e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15 (6); 1289-1294

Original Research Article

Study to Determine the Association of Cholelithiasis, Choledocholithiasis and Hypothyroidism

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Received: 20-03-2023 / Revised: 11-04-2023 / Accepted: 05-05-2023
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Conflict of interest: Nil

Abstract:

Introduction: Hypothyroidism causes dyslipidaemia and stasis of bile and sphincter of oddi dysfunction causing cholelithiasis and choledocholithiasis.

Aim: to study the prevalence of hypothyroidism in patients presenting with cholelithiasis/ choledocholithiasis.

Methods: This cross-sectional study was conducted on 100 patients having cholelithiasis/choledocholithiasis. All the patients were assessed for thyroid profile, lipid profile and prepared for cholecystectomy after abdominal ultrasound.

Results: Among 100 patients, the majority them were in 40–49 (40%) years age group, 24 (35.29%) of them were females and 16 (50.00%) were males. 26 patients have hypothyroidism (7- clinical and 19 – subclinical). The mean total cholesterol level was 151.46 ± 26.57 mg/dl in euthyroid and 232.34 ± 33.72 mg/dl in hypothyroid patients, mean LDL level was 95.27 ± 21.46 mg/dl in euthyroid and 153.92 ± 28.68 mg/dl in hypothyroid patients which was statistically significant ($p<0.0001$). Mean HDL level was comparable in all patients. Among the hypothyroidism patients 18 (69.29%) were female and 8 (30.77%) patients were male.

Conclusion: When treating patients with cholelithiasis or choledocholithiasis, physicians should be aware of the possible background of hypothyroidism and should consider evaluation of thyroid function in female patients at least 40 years of age.

Keywords: cholelithiasis, choledocholithiasis, hypothyroidism, dyslipidaemia

Introduction

It has been debated for many years whether thyroid disease can cause cholelithiasis. The prevalence of cholelithiasis has been reported to be approximately 5-26% in various countries [1]. The prevalence of cholelithiasis in central India is approximately 4%. [2] The etiology of cholelithiasis appears to be multifactorial. [3,4] In both animal and human studies, thyroxine (T4) has direct pro-relaxant effects on the sphincter of Oddi (SO) expressing thyroid hormone receptors β1 and β2. This pro-relaxation effect of T4 is mediated through a mechanism that requires the synthesis of new mRNA and protein, followed by activation of ATP-dependent K+ channels. Hypothyroidism has been shown to cause abnormalities in lipid metabolism, alter the rate of bile excretion, and lead to gallstone formation. Recent studies have demonstrated a relaxing effect of serum total thyroxine (T4) on the sphincter of Oddi in both humans and pigs. [5] [6] Some studies have

reported a high prevalence of hypothyroidism (both overt and subclinical) in cholelithiasis, with T4 A possible link between low levels and CBD stones is supported. [6] In patients with hypothyroidism, impaired cholesterol metabolism, impaired bile secretion, and impaired relaxation of the sphincter of Oddi are thought to contribute to cholelithiasis and bile duct stones (CBD). [7] Volzke et al. [8] showed an association between high levels of thyroid-stimulating hormone (TSH) and cholelithiasis. In 2003, Laukkarrinen et al. [9] and Yousif et al. [10] described the effect of hypothyroidism on biliary emptying time. Many other studies have shown a high prevalence of hypothyroidism (subclinical or clinical) of approximately 8.8% in patients with cholelithiasis. [4, 5, 8, 11] Studies have shown that Delhi has the highest incidence of cholelithiasis in women in the world, at 21.5 per 100,000 [12]. Cholelithiasis is common in healthy young to middle-aged people, with a prevalence of approximately 11% to 36%. The prevalence of hypothyroidism in India is approximately 10.95% and it is estimated that approximately 42 million people in India suffer from some form of thyroid disease. [13,14]

Aim: of the current study was to investigate the prevalence of clinical and subclinical hypothyroidism in patients with cholelithiasis.

Methods:

100 patients of each age group diagnosed with cholelithiasis. This prospective study conducted at Ajmer Medical College and Hospital. Patients with a history of thyroid surgery or previous exposure to radioactive iodine who were taking cholesterol-lowering drugs were excluded from the study. The study population was selected by a targeted sampling technique based on inclusion and exclusion criteria. Prior to selection, a routine medical history, physical examination, and investigations were performed to rule out comorbidities and general debility. Thyroid function tests including name, age, gender, patient ID (IP number), diagnosis, FT3, FT4, TSH and quantitative analysis of serum lipid profiles including serum total cholesterol, serum LDL cholesterol, serum triglycerides and serum HDL cholesterol were also done.

Statistical Analysis:

Data thus collected was analyzed by Epi info software of CDC. Quantitative variables expressed in frequency and quantitative variables expressed in mean and standard deviation. Statistical tests such as t-test, Chi-Square test, Pearson test were applied and p- value <0.05 was significant.

