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Original Research Article

Prevalence of Hypothyroidism in Patients Presenting with Cholelithiasis: A Prospective Observational Study from a Tertiary Care Centre in Eastern India

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Abstract

Background: Cholelithiasis and hypothyroidism are among the most prevalent surgical and endocrine conditions in tertiary care in India, sharing overlapping demographic profiles and mechanistic pathways. Despite a biologically plausible link through altered cholesterol metabolism, impaired gallbladder motility and sphincter of Oddi dysfunction, region-specific data on their coexistence remain sparse. This study aimed to determine the prevalence of hypothyroidism—both overt and subclinical—in patients with ultrasonographically confirmed cholelithiasis and to characterise associated metabolic derangements.

Methods: A prospective observational study was conducted from November 2023 to October 2025 at the Department of General Surgery, M.K.C.G. Medical College and Hospital, Berhampur, Odisha—a tertiary care teaching institution serving southern Odisha. Ninety-seven adult patients (aged 18–70 years) with sonologically confirmed symptomatic cholelithiasis were enrolled after applying predetermined inclusion and exclusion criteria. A sample size of 97 was derived from a reference prevalence of 20%, 80% power, $\alpha = 0.05$, and a precision of ±8% (calculated n = 96). Serum TSH, free T3 and total T4 were measured in all participants; thyroid status was classified as euthyroid, subclinical hypothyroid (elevated TSH, normal T3/T4) or clinically hypothyroid (elevated TSH with reduced T3/T4). Fasting lipid profile including total cholesterol, triglycerides, LDL and HDL was recorded. Statistical analysis used chi-square, one-way ANOVA with Tukey post-hoc test and Pearson correlation; $p < 0.05$ was taken as significant.

Results: The cohort (N = 97) had a mean age of 47.3 ± 12.6 years (range 18–70 years) and a female predominance of 73.2% (F:M = 2.7:1). Overall, 27.8% of cholelithiasis patients had hypothyroidism: 17.5% subclinical and 10.3% overt clinical hypothyroidism. Dyslipidaemia was present in 20.0% of euthyroid patients compared with 64.7% in subclinical and 80.0% in clinical hypothyroid patients ($\chi^2 = 22.680$, $p < 0.001$; OR 9.50, 95% CI 3.45–26.15). TSH showed significant positive correlations with total cholesterol ($r = 0.480$), triglycerides ($r = 0.537$) and LDL ($r = 0.562$), and an inverse correlation with HDL ($r = -0.462$), all $p < 0.001$. In a sensitivity analysis restricted to patients without complicated disease (no fever or jaundice; n = 60), the prevalence of hypothyroidism remained 23.3%. Age, gender, BMI and stone multiplicity did not show statistically significant associations with thyroid status.

Conclusion: More than one in four patients presenting with cholelithiasis to a tertiary surgical unit harboured hypothyroidism, with the subclinical variety predominating. Thyroid dysfunction was strongly linked to an atherogenic lipid profile and dyslipidaemia. The prevalence was robust across a sensitivity analysis excluding complicated cases. Incorporating thyroid function testing—at minimum, serum TSH—into the routine metabolic workup of cholelithiasis patients, particularly those with coexisting dyslipidaemia, appears clinically justified.

Keywords: Cholelithiasis; Hypothyroidism; Subclinical hypothyroidism; Dyslipidaemia; TSH; Gallstone disease; Cholecystectomy; Eastern India.

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Introduction

Gallstone disease remains one of the commonest reasons for elective abdominal surgery worldwide, and its burden is growing in India alongside rapid urbanisation and the rising prevalence of metabolic syndrome. Population-based data from the Gangetic basin have documented a substantial prevalence of gallbladder disease, with female gender, advancing age, multiparity and obesity emerging as dominant risk factors. [1] The condition exerts a significant economic cost through emergency admissions, cholecystectomy services and the management of complications such as acute cholecystitis, choledocholithiasis and gallstone pancreatitis.

