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A Study On Association Of Subclinical Hypothyroidism In Cases Of Cholelithiasis.

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ABSTRACT

The prevalence of gall bladder stones in India has been rising due to change in food habits, advanced investigations and increasing affordability. Stone formation depends on cholesterol concentration, supersaturation, nucleation and abnormal gall bladder motility leading to biliary stasis. Discussions done globally for decades on whether thyroid disorders can cause cholelithiasis explained various possibilities in thyroid failure which include; altered liver cholesterol metabolism, altered pro-relaxing effect of thyroxine on sphincter of Oddi and altered bile flow. To determine the association between gallstones and subclinical hypothyroidism. This prospective observational type of study was conducted in Department of General Surgery, Govt. Theni Medical College In the year 2021.Study found that subclinical hypothyroidism is a highly probable risk factor for development of gallstones especially for females. Undetected and untreated hypothyroidism in such patients will result in persistence of the basic pathophysiology responsible for the primary disease process resulting in recurrence and complications. Detailed history was taken to establish proper diagnosis and thorough physical examination was obtained in each patient. Data collection sheets were filled appropriately. After evaluation and preparation, patients who required surgical treatment were taken up for surgery. Meticulous techniques were practiced, and aseptic precautions were followed. After completing the collection of data, it was compiled in a systemic way for this study. After explaining the study and the investigative and operative procedures and their merits and demerits, expected results and possible complications, consent was obtained from all the patients/ legal guardians Data analysis was made both manually and by using computer. Calculated data was arranged in a systemic manner, and distributed in form of tables and figures and statistical analysis was done to evaluate the objectives of this study with the aid of Statistical Package for Social Science (SPSS). The size of the stone ranged from 3mm to 20mm. 43 Out of 47 (91.49%) were multiple stones and 4 out of 47 (8.51%) were single. 09 out of 12 hypothyroidisms (75%) patients had multiple stones and 01 out 35 (2.85%) patients of euthyroid had single stone. fisher exact test is 0.0459 and is statistically significant. Most of the stones were of pigment type and was 51.06% and cholesterol stones were 23.4%. In hypothyroid cases most stones were of cholesterol type 58.33% and In Euthyroid cases most stones were of pigment type. Chi square test value is 11.259 and p value = 0.00359. It is significant at P value ≤0.05. Subclinical hypothyroidism is more common in the CBD stone patients, compared with no gallstone controls, supporting our hypothesis that hypothyroidism might play a role in the forming of CBD stones. At minimum, women older than 60 yr. with CBD stones should be screened for borderline or overt subclinical hypothyroidism.

Keywords: Hypothyroidism, OfCholelithiasis, gall bladder stones, thyroid.

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INTRODUCTION

Gallstones are the most common pathology of biliary tree, can be classified into three main types: cholesterol, pigment (black, brown) or mixed stones. In USA and Europe, 80%cholesterol or mixed stones, whereas in Asia,80% are pigment stones. Gallstones may be single, multiple, large or small and those containing calcium salts are radio opaque (10%). Single stone consist of cholesterol and are uncommon, due to precipitation of cholesterol and calcium [1]. Pigment stones arise due to precipitation of concentrated bile pigmentMany studies were done to reveal the risk factor for biliary lithiasis and have focused on hyper saturation of cholesterol in bile as a critical step in nucleation process in formation of bile stone [2]. Thyroid disorder is a commonly prevalent condition among adults. There has been a discussion, for a decade, to conclude the association between thyroid disorder and gallstone formation.

There are several studies and explanations for the possible relation between subclinical hypothyroidism and gall stone disease, which include the known link between thyroid failure and disturbance in lipid metabolism, which may ultimately lead to change in composition of bile [3].

Moreover, the sphincter of Oddi express thyroid hormone receptors and thyroxine has a direct prorelaxing effect on it. The important functional factors that may promote gallstone formation are low bile flow and sphincter of Oddi dysfunction. The prevalence of subclinical hypothyroidism has never been studied before in gallstone patients before. If an increased prevalence of thyroid disorder will be found, it may have an effect on diagnostic and therapeutic work up of patient with gallstone.90% of all hypothyroid patients have elevated cholesterol level than in euthyroid patients. Hypothyroidism is the most common cause of secondary hypercholesterolemia [4,5].

