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RESEARCH ARTICLE
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TO DETERMINE THE INCIDENCE OF HYPOTHYROIDISM AMONG GALL STONE DISEASE PATIENTS AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Background

Gall stone disease is prevalent among the population and several etiological factors have been described for the genesis of gall stone disease. Thyroid dysfunction particularly hypothyroidism and its association with gall stone disease is not well established in literature despite being a topic of discussion for many years. Hypothyroidism can cause sphincter of Oddi dysfunction leading to biliary stasis leading to formation of gallstones. Serum hypercholesterolemia is also seen in hypothyroidism which can cause bile to supersaturate with cholesterol further leading to formation of gallstones.

Methods

A total of 260 patients with documented gall stone disease were included in the study. These patients were interviewed and clinically evaluated. Thyroid function test and serum cholesterol (fasting) was performed in all of them. The incidence of hypothyroidism was obtained and compared with the general public and correlation was calculated between hypothyroidism and hypercholesterolemia.

Results

Of the 260 patients included in the study, 25% were found to be hypothyroid. Among 65 hypothyroid patients, majority were females (16.9%). Subclinical hypothyroidism (20%) was commonest. Most of gall stone patients with hypothyroidism were found to be in the age group of 50-59 years of age. The prevalence of hypothyroidism in local population is 9.23%. Statistically, hypothyroidism was found to be significantly higher in patients with gallstone disease**.** 70 percent of hypothyroid patients also had hypercholesterolemia and a positive correlation between hypothyroidism and hypercholesterolemia was identified.

Conclusion

It can be concluded from the findings of this study that incidence of hypothyroidism is high among gall stone disease patients especially in middle aged females. Left undetected it may result in complications. Positive correlation between hypothyroidism and hypercholesterolemia was

identified. Clinicians should be aware of possible hypothyroid background and consider examining the thyroid profile at least in females over 30 years of age with gallstone disease, in which group the incidence of clinical and sub clinical hypothyroidism is the highest and initiate prompt and adequate thyroxine therapy.

Key Words: Gallstones; Hypothyroidism; Hypercholesterolemia; Incidence; Risk Factors; Sphincter of Oddi Dysfunction; Biliary Hypokinesia; Cholecystectomy; Thyroid Hormones; Thyroid Function Tests; Cholelithiaisis.

INTRODUCTION

Gall stone disease is common among the adult population worldwide and prevalence varies from 10% in western countries[1] and around 6% in India[2]

Multiple etiological factors have been described for the genesis of gall stone disease

- Cholesterol super saturation in the bile forms a majority, ~ 80% of gall bladder stones[3]
- Alteration in the level of bile acids, bile salts, lecithin (phospholipid) levels and thus altering the bile salt to cholesterol ratio.
- Biliary stasis
- Altered enterohepatic circulation- The main biliary constituents, cholesterol and bile acids, undergo an enterohepatic circulation passing through the liver, gallbladder and small intestine whereby they are modified, excreted or reabsorbed. Consequently, each disturbance in organ functionality can impact the enterohepatic circulation and thereby promote cholesterol gall stone disease.[4]
- Infections and infestation of the gall bladder and biliary tract.
- Increased bilirubin production.

Thyroid dysfunction particularly hypothyroidism and its association with gall stone disease is not well established in literature even though it has been a topic of discussion for many years. Thyroid dysfunction can impact bile flow rate and contribute to gallstone disease.[5] Physiological concentrations of T_4 have a pro-relaxing effect on sphincter of Oddi in humans and pigs leading to increased bile flow.[6,7] In hypothyroidism a profound sphincter of Oddi contraction has been observed, that leads to an enhanced storage time of gallbladder bile fluid and thereby promotes biliary supersaturation as well as precipitation of cholesterol crystals.[8] 90% of hypothyroid patients have elevated cholesterol levels,[9] triglyceride levels, or both. Hypothyroidism causes decreased LDL receptor activity leads failure of removal of cholesterol from serum. A decreased bile salt concentration has been reported in hypothyroidism. Serum hypercholesterolemia in hypothyroidism may cause bile to supersaturate with cholesterol giving rise to prolonged stasis of bile in the gallbladder further leading to stone formation. In addition to established risk factors like age, gender, obesity, obtaining the incidence of hypothyroidism among gall stone disease patients may identify a new risk factor. Furthermore, in patients with established gall stone disease, knowing the incidence of hypothyroidism, we can assess whether thyroid profile is warranted in such patients and thus screen for hypothyroidism.

