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Original Article

Surgery Section

Prevalence of Thyroid Dysfunction in Patients with Gallstone Disease: A Cross-sectional Study

CHINMAY DANGI[1], NILESH MEHTA[2], MITKUMAR V PATEL[3], URMILKUMAR LABANA[4], YASHASVI PATEL[5], DARSHIT DINESHBHAI PATEL[6], MOHIT BIMALBHAI GOSWAMI[7], AJAY CHAUHAN[8]

ABSTRACT

Introduction: Patients with gallstone disease have already been investigated for the prevalence of previously undetected thyroid dysfunction, and the findings point to a possible link between hypothyroidism and gallstone disease. This research was carried out to support the need for assessment of the thyroid status in patients presenting with gallstones.

Aim: To determine the prevalence of thyroid disorders and to study the relationship between thyroid dysfunction and sociodemographic variables in patients with gallstone disease.

Materials and Methods: A cross-sectional, observational, hospital-based study was carried out at Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India, in 117 patients with gallstones from January 2021 to June 2022. The sampling method was consecutive sampling. Standard baseline investigations and thyroid profiles were conducted. Operative and perioperative factors such as age (ranging from 18-80 years), sex, co-morbidities, radiological findings (number and size of stones, presence of Common Bile Duct (CBD) stones), thyroid profile, surgeries performed, and significance (p-value) of these factors were assessed based on the Chi-square test.

Results: The mean age of participants was 44 years. There were 37 (68%) males and 80 (32%) females. Of the 117 patients, 49 patients (41.9%) were found to have hypothyroidism, and the remaining 68 patients (58.1%) were euthyroid. Among these 49 patients, only 15 were known to have hypothyroidism, while the remaining 34 patients were newly diagnosed. Of the 49 patients, 30 were females and 19 were males. There was no significant association between hypothyroid state and gallstone formation in either males (p-value: 0.154) or females (p-value: 0.194).

Conclusion: A low prevalence of hypothyroidism was observed in both sexes. Further large population studies are needed to compare these findings.

Keywords: Choledocholithiasis, Cholelithiasis, Hypothyroidism, Sphincter of oddi dysfunction, Subclinical hypothyroidism

INTRODUCTION

Cholelithiasis is one of the most encountered intra-abdominal pathologies for a general surgeon. The three main categories are cholesterol, pigment (black or brown), and mixed stones. In Western nations, 80% of stones are cholesterol or mixed, but in Asia, 80% of stones are pigment [1]. The gallbladder may contain one or multiple stones. They form because of changes in the normal metabolism and transport of cholesterol through the hepatobiliary system [2]. The supersaturation of cholesterol in bile during the nucleation process has been emphasised as a key phase in the formation of gallstones in several research studies conducted in the West to discover risk factors for gallstones [3]. Among adults, thyroid diseases are a common medical condition. There has been debate over the past 10 years as to whether thyroid conditions can result in the formation of stones in the hepatobiliary system. A study has suggested that dysfunction of the thyroid gland and the pathophysiology of lipids are related, tending to modify the contents of bile [2]. Studies by Raghuvanshi BS et al., Laukkarinen J et al., Tombisana S et al., have also shown that hypothyroid patients have decreased biliary flow due to hypomotility [1,3,4]. Patients with gallstone disease have already been investigated for the prevalence of previously undetected thyroid dysfunction, and the findings point to a possible link between hypothyroidism and gallstone disease. The diagnosis and treatment of people with gallstones may be impacted if there is a higher prevalence of thyroid dysfunction [1,5-8]. Therefore, this research study was conducted to determine the prevalence of thyroid disorders in patients with gallstone disease.

MATERIALS AND METHODS

This cross-sectional, observational study was conducted at Department of General Surgery, Geetanjali Medical College and Hospital, Udaipur, India, on 117 patients from January 2021 to June 2022, after obtaining approval from the Institutional HREC (vide approval no. 2021/1879 dtd. 1/2/2021). Written informed consent was taken from patients or their guardians before proceeding with the study.

