Original Research Article

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Prevalence of subclinical hypothyroidism in cases of cholelithiasis

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ABSTRACT

Background: This prospective study was carried out to analyse the prevalence of subclinical hypothyroidism in patients of gall stones.

Methods: A prospective study was carried out in the Gandhi Medical College and associated Hamidia Hospital Bhopal from 2015 to 2016. Data was collected from patients who were admitted in surgical wards, with a provisional diagnosis of cholelithiasis. Patient was diagnosed cholelithiasis on abdominal ultrasonography and was tested for having subclinical hypothyroidism by testing fasting blood samples for serum TSH.

Results: A total of 50 patients of cholelithiasis were included in present study. Females were 42 out of 50 (84%) and males were 8 out of 50 (16%). Most common age group was 41-50 (36%) correct (insignificant at p<0.05). 12 (24%) out 50 patients were hypothyroid. Out of total 42 females 11(26.19 %) were hypothyroid (insignificant at p<0.05). All stones in hypothyroidism patients were >1cm and overall 58% stones were >1cm (statically significant P<0.05). 03 out of 12 hypothyroidisms (25%) patient had single stones while 9 (75%) patient have multiple stone (statically significant P value <0.05). In hypothyroid cases most stones were of cholesterol type (58%) (Statically significant at P value <0.05)

Conclusions: Early diagnosis of hypothyroid state at subclinical level by monitoring TSH level so that they can be treated at early stages and burden of Cholelithiasis thus can be prevented.

Keywords: Cholelithiasis, Hypothyroid, Subclinical

INTRODUCTION

Gall stone is a disease seen around 2-29% prevalence in Indian subcontinent. Its prevalence varies along demographics, age, and sex, geography of region, food habits, sedentary life style and obesity. Until now, Cholelithiasis was believed to occurring in sedentary peoples and was thought to be associated with lipid disorder. It was considered to be a disease of fat, forty, fertile, flatulent and female disease. Now focused had shifted to hypothyroidism association since last two decades as many patients with cholelithiasis are found to have hypothyroid. Hypothyroid is also quite common in

Indian population around 5-15%, and subclinical hypothyroidism around 8-12%. Usha Menon V reported high prevalence in India, quite often under diagnosed especially in mountain and hilly regions.¹

This population is masked due to absence of symptoms and is revealed on thyroid assays, chiefly TSH, which can have detrimental metabolic effects, may be reversible on thyroid replacement therapy. It was previously known to cause dyslipidemia, and this was thought to be the cause of cholelithiasis in these patients. But other mechanism such as decreased bile flow, gall bladder hypomotility, sphincter of oddi spastic changes due to hypothyroidism

had been implicated in study by Laukkarinen J group bile salt had also been implicated as target of TSH in hypothyroidism causing decrease in bile salt in bile changing composition of bile resulting in high cholesterol: bile salt ratio which is driving force for nucleation resulting in gall stones.2 Iniken J sand study suggests low bile flow due to motility disorders of bile duct and sphincter of oddi.3 Song study suggests bile acids functioning as regulator by promoting or suppressing transcription at nuclear level and sphincter of oddi dysfunction.⁴ Thus multiple mechanism are proposed to be action of thyroid hormone leading to gall stone formation. This study was conducted to explore patients prevalence of hypothyroidism in cholelithiasis, so that light on relation of hypothyroidism and cholelithiasis could be found.

METHODS

Data was collected from patients who were admitted in surgical wards of Hamidia hospital Bhopal, with a provisional diagnosis of cholelithiasis. Study was on patient diagnosed cholelithiasis on abdominal tested ultrasonography for having subclinical hypothyroidism by testing fasting blood samples for serum TSH. All patients underwent routine and special investigations if indicated. Patient was diagnosed with hypothyroidism on the basis of serum TSH value $>5.5 \mu IU/mL$.

Abdominal ultrasound was used for screening for cholelithiasis because its sensitivity and specificity is greater than 95% and is cheaper and easily available investigation.

Thyroid profile was done in microbiology department in Gandhi Medical College using fasting blood samples in patient diagnosed with cholelithiasis by using ultrasensitive sandwich chemiluminescent immunoassay for TSH having 100% specificity for hypothyroidism and >99% sensitivity and therefore it is useful initial screening method for diagnosing thyroid disorders. Normal range of TSH: $0.30\text{-}5.5\mu\text{IU/mL}$.

Stone analysis

Morphology and composition

The findings on gross examination were noted, and the stones recovered from the gallbladder were classified on the basis of their gross morphology. After the morphological study, gallstones were washed, dried and grinned to a powder. Powder was taken for chemical analysis.

Quantitive analysis of these gallstones was done in the department of biochemistry. The stones were classified into cholesterol (CS), pigment (PS), and mixed stones (MS). Total cholesterol was estimated by CHOD-PAP, total bilirubin by Diazo method, triglycerides by GPO-

PAP method, oxalate by the method described by Satyapal and Pundir based on colorimetric enzymatic method, calcium by O-cresolphthalein-complex one method, Phospholipid and inorganic phosphate were determined according to Fiske and Subba Rao.

It was a prospective observational study. The study was carried out on 50 patients satisfying inclusion criteria admitted in Hamidia Hospital, GMC, Bhopal, for a period of one year.

Inclusion criteria

All cases admitted to department of surgery, Hamidia hospital, Bhopal (Madhya Pradesh) with cholelithiasis as provisional diagnosis on abdominal ultrasonography.

Exclusion criteria

Patients with previous history of hypothyroidism or taking thyroid replacement for treatment.

Statistical analysis

Statistical analysis system (SAS) windows software 2014 is used for fisher exact test and chi square test for all prevalence variables comparing age, sex, type of stones with TSH, USG findings etc.