MATERIALS AND METHODS

The present study was conducted from February 2023 to March 2024. The study was set in Department of General Surgery at a tertiary care center, Mandya Institute of Medical Sciences, Mandya. Sample size was estimated using the formula,

$$n = Z^2 P(1\text{-}P)/d^2$$

Considering the prevalence of hypothyroidism as 28.5% among gall stone disease patients and the margin of the error at 20%, Z= 1.96, the minimum sample size needed is 251. This study has taken sample size as 260 patients.

Inclusion Criteria

- Patients with radiologically diagnosed gall stone disease willing to participate in the study after giving fully informed consent
- Patients attending surgical outpatient department or admitted at Mandya Institute of Medical Sciences Mandya with radiologically diagnosed gall stone disease.

Exclusion Criteria

- Pregnant women
- Patients on drugs such as phenytoin, carbamazepine, lithium, amiodarone that can affect thyroid function tests
- Already diagnosed hypothyroid patients
- History of thyroidectomy
- Serious underlying diseases such as sepsis, cholangitis.
- Age less than 20.

Investigations

- Ultrasonography of the abdomen
- Thyroid function test
- Fasting lipid profile data (serum cholesterol levels)

Procedure

Cases were selected in a non-random, time bound purposive method. Selected patients from the outpatient department of surgery and admitted patients in the General Surgery department were explained regarding their participation in the study. After obtaining their informed consent, a questionnaire was used to document data that included their demographic details, past and present medical history, drug history, symptoms related to hypothyroidism such as loss of appetite, gaining weight, tiredness, constipation, cold intolerance, menstrual disturbances. These patients were then examined and relevant findings documented. The ultrasound abdomen reports, thyroid profile and fasting lipid profile data was also documented in the proforma sheet. The normal serum value for T3 was taken as, between 80 – 200 ng/dl, T4 was taken as, between 5.1 – 14.1 mcg/dl, TSH was taken as, between 0.27 – 4.2 mIU/ml, cholesterol was taken as <200 mg/dl. All the data collection sheets were filled by the investigator himself. After completion of the data collection, appropriate treatment for their condition was administered. Patients that were found to be hypothyroid were started on thyroxine supplementation therapy.

Statistical Analysis

Data analysis was done both manually and by using computer. Data was entered in M.S. Office Excel software. Calculated data were arranged in systemic manner, presented in various table and figures. Statistical analysis to evaluate the objectives of this study was done with the help of Statistical Package for Social Science (SPSS) using descriptive statistics, like mean, standard deviation, percentage, inferential statistics like chi square test to know the association. The p value of less than 0.05 was considered significant.

RESULTS

Two hundred and sixty patients fulfilled the inclusion and exclusion criteria.

Age Group in Years	**Male**	**Female**
20-29	2	38
30-39	31	45
40-49	13	31
50-59	35	26
>60	15	24
Total	96	164

Table 1: Age and Sex distribution of gall stone patients

Mean age of patients were 44.1y and the commonest age group having gallstone disease was 30-39 years. 164 Patients were female and 96 were male. MALE: FEMALE Sex Ratio is 1:1.77. Gallstone disease is found to be 1.77 times more common in females than males.
Among the comorbidities, 35 patients had type 2 diabetes and 29 patients had essential hypertension while 12 patients had both comorbidities. The USG abdomen findings revealed 230 patients with only GB calculus, 8 patients with only CBD calculus and 30 patients with both GB and CBD calculus. 147 patients had multiple calculi and 113 patients had single calculus.

	All Patients	**Hypothyroid**	**Euthyroid**
Number of patients	260	65	195
Age (years)	Mean = 45.6	Mean = 50.18	Mean = 42.49
Male	36.93%	8.1%	28%
Female	63.07%	16.9%	46 %
Table 2: Demography and status of hypothyroidism			

Out of 260 gall stone disease patients 65 patients (25%) were hypothyroid of which 23 patients were males and 42 patients were female.

