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Original Research Article

Magnitude of hypothyroidism among patients of cholelithiasis in a tertiary care centre in rural West Bengal: a prospective study

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ABSTRACT

Background: Cholelithiasis is a common pathology of the gall bladder affecting about 10 to 15% of the adults in western countries and 2 to 29% in India. More than 80% of the patients with cholelithiasis are asymptomatic. Hypothyroidism may cause gall stone formation due to the hyperlipidemia, motility disorders affecting the bile duct and sphincter of Oddi.
Methods: This was a descriptive cross-sectional study conducted at Department of Surgery, Bankura Sammilani Medical College and Hospital, Bankura from March 2019 to February 2020 for duration of one and half year. The sample size was 54 and consecutive non-probability sampling technique was used for the sampling. All the collected data were recorded in a pre-designed proforma and analyzed in MS excel.
Results: Out of 54-patients with cholelithiasis, 28% patients were from the age group 45-54 years.40% patients were hypothyroid pre-dominantly females. Among 30-female patients 11 (26.82%) were hypothyroid and among 11-male patients 2 (15.38%) were hypothyroid. Hypothyroidism in male and female was statistically significant.
Conclusions: This study was introduced to determine the relationship between hypothyroidism and cholelithiasis. It was concluded that hypothyroidism was more common in female, obese and elder patients. The gender distribution of the hypothyroidism in patients with cholelithiasis was statistically significant while all other variables were statistically not significant.

Keywords: Hypothyroidism, Cholelithiasis, Hyperlipidemia, Billiary dyskinesia

INTRODUCTION

Around 10–15% of adults develop gallstones in the developed countries.[1] The prevalence of gall stone disease was estimated around 2-29% in India with significant differences in north and south India.[2] Hypothyroid is one of the most common endocrine disorder around 5-15% in Indian population and around 8-12% in sub clinical hypothyroidism was estimated. According to Usha Menon report, the high prevalence area in India quit often under diagnosed mainly in mountain and hilly regions.[3] The gallstone formation is a complex process involving factors affecting bile content and bile flow. An important factor in the forming of gall bladder stones is biliary stasis, which may be associated with sphincter of Oddi (SO) stenosis, SO dyskinesia, or bile duct strictures.[4-7] The previously diagnosed hypothyroidism in common bile duct (CBD) stone patients, compared with gallbladder stone patients are highly affected, 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 gall bladder stones and hypothyroidism.8 Both the animal and human SO have shown that thyroxine has a direct, pro-relaxing effect on the SO motility at physiological concentrations in Ex vivo experiments, may be mediated via thyroid hormone receptors-β1 and -β2, and the absence of T4

may cause an increased tension in the SO.[9-11] The net bile flow to the duodenum is decreased in hypothyroidism and increased in hyperthyroidism in rat, and in human cholescintigraphy the hepatic clearance of 99m Tecnetium diethyliminodiacetic acid is low, and the hilum duodenum transit time tends to be high in hypothyroidism.[12,13]

In general, about 95% of the gallbladder stones can be diagnosed with ultrasound. The primary hypothyroidism and the early thyroid failure is associated with an increased serum TSH concentration. The S-FT4 level is decreased in clinical hypothyroidism.14 In the subclinical form, an increased S-TSH level is associated with a normal S-FT4 level, and the patient is asymptomatic.[14] Subclinical hypothyroidism is a most prevalent condition among adult population; however, it is frequently not focused. Recently in the United Kingdom, the prevalence of subclinical hypothyroidism among was 2.6% among the healthy subjects. The prevalence of hypothyroidism (clinical and subclinical) is higher around 20% among women older than 60 years.[15] It is unremarkable whether treatment will improve quality of life in healthy, symptom-free patients who have abnormal TSH levels and normal FT4 levels.[16,17] Treatment of subclinical hypothyroidism is considered if it is associated with significant changes in the cholesterol level, cardiovascular effects, or neuromuscular symptoms. Some studies have reported that a positive effect on these symptoms may be corrected with early replacement therapy with l-thyroxine.[18,19] Brown pigment stones are formed secondary to biliary stasis, which is important factor leading to anaerobic bacterial degradation and precipitation of biliary lipids.[20,21]

