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Thyroid Profile in Gall Stone Diseases–A Comparative Study

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Abstract

Context: For decades, there has been a discussion, whether thyroid disorders could cause gallstone disease. These explanations include the known link between thyroid failure and disturbances of lipid metabolism 1 that may consecutively lead to a change of the composition of the bile.A population-based comparative study was performed to determine the association between thyroid profile and gall stone diseases.

Aims: To know the association between thyroid function change and gall stone formation.

Settings and Design: This is a tertiary care hospital done study descriptive observational study.

Methods and Material: This study was conducted in a tertiary care hospital of north Karnataka .The study duration was January 2018 to December 2018. A total of 1004 patients with gastrointestinal problems and Gallstone were selected randomly for the study.

Statistical analysis used: Statistical analysis was done using ratios and percentage.Comparative results were obtained using two group which were compared and calculated using independent t test for the TSH levels and T4 levels.

Results: There was no difference in the median values of S-TSH (3.06, range 0.27–4.2 vs. 2.8, range 0.28–7.40ulU/ml) and S-T4 (13, range 5.5–13.0 vs. 13.0, range 5.5.–13 ug/dl) between the groups .The prevalence of subclinical (S-TSH > 4.2ulU/ml;) hypothyroidism in women was 24% in Gallstone disease group and 2.3 than in the control group and in men 24% and 2% (total 5.5%) in the Gallstone disease group than in control group, respectively.

Conclusions: There is an association between change in thyroid function with gallstone disease.

Keywords: Cholelithiasis; Thyroid profile; Subclinical hypothyroidism.

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Introduction

The earliest known gallstone dates back to the twenty-first Egyptian Dynasty (1085-945 BC), having been discovered in the mummy of a priestess of Amen. This ancient specimen was unfortunately destroyed in the bombing of England during the second world-war. Gallstones or cholelithiasis were first described in the 5th century by the Greek physician Alexander Trallianus, who wrote about stones within the bile ducts. Carl Langenbach of Berlin was credited to have performed the first cholecystectomy or the surgical removal of the gallbladder in 1882.[1] The incidence varies widely in different part of world. For decades, there has been a discussion, whether thyroid disorders could cause gallstone disease. Particularly, there are several explanations for a possible relation between hypothyroidism and gallstone disease. These explanations include the known link between thyroid failure and disturbances of lipid metabolism[1] that may consecutively lead to a change of the composition of the bile. Recent studies[2] also demonstrated low bile flow in

hypothyroid subjects. Furthermore, the sphincter of Oddi expresses thyroid hormone receptors and thyroxin has a direct pro-relaxing effect on the sphincter.[3] Both low bile flow and sphincter of Oddi dys function are regarded as important functional mechanisms that may promote gallstone formation[4]. Other studies[5,6] found a proportion of previously diagnosed hypothyroidism of 8% and 6% in patients having common bile duct and gallbladder stones, respectively, compared to a proportion of only 1% in the controls. The usage of thyroxin was even suspected to dissolve gallstones[7].

Aims and Objectives:

To know the association between thyroid function changes and gall stone formation.

Subjects and Methods:

This study was conducted in a tertiary care hospital of north Karnataka .The study duration was January 2018 to December 2018. A total of 208 patients with gastrointestinal problems and Gallstone were selected from 1004 cases for the study .Radiological and other needful investigations and procedures were done to confirm the diagnosis and cases were managed accordingly.

Inclusion criterias:

1. Patients from both sexes of various age groups of 18yrs to 80 years of age.
2. All patients admitted with gastrointestinal problems were taken into consideration.

Exclusion criterias:

1. Patients less than 18 years and more than 80 years
2. Patients with h/o hypothyroidism, hyperthyroidism.
3. Pregnant women.
4. Patients who were on antiepileptic drugs.
5. Patients who were in septicemia
6. H/o hemolytic disorders
7. H/o hyper spleenism
8. Other illness not related to gastrointestinal disorders.

All routine laboratory investigations including Random blood sugar, Hemoglobin, Total leukocyte count, LFT including serum bilirubin, SGOT (AST), SGPT (ALT) Triglyceride, cholesterol, LDL, VLDL and HDL.

