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Prevalence of Hypothyroidism and Other Thyroid Disorders Among Patients With Cholelithiasis in a Tertiary Care Centre in South India: A Cross-Sectional Study

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ABSTRACT

Introduction: Thyroid dysfunction has been implicated in the pathogenesis of gallstone disease through its effects on lipid metabolism, bile composition, gallbladder motility, and sphincter of Oddi function. However, the prevalence of hypothyroidism and other thyroid disorders among patients with cholelithiasis remains variable across studies. This study aimed to determine the prevalence of hypothyroidism and other thyroid disorders among patients with cholelithiasis undergoing cholecystectomy and to describe their demographic and clinical characteristics.

Methodology: A hospital-based cross-sectional study was conducted among 120 consecutive patients with ultrasonographically confirmed cholelithiasis undergoing elective cholecystectomy at the Department of General Surgery, Government Medical College, Thiruvananthapuram, Kerala, between July 2019 and July 2020. Demographic and clinical details were collected using a structured proforma. Serum free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) levels were estimated using chemiluminescent microparticle immunoassay. Participants were categorized into euthyroid, hypothyroid, hyperthyroid, subclinical hypothyroid, and subclinical hyperthyroid groups. Data were analysed using SPSS version 16.0, and associations were assessed using the Chi-square test with a p-value <0.05 considered statistically significant.

Results: Of the 120 participants, 68 (56.7%) were euthyroid, while thyroid dysfunction was identified in 52 (43.3%). Hypothyroidism was observed in 29 (24.2%) participants, hyperthyroidism in 14 (11.7%), subclinical hyperthyroidism in 7 (5.8%), and subclinical hypothyroidism in 2 (1.7%). Among patients with thyroid dysfunction, hypothyroidism accounted for 59.6% of cases. Hypothyroidism was more common among older participants and females, whereas hyperthyroidism predominated in younger participants and males. Although hypothyroidism was more frequent among overweight and obese participants, no significant association was observed between BMI and thyroid dysfunction.

Conclusion: Thyroid dysfunction, particularly hypothyroidism, was common among patients with cholelithiasis undergoing cholecystectomy. The predominance of hypothyroidism among older adults and females suggests that thyroid function assessment may be beneficial in selected patients with gallstone disease to facilitate early diagnosis and appropriate management. Further multicentre prospective studies are warranted to clarify the causal relationship between thyroid dysfunction and cholelithiasis.

Keywords: *Cholelithiasis, Hypothyroidism, Thyroid Diseases, Cholecystectomy, Thyrotropin, Cross-Sectional Studies, Prevalence, Gallbladder Diseases.*

INTRODUCTION

Gallstone disease is one of the most common disorders encountered in general surgical practice and remains a significant cause of abdominal morbidity worldwide. [1] Cholelithiasis results from a complex interaction of genetic, metabolic, hormonal, and environmental factors affecting bile composition and gallbladder motility. [1,2] Thyroid hormones play an important role in regulating lipid metabolism, gastrointestinal motility, and biliary physiology, suggesting a possible association between thyroid dysfunction and gallstone formation. Thyroid disorders are common in the general population, and the many studies across world demonstrated a considerable burden of both overt and subclinical thyroid dysfunction among adults. [2]

Interest in the relationship between thyroid dysfunction and gallstone disease has increased over the past two decades. Laukkarinen et al. demonstrated reduced bile flow in patients with hypothyroidism, highlighting the potential role of thyroid hormones in maintaining normal biliary dynamics. [3] The prevalence of gallstone disease has been reported to range from 5% to 25% across different populations and geographic regions. [4] A study from Iran reported a prevalence of 6.3% and emphasized the influence of demographic and metabolic factors on gallstone formation. [5] Studies from India have reported a wide variation in the prevalence of gallstone disease, ranging from approximately 4% to 10%, with higher rates observed in northern regions compared to southern India. Recent Indian data have demonstrated substantial regional variation in gallstone disease prevalence, with rates ranging from 0.3% to 10.8% across different geographic regions of the country. The highest prevalence has been reported from northern and northeastern regions, including Mullanpur (10.8%) and Kamrup, Assam (10.7%), while considerably lower rates have been observed in western India. [6, 7] Several mechanisms have been proposed to explain the association between hypothyroidism and cholelithiasis, including disturbances in cholesterol metabolism, impaired bile secretion, delayed biliary emptying, and increased sphincter of Oddi tone. [8]