MATERIALS AND METHODS

This prospective observational type of study was conducted in Department of General Surgery, Govt. Theni Medical College In the year 2021.Study found that subclinical hypothyroidism is a highly probable risk factor for development of gallstones especially for females. Undetected and untreated hypothyroidism in such patients will result in persistence of the basic pathophysiology responsible for the primary disease process resulting in recurrence and complications.

Inclusion criteria: Patients admitted in surgical ward with provisional diagnosis of cholelithiasis on abdominal ultrasound

Exclusion criteria

- Those with previous history of hypothyroidism
- patients taking thyroid replacement drugs
- Abdominal ultrasound
- Thyroid profile (TSH)

Method of sampling was nonrandom, purposive. Short history and physical examination were conducted after admission of patients admitted in surgery department with features suggestive of extra hepatic biliary stones. Basic investigations were done which was followed by imaging studies. All patients were explained about the disease process and the appropriate line of management. All the information regarding the study was explained to the patients who were willing to participate in this study. Informed written consent was obtained. Detailed history was taken to establish proper diagnosis and thorough physical examination was obtained in each patient. Data collection sheets were filled appropriately. After evaluation and preparation, patients who required surgical treatment were taken up for surgery. Meticulous techniques were practiced, and aseptic precautions were followed. After completing the collection of data, it was compiled in a systemic way for this study. After explaining the study and the investigative and operative procedures and their merits and demerits, expected results and possible complications, consent was obtained from all the patients/ legal guardians. Those who agreed were involved in the study. No other additional investigation was done and did not have any significant risk. It did not cause any economic issues to the patient. The study was approved by the institutional ethical committee board prior to collection of data.

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Stastical analysis

Data was collected in an approved data form. Data analysis was made both manually and by using computer. Calculated data was arranged in a systemic manner, and distributed in form of tables and figures and statistical analysis was done to evaluate the objectives of this study with the aid of Statistical Package for Social Science (SPSS 19.0)

RESULTS

In present study 12 out of 50 (24%) of patients of cholelithiasis had hypothyroidism. In females 26.19% had hypothyroidism and in males had 12.5% hypothyroidism. Overall, 91.16% of hypothyroidism was in females. Fisher test value is 0.6606 is insignificant at $p<0.05$. This result was insignificant in our study despite higher prevalence and no relation was found between gender specific gall stone. This can be understood by higher prevalence of hypothyroidism in female. In present study most, common group was between 41-50 (36%). The chi-square statistic is 1.3106. The p-value is 0.85958 the result is not significant at $p<0.05$. The number of patients with cholelithiasis and hypothyroidism increase with age. In present study all stones in hypothyroidism patient were >1cm and overall, 58% stones were >1cm, fisher exact test value is 0.0005 and is statistically significant at $p<0.05$.

Most of the stones were of pigment type and was 51.06% and cholesterol stones were 23.4%.In hypothyroid cases most stones were of cholesterol type 58.33% and In Euthyroid cases most stones were of pigment type. Chi square test value is 11.259 and p value = 0.00359. It is significant at P value ≤0.05. 09 out of 12 hypothyroidisms (75%) patients had multiple stones and 01 out 35 (2.85%) patients of euthyroid had single stone. fisher exact test is 0.0459 and is statistically significant.

Table 1: Prevalence Of Thyroid Across Age Groups

Age group	Thyroid status		Total patient
	Euthyroid	Hypothyroid	with gallstone
10-20	2	0	2 (4%)
21-30	6	1	7 (14%)
31-40	7	2	09 (18%)
41-50	13	5	18 (36%)
>50	10	4	14 (28%)
Total	38	12	50

Table 2: Comparison of stone size with thyroid status.

Size of stone	Thyroid status		Total
on USG (mm)	Euthyroid	Hypothyroid	
<10 mm	21	0	21 (42%)
>10 mm	17	12	29 (58%)
Total	38	12	50

Table 3: Hypothyroidism prevalence against numberof stones.

