

“Correlation of Subclinical Hypothyroidism in Gall Bladder Stone Disease in A Tertiary Care Hospital”

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Abstract:

Introduction: In the present study has been made to study the association between sub-clinical hypothyroidism and biliary stone disease and establish if there is any clinical correlation between these two diseases.

Previously described that thyroid hormone are having a number of effects on cholesterol metabolism. In hypothyroidism serum cholesterol values rises which in turn leads to super saturation of bile with cholesterol, leading to gallbladder hypo motility, decreased contractibility and impaired filling, giving rise to prolonged residence and flow capacity of bile in the gallbladder. These events may contribute to the retention of cholesterol crystals, thereby allowing sufficient time for nucleation and continual growth into mature gall stones.

Aims and objectives: To study the occurrence of subclinical hypothyroidism and hypothyroidism in patients with gallstone disease, to compare the demographic profile of gallstone disease patients having subclinical hypothyroidism and hypothyroidism with gall stone disease patients who are euthyroid and to study the association of sub-clinical hypothyroidism with cholelithiasis and choledocholithiasis.

Materials and methods: The study was conducted in the Department of Surgery, Gauhati Medical College during the period 1st June 2019 to 31st May 2020.

STUDY TYPE: Cross-sectional study.

STUDY PERIOD: 1ST JUNE 2019 TO 31ST MAY 2020. **SOURCE OF DATA:** Patients who were admitted in surgical ward of department of surgery, GMCH, Guwahati with a provisional diagnosis of cholelithiasis. Study was on patients diagnosed cholelithiasis on abdominal ultrasonography.

SAMPLE SIZE: A total of 220 patients were included in the study.

SELECTION CRITERIA:

Inclusion criteria: Patients with cholelithiasis (the presence of gallstones on ultrasound).

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

Results and Observations: A cross-sectional study was conducted on the randomly selected patients with proven Gall stone disease in a total of 220 patients in Gauhati Medical College and Hospital, GUWAHATI for the period of one year. All patients who fit into the inclusion and exclusion criteria were evaluated.

Out of 220 patients 141(64.09%) were euthyroid, 61(27.73%) patients had sub clinical hypothyroidism and 18(8.18%) patients were of hypothyroidism. The prevalence of subclinical hypothyroidism in gall stone in this case study is having p value of 0.0042. This reflects association between sub-clinical hypothyroidism and gall stone disease is statistically significant.

Conclusion: This study concludes that there is a relationship between thyroid dysfunction particularly sub-clinical hypothyroidism and gallstone diseases. Subclinical hypothyroidism is more common than clinical hypothyroidism. Hypothyroidism has higher prevalence in females than males. There is an increased prevalence of subclinical hypothyroidism associated with the biliary stone disease. If subclinical hypothyroidism is diagnosed and treated timely, can reduce biliary stone disease patients significantly. Among the female hypothyroid patients, the incidence was highest above 40 years of age so we recommend that TSH level should be measured for every patient with gallstone disease above this age. Our recommendation is that every patient with gallstones above 40 years (especially females) should be screened for thyroid status, serum TSH may be used as serum marker so that hypothyroid status could be diagnosed at early stage and progression to full blown hypothyroidism is halted. The prevalence of subclinical hypothyroidism is more in choledocholithiasis patients than cholelithiasis, if subclinical hypothyroidism is diagnosed and treated timely, can reduce choledocholithiasis disease patients significantly.

So, we recommend that surgeon should be aware of thyroid background in patients with biliary stone disease, TSH should be measured as most of them are sub clinically hypothyroid patients.