Experimental studies have further strengthened this hypothesis. Thyroxine has been shown to exert a direct relaxing effect on the sphincter of Oddi, thereby facilitating bile flow into the duodenum. [9,10] Reduced thyroxine activity may therefore promote biliary stasis and favour gallstone formation. The physiological basis of these effects is supported by the established role of thyroid hormones in regulating metabolic processes and smooth muscle function throughout the body. [11, 12] The scientific rationale of the study was based on emerging evidence suggesting a possible association between thyroid dysfunction and gallstone disease through alterations in lipid metabolism, bile composition, biliary motility, and sphincter of Oddi function. [3, 6-8] Although several international studies have reported an increased prevalence of hypothyroidism among patients with cholelithiasis, data from the Indian population, particularly from South India, remain limited. The present study was undertaken to address this knowledge gap by evaluating the prevalence of hypothyroidism and other thyroid dysfunctions among patients with cholelithiasis in a tertiary care setting, thereby providing region-specific evidence on this clinically relevant association. Therefore, the present study was undertaken to determine the prevalence of hypothyroidism and other thyroid disorders among patients with cholelithiasis undergoing cholecystectomy in a tertiary care centre and to describe their demographic and clinical characteristics.

METHODOLOGY

Study Design, Setting, Duration

The present hospital-based cross-sectional study was conducted in the Department of General Surgery, Government Medical College, Thiruvananthapuram, Kerala, India. The study included patients with cholelithiasis who were admitted for elective cholecystectomy in the surgical wards of the institution. Data collection was carried out over a one-year period from July 2019 to July 2020.

Study population, Sample size, and Sampling

Inclusion criteria: The study included male and female patients diagnosed with cholelithiasis and admitted to the Department of General Surgery, Government Medical College, Thiruvananthapuram, for elective cholecystectomy during the study period. Participants who provided informed consent and fulfilled the eligibility criteria were enrolled consecutively.

Exclusion criteria: Patients with a history of thyroidectomy, previously diagnosed hypothyroidism receiving treatment, pregnancy, haemolytic disorders, and those receiving medications known to interfere with thyroid function tests, including phenytoin, carbamazepine, metoclopramide, amiodarone, and lithium, were excluded from the study.

The sample size was calculated based on a previous study by Singh et al that reported a prevalence of hypothyroidism of 24% among patients with gallstone disease. [12] Using the formula $n = 4pq/d^2$, where $p = 24$, $q = 76$, and absolute precision $(d) = 8\%$, the minimum required sample size was estimated to be 114. A total of 120 patients were included in the study. A consecutive sampling technique was employed. All eligible patients diagnosed with cholelithiasis and

admitted for elective cholecystectomy during the study period were approached for participation and enrolled consecutively after obtaining informed consent until the required sample size was achieved.

Method of data collection and study variables

Data were collected from patients with cholelithiasis admitted to the Department of General Surgery, Government Medical College, Thiruvananthapuram, who were scheduled for elective cholecystectomy. After obtaining informed consent, demographic and clinical information including age, sex, height, weight, and body mass index (BMI) were recorded using a structured data collection proforma. The diagnosis of cholelithiasis was confirmed by ultrasonography and intraoperative findings documented in the hospital records. Venous blood samples were collected from all participants for estimation of serum free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) levels using chemiluminescent microparticle immunoassay (CMIA). Based on thyroid function test results, participants were categorized as euthyroid, hypothyroid, hyperthyroid, subclinical hypothyroid, or subclinical hyperthyroid. The primary outcome variable was the prevalence of hypothyroidism and other thyroid dysfunctions among patients with cholelithiasis, while age, sex, and BMI were evaluated as associated clinical characteristics.