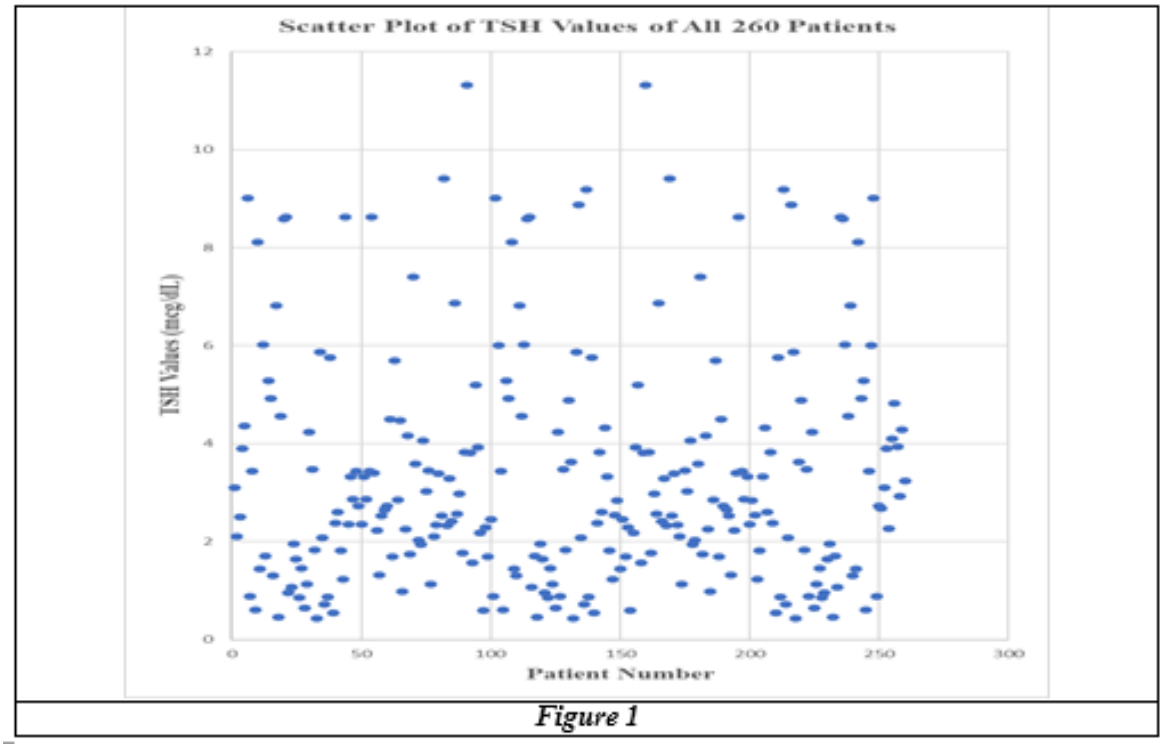

Figure 1

Age Group in Years	**Male**	**Female**
20-29	0	4
30-39	2	13
40-49	3	6
50-59	12	8
>60	6	11
Total	23	42
Table 3: Age and sex distribution of patients with gallstones and hypothyroidism		

