



Hypothyroidism as a Risk Factor for Choledocholithiasis

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ABSTRACT:

Background: Gallstone disease is a common world-wide health problem, with choledocholithiasis (CBD stones) as one of its complications. Hypothyroidism has been put forward as an etiological factor for gallstone formation based on its influence on lipid metabolism and biliary motility. This study assess the correlation between hypothyroidism and CBD stone formation and investigate thyroid function and lipid profile changes in affected patients.

Methods: The research was done in the hospital setting carried out using 140 study subjects, 70 patients with CBD stones and 70 healthy controls. The thyroid function tests and the lipid profile tests were done. The characteristics of CBD stones and the associated biliary conditions were compared in those with and without hypothyroidism.

Results: The prevalence of hypothyroidism was significantly greater among CBD stone patients (22.9%) compared to the control group (7.1%) ($p=0.0095$). The mean TSH levels were higher in the cases (3.6 ± 3 mIU/L) than in the controls (2.6 ± 1.5 mIU/L) ($p=0.0014$), along with decreased T3 and T4 levels in the cases. In cases total cholesterol and triglyceride levels along with reduced HDL levels in comparison to controls. An increased incidence of multiple CBD stones was seen in hypothyroid patients, at 62.5%. The incidence of associated pancreatitis was significantly lower in hypothyroid patients (25%) compared to non-hypothyroid patients (85.1%) ($p<0.0001$).

Conclusions: Hypothyroidism is associated to CBD stone development and dysfunctional thyroid function and lipid profile. Gallstone disease patients should be screened for thyroid dysfunction to detect and avoid complications.

1. Introduction

With incidence rates ranging from 2% to 29% in India and higher in northern populations than in southern ones, cholelithiasis, also known as gallstone disease, is a serious worldwide health concern. The most prominent explanations for the discrepancies include variations in nutrition, genetic predisposition, and dietary habits. The health system is heavily burdened by gallstones, which are mostly composed of cholesterol and can cause cholecystitis, choledocholithiasis, and pancreatitis [1-4]. Usually due to an excess of bilirubin or cholesterol or a lack of bile salts, gallstones develop when the bile held in the gallbladder hardens and includes material that forms stones [5]. Additionally, bile stasis and an increased risk of stone formation may result from the hypothyroid condition's inhibition of Oddi's sphincter relaxation [6]. A key factor in lipid metabolism is thyroid hormones, and hypothyroidism usually results in high

blood cholesterol levels, which encourage the formation of gallstones [7]. Both clinical and subclinical forms of hypothyroidism are common, and studies indicate that people with choledocholithiasis have a higher incidence of the condition [8]. Because thyroid problems can raise the likelihood of gallstone development and vice versa, screening for thyroid dysfunction is recommended to prevent the consequences of untreated hypothyroidism, especially in older adults and women with gallstones [9]. The correlation between choledocholithiasis and hypothyroidism highlights the necessity of a holistic approach to patient care, which includes monitoring thyroid function in those at risk for gallstone disease [10].

This study will determine how hypothyroidism and the development of CBD stones are related. Thyroid function tests and lipid profiles between CBD stone and control patients will be compared and contrasted in this



study. The type of CBD stones and related biliary diseases in hypothyroid and non-hypothyroid people are also examined in this study.

2. Methods

It's a case-control study, carried out within the hospital setting, that employed the case-control study design to explore the link between hypothyroidism and the development of common bile duct stones (choledocholithiasis). It sought to establish a change in lipid profile levels among CBD stone-presenting patients and controls. The research had 140 participants, where 70 were CBD stones-presenting patients and 70 age- and sex-matched healthy controls free of gallstone disease.

CBD stones patients were selected following their presentation, laboratory assessment, ultrasonography, and imaging confirmation studies like MRCP or ERCP. Data regarding age, sex, pre-existing health conditions, lifestyle factors, and thyroid function were collected using a questionnaire form.

Thyroid function tests, including serum TSH, T3, and T4 levels, were measured in the cases as well as in controls. Fasting samples were used for measuring the lipid profile, which consists of total cholesterol, triglycerides, HDL, and LDL.

Second, in the cases under study, the characteristics of CBD stones, such as if they were a single or multiple stone, existence of gall bladder stones (as single or multiple), presence of cholelithiasis associated with CBD stones, and pancreatitis in association, were studied. The characteristics among patients with hypothyroidism and without hypothyroidism in the case group were assessed to find associations of interest.

Appropriate tests were employed to examine the statistics. Continuous data were expressed as mean \pm SD and analysed using the unpaired t-test. We utilised frequency and percentage to present the categorical variables, which were analysed using the Chi-square test or Fisher's exact test for comparison. A p-value below 0.05 was deemed statistically significant.

