# **Original Research Article**

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# Gall stones and hypothyroidism: a double jeopardy

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# ABSTRACT

**Background:** Gall stones are one of the frequent biliary pathologies in the biliary system. Gall stones are deposition of bile pigments, cholesterol and calcium salts in the form of hard crystalline mass in the gall bladder. Saturation of bile in gall bladder, bile stasis due to sphincter of Oddi dysfunction, biliary sludge and change in chemical disproportion of bile are all risk factors for gall stone development. Thyroid disorders are also a very common endocrine pathology. On the Oddi sphincter, thyroid hormone receptors are present, and thyroxine has a strong relaxing effect on the sphincter. Hypothyroidism reduces the gall bladder contractility and causes lipid metabolism alteration which leads to biliary stasis. These promote the gall stone formation.

**Methods:** A single centre cross-sectional study, was done among 86 patients diagnosed with cholelithiasis clinically and confirmed by ultrasonography. All patients were subjected to thyroid profile test, liver function test, fasting lipid profile test. Patients with a history of hypothyroidism were excluded from the study.

**Results:** Among 86 study subjects, 29 (33.7%) of study subjects had hypothyroidism, out of which 21 (24.4%) had subclinical hypothyroidism, 8 (9.3%) had clinical hypothyroidism. Of the remaining subjects 4 (4.7%) were hyperthyroid and 53 (61.6%) were Euthyroid. A total of 24 subjects had dyslipidaemia of which (15) 62.5% had clinical and sub clinical hypothyroidism (p<0.001).

**Conclusions:** In the evolution of Gall stones in hypothyroid patients, decreased liver cholesterol metabolism, decreased bile emptying and decreased Oddi relaxation sphincter play a role. In our study there was a strong association between hypothyroidism and gall stones. Hypothyroid patients also had abnormal total cholesterol, triglycerides and ALP levels.

Keywords: Gall stones, Thyroid disorders, Dyslipidaemia, Bilirubin

#### **INTRODUCTION**

Gall stones are the most frequent biliary pathology. Stones in the gall bladder are small, hard crystalline balls abnormally developed from calcium salts, bile pigments and cholesterol.<sup>1</sup> Saturation of bile in gall bladder, bile stasis due to sphincter of Oddi dysfunction, biliary sludge and change in chemical disproportion of bile are all risk factors for gall stone development.<sup>2</sup> Thyroid disorders are also a very frequent endocrine pathology. Hypothyroidism produces elevated cholesterol levels leading to super saturation of the bile. Thyroid hormone has a negative effect on HMG Co-A reductase enzyme which in turn regulates cholesterol levels. As a result, decreased thyroid function leads to hypercholesterolemia and dyslipidaemia.<sup>3</sup> Thyroid hormone reduces the metabolism of cholesterol by acting on the liver, it also acts on hepatic sinusoids and regulates the metabolic activity.<sup>4</sup> The main factor that contributes to formation of cholesterol stones is super saturation of cholesterol by bile.5 the Hypothyroidism also decreases relaxing of the sphincter of causes gallbladder hypomotility, reduces Oddi, contractibility and decreases filling causing prolonged accumulation and decreased flow capacity of bile in the gallbladder.<sup>6</sup> This leads to decreased bile clearance which in turn causes nucleation and gall stone formation.<sup>7</sup> During anaesthesia, hypothyroidism may lead to decrease in spontaneous breathing, myocardial function depression, reduced plasma volume, baroreceptor function irregularity, hyponatremia, hypoglycaemia, anaemia, and impaired metabolism of hepatic drugs.<sup>8</sup>

#### **METHODS**

This study was a single centred cross-sectional observational study and was conducted at our institute. within the span of 18 months from February 2019 till August 2020. Considering the prevalence of hypothyroidism and using the formula  $n=4pq/L^2$ , with absolute precision error (L) of 11% and 10% non-response error, the sample size was calculated. All the patients who presented to out patient department with features of Gall stone disease or incidentally found silent gall stones were included in our study. Patients who were seriously ill and who had been previously diagnosed with thyroid disorders or Choledocholithiasis were excluded from this study. A total of 86 patients were included and informed written consent was taken from all patients before the initiation. A thorough history and clinical examination to check for thyroid disorders was done. Co-morbidities like diabetes and hypertension history were taken into account. All patients were subjected to thyroid profile test, liver function test and fasting lipid profile. All the data collected was entered in excel sheet and using SPSS software the statistical results were recorded

#### RESULTS

Our study was conducted among 86 patients who were diagnosed with cholelithiasis. Most of the patients belonged to the age group off 40-50 years with 66.3% being women and remaining 33.7% men. In the study population around 20 (23.2%) patients were hypertensive and 24 (27.9%) were diabetic. On detailed history we found 8 (9.3%) had features suggestive of hypothyroidism, 4 (4.7%) had features suggestive of hyperthyroidism out of which 1 (1.2%) had toxic symptoms. Based on the thyroid function test and values of T3, T4 and TSH, 53 (61.6%) subjects were Euthyroid, 21 (24.4%) subjects had subclinical hypothyroidism, 8 (9.3%) subjects were hyperthyroid.

