



Prevalence of subclinical hypothyroidism in diagnosed cases of gall stone disease: Prospective study from a tertiary care institute in Himalayan region

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Abstract

Gall stones are the most common biliary pathology, recent studies show that 10–15% of adult population in USA has gall stones (20 millions), 3% of them underwent cholecystectomy, 85% of them asymptomatic, 1–4% of them develop symptoms each year, females more affected than males 3:1^{1,2}. For decades there has been a discussion, whether thyroid disorders could cause gallstone disease. Interestingly it has been reported that the risk, in particular, for gall stones, increases in clinical and subclinical hypothyroidism. There are multiple factors that may contribute to the formation and/or accumulation of gall stones in hypothyroid patients, including decreased liver cholesterol metabolism, diminished bile secretion, and reduced Sphincter of Oddi relaxation.

Objective: To assess the prevalence of hypothyroidism in patients with gall stones and try to establish hypothyroidism as a possible etiological factor for gallstones formation.

Methods: A cross sectional study was carried out at IGMC & Hospital involving 149 patients with cholelithiasis admitted to the hospital during the period from April 2016 to October 2017. All patients were assessed by detailed clinical history and examination with appropriate investigations in form of abdominal USG, thyroid function tests and lipid profile.

Results: Out of 149 patients of gallstone, 120 patients were euthyroid and 29 patients were having subclinical hypothyroidism. Maximum number of patients belonged to the age group of 41-50 years (31.54%). Majority were female, i.e. 107 (72%). Out of the 29 patients diagnosed with subclinical hypothyroidism, 21(72%) were female .77(51.67%) patients presented with complaints of fatty dyspepsia followed by 57(38.25)% with biliary colic and 15(10.66%) with pain right hypochondrium.

Keywords: Hypothyroidism, Gall stones, Subclinical Thyroid dysfunction.

Introduction

The prevalence of gall stone disease is around 2-29% in the Indian subcontinent. Its prevalence varies along demography, age, sex, geography, food habits, sedentary life style and obesity. Until now, Cholelithiasis was believed to occur in

sedentary people and was thought to be associated with lipid disorder. It was considered to be a disease of fat, forty and fertile females. Now the focus has shifted to its association with hypothyroidism since many patients with cholelithiasis were found to have hypothyroidism

in the last two decades. Hypothyroidism, not only increases the risk for gallbladder stones^{3,4}, but also the risk for common bile duct (CBD) stones, in particular.⁵⁻⁷

Overt and subclinical hypothyroidism is also quite common in the Indian population, the prevalence being 5-15% and 8-12% respectively. These conditions are quite often under diagnosed, especially in mountain and hilly regions due to the absence of symptoms and are revealed only on thyroid assays, chiefly TSH.

Materials and Methods

Type of Study and Sample Size

Prospective time bound non randomized study done on all the patients of gall stone disease admitted in Department of Surgery, IGMC Shimla from June 2016 to may 2017.

Inclusion Criteria

Patients with ultrasound proven cholelithiasis.

Exclusion Criteria

Patients with a history of previously diagnosed or treated thyroid function abnormalities, history of thyroidectomy, ongoing pregnancy, serious underlying diseases, patients on oral contraceptives, sepsis or cholangitis and those prescribed medications known to affect the thyroid function test such as phenytoin, carbamazepine, metoclopramide, amiodarone, and lithium.

Study Design

The study population was divided according to the TSH and T3/T4 reference values that were provided by the laboratory into three groups:

1. Subclinical hypothyroidism: symptom free patients with TSH concentration above upper limit of normal range and normal values of T3/T4.
2. Clinical hypothyroidism: in which there are symptoms of hypothyroidism with TSH level above the upper limit and T3/T4 below normal limit.
3. Euthyroid group: in which clinical and lab tests are within normal range.

3-4 ml of venous blood was collected and sent to the central laboratory of hospital for the estimation of serum T3 T4 and TSH. The functional sensitivity of the TSH assay was 0.03 mIU/L. The reference range was 0.3-3 mIU/L.

The normal reference range for T3, T4 and TSH in laboratory is 80-210 ng/ml, 4.8-12 µg/dl and 0.35-4.94 µIU/ml. The minimum detectable concentration of T3 and T4 by this assay is estimated to be 0.2 ng/ml and .4 µg/dl respectively.

A complete clinical profile i.e. a detailed history was recorded and physical examination done. Routine blood examination, liver function test, thyroid function test and ultrasound abdomen was performed in every case at the time of admission.

USG abdomen was done using a 5 MHz transducer and a high resolution monitor. The sonographers were unaware of the participant's clinical and laboratory characteristics. Gallstones were present if the gallbladder contained echoes that moved with gravity except when the stones were large, a septum existed in the gallbladder or there was an enclosed infundibulum.¹² Cholelithiasis was defined as sonographically diagnosed gallstones.

Statistical Analysis

Data on quantitative characteristics were expressed as mean \pm SD. Data on qualitative characteristics were expressed as percentage values or absolute numbers as indicated. Comparisons between groups were made using χ^2 -test (nominal data) and analysis of variance (ANOVA, continuous data). Sex-stratified logistic regression was performed in order to evaluate independent relationships between thyroid function and cholelithiasis. All analyses were adjusted for age and further potential confounders. All statistical analyses were performed with SPSS software, version 11.0.5 (SPSS GmbH Software, Munich, Germany).

