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GALL STONES AND HYPOTHYROIDISM: A REVIEW OF SYNCHRONOUS FINDINGS

General Surgery

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ABSTRACT

Background: Cholelithiasis is considered to be the most common biliary pathology. Gall stones are deposition of bile pigments, cholesterol and calcium salts in the form of hard crystalline mass in the gall bladder. Thyroid disorders are also a very common endocrine pathology. The decreased thyroid-stimulating hormone (TSH) levels affect almost every nucleated cell in our body. On sphincter of Oddi, thyroid hormone receptors are present, and thyroxine has a strong relaxing effect on the sphincter. Hypothyroidism reduces the gall bladder contractility and causes lipid metabolism alteration which leads to biliary stasis. These promote the gall stone formation. **Methods:** A single centre observational study, was done among 273 patients diagnosed with cholelithiasis clinically and confirmed by ultrasonography. All patients were subjected to thyroid profile test, liver function test, fasting lipid profile test. Patient with history of hypothyroidism were excluded from the study. **Results:** Among 273 patients, 59 (21.6%) patients had hypothyroidism and 74 (27.1%) had subclinical hypothyroidism. A total 137 (50.2%) had overweight (BMI 25.0 – 29.9 kg/m²). Among all hypothyroid patients 36 (61.0%) patients had hypertriglyceridemia and 22 (37.3%) patients had hypercholesterolemia. Increased APL was found in 51 (86.4%) patients, among all hypothyroid patients. **Conclusions:** On analysis of gall stone in hypothyroid patients, decreased liver cholesterol metabolism, decreased bile emptying and decreased relaxation of sphincter of Oddi play a role. In our study there was a strong association between hypothyroidism and Cholelithiasis. Gall stone patients had also high BMI, abnormal total cholesterol, triglycerides and ALP levels.

KEYWORDS

Gall stones, Thyroid Disorders, Hypothyroidism, Dyslipidemia, BMI.

INTRODUCTION

First documented gall stones were found in mummy of a priestess of Amen during 21st Egyptian dynasty (1085-945 BC). Gall stones or cholelithiasis were first described by Greek Physician Alexander Trallianus in 5th century and first documented Cholecystectomy by Carl Langenbach of Berlin in 1882.[1] Incidence of gall stones are higher in South-east Asian countries with strong association of gall bladder carcinoma. Saturation of bile in gall bladder, bile stasis due to Sphincter of Oddi dysfunction, biliary sludge and change in chemical disproportion of bile are all risk factors for gall stone development.[2] Thyroid disorders are also significantly very concerned endocrine pathology. Supersaturation of bile due to increased cholesterol levels occurs in hypothyroidism. Thyroxine (T_4) and Tri-iodothyronine (T_3) have a negative effect on HMG Co-A reductase enzyme which regulates cholesterol levels. So, hypothyroidism in turn induces hypercholesterolemia and dyslipidemia and reduces cholesterol metabolism.[3] It also decreases sphincter of Oddi relaxation, leading to gall bladder hypomotility, reduced contractibility and decreases filling causing prolonged accumulation and reduced flow capacity of bile in gall bladder.[4] This leads to bile clearance causing nucleation and gall stone formation.[5]

The hypothyroidism disease itself can either be of hypothyroidism (overt) or subclinical type, in which the serum level of Thyroxine (T_4) is lesser than the expected normal.[6] In cases of serum thyroid hormones within normal lab level, but serum TSH level slightly raised, subclinical hypothyroidism (mild thyroid failure) is labelled.[7]

Aims & Objectives

This study is carried out to assess the possibility of a correlation between hypothyroidism and cholelithiasis.

Subjects & Methods: This study was conducted in a tertiary care hospital of West Bengal (KPC Medical College & Hospital). The study duration was January 2024 to January 2025. A total of 273 patients with gall stones were selected from 712 cases for the study. Radiological and other needful investigations and procedures were done to confirm the diagnosis and cases were managed accordingly.

Inclusion Criteria:

1. Patients of both sexes of various age groups of 18 years to 80 years of age.
2. All patients admitted with diagnosed GB stones were taken into consideration.

Exclusion Criteria:

1. Patients less than 18 years and more than 80 years.
2. Pregnant women.
3. Patients with history of thyroid cancer.
4. Patients who were on antiepileptic drugs.
5. Patients who were in septicemia.
6. History of hemolytic disorders.
7. History of hypersplenism.
8. Patients with diagnosed choledocholithiasis.

All routine laboratory investigations including Liver function test including serum bilirubin, Serum Glutamic-Oxaloactetic Transaminase (AST), Serum Glutamic Pyruvic Transaminase (ALT), Gamma-Glutamyl Transferase, Alkaline Phosphatase; Thyroid profile including Thyroid stimulating Hormone (TSH), Total Thyroxine (T_4), Total Triiodothyronine (T_3); Lipid profile including Total Cholesterol, Triglycerides, Low-density Lipoprotein (LDL).

