

FREQUENCY OF SUBCLINICAL HYPOTHYROIDISM AMONG DIAGNOSED CASES OF CHOLELITHIASIS

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ABSTRACT:

BACKGROUND & OBJECTIVE: Thyroid hormones act as foundation for the normal functioning of all the body hormones and body metabolism. The abnormality of thyroid hormones may lead to deranged lipid metabolism with abnormal relaxation of sphincter of oddi. This will cause stasis of bile in gallbladder and biliary channels leading to stone formation. The objective of the study is to determine the frequency of subclinical hypothyroidism among diagnosed cases of Cholelithiasis.

METHODOLOGY: This study was conducted in Surgical Department, Sandman Provincial Hospital Quetta, from January to December 2018. The study has been approved by the ethical review committee of Post Graduate Medical Institute Quetta. It is a cross-sectional study. A total of 193 patients with Cholelithiasis were included in the study. After informed written consent, blood was sent to laboratory for testing the levels of serum TSH, T3 and T4. Samples having TSH values more than 6.0mU/L and serum thyroxin within the normal range 9.0-19.0pmole/L, were labeled as subclinical hypothyroidism.

RESULTS: The data of all the patients between 35 to 62 years of age with Cholelithiasis during the study period was taken and analysis was performed. The inclusion and exclusion criteria were strictly considered. Mean \pm SD of age was 47.03 ± 5.401 with C.I (46.26-47.80) years. Out of 193 patients 25 (13%) were male and 168(87%) were female. Subclinical hypothyroidism was found to be in 16 (8.16%) patients and remaining 177(91.70%) patients were found normal.

CONCLUSION: It was concluded that the incidence of subclinical hypothyroidism in Cholelithiasis patients is low.

KEYWORDS: Cholelithiasis, Subclinical hypothyroidism, Disease management.

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INTRODUCTION:

Cholelithiasis is the most common biliary pathology and divided into three main types: cholesterol stones, pigment (black, brown) stones and the mixed stones. In western world almost 80% are cholesterol or mixed stones, whereas in eastern world, 80% are pigment stones. Cholesterol stones and mixed stones contain 51 – 99 % cholesterol and mixture of bile acid, bile pigment, phospholipids and calcium salts^[1]. The prevalence of Cholelithiasis was reported to be 8 to 26% in western countries^[2]. In Pakistan the estimated prevalence is 9.03%^[3].

Literature has shown that 2.4% female patients treated for hypothyroidism had cholecystectomy^[4]. Many factors are involved in the complex pathogenesis of Cholelithiasis. In hypothyroidism there may be increased risk of gallstone^[5] and common Bile Duct (CBD) stones^[6]. Impaired cholesterol metabolism^[7], decreased bile secretion^[8] and impaired sphincter of oddi relaxation^[9,10] may contribute to Cholelithiasis and CBD stone in patients with hypothyroidism. Another study by Volzke H^[11] revealed an independent relation between Cholelithiasis and high thyroid stimulating hormone (TSH). Johanna Laukkarinen^[12] in 2003 explained delayed emptying of biliary tract with hypothyroidism which is concordant with a study by Hassan Yousif H^[13] that there is relationship between increased serum TSH and Cholelithiasis. Gallstones are either single or multiple or they can be large or small. Radio-opaque stones are those containing calcium salts but radiolucent are seen as well. These radiolucent stones are composed of calcium bilirubinate and of asphalt like products derived from bilirubin degradation. Rarely single stones are seen, consisting of cholesterol due to pathology in physico-chemical equilibrium of cholesterol production and its metabolism^[13,14,15,16]. Studies are conducted in west which focused on supersaturation of cholesterol in bile as identified risk factors for biliary lithiasis^[14]. Thyroid disorders are common among adult population. Among infants it is noted to be 0.01%, among children it is seen in 0.2% whereas in adults and old age population it is noted to be 2.9% and 2.0% respectively^[17,18]. The gender distribution is seen to be 73%

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among females and 27% among males^[16,18]. Previously very little work has been done on thyroid disorders and cholelithiasis among healthy subjects. The prevalence of thyroid disorders in healthy individuals was 2.6% in a recent study in United Kingdom^[17].

The frequency of subclinical hypothyroidism among cholelithiasis is not studied well both nationally and internationally. Up till now the studies have shown a prevalence of 8.8% of subclinical hypothyroidism in gallstones patients^[14,19,20]. If it is found that there is high prevalence of subclinical hypothyroidism among gallstone patients than this may affect the diagnostic and therapeutic approach in gallstone patients. This study is conducted to assess the frequency of subclinical hypothyroidism in gallstone patients.

METHODOLOGY:

It was a cross sectional study. This study carried was out in the Department of Surgery, Sandman Provincial Hospital Quetta, from January 2018 to December 2018. The study has been approved by the ethical review committee of Sandman Provincial Hospital Quetta. This is cross-sectional study of 193 patients. The sample of 193 patients was taken by applying formula $Z^2 \times (1-P) / e^2$ where "Z" is 1.96, "P" is the proportion of disease prevalence that is 8.8%^[14] and "e" is the margin of error keeping 4%. The data was collected from the outpatient Department of Surgery. After taking informed written consent, the blood was sent to laboratory for testing the levels of serum TSH, T3 and T4. After suitable SI unit conversions patients having serum TSH level greater than 6.0 mU/L with normal serum thyroxin levels i.e. below 19.0 pmole/L were taken as subclinical hypothyroid. Inclusion criteria were all patients with Cholelithiasis between 35-62 years of age and of both sexes. Patients with previous history of hypothyroidism and on treatment for hypothyroidism were not included in study.

