Section: General Surgery

Original Research Article

ASSOCIATION BETWEEN CHOLELITHIASIS AND THYROXINE TREATED HYPOTHYROIDISM- A CROSS SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Cholelithiasis or gallstone disease is a common prevalent condition in India. It is said to be a multifactorial disease. Modifiable risk factors like age, gender, pregnancy and non-modifiable risk factors like genetics, metabolic disorders can cause cholesterol supersaturation of bile, cholesterol precipitation and stone formation. Many population based studies have found an association between hypothyroidism and cholelithiasis.[1] This cross-sectional study is done to investigate the prevalence and association between cholelithiasis and thyroxine treated hypothyroidism in our Institute. **Materials and Methods:** A study population of 211 patients with diagnosed cholelithiasis was taken for analysis. Serum TSH was used to assess thyroid function. Cholelithiasis was defined by symptoms of cholelithiasis and the presence of gallstones on ultrasound. Patients with a history of hypothyroidism who were on various doses of thyroxine and developed cholelithiasis were calculated and mentioned as prevalence in percentage form. The p value for causal association between thyroxine treated hypothyroidism and cholelithiasis, if TSH value of 6mg/dL is considered as cut off, was considered statistically significant if less than 0.05. Chi-Square test was used to find statistical significance. **Results:** Patients with thyroxine treated hypothyroidism with cholelithiasis were evaluated further to get causal association. Among the 211 patients who were diagnosed with cholelithiasis, 16 (7.58%) were found to be hypothyroid and are currently being treated with Thyroxine (83.5 +- 39.1) mcg/day. There were 12 patients in the sample (75%) who were euthyroid and 4 patients (25%) with high TSH levels. Patients with diagnosed hypothyroidism with cholelithiasis were more often of female gender (93.8%). The value for causal association between thyroxine treated hypothyroidism and cholelithiasis was 0.0001. **Conclusion:** Our study concludes that cholelithiasis has a multifactorial etiology. It has a strong correlation with hypothyroid state in the patient, the progression of which is seen irrespective of treatment with thyroxine supplement.

INTRODUCTION

Cholelithiasis or gallstone disease (GD) is a hepatobiliary disease, caused by impaired metabolism of cholesterol, bilirubin and bile acids. It is a multifactorial disease, the causes of which are age, gender, genetic factors, obesity, prolonged fasting, pregnancy, metabolic disorders like hypothyroidism etc which contribute to cholesterol supersaturation of bile, cholesterol precipitation and crystallisation core formation.

It maybe also be due to impairment of basic gallbladder functions like contraction, absorption, secretion etc.[2]

In cholesterol metabolism when cholesterol concentration exceeds the solubilizing capacity of bile it leads to supersaturation of bile. Unilamellar vesicles are formed which ultimately undergo

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nucleation in the presence of mucin and calcium for cholesterol monohydrate crystals. These crystals form microstones which in turn form a gallstone.[3]
Thyroid hormones are the main regulators in lipid metabolism by stimulating the mobilisation and degradation of lipids and de-novo fatty acid synthesis in the liver. Increased cholesterol levels in hypothyroidism is mainly because of a reduction in LDL receptor activity. This reduced LDL receptor activity is because of the effect of thyroid hormone on serum regulatory element-binding protein-2(SREBP-2). Hypercholesterolemia causes supersaturation of bile which leads to cholesterol crystal formation.[4]
Though many population based studies correlate cholelithiasis with hypothyroidism,[1] we studied the actual prevalence of the disease among patients with thyroxine treated hypothyroidism by using a cross–sectional study in our institute.

MATERIALS AND METHODS

This study is a cross-sectional study conducted at Apollo Institute of Medical and Sciences and Research, in the General Surgery Department, in Hyderabad to investigate the prevalence and association between cholelithiasis and thyroxine treated hypothyroidism. A study sample of 211 with diagnosed cholelithiasis was taken. Cholelithiasis was defined by either symptoms of cholelithiasis or the presence of gallstones on ultrasound. Patients having history of syndrome X, hyperlipidemia, Diabetes mellitus, Non-alcoholic steatohepatitis were excluded from the study.
The patients were asked about the history of hypothyroidism. Those with hypothyroidism were asked about treatment details with thyroxine, including the dosage. Thyroid profile was checked in all to fit objective evidence of thyroid control. Patients with a history of hypothyroidism who were on various doses of thyroxine and developed cholelithiasis were calculated and mentioned as prevalence in percentage form.
Considering the prevalence of cholelithiasis in Hyderabad to be 9.03,[5] the study required a sample size of 211 for estimating the expected proportion with 5% absolute precision and 95% confidence interval.[6] Proportions were calculated for cholelithiasis and hypothyroidism. Chi-square test was used to study the association between cholelithiasis and hypothyroidism. P value was considered significant if less than 0.05.

