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Prevalence of hypothyroidism among patients with cholelithiasis in a tertiary care centre

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Abstract

Background: Cholelithiasis is a prevalent gallbladder pathology that affects 10 to 15% of persons in the Western world and 2 to 29% in India. More than 80% of cholelithiasis patients are asymptomatic. Hypothyroidism results in dyslipidemia, bile stasis, and Sphincter of Oddi malfunction, which leads to cholelithiasis and choledocholithiasis. As a result, patients with hypothyroidism should be tested for gall stones, which can be treated before difficulties arise.

Aim: Study aimed to find the prevalence of hypothyroidism in patients with cholelithiasis.

Materials and Method: The present study was a prospective study conducted in a tertiary care centre in South India. The study included 45 consecutive patients diagnosed with Cholelithiasis by USG Abdomen, attending the General Surgery Out Patient Department (OPD), above the age of 18 years, either symptomatic or asymptomatic, irrespective of undergoing Cholecystectomy or not, between the period of June 2022 and May 2023. Patient was diagnosed cholelithiasis on abdominal ultrasonography and was tested for having subclinical hypothyroidism by testing fasting blood samples for serum TSH, free T3 and T4 levels. Results were analysed using SPSS 20.0 version and the association was tested using Chi square test.

Results: Of the 45 total patients, 24 (53.33%) were between the ages of 30 and 50, 16 (35.56%) were under 30, and 5 (11.11%) were beyond 50. The age distribution was 43.24 +/- 9.38 years. In comparison to men, who accounted for 21 patients (46.67%), women made up 24 patients (53.33%). Of the 45 individuals, 28 (62.22%) were euthyroid and 17 (37.78%) were hypothyroid. Of the hypothyroid individuals, 3 (6.67%) had subclinical hypothyroidism, and 14 (31.11%) had clinical hypothyroidism. A statistically significant difference was seen when age and thyroid status were correlated (p=0.004). There was no statistically significant

difference in the correlation between thyroid status and the amount of gallstones by gender.

Conclusion: In the present study, hypothyroidism was identified in over one-third of cholelithiasis patients, with a significant frequency of subclinical hypothyroidism. Most importantly, physicians treating patients with gall stones should be aware of the potential hypothyroid background and think about testing thyroid function, especially in female patients over 30 years, who have the highest prevalence of both clinical and subclinical hypothyroidism.

Keywords: Cholelithiasis, Hypothyroidism, Hyperlipidemia, Sphincter of Oddi.

Introduction

Gallstone disease prevalence in India was found to be between 2 and 29%, with notable variations between the northern and southern regions of the country.[1] One of the most prevalent endocrine disorders is hypothyroidism, which affects 5–15% of Indians overall and 8–12% of them with subclinical hypothyroidism.[2]

Gallstones are divided into three types: cholesterol stones, pigment stones, and mixed stones. Whereas 80% of stones in Asia are pigment stones, 80% of stones in the USA and Europe are cholesterol or mixed stones. Cholesterol or mixed stones are composed of between 51 and 99 percent cholesterol together with phospholipids, bile acids, calcium salts, and bile pigments.[3] In general, stones come in a variety of sizes and shapes. They can be faceted, hard, or irregularly shaped like mulberries.[4]

Gallstone pathogenesis is a complicated process that involves variables that impact the flow and content of bile. Biliary stasis, which can be brought on by bile duct strictures, dyskinesia, or sphincter of Oddi stenosis, is a critical component in the formation of bile duct stones. It is believed that failure of the sphincter of Oddi and poor bile flow are significant functional processes that could encourage the production of gallstones.[5,6]

The most frequent cause of secondary hypercholesterolemia is hypothyroidism.[7]Hypothyroid patients have blood cholesterol levels that are generally 50% higher than euthyroid people, and 90% of those who are people with hypothyroidism have high cholesterol levels.[8] Research has revealed a connection between thyroid dysfunction and disruptions in lipid metabolism, which may ultimately result in alterations to the bile's composition.

