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Original research article

To Study The Relationship Between Hypothyroidism And Cholelithiasis In Patients Attending A Tertiary Care Hospital

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Abstract

Introduction: Since decades, there has been a discussion, whether thyroid disorders could cause gallstone disease. Gall stone disease is most common biliary pathology accounting to 2-29%.
prevalence in India. Its prevalence varies among demography, age, sex, food habits, sedentary life style, and obesity. It is considered as a disease of fat, forty, fertile, flatulent, and female. Both cholelithiasis and hypothyroidism are more prevalent in females than males. Hypothyroidism increases GB stones and also CBD stones.

Methodology: The present study is a Hospital Based prospective study which is time bound. This study was conducted during the period of January 2023 to March 2024 (15 months). Total 80 patients were included in these studies that are diagnosed with Cases admitted in the department of General Surgery at Government Siddhartha Medical College, and satisfying the inclusion criteria. Inclusion Criteria is 1. Patients who are diagnosed as Cholelithiasis by abdominal ultra-sonogram and who are willing to participate in study. 2. Age >13 years. 3. Patients with known hypothyroidism. 4. Patients with subclinical hypothyroidism.

Results: In the present study 16 patients are hypothyroid, 6 patients are sub clinical hypothyroid out of 80 patients of cholelithiasis. 58 out of 80 are in euthyroid state (72.5%).

Conclusion: Cholelithiasis is most common in 41-50 yrs age group. Significant number of females was affected by gallstone disease. Prevalence of hypothyroidism and subclinical hypothyroidism in this study is 20% and 7.5%. 18 out of 22 patients has size of the stone >1 cm and 61 out of 80 had multiple stones, 19 out of 80 had single stones. Most of the patients had multiple stones. All the study cases underwent cholecystectomy.

Keywords: Cholelithiasis, hypothyroid, sub cinical hypothyroid, prevalence, ultra-sonogram

Introduction

Prevalence of hypothyroidism in females: males - 3: 1. Prevalence of cholelithiasis in Females: Males - 2.9:1. The pathogenesis of gall stones includes both altered bile content and flow. Many studies reveal that thyroid hormone dysfunction can lead to disturbance in both bile formation and flow as hypothyroidism can lead to dyslipidemia promotes gall stone formation.

Hypothyroidism can decrease the bile salts in bile leads to altered bile salt cholesterol ratio. Hypothyroidism decreases gall bladder motility and bile flow. Sphincter of oddi expresses thyroid hormone receptors and thyroxine has direct pro relaxing effect on the sphincter of oddi that expresses thyroid hormone receptors beta1, beta2. This pro relaxing effect of T4 is mediated through a mechanism that requires new mRNA and protein synthesis and subsequently result in the activation of ATP dependent K+ Channels [3]. Low bile flow and sphincter of oddi dysfunction both are regarded as important mechanisms that might promote gallstone formation. As multiple mechanisms are involved in thyroid hormone dysfunction and gall stone formation studies must be done to enlighten this aspect so as to arrive at early diagnosis and treatment of subclinical hypothyroidism may prevent gall stone formation.

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The aim of this current study is to find the correlation between hypothyroidism in cholelithiasis patients. The objectives are:

1. To study the prevalence of hypothyroidism in cholelithiasis patients.
2. To study the prevalence of subclinical hypothyroidism in cholelithiasis patients.
3. To study the age and sex distribution of subclinical hypothyroidism and hypothyroidism in cholelithiasis patients.
4. To study the ultrasonography findings of patients with subclinical hypothyroidism and hypothyroidism.

Materials and Methods

The present study is a Hospital Based prospective study which is time bound. This study was conducted during the period of January 2023 to March 2024 (15 months). Total 80 patients were included in these studies that are diagnosed with Cases admitted in the department of General Surgery at Government Siddhartha Medical College, and satisfying the inclusion criteria.

Inclusion criteria

1. Patients who are diagnosed as Cholelithiasis by abdominal ultra-sonogram and who are willing to participate in study.
2. Age >13 years.
3. Patients with known hypothyroidism.
4. Patients with subclinical hypothyroidism.

