STUDY THE ASSOCIATION BETWEEN THYROID DISORDER AND GALL STONE DISEASES (CHOLELITHIASIS & CHOLEDODCHOLITHIASIS)
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ABSTRACT: Biliary stone diseases are one of the most common conditions that are prevalent among adult population. Biliary stone diseases include cholelithiasis and choledocholithiasis. The prevalence of cholelithiasis among adult population is 10-12%;¹-³ the prevalence of choledocholithiasis among cholelithiasis patients varies from 8-16%.⁴,⁵ The prevalence of biliary stone diseases increases with age with female to male ratio of 4:1,⁶ but in our region prevalence of biliary stone diseases is very high in female patients.

KEYWORDS: Thyroid Disorder, Gall Stone Diseases, Cholelithiasis, Choledocholithiasis.

INTRODUCTION: The pathogenesis of biliary stone diseases is a complex process involving factors affecting bile content and bile flow. A crucial factor for the formation of CBD stone is biliary stasis,⁷ which may be caused by sphincter of Oddi (SO) stenosis, SO dyskinesia & CBD stricture.⁸-¹⁰ For decades, there has been a discussion whether thyroid disorders could cause biliary stone diseases.

There are several possible explanations for the relation between thyroid disorders with biliary stone diseases. In hypothyroidism, the lack of thyroxine causes:

1. Decreases liver cholesterol metabolism¹¹ resulting in bile cholesterol supersaturation, which in turn impairs the motility¹², contractility¹³ and filling¹⁴ of the gallbladder, contributing to the retention of cholesterol crystals and to the nucleation and growth of gallstones¹².
2. Diminishes bile secretion from hepatocytes¹⁵ resulting in impaired clearance of precipitates from the bile ducts.
3. Reduces SO relaxation¹⁶,¹⁷ resulting in delayed bile flow¹⁸,¹⁹ and thus the formation and accumulation of CBD stones.

Hypothyroidism decreases liver cholesterol metabolism

A 90% of hypothyroid patients have elevated cholesterol levels, triglyceride levels, or both. In hypothyroidism, decreased LDL receptor activity leads to impaired removal of cholesterol from the serum and reduced regulation of HMG-CoA reductase expression leads to decreased cholesterol synthesis.

Hypothyroidism may reduce hepatic bile secretion.

Hepatocytic bile secretion may not be significantly reduced in humans in the early phase of hypothyroidism, but decreased bile secretion in prolonged hypothyroidism has been reported¹⁵, whereas hyperthyroidism seems to have no effect. Thus decreased bile hepatic secretion may have at least some impact on the delayed bile flow in prolonged hypothyroidism.

Hypothyroidism reduces bile flow into the duodenum.
In a prospective human study, hepatic clearance was significantly decreased and the hilum-duodenum transit time had a tendency to increase in the hypothyroid stage after thyroidectomy, when compared to the euthyrotic stage in the same patients. Hepatic maximal uptake and the appearance of radioactivity in the large bile ducts at the hepatic hilum were similar in the hypothyroid and euthyrotic stages of this study. The findings were not attributable to different hepatic secretion but strongly suggested that bile flow into the duodenum is reduced in the hypothyroid stage. This could be due to changes in bile composition and gallbladder motility, and because of changes in the resistance to flow, that is, in the SO motility.

**Diagnosis:**

The patients were divided into two groups: Group A and Group B.

- Group A included 100 patients with cholelithiasis or choledocholithiasis or both (prior history of cholecystectomy or the presence of gallstones or CBD stones on ultrasound abdomen) admitted in the surgical ward.

- Group B included 100 surgical patients of abdominal pathology other than gall bladder and CBD stone diseases or H/O cholecystectomy performed or gall stones detected at ultrasonography.

In this study Transabdominal ultrasound was the investigation used to diagnose cholelithiasis and choledocholithiasis. In this study Ultrasound abdomen was done in a single centre, Department of radiology, SPMC, Bikaner as ultrasound is operator dependent imaging modality. Ultrasound is a sensitive, inexpensive, reliable and reproducible test to evaluate most of the biliary tree. Therefore this modality is the choice for initial investigation of symptoms of biliary diseases. Gall bladder diseases are regularly diagnosed by Ultrasound because of its superficial location and no overlying bowel gas enables its evaluation. Ultrasound has a high specificity and sensitivity for cholelithiasis. Ultrasound also identifies CBD stones.

Thyroid function tests like serum TSH(0.270 - 4.20 µIU/ml), T₃ (1.30 - 3.10 nmol/l), T₄ (5.13 - 14.06 µg/dl) were measured by Electrochemiluminescence (ECL) using morning fasting blood samples in the Biochemistry Department, SPMC, Bikaner. ECL is a third generation thyroid function assay, has high sensitivity 97% and high specificity provides results within 18 minutes, less affected by non-thyroidal disease process and change of hormonal binding proteins.

In a retrospective study on patients over 60 years of age, it was noted for the first time that CBD stone patients have significantly more diagnosed hypothyroidism (11%), not only when compared to control patients from whom gallstones had been excluded (2%), but also when compared to gallbladder stone patients without CBD stones (6%). This finding suggested that factors other than merely those affecting cholesterol metabolism, for example, specific effects on bile flow, might be behind the association between CBD stones and hypothyroidism.

Inkinen et al study noted a proportion of previously diagnosed hypothyroidism of 8% and 6% in patients having CBD stones and gall bladder stones respectively compared to a proportion of only 1% in the controls. This indicates clearly the increased prevalence of CBD stones in hypothyroid patient than gall bladder stone.

**DISCUSSION:** Gallstone disease (GSD) is a worldwide disease and it remains to be one of the most common health problems leading to surgical intervention. Since two decades, there has been a discussion whether thyroid disorders could cause biliary stone diseases. Earlier studies showed
that hypothyroidism is more prevalent among gall stone patients. Further studies have found that CBD stones patients have significantly more often diagnosed hypothyroidism than gall bladder stone patients or controls, which could be explained by the delayed emptying of the biliary tract, due to the lack of pro relaxing effect of T4 on the sphincter of Oddi contractility.17

In this study, we investigated the overall association between thyroid disorders and biliary stone diseases which included cholelithiasis and choledocholithiasis. Our study included 200 patients 100 each in study and control group. Both study and control groups were matched for age and sex.

In our study out of 7 hypothyroid patients, 6 were females and 1 was male. The higher proportion of hypothyroidism in women with biliary stone disease compared to men was mainly due the earlier symptomatology of biliary stone disease in women as well as the higher incidence of thyroid disease in women in general. This leads to an earlier detection and treatment of hypothyroidism in women.

CONCLUSION: This study concludes that
1. There is a significant association between thyroid disorders particularly hypothyroidism and biliary stone diseases.
2. Hypothyroidism is more common in CBD stone patients than GB stone patients.
3. Subclinical hypothyroidism is more common than clinical hypothyroidism.
4. Hypothyroidism has higher prevalence in females than males.
5. Patients > 60 years age with hypothyroidism are more likely to have hypothyroidism. so we recommend that surgeon should be aware of thyroid background in patients of biliary stone diseases, TSH should be measured as most are subclinically hypothyroid with special consideration to patients of > 60 years age group.

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