The hypothyroid state is thought to be reducing the sphincter of Oddi's tendency to relax, which causes bile supersaturation with cholesterol. This, in turn, causes the gall bladder to become hypomotile, less contractible, and to fill abnormally. This, in turn, increases the amount of time that bile spends in the gallbladder and its capacity to flow, which causes bile stasis. Eventually, this leads to the initiation of bile supersaturation and the formation of gall stones.[9]

Hypothyroidism has been linked to decreased bilirubin excretion because of reduced activity of UDP glucuronyl transferase in several studies. In certain instances, the use of thyroxine has been suggested to dissolve gallstones and CBD stones. Additionally, the oddi sphincter expresses receptors for thyroid hormones, and thyroxin directly promotes relaxation in the sphincter. On the contrary, a small number of studies have demonstrated that hyperthyroidism may also tend to cause hepatic nuclear receptor gene over expression, which is a critical component of cholesterol metabolism and can lead to the development of cholesterol gallstones.[10]

As a result, multiple hypotheses have been put out to explain how thyroid hormone causes gallstones to form. This study was conducted to explore prevalence of hypothyroidism in patients of cholelithiasis by assessing

levels of Serum TSH (Thyroid Stimulating Hormone), free T3 (Triiodothyronine) and free T4 (Thyroxine).

Materials and Methods

This cross-sectional observational study was conducted in Department of General Surgery, Sree Mookambika Institute of Medical Sciences, Kulasekharam. The study included all consecutive patients diagnosed with Cholelithiasis by USG Abdomen, attending the General Surgery Out Patient Department (OPD), above the age of 18 years, either symptomatic or asymptomatic, irrespective of undergoing Cholecystectomy or not, between the period of June 2022 and May 2023. Those who were not willing to participate in the study, patients who had undergone thyroid surgery and thyroid supplementation, and pregnant women were excluded from the study. A total of 45 patients were recruited in the present study.

Detailed history and clinical examination done, variables like age, sex, number of gall stones, USG neck findings noted. Blood samples were collected from each patient. T3, T4 and TSH were assessed in the fasting serum samples of the study subjects using Beckman Coulter automated immunoassay method technology. The normal range of TSH was 0.34-5.2mU/L, 2.5-3.9pg/ml for free T3 and 0.6-1.1 ng/dL for free T4.

Individuals without symptoms who had a serum TSH of more than 5.2 mIU/l were classified as subclinical hypothyroid, while those who did had symptoms were classified as clinically hypothyroid. Individuals classified as euthyroid had normal serum TSH, free T3, and free T4 levels. Overt hyperthyroidism was defined by low TSH and high free T4 levels.

Statistical Analysis was carried out using SPSS 20.0 version. The collected data were entered in the MS excel spread sheet. Descriptive statistics (frequency, percentage) were evaluated using mean, standard deviation and 95% Confidence Interval. Chi square test was done to assess statistical significance. A p value less than 0.05 was considered statistically significant.

Observation and Results

Among the total 45 patients, 24(53.33%) patients were between 30-50 years, 16(35.56%) patients were less than 30 years and 5(11.11%) patients were more than 50 years. The mean age was 43.24±9.38 years. The maximum numbers of patients were females 24(53.33%) compared to males 21(46.67%).

Out of 54 patients, 17(37.78%) were hypothyroid and 28(62.22%) were euthyroid. Among the hypothyroid patients, 3 (6.67%) had clinical hypothyroidism and 14 (31.11%) had subclinical hypothyroidism. The mean and Standard deviation of Thyroid function test was given in Table 1.

Age (years)	Mean	Standard Deviation
FT3(pg/ml)	1.5±0.76	0.816
FT4(ng/dl)	1.07±0.38	1.286
TSH(µIU/ml)	6.98±2.14	6.58

Table 1: Mean values of T3, T4 and TSH.

On correlating age and thyroid status showed statistically significant difference with p=0.004 (Table 2). Correlation between gender and thyroid status showed p value of 0.078, which was not statistically significant. (Table 3).

Age (years)	Hypothyroid	Euthyroid	p value
<30	9(56.25%)	7(43.75%)	0.004
30 – 50	8(33.33%)	16(66.67%)	
>50	0(0%)	5(100%)	

Table 2: Comparison of age with thyroid status

Gender	Hypothyroid	Euthyroid	p value
Male	4(19.5%	17(80.95%)	0.078
Female	13(54.17%)	11(45.83%)	

Table 3: Comparison of gender with thyroid status

Among the 45 patients, 17(37.78%) had single gall stone and 28(62.22%) had multiple gall stones. Correlation between gender and thyroid status showed p value of 0.098, which was not statistically significant (Table 4).

