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Research Article

THYROID FUNCTION ABNORMALITIES IN PATIENTS WITH CHOLELITHIASIS: A HOSPITAL-BASED CROSS-SECTIONAL STUDY

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ABSTRACT

Objective: The objective of the study is to analyze the association between thyroid function abnormalities and cholelithiasis, focusing on the prevalence and types of thyroid dysfunctions in patients with gallstone disease compared to a healthy control group.

Methods: A comparative, hospital-based cross-sectional study was conducted in the department of general surgery at a tertiary care medical college. The study included 60 patients diagnosed with cholelithiasis (Group A) and 60 age-matched healthy individuals (Group B). Detailed history, physical examinations, ultrasound imaging, and thyroid function tests (TFTs) were performed. TFTs included measurements of free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone. Patients were categorized based on thyroid status into euthyroid, subclinical and clinical hypothyroidism, and hyperthyroidism. Statistical analysis was performed using SPSS version 21.0, with significance set at $p<0.05$.

Results: The study revealed a female preponderance in cholelithiasis cases (76.67% in Group A vs. 65.00% in Group B). The mean age and BMI were comparable between the groups. Thyroid function abnormalities were more prevalent in the cholelithiasis group ($p=0.0251$), with a higher incidence of hypothyroidism compared to the control group. Subclinical hypothyroidism was the most common thyroid dysfunction in cholelithiasis patients. Common complaints in the cholelithiasis group included anemia, menstrual irregularities, skin changes, and weakness.

Conclusion: The study demonstrates a significant association between cholelithiasis and thyroid function abnormalities, particularly hypothyroidism. The findings suggest the need for routine thyroid function evaluation in patients with cholelithiasis, which could influence management strategies and improve patient outcomes.

Keywords: Cholelithiasis, Thyroid function abnormalities, Hypothyroidism, Management.

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INTRODUCTION

Cholelithiasis is characterized by the formation of stones within the gallbladder. This pathological state results from an imbalance in the composition of bile which leads to the precipitation of cholesterol and bilirubin [1]. The pathophysiology of cholelithiasis involves various factors including supersaturation of cholesterol in bile, gallbladder hypomotility, and the nucleation of cholesterol crystals. Predisposing factors for cholelithiasis include obesity, rapid weight loss, age, female gender, and genetic predispositions. Clinical features may range from asymptomatic gallstones to severe abdominal pain, jaundice, and cholecystitis [2].

The confirmation of diagnosis of cholelithiasis is primarily done based on imaging. Ultrasonography (US) is the modality of choice due to its non-invasive nature, high sensitivity, and specificity for the diagnosis of cholelithiasis. US can effectively detect gallstones and provide information on gallbladder wall thickening and biliary duct dilation which are indicative of complications such as acute cholecystitis [3]. The role of computed tomography (CT) in diagnosing cholelithiasis is limited due to its lower sensitivity in detecting small gallstones. However, CT is immensely valuable in evaluating complications of gallstone disease (GSD) such as cholecystitis, and in identifying pancreatitis which in many cases is an associated condition in patients with cholelithiasis [4].

The management of cholelithiasis can be divided into medical and surgical management. Medical management is usually reserved for those patients who are either asymptomatic or those in whom there is a contraindication to surgical interventions [5]. The medical therapy may consist of ursodeoxycholic acid, which works by dissolving cholesterol gallstones. This method is most effective for small, cholesterol-rich stones in a functioning gallbladder. In addition to pharmacological therapy, maintaining a healthy diet low in fats and cholesterol, regular exercise, and weight management are crucial lifestyle modifications recommended to prevent gallstone formation and growth [6]. If cholecystitis is suspected, then antibiotics and non-steroidal anti-inflammatory drugs can also be given. In cases not amenable to non-surgical management, cholecystectomy is the definitive and standard treatment. Minimally invasive laparoscopic cholecystectomy is becoming the surgical procedure of choice in cases of cholelithiasis due to its minimally invasive nature, reduced post-operative pain, shorter hospital stays, and quicker recovery. For complicated cases, procedures such as ERCP may be used. Post-surgery, patients generally resume normal activities quickly, though dietary adjustments are often needed. Surgical treatment effectively minimizes recurrence risks [7].