Inclusion criteria: Patients in the age group of 18-80 years, patients with the radiological finding of gallstone disease,patients with controlled co-morbid conditions (diabetes mellitus, hypertension) were included in the study.

Exclusion criteria: Patients with previous history of thyroid surgery and taking thyroid replacement for treatment, stones in the pancreatic duct, patients with cholangitis, pregnant females, patients on drugs causing hypothyroidism: Amiodarone, Lithium, antidepressants, Phenytoin, Interferon, Imatinib, patients on drugs causing gallstones: Estrogen/OCPs, Fenofibrate, Gemfibrozil were excluded from the study.

Study Procedure

The sampling process was consecutive. After admitting patients with a radiological finding of gallstones, a thorough history was obtained, and a clinical examination was conducted. Standard baseline blood investigations, including lipid profiles and liver function tests (S. bilirubin total, direct, indirect), were performed. The disease process and potential management options were explained to patients/guardians. For analysis of the patient's thyroid profile, a morning fasting blood sample was sent to the Biochemistry Laboratory in Geetanjali Hospital, Udaipur, and analysed using the Chemiluminescence method on the Vitros ECIQ instrument. The patients' thyroid status, whether euthyroid, hypothyroid, or hyperthyroid, was noted. Patients with serum Thyroid Stimulating Hormone (TSH) levels between 0.5 and 4.9 mIU/L were considered normal. Subclinical hypothyroidism was

defined as serum TSH levels between 5 and 10 mIU/L with normal T3 and T4 levels. TSH concentrations greater than 10 mIU/L were considered clinical hypothyroidism [9]. The patient's treatment plan, whether conservative or surgical, was chosen after a thorough review. The investigator immediately recorded all the information on the data collection sheets. Hypothyroidism was considered as the dependent variable. Independent variables that were considered included:

- Age (ranging from 18 years to 80 years),
- Sex (male or female),
- Co-morbidities (hypertension, diabetes),
- Ultrasound findings (number and size of stones, presence of CBD stones),
- Thyroid profile (T3, T4, TSH),
- Surgeries performed (laparoscopic/open cholecystectomy, CBD exploration).

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS version 25.0) software was used for statistical analysis. The Chi-square test was applied for non parametric values, and a p-value of <0.05 was considered significant.

RESULTS

The selected patients' ages ranged from 18 to 80 years. The mean age of the study population was 44±11.16 years, which was statistically not significant. There were 32% males and 68% female patients in this study [Table/Fig-1]. The most common co-morbidity present was hypertension, seen in 15 (12.8%) patients [Table/Fig-2]. Forty-nine patients (41.9%) were found to have hypothyroidism, and the remaining 68 patients (58.1%) were found to be euthyroid [Table/Fig-3]. Only 15 of these individuals had known hypothyroidism, while the remaining 34 were newly diagnosed. Out of the 49 hypothyroid patients, 30 were female and 19 were male. The predominant age group was 40-49 years, with a mean age of 45 (±8.9) years [Table/Fig-4].

Age (years)	Gender n (%)		Total (p-value)
	Female	Male	
18-29	8 (6.8)	4 (3.4)	12 (0.686)
30-39	16 (13.6)	9 (7.6)	25 (4.99)
40-49	22 (18.8)	10 (8.5)	32 (0.582)
50-59	22 (18.8)	8 (6.8)	30 (3.32)
60-69	10 (8.5)	4 (3.4)	14 (2.36)
70-79	2 (1.7)	2 (1.7)	4 (1.33)
Total	80 (0.839) (68%)	37 (0.010) (32%)	117

[Table/Fig-1]: Age and gender distribution of patients with gallstones.

Associated co-morbid conditions	n (%)
No co-morbidities	90 (76.9)
Diabetes mellitus	8 (6.8)
Both hypertension and diabetes	4 (3.4)
Hypertension	15 (12.8)
Total number of patients	117 (100)

[Table/Fig-2]: Co-morbid conditions.