Gall stones	Hypothyroid	Euthyroid	p value
Single	5(29.41%)	12(70.59%)	0.078
Multiple	22(78.57%)	6(21.43%)	

Table 4: Comparison of number of Gall stones with thyroid status

Discussion

While cholelithiasis affects 24% of people in affluent nations, it is not as common in less developed regions of the world, despite being a major cause of morbidity worldwide.[11] This study examined potential correlations among serum TSH levels and gallstone development.

In the current study, the majority of patients (30.33%) were between the age group of 30 and 50. The average age of the patients was 43.24±9.38 years, with 24 (53.33%) females and 21 (46.67%) men, respectively. According to Maji J et al.[12] 28% of the patients were in the 45–54 age range and Females made up the majority of the 40% of hypothyroid patients. In the study by Ghafoor MT et al.[13] subclinical hypothyroid condition affected those over the age of 55, while the peak age group for instances of hypothyroidism was 36–55 years of age.

Of the 54 patients, 17 (37.78%) were hypothyroid. There were 3 cases (6.67%) of clinical hypothyroidism and 14 cases (31.11%) of subclinical hypothyroidism. In the study by Maji J et al.[12] subclinical hypothyroidism and clinical hypothyroidism were observed in 10 (18.5%) patients and 3 (5.55%) individuals, respectively. In their study, Rahman K et al.[14] found that 64 (68.1%) of the patients were euthyroid and 30 (31.9%) were hypothyroid. There were 27 (28.7%) patients with subclinical hypothyroidism and 3 (3.2%) with clinical hypothyroidism among the hypothyroid patients. The p-value for the prevalence of subclinical hypothyroidism in gallstones in the study by Kumar G et al.[15] was 0.0042. This was a statistically significant correlation between sub-clinical hypothyroidism and gallstone disease. These findings were comparable to the present study.

According to Singh RR et al.[16] 24%, 64%, and 12% of males with gallstones had hypothyroid, euthyroid, or hyperthyroid diagnoses, respectively. The proportion of females identified with hypothyroid, euthyroid, or hyperthyroid conditions, respectively, was 24.4%, 65.85%, and 1% of those with gallstones.

Similarly, in the study carried out by Ghadhban BR et al.[17] the majority of the patients were between the ages of 36 and 50, with 84 (81.6%) being females and 19 (18.4%) being males. Of the total number of patients, eight (7.8%) were determined to have subclinical hypothyroidism and 95 (92.2%) were found to be euthyroid, with female gender predominance at 81.6% in subclinical hypothyroid group.

High serum TSH levels and age were found to be significantly correlated in the current study (p=0.004), although there was no significant link observed with gender (p=0.078) or the number of gallstones (p=0.078) ($p<0.05$ was significant). Rahman K et al.[14] observed no statistically significant association between elevated serum TSH levels with age (p=0.775), gender (p=0.464), or number of gall stones (p=0.586)

The probability of having hypothyroidism was found to be strongly adversely correlated (p=0.017) with increasing age, according to Nair KP et al.[18] Females were 19% less likely than males to develop hypothyroidism, however this difference was not statistically significant. In a study conducted by Raghuwanshi BS et al.[19] 3 out of 12 hypothyroidism

patients (25%) had single stones, while 9 (75%) had numerous stones (statically significant P value 0.05). The majority of stones (58%) in hypothyroid patients were of the cholesterol type, and this was statistically significant at P value≤0.05.

Conclusion

Hypothyroidism, or subclinical hypothyroidism, has been linked in a number of recent research. The increased frequency of hypothyroidism in gallbladder stone patients points to modifications in the sphincter of Oddi's function in particular, as well as changes in cholesterol metabolism and bile excretion rate. Above all, in treating patients with microlithiasis or biliary stones, physicians should be cognizant of the potential hypothyroid background and think about testing thyroid function, especially in female patients, who have the highest rate of both subclinical and clinical hypothyroidism and should be examined for thyroid function.

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