Interestingly, emerging research indicates a potential link between thyroid function abnormalities and cholelithiasis. Thyroid hormones play a crucial role in lipid metabolism, gastrointestinal motility, and gallbladder function. Alterations in thyroid function such as hypothyroidism can lead to dyslipidemia and bile stasis predisposing an individual to cholelithiasis [8]. Conversely, hyperthyroidism might increase bile acid synthesis and cholesterol turnover which could also contribute to gallstone formation. The common thyroid function abnormalities observed in patients with cholelithiasis include variations in serum concentrations of thyroid-stimulating

hormone (TSH), triiodothyronine (T3), and thyroxine (T4). The exact pathophysiological mechanisms linking thyroid dysfunction and GSD are still being investigated. Various studies suggest altered bile composition, decreased gallbladder motility, and changes in cholesterol metabolism as potential causes of cholelithiasis [9].

With this background, we conducted this hospital-based comparative study to analyze the thyroid function abnormalities in patients with cholelithiasis.

METHODS

This was a comparative study conducted in the department of general surgery of a tertiary care medical college situated in an urban area. Sixty patients diagnosed to be having cholelithiasis (Group A) were included in this study based on pre-defined inclusion and exclusion criteria. Sixty healthy individuals were enrolled as the control group (Group B). Informed written consent was obtained from all the cases and individuals in the control group. The sample size was calculated based on a pilot study on the topic of thyroid function abnormalities in cholelithiasis, assuming 90% power and 95% confidence interval, the sample size required was 60 patients therefore we included 60 patients in our study.

A detailed history of all individuals including age, gender, history of medications, physical activity level, any previous abdominal surgery, eating habits, and lifestyle was obtained. Height and weight were noted and BMI was calculated. All patients underwent an ultrasound examination. In cases of patients with cholelithiasis, it was done to confirm the presence of cholelithiasis and to rule out associated abnormalities such as cholecystitis and choledocholithiasis whereas in individuals in control group, it was done to rule out the possibility of asymptomatic cholelithiasis. Thyroid function tests (TFTs), including free triiodothyronine (FT3), free thyroxine (FT4), and TSH, were performed on all participants. These tests were conducted in the morning before breakfast. The normal reference ranges for TFTs were taken as 0.8–2 ng/mL for T3, 5.5–12.2 µg/dL for T4, and 0.6–4.5 µIU/mL for TSH. A comparison of TFTs was done between the cholelithiasis group and individuals in control group. Based on thyroid function reports and clinical features patients were divided into five distinct groups, namely subclinical hypothyroidism (SCH) (characterized by elevated TSH levels with normal FT3 and FT4 and absent clinical symptoms), clinical hypothyroidism (identified by elevated TSH and decreased FT3 and FT4 levels, accompanied by clinical symptoms), subclinical hyperthyroidism (marked by decreased TSH levels with normal FT3 and FT4 and no clinical symptoms), and clinical hyperthyroidism (TSH levels are decreased, FT3 and FT4 levels are elevated, and clinical symptoms are present) and euthyroid status, where patients exhibit normal TSH, FT3 and FT4 levels, and lack thyroid-related clinical symptoms.

The statistical analysis utilized SPSS version 21.0, presenting quantitative data as mean and standard deviation, while qualitative data were summarized using frequency and percentage tables. Unpaired t-tests were employed for quantitative data, and Chi-square tests were used for qualitative data. Statistical significance was set at $p<0.05$.

Inclusion criteria

1. Sixty patients with cholelithiasis were diagnosed based on ultrasound imaging (cases) and similar numbers of age-matched healthy individuals (control group)
2. Age more than 18 years
3. Those who gave informed and written consent to be part of the study.

Exclusion criteria

1. Those who refused consent
2. Those below 18 years of age
3. Known cases of hypothyroidism or hyperthyroidism
4. History of thyroid surgery or those who had undergone thyroidectomy
5. Patients on medications known to alter thyroid functions such as metformin, lithium, amiodarone, or glucocorticoids.

