Study of pattern of Subclinical Hypothyroidism among cases with Cholelithiasis - A Cross Sectional Study

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Abstract

Background: Gallbladder stones have become more common in India as a result of dietary changes, better diagnostic techniques, and easier access to healthcare. Given that there exist a potential connection between thyroid conditions and cholelithiasis has been discussed for decades on a global scale. This relationship may be misunderstood or exaggerated by confusing characteristics including female sex and obesity, which are risk factors for both gallstones and SCH. Thus, the goal of this study was to look at the relationship between gallstone disease and subclinical hypothyroidism.

Methods: This cross-sectional research was carried out among patients with cholelithiasis who visited the general surgery outpatient department (OPD) at Sri Devaraj Medical College in Kolar. A total of 124 cholelithiasis cases were included. All participants were subjected to fasting thyroid profile and interpreted. SPSS-Version 21 was used to evaluate the data after it was entered into an Excel sheet.

Results: The vast majority of cases are in the 31–40 age range, with a notable female preponderance. Furthermore, according to BMI, 59.6%, 27.4%, and 12.9% of patients were classified as normal, overweight, or obese, respectively. The prevalence of SCH and hypothyroidism was found to be 27.4% and 7.3%, respectively, with 65.3% of patients being euthyroid, according to the interpretation of the thyroid profile. There was no discernible correlation found when evaluating the relationship between thyroid health and age. However, a substantial correlation was found when evaluating the relationship between the participant's thyroid condition and gender and BMI.

Conclusion: According to this study, SCH was present in 27.4% of cholelithiasis patients, which is a noteworthy occurrence. The remainder people were euthyroid, whereas 7.3% had hypothyroidism. This study also found a greater incidence among females. Furthermore, a greater BMI is one specific risk factor for cholelithiasis.

Key words: Cholelithiasis, Thyroid dysfunction, subclinical hypothyroidism

Introduction

The most prevalent biliary pathology in the world is gallstone disease, sometimes referred to as cholelithiasis, with significant regional variations in incidence rates[1]. In India, it is thought to afflict roughly 4% of the population, whereas in the US, it affects between 10% and 15% of the population[2,3]. Gallbladder stones have become more common in India as a result of dietary changes, better diagnostic techniques, and easier access to healthcare. According to a gallstone survey, South Asians were seven times more likely than other ethnic groups to have gallbladder stones[4]. Depending on their makeup, gallstones might be mixed, cholesterol, or pigmented[5]. A bile chemical imbalance caused by the precipitation of one or more bile constituents in the gallbladder is the most frequent cause of gallstone formation[4]. Hypothyroidism is thought to be a contributing factor in the complicated and multifaceted process of gallstone development[5].

The potential connection between thyroid conditions and cholelithiasis has been discussed for decades on a global scale. Elevated blood thyroid-stimulating hormone (TSH) levels in spite of normal serum free thyroxine (T4) levels are the hallmark of subclinical hypothyroidism. It tends to rise with age and is more common in women. The most significant consequence is that subclinical hypothyroidism (SCH) has a high probability of developing into clinical hypothyroidism. Because the sphincter of Oddi, which expresses the thyroid hormone receptors β1 and β2, has a diminished pro-relaxing propensity, hypothyroidism may cause a delay in biliary system emptying. Patients may experience bile stasis as a result, increasing their risk of gallstones[6]. The increasing incidence of hypothyroidism, which may be linked to gallstones, may affect how individuals with gallstones are diagnosed and treated.

Bile flow is frequently diminished in hypothyroidism because the sphincter of Oddi, which is thought to express thyroid hormone receptors, is less active. The sphincter is directly relaxed by thyroxine, and a lack of it in hypothyroid conditions can cause biliary stasis, which is a crucial component in the development of gallstones[7]. The digestive tract's motility is frequently compromised in hypothyroidism, which lowers the amount of bile that enters the duodenum[7].