Thyroid function test: - T3, T4 (Normal range 5.5-13ug/dl),

Serum thyrotropin (TSH) (normal range 0.27-4.20lU/ml), was analyzed by immune chemiluminescent procedures. All TSH measurements were performed in one central laboratory.

Method

1. *For study group*: -The Patients were diagnosed by USG (Ultrasonography), or MRCP, past h/o Cholecystectomy to have gallstone disease.
2. *For Control group*: - Neither did the patients have a history of gallstone disease or stones at ultrasonography performed during the study.

Then both groups Blood samples were taken, and laboratory parameters were analyzed in a central laboratory. All TSH, T3, T4 measurements were performed in one central laboratory

Primary study endpoint

At the end of the study patient were categorized as:-

Gallstone disease

Non Gallstone disease

Statistical analysis

Statistical analysis was done by using simple ratio and percentages. Microsoft 2010 was used to generate tables.Two groups were compared and calculated using independent t test for the TSH levels and T4 levels.

Result

Age and gender of the patients were similarly distributed in groups I (CBD stone) and II (control). There were 208 Gallstone disease and 796 in the control group. Median age was 50 (range 20–80) and 40 (18–80) yrs. At the time of hospitalization in the Gallstone disease and control patients, respectively. Differences were no significant between the groups. None of the patients included in the study were septic. None of the patients recruited into the study had symptoms of hypothyroidism. There was no difference in the median values of S-TSH (3.06, range 0.27–4.2 vs. 2.8, range 0.28–7.40ulU/ml) and S-T4 (13, range 5.5–13.0 vs. 13.0, range 5.5.–13 ug/dl) between the groups'-TSH was above the upper normal range (>4.20 ulU/ml; subclinical hypothyroidism) in 46 gallstone disease patients (22%), compared with two controls (2%; P = 0.05). In each grade the prevalence of subclinical or borderline subclinical

hypothyroidism was higher in Gallstone disease patients than the control patients. The prevalence of subclinical (S-TSH > 4.2ulU/ml;) hypothyroidism in women was 24% in Gallstone disease group and 2.3 than in the control group and in men 24% and 2% (total 5.5%) in the Gallstone disease group than in control group, respectively. There were 12 patients (2%) in the control group (none in gallstone disease group) had S-T4 within the normal range.

Table 1: Levels of Thyroid stimulating hormone levels in gallstone disease patient.

TSHulU/ml	Number of cases	Percentage %
0.0-0.27	2	1
0.27-4.20	160	77
4.20-18	46	22
Total	208	100

Table 2: Levels of thyroid stimulating hormone in Non gallstone disease patient.

TSHulU/ml	Number of cases	Percentage%
0.0-0.27	0	0
0.27-4.20	784	98
4.20-18	12	2
Total	796	100

Table 3: Serum T_4 levels in gallstone disease patient.

T_4 ug/dl	No of cases	Percentage %
1.0-5.49	8	4
5.5-13	195	94
13-18	5	2
Total	208	100

Table 4: Serum T_4 level in non-Gallstone disease patient.

T_4 ug/dl	Number of cases	Percentage %
1.0-5.49	15	2
5.5-13	764	96
13-18	17	2
Total	796	100

Table 5: Levels of thyroid stimulating hormone in Female Gallstone disease patient.

TSHulU/ml	Number of cases	Percentage %
0.0-.27	2	1
.27-4.2	128	75
4.20-18	40	24
Total	170	100

Discussion

Earlier, an association between cholelithiasis and cbdstones (Gallstone disease) and diagnosed hypothyroidism and delayed emptying of the biliary tract in experimental and clinical hypothyroidism have been shown, explained at least partly by the lack of the prorelaxing effect of T4 on the sphincter of Oddi contractility.[8] In this study wefurther investigated the prevalence of previously undiagnosed thyroid function abnormalities in gallstone disease patients. To our knowledge It was found that in the CBD stone patients, subclinical hypothyroidism are significantly more common, compared with the non-gallstone controls(10.2 vs. 2.8%; P = 0.026), the prevalence in the subgroup of women older than 60 yrs. Being as high as 23.8%, compared with 1.8% in the control patients. In our study also it was found that in the gallstone disease patients, subclinical hypothyroidism are significantly more common, compared with the non-gallstone controls (22 vs. 2%; P =0.025).