Exclusion criteria

1. Who underwent total thyroidectomy / pregnant / sepsis / severe illness.
2. Who are taking drugs known to affect thyroid functions like phenytoin, carbamazepine, phenobarbitones, rifampicin, amiodarone, lithium, estrogens, glucocorticoids etc.
3. Children below 13 years of age.
4. Post cholecystectomy patients.

Methods

In the patients who fulfilled the inclusion criteria, detailed history and clinical examination was done. They are subjected to biochemical investigations like Complete blood count, Blood sugar by glucose oxidase method, Blood urea, Serum creatinine, Fasting serum thyroid profile [4-6], Ultrasound abdomen. Then, patients are subjected to thyroid function tests by collecting 3-4 ml of venous blood from the peripheral vein after 12 hours of fasting and sending them to the lab to estimate T3, T4, and TSH. Abdominal ultrasound is taken as a reference for Cholelithiasis' diagnosis.

Before collection of data, all subjects were briefed about the purpose of the study and written informed consent was obtained. All investigations were done free of cost and no financial burden imposed on the patient.

Statistical analysis was done by spreading the data over the excel sheet. Expressing the data in percentages and projecting the data as tables and relevant diagrams. SPSS software version 26 is used to do Chi square (p<0.05 is considered significant) and ANOVA test wherever applicable.

Results

From the present study the following results were observed. Total 80 cases of cholelithiasis were enrolled in this study.

Table 1: Prevalence of hypothyroidism and SCH among the patients included in this study

No. of patients	Euthyroid	Hypothyroid	Subclinical Hypothyroid
80 (n)	58 (72.5%)	16 (20%)	6 (7.5%)

In the present study 16 patients are hypothyroid, 6 patients are sub clinical hypothyroid out of 80 patients of cholelithiasis. 58 out of 80 are in euthyroid state (72.5%).

In the present study females were 60 out of 80 (75%) and males were 20 out of 80(25%). It is most

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common in females as both hypothyroidism and cholelithiasis are common in females.

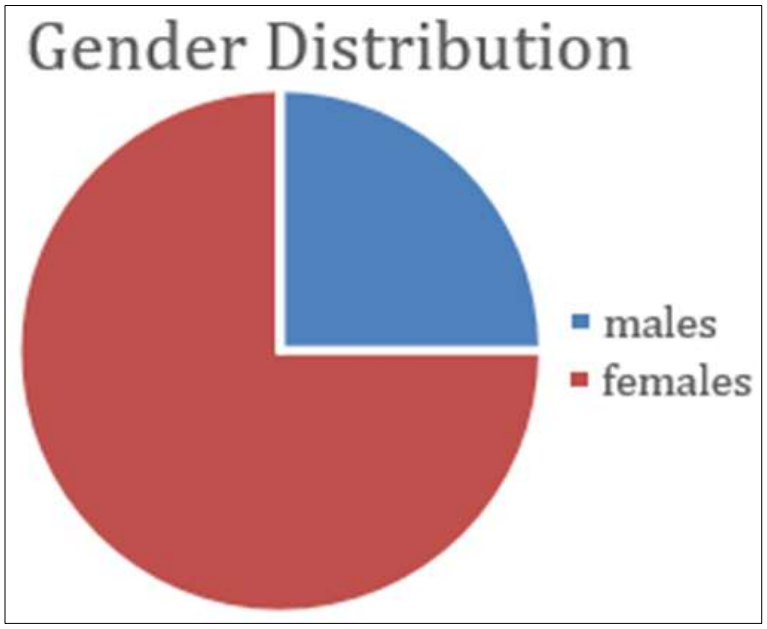

Fig 1: Showing gender distribution of the patients included in this study

Out of total 80 cases 20 were males, 60 were females.
In females (12 out of 60) 20% had hypothyroidism, (6 out of 60) 10% had subclinical hypothyroidism and in males (4 out of 20) 20% had hypothyroidism. Overall (12 out of 16) 75% of hypothyroidism was in females, (6 out of 6) 100% subclinical hypothyroid was in females. ANOVA test value is 2.94 is insignificant p is 0.196.