Furthermore, research has linked hypothyroidism to lower bilirubin excretion, mostly as a result of reduced UDP glucuronyl transferase activity[8]. In light of these factors, the current study is to examine the frequency of undiagnosed hypothyroidism in cholelithiasis patients as well as the possibility that hypothyroidism contributes to gallstone disease in the Gujarati region. This study may contribute to a more thorough knowledge of the connection between gallbladder disease and thyroid function.

A potential causative relationship between SCH and cholelithiasis has been suggested by a number of studies conducted in various populations. The directionality or strength of the association is still up for discussion, and these findings are still inconsistent. This relationship may be misunderstood or exaggerated by confusing characteristics including female sex and obesity, which are risk factors for both gallstones and SCH. To further investigate the association

while accounting for potential confounders, a well-designed case-control research is required. Thus, the goal of this study was to look at the relationship between gallstone disease and subclinical hypothyroidism[9].

Methods

This cross-sectional research was carried out among patients with cholelithiasis who visited the general surgery outpatient department (OPD) at Sri Devaraj Medical College in Kolar between November 2025 and January 2026. Patients of both sexes and participants ranging in age from 18 to 80 were included. The study excluded patients with common bile duct stones and cholangitis, those on medications that alter thyroid function test results, those receiving treatment for thyroid abnormalities, those experiencing rapid weight loss as a result of gastric bypass surgery, those following a low-calorie diet, and those with dyslipidemia. With 7% absolute accuracy and 95% confidence, the sample size of 124 was calculated using the prevalence of 19.4% as stated by Sinha SR et al[10]. As a result, a total of 124 cholelithiasis cases were included.

The Institutional Human Ethics Committee granted ethical committee clearance for this investigation. The lead investigator used a pre-structured proforma to evaluate the subjects' clinical presentation and demographics after obtaining written informed permission. The lead investigator then evaluated each participant's comprehensive medical history and performed a clinical examination. All participants were subjected to fasting thyroid profile and Patients were deemed euthyroid if their blood TSH levels were between 0.5 and 4.9 mIU/L and their T3 and T4 levels were normal. Serum TSH values between 5 and 10 mIU/L with normal T3 and T4 levels were considered SCH. Clinical hypothyroidism was defined as TSH levels higher than 10 mIU/L [12]. SPSS-Version 21 was used to evaluate the data after it was entered into an Excel sheet. For quantitative variables, descriptive statistics were computed using the mean, standard deviation, and proportions (%). The Kruskal-Wallis H test and the Chi Square test were employed to test the hypothesis. A p-value of less than 0.05 was regarded as statistically significant.

Results

In this study the mean age of the study participants was reported as 42.3 years with SD of 14.3 years. Notably majority of cases belongs of age group 31-40 years of age with remarkable female predominance. Additionally, based on BMI there were 59.6%, 27.4% and 12.9% of cases belongs to normal, overweight and obese BMI, respectively. Notably based on the interpretation of thyroid profile, the prevalence of SCH and hypothyroidism were reported as 27.4% and 7.3%, respectively with 65.3% euthyroid cases. Mean TSH, mean T3 and mean T4 were reported as 4.9±3.3mIU/L, 1.6±1.2mIU/L and 9.6±3.2mIU/L respectively (Table 1).

Table 1: Clinical Profile of the Study participants

Parameter	Frequency	Percentage
Age group		
≤ 30 years	32	25.8
31-40 years	35	28.2
41-50 years	33	26.6
51-60 years	9	7.3
> 60 years	15	12.1
Total	124	100.0
Gender		
Female	112	90.3
Male	12	9.7
Total	124	100.0
BMI		
Normal	74	59.6
Overweight	34	27.4
Obese	16	12.9
Total	124	100.0
Interpretation of Thyroid profile		
Euthyroid	81	65.3
SCH	34	27.4
Hypothyroidism	9	7.3
Total	124	100.0

On assessing the association between the age and the thyroid status, there was no significant association noted. However on assessing the association between the gender and BMI with the thyroid status of the participant, significant association was noted (Table 2).

