

PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN COMMON BILE DUCT STONE PATIENTS

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ABSTRACT

Subclinical thyroid dysfunction is a common laboratory diagnosis characterized by an abnormal high serum thyrotropin (TSH) concentration with normal free triiodothyronine (T3) and thyroxine (T4) levels. Refinements in serum thyrotropin measurements during the past few decades have resulted in a sharp increase in the diagnosis of thyroid dysfunction, mirroring the tendency towards early diagnosis of many other conditions such as hyper lipidemia for which early treatment appears beneficial. Various studies have been done regarding subclinical thyroid dysfunction and its clinical relevance in common bile duct (CBD) stone patients.

This study of subclinical hypothyroidism was done on 30 common bile duct stone patients, admitted in Department of General Surgery. The aim of the study was to find out the prevalence of subclinical hypothyroidism in common bile duct stone patients.

Key words: subclinical hypothyroidism, common bile duct stone, thyroid dysfunction

INTRODUCTION

While screening patients for thyroid disease, physicians often find increased TSH levels in patients whose free T4 levels are not below normal. This state, termed “subclinical hypothyroidism”, is most commonly an early stage of hypothyroidism. Although the condition may resolve or remain unchanged, within a few years in some patients, overt hypothyroidism develops, with low free T4 levels as well as a raised TSH level. The likelihood that this will happen increases with greater TSH elevations and detectable antithyroid antibodies. Because patients with subclinical hypothyroidism sometimes have subtle hypothyroid symptoms and may have mild abnormalities of serum lipoproteins and cardiac function, patients with definite and persistent TSH elevation should be considered for thyroid treatment.¹

Hypothyroidism is quite common in older persons. Clinical suspicion of hypothyroidism may be delayed in elderly patients because symptoms such as fatigue and constipation, and other early manifestations of thyroid failure may be attributed to aging itself. The high prevalence of thyroid failure and the difficulty of making an early clinical diagnosis in older persons suggest that screening for hypothyroidism might be useful in this group, especially since a simple test, the serum TSH level, is available.¹

Studies have shown increased prevalence of subclinical hypothyroidism in CBD stone patients. There are multiple factors that may contribute to the formation of CBD stones in hypothyroid patients including decreased liver cholesterol metabolism, diminished bile secretion and reduced sphincter of oddi (SO) relaxation. While treating patients with CBD stones, the clinicians should be aware of the

possible hypothyroid background, and consider the need for thyroid function assessment in these patients.²

A crucial factor in the formation of bile duct stones is biliary stasis³ which may be caused for example by SO stenosis, SO dyskinesia or bile duct strictures.⁴⁻⁶

Studies have shown that thyroxine has a direct prorelaxing effect on the sphincter of oddi (SO) motility at physiological concentration, possibly mediated via thyroid hormone receptors β_1 and β_2 and absence of thyroxine may thus result in an increased tension in the SO.^{7,8}

Laukkanen et al (2007) studied the prevalence of previously undiagnosed subclinical hypothyroidism in CBD stone patients compared to non gallstone controls on the basis of serum free thyroxine (T4) and thyrotropin (TSH). 5.3% and 5% (total 10.3%) of CBD stone patients were diagnosed to have subclinical and borderline-subclinical hypothyroidism compared to 1.4% and 1.4% (Total 2.8%) in the control group respectively. They concluded that subclinical hypothyroidism is more common in the CBD stone patients compared to non gallstone controls.⁹

Yadav et al (2013) studied the influence of thyroid hormones on biochemical parameters of liver function. The liver enzyme Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Alkaline phosphatase (ALP) were increased in subclinically hypothyroid patients and in overt hypothyroid cases as compared to the controls.¹⁰

MATERIAL AND METHODS

The present study was conducted on 30 CBD stone patients, admitted in Deptt. of Surgery. The aim was to find out the prevalence of subclinical hypothyroidism in CBD stone patients. In each case of CBD stone, the diagnosis was made from history, physical findings and USG Abdomen. Subclinical hypothyroidism was diagnosed in symptom free patients on the bases of Thyroid Function tests (T3, T4, TSH).

Only those cases with age more than 18 yrs were included in the study. Both the male and female sexes were included in the study.

SAMPLE COLLECTION

From Morning blood samples (5 ml), serum free thyroxine (T4), triiodothyronine (T3) and thyrotropin (TSH) were analysed. The symptom free patients with TSH concentration above the upper limit of the normal range and T3 and T4 within normal range were considered as subclinically hypothyroid.

Accepted Normal Values

T3	0.49 – 2.02 ng/ml	Method ELISA
T4	4.7-12.8 μ g/dl	Method ELISA
TSH	0.44–3.45 μ IU/mL	Method ELISA

Exclusion Criteria

1. Pregnant Patients
2. Patients with phenytoin or carbamazepine or amiodarone therapy.
3. Patients with history of treated or diagnosed thyroid function abnormalities.