RESULTS

The analysis of the patients based on gender distribution showed that in cases of patients with cholelithiasis there were out of 60 cases there were 46 (76.67%) females and 14 (23.33%) males. Whereas in control group, there were 39 (65.00%) females and 21 (35.00%) males. There was an overall female preponderance in both groups. The gender distribution was found to be comparable in both groups with no statistically significant difference (p=0.2286) (Table 1).

The most commonly affected age group in cholelithiasis group was found to be 51–60 years (40%) followed by 41–50 years (25%) and above 60 years (26.67%). The mean age of cholelithiasis group was found to be 52.34±12.36 years. The mean age of control group was found to be 49.12±14.28 years. The mean age of both groups was found to be comparable with no statistically significant difference (p=0.1892) (Table 2).

The analysis of patients based on body mass index showed that in Group A, majority of the patients were either overweight (60%) or obese (30%) and only 6 (10%) had a normal BMI. Whereas in Group B 32 (53.33%), patients had normal weight, 20 (33.33%) patients were overweight, and 8 (13.33%) patients were obese. The mean BMI of cholelithiasis was high as compared to control group and the difference was found to be statistically significant (p=0.047) (Table 3).

The TFTs of both groups were done, and the patients were compared for incidence of thyroid abnormalities. In Group A, the majority (61.67%) of the patients were euthyroid, whereas 35% (21 cases) had hypothyroidism, and hyperthyroidism was seen in 2 (3.33%) patients. In Group B, the majority of the patients were euthyroid (81.67%) and hypothyroidism was seen in 11 (18.33%) cases. There was no case of hyperthyroidism in Group B. The incidence of thyroid function abnormalities was more in Group A as compared to Group B and the difference was found to be statistically significant (p=0.0251) (Table 4).

Out of the 14 males in Group A (cholelithiasis group), 3 (21.43%) patients had thyroid function abnormalities whereas among 46 females, 20 (43.48%) were found to have thyroid function abnormalities. Among Group B (health individuals), out of 21 males 2 (9.52%) had hypothyroidism and among 39 females, 7 (17.95%) were found to have hypothyroidism on TFT (Table 5).

Table 1: Comparison of gender distribution of the studied cases

Gender distribution	Group A		Group B	
	Cases	Percentage	Cases	Percentage
Males	14	23.33	21	35.00
Females	46	76.67	39	65.00
Total	60	100.00	60	100.00

p=0.2286 (Not significant)

Table 2: Comparison of age groups in the studied cases

Age group	Group A		Group B	
	No of patients	Percentage	No of patients	Percentage
18–30 years	2	3.33	5	8.33
31–40 years	3	5.00	7	11.67
41–50 years	15	25.00	15	25.00
51–60 years	24	40.00	25	41.67
>60 years	16	26.67	8	13.33
Total	60	100.00	60	100.00
	Mean Age: 52.34±12.36		Mean Age: 49.12±14.28	

p=0.1892 (Not Significant)

Table 3: Comparison of body mass index of the studied cases

Body mass index	Group A		Group B	
	Number of patients	Percentage	Number of patients	Percentage
Healthy Weight (18.5–24.9)	6	10.00	32	53.33
Overweight (25–29.9)	36	60.00	20	33.33
Obese (30 or above)	18	30.00	8	13.33
Total	60	100.00	60	100.00
	28.12±9.86		24.76±8.42	

p=0.047 (Significant)

Table 4: Thyroid function abnormalities in both the groups

Thyroid status	Group A		Group B	
	No of cases	Percentage	No of cases	Percentage
Euthyroid	37	61.67	49	81.67
Hypothyroidism	21	35.00	11	18.33
Hyperthyroidism	2	3.33	0	0.00
Total	60	100.00	60	100.00

p=0.0251 (Not significant)

Table 5: Gender-wise distribution of thyroid function abnormalities in both groups

Thyroid status	Group A		Group B	
	Male	Female	Male	Female
Euthyroid	11	26	19	32
Hypothyroidism	3	18	2	7
Hyperthyroidism	0	2	0	0
Total	14	46	21	39

Among 23 patients with cholelithiasis, majority of the patients (65.22%) had SCH whereas clinical hypothyroidism was seen in 6 (26.09%) patients. Hyperthyroidism was observed in 2 (8.70%) patients. Among healthy individuals, out of 11 patients having thyroid function abnormalities, 8 (72.73%) had clinical hypothyroidism, and 3 (27.27%) had SCH (Fig. 1).

