

# Hypothyroidism and Gallstone Connection: A Tertiary Hospital-Based Observational Cross-sectional Analysis in North East India

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## Abstract

**Background:** Gallstone is one of the most common pathologies of biliary tree and the prevalence varies according to age, sex, and geography of the region. It is also related to certain food habits, and lifestyle. Increase in serum cholesterol in hypothyroidism, predisposes to supersaturation of bile with cholesterol and later stone formation.

**Materials and Methods:** This is an observational cross-sectional study with sample size of 100 cases, between 10 and 70 years with asymptomatic or symptomatic cholelithiasis and/or choledocholithiasis with body mass index = 18.5–25 kg/m<sup>2</sup>, done over a period of 12 months after taking consent. Different variables were studied, such as age, sex, thyroid function test, diagnosis, procedure done, and type of stone.

**Results:** This cross-sectional study revealed that females were more commonly affected with gallstone disease. The mean age of presentation was 42 years, and the least affected age group was below 20 years. The prevalence of hypothyroidism was 45% (both clinical and subclinical) among the cases. Clinical hypothyroidism in females with gallstone was found to be statistically significant ( $P < 0.05$ ). Cholesterol stones were most common with a significant association between female sex and the type of stone (cholesterol vs. non-cholesterol), with a  $P = 0.042$ .

**Conclusion:** The present cross-sectional study conducted at a tertiary care hospital in North-east India concluded a significant association between gallstone disease and hypothyroidism. However, further research needs to be carried out with a bigger sample size to establish this correlation.

**Key words:** Choledocholithiasis, Cholelithiasis, Gallstone, Hypothyroidism, Subclinical hypothyroidism

## INTRODUCTION

Archaeological evidence indicates that around 2000 years ago, young Egyptian women had gallstones during the period of the Roman Empire.<sup>[1]</sup>

Gallstone is the most commonly encountered problem of the biliary tree.<sup>[2]</sup>

It is usually secondary to an abnormality in lipid and bile salt levels, which causes accumulation of the bile salts in the gallbladder cavity.<sup>[3]</sup>

Its prevalence varies according to demographics, age, sex, geography of the region, food habits, sedentary lifestyle, and obesity.<sup>[4,5]</sup>

The action of hormones secreted by the thyroid gland on cholesterol metabolism is well established.<sup>[6]</sup> Thyroxine has a direct pro relaxing effect. The smooth muscles on the sphincter of Oddi possess thyroid hormone receptors.<sup>[7]</sup> Hence a decrease in thyroid function leads to less relaxation of Sphincter of Oddi and causes stagnation of bile in the gallbladder. Hypothyroidism causes increase in serum cholesterol, hence leads to the disturbance in

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lipid metabolism which causes supersaturation of bile with cholesterol. This contributed to the development of cholesterol stones.<sup>[8]</sup> Bile flow in hypothyroid patients is slowed down, which leads to stagnation of bile in gallbladder, giving more time for the nucleation process for gallstone formation.<sup>[9]</sup> In hypothyroidism, the conjugation of bilirubin gets affected, due to the decreased effect of UDP glucuronyl transferase, which in turn leads to increase in the unconjugated bilirubin and results in formation of pigment stones.

Several studies conducted so far have either found an association or no association of gallstone disease with hypothyroidism. The relationship remains debatable. Hence, the present research attempts to understand the same potential relation in the present setting and among a defined population.

## MATERIALS AND METHODS

Type and timeline of study: Observational cross-sectional study in a tertiary care hospital over 12 months

Sample size: 100 cases

### Inclusion Criteria

1. Patients between 10 and 70 years with asymptomatic or symptomatic cholelithiasis and body mass index (BMI) = 18.5–25 kg/m<sup>2</sup>
2. Patients between 10 and 70 years with asymptomatic or symptomatic choledocholithiasis and BMI = 18.5–25 kg/m<sup>2</sup>
3. Eligible patients who give consent for the study.