Data analysis and ethical consideration

The collected data were entered into Microsoft Excel and analysed using Statistical Package for the Social Sciences (SPSS) version 16.0. Continuous variables were summarized as mean ± standard deviation (SD), while categorical variables were expressed as frequencies and percentages. The distribution of thyroid function status among patients with cholelithiasis was assessed, and associations between thyroid dysfunction and selected demographic and clinical variables were evaluated using the Chi-square test. A p-value of <0.05 was considered statistically significant.

All participants were informed about the objectives of the study, and written informed consent was obtained prior to enrolment. Confidentiality and anonymity of participant information were maintained throughout the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of Government Medical College, Thiruvananthapuram, prior to commencement of the study, with reference number HEC.No.07/01/2019/MCT

RESULTS

Sociodemographic and clinical features (n=120)

Among the 120 patients with cholelithiasis included in the study, the largest proportion belonged to the 41–50 years age group (36.7%), followed by 31–40 years (25.8%). Females constituted a slightly higher proportion of the study population than males (52.5% vs. 47.5%). With regard to nutritional status, the majority of participants (67.5%) had a BMI between 25 and 29.9 kg/m², while only 4.2% had a BMI of ≥30 kg/m². **(Table -1)**

Distribution of Thyroid Function Status (n=120)

Among the 120 patients with cholelithiasis included in the study, 68 (56.7%) were euthyroid. Thyroid dysfunction was identified in 52 (43.3%) participants, of whom 29 (24.2%) had hypothyroidism, 14 (11.7%) had hyperthyroidism, 7 (5.8%) had subclinical hyperthyroidism, and 2 (1.7%) had subclinical hypothyroidism. Euthyroid status was the most common thyroid profile observed among the study participants **(Figure 1), (Table 2).** Among the 52 patients identified with thyroid dysfunction, hypothyroidism was the predominant abnormality, accounting for 31 (59.6%) cases, while hyperthyroidism was observed in 21 (40.4%) cases. **(Figure 2)**

Relationship Between Age, Sex, BMI and Type of Thyroid Dysfunction (n=120)

Hypothyroidism was more common among older participants, accounting for 73.7% of thyroid dysfunction cases in the 41–50 years age group and 72.7% among those aged above 50 years, whereas hyperthyroidism was relatively more frequent among participants aged less than 30 years (75.0%). A statistically significant association was observed between age group and type of thyroid dysfunction ($\chi^2 = 8.21$, $p = 0.042$). Similarly, females demonstrated a significantly higher prevalence of hypothyroidism than males (74.2% vs. 38.1%), while hyperthyroidism was more common among males than females (61.9% vs. 25.8%) ($\chi^2 = 6.54$, $p = 0.011$). Although hypothyroidism was more frequently observed among participants with a BMI ≥30 kg/m² (75.0%) and those with a BMI of 25–29.9 kg/m² (64.7%), the association between BMI category and type of thyroid dysfunction was not statistically significant ($\chi^2 = 2.31$, $p = 0.315$). **(Table-3)**

TABLES

Table 1: Sociodemographic and clinical characteristics of study participants (N = 120)

Variable	Frequency (n)	Percentage (%)
Age group (years)		
<30	19	15.8
31–40	31	25.8
41–50	44	36.7
>50	26	21.7

Sex		
Male	57	47.5
Female	63	52.5
BMI (kg/m²)		
<18.5	3	2.5
18.5–24.9	31	25.8
25–29.9	81	67.5
≥30	5	4.2

Table 2. Distribution of Thyroid Function Status among patients with cholelithiasis (N = 120)

Thyroid status	Frequency (n)	Percentage (%)
Euthyroid	68	56.7
Hypothyroid	29	24.2
Hyperthyroid	14	11.7
Subclinical hyperthyroidism	7	5.8
Subclinical hypothyroidism	2	1.7
Total	**120**	**100.0**

Table 3. Association of Age Group, Sex and BMI with Type of Thyroid Dysfunction (N = 52)