Key Words: *subclinical hypothyroidism, cholelithiasis, choledocholithiasis, prevalence, gallstone, cross-sectional, ultrasonography.*

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I. Introduction:

Gall stone (cholelithiasis) is the most common biliary pathology both in India and western countries. Geography plays an important role in the prevalence of cholelithiasis and also the type of stone. In western countries 10-20% of adults develop gallstones and 65% to 80% are asymptomatic. In Indian population, 10% to 12% of adults develop gallstones. In patients with gallbladder stones the prevalence of common bile duct stones ranges from 6 to 12%. One gallstone survey suggested that gallbladder stones occurred 7 times more commonly in north Indian than in south Indian. This reflects combined differences in environmental, dietary, and genetic factors.

Bile stasis, bactibilia, chemical imbalances, pH imbalances, change in bile composition and formation of sludge are among the principle factors thought to lead to formation of gallstones. Imbalance of bile salt and cholesterol concentrations that leads to precipitation inside the gallbladder. The gallstones formation is complex process which involves factors affecting bile content and bile flow. A crucial factor in the forming of bile duct stones is biliary stasis, which can be caused by sphincter of Oddi (SO) stenosis, SO dyskinesia or bile duct strictures.

Gallstones may be single or multiple, large or small those containing calcium salts are radio-opaque. Single stone is uncommon but usually consist mainly of cholesterol and arise due to a disorder of the physio-chemical equilibrium which normally maintains cholesterol in micellar form in the bile.

Thyroid diseases are, arguably, among the commonest endocrine disorders worldwide. India too is no exception. For decades there has been discussion whether thyroid disorders could cause gall stone disease. There could be several explanations for possible relation between hypothyroidism and gall stone disease.

Previously described that thyroid hormone is having a number of effects on cholesterol metabolism. In hypothyroidism serum cholesterol values rises which in turn leads to super saturation of bile with cholesterol, leading to gallbladder hypo motility, decreased contractibility and impaired filling, giving rise to prolonged residence and flow capacity of bile in the gallbladder. These events may contribute to the retention of cholesterol crystals, thereby allowing sufficient time for nucleation and continual growth into mature gall stones. In addition, the rate of bile secretion may be decreased, physically impairing clearance of precipitates from the bile ducts and gallbladder. Furthermore, the sphincter of oddi described to have a thyroid hormone receptors. Thyroxin has a direct pro relaxing effect on the sphincter. Both low bile flow and sphincter of oddi dysfunction are regarded as important functional mechanism that may promote gall stone formation. Likewise low levels of T4 have an effect in relaxing the sphincter of Oddi, leading to biliary stasis and stone formation. A crucial factor in forming of bile duct stones is biliary stasis, which may be caused by sphincter of oddi stenosis, dyskinesia, or bile duct strictures. Recent studies concentrate on gall stones and thyroid hormones – T3 and T4 have effect on both bile content and bile flow.

A positive correlation was found between diagnosed gall stones and sub-clinical hypothyroidism in the various studies, therefore it is further investigated the possible reasons for this clinical association between gallstone and subclinical hypothyroidism. In the present study has been made to study the association between sub-clinical hypothyroidism and biliary stone disease and establish if there is any clinical correlation between these two diseases.

AIM:

To study the occurrence of subclinical hypothyroidism and hypothyroidism in patients with gallstone disease, to compare the demographic profile of gallstone disease patients having subclinical hypothyroidism and hypothyroidism with gall stone disease patients who are euthyroid and to study the association of sub-clinical hypothyroidism with cholelithiasis and choledocholithiasis.

II. Material & Methods:

The study was conducted in the Department of Surgery, Gauhati Medical College during the period 1st June 2019 to 31st May 2020.

STUDY TYPE: Cross-sectional study.

STUDY PERIOD: 1ST JUNE 2019 TO 31ST MAY 2020.

SOURCE OF DATA: Patients who were admitted in surgical ward of department of surgery, GMCH, Guwahati with a provisional diagnosis of cholelithiasis. Study was on patients diagnosed cholelithiasis on abdominal ultrasonography.

SAMPLE SIZE: A total of 220 patients were included in the study.