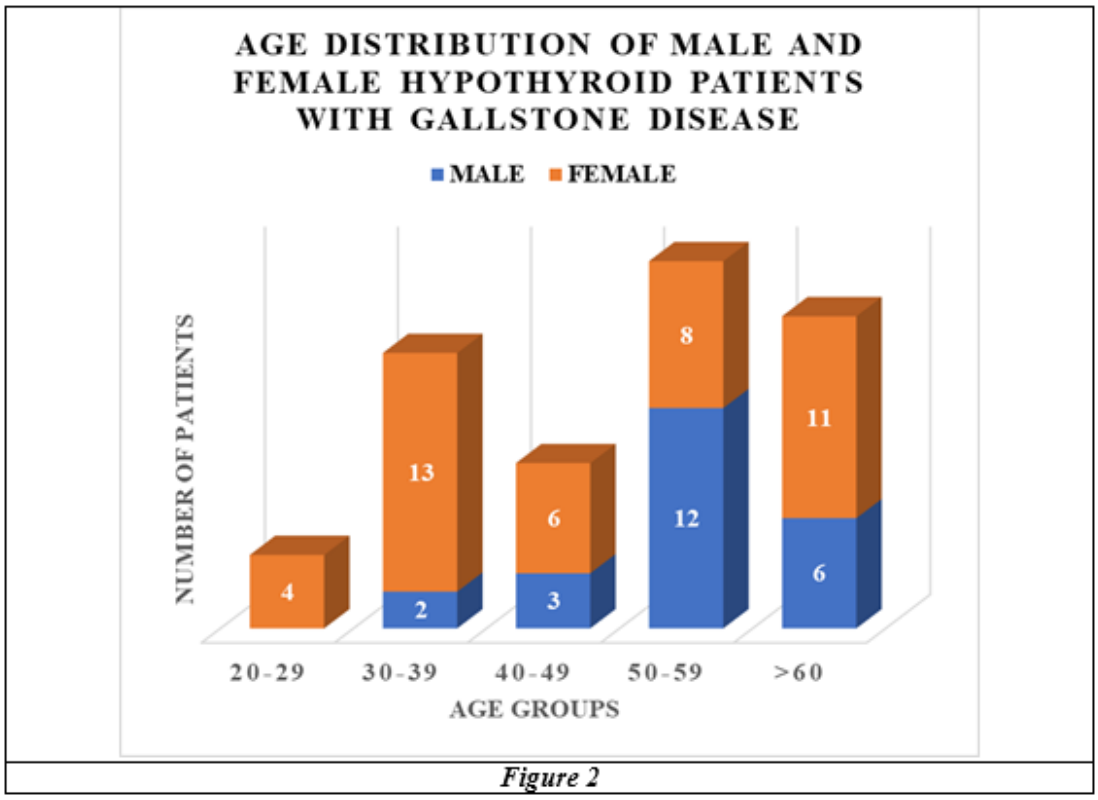

Figure 2

Among the 65 patients that were hypothyroid of, 52 were sub-clinically hypothyroid (19 male and 33 female) and 13 were clinically hypothyroid (4 male and 9 female).

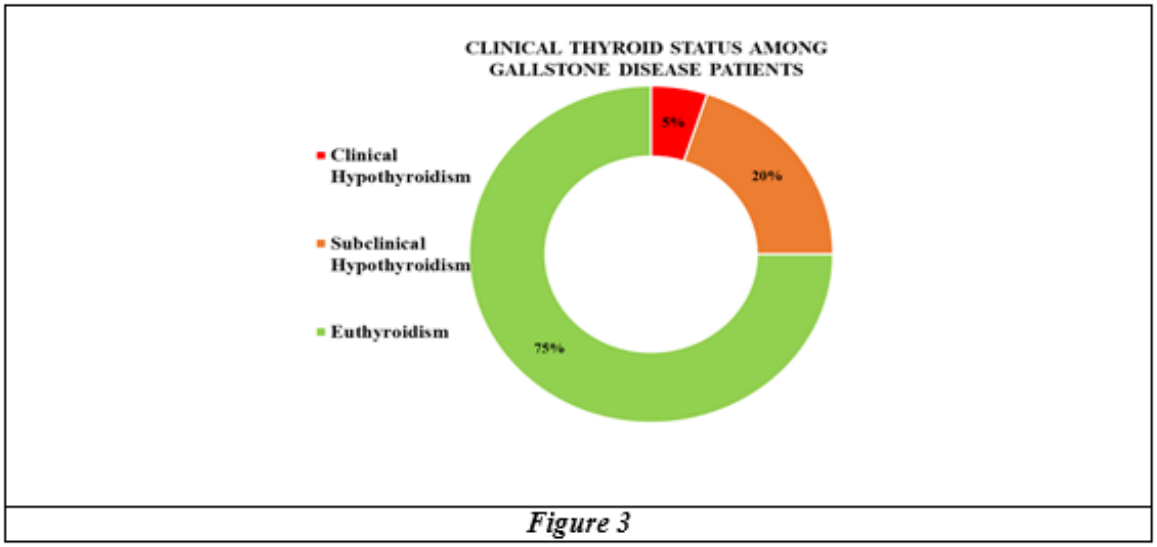

Figure 3

156 Patients (60%) had hypercholesterolemia of which 66 were male and 90 were female. The remaining 104 patients (40%) had normocholesterolemia of which 30 were male and 74 were female.