The analysis of patients based on presenting complaints showed that in cholelithiasis groups, anemia (17/60), menstrual irregularities (16/60), skin changes (14/60), and weakness (14/60) were the common complaints other than those attributable to cholelithiasis. Whereas in the control group, anemia (11/60) and menstrual irregularities were common complaints (5/60) (Fig. 2).

DISCUSSION

The relationship between thyroid function abnormalities and cholelithiasis shows an intricate relationship between endocrine function in cases with gastrointestinal pathologies. It is well known that the thyroid hormones play a crucial role in regulating lipid metabolism and hypothyroidism can significantly alter lipid metabolism and bile composition. This alteration can lead to an increased risk of gallstone formation [10]. Hypothyroidism is also associated with reduced bile flow and altered cholesterol metabolism, both of which are key factors in the pathogenesis of cholelithiasis. In addition to this, thyroid disorders can impact the motility of the gallbladder, further contributing to gallstone formation. While the exact mechanisms linking these conditions are still being studied, the evidence suggests a bidirectional relationship between cholelithiasis and thyroid functional abnormalities. Hence, not only thyroid function abnormalities predispose an individual for the development of cholelithiasis but also cholelithiasis may cause thyroid function abnormalities [11].

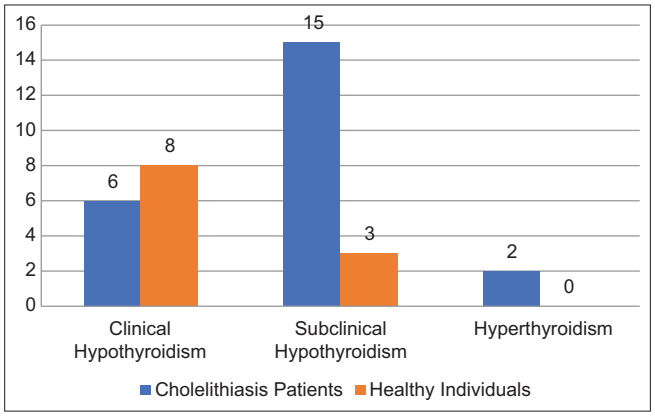

Fig. 1: Distribution of various thyroid function abnormalities in studied groups

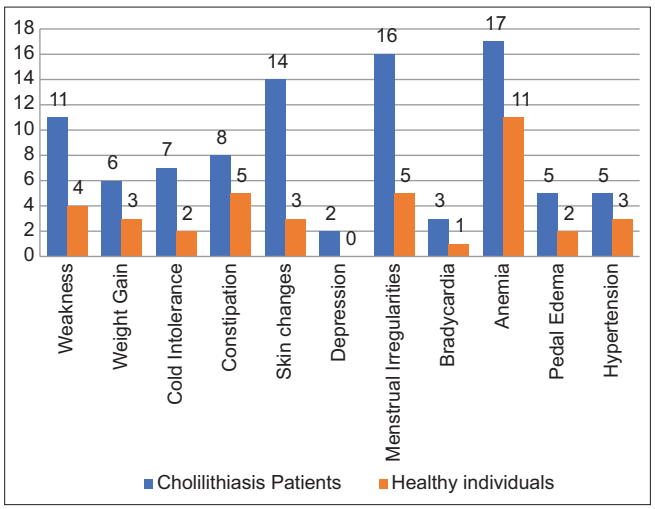

Fig. 2: Comparison of signs and symptoms in studied cases

In our study, among the cholelithiasis group, out of 60 cases, there were 46 (76.67%) females and 14 (23.33%) males. This female preponderance in cases of cholelithiasis has been reported by the majority of the studies. Dhar *et al*. conducted a community-based study to investigate the prevalence of GSD and its association with various factors [12]. The methodology involved inviting 1,332 individuals aged 15 years and above from two villages, with a response rate of 80% (1,058 participants). The study found a 5.4% prevalence of GSD, characterized by current cholelithiasis or a history of cholecystectomy. Notably, the prevalence was higher in women (7.7%) compared to men (3.3%). An increase in prevalence rates was observed with age, rising from 0.9% in those under 30 years to 10% in individuals over 50 years. A significant correlation was also noted between obesity and GSD, with 48.1% of obese subjects having GSD compared to 3.2% of