Also, patients' weight (Kg) and height (Meter) was recorded to calculate Body Mass Index (BMI).

RESULTS

Our study was conducted among 273 patients who were diagnosed with cholelithiasis by sonography. Most of the patients were women 171 (62.6%) and rest were men 102 (37.4%). **(Figure 1)**

Gender	Frequency	Percentage
Men	102	37.4%
Women	171	62.6%
Total	273	100%

Figure 1: Gender Distribution Among Study Population

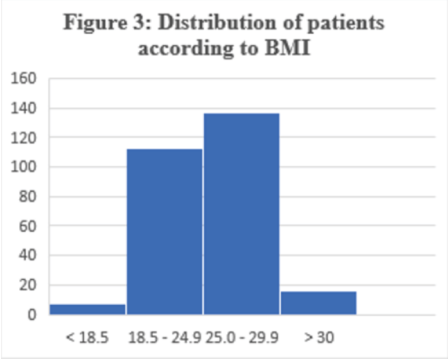
In our study majority of patients were between 31 – 50 years (58.3%) and below 30 years were 23 patients (8.4%). **(Figure 2)**

Age	Frequency	Percentage

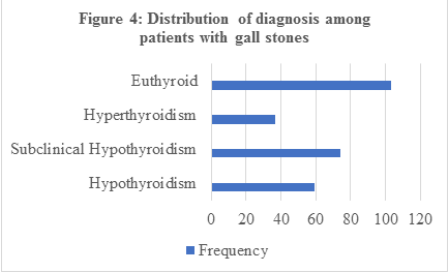
18-30 years	23	8.4%
31-50 years	159	58.3%
51-80 years	91	33.3%
Total	273	100%

Figure 2: Age Distribution Among Study Population

In our study, we found out that the maximum number of patients, 137 (50.2%), fell into group having a BMI of 25.0 – 29.9 kg/m^2 which is overweight. 113 patients (41.4%) had a BMI 18.5 – 24.9 kg/m^2 which was labelled as normal weight. **(Figure 3)**



Among all 273 patients 59 patients (21.6%) had increased TSH and decreased T_4, with features of hypothyroidism, 74 patients (27.1%) had increased TSH but normal T_4 so subclinical hypothyroidism, 103 patients (37.7%) were euthyroid and 37 patients (13.6%) were hyperthyroid. **(Figure 4)**



All the patients were also subjected to liver function test and lipid profile and we found that albumin level was low in 15 patients (5.5%), who had hypothyroidism and in 7 patients (2.6%), who had subclinical hypothyroidism as compared to 0 patient, who had hyperthyroidism and 6 patients (2.2%), who were euthyroid. Alkaline phosphatase was high in 51 patients (18.7%), who had clinical hypothyroidism and in 56 patients (20.5%), who had subclinical hypothyroidism in comparison with 0 patient, among both in euthyroid and hyperthyroid patients. **(Figure 5)**

Variables		Clinical Hypothyroidism	Subclinical Hypothyroidism	Hyperthyroidism	Euthyroid
Albumin	**Low**	15 (5.5%)	7 (2.6%)	0 (0%)	6 (2.2%)
	Normal	44 (16.1%)	67 (24.5%)	37 (13.6%)	97 (35.6%)
Direct Bilirubin	**Normal**	59 (21.6%)	70 (25.6%)	37 (13.6%)	101 (37.0%)
	High	0 (0%)	4 (1.5%)	0 (0%)	2 (0.7%)
ALP	**Normal**	8 (2.9%)	18 (6.6%)	37 (13.6%)	103 (37.7%)
	High	51 (18.7%)	56 (20.5%)	0 (0%)	0 (0%)

Figure 5: Thyroid profile and liver function test

Among all patients 22 patients (8.1%) had high total cholesterol, who had clinical hypothyroidism, 36 patients (13.1%) had high triglycerides, who had subclinical hypothyroidism as compare to 10 patients (3.7%) had high cholesterol, who were hyperthyroid and 88 patients (32.2%) had high triglycerides, who were euthyroid. High LDL was found in 15 patients (5.5%), who had hypothyroidism and 25 patients (9.2%), who had subclinical hypothyroidism. **(Figure 6)**

Variables		Hypothyroidism	Subclinical Hypothyroidism	Hyperthyroid	Euthyroid
Total Cholesterol	**Normal**	37 (13.6%)	32 (11.7%)	10 (3.7%)	88 (32.2%)
	High	22 (8.1%)	42 (15.4%)	27 (9.9%)	15 (5.5%)
Triglycerides	**Normal**	23 (8.4%)	21 (7.7%)	28 (10.3%)	82 (30.0%)
	High	36 (13.2%)	53 (19.4%)	9 (3.3%)	21 (7.7%)
LDL	**Normal**	44 (16.1%)	49 (18.0%)	27 (9.9%)	64 (23.4%)
	High	15 (5.5%)	25 (9.2%)	10 (3.7%)	39 14.3%)

