Research Paper

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Prevalence of Subclinical Hypothyroidism in Gall Stone Disease- A One Year Study

Medical Science

KEYWORDS : Cholelithiasis, hypothyroidism, hyperlipidemia

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ABSTRACT

For decades there has been discussion whether thyroid disorders could cause gall stone diseases. There could be several explanations for possible relation between hypothyroidism and gall stone disease. A cross sectional study was done in Dept of General Surgery, MCH Trivandrum between the period May 1st 2014 to April 31st 2015 to know the prevalence of subclinical hypothyroidism in patients with symptomatic gall stone disease in a tertiary care centre and its statistical significance. During which period total of 93 patients with gall stone disease were studied to see the relation between hypothyroidism and gall stones. For every patient with diagnosed gallstone, full history and clinical examination was taken and laboratory blood test for T3, T4 and TSH. Out of 92 patients with gallstone 50 (54.3%) were females and 42 (45.7%) males. Thyroid disorder in form of subclinical hypothyroidism was found in 12 (13%), (from this percentage 10 (83.3%) were females and males were 2 (16.7%). From 92 cases with gallstones diseases 7(7.6%) cases complaining from goitre. Peak age was less than 40 years. In this study, the higher proportion of hypothyroidism in women with cholelithiasis compared to men was mainly due the earlier symptomatology of gallstone disease in women as well as the higher incidence of thyroid disease in women in general. This leads to an earlier detection and treatment of hypothyroidism in women .Female patients with Gallstones should be checked for serum TSH, T3 and T4 because of high incidence of hypothyroidism among group.

Introduction:

Gallstones are the most common biliary pathology, can be divided into three main types: cholesterol, pigment (black, brown) or mixed stones. In the USA and Europe, 80% are cholesterol or mixed stones, where as in Asia, 80% are pigment stones. Cholesterol or mixed stones contain 51 – 99 % cholesterol plus admixture of calcium salts, bile acids, bile pigment and phospholipids .Gallstones may be single or multiple, large or small those containing calcium salts are radio-opaque. Single stones are uncommon but usually consist mainly of cholesterol and arise due to a disorder of the physico-chemical equilibrium which normally maintains cholesterol in micellar form in the bile, small amount of cholesterol and traces of iron where been detected. Many studies were done to identify risk factor for biliary lithiasis in the west have focused on hypersaturation of cholesterol in bile in nucleation process a critical step in the genesis of bile stone .Thyroid disorder is a prevalent condition among adult population; however, it is frequently over looked. The previous studies about the prevalence of thyroid disorders among healthy subjects are few in number. The recent study from United Kingdom; the prevalence of thyroid disorders among healthy subjects was 2.6%. For decade; there has been a discussion, whether thyroid disorders could cause gallstone disease. Particularly, there are several explanations for a possible relation between hypothyroidism and gallstone disease; these explanations include the known link between thyroid failure and disturbances of lipid metabolism that may consecutively lead to change of composition of the bile. Recent studies also demonstrated low bile flow in hypothyroid subjects. Furthermore, the sphincter of oddi expresses thyroid hormone receptors and thyroxine has a direct prorelaxing effect on the sphincter. Both low bile flow and sphincter of oddi dysfunction are regarded as important functional mechanisms that may promote gallstone formation.The usage of thyroxine was even suspected to dissolve gallstones, however, a spontaneous passage of the stone to the duodenum could be excluded in this case report .In western countries 10-12% of adults develop gallstones. The prevalence of common bile duct (CBD) stones in patients with gallstones varies from 8 to 16% .The pathogenesis of gallstones is complex process involving factors affecting bile content and bile flow. A crucial factor in the forming of bile duct stones is biliary stasis , which may be caused for examples by sphincter of oddi stenosis ,dyskinesia, or bile duct strictures. The prevalence of previously undiagnosed thyroid function abnormalities has never been studied in gallstone patients before .If an increased prevalence of thyroid disorders will be found, it might have an effect on the diagnostic and therapeutic work up of patient with gallstone. Hypothyroidism is the most common cause of secondary hypercholesterolemia, patients with hypothyroidism have serum level of cholesterol approximately 50% higher than level in euthyroid patients and 90% of all hypothyroid patients have elevated cholesterol level.