Age groups (years)	Thyroid status		Total
	Euthyroidism	Hypothyroidism	
18-29	5	7	12
30-39	13	12	25
40-49	16	16	32
50-59	23	7	30
60-69	8	6	14
70-79	3	1	4
Total	68 (p-value- 0.409)	49 (p-value- 0.194)	117

[Table/Fig-3]: Age assessment in patients of gallstone disease and associated thyroid status.

Age (years)	Male	Female
18-29	3 (6.1)	4 (8.1)
30-39	7 (14.2)	5 (10.2)
40-49	6 (12.2)	10 (20.4)
50-59	0	7 (14.2)
60-69	3 (6.1)	3 (6.1)
70-80	0	1 (2.04)
Total	19 (38.7)	30 (61.2)

[Table/Fig-4]: Gender distribution of gallstone patients with hypothyroidism.

It was observed that 82 patients (70.1%) had multiple stones in their gallbladder 35 patients (29.9%) had a single stone in their gallbladder and eight patients had CBD stones. There was no significant association between hypothyroid state and gallstone formation in either males (p-value: 0.154) or females (p-value: 0.194).

In the assessment of thyroid profiles, the mean and standard deviation were found to be as follows for hypothyroid patients: T3 (2.544±1.051), T4 (6.323±2.33), and TSH (5.728±4.235) [Table/Fig-5].

Variable	T3	T4	TSH
Hypothyroid	2.54±1.05	6.32±2.33	5.72±4.23
Euthyroid	1.88±0.65	7.54±3.12	3.49±2.80
p-value	0.765	0.533	0.454

[Table/Fig-5]: Assessment of thyroid hormone levels.

Both laparoscopic and open treatments were used to handle the patients. Out of the 115 patients who underwent laparoscopic cholecystectomy, two patients had to be converted to an open operation due to bleeding, adhesions, and other intraoperative difficulties. Additionally, eight patients (6.8%) underwent CBD exploration along with cholecystectomy. Among all hypothyroid patients, one patient underwent open cholecystectomy, and 48 underwent laparoscopic cholecystectomy. Out of these 48 patients, five also underwent CBD exploration for managing CBD stones. The postoperative conditions were stable.

DISCUSSION

To assess the importance of thyroid dysfunction as a contributing factor and determine whether thyroid profile should be included in routine investigations for patients with gallstone disease, this study aimed to determine the prevalence of thyroid dysfunction in such patients. All 117 patients underwent a thyroid profile assessment, and it was found that 49 patients (41.9%) had hypothyroidism, which was statistically insignificant with a p-value of 0.194. The remaining 68 patients were found to be euthyroid.

Among these individuals, only 15 had a known diagnosis of hypothyroidism, while the remaining 34 were newly diagnosed. Out of the 49 patients with hypothyroidism, 30 were females and 19 were males, but the difference between the sexes was not statistically significant. This finding was consistent with studies conducted by Raghuvanshi BS et al., (24% prevalence) and Watali YZ et al., (14% prevalence) [1,7].

In the study by Tombisana S et al., the highest number of patients with hypothyroidism belonged to the age group of 46-55 years, comprising 17 individuals (39.5%). The youngest patient was 21 years old. Among the 126 female patients in the same study, 29 (23.1%) had hypothyroidism, and 6 (4.7%) had hyperthyroidism. For male patients, 14 (18.9%) had hypothyroidism, and 3 (3.9%) had hyperthyroidism [4].

Another study by Laukkarinen J et al., reviewed multiple articles on the association [5]. They found that in seven patients with

diagnosed untreated hypothyroidism, the patients had low FT4 levels (4.5 pmol/L [3.8-6.4] vs 18.2 pmol/L [14.5-26.9]; p<0.001) and high TSH levels (75.6 pmol/L [41-180] vs 0.6 pmol/L [0.1-2.4]; p=0.002) compared to the euthyroid stage in gallstone patients. Their previous study also suggested a 7% prevalence in 2002 [10].