Figure 6: Thyroid Profile And Lipid Profile Test

DISCUSSION

Our study was conducted among 273 patients with radiological evidence of cholelithiasis. In our study women predominance (62.6%) was seen as compared to the men. Numerous studies confirmed what we found in our research: females had higher prevalence of cholelithiasis than males. [8-11] The higher incidence of gall stones in women was in concordance to Ghadhban et al. study (81.6%). [12] Sarda et al., Rajan et al. and Sachdeva et al. showed similar results as our study showing female preponderance. [8-10] Because of sex hormones and pregnancy women are supposed to be at higher risk and traditional epidemiologic studies corroborate this. Effect of oestrogen on blood becomes hypercholesterolemic and lithogenic by increasing release of biliary cholesterol. [10]

Mostly affected age group is 31-50 years (58.3%) in our study. In their research Herman et al. have documented a comparable frequency. [13] Shaffer et al. performed an extensive survey, including patients from all over the world, and concluded that, as you age, the likelihood of developing gall stones increases. [14] Age causes a decrease in bile acid production, an increase in cholesterol production in bile and biliary cholesterol saturation. The bile acid synthesis rate-limiting enzyme Cholesterol 7a-hydroxylase (CYP7A1), is less active. [15-16] Additionally, as people age, more risk factors may build up, resulting in lithogenesis. [17]

As per our study, we found out that, the most significant number of patients, 137 (50.2%) fell into the group who had a BMI of 25.0 – 29.9 kg/m^2 which is overweight. 16 patients (5.8%) were found to have a BMI >30 kg/m^2 who were labelled as obese. The study published by Sarhan et al. and Sodhi et al. kept forward that a high BMI may contribute to lithogenesis. [18-19] Alexander et al. and Hayat et al. stated that increased cholesterol in blood and high BMI increases risk of gall stones. [20-21]

Our study found that, out of 273 patients, 103 (37.7%) were euthyroid, 59 (21.6%) had hypothyroidism and 74 (27.1%) had subclinical hypothyroidism. Völzke et al. found a connection between increased TSH levels and gall stones that can be found in sonography. [22] Kotwal et al. and Rinchen et al. found that 14.4% of the patients with hypothyroidism in Sikkim, India, also had cholelithiasis. [23] Yousif et al. study found similar outcomes as those by Ibrahim et al. and Abdulbary et al. [24-25] Arbab et al. published that 16 out of 193 (8.16%) patients who had cholecystectomy done due to cholelithiasis also were diagnosed with hypothyroidism. [26]

Our study showed that dyslipidemia in hypothyroidism is much higher as compared to euthyroid patients. Marwaha et al. in his study showed that in adults with hypothyroidism there was a significant increase in serum total cholesterol and LDL levels. [27] Hussain et al. in his study showed significantly high cholesterol, Triglycerides and LDL among subclinical hypothyroid patients compared to the controls. [28] Pedrelli et al. showed increased levels of total cholesterol and LDL among hypothyroidism patients. [29] We attribute this to the effect of thyroid hormone on HMG Co A reductase enzyme and the influence of Thyroxine in lipid metabolism in Liver. [30] This finding in however in contraindication to Ahmmed Hassan Issa et al., who in his study among 232 patients, 175 patients with dyslipidemia proved that only 25 were hypothyroid. [31]

Alkaline phosphatase, an enzyme produced by the biliary epithelium, was found to be in increased in 56 patients, all who had hypothyroidism. ALP was normal in both euthyroid and hyperthyroid patients. This could be secondary due to lack of effect of thyroid hormone on special receptors which facilitates biliary motility.[32] Lack of thyroxine promotes bile stasis and sphincter of Oddi dysfunction which in turn increase biliary pressure and ALP levels. This is a significant finding as these patients may eventually develop choledocholithiasis. In other studies, conducted by Steenbergen et al. and Inkinen et al. stated that the increased incidence of biliary stones in hypothyroidism is due to hypercholesterolemia, hypotonia of GB and reduced excretion of bilirubin. [33-34]

Limitations:
Our study had small sample size, conducted in a single centre and patients with choledocholithiasis were excluded from this study. We propose to conduct a multi-centre, large population-based study in order to provide a higher level of evidence.

CONCLUSION:

Our present study concludes that there is a correlation between cholelithiasis and hypothyroidism. The prevalence of cholelithiasis and hypothyroidism is higher in females. Most patients with cholelithiasis and hypothyroidism are elderly patients (>31years). The study also denotes the incidence of cholelithiasis and hypothyroidism is higher in overweight patients (BMI >25 kg/m^2).

To conclude we propose that all patients with cholelithiasis and dyslipidemia must be evaluated for thyroid function abnormalities in patients with hypothyroidism. ALP levels must be evaluated as there is a higher chance of incidence of primary biliary stones due to biliary dysmotility and sphincter of Oddi dysfunction.

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