Hypothyroidism, which encompasses both overt thyroid failure and the biochemically milder subclinical form, is among the most frequent endocrine disorders encountered in Indian adult populations. A multicentre national survey spanning eight cities estimated that a considerable proportion of adults have biochemical hypothyroidism, a large fraction of whom remain undetected without active screening. [2] The condition predisposes individuals to secondary hypercholesterolaemia by impairing hepatic LDL receptor-mediated clearance and reducing bile acid synthesis, thereby increasing biliary cholesterol content and creating a lithogenic bile environment. In hypothyroid states, thyroid hormone-dependent smooth muscle contractility is reduced, affecting both gallbladder emptying and sphincter of Oddi relaxation, which further promotes bile stasis and crystal nucleation. [3-5]

Registry-based cohort studies from Scandinavia have documented a significantly higher rate of bile duct stone procedures among hypothyroid patients than in the general population, particularly in those above 60 years, suggesting that thyroid dysfunction may be an independent risk factor not only for gallbladder stone formation but also for ductal stone retention. [6] More recent Indian observational data have begun to explore this relationship, consistently finding that 12–22% of cholelithiasis patients harbour previously unrecognised hypothyroidism, with the subclinical variety predominating. [7-12] Despite these emerging reports, region-specific data from eastern India remain limited, and most available studies have not simultaneously characterised the lipid profile, body composition and ultrasonographic stone characteristics across thyroid status subgroups. Understanding the extent and metabolic correlates of hypothyroidism in patients who present to a tertiary surgical unit with gallstone disease has direct implications for perioperative risk stratification, metabolic optimisation before cholecystectomy, and the rational use of thyroid function testing in surgical practice. We hypothesised that the prevalence of hypothyroidism among patients presenting with symptomatic cholelithiasis to a tertiary surgical unit would exceed the estimated 10–15% background prevalence of hypothyroidism in the Indian adult population. [2] The present study was therefore designed to: (1) determine the prevalence of hypothyroidism among patients with ultrasonographically confirmed cholelithiasis; (2) characterise the associated biochemical and metabolic profile across thyroid status categories; and (3) examine the relationship between thyroid dysfunction and the clinical and imaging features of gallstone disease.

Materials and Methods

Study Design, Setting and Period: This was a prospective, hospital-based, observational study conducted from November 2023 to October 2025 in the Department of General Surgery, M.K.C.G. Medical College and Hospital, Berhampur, Odisha—a tertiary care teaching institution serving southern Odisha with a large catchment from the districts of Ganjam, Gajapati and Kandhamal. Ethical clearance was obtained from the Institutional Ethics Committee prior to enrolment (IEC/MKCG/2024/21/08), and the study adhered to the guidelines of the Indian Council of Medical Research and the principles of the Declaration of Helsinki (2000). Written informed consent was obtained from every participant. There was no post-operative follow-up; all measurements were cross-sectional at the time of admission for planned cholecystectomy.

Study Size: A formal sample size calculation was performed a priori using the formula $n = z^2 \times p(1-p)/d^2$, where $z = 1.96$ (two-tailed $\alpha = 0.05$), $p = 0.20$ (estimated hypothyroidism prevalence in cholelithiasis patients from prior Indian studies [7,8]), and $d = 0.08$ (acceptable margin of error ±8%). This yielded a required sample of 96 patients; 97 were enrolled over the study period.

Participants: Adult patients aged 18–70 years presenting with symptomatic cholelithiasis confirmed by abdominal ultrasonography (USG) were eligible for inclusion.

Exclusion criteria were: previously established diagnosis of any thyroid disorder (including those on levothyroxine or antithyroid medications); known liver disease or cirrhosis; active malignancy; pregnancy or lactation; current use of medications known to interfere with thyroid function (amiodarone, lithium, glucocorticoids, iodine-containing contrast media); and incomplete thyroid profile or lipid data. After applying these

criteria, 97 patients constituted the final study cohort. No patients were lost after enrolment.