3. Results

The mean age of the cases was 52.3 ± 17.6 years, while that of the controls was 51 ± 18 years, and there was no statistically significant difference ($p=0.646$), indicating adequate age matching. The case group had a greater female predominance at 57.1% compared to the control group, which was 44.3%, with no statistical significance ($p=0.1295$). Type 2 Diabetes Mellitus was noted in 31.42% of cases and 22.85% of controls, whereas Hypertension occurred in 30% of cases and 27.14% of controls, but these were not statistically significant.

Hypothyroidism was significantly more prevalent in the case group at 22.9% compared with the control group at 7.1% ($P: 0.0095$). It is shown in Table 1.

The mean TSH levels were elevated in the cases (3.6 ± 3 mIU/L) in contrast to the controls (2.6 ± 1.5 mIU/L), with a statistically significant p-value of 0.0014. The mean levels of T3 and T4 were reduced in the control group when contrasted with the case group. The mean T3 level in the cases was 2.7 ± 1 ng/ml, in the control group it was 1.4 ± 0.4 ng/ml ($p=0.0005$). The mean T4 level was 1.24 ± 0.61 ng/dl for the cases and 0.98 ± 0.26 ng/dl for the controls ($p=0.001$). It is shown in Table 2. The case group possessed a significantly higher mean Total Cholesterol level (171.9 ± 56.9 mg/dL) than controls (153.3 ± 30.1 mg/dL) (p -value = 0.0017). Cases possessed a significantly higher mean Triglyceride (TG) level (121.3 ± 45.8 mg/dL) than controls (85.5 ± 30.8 mg/dL) with a p-value of 0.0005. The patients in case group had significantly lower HDL concentrations (37.2 ± 10.9 mg/dL) than controls (51.2 ± 8.9 mg/dL), indicative of dyslipidaemia (p -value = 0.0005). The levels of LDL were not significantly different in patients (92 ± 38.5 mg/dL) and controls (86.7 ± 24.8 mg/dL), with a p-value of 0.340. It is shown in Table 3.

Hypothyroid subjects had more than one CBD stone in 62.5% and single CBD stones in 37.5%. Single CBD stones were more common (59.3%) than multiple stones (40.7%) in non-hypothyroid subjects, but the difference was not significant ($p=0.1471$). Both groups of patients had a number of gall bladder stones—56.2% in hypothyroid and 68.5% in non-hypothyroid patients. Single and numerous gall bladder stones did not vary. Cholelithiasis was diagnosed in 68.7% of non-hypothyroid patients and 85.1% of hypothyroid subjects ($p=0.1419$). non-hypothyroid patients had a much higher incidence of associated pancreatitis (85.1%) than hypothyroid patients (25%), reflecting a highly significant difference ($p<0.0001$). It is shown in table 4.

4. Discussion

The relationship between hypothyroidism and the development of CBD stones is examined in this study. In particular, the thyroid function test and lipid profile of CBD stone patients and controls will be compared. In both hypothyroid and non-hypothyroid individuals, the research will also ascertain the makeup of CBD stones and the frequency of concurrent biliary illness.

Gallstones affect around 6.1% of people globally, with a greater frequency in South American and female populations. In India, the frequency varies significantly by area, with northern inhabitants having a prevalence that is two to four times greater than that of southern



groups. In the Indian population, prevalence has been reported to range from 2% to 29% [11, 12, 2]. Research has shown a strong correlation between CBD stones and hypothyroidism that has already been identified [13].

With a p-value of 0.0095, the case group (22.9%) had a significantly greater prevalence of hypothyroidism than controls (7.1%), confirming earlier studies linking hypothyroidism to CBD stones. Subclinical hypothyroidism was discovered in 1.4% of controls and 5.3% of patients with CBD stones, suggesting a substantial correlation. Women over 60 had a 11.4% prevalence of CBD stones, whereas controls had a 1.8% prevalence [14].

Results from thyroid function tests in individuals with CBD stones, such as lower T3 and T4 and higher mean TSH, are in line with earlier studies. According to Ajdarkosh et al., individuals with CBD stones had lower HDL cholesterol, higher mean TSH, and higher triglyceride levels than controls. According to these findings, lipid metabolic problems and thyroid dysfunction may be linked to CBD stones [15]. The idea that thyroid problems may be the cause of CBD stones is supported by Laukkanen et al.'s discovery that patients with CBD stones had a higher frequency of subclinical hypothyroidism than controls [14].