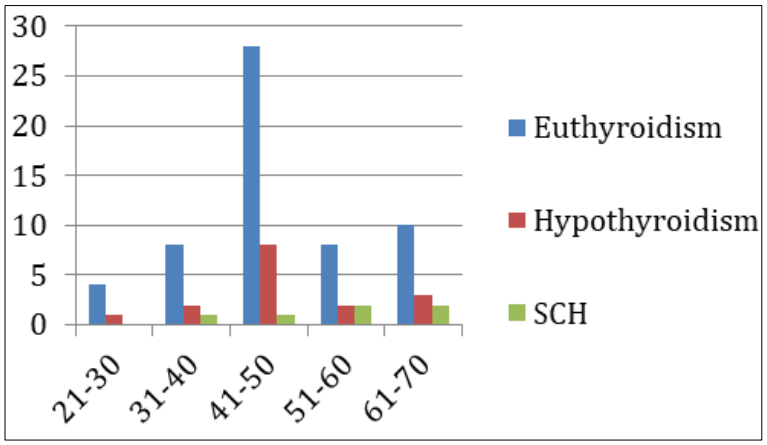

Fig 2: Prevalence of hypothyroidism and sub clinical hypothyroidism across age groups

In this study most common age group was between 41-50 (46.25%). The ANOVA statistic test value is 4.69. The p-value is 0.031 and the result is significant at $p<0.05$. Next most common age group is 61 to 70 years representing 18.75% i.e., 14 patients, followed by 51-60 years age group representing 15% i.e., 12 patients. Least common in the age group of 21-30 (6.25%) that is 5 patients. This may be due to time required for gall stone formation in patients with hypothyroidism patients is long. So prevalence is less in younger age groups compared to older age groups. The number of patients with hypothyroidism increases with age.
In younger age group the cause for cholelithiasis may be due other causes like hemolytic anemias, sickle cell anemia, and thalassemia. In these cases the stones are multiple and are pigmented stones or mixed stones rather than pure cholesterol stones.

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Table 2: Comparison of size of the stone with thyroid status

Size of the stone	Euthyroid	Hypo + SCH	Total
<10 mm	34	4	38 (47.5%)
>10 mm	24	18	42 (52.5%)
Total	58	22	80

In present study (18out of 22) 81.8% stones in hypothyroidism and SCH patients were >1cm and overall (42 out of 80) 52.5% stones were >1cm, fisher exact test value is 0.0022 and is statistically significant at $p<0.01$.

61 Out of 80 (76.25%) were multiple stones and 19 out of 80 (23.75%) had single stones. Most of the patients have multiple stones on abdominal ultrasonography examination.