All the patients were also subjected to liver function test and lipid profile and we found that albumin level was low in 7 (8.1%) patients and 2 (2.3%) subjects had high direct bilirubin level. Out of 29 subjects who had hypothyroidism, 15 (51.7%) had high cholesterol levels and 20 (68.9%) had high triglycerides as compared to patients with euthyroid status [Total = 53 patients, 1 (1.8%) had high cholesterol and 11 (20.7%) had high Triglycerides]. 23 (79.3%) of hypothyroid patients also has elevated ALP as compared to 0 in Euthyroid patients.





Figure 1: Age distribution among study population.



Variables		Diagnosis of thyroid disorders (%)				
		Clinical hypothyroidism	Subclinical hypothyroidism	Hyperthyroidism	Euthyroid	P value
Albumin	Low	2 (28.6)	2 (28.6)	0	3 (42.9)	0.22
	Normal	6 (7.6)	19 (24.1)	4 (5.1)	50 (63.3)	
Direct Bilirubin	Normal	8 (9.5)	20 (23.8)	4 (4.8)	52 (61.9)	0.623
	High	0	1 (50)	0	1 (50)	
ALP	Normal	1 (1.6)	5 (7.9)	4 (6.3)	53 (84.1)	<0.001*
	High	7 (30.4)	16 (69.6)	0	0	

#### Table 1: Thyroid profile and liver function test.

Variables		Diagnosis of thyroi				
		Clinical hypothyroidism	Subclinical hypothyroidism	Hyperthyroidism	Euthyroid	P value
Cholester ol	Normal	5 (8.1)	9 (14.5)	3 (4.8)	45 (72.6)	0.002*
	High	3 (12.5)	12 (50)	8 (33.3)	1 (4.2)	
TG	Normal	3 (5.6)	6 (11.1)	3 (5.6)	42 (77.8)	<0.001*
	High	5 (15.6)	15 (46.9)	1 (3.1)	11 (34.4)	
LDL	Normal	6 (10.7)	14 (25)	3 (5.4)	33 (58.9)	0.93
	High	2 (6.7)	7 (23.3)	1 (3.3)	20 (66.7)	

## Table 2: Hypothyroidism versus dyslipidaemia.

## DISCUSSION

Our study was conducted among a total of 86 subjects with radiological evidence of cholelithiasis. There was a predominance of women (66.3%) as compared to the men. The higher incidence of gall stones in women was in concordance to a study done by Ghadhban et al.<sup>9</sup>

The results of our study are comparable with a study conducted by Ahmmed et al who demonstrated that among 232 patients with cholelithiasis, 13.2% were hypothyroid and among those 68.8% were subclinical hypothyroid and 31.2% were clinical hypothyroid.<sup>10</sup> The strong influence of thyroid hormones on both lipid metabolism as well as in the motor function of the biliary system paves way for this high incidence in hypothyroidism. However, Watali et al in his cross-sectional study of 200 patients remarked that there was no strong association between gall stone disease and hypothyroidism.<sup>11</sup>

Our study showed that dyslipidaemia in hypothyroidism is much higher as compared to euthyroid patients (p<0.001). Marwaha et al in hi study showed that in adults with hypothyroidism there was a significant increase in serum total cholesterol and LDL values.<sup>12</sup> Moreover, Hussain et al in his study showed significantly high levels of total cholesterol, triglycerides and LDL among sub clinical hypothyroid patients compared to the controls.<sup>13</sup> Likewise, Pedrelli et al showed increased levels of total cholesterol and LDL among hypothyroidism patients.<sup>14</sup> We attribute this to the effect of thyroid hormone on HMG CoA Reductase Enzyme, and the influence of Thyroxine in lipid metabolism in liver.<sup>15</sup> This finding is however in contradiction to Ahmmed Hassan Issa et al, who in his study among 232 patients, 175 patients with dyslipidaemia proved that only 25 were hypothyroid stating there was no correlation between hypothyroidism and cholelithiasis (p=0.92).<sup>10</sup>

Alkaline phosphatase, an enzyme produced by the biliary epithelium, was found to be in increased in 23 patients, all of who had hypothyroidism. Alkaline phosphatase was normal in Euthyroid and hyperthyroid patients. This could be secondary due to the lack of effect of Thyroid hormone on special receptors which facilitate biliary motility.<sup>16</sup> Lack of thyroxine promotes bile stasis and sphincter on Oddi dysfunction which in turn increases biliary pressures and Alkaline phosphatase levels. This is a significant finding as these patients may eventually develop Choledocholithiasis. In other studies, conducted by Steenbergen et al and Inkinen et al in their stated that the increased incidence of biliary stones in hypothyroidism is due to hypercholesterolemia, hypotonia of the gall bladder and reduced excretion of bilirubin.<sup>17,18</sup>

The limitations of our study are small sample size, conducted in a simple centre and patients with choledocholithiasis were excluded from this study. We propose to conduct a multi-centric, large population-based studies in order to provide a higher level of evidence.

# CONCLUSION

To conclude we propose that all patients with cholelithiasis and dyslipidaemia must be evaluated for thyroid function abnormalities in patients with hypothyroidism. Alkaline phosphatase levels must be evaluated as there is a higher chance of incidence of primary biliary stones due to biliary dysmotility and sphincter of Oddi dysfunction.

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