Table 2: Association between clinical profile and thyroid status

Variables	Euthyroid	SCH	Hypothyroidism	p value
Age group				
≤ 30 years	26 (21)	5 (4.0)	1 (0.8)	0.413
31-40 years	20 (16.1)	12 (9.7)	3 (2.4)	
41-50 years	21 (16.9)	9 (7.3)	3 (2.4)	
51-60 years	7 (5.6)	2 (1.6)	0 (0.0)	
> 60 years	7 (5.6)	6 (4.8)	2 (1.6)	
Total	81 (65.3)	34 (27.4)	9 (7.3)	
Gender				

Female	76 (61.3)	27 (21.8)	9 (7.3)	0.035*
Male	5 (4.0)	7 (5.6)	0 (0.0)	
Total	81 (65.3)	34 (27.4)	9 (7.3)	
BMI				
Normal	55 (44.4)	16 (12.9)	3 (2.4)	0.004*
Overweight	23 (18.5)	9 (7.3)	2 (1.6)	
Obese	3 (2.4)	9 (7.3)	4 (3.2)	
Total	81 (65.3)	34 (27.4)	9 (7.3)	

*Significant (Chi Square Test)

Mean TSH and mean T4 were significantly differs with the thyroid status of the study participants however mean T3 does not differ significantly (Table 3).

Table 3: Mean difference in thyroid parameters based on thyroid status

Parameter	Euthyroid	SCH	Hypothyroidism	p value
Mean TSH (mIU/L)	3.2±1.1	7.0±1.6	13.6±3.7	0.000*
Mean T3 (mIU/L)	1.7±1.4	1.3±0.8	1.3±0.8	0.202
Mean T4 (mIU/L)	9.8±3.1	10.1±3.1	6.5±3.4	0.007*

*Significant (Kruskal-Wallis H test)

Discussion

In the present study, the prevalence of SCH among cases with cholelithiasis was reported as 27.4% and clinical hypothyroidism was reported as 7.3%. These findings were in line with the findings of Sinha SR et al[10] who sought to determine the prevalence of GSD and thyroid conditions. They reported that of the 180 individuals, 1.7% had hyperthyroidism, 19.4% had SCH, 11.1% had clinical hypothyroidism, and 67.8% were euthyroid. Dyslipidemias were seen in 67.3% of the 55 individuals with hypothyroidism. They stated that 30% of GSD patients had hypothyroidism, with a preponderance of females. Thyroid dysfunction should be assessed in all GSD patients with dyslipidemia as hypothyroidism is a unique risk factor for cholelithiasis. According to Ghadhaban BR et al[11]., 18.4% of them were men and 81.6% of them were women. Of the total number of patients, 7.8% had SCH and 92.2% were determined to be euthyroid; 81.6% of the patients in the subclinical hypothyroid group were female. The majority of individuals with SCH had a positive family history (75%) and a negative family history (25%), however the incidence among men was found to be 18.4%. They asserted that there is a gender-specific correlation between gallstone disease and SCH because this study found a statistically significant increase in the prevalence of SCH among females aged 40 and older, as well as a positive family history and a single abdominal gallstone. Khurana HK et al[12] looked at the connection between gallstone disease and SCH. They reported that 38.9% of the 239 individuals had SCH. The majority of SCH patients (58.1%) were between the ages of 33 and 46. 74.2% of SCH patients were female. Compared to individuals with normal thyroid status, those with

subclinical thyroid status were more likely to have more calculi, bigger stones, and a positive family history. Multiple calculi, a stone bigger than 10 mm, and a positive family history of hypothyroidism were all identified as independent risk factors for SCH. They came to the conclusion that SCH could be a major risk factor for gallstone illness, emphasizing the significance of regular thyroid function testing for cholelithiasis patients.