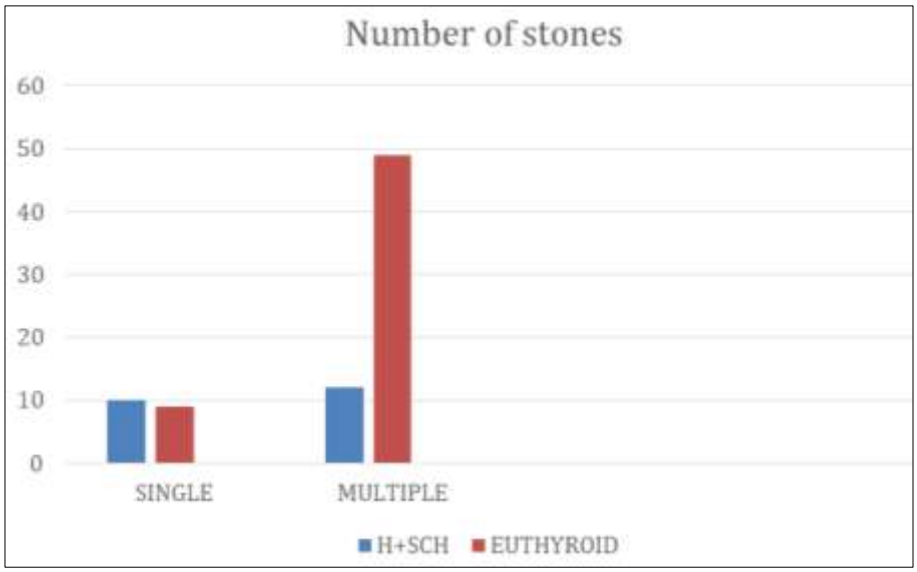

Fig 3: Hypothyroidism prevalence against number of stones

12 out of 22 hypothyroidism (54.54%) patients had multiple stones, and 9 out 58 (15.51%) patients of euthyroid had a single gallstone. The Fisher exact test is 0.0081 and is statistically significant. Multiple stones are common in both hypothyroidism patients and euthyroidism patients, representing 54.54%, 84.48%, respectively. But in our study, single stones are common in hypothyroidism than in euthyroidism, with prevalence rates of 45.45%, 15.51%, respectively.

Table 3: Signs and symptoms of patients in this study

Symptoms and signs	Yes	No
Abdominal pain	64 (80%)	16 (20%)
vomiting	58 (72.5%)	22 (27.5%)
Fatigue	44 (55%)	36 (45%)
Weight gain	24 (30%)	56 (70%)
constipation	26 (32.5%)	54 (67.5)
Menstrual disturbances	12 (15%)	68 (85%)
Obesity	60 (75%)	20 (25%)
Dry skin texture	22 (27.5%)	58 (72.5%)
Hair loss	10 (12.5%)	70 (87.5%)
RHC tenderness	36 (45%)	44 (55%)

In this study, abdominal pain was the most common symptom presenting in 80%, i.e., 64 patients. Obesity is also a common finding (75%), along with easy fatigability. Among the specific symptoms of hypothyroidism, easy fatigability was the most common symptom presenting in 55% followed by constipation (32.5%), weight gain (30%), dry skin texture (27.5%). Menstrual abnormalities are present in most of patients. The most common abnormality is menorrhagia. It is common in patients with subclinical hypothyroidism. This may be due to the similar effect of TSH hormone on the female genital

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system as a follicular stimulating hormone. So that in hyperthyroidism, either amenorrhea or hypomenorrhea may be present. This is due to the negative feedback effect of TSH hormone on the pituitary gland.

Table 4: Symptoms based on the thyroid status of the patient in this study

Clinical features	Present (or) absent	Euthyroid	Hypothyroid	SCH
Fatigue	Yes	26 (32.5%)	14 (17.5%)	4 (5%)
	No	32 (40%)	2 (2.5%)	2 (2.5%)
Weight gain	Yes	11 (13.75%)	12 (15%)	1 (1.25%)
	No	47 (58.75%)	4 (5%)	5 (6.25%)
Constipation	Yes	15 (18.75%)	10 (12.5%)	1 (1.25%)
	No	43 (53.75%)	6 (7.5%)	5 (6.25%)
Menstrual disturbances	Yes	3 (3.75%)	9 (11.25%)	0 (0%)
	No	55 (68.75%)	7 (8.75%)	6 (7.5%)
Anemia	Yes	16 (20%)	6 (7.5%)	0 (0%)
	No	42 (52.5%)	10 (12.5%)	6 (7.5%)
Obesity	Yes	44 (55%)	16 (20%)	0 (0%)
	No	14 (17.5%)	0 (0%)	6 (7.5%)
Skin texture	Dry	8 (10%)	14 (17.5%)	0 (0%)
	Moist	50 (62.5%)	2 (2.5%)	6 (7.5%)
Hair loss	Yes	6 (7.5%)	4 (5%)	0 (0%)
	No	52 (65%)	12 (15%)	6 (7.5%)

Obesity is the most common finding observed in this study who is euthyroid (55%) followed by fatigue (32.5%) and anemia (20%).Obesity (20%) followed by dry skin texture (17.5%) and fatigue (17.5%) is also seen in hypothyroid cases. Sub clinical thyroid no significant changes were observed.