The two study groups were well comparable for age and gender distribution. Because of the possible effects on the serum thyroid values, patients with phenytoin or carbamazepine therapy as well as pregnant patients were excluded from both of the groups. The group I patients were diagnosed by USG to have gallstone disease. Base on a normal serum bilirubin level, none of the control patients had signs of biliary stasis. Neither did the control patients have a history of gallstone disease or stones at ultrasonography performed during the study. In general, at ultrasonography about 95% of the gallbladder stones can be diagnosed.[9] With a negligible false-positive rate, because there was no suspicion of Gallstone disease in the control patients, no imaging techniques except for ultrasonography (e.g. Magnetic resonance cholangio pancreatography).

The laboratory hallmark of primary hypothyroidism and the most sensitive test for detecting early thyroid failure is an increased S-TSH concentration. The S-T4 level is decreased in clinical hypothyroidism.[10] In the subclinical form, an increased S-TSH level is accompanied by a normal S-T4 level, and the patient is asymptomatic.[11] In the present study, none of the patients was clinically hypothyroid. It was recognized that in 22% of the patients with Gallstone disease, S-TSH levels were above the upper limit of the normal range (defined as subclinical hypothyroidism), compared with 2% in the control patients (p=0.025). Furthermore, as many as 46 patients (22%) in the gallstone disease group had S-TSH levels above or close to the upper limit of the normal range (defined as subclinical hypothyroidism). Thus, subclinical hypothyroidism is significantly more common in patients with gallstone disease, compared with non-gallstone control patients. In this study setting,

the thyroid function serum determinations were done only once in each individual, and the findings are thus not based on a recording of a persistent abnormality. However, the measuring of the thyroid values was done similarly in both of the groups.

Subclinical hypothyroidism is a prevalent condition among adult population; however, it is frequently overlooked. The previous studies about the prevalence of subclinical hypothyroidism among health subjects are few in number. Of the current study. In a recent study from the United Kingdom,[12] the prevalence of subclinical hypothyroidism among healthy subjects was 2.6%, which is somewhat higher compared with the prevalence of hypothyroidism among the control patients in the present study (2%). The prevalence of hypothyroidism (clinical plus subclinical) among women as high as 24%.[13] In the present study, the prevalence of subclinical hypothyroidism in men and women patients compared with 1% in the control patients. The currently diagnosed 24% prevalence of subclinical hypothyroidism and the previously diagnosed 11% prevalence of hypothyroidism[14] in female CBD stone patients older than 60 yrs. Support the findings of Dickey and Feld[15] and suggest that at least this subgroup of patients might need to be screened for current thyroid dysfunction. It is uncertain whether treatment will improve quality of life in healthy, symptom-free patients who have abnormal TSH levels and normal st4 levels.[14,15] The pathogenesis of gallstones is a complex process involving factors affecting bile content and bile flow. Brown pigment stones are formed secondary to biliary stasis,[16] which is the major factor leading to anaerobic bacterial degradation and precipitation of biliary lipids

In the present study, we did study the thyroid values in gallbladder stone patients without CBD stones. If the effect of T4 or the absence of T4 affected only the cholesterol metabolism and the hepatic bile secretion, the patients with gallbladder and CBD stones would presumably evince an equally increased prevalence of diagnosed or subclinical hypothyroidism. In a previous study, it was, however, noted the CBD stone patients had two times more previously diagnosed hypothyroidism than the gallbladder stone patients.[17]

In a previous study,[11] the CBD stone patients with diagnosed hypothyroidism were already receiving T4 replacement therapy and were already euthyreotic in clinical and laboratory evaluation at the time of the diagnosis of CBD stones. Thus, CBD stone formation may already begin during the period of undiagnosed or subclinical hypothyroidism, later T4 replacement therapy not having enough effect on clearance of stones already formed. The findings of the present study are not in contrast with this hypothesis. There is only one case report that describes gallstone disappearance after treatment with T4.[15] There are currently no data to suggest whether therapeutic doses of T4 could prevent gallstone formation. In conclusion, subclinical hypothyroidism is more common in the gallstone disease patients, compared with the non-gallstone controls, which supports our previous hypothesis that hypothyroidism, and might play a role in the forming of gallstone. Further studies are needed to investigate whether early treatment of subclinical or clinical hypothyroidism could prevent the gallstones in these patients. For offered replacement therapy, a positive effect on the symptoms associated with subclinical hypothyroidism as a possible achievement.