Thyroid hormones are related with cholesterol metabolism.[22] When serum cholesterol values rise in hypothyroidism, bile may also become supersaturated with cholesterol, leading to gallbladder hypomotility, low contractility, and filling impairement, giving rise to a prolonged stasis of bile in the gallbladder.[21,23,24] It may cause the retention of cholesterol crystals, allowing sufficient time for nucleation and continual growth into mature gallstones.[22] Besides the rate of bile secretion may be reduced, physically impairing clearance of precipitates from the bile ducts and gallbladder. Thyroid hormones are well known to have an enterohepatic circulation.[25-27] So it may cause to impair bile acid secretion in a patient could interfere with the enterohepatic circulation of T4, enhance thyroid hormone clearance, and provoke hypothyroidism in an individual with low thyroid reserve, example- due to autoimmune thyroiditis.

METHODS

It is a hospital based cross-sectional descriptive study. The study has been carried out after ethical clearance from the Institutional Ethical Committee in the Department of General Surgery and Department of Biochemistry in Bankura Sammilani Medical College and Hospital, Bankura, West Bengal from from March 2019 to August 2020. The study population comprised of total 54 patients, satisfying below mentioned inclusion and exclusion criteria. The primary data for this study were patient's details and investigation reports, collected in predesigned case record form.

The study population will be selected from all cases admitted to Department surgery both men and women with cholelithiasis as diagnosis on abdominal ultasonography in a given period of time.

Sample size

Sample size for the proposed study will be calculated based on a formula used for cross-sectional study. It is

$$n = z2pq \div l2$$

Where z=1.96 (two tailed) at 90 percent confidence interval, P=prevalence of event of interest (hypothyroidism), q=compliment of p (100-p), l=acceptance error around the reported prevalence (p).

As prevalence of hypothyroidism around 5-15%, Considering 15%, prevalence

$$n = z2pq \div l2 = (1.96)2 \times 15 \times (100 - 15) \div 10 \times 10$$

$$= 4898.04 \div 100$$

$$= 48.98 = 49$$

Considering 10 percent of non-respondent=49×10 percent =4.9. So, sample size=49+4.9=53.9=54.

Sampling design

As per record 3 to 4 such patients get admitted in general surgery department daily in each unit data collection from the proposed study will be continued for the eleven month i.e. 44 (forty four weeks). Data collection for the proposed study has been planned to be done twice in a week basis.

The two days of a week will be selected via simple random sampling method using lottery technique conducted at the start of each week. One each day of data collection one eligible patient will be chosen via simple random sampling technique using lottery. This process will be going on repeated until the desired number of sample collected.

Inclusion criteria

Both male and female patients who have admitted in the Department of General Surgery, BSMCH with cholelithiasis as diagnosis on abdominal ultasonography.

Exclusion criteria

Excluded were patients with a history- treated diagnosed thyroid function abnormalities, thyroidectomy, pregnancy, serious underlying disease-sepsis or cholangitis, those prescribed medications known to affect the thyroid function tests such as- phenytoin, carbamazepine, metoclopramide, amiodarone, and lithium, Patients who had not given consent.

Study variables

The prevalence variables comparing age, sex, serum T3, T4, TSH, USG finding about stone.

Allocation of patient in the study arms

All the patients admitted in surgical department, radiologically diagnosed gall stone disease in a one and half year given period of time.

Study techniques

Details of cases, full history, clinical examination, and symptoms and signs of hypothyroidism (loss of appetite, gaining weight tiredness, constipation, cold intolerance, menstrual disturbances, bradycardia, presence or absence of goiter etc).

Within one-year, total number of gall stones patients admitted in this hospital are calculated. Every patient thyroid profile will be done and observed all these things with inclusion criteria.

Study tools and procedure

USG of whole abdomen. Thyroid function tests (T3, T4, TSH). History taking, on table BMI calculation. Proforma.

Data analysis

Data entry and statistical analysis were done using MS excel. The collected data were entered in the MS excel spread sheet. The accuracy of the data was checked and any error found was corrected before actual analysis. Descriptive statistics (frequency, percentage) were used to summarize and describe the findings. Pie and bar diagrams were also used to present the findings.

RESULTS

Around 24.07% of the cholelithiasis patient under study, i.e. 13 patients were diagnosed with hypothyroidism and 75.92%, i.e. 41 patients were euthyroid of which 3/4th (75.92%) of the study population were female and rest 24.02% were male.