Discussion

This study is conducted on 80 patients. Patients were admitted in Government general hospital for cholelithiasis and all patients were undergone cholecystectomy. All patients had cholelithiasis diagnosed by abdominal ultrasonography study. Hypothyroid patients will have biliary stasis because of delayed emptying of bile from the biliary tract into the duodenum. This is due to the decreased pro-relaxing action of thyroxine on the sphincter of Oddi in hypothyroid individuals. There were 60 (75%) female patient and 20 (25%) male patients in our study. This is due to prevalence of cholelithiasis is high in females. Sex hormones and Pregnancy are believed to cause women at a higher risk. Male to female ratio in this study was 1:3.Bansal's *et al.* [7], study found 35% males and 65% females in their study of 104 patients. In another study Bhattacharya *et al.* [8] showed 28.6% were male and 71.4% were female. Sharma *et al.* [9] study showed that 70% female and 30% males in their study.

In this study 16 patients were hypothyroid, 6 patients were sub clinical hypothyroid out of 80 patients characterize by increased TSH from the standard value in their thyroid profile, with the prevalence rate of 20%, 7.5% respectively. In other studies, 8% prevalence was found in the study of Ahmad MM *et al.* [10].14.4% prevalence is found to have cholelithiasis in Kotwal's *et al.* [11] study in Sikkim. In Ibrahim *et al.* study [12], total 50 patients were studied in which 12 were diagnosed as SCH in which 11 (91.6%) were females and 1(8.33%) was male.

In our study, there was increased prevalence of cholelithiasis, subclinical hypothyroidism and hypothyroidism in >40 year age group. The number of patients with hypothyroidism and cholelithiasis are increase with age. 13 out of 64 comprising 20.31% were hypothyroid and 5 out of 64 i.e.7.81 were subclinical hypothyroid in >40 years age. 03 out of 16 comprising 18.75 were hypothyroid and 1 out of 16 i.e.6.25% were subclinical hypothyroid in <40 years age group. In the study conducted by Hassan *et al.* [13], total 225 patients were studied. Out of which, in less than 40 yrs. age group 3 were subclinical hypothyroid and none of them were hypothyroid.

In this study 18 out of 22 Stones in Hypothyroidism patients were >1 cm. Overall, 52.5% of stones are >1cm, fisher exact test value is 0.0022 and is statistically significant as $p<0.01$. 61 out of 80 (76.25%) were multiple stone and 19 out of 80 (23.75%) were single. 12 out of 22 hypothyroidism (54.54%) patient had multiple stones and 09 out 58(15.517%) patient of euthyroid had a single stone. In the study conducted by Ibrahim *et al.* [12], total 50 patients of cholelithiasis were studied. Of which 12 out of 50

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were hypothyroid. All stones in hypothyroidism was >1cm. 3 out of 12 hypothyroidism had single stone, 9 patients had multiple stones.

Conclusion

Cholelithiasis is most common in 41-50 yrs. age group. Significant number of females was affected by gallstone disease. Prevalence of hypothyroidism and subclinical hypothyroidism in this study is 20% and 7.5%. Gender wise prevalence in this study was higher in females, among the 60 females with cholelithiasis, 12 were diagnosed as having hypothyroid and 6 were subclinical hypothyroid. Among the total 20 males, 4 diagnosed as hypothyroid and none of the males were subclinical hypothyroid. In present study, 18 out of 22 patients has size of the stone >1cm and 61 out of 80 had multiple stones, 19 out of 80 had single stones. Most of the patients had multiple stones. All the study cases underwent cholecystectomy. As most patients were in greater than 40 years of age, it can be explained by the time needed for stone formation by the effect of increased TSH in hypothyroidism. This study corroborated with other studies as mentioned in the discussion part. Thus leading to further understanding the relation between cholelithiasis and hypothyroidism. In the future extensive population studies are needed in this direction to compare these findings. To recommend screening and early diagnosis of hypothyroid state at the subclinical level by regularly monitoring TSH. They can be identified and treated at early stages and the burden of cholelithiasis can be prevented at least in this subgroup.

Conflict of Interest

None to be declared.

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