RESULTS

Cholelithiasis was defined by symptoms of cholelithiasis and the presence of gallstones on ultrasound.
Among 211 diagnosed cases of cholelithiasis, there were 16 patients with Thyroxine treated hypothyroidism. (7.6%). Serum TSH was used to assess functional thyroid status.
The normal TSH value for the study was taken as 6 mIU/mL.
There were 12 patients in the sample (75%) with normal TSH and 4 patients (25%) with high TSH levels.
The three groups were compared with baseline demographic and clinical characteristics. [Table 1]
Patients with diagnosed hypothyroidism with cholelithiasis were more often of female gender. There were 78 male patients (37%) and 133 female patients (63%) in total population. [Table 2] The ratio was 1:15 for patients with hypothyroidism.
The mean age of patients in the sample was 44.31 +- 2.370. [Table 3]
In patients with history of cholelithiasis and hypothyroidism, the average dose of Thyroxine used by the patients was 83.5 +- 39.1. [Table 4]
The no. of years since diagnosis of hypothyroidism was taken into consideration and the average was 6.72 +- 7.58. [Table 4]

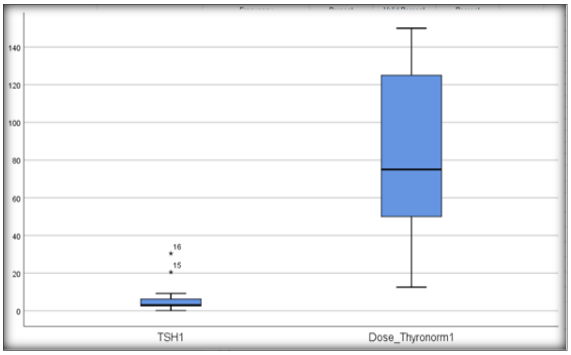

Figure 1

Among 211 patients, 16 were on various doses of Thyroxine for hypothyroidism, out of which 4 were uncontrolled. The causal association with the chi-square test gave the two-tailed P value of 0.0001. The association is considered to be statistically significant.

Table 1

TSH (mIU/L)	frequency	percent	Valid percent	Cumulative percent
<6	12	75.0	75.0	75.0
>=6	4	25.0	25.0	100.0
Total pts with history of hypothyroidism	16	100.0	100.0	

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Table 2

	frequency	percent	Cumulative percent
female	133	63	63
male	78	37	100.0
total	211	100.0	

Table 3

	N	Minimum	Maximum	Mean	Std. Deviation
Age	211	26	67	44.31	12.370

Table 4

	N	Minimum	Maximum	Mean	Std. Deviation
Thyroxine dose for hypothyroid patients	16	12.50	150.00	83.5938	39.18938
Years of hypothyroidism	16	0.17	30.00	6.7244	7.58828
TSH in hypothyroid patients	16	0.09	30.44	6.3061	8.02655
Valid N	16				

Table 5

	TSH level <6	TSH level >6	Total
Thyroxine treated hypothyroidism	12	4	16
Euthyroid patients	195	0	195
Total patients with cholelithiasis	207	4	211

DISCUSSION

In our study consisting of a sample population of 211 patients with diagnosed cholelithiasis,133 were of female gender (63%) and 78 were of male gender (37%). Of these 211 patients, 16 patients were also found to be hypothyroid (7.6%).

Among the 16 patients with hypothyroidism and cholelithiasis, the ratio of males to females was 1:15 and the mean age of the sample population was found to be 44.3 years.

In another study Association between thyroid function and gallstone disease, the hypothyroid patients with cholelithiasis were also more often of female gender (69.8 %) and the mean age was 51.1 years.[7].In the study The prevalence and correlation between subclinical hypothyroidism and gall stone disease in Baghdad teaching hospital, the mean age of patients was 43 years and 81.6% of them were females.[8]

Our study correlates to the aforementioned studies in finding a similar mean age and the prevalence of hypothyroidism with cholelithiasis to be more often in female populations.

Our study shows the prevalence of hypothyroidism in diagnosed cholelithiasis patients to be 7.6%.

The study Prevalence of Thyroid Disorder in Gallstone Disease Patients: A Cross-Sectional Study showed that the prevalence of hypothyroidism in patients with gallstone disease was 30%.[9]

The study Gallstones and hypothyroidism: a double jeopardy shows that the prevalence of hypothyroidism in diagnosed cholelithiasis was 33.7%.[8]

A study The prevalence of hypothyroidism in patients with gallstone disease was conducted in Iraq which showed the prevalence of hypothyroidism in patients with diagnosed cholelithiasis to be 13.8%. 75.4% of the diagnosed hypothyroid patients had an increased lipid profile while 57% had a normal lipid profile which may have been the cause.[10]

This cross-sectional study is done to investigate the prevalence and association between cholelithiasis and thyroxine treated hypothyroidism in our Institute. A sample population of 211 patients diagnosed with cholelithiasis was taken, out of which 16 patients were being treated for hypothyroidism with various doses of thyroxine. The causal association with the chi-square test gave the two-tailed P value of 0.0001, hence the association is considered to be statistically significant, correlating to the aforementioned studies.

CONCLUSION

Our study conclusively demonstrates that cholelithiasis is multifactorial in nature, with a strong correlation to hypothyroidism. Furthermore, we found that thyroxine treatment does not halt disease progression, underscoring the need for a comprehensive approach to management.

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