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Original Research Article

Prevalence of undiagnosed hypothyroidism in patients with gall bladder stones in Belagavi

Ramesh S. Koujalagi, Vinod Karagi, Abhijit S. Gogate, Athira C.*

Department of General Surgery, J. N. M. C., Belagavi, Karnataka, India

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***Correspondence:**
Dr. Athira C.,
E-mail: drathiracmenon@gmail.com

ABSTRACT

Background: Contribution of hypothyroidism to gallstone formation is debated over years. With this background, the study intended to analyze the prevalence of undiagnosed hypothyroidism in patients with cholelithiasis. The aim is to understand the prevalence of hypothyroidism in patients with gallstones.
Methods: A prospective, hospital-based study was done on 100 patients admitted for the management of gall stone disease in Belagavi. After initial screening, a detailed history was obtained with special reference to symptomatology and the risk factors as per proforma from patients meeting selection criteria. Thyroid function test was done on all eligible patients. Patients were divided into three groups of Euthyroid, Subclinical hypothyroid and clinical hypothyroidism. Statistical analysis used. Percentage of gall stones in different age groups and gender of the study population was calculated followed by prevalence of hypothyroidism and subclinical hypothyroidism in all the patients included.
Results: Among the study population, 40% were male and 60% were female. 23 of them have subclinical hypothyroidism and 6 of them were diagnosed with hypothyroidism. Majority of subclinical hypothyroid patients (39.13%) were aged 41-60 years. Hypothyroid symptoms were shown by the study population with unknown thyroid status.
Conclusions: The prevalence of hypothyroidism in cholelithiasis is 29% in the study and is significant. The study demands further studies to consider hypothyroidism as a cause /risk factor for biliary calculus.

Keywords: Hypothyroidism, Gallbladder stones, Thyroid function test, Biliary tree

INTRODUCTION

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.[1]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.[2]

In Belagavi, a larger number are affected with cholelithiasis and the prevalence of undiagnosed hypothyroidism in cholelithiasis has never been studied. With this background, the study intends to analyze the prevalence of undiagnosed hypothyroidism in patients with cholelithiasis and tries to establish hypothyroidism as a probable cause for biliary stones in Belagavi.

METHODS

After an institutional ethical clearance, a prospective, hospital based cross-sectional study was done on patients admitted for the management of gall stone disease in the

department of general surgery in Belagavi during January 2019 to December 2019. The source of the data: Gall stone disease patients getting admitted to the surgery wards. All patients with cholelithiasis were included. Patients with history of hypothyroidism/thyroidectomy, hemolytic diseases, concomitant co-morbidities especially diabetes mellitus type II, renal stones, stones in pancreatic duct, women taking oral contraceptive pills/ pregnant, patients with cholangitis and those on phenytoin, carbamazepine, metoclopramide, amiodarone, and lithium were excluded from the study.

Sampling was done through universal sampling technique. The sample size calculation was calculated based on the following formula;

$$n=\frac{Z^2\times p\times q}{d^2},$$

where,

n=sample size,

Z=1.96 approximated to 2 (considering confidence as 95%),

p=prevalence,

q=100-p and

d=absolute precision.

One-year cross sectional study by Maharajan et al in Tamil Nadu showed a prevalence of 38% hypothyroidism among patients with gallbladder stones.[3] In this current study, expecting comparable results with 95% confidence levels and 10% absolute precision in the result, the study requires a minimum of 94 subjects. So, p=38, q=62 and d=10; (n=94.2).