Materials and Methods:

A cross sectional study was done in Dept. of General Surgery MCH, Trivandrum between 1st of May 2014 and 31st of April 2015 in which 92 patients with gallstones were taken, full history and clinical examination including name, age, sex – etc. and symptoms and signs of

hypothyroidism including (loss of appetite, gaining weight, tiredness, constipation, cold intolerance, menstrual disturbances, bradycardia, presence or absence of goiter etc.) Investigations included were serum Hb, Serum Cholesterol, level of serumT3, T4, and TSH. Patients were divided according to history, clinical examination and laboratory test (T3, T4, TSH) into 2 groups: 1. Subclinical hypothyroidism includes the symptom free patients with TSH concentrations above the upper limit of normal range and T4 and / or T3 being normal limit. (According to our laboratory readings) 2. Euthyroid group where clinical and laboratory tests were normal. All these groups may present with or without goiter. Already diagnosed hypothyroid patients were excluded from the study. All Patients with cholelithiasis, choledocholithiasis (presence of gallstones on ultrasound during the study period was included. Patients with previous history of hypothyroidism on treatment and pregnant were excluded.

Results:

Above mentioned variables where studied among 92 patients and the results were analyzed statistically based on SPSS program (Statistical Package for the Social Sciences).

Sample characteristic's

Age group wise distribution of cases was analyzed , which showed maximum number of cases in the age group < 40 which was closely followed by 41 – 50 age group.

Clinical variables of samples

Regarding the clinical variables of subjects 27.2% presented with pain, 81.5% with dyspepsia, 28.3% with jaundice, and 28.3% with fever, 7.6% with necks swelling, 1.1% with pressure symptoms, 14.1% with symptoms of hyperthyroidism, 31.5% with symptoms of Diabetes Mellitus, 30.4% with HTN and 19.6% with hyper cholesterolemia. Among the subjects 27.2% were having habit of smoking, 25% of alcoholism, 22% had icterus and 19% were obese.

Prevalence of Hypothyroidism

Table 1: Percentage and frequency distribution of subjects according to presence of hypothyroidism

Hypothyroidism	Frequency	Percent
Present	12	13.0
Absent	80	87.0

Association of Hypothyroidism with selected variables

Table 2: Comparison of age based on hypothyroidism

Age	Absent		Present		Odds (95% CI)
	Count	Percent	Count	Percent	
<=40	27	81.8	6	18.2	2.78 (0.51 – 15.06)
41 - 50	28	87.5	4	12.5	1.79 (0.30 – 10.60)
>50	25	92.6	2	7.4	1

χ^2 = 1.53, p = 0.465

Table 3: Comparison of sex based on hypothyroidism

Sex	Absent		Present		Odds (95% CI)
	Count	Percent	Count	Percent	
Male	40	95.2	2	4.8	1
Female	40	80.0	10	20.0	5.0 (1.03 – 24.28)

χ^2 = 4.67*, p = 0.031

Table 4: Comparison of DM based on hypothyroidism

DM	Absent		Present		Odds (95% CI)
	Count	Percent	Count	Percent	
Yes	27	93.1	2	6.9	1
No	53	84.1	10	15.9	2.55 (0.52 – 12.45)

χ^2 = 1.41, p = 0.235

Table 5: Comparison of HTN based on hypothyroidism

HTN	Absent		Present		Odds (95% CI)
	Count	Percent	Count	Percent	
Yes	26	92.9	2	7.1	1
No	54	84.4	10	15.6	2.41 (0.49 – 11.79)

χ^2 = 1.24, p = 0.266

Table 6: Comparison of hyper cholesterolemia based on hypothyroidism

Hyper cholesterolemia	Absent		Present		Odds (95% CI)
	Count	Percent	Count	Percent	
Yes	18	100.0	0	0.0	1
No	62	83.8	12	16.2	0.01 (0 – 0)