In another study, the prevalence of SCH in instances of cholelithiasis was found by Arbab R et al[13]. They reported that 87% of the 193 patients were female and 13% were male. 91.7% of patients were determined to be normal, whereas 8.16% of patients had SCH. It was determined that individuals with cholelithiasis have a low rate of SCH. The purpose of Swami YK et al.'s[14] study was to find out how common SCH is in gallstone patients and whether it may contribute to the development of gallstones. Thirty-two of the 160 patients had SCH and six had overt hypothyroidism, making up 23.8% of the total. The prevalence of hypothyroidism was higher in women (32.3%) than in men (19.4%). Right hypochondrial discomfort, fatty dyspepsia, and biliary colic were prevalent symptoms. The study shows a strong correlation between gallstone disease and hypothyroidism, especially SCH. In patients with gallstone disease, Dang C et al[15]. assessed the frequency of thyroid abnormalities and investigated the connection between thyroid dysfunction and sociodemographic factors. They reported that the participants' average age was 44. There were 32% females and 68% men. Of the 117 individuals, 58.1% had euthyroidism and 41.9% had hypothyroidism. Of these 49 individuals, only 15 had a history of hypothyroidism, while the remaining 34 had just received a diagnosis. There were 19 men and 30 women among the 49 patients. In both males and females, there was no discernible correlation between hypothyroidism and the development of gallstones. They came to the conclusion that both sexes had low rates of hypothyroidism.

Additionally, the relationship between thyroid function tests and gallstone disease diagnoses was evaluated by Wali MI et al[16]. The study's median age was 40 years, with 71.5% of participants being female and 28.5% being male. 18.5% of patients had hypothyroidism, a thyroid condition; 19.6% of these patients were female and 15.8% were male. 10.5% of the 37 instances with hypothyroidism were subclinical, while 8% were symptomatic. Clinically, a high TSH level in 37 out of 200 individuals is not statistically significant. Nonetheless, there is a statistically significant correlation between low T3 levels and elevated TSH in clinical hypothyroidism. Their investigation found that whereas low T3 with high TSH was statistically significant, high TSH levels in individuals with biliary calculi were not statistically significant. The relationship between SCH and gallstone disease was also evaluated by Biswas S et al[17]. SCH was found to be substantially more common in the case group (30%) compared to the controls (17.5%). The most prevalent kind was cholesterol stones, which were mostly seen in hypothyroid individuals (87.5%). The most common demographic characteristics were female sex and age between 30 and 50. Gallstone disease and SCH were shown to be significantly correlated. Their research identifies a possible connection between cholelithiasis and SCH, particularly in middle-aged women with stones that are high in cholesterol.

In consistent with this study, Kumar G et al[18] investigated the prevalence of hypothyroidism and SCH in gallstone disease patients. Of the 220 individuals, 8.2% had hypothyroidism, 27.7% had SCH, and 64.1% were euthyroid. In this case study, SCH was prevalent in gallstones. This is a statistically significant correlation between gallstone disease and SCH. This study suggests that gallstone disorders and thyroid malfunction, namely SCH, are related. Compared to clinical hypothyroidism, SCH is more prevalent. Subclinical and borderline-SCH were identified in 5.3% and 5.0% of CBD stone patients, respectively, compared to 1.4% and 1.4% in the control group, according to Laukkarinen J et al[19]. SCH in women over 60 was found in 11.4% of CBD stone patients and 1.8% of control patients, whereas subclinical plus borderline-SCH was found in 23.8% of CBD stone patients and 1.8% of control patients. They asserted that, in comparison to non-gallstone controls, SCH is more prevalent in CBD stone patients. According to Maji J et al[20], 28% of the 54 patients with cholelithiasis were between the ages of 45 and 54.40% of patients, mostly women, had hypothyroidism. 26.8% of the 30 female patients and 15.4% of the 11 male patients had hypothyroidism. Both male and female hypothyroidism was statistically significant. The purpose of this study was to ascertain if hypothyroidism and cholelithiasis are related. It was determined that older, female, and obese patients were more likely to have hypothyroidism.