Participant flow: During the study period, 138 patients presented with ultrasonographically confirmed cholelithiasis. Of these, 41 were excluded: 14 had a pre-existing thyroid diagnosis (on levothyroxine or antithyroid medications); 9 had known liver disease; 5 were pregnant; 7 were on thyroid-interfering medications; and 6 had incomplete laboratory data. The remaining 97 patients were enrolled and all 97 had complete data for analysis.

Data Collection: A structured case record form captured: demographic information (age, sex, body mass index); clinical presentation (symptom type and duration); comorbidities (hypertension, impaired fasting glucose); and current medications. BMI was calculated from measured height and weight and categorised according to Asian cut-offs: underweight (<18.5), normal (18.5–24.9), overweight (25.0–29.9) and obese (≥30.0 kg/m²). Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or current antihypertensive use. Impaired fasting glucose was defined as fasting blood sugar 100–125 mg/dL; no patient had a fasting blood sugar ≥126 mg/dL (diabetes mellitus). Ultrasonographic findings—stone number, size, gallbladder wall thickening, biliary sludge and common bile duct (CBD) diameter—were recorded from reports obtained on a Philips EPIQ 5 machine using standardised protocols by a single experienced radiologist blinded to the thyroid function results.

Laboratory Investigations: Fasting venous blood samples were obtained in the morning. Serum TSH was measured by third-generation immuno chemiluminometric assay (reference range 0.5–5.0 mIU/L); serum free T3 (reference 2.3–4.2 pg/mL) and serum total T4 (reference 5.1–12.1 µg/dL) were measured by electrochemiluminescence immunoassay. Thyroid status was defined as: euthyroid (TSH 0.5–5.0 mIU/L with normal T3/T4); subclinical hypothyroidism (TSH > 5.0 mIU/L with normal T3/T4); and clinical hypothyroidism (TSH > 10 mIU/L with reduced T3 and/or T4). All thyroid function tests were performed on a single fasting sample; no confirmatory repeat TSH was obtained.

Fasting lipid profile included total cholesterol, triglycerides, LDL cholesterol (calculated by the Friedewald formula) and HDL cholesterol. Dyslipidaemia was defined according to NCEP-ATP III criteria as the presence of one or more of the following: total cholesterol ≥200 mg/dL; LDL cholesterol ≥130 mg/dL; triglycerides ≥150 mg/dL; or low HDL cholesterol (<40 mg/dL in men, <50 mg/dL in women). Additional investigations included haemoglobin, fasting blood sugar, serum bilirubin (total and direct), SGOT, SGPT, ALP, serum urea and creatinine.

Bias Minimisation: Several steps were taken to reduce bias. To minimise selection bias, all consecutive eligible patients presenting during the study period were enrolled rather than selective recruitment. Information bias was reduced by using standardised, validated assay platforms and a single structured proforma; however, TSH was measured on one occasion only, and regression dilution bias cannot be excluded. Observer bias in ultrasonographic reporting was minimised by performing all scans on the same machine using standardised protocols with the radiologist blinded to thyroid function results. Patients already known to have thyroid disease were excluded to prevent prior-diagnosis bias.

Residual confounding from factors such as insulin resistance, parity, oral contraceptive use and dietary fat intake was not fully controlled; these limitations are addressed in the Discussion. As this is a hospital-based tertiary care study, referral bias is inherent: the cohort is likely enriched for more symptomatic and complicated presentations compared with community-based or primary care populations, and the prevalence of hypothyroidism reported here may be higher than would be observed in a community-screening context.