Among 13 cholelithiasis patient with diagnosed hypothyroidism 3 (24.08%) presented with clinical symptoms of hypothyroidism, rest 10 (76.92%) were suffering from subclinical hypothyroidism.

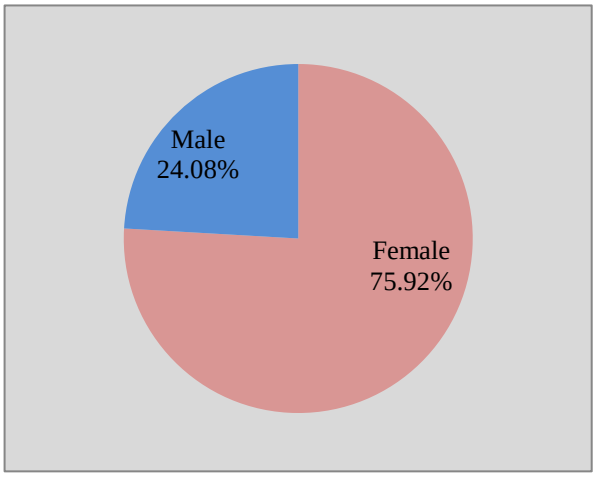

Figure 1: Distribution of study population according to gender(n=54).

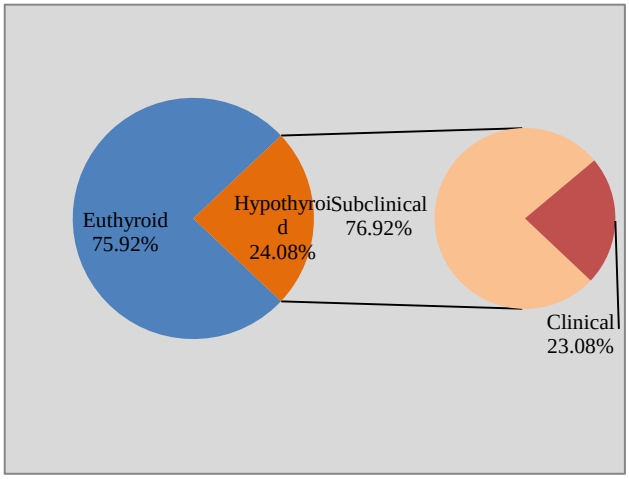

Figure 2: Distribution of study population according to thyroid status (n=54).

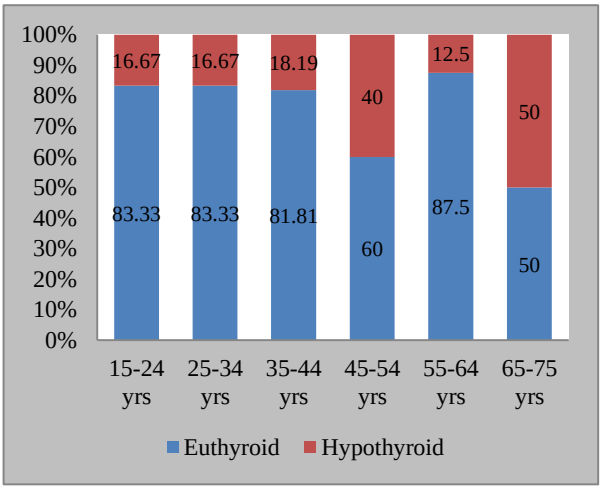

Figure 3: Distribution of study population according to age and thyroid status (n=54).

Out of 54 cholelithiasis patients under the study, maximum (28%) belonged in the age group of 45-54 years followed by 22% in the 25-34 years age group. Around 11% were in the 15-24 years age group, and only 4% of the patients belonged to 65-75 years age group.

Table 1: Distribution of study population according to gender and thyroid status (n=54).

Sex	Euthyroid frequency (%)	Hypothyroid frequency (%)	Total frequency (%)
Male	11 (84.61)	2 (15.38)	13 (100)
Female	30 (73.17)	11 (26.82)	41 (100)
Total	41 (75.92)	13 (24.07)	54 (100)

Table 2: Distribution of study population according to sex and subclinical, clinical hypothyroidism (n=54).