Variable	Hypothyroid n (%)	Hyperthyroid n (%)	Total	χ^2	p value
Age group (years)				**8.21**	**0.042**
<30	2 (25.0)	6 (75.0)	8		
31–40	7 (50.0)	7 (50.0)	14		
41–50	14 (73.7)	5 (26.3)	19		
>50	8 (72.7)	3 (27.3)	11		
Sex				**6.54**	**0.011**
Male	8 (38.1)	13 (61.9)	21		
Female	23 (74.2)	8 (25.8)	31		
BMI (kg/m²)				**2.31**	**0.315**
<25	6 (42.9)	8 (57.1)	14		
25–29.9	22 (64.7)	12 (35.3)	34		
≥30	3 (75.0)	1 (25.0)	4		

FIGURES

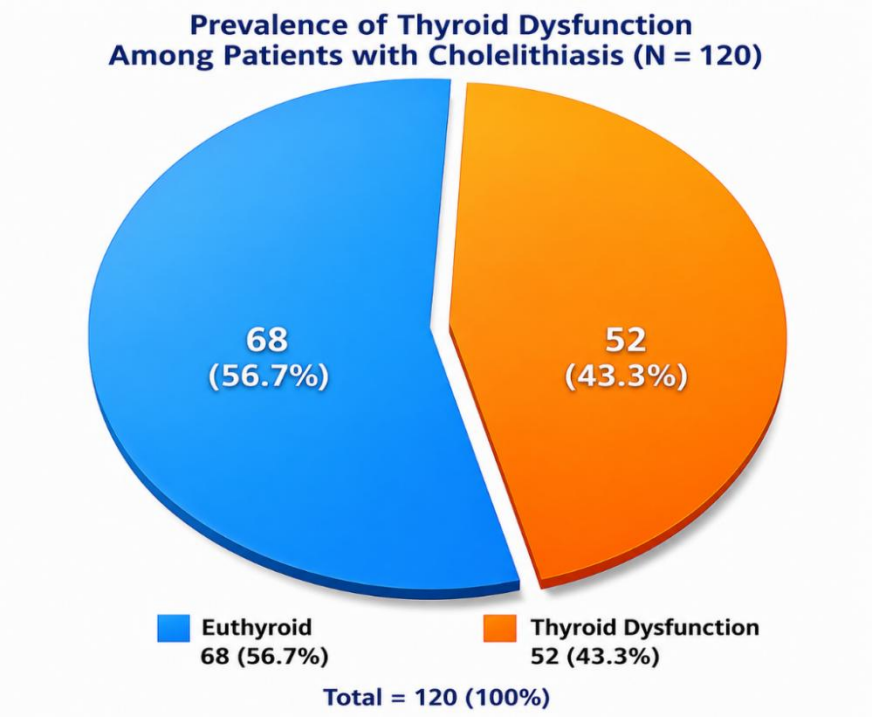

Figure 1: Prevalence of thyroid dysfunction in patients with cholelithiasis (N=120)

