Female	30 (51.7%)	28 (48.3%)

Table 3. Distribution According to Age, Sex and Subclinical, Clinical Hypothyroidism

	Euthyroid (N=62)	Hypothyroid (N=38)	
		Subclinical Hypothyroid (N=22)	Clinical Hypothyroid (N=16)
Age			
<20	4 (100%)	0 (0)	0 (0)
21-30	16 (88.9%)	2 (11.1%)	0 (0)
31-40	10 (55.6%)	2 (11.1%)	6 (33.3%)
>41	32 (53.3%)	18 (30%)	10 (16.7%)
Gender			
Male	32 (76.2%)	6 (14.3%)	4 (9.5%)
Female	30 (51.7%)	16 (27.6%)	12 (20.7%)

Distribution According to Comorbidities: Diabetes was the predominant co- morbidity in this study- in 21% of the patients.

Table 4. Distribution According to Comorbidities

Co- Morbidity	Number	Percentage
Diabetes Mellitus	16	16.0
Hypertension	21	21.0
Both DM and HT	8	8.0
No co morbidity	53	55.0

Symptoms and Signs of the Patients in the Study: Abdominal pain was the most common symptom presenting in 34%, i.e. 34 patients. Among the specific symptoms of hypothyroidism, easy fatigability was the most common symptom presenting in 16%, i.e. 16 patients. (Table 4)

Table 5. Distribution According to Symptoms and Signs of the Patients in the Study

Symptoms and Signs	Yes	No
Abdominal pain	34 (34%)	66 (66%)
Vomiting	18 (18%)	82 (82%)

Fatigue	16 (16%)	84 (84%)
Weight gain	14 (14%)	86 (86%)
Constipation	12 (12%)	88 (88%)
Hoarseness	2 (2%)	98 (98%)
Menstrual disturbance	6 (6%)	94 (94%)
Obesity	10 (10%)	90 (90%)
Dry skin texture	2 (2%)	98 (98%)
Hair loss	6 (6%)	94 (94%)
Right hypochondrial tenderness	10 (10%)	90 (90%)

USG Findings among the Study Group: Among the study group, 68.0%, i.e. 68 patients had multiple calculi alone, 23.0%, i.e. 23 patients had single calculi, 5 (5%) patients had GB + CBD calculi and CBD calculi alone was seen in 4(4%) patients. Patients with multiple calculi were more common. (Table 5)

Association of USG Findings with Thyroid Status: Among 38 patients of hypothyroidism, 22 patients had multiple calculi alone and two patient had multiple calculi with distended gallbladder. (Table 5)

Table 6. Distribution According to USG findings

USG Findings	Euthyroid	Hypothyroid	Total Patients
MC	44 (70.9%)	24 (63.1%)	68 (68%)
SC	13 (20.9%)	10 (26.3%)	23 (23%)
MC+CBD	3 (4.8%)	2 (5.3%)	5 (5%)
CBD alone	2 (3.2%)	2 (5.3%)	4 (4%)
Total	62 (100%)	38 (100%)	100 (100%)

DISCUSSION

This prospective observational study, conducted at Index Medical College Hospital & Research Centre, Indore, involved 100 patients diagnosed with cholelithiasis, including gallstones and/or common bile duct stones. The study sought to determine whether thyroid profiles should be integrated into routine examinations for individuals with cholelithiasis, potentially highlighting thyroid dysfunction as a contributory factor in gallstone formation. GSDs are one of the most common conditions encountered by surgeons, with an incidence ranging from 5% to 30%. Risk factors for gallstone formation include gender, age, obesity, and co-morbidities, with hypothyroidism also considered a potential risk factor. A study by Watali YZ et al. [14] found a higher prevalence of hypothyroidism in patients with cholelithiasis compared to those without, though this difference was not statistically significant. In our study, we observed a high prevalence of hypothyroidism in patients with cholelithiasis i.e., 38%, a finding consistent with a study by Kotwal et al. [15] and Subramani B et al. [6] Other research has reported varying prevalence rates, ranging from 8% to 24%.[7,16]

Among the study group, 60% were in the age group of >41 yrs. This was in concurrence with studies done by M Ali et al.[1], Sinha SR et al.[2] and Subramani B et al. [6] Among the study group, 58.0% are females and 42.0% are males. Women were predominant at 58 (58%) compared to men at 42 (42%). This finding is in accordance with the study conducted by Ghadhban et al.[17], M Ali et al.[1] and Subramani B et al.[6]. An evaluation of the thyroid profile was performed for each of the 100 patients, and the results revealed that 22 (22%) patients had subclinical hypothyroidism and 16 (16%) patients with clinical hypothyroidism and the other 62 (62%) patients were found to be euthyroid. A similar study by Tombisana et al. [12] identified the highest prevalence of hypothyroidism in the 46-55 age group, with 39.5% of patients in this range. Among 126 female participants, 23.1% had hypothyroidism and 4.7% had hyperthyroidism. In male participants, 18.9% were hypothyroid and 3.9% were hyperthyroid. These results align with the findings from our study.

In the present study, diabetes was the most common co-morbidity, affecting 21% of patients. Abdominal pain was the leading symptom, seen in 34% of patients, while easy fatigability was the most common hypothyroid-specific symptom, reported by 16%. These findings align with the study by Subramani B et al.[6]

In ultrasound findings of cholelithiasis, 68%, i.e. 68 patients had multiple calculi alone with 24 patients having hypothyroidism. Earlier observational studies have indicated a positive correlation between thyroid disorders and the development of gallstone disease (GSD). Inkinen et al. [18] found an association between hypothyroidism and the formation of common bile duct stones and GSD. Similarly, Völzke et al.[19], in a study of 3,749 individuals aged 20 to 79, identified an independent correlation between GSD and elevated serum TSH levels, although this correlation was not observed in female patients. However, other research has shown that women are more susceptible to both GSD and thyroid disorders. Additionally, patients with cholelithiasis exhibit a higher prevalence of both subclinical and clinical hypothyroidism.

This increased prevalence suggests that thyroid status should be carefully considered in the diagnostic and therapeutic management of cholelithiasis. Screening for thyroid function, particularly measuring TSH, is recommended, especially for patients over 40 years old. Hypothyroidism should be recognized as a distinct risk factor in cholelithiasis patients.

The study's limitations include its single-center design, which may limit the generalizability of the findings. To validate these results and make recommendations for thyroid dysfunction screening, a longer duration and larger sample size are needed. This can be achieved through a multicenter trial to enhance the robustness and applicability of the findings.

CONCLUSION

The findings of this study suggest that hypothyroidism is a likely risk factor for the development of gallstones, particularly in middle-aged females. Clinicians should be aware of this association and consider screening for thyroid dysfunction, especially in females over 40 years of age, where the prevalence of both clinical and subclinical hypothyroidism is highest.

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