χ^2 = 3.36, p = 0.067

Discussion:

During last two decades the etiologies of Gall stones have been evaluated more seriously. In addition to classic risk factors such as age, gender, obesity and genetics, the associations between gall stones and delayed emptying of the biliary tract in hypothyroidism have been shown. This is related to lack of the pro relaxing effect of the thyroid hormone on SO contractility. In this study we have evaluated the prevalence of thyroid dysfunction in patients with gall stones diseases. Serum TSH is a hallmark of thyroid dysfunction. The subclinical form of hypothyroidism is characterized by increased serum TSH levels along with normal serum FT4 levels and a lack of clinical symptoms. The mean TSH levels in the present study among the case group were higher than the control group. There were more females with subclinical hypothyroidism with gall stone disease.

This can possibly be attributed to the fact that females have usually been more considered to have thyroid dysfunction. A study by Laukkarinen has shown subclinical hypothyroidism to be a common problem among patients with CBD stones. He concluded that hypothyroidism played a role in the formation of CBD stones secondary of its effects on SO relaxation; which in turn might be influence on emptying of the biliary system. The pro-relaxing effect of T4 on SO has been previously reported. The present study, there was a close relation between T4 levels according to binary analysis with gall stone diseases (p<0.01) which was similar to earlier studies, however this was not confirmed in multivariate analysis. Some studies have reported that thyroxin replacement therapy has a positive effect on cholesterol level, cardiovascular, neuromuscular and choledolithiasis. We did evaluate the influence of thyroxin replacement therapy and the results where the same.

It is expected that increasing age increases subjects' exposure to risk factors of gall stones or thyroid dysfunctions. In our study there was no association between age and thyroid disorders which might be related to the number of patients. This correlation has been reported in different studies. In one study on cadavers there was a positive relationship between age and prevalence of cholelithiasis. According to different studies, among the elderly, the rate of hyperthyroidism was 2.1-6% and for hypothyroidism it was 2.0-2.9%. The prevalence of subclinical hypothyroidism in women older than 60 years of age was 11.4% in CBD-stone patients compared with 1.8 % in control patients.

We have also evaluated metabolic factors in the study group. Obesity is considered as a risk factor for gallstones. Supersaturated bile among obese subjects may be there before this phenomenon. In our study, there were more overweight cases compared to controls which supported results from previous studies.

Patients with hypothyroidism are more prone to have high serum cholesterol levels. The mechanism of thyroid hormones on cholesterol metabolism is multifactorial. Thyroid hormones influence the synthesis, absorption and usage of cholesterol. In the present study, although the mean cholesterol levels in the case group was not comparable with the control group; differences were observed in mean HDL, LDL, and TG levels. These results were almost consistent with other studies. In regression multivariate analysis, we concluded that serum- TSH level was an independent factor that could be considered a risk factor for the formation of Gall stones.

In conclusion, thyroid dysfunction is more common among patients with Gall stones and it may be a risk factor for biliary stone formation. This may be attributed to the absence of the pro-relaxing effects of thyroid hormones. Earlier, an association between gallstone and diagnosed hypothyroidism and delayed emptying of the biliary tract in experimental and clinical hypothyroidism has been shown, explained at least partly by the lack of prorelaxing effect of T4 on the sphincter of oddi contractility. In this study we further investigated the prevalence of previously undiagnosed hypothyroid abnormalities in gallstone patients. The this study , the higher proportion of hypothyroidism in women with cholelithiasis compared to men was mainly due the earlier symptomatology of gallstone disease in women as well

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as the higher incidence of thyroid disease in women in general. This leads to an earlier detection and treatment of hypothyroidism in women.

In summary, several recent studies report an association between hypothyroidism, or subclinical hypothyroidism, and gall stones. The higher prevalence of hypothyroidism in gall stone patients is due to altered cholesterol metabolism, or bile excretion rate, but particularly changes in the function of the SO that may underline the association between gall bladder stones, CBD stones and hypothyroidism. In our study the prevalence of subclinical hypothyroidism was 13% of the total Patients. And there was no significant relationship between age group involved and sex involved.

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