No. ofstones	Thyroid status		Total
	Euthyroid	Hypothyroid	
Single	01	03 (25%)	04
Multiple	34	09 (75%)	43
Total	35	12	47

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Table 4: Type of stone with thyroid status

Compositionand type of stone	Thyroid status		Total
	EuthyroidN = 35	HypothyroidN = 12	
Cholesterol	04 (11.42%)	07 (58.33%)	11
Mixed	11 (31.42%)	01 (8.33%)	12
Pigment	20 (57.14%)	04 (33.33%)	24
Total	35	12	47

DISCUSSION

The prevalence of common bile duct (CBD) stones in patients with gallbladder stones varies from 8 to 16%). The pathogenesis of gallstones is a complex process involving factors affecting bile content and bile flow. A crucial factor in the forming of bile duct stones is biliary stasis which may be caused for example by sphincter of Oddi (SO) stenosis, SO dyskinesia, or bile duct strictures [6]. Previously it has been shown that CBD stone patients have significantly more often diagnosed hypothyroidism, compared with gallbladder stone patients or controls [7]. The higher prevalence of previously diagnosed hypothyroidism in CBD stone patients, compared with gallbladder stone patients, suggests that factors other than merely changes in the cholesterol metabolism or bile excretion rate, particularly changes in the function of the SO, also may be behind the association between CBD stones and hypothyroidism. *Ex vivo* experiments with both the pig and human SO have shown that thyroxine has a direct, prorelaxing effect on the SO motility at physiological concentrations, possibly mediated via thyroid hormone receptors-β_1 and -β_2, and the absence of T_4 may thus result in an increased tension in the SO In the rat the net bile flow to the duodenum is reduced in hypothyroidism and enhanced in hyperthyroidism and in human cholescintigraphy the hepatic clearance of ^{99m}Tecnetium diethyliminodiacetic acid is decreased, and the hilum duodenum transit time tends to be increased in hypothyroidism [8]. The reduced prorelaxing effect of T_4 on the SO in hypothyroidism shown in the experimental investigations may thus result in delayed emptying of the biliary tract, and, together with the possible cholesterol load in the bile and decreased hepatocytic excretion rate, may compose an important explanation for the increased association of CBD stones and hypothyroidism. There were 42 (84%) female patient and 8 male patientsin our study [9]. This is because prevalence of cholelithiasisis higher in females. Pregnancy and sex hormones are believed to place women at a higher risk, and the view has been supported by several classical epidemiologicstudies. 12 patients out of 50 showed hypothyroidisms characterize by increased TSH from normal value in their thyroid profile, with prevalence rate of 24% [10]. In other Indian studies, 8% prevalence was found in study of Ahmad MM. 14.4 % patients were found to have cholelithiasis in study conducted by Ibrahim SL et.al Most of the cases (12 of 16; 75%) with S-TSH values over 6.0 mU·liter^{-1} (subclinical hypothyroidism; grades III-IV) in the CBD stone group were found in women older than 60 yr; in this subgroup the prevalence was 11.4% (12 of 105) in the CBD stone and 1.8% (one of 56) in the control group (P = 0.032) [11]. In women older than 60 yr in CBD stone patients, the prevalence of grades I-IV (S-TSH ≥ 5.0 mU·liter^{-1}) subclinical plus borderline subclinical hypothyroidism was 25 of 105 (23.8%), compared with one of 56 (1.8%) in the control group (P = 0.012). There were two patients (1.4%) in the control group (none in CBD stone group) who were recognized to have S-TSH values below the lower normal limit (<0.4 mU·liter^{-1}) [12]. Of these two patients, one had S-FT4 above the upper normal limit (>19.0 pmol·liter^{-1}), and the other had S-FT4 within the normal range [13]. In addition, one patient in group I with S-TSH within the normal range (0.3%) had S-FT4 above the upper normal range. There was no statistical difference between the two groups.In the general linear model multivariate analysis, patient group, age, and gender were associated with the level (grades I-IV) of thyroid function [14,15].

CONCLUSION

This study was conducted to explore prevalence of hypothyroidism in patients of cholelithiasis, so that light on relation of hypothyroidism and cholelithiasis could be found. In our study, as expected majority of patients were females as both hypothyroid and cholelithiasis is common in females and most of our patients were in forty and fifty age group. 24% patients were diagnosed with hypothyroidism, hypothyroid patients were detected on surgery to have multiple stones and most of these stones were yellow in color and that to be cholesterol stones as most common type. As most patients were in greater than forty years, it can be explained by time needed for stone formation due to effect of increased TSH.

This study corroborated earlier studies as mentioned in discussion part, and lead further to understanding relation of hypothyroidism and cholelithiasis. Further large population studies are needed in this direction to compare these findings leading to recommendations for screening for early diagnosis of hypothyroid state at subclinical level by regularly monitoring TSH so that they can be treated at early stages and burden of cholelithiasis thus can be prevented at least in this subgroup.

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