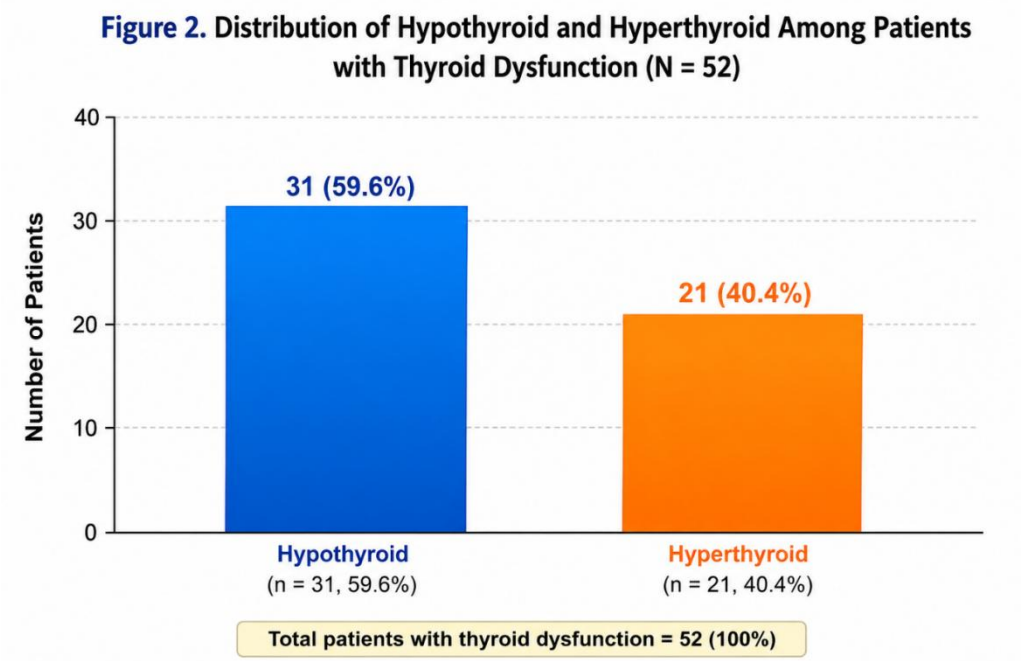

Figure 2. Distribution of Hypothyroid and Hyperthyroid Disorders Among Patients with Thyroid Dysfunction (N = 52)

DISCUSSION

In the present study, thyroid dysfunction was identified in 43.3% of patients with cholelithiasis, with hypothyroidism accounting for 24.2% of all participants and representing 59.6% of all thyroid dysfunction cases, while hyperthyroidism constituted 17.5% of the study population and 40.4% of thyroid dysfunction cases. The proportion of hypothyroidism and other thyroid dysfunctions observed in the present study was higher than that reported in several previous studies. Inkinen et al. [13] reported hypothyroidism in only 6% of patients with gallbladder stones and 11% of patients with common bile duct stones, compared with the substantially higher prevalence of hypothyroid disorders observed in our cohort. Similarly, Laukkarinen et al. [14, 15] documented subclinical hypothyroidism in 5.3% of common bile duct stone patients, while only 1.0% of controls were affected, supporting the association between biliary stone disease and thyroid dysfunction. Similar to our study, review by Kulkarni et al. [16], concluded that both clinical and subclinical hypothyroidism occur more frequently among patients with cholelithiasis. Megalai Mani et al. [17] reported euthyroid status in 86.7% of cholelithiasis patients, with only 10.0% having subclinical hypothyroidism and 3.3% having overt hypothyroidism, whereas a considerably lower proportion of euthyroid individuals and a higher burden of thyroid dysfunction were observed in the present study. Likewise, Singha et al. [18] found clinical, subclinical, and borderline subclinical hypothyroidism in 2.2%, 5.0%, and 6.6% of cholelithiasis patients, respectively, giving an overall prevalence of 13.8%, which was lower than that observed in our study. The female predominance and increasing frequency of hypothyroidism with advancing age observed in our study were also consistent with the findings of Singha et al. [18], who reported that hypothyroidism was particularly common among women aged above 50 years, with a prevalence of 32.4%. Furthermore, Volzke et al. [19] demonstrated a significant association between elevated serum TSH levels and cholelithiasis among males (OR 3.77; 95% CI: 1.06–13.41), highlighting the potential contribution of thyroid dysfunction to gallstone pathogenesis. The higher prevalence of thyroid dysfunction observed in the present study compared to earlier reports may be attributed to differences in study population, geographic variation, inclusion of all thyroid dysfunction categories, and variations in diagnostic criteria and thyroid function assessment. The overall findings of our study are in agreement with the previous studies which concluded that both clinical and subclinical hypothyroidism occur more frequently among patients with cholelithiasis and may contribute to gallstone formation through impaired sphincter of Oddi relaxation and biliary stasis. The similarity in findings across studies may be attributed to the comparable demographic profile of patients with cholelithiasis, particularly the predominance of middle-aged and older adults and females, who are at an increased risk of hypothyroidism.