non-obese subjects. Interestingly, a majority (71.9%) of the subjects with GSD were asymptomatic. Based on these findings, the authors concluded that approximately 5% of the rural Bangladeshi community evaluated has GSD. They identified higher age, female gender, obesity, and higher socioeconomic class as factors associated with a higher prevalence of GSD. Similar risk factors (including female gender to be one of the significant risk factors) were also reported by authors such as Chen *et al*. [13] and Thijs *et al*. [14].

In this study, in Group A, the majority (61.67%) of the patients were euthyroid, whereas 35% (21 cases) had hypothyroidism, and hyperthyroidism was seen in 2 (3.33%) patients. In Group B majority of the patients were euthyroid (81.67%) and hypothyroidism was seen in 11 (18.33%) cases. There was no case of hyperthyroidism in Group B. Rahman *et al*. conducted a cross-sectional study to find out whether there is any association between cholelithiasis and thyroid profile in patients undergoing elective cholecystectomy for gallstone disease and to find the difference in the chemical composition of gallstones in these patients [15]. The research involved 300 patients divided into 150 cases (patients with GSD undergoing cholecystectomy) and 150 controls (without asymptomatic cholelithiasis). Fasting blood samples were collected for serum T3, T4, free T4, and TSH measurements. The gallstones were also examined for their morphology and biochemical composition. The results indicated a significant female predominance in the cholelithiasis group, with a 4:1 female-to-male ratio. Hypothyroidism prevalence was notably higher in the cholelithiasis group (38.6%) compared to the control group (22%). SCH was observed in 30.0% of cases versus 17.3% in controls, with a majority of hypothyroid cholelithiasis patients being female. In addition, cholesterol stones were more prevalent in hypothyroid patients (93.1%) than in euthyroid patients (69.6%). Based on these findings, the authors concluded that hypothyroidism was more common in patients with gallstones compared to controls, with a higher prevalence among females. They suggest that thyroid function should be considered in patients with GSD. A similar high prevalence of thyroid function abnormalities in patients with gallstones was also reported by authors such as Ravi *et al.* [16] and Kube and Zwanziger [17].

In this study in cholelithiasis group anemia, menstrual irregularities, skin changes, and weakness were the common complaints other than those attributable to cholelithiasis. Whereas in control group, anemia and menstrual irregularities were common complaints. Khan *et al*. conducted a retrospective chart analysis of prospectively collected data in a cross-sectional study to determine the frequency, clinical presentations, and treatment indications of SCH [18]. The study reviewed the medical records of 4,448 patients, with 2,760 diagnosed with thyroid disorders and 260 (9.42%) with SCH. Patients ranged from 12 to 70 years and had TSH > 4 mIU/l with normal FT3 and FT4 levels. Those with chronic systemic diseases were excluded. The results showed that 93.8% of the SCH patients were female, with common symptoms including lethargy (56.2%), weight increase (39.2%), and menstrual irregularities (34.6%). Most patients (68.1%) had a TSH level of <10 mIU/l, whereas 31.9% had TSH ≥10 mIU/l. Thyroxine treatment was given to 70.4% of these patients. Treatment indications included TSH ≥10 mIU/l, subfertility, symptoms suggestive of hypothyroidism, and high antibody titers. The study concluded that SCH is prevalent in the population, with lethargy being a common complaint. Treatment was typically indicated for patients with a TSH ≥10 mIU/l, as well as those with troublesome hypothyroidism symptoms and subfertility at lower TSH levels. Similar findings were also reported by authors such as Yoo and Chung [19] and Fatourechi [20].

CONCLUSION

Our study highlights significant associations between cholelithiasis and thyroid function abnormalities. Predominantly affecting females, the study found a higher prevalence of thyroid dysfunction in patients with cholelithiasis compared to healthy controls. The data indicates a propensity to develop SCH in the cholelithiasis group. These findings underscore the importance of evaluating thyroid function in patients with cholelithiasis, which could have implications for management and prognosis.

CONFLICT OF INTEREST

None.

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