Statistical Analysis: Data were entered into Microsoft Excel 2016 and analysed using IBM SPSS version 20.0. All analyses were complete-case; as no data were missing in the final cohort of 97 patients, no imputation was required. Categorical variables were expressed as frequencies and percentages and compared using Pearson's chi-square test (or Fisher's exact test where expected cell counts < 5). Continuous variables were expressed as mean ± standard deviation (SD) and compared across the three thyroid status groups using one-way ANOVA with Tukey's Honestly Significant Difference (HSD) post-hoc test for pairwise comparisons. Pearson correlation coefficients were calculated to quantify the relationship between TSH and lipid parameters. Unadjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated for the association between hypothyroid status and dyslipidaemia. No multivariable regression was performed owing to the limited sample size relative to the number of potential confounders; this is acknowledged as a limitation. A pre-specified sensitivity analysis was performed restricting the cohort to patients without complicated gallstone disease (defined as the absence of fever and jaundice) to assess whether the prevalence estimate was driven by complicated presentations. A pre-planned sex-stratified subgroup analysis examined the prevalence of hypothyroidism separately in female and male

patients. A p-value of < 0.05 was considered statistically significant throughout.

Results

Participant Flow and Demographic Profile: Of 138 patients presenting with ultrasonographically confirmed cholelithiasis during the study period, 41 were excluded (14 prior thyroid diagnosis, 9 liver disease, 5 pregnancy, 7 on thyroid-interfering medications, 6 incomplete data), leaving 97 for analysis; complete data were available for all 97. The mean age was 47.3 ± 12.6 years (range 18–70 years). The 46–55 year age group was the largest cohort (32.0%), followed by the 36–45 year group (23.7%); 55.7% of patients were above 45 years (Table 1). Female patients constituted 73.2% (n = 71) and males 26.8% (n = 26), yielding a female-to-male ratio of 2.7:1. BMI distribution: underweight 6.2% (n = 6), normal 27.8% (n = 27), overweight 42.3% (n = 41), obese 23.7% (n = 23); combined overweight-plus-obese 66.0%; mean BMI 26.5 ± 4.9 kg/m².

Comorbidities: hypertension was present in 45.4% (n = 44; SBP ≥140 or DBP ≥90 mmHg). Impaired fasting glucose (FBS 100–125 mg/dL) was found in 43.3% (n = 42); no patient met the diagnostic criterion for diabetes mellitus (FBS ≥126 mg/dL).

Mean haemoglobin was 13.2 ± 1.4 g/dL; anaemia (Hb < 12 g/dL in women, < 13 g/dL in men) was present in 17 patients (17.5%). Liver function tests were within normal limits across all thyroid status groups (Table 2).

Table 1: Baseline characteristics of the study cohort (N = 97)

Characteristic	Total (N=97)	Euthyroid (n=70)	Subclinical Hypo (n=17)	Clinical Hypo (n=10)	p-value
Age (years), mean ± SD	47.3 ± 12.6	47.4 ± 12.7	47.2 ± 13.0	46.9 ± 12.0	0.940
Female gender, n (%)	71 (73.2%)	49 (70.0%)	14 (82.4%)	8 (80.0%)	0.515
BMI (kg/m²), mean ± SD	26.5 ± 4.9	26.2 ± 4.8	27.1 ± 5.2	26.9 ± 5.0	0.514
Overweight or Obese, n (%)	64 (66.0%)	45 (64.3%)	13 (76.5%)	8 (80.0%)	0.514
Hypertension, n (%)	44 (45.4%)	35 (50.0%)	4 (23.5%)	5 (50.0%)	0.163
Impaired fasting glucose, n (%)	42 (43.3%)	30 (42.9%)	8 (47.1%)	4 (40.0%)	0.940
Multiple gallstones, n (%)	60 (61.9%)	41 (58.6%)	11 (64.7%)	8 (80.0%)	0.412
GB wall thickening, n (%)	23 (23.7%)	17 (24.3%)	4 (23.5%)	2 (20.0%)	0.951
Biliary sludge, n (%)	17 (17.5%)	12 (17.1%)	3 (17.6%)	2 (20.0%)	0.969
CBD dilatation, n (%)	12 (12.4%)	9 (12.9%)	2 (11.8%)	1 (10.0%)	0.968
Fever (complicated), n (%)	27 (27.8%)	18 (25.7%)	5 (29.4%)	4 (40.0%)	0.565
Jaundice, n (%)	17 (17.5%)	13 (18.6%)	3 (17.6%)	1 (10.0%)	0.778

SD = standard deviation. p-values from chi-square test (categorical) or one-way ANOVA (continuous). Hypertension defined as SBP ≥140 or DBP ≥90 mmHg. Impaired fasting glucose = FBS 100–125 mg/dL; no patient had FBS ≥126 mg/dL.