The prevalence of thyroid dysfunction observed in the present study (43.3%) was substantially higher than that reported by Gadhban et al. [20], who identified subclinical hypothyroidism in only 7.8% of patients, with 92.2% remaining euthyroid. Fayziyev et al. [21] reported a higher prevalence of subclinical hypothyroidism (32.2%) and overt hypothyroidism (16.4%) among patients with cholelithiasis compared with healthy controls, further supporting the association between thyroid dysfunction and gallstone disease. The prevalence of hypothyroidism in our study (24.2%) was comparable to that reported by Arun N et al. [22], who documented hypothyroidism in 23% of patients with gallstone

disease, but was higher than the prevalence reported by Mukthar Ali et al. [23] and Ajdarkosh et al. [24], who found hypothyroidism in 14.4% and 11.3% of patients, respectively. Similarly, Arbab et al. [25] observed subclinical hypothyroidism in only 8.16% of patients, whereas Dangi et al. [26] reported a markedly higher prevalence of hypothyroidism (41.9%) than that observed in the present study. The female predominance of hypothyroidism and its greater occurrence in older age groups observed in our study were also consistent with the findings reported by Mukthar Ali et al. [23], Arbab et al. [25], and Dangi et al. [26]. The variations in prevalence across studies may be attributed to differences in study design, sample characteristics, diagnostic criteria, thyroid function assessment methods, and geographic factors. Collectively, the available evidence indicates that thyroid dysfunction is more frequently encountered among patients with cholelithiasis, supporting the importance of considering thyroid function assessment as part of the clinical evaluation in selected high-risk patients. The observed similarities may also be due to comparable demographic profiles across studies, particularly the predominance of middle-aged and older adults and the higher proportion of female participants, who are known to have an increased risk of both thyroid dysfunction and gallstone disease.

The prevalence of thyroid dysfunction observed in the present study (43.3%) was considerably higher than that reported by Jabini et al. [27], who documented an overall hypothyroidism prevalence of 9.9%, comprising 5.6% clinical and 4.3% subclinical hypothyroidism among patients with gallbladder sludge and stones. Similarly, the prevalence of hypothyroidism in our study (24.2%) was lower than the 40.0% reported by Maji et al. [28] but substantially higher than the prevalence reported by Murasingh et al. [29], who observed clinical hypothyroidism in 5.5% and subclinical hypothyroidism in 26.0% of patients, and by Rohan et al. [30], who identified elevated TSH levels in only 9.1% of patients. The prevalence of hypothyroidism in our study was comparable to that reported by Karthikeyan et al. [31], who demonstrated hypothyroidism in 22.9% of patients with common bile duct stones, and Aranya et al. [32], who reported hypothyroidism in 26.0% of patients with cholelithiasis. Likewise, Sinha et al. [33] and Bhavani et al. [34] documented lower prevalences of hypothyroidism of 19.4% and elevated TSH in 15.7% of patients, respectively. These similarities and differences may be attributed to variations in study populations, inclusion criteria, thyroid function assessment, geographic factors, and the spectrum of gallstone disease evaluated across studies.

The female predominance of hypothyroidism observed in the present study was in agreement with the findings of Maji et al. [28], Sinha et al. [33], Bhavani et al. [34], and Biswas et al [35], all of whom reported a higher burden of thyroid dysfunction among women with cholelithiasis. Similarly, the greater occurrence of hypothyroidism among older participants in our study corresponded with the observations of Rohan et al. [30], who reported raised TSH predominantly in patients aged 61–80 years, and Sidduri et al. [36], who found subclinical hypothyroidism in 36% of patients aged above 50 years compared with 22% among younger individuals. Furthermore, Biswas et al. [35] demonstrated a significantly higher prevalence of subclinical hypothyroidism among cases than controls (30.0% vs. 17.5%), while Sidduri et al. [36] reported subclinical hypothyroidism in 30.0% of cases compared with 9.1% of controls, further supporting the association between thyroid dysfunction and gallstone disease. The overall consistency of these findings may be explained by the shared pathophysiological effects of thyroid hormone deficiency on lipid metabolism, biliary motility, gallbladder emptying, and sphincter of Oddi relaxation, together with the predominance of middle-aged and female patients across most study populations.

Although the overall findings of the present study were largely consistent with previous reports, minor variations in the prevalence of hypothyroidism and other thyroid dysfunctions were observed. These differences may be attributed to variations in sample size, study design, geographic location, demographic characteristics, inclusion and exclusion criteria, spectrum of gallstone disease studied, thyroid function assessment methods, and differences in laboratory assays and diagnostic cut-off values used across studies. In short, the present study adds to the growing body of evidence supporting an association between thyroid dysfunction and cholelithiasis, particularly among middle-aged and older women. Nevertheless, well-designed multicentre prospective studies with larger sample sizes are warranted to confirm these findings and establish evidence-based recommendations for thyroid screening in patients with gallstone disease.