Methodology

The patients were screened first as per the proforma. To all patients meeting the selection criteria, informed written consent to participate in the study was given and explained about the study and its implications. Detailed history was obtained with special reference to symptomatology and the risk factors as per proforma. Clinical examination was performed, and findings were recorded as per proforma. Thyroid function test was done on all eligible patients. Serum TSH level is usually the initial laboratory test for screening of dysfunction of thyroid if absence of hypothalamic/pituitary pathology is confirmed. Thyroid dysfunction is confirmed in presence of raised or reduced S.TSH levels but cannot diagnose the cause. Hyperthyroidism is diagnosed with reduced TSH and high serum levels of free T4 (FT4) and/or free T3 (FT3). Patients were divided according to history, clinical examination and laboratory test (free T3, free T4 and TSH) into three groups according to hospital values, serum TSH: 0.27-4.2 microIU/ml, F.T4: 0.93-1.7 mg/dl, free T3: 2-4.4 mg/dl. Group 1: euthyroid group; clinical and laboratory tests were normal. Group 2: subclinical hypothyroidism; asymptomatic and with TSH concentration above the upper limit of normal range and FT4 and/or FT3 within normal limits (According to our laboratory readings). Group 3: clinical hypothyroidism; symptomatic and with TSH level above the upper limit and FT4 and/or FT3 decrease below the normal limit.

Statistical analysis

Data collected was entered in MS Excel spread sheet, analysed and expressed as percentage.

RESULTS

A total of 100 random patients meeting the selection criteria were included and their data was collected. 40 % were male and 60% were female. Among the 100 patients, 2 patients were below 20 years, 31 patients were in the range of 21 to 40 years, and 28 were between 41 to 60 years, 34 patients fall between 61 to 80 years of age. There were 5 patients who are above 80 years. Among 100 patients, 71 of them were euthyroid and 23 of them were identified to have subclinical hypothyroidism and 6 of them were diagnosed with hypothyroidism (Figure 1).

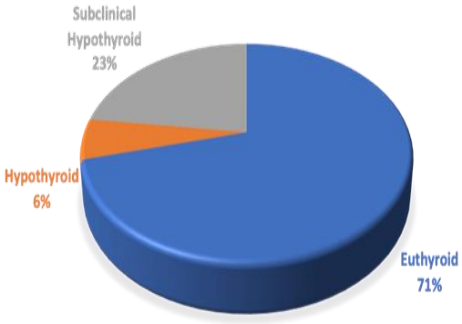

Figure 1: Thyroid status among included patients.

Of 71 euthyroid patients, 38 were female and 33 were male. In the case of subclinical hypothyroidism, there were 17 females and 6 males. Out of 6 % clinical hypothyroidism, there were 5 females and only 1 male. 75.8% females and 24.1% males were diagnosed as hypothyroid in the study (Table 1).

Table 1: Gender distribution of thyroid status.

Sex	Euthyroid	Hypothyroid	Subclinical hypothyroid
Female	38	5	17
Male	33	1	6

Among the 71 euthyroid patients, there was only 1 female patient in the age group of below 21 years. Between 21-40 years, 19 were female and 4 were male. However, in 41 -60 years, female & male patients were 9 and 10 respectively. There was higher number of male patients (18 patients) in the age range of 61-80 years where female patients were only 4. There were 2 female and 1 male patients in the age group of above 80 years (Figure 2). Among the 23 subclinical hypothyroid patients, only 1 female was in the group range of below 20 years. Similarly, in 21-40 years age group, there were 5 female patients, and no male was found. Of 9 patients in group of 41-60 years, 78% were female and 22% were male. Among the 7 between 61-80 years, 4 were female patients and 3 were male. Only 1 female patient was found in the age range of more than 80 years (Figure 3). Out of the 6 cases of hypothyroidism, 50% were female, in group of 41-60 years. One female and male patients were in age group of 61-80 years. Above 80 years, only one female patient was found (Figure 4).

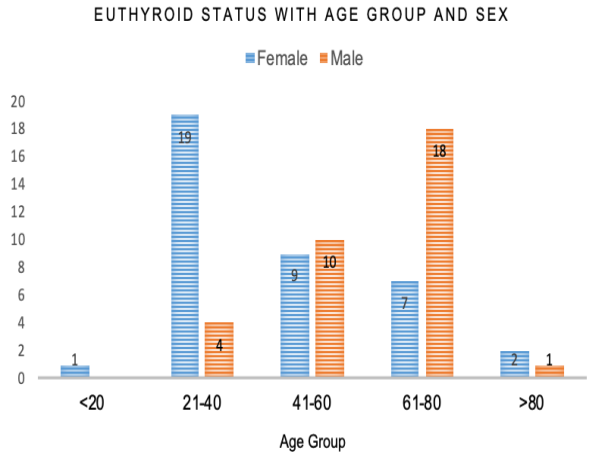

Figure 2: Euthyroid status with age group and sex.