Clinical Presentation: Right upper quadrant pain was the dominant symptom, affecting 91.8% (89/97) of patients. Dyspepsia was reported in 68.0% (66/97), vomiting in 45.4% (44/97), fever in 27.8% (27/97) and jaundice in 17.5% (17/97).

Hypothyroid-related symptoms were also captured: weakness in 42.3% (41/97), weight gain in 35.1% (34/97), constipation in 30.9% (30/97), dry skin in 25.8% (25/97), cold intolerance in 23.7% (23/97) and swelling of the face and limbs in 17.5% (17/97). None of these hypothyroid symptoms differed significantly between the hypothyroid and euthyroid groups (all p > 0.19), consistent with the predominantly subclinical nature of thyroid dysfunction in this cohort.

Thyroid Status Distribution: Overall, 27.8% (27/97) of patients had hypothyroidism: 17.5% (17/97) subclinical and 10.3% (10/97) clinical hypothyroidism, while 72.2% (70/97) were euthyroid (Table 2). The predominance of subclinical over overt disease (ratio 1.7:1) indicates that a substantial fraction of thyroid dysfunction in this population would have remained undetected without biochemical screening.

Table 2: Thyroid hormone and liver function profile by thyroid status group

Parameter	Euthyroid (n=70)	Subclinical Hypo (n=17)	Clinical Hypo (n=10)	p-value
TSH (mIU/L), mean ± SD	2.35 ± 0.86	7.86 ± 1.56	18.53 ± 3.55	< 0.001
T3 (ng/mL), mean ± SD	1.40 ± 0.30	1.30 ± 0.30	0.70 ± 0.20	< 0.001
T4 (µg/dL), mean ± SD	8.00 ± 1.50	6.50 ± 1.30	3.00 ± 1.00	< 0.001
Haemoglobin (g/dL)	13.2 ± 1.4	13.3 ± 1.5	13.0 ± 1.3	0.893
Total Bilirubin (mg/dL)	0.7 ± 0.3	0.7 ± 0.3	0.7 ± 0.2	0.986
SGOT (U/L)	32.6 ± 7.5	34.4 ± 8.0	33.0 ± 7.2	0.660
SGPT (U/L)	32.5 ± 10.1	32.7 ± 11.8	31.5 ± 10.0	0.952
ALP (U/L)	83.2 ± 22.1	85.9 ± 15.8	78.7 ± 20.4	0.635

All comparisons by one-way ANOVA. Post-hoc Tukey HSD confirmed significant inter-group differences for TSH, T3 and T4 (all $p < 0.001$). Liver function tests did not differ across thyroid status groups.

Association of Age, Gender and BMI with Thyroid Status: No statistically significant association was found between age group and thyroid status ($\chi^2 = 4.160$, df = 10, $p = 0.940$), confirming that thyroid dysfunction was distributed across all adult age categories.

In the pre-specified sex-stratified analysis, hypothyroidism prevalence was 31.0% in females (22/71) and 19.2% in males (5/26); the difference did not reach statistical significance ($\chi^2 = 1.327$, df = 2, $p = 0.515$; Fisher's exact OR 1.89, 95% CI 0.64–5.62). The limited male sample (n = 26) was underpowered to detect a clinically meaningful sex difference. BMI category was not significantly associated with thyroid status ($\chi^2 = 5.235$, df = 6, $p = 0.514$); numerically, hypothyroidism was more common in overweight (34.1%) and obese (34.8%) patients than in those with normal BMI (14.8%) or underweight patients (16.7%).