Patients with common bile duct (CBD) stones had their thyroid function patterns assessed by Ajdarkosh H et al[21]. They discovered that the patients' mean TSH (2.6 mg/dl) was greater than that of the control group (2.5 mg/dl). Serum TSH levels more than 5 MU/L were detected in 30.6% of patients and 22.5% of controls with SCH. In 11.3% of patients and 10.8% of the control group, hypothyroidism was found. They came to the conclusion that bile duct stones and thyroid conditions were related. The frequency of hypothyroidism in cholelithiasis patients was found by Ali M et al[22]. They observed that 47.1% of the 174 cholelithiasis patients were between the ages of 41 and 50.Hypothyroidism affected 14.4% of patients, mostly women. 20.6% of the 97 female patients and 6.5% of the 77 male patients had hypothyroidism. Both male and female hypothyroidism was statistically significant. The purpose of this study was to ascertain if hypothyroidism and cholelithiasis are related. It was determined that older, female, and obese patients were more likely to have hypothyroidism. The frequency of undetected thyroid dysfunction in CBD stone patients was examined by Sidduri S et al[23]. They discovered that the average TSH levels in the patients and controls were 2.58 and 3.57, respectively. 30% of patients had SCH, compared to 9.09% of controls. SCH was more common in individuals over 50 in the CBD stone group (36%) than in those under 50 (22%). SCH was more common in women (23%) than in men (11%). They asserted that compared to controls, SCH was more prevalent among CBD stone patients. In CBD patients over 50, SCH was more common. Females were more likely than males to have SCH among CBD stone patients. The frequency of undetected hypothyroidism in individuals with cholelithiasis was discovered by Singha D et al[24]. They said that clinical, subclinical, and borderline SCH were identified in 2.2%, 5.0%, and 6.6% (a total of 13.8%) of the cholelithiasis patients. The incidence of clinical and subclinical plus borderline hypothyroidism in women over 50 was 6.8% and 25.6%, respectively, whereas the prevalence of clinical plus subclinical plus borderline-SCH in patients with cholelithiasis was 32.4%. Even

though the study identified a low incidence of hypothyroidism, it is clear that subclinical and borderline SCH were far more prevalent than clinical hypothyroidism, and that the frequency increased with age.

According to Kumar PKH et al[25]., 17.5% of gallstone patients had SCH, which was more common in females (21%) than in males (10%). This gender difference was statistically significant. There were comorbid conditions: 14% of the patients had hypertension, and 15.8% had diabetes mellitus. These results demonstrate a strong correlation between gallstone disease and SCH, particularly in females. The rate of hypothyroidism in cholelithiasis cases that were identified was assessed by Arun N et al[26]. They reported that gallstone disease was associated with a significant frequency of hypothyroidism (23%). Just 6% of participants with gallstone disease were obese in this research. Additionally, they discovered that 73% of the hypothyroid research participants were fat. According to Vineet T et al[27]., 23% of persons who have never had thyroid illness have increased blood TSH. Although the age range of 31 to 40 years old had the highest number of people with raised TSH, the age group of 41 to 50 years old had the highest proportion (42.9%). Compared to the proportion of patients with elevated serum TSH levels, a substantial 33% of patients exhibited elevated fasting bile TSH levels with a female majority. The proportion of patients with increased biliary TSH was greater in the 41–50 age group (57.1%) than in the 31–40 age group. They asserted that in female gallstone disease patients, a statistically significant independent connection was found between serum TSH and fasting bile TSH. The connection between hypothyroidism and cholelithiasis was established by Kulkarni V et al[28]. They reported that a higher percentage of patients (82.7%) were over 40, with a plurality of women (61.5%). The group with a BMI higher than normal had more individuals with cholelithiasis (57.6%). Patients with a BMI over normal were also more likely to have both hypothyroidism and cholelithiasis. Pain in the right hypochondriac area was reported by the majority of symptomatic individuals (88.5%). Of these 52 individuals, 43 were euthyroid, and 17.3% had hypothyroidism (seven were subclinical, and two had overt clinical symptoms and signs). Their research confirmed the link between hypothyroidism and cholelithiasis.

Conclusion

This study indicated that 27.4% of cholelithiasis patients had SCH, which is a significant prevalence. 7.3% had hypothyroidism, whereas the remaining individuals were euthyroid. Additionally, a higher frequency among females was discovered in this investigation. Additionally, one particular risk factor for cholelithiasis is a higher BMI. Furthermore, we advise thyroid dysfunction screening for all cholelithiasis patients.

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