RESULTS

Present study was carried out in Department of Surgery, Gandhi Medical Collage Bhopal and associated Hamidia Hospital between March 2015 to September 2016. Total 50 cases of cholelithiasis were enrolled in these studies 47 out of 50 undergone cholecystectomies. In present study females were 42 out of 50 (84%) and males were 8 out of 50(16%).

Table 1: Prevalence of hypothyroidism.

(N=50)	Euthyroid	Hypothyroid
Number of patient	38(76%)	12 (24%)

In present study 12 out of 50 (24%) of patients of cholelithiasis had hypothyroidism.

Table 2: Sex wise prevalence of hypothyroidism.

Com	Thyroid status	Total	
Sex	Euthyroid	Hypothyroid	Total
Female	31 (73.80%)	11 (26.19%)	42
Male	07 (87.50%)	01 (12.5%)	08
Total	38	12	50

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.

Table 3: Prevalence of thyroid across age groups.

Age	Thyroid status		Total patient	
group	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 4: Comparison of stone size with thyroid status.

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

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.

Table 5: Comparison of patients having number of stone.

n=47	Multiple	Single	Total
Number of patients	43 (91.49%)	4 (8.51%)	47

43 Out of 47 (91.49%) were multiple stones and 4 out of 47 (8.51%) were single.

Table 6: Hypothyroidism prevalence against number of stones.

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

09 out of 12 hypothyroidisms (75%) patients had multiple stones and 01 out 35 (2.85%) patient of euthyroid had single stone. fisher exact test is 0.0459 and is statistically significant.

Table 7: Type of stone in patients.

N=47	Pigment	Cholesterol	Mixed	Total
No. of patient	24 (51.06%)	11 (23.40%)	12 (25.53%)	47

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 .

Table 8: Type of stone with thyroid status.

Composition	Thyroid status			
and type of stone	Euthyroid N = 35	Hypothyroid N = 12	Total	
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

This is a Hospital based study conducted on 50 patients. Patients were admitted in our hospital for cholelithiasis and 47 out of 50 underwent cholecystectomy. All patients have cholelithiasis in their abdominal ultrasonography study.

Sex wise distribution of patients

There were 42 (84%) female patient and 8 male patients in our study. This is because prevalence of cholelithiasis is 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 epidemiologic studies.

Male to female ratio in this study was 1:5.25. Bansal found 65% females and 35% males in their study of 104 patients.⁵ Similarly Bhattacharya showed 71.4% were female; 28.6 % were male.⁶ Similarly, Sharma study had 70% females and 30 % males in their study.⁷

Prevalence of hypothyroidism

12 patients out of 50 showed hypothyroidisms characterize by increased TSH from normal value in their thyroid profile, with prevalence rate of 24%. 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 Kotwal in Sikkim.^{8,9}

This can be due to higher number of patients having undiagnosed or subclinical hypothyroidism. As radiological investigations are easily available, increasing number of patients are being diagnosed cholelithiasis on ultrasonography. Topographical and demographic differences are present in different studies.

Sex wise prevalence of hypothyroidism

Total patients of hypothyroid were 12, out of 12 patients. 11 were female i.e. 91.66% contribution in females and 1 out of 12 patient accounting for 8.34% of hypothyroid in males. In study by Stephan it was 83.3% in females and 16.7% males. 10 11 out of 42 females (21.15%) had hypothyroidism. 01 out of 8 males (12.5%) had hypothyroidism. Previous studies show prevalence of 4.8% in males and 20% in females respectively in study conducted by Stephan outside India. 10 In the study by Ibrahim. group, males having hypothyroidism 13.20 % and in females it was 95.47%.¹¹ Fisher test value is 0.6606 is insignificant at p<0.05 the results were 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 females.

Prevalence of thyroid across age groups

In our study, there was higher prevalence of hypothyroidism and cholelithiasis in age group >40 year. The number of patients with cholelithiasis and hypothyroidism increase with age. 09 out of 32 comprising 28.12% were hypothyroid in >40 and 03 out of 18 comprising 16.66% in <40 age group, out of these, 2 patients were of thalassemia major operated for gall stones, confounding increased prevalence in this group. But still the result was insignificant across age groups. Study by Khuroo and Pradhan SB corroborated this finding. 12,13 This can be accounted by early appearance of symptom of hypothyroidism in younger age group and patient start seeking treatment for hypothyroidism early, these cases are therefore excluded from our study.

Comparison of stone with size, number and type with thyroid status.

In this 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 as p<0.05. 43 out of47 (91.49%) were multiple stone and 4 out of 47 (8.51%) were single. 09 out of 12 hypothyroidisms (75%) patient had multiple stones and 01 out 35(2.85%) patient of euthyroid had single stone.

In this study, 24 out of 47 (51.1%) were pigment stone, 12 out of 47 mixed (25.53%) and 11 out of 47 i.e. (23.4%) cholesterol stones on morphological ground and on chemical analysis. In the study by Chandran P mixed stone were 38%, cholesterol 36% and pigment 26%. ¹⁴ In other study done by Taher MA cholesterol stone was

most common i.e. 49.3% followed by mixed (33.3%) than pigment (17.3%).¹5 7 out of 12(58.33%) cholesterol stone patient was hypothyroid, and it had significant association with hypothyroid. Chi square test value is 11.259 and p value = 0.00359, It is significant at p value ≤0.05. Similarly, stone size of >1cm had strong correlation with thyroid and multiple stones in gall bladder were having strong correlation with hypothyroidism as was in study by Bansal.⁵

In patients having hypothyroidism, cholesterol stones were found with higher prevalence and there was statistical significance with these stones. Similar findings were corroborated in Ibrahim study and study by Yousif.

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 vellow 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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Ethical approval: The study was approved by the

Institutional Ethics Committee

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