Lipid Profile and Dyslipidaemia by Thyroid Status: A significant stepwise deterioration of the lipid profile was observed across thyroid categories. Mean total cholesterol rose from 183.9 ± 30.4 mg/dL (euthyroid) to 224.8 ± 42.7 mg/dL (subclinical) and 249.0 ± 35.1 mg/dL (clinical hypothyroidism) (ANOVA $F = 23.558$, $p < 0.001$). Triglycerides followed a parallel gradient (138.7, 188.5 and 243.3 mg/dL respectively; $F = 24.537$, $p < 0.001$). LDL increased from 112.2 to 149.6 to 172.8 mg/dL ($F = 30.995$, $p < 0.001$), while HDL fell from 45.9 to 35.8 to 33.0 mg/dL ($F = 18.999$, $p < 0.001$), indicating a progressively atherogenic lipid pattern with worsening thyroid function (Table 3). These represent a 35% increase in total cholesterol and a 54% increase in LDL from euthyroid to clinical hypothyroidism.

Table 3: Lipid profile by thyroid status group (mg/dL, mean ± SD)

Lipid Parameter	Euthyroid (n=70)	Subclinical Hypo (n=17)	Clinical Hypo (n=10)	p-value
Total Cholesterol	183.9 ± 30.4	224.8 ± 42.7	249.0 ± 35.1	< 0.001
Triglycerides	138.7 ± 45.8	188.5 ± 59.8	243.3 ± 43.8	< 0.001
LDL Cholesterol	112.2 ± 25.4	149.6 ± 30.8	172.8 ± 29.9	< 0.001
HDL Cholesterol	45.9 ± 7.8	35.8 ± 9.2	33.0 ± 7.6	< 0.001
Dyslipidaemia, n (%)	14 (20.0%)	11 (64.7%)	8 (80.0%)	< 0.001

ANOVA F-statistics: Total Cholesterol F=23.558; Triglycerides F=24.537; LDL F=30.995; HDL F=18.999. All inter-group differences significant at $p < 0.001$ by Tukey post-hoc test. Dyslipidaemia defined per NCEP-ATP III: TC ≥200 mg/dL, or LDL ≥130 mg/dL, or TG ≥150 mg/dL, or HDL <40 mg/dL (men) / <50 mg/dL (women). χ^2 for dyslipidaemia across groups = 22.680, df = 2, $p < 0.001$; unadjusted OR for hypothyroid vs euthyroid = 9.50 (95% CI 3.45–26.15). Overall NCEP-ATP III dyslipidaemia component breakdown in the full cohort: TC ≥200 mg/dL in 40.2% (n=39); LDL ≥130 mg/dL in 36.1% (n=35); TG ≥150 mg/dL in 43.3% (n=42); low HDL (sex-specific) in 60.8% (n=59).

Correlation between TSH and Lipid Parameters: Pearson correlation analysis revealed moderate positive correlations between TSH and total cholesterol ($r = 0.480$, $p < 0.001$), triglycerides ($r = 0.537$, $p < 0.001$) and LDL ($r = 0.562$, $p < 0.001$), and a moderate inverse correlation between TSH and HDL ($r = -0.462$, $p < 0.001$), confirming a dose-response relationship between the degree of thyroid hypofunction and severity of lipid abnormalities (Table 4).

Table 4: Pearson correlation between serum TSH and lipid parameters (N = 97)

Lipid Parameter	Pearson r	p-value	Interpretation
Total Cholesterol	0.480	< 0.001	Moderate positive
Triglycerides	0.537	< 0.001	Moderate positive
LDL Cholesterol	0.562	< 0.001	Moderate positive
HDL Cholesterol	−0.462	< 0.001	Moderate negative

All correlations significant at $p < 0.001$.