SELECTION CRITERIA:

Inclusion criteria: Patients with cholelithiasis (the presence of gallstones on ultrasound)

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III. Results And Observations:

A cross-sectional study was conducted on the randomly selected patients with proven Gall stone disease in a total of 220 patients in Gauhati Medical College and Hospital, GUWAHATI for the period of one year (from 1st june 2019 to 31st may 2020). All patients who fit into the inclusion and exclusion criteria were evaluated.

Of the 220 cases selected 62 (28.18%) were males and 158 (71.82%) were females. In this study, female are more as compared to male, may be due to earlier symptomatology of gallstone disease as well as higher incidence of thyroid disease in women.

Out of the 220 patients, 62 (28.18%) were males and 158 (71.82%) were females. The ratio of male to female distribution is 1:2.55.

The most common age group in males were 40 – 49 years (7.73%) and mean age of male patients were 41.87years \pm 13.17SD, in females were 30 – 39 years (22.73%) mean age of female patients were 41.53years \pm 13.15SD and overall, the most common age group was 30 – 39 years 64 (29.09%).

The p value of mean age distribution of gallstone disease in both gender is 0.4316 and the difference was statistically not significant.

Out of 220 patients 141(64.09%) were euthyroid ,61(27.73%) patients had sub clinical hypothyroidism and 18(8.18%) patients were of hypothyroidism. The prevalence of subclinical hypothyroidism in gall stone in my case study is having p value is 0.0042 this reflects association between sub-clinical hypothyroidism and gall stone disease statistically significant.

Of the 220 patients, 141 (64.09%) were euthyroid, 61 (27.73%) had sub clinical hypothyroid and 18 (8.18%) were hypothyroid patients.

The prevalence of thyroid dysfunction in males across different age group, showing 53 (24.09%) females out of 62 males, mostly were euthyroid, 40 – 49 years age group had 3(1.13%) sub clinical hypothyroid and 40 – 49 years & 50 - 59 years age group had 1(0.45%) hypothyroid. The mean age of gallstone disease patients with sub-clinical hypothyroidism and hypothyroidism was 41.52 \pm 13.21SD. and mean age of gallstone disease patients with euthyroid status was 41.53 \pm 13.15SD. The difference in mean age was statistically not significant (p value – 0.4978).

88 (40.00%) females out of 158 females, mostly were euthyroid, 40 – 49 years age group had 19 (8.64%) sub clinical hypothyroid and 30 – 39 years age group had 11(5.00%) hypothyroid.

88 (40.00%) females out of 158 females, mostly were euthyroid, 40 – 49 years age group had 19(8.64%) sub clinical hypothyroid and 30 – 39 years age group had 11(5.00%) hypothyroid.

Out of 220 cholelithiasis patients, 35 (15.91%) also had choledocholithiasis.

Out of 62 male patients,11(17.74%) patients had choledocholithiasis, and out of 158 female patients,24 had choledocholithiasis. The gender difference was statistically not significant (p value- 0.4155).

Out of 220 sample population, 141 were euthyroid. Out of these 141, 15 had choledocholithiasis. The proportion of patients with choledocholithiasis amongst euthyroid patients is 10.63%

Out of 220 sample population, 79 had thyroid dysfunction. Out of these 79, 20 had choledocholithiasis. The proportion of patients with choledocholithiasis amongst patients with thyroid dysfunction is 25.32%.

Out of 35 choledocholithiasis patients, 15 patients were euthyroid, 18 had subclinical hypothyroidism and 2 had hypothyroidism.

Out of 35 choledocholithiasis patients, 15(42.86%) patients were euthyroid, and 20(57.14%) patients had subclinical hypothyroidism plus hypothyroidism. Out of 185 cholelithiasis patients, 126(68.11%) patients were euthyroid, and 59(31.89%) patients had subclinical hypothyroidism plus hypothyroidism. The difference was statistically significant (p value – 0.0044).