According to Sidduri et al., 30% of patients with CBD stones had subclinical hypothyroidism (SCH), compared to 9.09% of controls, with a very significant p-value (< 0.05). Patients revealed substantially higher mean TSH levels (3.57 ± 1.7) than controls (2.58 ± 0.67 ; $p = 0.0029$). Low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC) were elevated in individuals with CBD stones, suggesting a link between SCH, dyslipidemia, and CBD stone development [16]. Singh et al. observed 27.7% hypothyroid, 61.1% euthyroid, and 1.1% hyperthyroid in female CBD stone patients. Sixty-two percent of male CBD stone patients were euthyroid, 18.75% were hyperthyroid, and 18% were hypothyroid [17]. According to these results, hypothyroidism is significantly more common in CBD stone victims.

Previous research provides strong support for our findings that patients with CBD stones have altered lipid profiles. According to Saldanha et al., the majority of these patients had abnormal lipid profiles, particularly low HDL and high LDL and VLDL levels [18]. High serum LDL and low HDL concentrations were found to be strongly associated with an increased risk of biliary calculus by Jiwen Wang et al. [19].

In hypothyroid individuals, our study found that the incidence of numerous CBD stones was greater than that of single stones. Hypothyroidism was detected in 8% of CBD stone patients, compared to 1% in the control

group, according to Inkinen et al. [13]. According to Teguh et al., hypothyroidism was discovered in 27.7% of female patients with CBD stones and 24% of male gallstone patients [20]. According to Rassam et al., subclinical hypothyroidism was found in 7.8% of these individuals, with a higher frequency in females aged 36 to 50 [21]. Gallstones can develop when bile becomes less soluble and crystallizes as a result of supersaturation brought on by elevated cholesterol levels [6].

The link between hypothyroidism and the pathophysiology of CBD stones emphasizes the importance of a methodical approach to patient assessment and care, including the use of thyroid function testing in biliary stone disease diagnosis and treatment planning.

The study's methodology limited its breadth, since it only involved one center and a small sample size, which might have an impact on how broadly the results can be applied. The degree and duration of hypothyroidism were not evaluated. Genetics and diet were not considered factors.

5. Conclusion

This study illustrates a correlation between CBD stone and hypothyroidism. CBD stone patients had thyroid dysfunction and dyslipidaemia. Hypothyroidism elevates the risk for biliary stone by affecting lipid metabolism. Pancreatitis, multiple stones, and gallbladder stones were more common in hypothyroid CBD stone patients. Detection and treatment of thyroid disorders in early stages among CBD stone patients can prevent morbidity due to gallstones.

Further large-scale research is required to establish this association and explore the benefits of thyroid function monitoring in patients with biliary stone disease.

Table 1: Comparison of demographic characteristics, comorbidities and lifestyle factors

Variables	Cases (n=70)	Controls (n=70)	p-value
Age	52.3 ± 17.6	51 ± 18	0.646
Sex			0.1295
-Female	40 (57.1%)	31 (44.3%)	
-Male	30 (42.9%)	39 (55.7%)	



Co-morbidities			
-DM	22(31.42%)	16(22.85%)	0.2559
-HTN	21(30%)	19(27.14%)	0.7093
-CAD	7(10%)	4(5.71%)	0.3478
-Hypothyroidism	16(22.9%)	5(7.1%)	0.0095*
Lifestyle factors			
-Alcohol consumption	12(17.1%)	16(22.9%)	0.3997
-Smoking	11(15.7%)	9(12.9%)	0.6303

Table 2: Comparison of thyroid function parameters

Lipid Parameters	Cases (n=70) (Mean ± SD)	Controls (n=70) (Mean ± SD)	P-value
Total Cholesterol (TC)	171.9±56.9	153.3±30.1	0.0017*
Triglycerides (TG)	121.3±45.8	85.5±30.8	0.0005*
HDL	37.2±10.9	51.2±8.9	0.0005*
LDL	92±38.5	86.7±24.8	0.34

Table 3: Lipid profile comparison between cases and controls

Thyroid Parameters	Cases (n=70) (Mean ± SD)	Controls (n=70) (Mean ± SD)	P-value
TSH	3.6±3	2.6±1.5	0.0014*
T3	2.7±1	1.4±0.4	0.0005*
T4	1.24±0.61	0.98±0.26	0.001*

Table 4: Characteristics of CBD stones and gall bladder stones in case group with and without hypothyroidism

Characteristics	With Hypothyroidism (N=16)	Without Hypothyroidism (N=54)	P-value
CBD stone			
-Single	6 (37.5%)	32 (59.3%)	0.1471
-Multiple	7 (43.7%)	22 (40.7%)	0.8317
Gall bladder stone			
- Single	0 (0%)	9 (16.7%)	0.0821
Multiple	9 (56.2%)	37 (68.5%)	0.3662
Associated Cholelithiasis	11 (68.7%)	46 (85.1%)	0.1419
Associated Pancreatitis	4 (25%)	46 (85.1%)	< 0.0001*



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