### Exclusion Criteria

1. Patients with a previous history of hypothyroidism or thyroid intervention or already on treatment
2. Patients with a history of cirrhosis, crohn's disease
3. Pregnant
4. Patients on oral contraceptive
5. Patients who don't give consent for the study
6. Patients below 10 or above 70 years of age.

### Data Collection

Data were collected using a pre-tested structured questionnaire, from all the cases by direct interview after getting informed written consent.

### Variables Studied

1. Age
2. Sex
3. Thyroid function status
4. Type of stone

5. Diagnosis
6. Operative procedure.

### Working Definitions

- Subclinical hypothyroidism – thyroid-stimulating hormone (TSH) more than 4.05 mIU/L with normal Free T4 level
- Clinical hypothyroidism – TSH more than 4.05 mIU/L with Free T4 level of <10 pmol/L and/OR Free T3 level <4.26 pmol/L.

## RESULTS

1. The age-group distribution of 100 patients showed an average age of 42 years to be most affected.
2. Gender distribution indicates a 1.3 times higher representation of females in the study population compared to males.
3. Clinical hypothyroidism in females with gallstones was found to be statistically significant ( $P < 0.05$ ).
4. The majority of patients had cholelithiasis.
5. The most common type of stone is cholesterol stones, with significant association between female and cholesterol stones ( $P = 0.042$ ).
6. A majority underwent laparoscopic cholecystectomy (95%) and 5% of patients underwent open common bile duct (CBD) exploration.

## DISCUSSION

The present study observed the gender-based distribution of 100 patients, where 56% are female, and 44% are male. This indicates a 1.3 times higher representation of females in the study population compared to males. In 2005, Völzke *et al.* conducted research in Pomeria, Central Europe and concluded that the proportion of cholelithiasis among males and females was 14.4% and 25.3%, respectively.<sup>[10]</sup> In 2015, Ahmad *et al.* did a study and found that out of a total of 50 patients of cholelithiasis 84% were female and males 16%. The most common age group was 41–50 (36%) correct (insignificant at  $P < 0.05$ ) 12 (24%).<sup>[11]</sup>

This study showed an average age of 42 years to be most commonly affected. 4%. In the age group <20 years and more than 40 years, female preponderance is seen. However, in the age group from 21 years to 40 years, males are more affected. In 2019, Tombisana *et al.* observed that the maximum number of cholelithiasis patients with hypothyroidism were in the age group of 46–55 years comprising 39.5%. The minimum age recorded was 21 years.<sup>[12]</sup> In 2020, Wali *et al.* conducted a study to know the association of thyroid functions tests in diagnosed