Thus, we can conclude that the occurrence of thyroid dysfunction in the form of Subclinical hypothyroidism and hypothyroidism is more common among choledocholithiasis patients in comparison to cholelithiasis patients.

IV. Summary:

The present cross sectional study was conducted from 1st June 2019 to 31st may 2020 on 220 selected patients with gall stones disease in the Department of General Surgery, Gauhati Medical College, Guwahati to find the prevalence of sub-clinical hypothyroidism in diagnosed cholelithiasis patients and was aimed to find the role of sub-clinical hypothyroidism in development of gallstones and to add the thyroid function test as a part of routine workup in biliary stone patients.

Most of the Gall stone patients were in the age group of 30-39 years (29.09%).

Among these patients, 28.18% were males; 71.82% were females and Male to female ratio: 1:2.55. Females were the predominant group.

On evaluation of patients with USG abdomen, 84.09% had gall Bladder stone and 15.91% had CBD calculi.

In 220 patients, 27.73% patients were found to be sub-clinical hypothyroid, 8.18% patients were found to be hypothyroid and 64.09% patients found to be Euthyroid. The association between sub-clinical hypothyroidism and gall stone disease was found to be statistically significant in the present study (p value =0.0042).

Among 79 thyroid dysfunction patients, 9 patients (11.39%) were males and 70 patients (88.61%) were females. Thus, out of 62 males patients having gallstone disease ,9(14.51%) males had thyroid dysfunction and out of 158 female patients ,70(44.30%) females had thyroid dysfunction. The difference was statistically significant (p value is less than 0.005).

Most of gall stone patients with sub-clinical hypothyroidism were found to be in the age group of 40-49 years of age. Similarly, most of the females gall stone patients with sub-clinical hypothyroidism were found to be in the age group of 40-49 years of age.

Out of 62 male patients, 11 (17.74%) patients had choledocholithiasis, and out of 158 female patients, 24 patients (15.19%) had choledocholithiasis. Out of 35 choledocholithiasis patients, 15(42.86%) patients were euthyroid, 18(51.43%) had subclinical hypothyroidism and 2(5.71%) had hypothyroidism. This indicates that subclinical hypothyroidism and hypothyroidism is associated with increased incidence of choledocholithiasis as compared to the euthyroid group (p=0.0044).

Out of 35 choledocholithiasis patients, 15(42.86%) patients were euthyroid, and 20(57.14%) patients had subclinical hypothyroidism plus hypothyroidism. Out of 185 only cholelithiasis patients, 126(68.11%) patients were euthyroid, and 59(31.89%) patients had subclinical hypothyroidism plus hypothyroidism. Thus, hypothyroidism was found to be associated with increased incidence of choledocholithiasis as compared to cholelithiasis, the difference being statistically significant (p value = 0.0044).

Patients were managed with laparoscopic and, open procedures. 55.91% patients underwent laparoscopic cholecystectomy, 28.18% patients were treated with open cholecystectomy and 15.91% patients managed with open cholecystectomy with CBD exploration surgery.

Subclinical hypothyroidism is a thyroid dysfunction with elevated serum TSH and normal T3 and T4 levels. Thyroid hormones influence the cholesterol metabolism and also have a pro-relaxing effect on the sphincter of Oddi. Whenever the thyroid function is disturbed-decreased T3 T4 levels will lead to gall stone formation. From the above 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 - 49. 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.

V. Discussion:

Earlier, an association between gallstone, diagnosed hypothyroidism and delayed emptying of the biliary tract is shown. This relation was showed with a help of experimental and clinical hypothyroidism, explained at least partly by the lack of pro relaxing effect of T4 on the sphincter of oddi contractility. In recent years, experiments have demonstrated that low bile flow and sphincter of Oddi dysfunction are important functional mechanisms that may promote biliary stone formation.