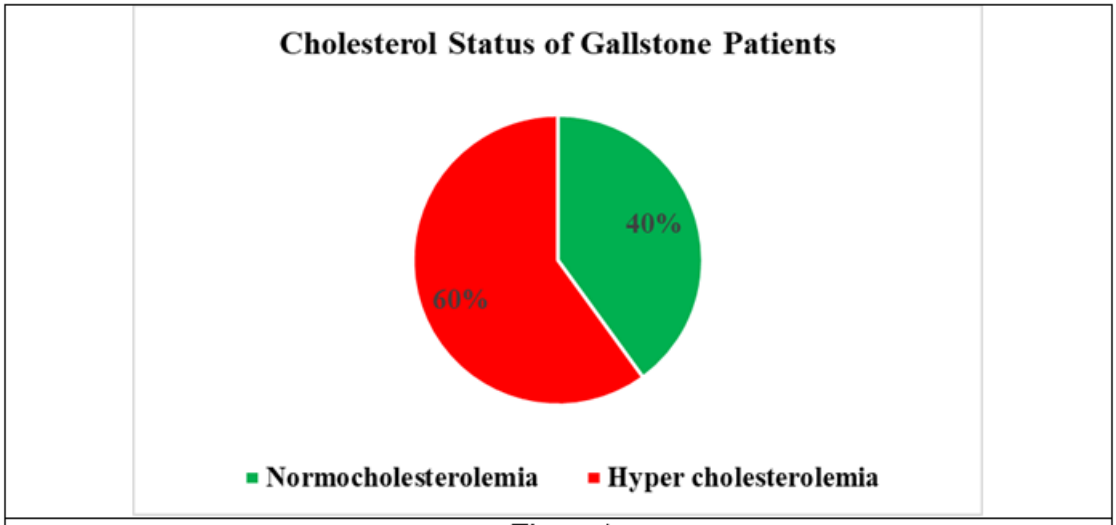

Figure 4

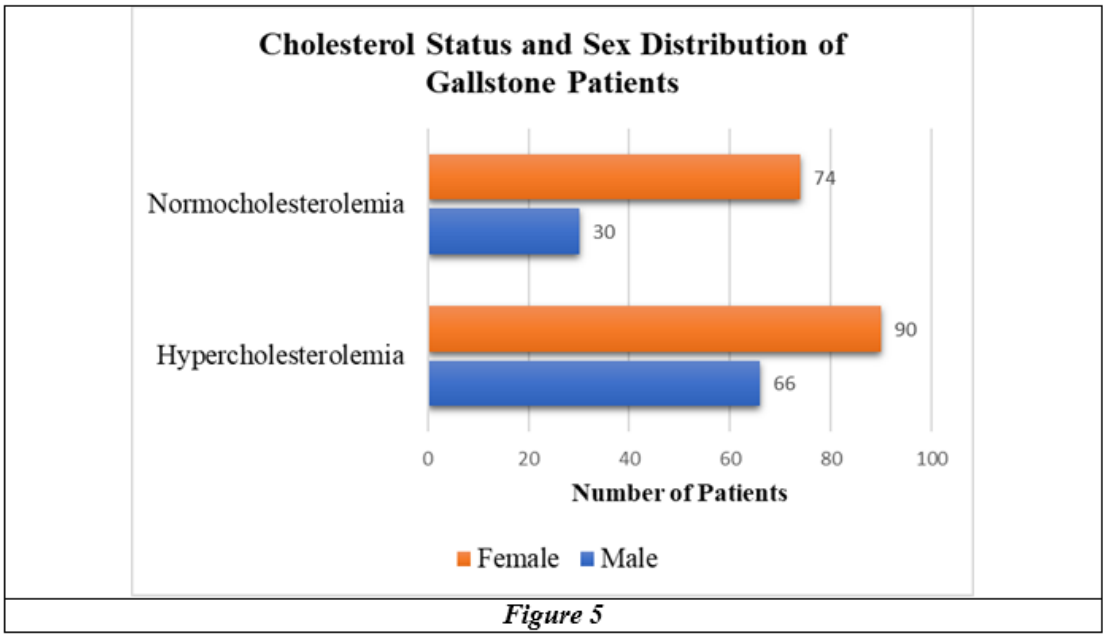

Figure 5

Age Group in Years	Male	Female
20-29	0	9
30-39	13	23
40-49	12	15
50-59	27	21
>60	14	22
Total	66	90