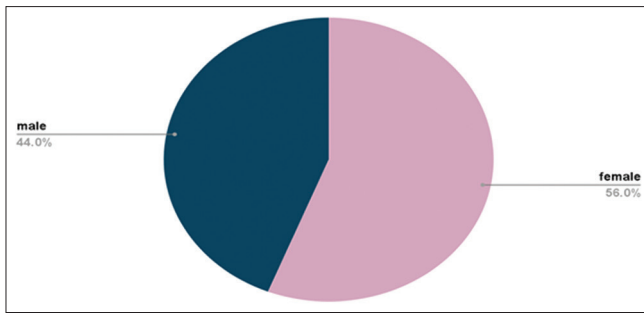


Figure 1: Gender distribution

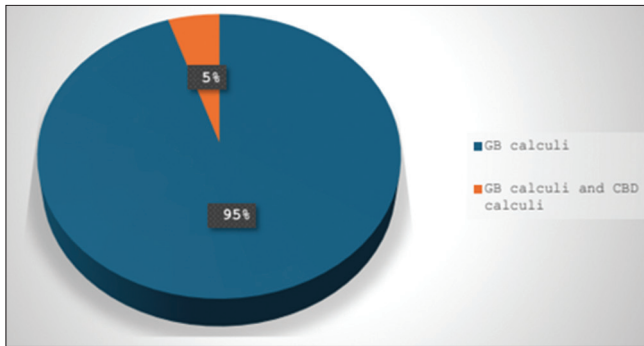


Figure 2: Diagnosis of patients

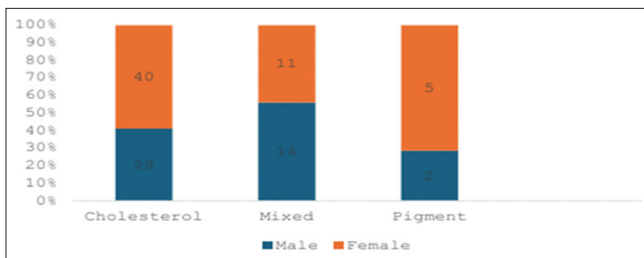


Figure 3: Gallstone type

Table 1: Age group distribution

Age group (years)	Percentage (Frequency)
<20	4
21–30	19
31–40	25
41–50	23
51–60	18
61–70	11

Table 2: Thyroid function status

Thyroid function status	Frequency			P-value
	Male	Female	Total	
Euthyroid	25	30	55	
Subclinical hypothyroidism	15	12	27	>0.05
Clinical hypothyroidism	4	14	18	<0.05

cases of gallstone disease. 43 (71.5%) were females and 57 (28.5%) were males with a median age of 40 years. Thyroid disorder in the form of hypothyroidism was

found in 37 (18.5%) patients (higher TSH levels than normal value for their age), 28 (19.6%) were females and 9 (15.8%) males.<sup>[13]</sup> The most common type of stone found in our study was cholesterol followed by mixed followed by pigment. Rasool *et al.* found the most common gallstones were mixed stones with 80.7%, followed by cholesterol stones with 13.5% and pigment stones with 5.8%.<sup>[14]</sup> Qiao *et al.* conducted study on systemic classification of gallbladder stones and found cholesterol stones to be most common in the study population.<sup>[15]</sup>

Among the total participants, 55% were euthyroid, 27% subclinical hypothyroid, and 18% clinical hypothyroid cases were identified categories. The statistical analysis revealed a significant difference ( $P = 0.03$ ) between male and female in clinical and subclinical hypothyroidism who developed gallstones. A prospective study conducted in 2007 (Laukkanen *et al.*) showed that subclinical hypothyroidism is more common in biliary stone disease. The prevalence of subclinical hypothyroidism in biliary stone patients found to be 5.3% and in control patients found to be 1.4%. A total of 5.3 and 5.0% (total 10.2%; 31 of 303) of the CBD stone patients were diagnosed to have subclinical and borderline-subclinical hypothyroidism, compared with 1.4% ( $P = 0.05$ ) and 1.4% (total 2.8%, four of 142;  $P = 0.026$ ) in the control group, respectively.<sup>[16]</sup> In 2019, Tombisana *et al.* observed that among the seven choledocholithiasis patients with hypothyroidism, five were subclinical with 71.4% of the cases.<sup>[12]</sup> Zaini and Zwain, in Iraq, showed that gallstone has a relatively high incidence of hypothyroidism in patients between the age group of 51–60 years. Out of 225 patients with gallstone 198 (88%) were females and 27 (12%) males. Thyroid disorder in the form of hypothyroidism was found in 24 patients (10.6%), (from this percentage 22 (9.7%) were females.<sup>[17]</sup> 95% of the patients were diagnosed with stone in gallbladder and 5% as having stone in both gallbladder and CBD. A majority, 95%, underwent laparoscopic cholecystectomy, while 5% required open cholecystectomy with CBD exploration.

## CONCLUSION

There is a high prevalence of hypothyroidism (both clinical and subclinical combined, 45%) among the patients of gallstone. Clinical hypothyroidism in females with gallstone was found to be statistically significant ( $P < 0.05$ ). Hence, it is observed that hypothyroid is a risk factor for the development of gallstones. Most of the gallstones were found to be cholesterol stones with a significant association with female sex ( $P = 0.042$ ). Surgeons should be aware of possible associated hypothyroidism in gallstone disease patients and should consider evaluating the thyroid profile pre-operatively, although further research needs

to be carried out with bigger sample size to establish this correlation of hypothyroidism in gall stone disease patients.

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