Sex	Euthyroid (%)	Subclinical hypothyroid (%)	Clinical hypothyroid (%)	Total (%)
Male	11 (84.61)	1 (9.09)	1 (9.09)	13 (100)
Female	30 (73.17)	9 (21.95)	2 (4.87)	41 (100)
Total	41 (75.92)	10 (18.51)	3 (5.55)	54 (100)

Proportion of cholelithiasis patient suffering from hypothyroid was height in the age group of 65-75 years (50%) followed by the age group of 45-54 years (40%).

Proportion of hypothyroid was higher among female with compare to male (26.82% versus 15.38%).

In our study 24.06% patients were detected as hypothyroidism, in which subclinical hypothyroidism and clinical hypothyroidism were 18.51%, 5.55% respectively. Among the subclinical hypothyroidism and clinical hypothyroidism the female and male ratio were 21.95% versus 9.09% and 4.87% versus 9.09% respectively.

DISCUSSION

In our study was done in Bankura Sammilani Medical College and Hospital, Bankura on 54 patients of cholelithiasis diagnosed with ultrasonogram in the Department of General Surgery. All the patients were screened with Thyroid function test (TSH, T3, T4). Among the study group, 41 (75.92%) patients were females and 13 (24.02%) patients were male. The maximum number of patients 15 (27.77%) were present in 45-54 years age group.

The similar type of age group was detected in various literature likewise Nath et al (51-60 years); Singha et al (>40 years); Ghimire et al (>40 years).[28-30]

The euthyroid patients were 41 (75.92%) and the hypothyroidism patients were 13 (24.08%) out of 54 patients in this study. The prevalence of hypothyroidism was 24.08% in the study.

The association between hypothyroidism and cholelithiasis was seen in Nath et al (38%); Pushpalatha et al, Mohanan et al (23%); Singh et al (27%); Hassan et al (38.6%); Ghimire et al (26.7%); Singha et al (13.8%); Manimegalai et al (13.3%); Volzke et al (1.2%).[28-35]

In our study the subclinical hypothyroidism and the clinical hypothyroidism among hypothyroid was seen viz 10 (18.5%) patients, 3 (5.55%) patients respectively.

The similar type of study was seen in previous study like Ghimire et al viz 21.1% and 5.6%; Nath et al 22% and 16%; Manimegalai et al 10% and 3.33%; Singha et al 11.6% and 2.2%; Ahmed et al 9.5% and 4.31%.[30-36]

Limitations of the study

As this study has been carried out over a limited period of time with a limited number of patients and there was lack of financial and infrastructural support, it could not have been large enough to be of reasonable precision. The follow up period was not long enough to comment about recurrence in patients with hypothyroidism and the response of the patients to thyroid medications. All the facts and figures mentioned here may considerably vary from those of large series covering wide range of time, but still then, as the cases of this study were collected from a tertiary level hospital in our country, this study has some credentials in reflecting the facts regarding prevalence of hypothyroidism in cholelithiasis patients and its possible correlation with the natural progression of the disease process.

CONCLUSION

Several recent studies report an association between hypothyroidism, or subclinical hypothyroidism. The higher prevalence of hypothyroidism in gallbladder stone patients suggests that not only changes in the cholesterol metabolism, or bile excretion rate, but particularly changes in the function of the sphincter of oddi (SO). It seems likely that the lack of thyroxine in hypothyroidism gives rise to a reduction in bile flow in many ways. In addition to the increased cholesterol load in bile and the reduced bile secretion rate, the deficiency of the prorelaxant effect of thyroxine on the SO appears to be a crucial factor leading to the reduced bile flow in hypothyroidism. The initial formation of bile cholesterol

crystals may begin during the untreated period of hypothyroidism, and the stones may continue to develop or mature even after the thyroxine replacement therapy has begun. It is possible that thyroxine replacement therapy is not sufficient in all patients to maintain normal SO function, causing increased risk of biliary stone formation. Studies with subclinical hypothyroid patients have demonstrated that a positive effect on the changes in the serum cholesterol level, on cardiovascular effects, or on neuromuscular symptoms may be achieved with early replacement treatment with thyroxine, and it can be assumed that patients at risk of forming biliary stones due to subclinical hypothyroidism may also benefit from such early treatment. Most importantly, when treating patients with biliary stones or microlithiasis, clinicians should be aware of the possible hypothyroid background and consider examining the thyroid function, at least in female patients over 45 years of age, in which group the prevalence of clinical and subclinical hypothyroidism is the highest.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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