Table 4: Age distribution of patients with gallstones and hypercholesterolemia

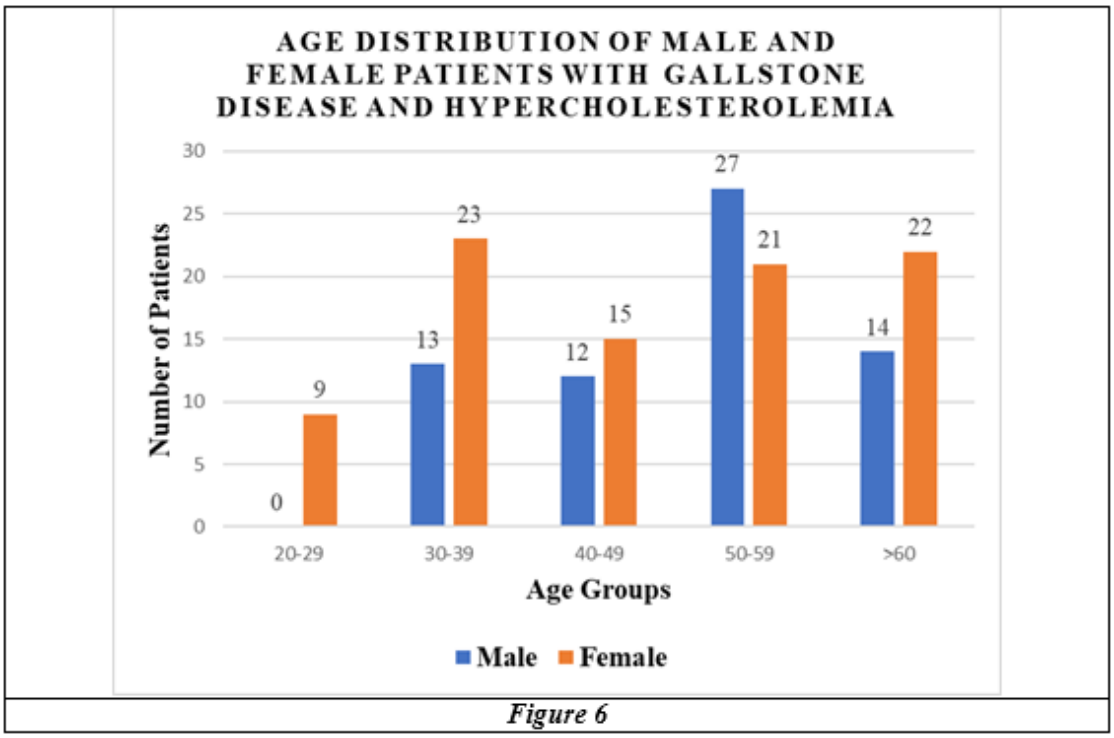

Figure 6

Serum Cholesterol	Number of Hypothyroid Patients
Hypercholesterolemia	46 (70.76%)
Normocholesterolemia	19 (29.24%)

Table 5: Status of serum cholesterol in hypothyroid gallstone disease patients

Among the 46 hypothyroid hypercholesterolemic patients, 33 patients (50.76%) had subclinical hypothyroidism and 13 (20%) had clinical hyperthyroidism.