Results:

The mean age of the overall patient population for the study was 45.97 ± 11.73 years and it ranges between 20 years to 70 years. Majority of the patients are in the age range of 40 to 49. 32% of the patients are male and the rest 68% are female.

Table 1: Socio demography

Age Groups	Male	Female	Total (%)
20 – 29	3	6	9.00
30 – 39	3	19	22.00
40 – 49	16	24	40.00
50 – 59	6	13	19.00
60 – 70	4	6	10.00
Total	**32**	**68**	**100**

Total 38% patients have comorbidites (12 have diabetes mellitus, 19 have HTN and 7 have both).

Hypertension (19%) was the predominant co- morbidity followed by diabetes mellitus (12%) among the study subjects.Across the

study population, patients with cholelithiasis, most often presented with multiple gallstones (62%), followed by a single gallstone (29%). Most patients with cholelithiasis and hypothyroidism had multiple gallbladder stones (42.31%), followed by single gallstones and CBD stones (42.31%), and only 7.69% patients had CBD + GB stones.

Table 3: Radiological findings

Radiological finding	Euthyoroid	Hypothyoid	Total	(%)
GB – Single stone	20	9	29	29.00
GB – Multiple stone	51	11	62	62.00
CBD stone	1	2	3	3.00
Both GB & CBD	2	4	6	6.00
Total	**74**	**26**	**100**	**100**

26% of patients with cholelithiasis/ choledocholithiasis had hypothyroidism. Among these hypothyroidism patients 2 male and 5 female patients had clinical hypothyroidism and 6 male and 13 female had sub clinical hypothyroidism.

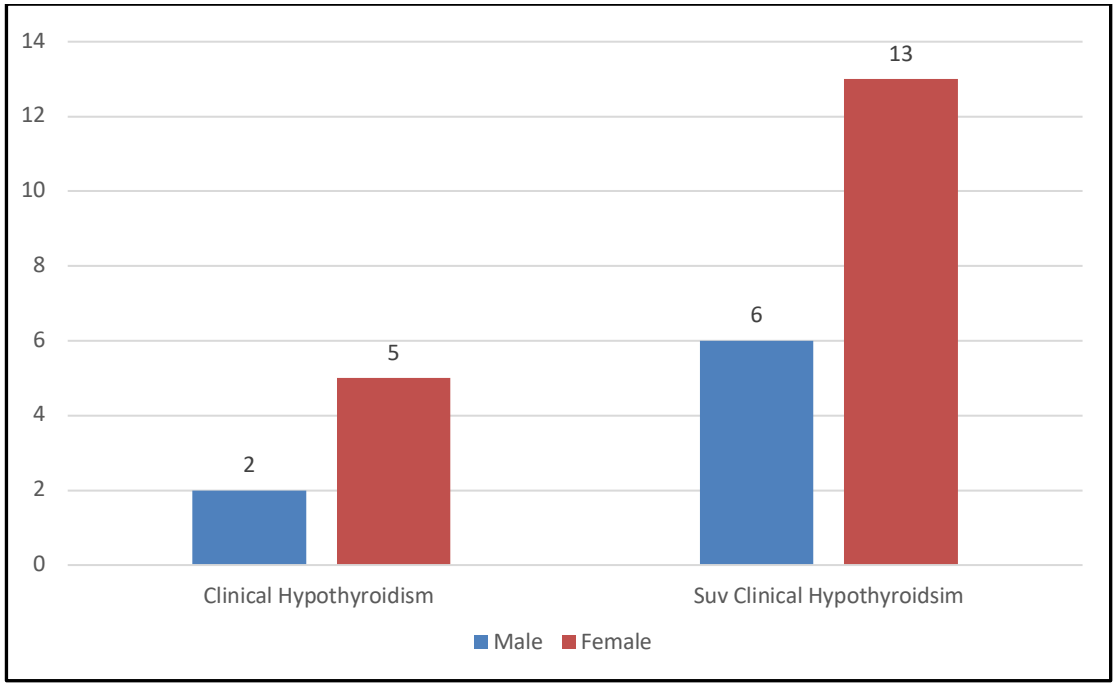

Figure 1: Gender wise distribution of hypothyroidism patients

Lipid profile of study population showed that in 76.93% hypothyroid patients had serum cholesterol levels >200 mg/dl in comparison to euthyroid patients where only 21.62 % patients had serum cholesterol levels >200 mg/dl. This difference in serum cholesterol level was statistically significant (p=0.0001). Serum TC and LDL were statistically higher in hypothyroidism whereas serum HDL cholesterol levels were statistically insignificant.