A cross-sectional study was conducted on the Prevalence of sub clinical hypothyroidism in patients with proven Gall stone disease in a total of 220 patients in GMCH Guwahati from the period of 1st June 2019 to 31st may 2020. All patients who fit the inclusion criteria were evaluated clinically and Thyroid function test was performed.

In our study, it was thus found to be more common among females as compared to males with a ratio of 2.55:1.

Overall, the most common age group was 30 – 49 years 64 (41.82%), the most common age group in males were 40 – 49 years 17 (7.73%), in females were 30 – 39 years 50 (22.73%).

In our present study, prevalence of thyroid dysfunction as 64.09% were euthyroid, 27.73% had sub clinical hypothyroid and 8.18% were hypothyroid patients.

In our present study, prevalence of thyroid dysfunction in males as 85.48% were euthyroid, 11.29 % had sub clinical hypothyroid and 3.23% were hypothyroid patients.

In our present study prevalence of sub clinical hypothyroidism and hypothyroidism are 34.18% and 10.13%.

In our present study highest prevalence of sub clinical hypothyroidism and hypothyroidism fall under 40 – 49 years and 30 – 39 years age groups.

In our present study, prevalence of highest thyroid dysfunction age groups in males are 40 – 49 years (98.42%) were euthyroid, 40 – 49 years (1.13%) had sub clinical hypothyroid and 50 – 59 (0.45%) were hypothyroid patients.

Thyroid function tests were performed in all 220 patients, 159 (72.27%) were euthyroid, 34 (15.45%) were subclinical hypothyroidism, and 27 (12.27%) had hypothyroidism.

A prevalence rate of 27.73% was seen in the study population which is consistent with the rates obtained by similar studies in India.

In our present study, out of 220 patients, 35 (15.91%) had choledocholithiasis. In the present study, out of 62 male patients, 11(17.74%) patients had choledocholithiasis, and out of 158 female patients, 24(15.19%) had choledocholithiasis. The gender difference was statistically not significant (p value- 0.4155).

In the present study, out of 35 choledocholithiasis patients, 15(42.86%) patients were euthyroid, 18(51.43%) had subclinical hypothyroidism and 2(5.71%) had hypothyroidism.

Out of 35 choledocholithiasis patients, 15(42.86%) patients were euthyroid, and 20(57.14%) patients had subclinical hypothyroidism plus hypothyroidism. Out of 185 only cholelithiasis patients, 126(68.11%) patients were euthyroid, and 59(31.89%) patients had subclinical hypothyroidism plus hypothyroidism. The difference was statistically significant (p value – 0.0044).

In all the study population surgical interventions done 123 (55.91%) underwent laparoscopic cholecystectomy, 62 (28.18%) underwent open cholecystectomy, 35 (15.91%) underwent an Open cholecystectomy with CBD exploration.

VI. Conclusion:

This study concludes that there is a relationship between thyroid dysfunction particularly sub-clinical hypothyroidism and gallstone diseases. Subclinical hypothyroidism is more common than clinical hypothyroidism. Hypothyroidism has higher prevalence in females than males. There is an increased prevalence of subclinical hypothyroidism associated with the biliary stone disease. If subclinical hypothyroidism is diagnosed and treated timely, can reduce biliary stone disease patients significantly. Among the female hypothyroid patients, the incidence was highest above 40 years of age so we recommend that TSH level should be measured for every patient with gallstone disease above this age. Our recommendation is that every patient with gallstones above 40 years (especially females) should be screened for thyroid status, serum TSH may be used as serum marker so that hypothyroid status could be diagnosed at early stage and progression to full blown hypothyroidism is halted. The prevalence of subclinical hypothyroidism is more in choledocholithiasis patients than cholelithiasis, if subclinical hypothyroidism is diagnosed and treated timely, can reduce choledocholithiasis disease patients significantly.

So, we recommend that surgeon should be aware of thyroid background in patients with biliary stone disease, TSH should be measured as most of them are sub clinically hypothyroid patients.

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