This suggests that thyroid dysfunction is associated with changes in bile composition and excretion rate, as well as changes in biliary emptying. These changes may be the probable causes for the increased prevalence of gallstones in hypothyroidism. This inference raises the possibility that changes in the Sphincter of Oddi's function, rather than changes in cholesterol metabolism or bile excretion rate, may be the driving force behind the link between CBD stones and hypothyroidism [5].

A study conducted by Singh AK et al., showed hypothyroid disorders in 20% of male cholelithiasis patients, while euthyroid status was observed in 72.5%. Among female cholelithiasis patients, hypothyroid disorder was found in 14% and hyperthyroid disease in 7% [11].

In the thyroid profile assessment in present study, the mean and standard deviation were found to be as follows: T3 (2.544±1.051), T4 (6.323±2.33), and TSH (5.728±4.235), respectively. The mean TSH value for the predominant age group (40-49) was 6.81, and for the predominant gender (female) was 5.65.

In the study by Raghuvanshi BS et al., 12 out of 50 patients showed hypothyroidism characterised by increased TSH levels in their thyroid profile, with a prevalence rate of 24%. Another study conducted by Völzke H et al., showed that out of 385 people, 10.3% had low serum TSH levels, 88.6% had normal levels, and 1.1% had high levels. The analysis showed a higher percentage of cholelithiasis in males with low serum TSH levels. However, their investigation did not find direct evidence of a link between high blood TSH levels and gallstone disease in females [6].

A similar cross-sectional study conducted by Ghadhban BR and Abid FN found that out of the total number of patients, 8 (7.8%) had subclinical hypothyroidism, and 95 (92.2%) were euthyroid. The subclinical hypothyroid group showed a female gender predominance with 81.6%, while the prevalence among males was 18.4%. This study showed a gender-specific relationship to gallstone disease [12].

In patients with high TSH values, multiple stones were seen in 67.3% and 32.7% had a single stone in their gallbladder. Additionally, five patients had stones in the common bile duct. These findings are similar to the conclusions of the study by Laukkarinen J et al., which showed a high prevalence of subclinical hypothyroidism in CBD stone patients. Specifically, five out of eight patients with CBD stones had subclinical hypothyroidism [10].

Limitation(s)

The study duration was short, and the sample size was small. Previous studies by Raghuvanshi BS et al., Singh J, Laukkarinen J et al., and Vanderpump MP et al., have shown an increased prevalence of subclinical thyroid dysfunction in patients with choledocholithiasis and its potential correlation. However, due to small sample size in present study, the results were insufficient to make definitive conclusions. Further evaluation is needed to explore the association between choledocholithiasis and thyroid dysfunction, particularly in larger population studies [1,8,10,13]. Present study data was insufficient to comment on any association between changes in thyroid function and the postcholecystectomy patient status.

CONCLUSION(S)

There was no significant association between hypothyroidism and gallstone formation in present study. The prevalence of hypothyroidism was low, suggesting no effect of thyroid dysfunction on the formation of gallstones. Further large population studies are needed to compare these findings and provide recommendations for screening and early diagnosis of subclinical hypothyroidism through regular TSH monitoring. Early treatment of subclinical hypothyroidism may help prevent the burden of cholelithiasis in this subgroup of patients.

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PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Student, Department of General Surgery, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
2. Associate Professor, Department of General Surgery, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
3. Assistant Professor, Department of General Surgery, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
4. Senior Resident, Department of General Surgery, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
5. Assistant Professor, Department of General Surgery, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
6. Postgraduate Student, Department of General Surgery, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
7. Postgraduate Student, Department of General Surgery, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
8. Professor, Department of General Surgery, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Chinmay Dangi,
217, Subhash Nagar, Near New Passport Office, Udaipur-313004, Rajasthan, India.
E-mail: dangichinmay@gmail.com

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