Statistical analysis was done on SPSS-22. Chi square test was applied for checking association among parameters included in this study.

RESULTS:

Out of 193 subjects, 25 (13%) were male and 168(87%) were female. Among them 2(12.5%) males and 14(87.5%) females had subclinical hypothyroidism. Statistically there was no significant association between hypothyroidism and gender ($p=0.657$). Mean \pm SD of age of study subjects was 47.03 ± 5.401 . Out of 193 subjects, 16(8.16%) have subclinical hypothyroidism while 177(91.70%) were not

having subclinical hypothyroidism. Among the patients with subclinical hypothyroidism, 13(81.25%)patients of 38 to 48 years of age group and only 3(18.75%) patients with in 49 to 62 years of age group were subclinically hypothyroid. The comparison of frequency of subclinical hypothyroid in various age groups was not significant (table-I). As far as the socio-economic status of the subjects having subclinical hypothyroidism was concerned, 8(50.0%) among poor class were subclinically hypothyroid whereas 4(25.0%) patients among both middle and upper class were subclinically hypothyroid as shown in (table-II).

Table-I: Age Distribution N=193.

Age Group	Subclinical Hypothyroidism		Chi –square	p-value
	Yes n (%)	No n (%)		
27-37	0 (0%)	4(2.25%)	2.964	0.202
38-48	13(81.25%)	104(58.75%)		
49-62	3(18.75%)	69(38.98%)		
Total	16(8.16%)	177(91.70%)		

Table-II: Stratification of socio economic status N=193.

Socio Economic Status	Subclinical Hypothyroidism		Chi-square	p-value
	Yes	No		
Poor Class	8(50%)	109(61.58%)	1.982	0.660
Middle Class	4(25%)	35(19.77%)		
Upper Class	4(25%)	33(18.64%)		
Total	16(8.29%)	177(91.70%)		

DISCUSSION:

The aim of the study was to determine the frequency of subclinical hypothyroidism in diagnosed cases of Cholelithiasis. Previously the association between cholelithiasis and hypothyroidism effecting biliary tract drainage has been shown, this is explained as due to lack of relaxing effect of T4 on the smooth muscles of

sphincter of oddi ^[21, 22, 23, 24]. In this study we considered the frequency of undiagnosed subclinical hypothyroid abnormalities among gallstone patients. The most sensitive laboratory investigation in primary hypothyroidism and the most reliable detector of early thyroid failure is serum TSH concentration ^[25]. Patients with normal T4 and T3 levels, but raised serum TSH levels and

clinically asymptomatic are labeled as subclinical hypothyroidism^[26,27]. We studied that the frequency of hypothyroidism with cholelithiasis among females is higher as compared to males. This might be due to early reporting of symptoms of gallstones among female as well as the higher number of females with thyroid disease as compared to males. This leads to an early diagnosis and treatment of both cholelithiasis and hypothyroidism among females. The Serum TSH level is most sensitive test for thyroid failures. T4 levels are reduced in clinical hypothyroidism but remains unchanged in subclinical hypothyroidism^[21,28-31].

In our study majority of the patients had age between 38-62 years, while in a study by Mercado MA^[29] reported older females of above 60 years of age. Another study concluded higher gallstones prevalence in women above 65 years of age, this probably is contributed due to sex hormone imbalance among females of this age group^[4].

This study showed that 25 (13%) patients were male and 168(87%) were female, among them 2(12.5%) males and 14(87.5%) females had subclinical hypothyroidism. As compared with the study of Laukkanen J, et al^[22] there was 82.6% females and 17.4% males with subclinical hypothyroidism which is comparable with current study.

Thyroid hormone has multiple effects on metabolism as well as on cholesterol metabolism^[21,22]. In hypothyroidism when the metabolism of cholesterol is affected, the value of serum cholesterol increases leading to super saturation in bile as well. The sluggish metabolism and body function may also lead to gallbladder hypomotility^[20,21,23], depressed contractility^[22], impaired filling and impaired contractility of sphincter of oddi. This leads to prolonged stasis of bile in the gall bladder. This will lead to retention of cholesterol crystals, with ample time for nucleation and continual growth for mature gallstones^[25]. Along with this, the rate of bile secretion is decreased^[16], thus impairing the clearance of the bile ducts and gallbladder. In our study, we studied TSH values in cholelithiasis patients. If the absence of T4 affects the cholesterol metabolism and hepatic biliary secretion, the patients with gallbladder and CBD stones will have equal increase in prevalence of subclinical hypothyroidism. In

some studies, it was seen that CBD stone patients had two times more chances of diagnosis of hypothyroid than the gallbladder stone patients^[25,26]. This can be due to the previously discussed reduced prorelaxing effect of T4 on the hypothyroidism^[22], resulting in delayed emptying of the biliary duct into the duodenum^[26], this may lead to formation of CBD stones.

In study done by Tuveri et al^[30], 11.4% prevalence of subclinical hypothyroidism in gallstone patients was recorded which is contrary to our study.

It has been claimed and discussed that thyroid abnormality may lead to cholelithiasis. In our setup we did not find any significant association between subclinical hypothyroidism and cholelithiasis. Therefore in our setup we don't recommend thyroid evaluation in cholelithiasis patients.

CONCLUSION:

It is concluded that the incidence of subclinical hypothyroidism in Cholelithiasis patients was 8% which was same as other studies reported. Further research is required to see that either early treatment of subclinical or clinical hypothyroidism would be beneficial for preventing gallstones and CBD stones or not.

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Authors' Contribution:

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Abdullah Khan: Methodology and frame work of study design.

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