Table 4: Serum Total Cholesterol Levels in Hypothyroidism patients

Sr Total Cholesterol levels	Gall Stone in Euthyroid patients		Gall stone with hypothyroidism		Chi square	P value
	no	%	no	%		
<200 mg/dl	58	78.38	6	23.07	25.539	**0.0001 (S)**
>200 mg/dl	16	21.62	20	76.93		
Total	**74**	**100.00**	**26**	**100.00**		
Mean (mg/dl)	**151.46 ± 44.95 44.95**		**232.35 ± 35.63**		**<0.0001 (S)**	
Mean HDL	**37.68 ± 5.56 44.95**		**36.81 ± 5.40**		**0.491 (NS)**	
Meal LDL	**96.43 ± 12.97 44.95**		**153.92 ± 13.09**		**<0.0001 (S)**	

Most patients were treated with laparoscopic cholecystectomy (75%), 3 patients with CBD stones were treated with ERCP, and of a total of 6 patients with GB and CBD stones, 4 were ERCP + lap chole and 2 with CBD exploration. Nine patients received conservative treatment.

Table5: Management of the study subjects

Procedure	Patients in Euthyroid state	Patients in Hypothyroid state	Total
Lap. Cholecystectomy	59	16	75
Open / Lap. Converted	4	3	7
Open + CBD	1	1	2
ERCP	1	2	3
ERCP + Lap.	1	3	4
Conservative	8	1	9
Total	**74**	**26**	**100**

Discussion:

Gall stone development affected by the multiple risk factors. Management of gall stone consists of diagnosis with the help of imaging modalities followed by conservative or by surgery. However, till now hypothyroidism is not proven risk factor for gallstones.

In our study mean age was 45.97 ± 11.43 yrs with range of 20 - 70 years, 32 were male and male to female ratio is 1: 2.125. This is showed in studies that in female patient prevalence of cholelithiasis are higher. Several studies supported that pregnancy and sex hormones increases the risk of gall stone diseases. [1] When comorbid factors were analyzed, HTN was the main comorbid factor, followed by diabetes. HTN was found to be a comorbid factor in 19 of her patients (19.00%). DM he was found to be a comorbid factor in 12 people (12.00%). Seven patients had both DM and HT. As mentioned above, cholelithiasis is a disease of the elderly, so hypertension and diabetes were the main concomitant factors. There was no evidence of a significant association with cholelithiasis. Similarly reported by Patel AM et al (2022) [15], Sachdeva et al. [16] and Gupta et al. [17].

In our study 26 patients (26.00%) had hypothyroidism. 18 (69.23%) patients out of 26 were female and only 8 (30.77%) were male among hypothyroidism patients. Of these 26 patients, only 7 had clinical hypothyroidism and the remaining 19 were diagnosed with hypothyroidism. Of these 26 patients, 18 of whom were females, Similarly reported by Ibrahim SL et al[18] and Koujalagi RS et al [19].

In our study, 64 patients had total cholesterol levels of 200 mg/dl. Of these, 16

patients were euthyroid and 20 were hypothyroid. These findings were statistically significant (p=0.0001). Mean total cholesterol levels were 151.46 ± 44.95 mg/dl in euthyroid patients and 232.35 ± 35.63 mg/dl in hypothyroid patients. This difference was significantly higher in hypothyroid patients (p<0.0001), similarly reported by Patel AM et al (2022) [15] and Kumar DV et al (2019) [3]. Similarly, Khan MAH et al [20] showed significant high total cholesterol (p<0.001) among hypothyroidism cases (n=80) where it was 241.56 ± 60.05 mg/dl when compared to euthyroid controls (n=31) where it was 146.94 ± 23.21 mg/dl.

Mean HDL cholesterol levels were 37.68 ± 5.56 mg/dl in euthyroid patients and 36.81 ± 5.40 mg/dl in hypothyroid patients. This difference in serum HDL cholesterol levels was similar in both groups (p=0.491). Mean LDL cholesterol levels were 96.43 ± 12.97 mg/dl in euthyroid patients and 153.92 ± 13.09 mg/dl in hypothyroid patients. This difference was significantly higher in hypothyroid patients (p<0.0001).

HDL cholesterol was comparable in the studies done by Lee WY et al [21] and Efstathiadou Z et al [22] where serum HDL level in subclinical hypothyroidism was statistically comparable when compared to euthyroid control.

In our study evaluating USG and CT patients, 62 patients (62%) had multiple gallbladder stones and 29 patients (29%) had a single gallbladder stone. Three patients had CBD stones and six patients had both CBD and GB stones. Of the total 26 hypothyroid patients who underwent radiological examination, 11 (42.31%) had multiple gallbladder stones and 9 (34.61%) had a single gallbladder stone. Two patients had CBD stones and four patients had both CBD and GB stones. Similarly seen by Patel AM et al[15].

Conclusion: When treating patients with cholelithiasis or choledocholithiasis, physicians should be aware of the possible background of hypothyroidism and should consider evaluation of thyroid function in female patients at least 40 years of age.

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