Ultrasonographic Findings and Stone Characteristics: Multiple gallstones were present in 61.9% (60/97) and a single stone in 38.1% (37/97). Associated sonographic features included gallbladder wall thickening in 23.7% (23/97), biliary sludge in 17.5% (17/97) and CBD dilatation in 12.4% (12/97). Stone multiplicity was not significantly associated with thyroid status ($\chi^2 = 1.774$, df = 2, $p = 0.412$); however, a directional tendency towards multiple stones was noted in hypothyroid patients (70.4%, 19/27) compared with euthyroid patients (58.6%, 41/70). Stone composition analysis was not performed.

Sensitivity and Subgroup Analyses: In the pre-specified sensitivity analysis restricted to patients without complicated disease (no fever and no

jaundice; n = 60), 14 of 60 patients (23.3%) had hypothyroidism (subclinical: 8/60 = 13.3%; clinical: 6/60 = 10.0%). This confirms that the overall prevalence estimate of 27.8% was not substantially inflated by inclusion of complicated presentations.

In the sex-stratified analysis, hypothyroidism was detected in 31.0% of females (22/71) and 19.2% of males (5/26). The lipid gradient across thyroid status categories was observed in both sexes; however, the small male subgroup (n = 26) precluded definitive sex-specific statistical conclusions.

Discussion

The central observation of this study is that more than a quarter of patients (27.8%) presenting to a tertiary surgical unit with ultrasonographically confirmed cholelithiasis had biochemical evidence of hypothyroidism, and that the subclinical variety (17.5%) outnumbered overt clinical hypothyroidism (10.3%) by a ratio of nearly 2:1. This pattern carries an important practical implication: most thyroid dysfunction in this population was clinically silent and would have gone undetected without targeted biochemical screening. The prevalence reported here is notably higher than the 10–22% range from comparable Indian and international series, [7-12] which may partly reflect differences in referral patterns at this tertiary centre—a finding supported by our sensitivity analysis, which demonstrated a prevalence of 23.3% even when patients with fever or jaundice (suggestive of complicated disease) were excluded. The residual elevation over background population prevalence estimates of 10–15% [2] likely reflects a genuine association rather than referral artefact alone. The pathophysiological basis for the observed association is well established. Thyroid hormones regulate hepatic LDL receptor expression and bile acid synthesis; deficiency leads to both elevated biliary cholesterol content and impaired enterohepatic clearance, creating supersaturated bile that nucleates cholesterol crystals. [3] Simultaneously, reduced thyroid hormone activity diminishes gallbladder smooth muscle contractility and impairs sphincter of Oddi relaxation, prolonging bile residence time and favouring crystal aggregation. [4.5] The graded deterioration of the lipid profile across the euthyroid, subclinical and clinical hypothyroid categories—with total cholesterol rising by 35% and LDL by 54% from euthyroid to clinical hypothyroidism—provides quantitative support for this mechanistic framework and is consistent with the finding that 80.0% of clinically hypothyroid patients had dyslipidaemia compared with 20.0% of euthyroid patients. The unadjusted OR for dyslipidaemia in hypothyroid versus euthyroid patients was 9.50 (95% CI 3.45–26.15), a clinically and statistically substantial effect size.

The moderate positive correlations between TSH and atherogenic lipid fractions (r = 0.480–0.562) and the inverse correlation with cardioprotective HDL (r = −0.462) establish that rising TSH—even within the subclinical range—is a quantifiable marker of metabolic deterioration. This is clinically important because subclinical hypothyroidism is frequently dismissed as a benign biochemical finding; the present data indicate that it carries a substantial lipid burden with potential implications for both biliary stone formation and cardiovascular risk.