CONCLUSION

The present study demonstrated that thyroid dysfunction was identified in 43.3% of patients with cholelithiasis undergoing cholecystectomy, with hypothyroidism being the predominant abnormality, affecting 24.2% of patients and accounting for 59.6% of all thyroid dysfunction cases. Hypothyroidism was more frequently observed among older individuals and females, suggesting that advancing age and female sex may increase susceptibility to thyroid dysfunction in patients with gallstone disease. The higher occurrence of hypothyroidism in this population may be explained by thyroid hormone deficiency-induced alterations in lipid metabolism, impaired bile secretion, reduced gallbladder motility, and diminished sphincter of Oddi relaxation, all of which promote biliary stasis and facilitate gallstone formation. Although hypothyroidism was more common among overweight and obese participants, no significant association was observed between BMI and the type of thyroid dysfunction, indicating that factors other than adiposity may play a greater role in the thyroid–gallstone relationship. These findings support the consideration of thyroid function assessment in patients with cholelithiasis, particularly in middle-aged and older women, to facilitate early diagnosis and appropriate

management. Further large-scale, multicentre prospective studies are warranted to establish the causal relationship between thyroid dysfunction and gallstone disease and to determine whether early detection and treatment of thyroid disorders can reduce the risk of gallstone formation and its associated complications.

RECOMMENDATIONS

The findings of the present study emphasize the need to consider routine thyroid function assessment in patients with cholelithiasis, particularly among middle-aged and older adults and female patients, who demonstrated a higher prevalence of hypothyroidism. Incorporating serum TSH, FT3, and FT4 estimation into the preoperative evaluation of patients undergoing cholecystectomy may facilitate the early detection of previously unrecognized thyroid dysfunction and enable timely referral for appropriate endocrine management. Considering the high prevalence of thyroid dysfunction observed in this study, clinicians should maintain a greater index of suspicion for underlying thyroid disorders in patients presenting with gallstone disease, especially in the absence of other identifiable risk factors. Early diagnosis and appropriate treatment of hypothyroidism may improve metabolic abnormalities, optimize perioperative care, and potentially reduce biliary stasis and the progression or recurrence of gallstone disease, although this warrants further investigation. From a public health perspective, targeted screening of high-risk cholelithiasis patients rather than universal screening may represent a cost-effective strategy. Future large-scale multicentre prospective studies are recommended to validate these findings, evaluate the long-term impact of thyroid hormone replacement on gallstone outcomes, and develop evidence-based recommendations for thyroid screening in patients with cholelithiasis.

LIMITATIONS

The limitations and shortcomings are inherent to research endeavors, often stemming from constraints on resources, funding, access to information, or the absence of a flawless system to follow. Being a single-centre, hospital-based cross-sectional study, the findings may not be generalizable to the wider population and the study design precludes establishing a causal relationship between thyroid dysfunction and cholelithiasis. The relatively small sample size and inclusion of only patients undergoing elective cholecystectomy may have introduced selection bias. In addition, the absence of a control group without cholelithiasis and the lack of long-term follow-up limited the assessment of the temporal relationship between thyroid dysfunction and gallstone disease.

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DECLARATIONS

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Conflict of interest: The authors of this article declare that they have no financial or personal relationships with other individuals or organizations that could inappropriately influence or bias their work. There are no employment affiliations, consultancies, stock ownership, honoraria, paid expert testimonies, patent applications/registrations, or any other financial or personal relationships that could be perceived as a conflict of interest in connection with this research.

Furthermore, there are no non-financial relationships, such as partnerships, collaborations, or affiliations of any nature, that could potentially affect the objectivity, integrity, or impartiality of this study. The authors have not been involved in the development of any system or technology under evaluation in this study. This article is presented with full transparency and adherence to ethical standards, and the authors affirm that there are no conflicts of interest that could compromise the credibility or validity of the research presented herein.

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