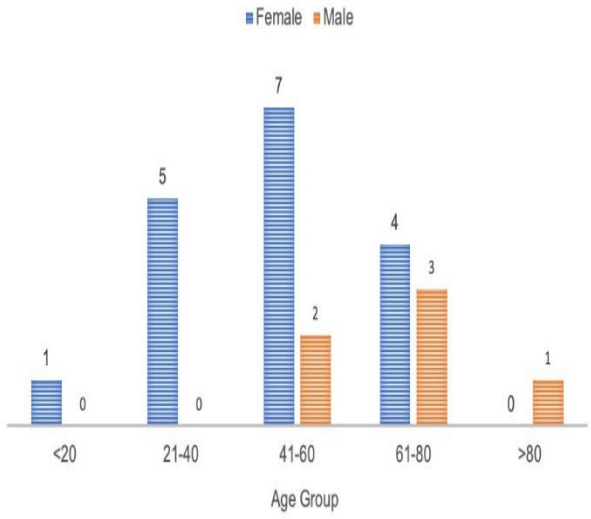

Figure 3: Subclinical hypothyroid status against age and gender.

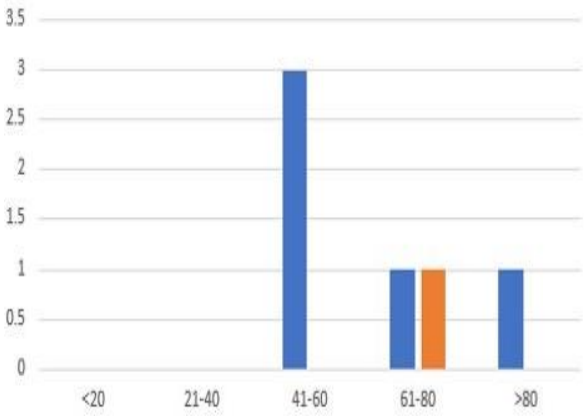

Figure 4: Hypothyroid status with age and gender.

DISCUSSION

Pathogenesis of gallstone is multifactorial and complex, which affects bile composition and its flow.[1,2] This study focuses on the prevalence of hypothyroidism in gall stones since hypothyroidism is known to alter hepatic cholesterol metabolism and it reduces bile secretion in liver. Studies have identified presence of thyroid receptors in Sphincter of Oddi causing a pro-relaxing effect.[7,8] This reflects the formation of gallstones in hypothyroidism.

In this study, 100 random patients meeting the selection criteria were included after taking informed consent. Out of which, 40% were males and 60% were females. After assessing symptoms and signs, a thyroid profile was sent for all. Among 100 patients, 29% were found to have hypothyroidism of which 23 were identified to have subclinical hypothyroidism and 6 were diagnosed with hypothyroidism. Many challenging studies are done all over the world to know the association between thyroid status and biliary stones over the years. In 2003, Laukkarinen et al. conducted a case control study in 2 stages by doing 99 mTc cholescintigraphy on untreated hypothyroid patients, before and after levothyroxine supplementation & making them euthyroid in Finland.[4-6] The current study did not include but gives a scope for a future interventional study with thyroxin supplementation and study on effects of thyroxin on the size of gall bladder calculi.