The absence of significant associations between thyroid status and age, gender, BMI or stone multiplicity deserves careful interpretation. The lack of age-stratified clustering argues against limiting thyroid function testing to older patients alone within a cholelithiasis cohort. In the sex-stratified analysis, the prevalence was 31.0% in females and 19.2% in males (OR 1.89, p = 0.313); non-significance is likely a consequence of limited male numbers (n = 26) rather than a true absence of sex effect. The finding that nearly one in five male cholelithiasis patients had hypothyroidism in this cohort is itself clinically meaningful. The numerically higher prevalence of hypothyroidism in overweight (34.1%) and obese (34.8%) patients compared with normal-BMI patients (14.8%) suggests that metabolic effects of thyroid dysfunction on gallstone formation may compound, but not fully depend on, excess adiposity. The perioperative relevance of undiagnosed hypothyroidism is frequently underappreciated. Even subclinical hypothyroidism has been associated with impaired myocardial contractility, diastolic dysfunction, hypertension and increased sensitivity to anaesthetic agents. The high background prevalence of hypertension (45.4%) and impaired fasting glucose (43.3%) in this cohort underscores the metabolic vulnerability of the surgical cholelithiasis population, in whom undiagnosed thyroid dysfunction adds a further modifiable endocrine risk factor. [13]

Several limitations of this study must be acknowledged. First, the single-centre tertiary design introduces referral bias (direction: upward prevalence estimate), though the sensitivity analysis restricted to uncomplicated cases mitigates this concern. Second, the sample size, while formally calculated and adequate for the primary prevalence estimate, was insufficient for multivariable regression or definitive sex-stratified conclusions. Third, the observational cross-sectional design precludes causal inference: whether hypothyroidism preceded or followed cholelithiasis cannot be determined. Fourth, TSH was measured on a single occasion without

confirmatory repeat, introducing potential regression-dilution bias that could attenuate the true association. Fifth, stone composition analysis was not performed, limiting conclusions about stone type; the pronounced lipid gradient makes a predominance of cholesterol stones biologically plausible. Sixth, important potential confounders—insulin resistance, parity, oral contraceptive use and dietary fat intake—were not fully characterised, and no multivariable-adjusted estimates are available. Seventh, the absence of a matched non-cholelithiasis control group prevents formal calculation of the relative risk attributable to hypothyroidism above background population prevalence. Finally, the absence of post-cholecystectomy follow-up data means that the impact of treating subclinical hypothyroidism on stone recurrence cannot be assessed.

Conclusion

Hypothyroidism—predominantly in its subclinical form—was detected in 27.8% of patients presenting with cholelithiasis to a tertiary surgical unit in eastern India. This prevalence was robust in a sensitivity analysis excluding complicated presentations (23.3%). Thyroid dysfunction was strongly associated with an atherogenic lipid profile and a high burden of dyslipidaemia, with an unadjusted OR of 9.50 (95% CI 3.45–26.15) for dyslipidaemia in hypothyroid versus euthyroid patients and a dose-response relationship between TSH and lipid abnormalities.

Age, gender, BMI and stone multiplicity did not independently predict thyroid status, indicating that demographic-based selective testing would miss a clinically significant number of cases. These findings support integration of serum TSH estimation into the routine metabolic workup of patients with symptomatic cholelithiasis, particularly when dyslipidaemia or hypothyroid symptoms are concurrently present. Prospective controlled studies with longer follow-up, stone composition analysis and multivariable adjustment are needed to confirm these associations and to determine whether early treatment of subclinical hypothyroidism reduces gallstone recurrence after cholecystectomy.

Declarations

Ethical approval and consent to participate: Ethical clearance was obtained from the Institutional Ethics Committee of M.K.C.G. Medical College and Hospital (IEC/MKCG/2024/21/08) prior to enrolment. Written informed consent was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki (2000) and ICMR guidelines.

Authors' contributions: CSM conceived the study, collected and analysed data, and drafted the manuscript. RRM supervised data collection, provided critical guidance on methodology and revised the manuscript. SPP provided overall academic supervision and critically reviewed the final draft. All authors approved the final version.

Data availability: The master dataset is available from the corresponding author on reasonable request.

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