	Clinical Hypo - thyroidism	Subclinical Hypo - thyroidism	Total Hypo - thyroidism	Euthyroi - dism	Borderline Subclinical Hypothyro - idism
Males	1	1	2	6	1
Females	0	8	8	12	1
Total	1	9	10	18	2

Table 1 : Distribution of males and females according to hypothyroidism

The prevalence of subclinical hypothyroidism, in our study

- ❖ Overall : 9/30 (30%)
- ❖ In women : 8/21 (38.09%)
- ❖ In men : 1/9 (11.11%)
- ❖ Borderline : 2/30 (6.67%)

Age groups	Clinical Hypo - thyroidism	Subclinical Hypo - thyroidism	Total Hypo - thyroidism	Euthyr - oidism	Borderline Subclinical Hypo - thyroidism
21 - 30	0	1	1	0	0
31 - 40	1	0	1	2	0
41 - 50	0	2	2	5	1
51 - 60	0	4	4	3	0
61 - 70	0	2	2	5	1
71 - 80	0	0	0	3	0
Total	1	9	10	18	2

Table 2 : Distribution of patients of different age groups according to hypothyroidism

The prevalence of subclinical hypothyroidism, in our study

- ❖ In the patients older than 50 years : 6/17 (35.29%)
- ❖ In patients older than 60 years : 2/10 (20%)
- ❖ Most of the cases of subclinical hypothyroidism (5/9 = 55.56%) were found in women older than 50 years.
- ❖ In women above 60 years of age : 2/9 (22.22%)

	Euthyroid patients	Subclinically Hypothyroid patients
Bilirubin (mg/dl) (Mean value)	1.16±0.18	1.64±0.29
AST (IU/L) (Mean value)	49.54±10.62	70.56±15.56
ALT (IU/L) (Mean value)	47.64±10.18	81.67±19.97
ALP (IU/L) (Mean value)	181.81±38.45	276.22±78.72

Table 3: Comparison between the various liver enzymes in euthyroid and subclinically hypothyroid patients.

In our study the liver enzymes Bilirubin, ALP, AST and ALT showed higher values in subclinically hypothyroid patients as compared to the euthyroid patients.

DISCUSSION

Recent studies report an association between hypothyroidism, or subclinical hypothyroidism, and CBD stones. The higher prevalence of hypothyroidism in CBD stone patients compared to gallbladder stone patients suggests that not only changes in the cholesterol metabolism, or bile excretion rate, but particularly changes in the function of the sphincter of oddi (SO) that may underline the association between CBD stones and hypothyroidism. It seems likely that the lack of T4 in hypothyroidism gives rise to a reduction in bile flow in many ways. In addition to the increased cholesterol load in bile and the reduced bile secretion rate, the deficiency of the prorelaxant effect of T4 on the SO appears to be a crucial factor leading to the reduced bile flow in hypothyroidism. Studies with subclinical hypothyroid patients have demonstrated that a positive effect on the changes in the serum cholesterol level, on cardiovascular effects, or on neuromuscular symptoms may be achieved with early replacement treatment with thyroxine and it can be assumed that patients at risk of forming CBD stones due to subclinical hypothyroidism may also benefit from such early treatment. Most importantly, when treating patients with CBD stones, clinicians should be aware of the possible hypothyroid background and consider examining the thyroid function, at least in female patients over 60 years of age, in which group the prevalence of subclinical hypothyroidism is the highest.¹¹

In our study, the prevalence of subclinical hypothyroidism was 30%, the prevalence of borderline subclinical hypothyroidism was 6.67% (total 36.67%). In the study done by Laukkarinen et al⁹ (2007), in CBD stone patients the prevalence of subclinical hypothyroidism was 5.3%, prevalence of borderline subclinical hypothyroidism was 5% (total 10.2%) compared to 1.4% and 1.4% respectively (total 2.8%, 4/142) in the control group.

In the present study, the prevalence of subclinical hypothyroidism in women older than 50 years was 41.67% in the CBD stone patients. The prevalence of subclinical hypothyroidism in women older than 60 years in our study was 28.57% in the CBD stone patients (as compared to 11.4% in CBD stone and 1.8% in control patients in the study done by Laukkarinen et al⁹ in 2007).

In our study the liver enzymes Bilirubin, AST, ALT and ALP showed higher values in subclinically hypothyroid patients as compared to the euthyroid patients. These findings suggest that the reduced prorelaxing effect of T4 on the SO may result in delayed emptying of the biliary tract and together with the changes in cholesterol metabolism and decreased hepatocyte excretion rate, may compose an important explanation for the increased association of CBD stones and hypothyroidism. In the study done by Yadav et al¹⁰ (2013) also, AST, ALT and ALP showed higher values in subclinically hypothyroid patients as compared to the euthyroid patients.

Subclinical hypothyroidism is a prevalent condition among adult population, however it is frequently overlooked. The previous studies about the prevalence of subclinical hypothyroidism in CBD stone patients are very few in number.

CONCLUSION

In conclusion, subclinical hypothyroidism is common in CBD stone patients, which supports the hypothesis that hypothyroidism might play a role in the formation of CBD stones. Further studies are needed to investigate whether early treatment of subclinical or clinical hypothyroidism could prevent the CBD stones in these patients. At least a subgroup of CBD stone patients i.e. women older than 50 years should be screened for thyroid function and offered replacement therapy if required.

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