In Iran, Ajdarkosh et al did a case control study in 2013 to know the association between clinical and subclinical hypothyroidism and stones in biliary tract and recommends thyroid profile test in all patients with biliary stones as there is strong association between them and thought hypothyroidism as a predisposing factor for the passage of gall stones to CBD.[13] An observational study by Singh et al in Punjab during 2014-2016 to understand the prevalence of hypothyroidism in cholelithiasis showed a similar gender distribution to the current study and concluded that there is no significant relation between thyroid status and biliary calculi.[15] In the

current study, the prevalence of thyroid dysfunction among patients with only cholelithiasis were studied and noted that 36.6% females and 17.5% males were diagnosed with hypothyroidism. None of the patients in the current study was diagnosed to have hyperthyroidism. The current study is contradicting with Singh et al study and showed a significant prevalence of 29% hypothyroidism in patients with gallstones.

Cross sectional study by Singha et al among 500 patients with cholelithiasis was done during 2014-2016 in North-East India.[16] They reported 13.8% hypothyroidism in their study, and all were females. The prevalence rate was higher in the current study compared to Singha et al with sex distribution of 75.8% females and 24.1% males, highlighting the higher prevalence among females. Watali et al studied the association of hypothyroidism in gallbladder stones in Delhi on 200 patients with upper abdominal pain for duration of one year in 2017and showed no association between hypothyroidism and gallstones.[17] Incidence of hypothyroidism noted in Watali et al study was high in patients aged above 50 years, which goes along with this current study.

In Madhya Pradesh, Brijendra et al did a study during 2015-2016 on 50 patients with gallstones. Gender distribution was 84% females and a 16% male which is higher compared to the current study distribution of 60% females and 40% males. Brijendra et al reports 24% prevalence of hypothyroidism in the total study population with a majority of 91% among females. However, Brijendra et al could not show any significant relation between gallstones specific to gender and hypothyroidism.[18] The study by Manjusha et al done in South India during 2016-2018 on 100 patients with cholelithiasis showed a prevalence of 14% hypothyroidism and majority of the patients were aged more than 40.[20] The current study showed a higher prevalence of 29% hypothyroidism in gallstones. Even though this current study excluded patients with known comorbidities causing gallstones, by Manjusha et.al found no significance between subclinical hypothyroidism and patient comorbidities like diabetes, hypertension, hypercholesterolemia, obesity, smoking or alcohol consumption. Manjusha et al noticed that patients diagnosed with hypothyroidism had larger gallstones compared to euthyroid patients. Moderate positive correlation was found between the two and suggested strong significance between hypothyroidism and size of gall stones. Only 75% hypothyroid patients had multiple calculi in Manjusha et al study, whereas present study observed that 100% patients with clinical hypothyroid and 78% with subclinical hypothyroidism was having multiple calculi in gall bladder. This reflects that hypothyroid state is having more risk of developing larger and multiple stones in gallbladder. A study done in Northeast India for duration of 6 months in 2018 by Das et al was a case control study to know the prevalence of hypothyroidism in gallstones showed a significant association between hypothyroidism and gallstones statistically.[21] The current study shows a significant prevalence of 29% hypothyroidism in patients with gall bladder stones with higher prevalence among elderly females. The higher prevalence among females could not be proved statistically in most of the studies since prevalence of gall stones itself in female gender is high. The current study lacks information about relationship between serum TSH levels and size and number of the calculi to find if raised TSH level can increase calculi size and number. Further studies on early diagnosis and treatment of hypothyroidism causing prevention or reduction in the size of biliary calculi should be done so that we can conclude with hypothyroidism as a specific risk factor for cholelithiasis and all patients with gall stones should be screened for thyroid dysfunction.

CONCLUSION

The prevalence of hypothyroidism in cholelithiasis is 29% in the study and is significant. 23% were diagnosed with subclinical and 6% with clinical hypothyroidism. This study also shows higher prevalence among females aged more than 40 years of age. Hypothyroid symptoms were shown by the study population with unknown thyroid status which highly recommends thyroid profile testing preoperatively. Further studies on early diagnosis and treatment of hypothyroidism causing prevention or reduction in the size of biliary calculi should be done so that we can conclude with hypothyroidism as a specific risk factor for cholelithiasis and all patients with gall stones should be screened for thyroid dysfunction.

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

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