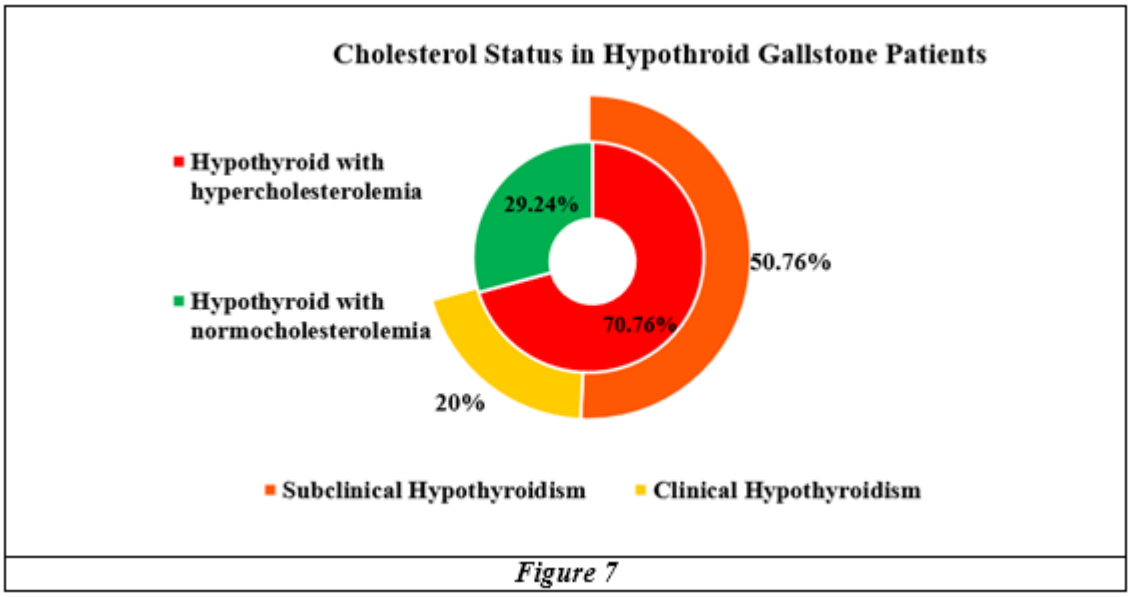

Figure 7

Off the total 156 hypercholesterolemic gallstone patients, 110 patients (71%) were euthyroid and 46 patients (29%) were hypothyroid.

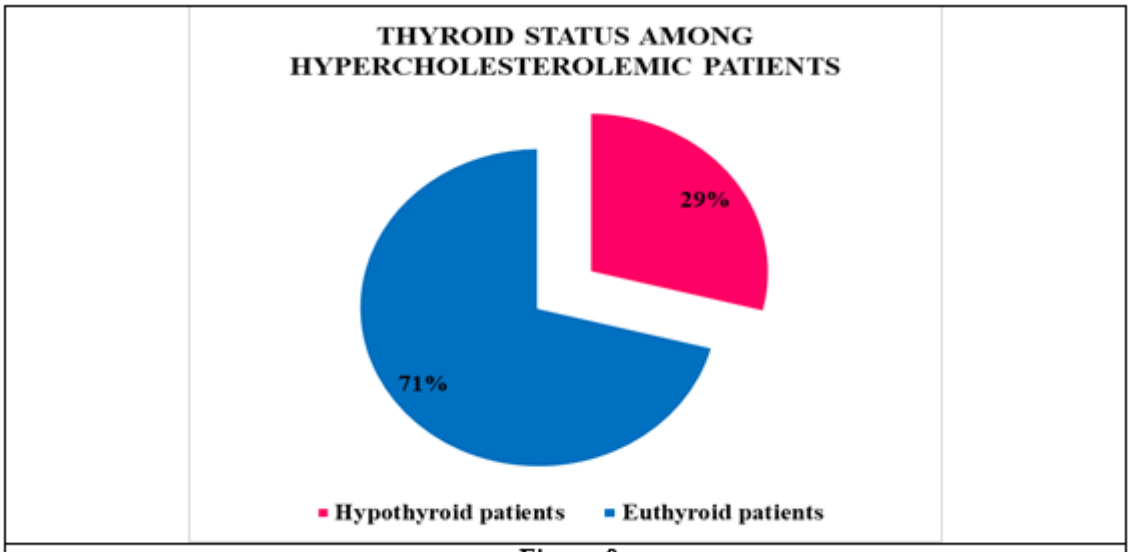

Figure 8

Statistical Analysis

In this study out of 260 patients with biliary stones 25% of patient (65 in number) were hypothyroid.

Prevalence of patients with hypothyroidism in Local population is 9.23%[10]

We plotted 2x2 Contingency table and used χ^2 test to analyze the data and got following results.

Thyroid Status	**Patients**	**Population**
Hypothyroid	65	9.23
Euthyroid	195	90.77
Table 6: 2x2 contingency table		

The χ^2 value is 11.3219. The *p*-value is .00766.

The **result is significant** at $p < .05$

Hypothyroidism is significantly associated with gallstone disease.

In this study out of 260 patients with biliary stones 25% of patient (65 in number) were hypothyroid. 70.76% of these hypothyroid patients (46 in number) also had hypercholesterolemia. The Spearman rho coefficient of correlation is $\mathbf{r_s = 0.30398}$

Thyroid Status	**Hypercholesterolemia**	**Normocholesterolemia**
Hypothyroid	46	19
Euthyroid	110	85
Table 7: 2x2 contingency table for hypothyroidism and hypercholesterolemia		

The χ^2 value is 4.188. The *p*-value is .04071. The result is significant at $p < .05$. There is a positive correlation between hypothyroidism and hypercholesterolemia.