Observations and Results

Table 1 Age-group based distribution of Patients (n=149)

Age Group	Frequency	Percentage
<10 Years	1	0.67 %
11-20 Years	1	0.67 %
21-30 Years	10	6.71%
31-40 Years	35	23.48%
41-50 Years	47	31.54%
51-60 Years	27	18.12%
61-70 Years	24	16.10%
71-80 Years	4	2.68%
Total	149	100%

Table 2 Gender wise distribution of Patients (n=149)

Sex	Frequency	Percentage
Female	107	72%
Male	42	28%
Total	149	100%

Table 3 Thyroid function status of enrolled patients

TFT	Frequency	Percentage
Euthyroid	120	80.5%
Subclinical Hypothyroid	29	19.5%
Total	149	100%

Table 4 Gender-wise distribution of patients with Subclinical hypothyroidism (n=29)

Sex	Subclinical hypothyroidism (n=29)
Female	21 (72%)
Male	8 (28%)
Total	29 (100%)

Table 5 Symptoms-based distribution of patients (n=149)

Symptoms of	Frequency	Percentage
Cholelithiasis		
Biliary colic	57	38.25%
Fatty dyspepsia	77	51.67%
Pain Right Hypochondrium	15	10.66%
Total	149	100%

Table 6 Symptoms-based Gender Wise distribution of patients(n=149)

Sex	History of Biliary colic	Fatty dyspepsia	Pain Right Hypochondrium
Female	44	50	13
Male	13	27	2
Total	57	77	15

Discussion

The relatively small number of patients resulted from the exclusion of patients with Previously known thyroid disorder who were 102 patients. The patients were excluded due to previous thyroid surgery, receiving thyroid medication, with cholelithiasis and ingestion of radioactive iodine administration. Subclinical hypothyroidism is a predominant disorder among adult population; however, it is often overlooked.

Age Distribution

In our study, youngest patient was of 8 years of age and eldest was 74 years old. Majority of patients were in the age group of 41-50 years (31.54%) and this can be contributed to the sex hormone imbalance of this age group which is similar to the study done by **Ahmed et al⁸** where eight patients of total 100 patients who were detected as having subclinical hypothyroidism were in the age group of 41–70 years. Among 8 patients detected as hypothyroid in the study group, 5 were in the age group of 51–60 years illuminating an increasing occurrence of sub clinical hypothyroidism with age.

Age is a main risk factor for gallstones formation, the age of 40 years appears to denote the cut-off between relatively low and high rates of cholecystectomies. Between the ages of 40 and 69 years, the incidence is 4 times higher than in younger subjects. **Laukkarinen et al.⁹** study show that thyroid function abnormalities even mild and preclinical should be screened in patients with gallstones' especially in women above 60 years. This matched with our result study about age group and its distribution because with increasing age there is decrease in water contents of body which may reach 45% of body weight, this is due to decrease in lean (muscle) mass of the body which may lead to more concentrated body fluids and excretions and more deposition of solid contents of the excretions which may lead to nucleation and formation of gall stone.

Sex Distribution

Of the 149 patients, majority were female, i.e. 107 (72%). The three F's associated with gall stones i.e. Forty, Fatty and Fertile female is well known worldwide. This study also supports the above said saying by giving a recording of 72% of gall stones in women compared to 28% in men which is in concordance with a study conducted by **Volzke H et al**¹⁰ showing that women were affected nearly twice as often as men, while gallstones were only slightly more often detected by ultrasound in women than in men.

Thyroid Function Status

Out of 149 patients subjects, 120(80.5%) were found to be euthyroid whereas 29(19.5%) were found to be in the range of subclinical hypothyroidism.

In a study done by **Johanna et al**¹¹ in 2007, the prevalence of subclinical hypothyroidism was 11.4%, which is close to that of our study (19.5%).

Out of the 29 patients diagnosed with subclinical hypothyroidism, 21(72%) were female and 8(28%) were male which is in concordance with study done by **Volzke H et al**¹⁰ on earlier diagnosis and treatment of hypothyroidism in women compared to men. This assumption is supported by the fact that the association between high serum TSH levels and cholelithiasis was mainly found in females with sonographically detected gallstones as proved in our study and still more predominant in female gender.

Conclusion

From our study, it is evident that subclinical hypothyroidism is also associated with gall stones and that too in women, in the age group of more than 40. Most importantly, when treating patients with gall stones or microlithiasis, clinicians should be aware of the possible hypothyroid background and consider examining the thyroid function, at least in female patients over 40 years of age, in which group the prevalence of clinical and subclinical hypothyroidism is the highest. Since it is associated with increased serum TSH alone, this

can be used as a serum marker and further complications of gall stones can be avoided.

Ethical Approval: Yes Ethical Approval and patient consent were taken under supervision of ethical committee of surgery, Department of Surgery, IGMC SHIMLA.

Sources of Funding: There is no funding for my research.

Conflicts of Interest: There is no conflict of interest.

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