Conclusion

There is an association between changes in thyroid function with gallstone disease.

***Conflict of Interest*:** nil

References

1. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med 2000;160: 526-534
2. Laukkarinen J, Sand J, Saaristo R, Salmi J, Turjanmaa V, Vehkalahti P, Nordback I. Is bile flow reduced in patients with hypothyroidism? Surgery 2003; 133: 288-293
3. Inkinen J, Sand J, Arvola P, Porsti I, Nordback I. Direct effect of thyroxine on pig sphincter of Oddi contractility. Dig Dis Sci 2001; 46: 182-186
4. Cicala M, Habib FI, Fiocca F, Pallotta N, Corazziari E. Increased sphincter of Oddi basal pressure in patients affected by gall stone disease: a role for biliary stasis and colicky pain? Gut 2001; 48: 414-417
5. Honore LH. A significant association between symptomatic cholesterol cholelithiasis and treated hypothyroidism in women. J Med 1981; 12: 199-203
6. Inkinen J, Sand J, Nordback I. Association between common bile duct stones and treated hypothyroidism . Hepatogastroenterology 2001; 47: 919-921

7. Vassilakis JS, Nicolopoulos N. Dissolution of gallstones following thyroxine administration. A case report. Hepatogastroenterology 1981; 28: 60-61

8. Borgman RF, Haselden FH. Cholelithiasis in rabbits: effects of bile constituents and hormones on dissolution of gallstones. Am J Vet Res 1969; 30: 107-112

9. La Vecchia C, Negri E, D'Avanzo B, Franceschi S, Boyle P. Risk factors for gallstone disease requiring surgery. Int J Epidemiology 1991; 20: 209-215

10. John U, Greiner B, Hensel E, Lüdemann J, Piek M, Sauer S, Adam C, Born G, Alte D, Greiser E, Haertel U, Hense HW, Haerting J, Willich S, Kessler C. Study of health in Pomerania(SHIP): a health examination survey in an East German region: objectives and design. Soz Präventivmed 2001; 46: 186-194

11. Völzke H, Lüdemann J, Robinson DM, Spieker KW, Schwahn C, Kramer A, John U, Meng W. The prevalence of undiagnosed thyroid disorders in a former iodine deficient area. Thyroid 2003; 13: 803–810

12. Loria P, Dilengite MA, Bozzoli M, Carubbi F, Messora R, Sassatelli R, Bertolotti M, Tampieri A, Tartoni PL, Cassinadri M, Della Ciana M, Contemori M, Save N, Sordi B, Alimenti G, Fabrizi F, Buciuni A, Carulli N. Prevalence rates of gallstone disease in Italy. The Chianciano population study. Eur J Epidemiology 1994; 10: 143-150

13. Trotman BW, Soloway RD. Pigment vs. cholesterol cholelithiasis: clinical and epidemiological aspects. Am J Dig Dis 1975; 20: 735-740

14. Laukkarinen J, Koobi P, Kalliovalkama J, Sand J, Mattila J, Turjanmaa V, Porsti I, Nordback I. Bile flow to the duodenum is reduced in hypothyreosis and enhanced in hyperthyreosis. Neurogastroenterol Motil 2002; 14: 183-188

15. Bergman F, van der Linden W. Further studies on the influence of thyroxine on gallstone formation in hamsters. Acta Chir Scand 1966; 131: 319-328

16. Berndt H, Nürnberg D, Pannwitz H. Prävalenz der Cholelithiasis. Ergebnisse einer epidemiologischen Studie mittels Sonographie in der DDR. [Prevalence of cholelithiasis. Results of an epidemiologic study using sonography in East Germany]. Z Gastroenterol 1989; 27: 662-666

17. Martinez de Pancorbo C, Carballo F, Horcajo P, Aldeguer M, de la Villa I, Nieto E, Gaspar MJ, de la Morena J. Prevalence and associated factors for gallstone disease: results of a population survey in Spain. J Clin Epidemiology 1997; 50: 1347-1355