DISCUSSION

This study was conducted with 260 selected patients with radiologically confirmed gallstones or CBD stones or both, attending the out-patient department or admitted under Department of General Surgery, at a tertiary care hospital, Mandya Institute of Medical Sciences, Mandya. The study was done in order to determine the incidence of hypothyroidism among patients with gallstones or biliary duct stones, in view of identifying hypothyroidism as a causative factor for the disease condition. The second objective of the study was to see if there was any correlation between hypothyroidism and hypercholesterolemia which is often seen in gallstone disease patients.

Gall stones found to be most common in the age group of 30-39 years. Mean age is 44.4y. Among these patients, 96 patients (36.93%) were male and 164 patients (63.07%) were female. The male: female ratio was found to be 1:1.77. Thus, females were predominantly affected. Among the comorbidities, 35 patients had type 2 diabetes and 29 patients had essential hypertension while 12 patients had both comorbidities. Diabetes is the predominant comorbidity associated with gallstones. Ultrasonography of the abdomen in these patients revealed GB calculi in most patients, GB Calculus with CBD calculi in 22 patients and isolated CBD calculus in 8 individuals. The stones were predominantly multiple in number.

Among these 260 patients, 65 patients (25%) were found to be hypothyroid and 195 patients (75%) were euthyroid. This is comparable with other Indian studies such as Ahmed Hasan Issa et al[11] study, Brijendra Singh Raghuwanshi et al[12] study and Saravanan Sanniyasi et al[13] study in which percentage of hypothyroid patients found to be 13.8%, 24% and 28.5% respectively.

Among the 65 hypothyroid patients, 65 % of the individuals were female and 35% of hypothyroid individuals were male. The mean age was 50.18 years. Most of gall stone patients with hypothyroidism were found to be in the age group of 50- 59 years of age.

Among the 65 hypothyroid patients, 13 were clinically hypothyroid while 52 patients showed subclinical hypothyroidism. All hypothyroid patients were started with thyroxine supplementation therapy.

On statistical analysis using $\chi 2$ test results were found to be significant at $p < .05$. The $\chi 2$ value is 11.3219. The p-value is .000766. Hence Hypothyroidism is significantly associated with gallstone disease.

Among the 65 hypothyroid patients in the study 46 patients had hypercholesterolemia. Thus, 70 percent of the patients with gallstone and hypothyroidism also had hypercholesterolemia. The Spearman correlation coefficient was calculated to be 0.303 and was found to be significant at $p<0.05$. Thus, there exists a positive correlation between hypothyroidism and hypercholesterolemia.

It is also noteworthy that despite there being a correlation between hypothyroidism and hypercholesterolemia, 56% of euthyroid patients (110 in number) among total of 195 euthyroid patients also had hypercholesterolemia. This proves that hypercholesterolemia has multiple etiopathogenesis and hypothyroidism is just one among them.

LIMITATIONS OF THE STUDY

- Assessment of composition of gall stones not done.
- Assessment of mobility of biliary tract not done to demonstrate decreased rate of bile flow in hypothyroid patients.
- Assessment for other genetic and etiopathogenic factors for hypercholesterolemia not done.

Despite this study having some limitations, it has some credentials in reflecting the facts regarding association between hypothyroidism and gall stone patients and its positive correlation with hypercholesterolemia in gall stone disease and can aid in further research regarding the same. This study also recommends the evaluation of thyroid function in gall stone disease individuals as part of the general workup as there is such high incidence of hypothyroidism among gallstone disease patients and is significantly associated with it.

CONCLUSION

This study was conducted in Department of General surgery, at a tertiary care hospital, Mandya Institute of Medical Sciences, Mandya. There is a high incidence of hypothyroidism in patients with biliary stone disease compared to general population. It can be concluded from the findings of this study that hypothyroidism is a probable risk factor for development of gallstones especially in middle aged females. Undetected hypothyroidism in the form of subclinical hypothyroidism and untreated or inadequately treated hypothyroidism in such patients will result in complications. Clinicians should be aware of possible hypothyroid background in such cases and consider examining the thyroid profile in females over 30 years of age and males over 50 years of age, in which group the incidence of clinical and sub clinical hypothyroidism is the highest. There also

exists a positive correlation between hypothyroidism and hypercholesterolemia. Hypothyroidism is one of the many etio-pathogenic factors which can cause hypercholesterolemia and can further impact gallstone disease and it progression. Thus, prompt evaluation along with early and adequate treatment of hypothyroidism with thyroxine supplementation is advised in such gallstone disease patients.

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