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Study of Thyroid Profile, BMI and Lipid Profile in Pathogenesis of Gall Stones

Dr. Poojan Purohit[1], Dr. Latika Sharma[2], Dr. Aamir Hussain Usmani[3], Dr. Harsh Bagla[4], Dr. Chetan Sharma*[5]

[1,2,3,4,5] Dept. of General Surgery, Dr. S.N. Medical College, and Associated Hospitals, Jodhpur

Background: To assess role of T3, T4 and TSH as a thyroid profile , serum lipid profile parameters , BMI in patients of gall stone disease.

Method: Patients who were admitted in Department of Surgery.

Results: Male to female ratio was 1:3.54, showing females have more prevalence of gallstone disease than males. The overall majority of patient age was between 46-60 years, in males majority of age was 61-75 years (10%) while in females it was 46-60 years (34%).In this study, the most common diagnosis was cholelithiasis (72%). Thyroid disorder in the form of hypothyroidism was found in 3(6%) patients, in which 3(6%) were females and no male was hypothyroid in this study. In this study, out of 50 gallstone disease patients, 21 (42%) had LDL-C⩾100mg/dl. Females had higher LDL-C than males. When BMI was studied in there so patients, 24(48%) had BMI in the ⩾25 kg/m2. Amongst those having higher BMI, 3(6%) were categorized as having obesity and rest (42%) as overweight. 20 females (40%) had higher BMI and 4(8%) males tend to have higher BMI.

Conclusions: There is no statistically significant correlation between deranged thyroid profile and gallstone disease. Dyslipidaemia and Higher BMI (⩾25kg/m2) had statistically significant association with gallstone disease patients.

Keywords: Thyroid, Dyslipidaemia, BMI .

INTRODUCTION

Gallstone disease is a very common gastro–intestinal disorder which is present world wide[(1)]. They may form because of many different disorders and the basis for it is impaired metabolism of cholesterol, bilirubin and bile acid and is characterized by formation of stones in hepatic or common bile duct or gallbladder[(2, 3)].

Gallstones are classified into cholesterol stones, pigment stone and mixed stones. There are three stages of gallstone formation–super saturation, nucleation and aggregation. Relative concentration of cholesterol, bile salt and phospholipids determine solubility in bile and cholesterol precipitation results in imbalance of these three components in bile[(4)]. Changes in the bile composition are closely related to disorders of lipid metabolism in liver. The prevalence of gallstones is related to many factors including age, gender, ethnicity, obesity, pregnancy, dietary factors, etc.[(5)].Many studies have been conducted so far to identify risk factor for cholelithiasis in west. They have focused on hyper saturation of cholesterol in bile in the nucleation process which is a key step in the genesis of gall stone[(6)]. For decades, 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 known link between thyroid failure and disturbances of lipid metabolism that may consecutively lead to change of composition of bile[(7)]. Further, sphincter of Oddi expresses thyroid hormone receptors and thyroxine has a direct pro–relaxing effect on sphincter[(8)], recent studies have also demonstrated low bile flow in hypothyroid patients[(9)]. Both the low bile flow and sphincter of Oddi dysfunction are regarded as important functional mechanisms that may promote gall stone formation[(10)].

In recent years, an effort has been made to know path physiological basis of gallstone formation. Role of serum lipids in the etiology of cholelithiasis is very important and in cholesterol gall stones serum lipids are altered, hence one of the aims of this study is to determine and analyze the changes in lipid profile parameter which are responsible for the causation of biliary calculi. Some investigators have reported that gallstones patients have hyperlipidaemia. Cholesterol gallstones results from the secretion by the liver of bile super saturated with cholesterol. This results in cholesterol crystallization. This occurs in association with high calorie and cholesterol richdiet, obesity or from increased activity

of hydroxyl methyl glutaryl CoA (HMG–CoA) reductase, the rate limiting enzyme of hepatic cholesterol synthesis and increased hepatic up take of cholesterol from blood[11].

Obesity is a major risk factor for gall stones[12,13]. The most important factor that influence excretion and concentration of lithogenic and inhibitory substances are diet and related metabolic disorders.

Large body size was suggested to be associated with higher risk of gall stone formation[12]. Also a large clinical study showed that being even moderately overweight increases the risk for developing gallstones. The most likely reason is the amount of bilesalt in bile in reduced, resulting in more cholesterol[14].

BMI correlates with body fat. It is a better estimate of body fat than body weight and has advantages over ideal body weight estimation unlike the ideal body weight tables that were based on mortality data alone BMI correlates with morbidity. It is used for both men & women[15]. Hence, in this study our aim is also to correlate obesity (BMI) with gallstone disease.

Aims and Objectives
To estimate T3, T4 and TSH as a thyroid profile, serum lipid profile parameters, BMI in patients of gall stone disease.

MATERIAL AND METHODS

It was a Prospective study with a total of 50 patients. Patients who were admitted in Department of Surgery. Dr. S.N. Medical College, and Associated Hospitals, Jodhpur from June 2014-December 2014 & diagnosed as having gallstone disease by ultrasonography (USG)

Following patients were excluded

Patients <15 year and >75 years of age, Terminally ill patients.
Patients already on thyroid replacement drugs, who are on cholesterol lowering drugs/or diagnosed as having lipidemia.
Patients on enteral feeding.

Method of collection of data

Details of cases are recorded with USG abdomen and pelvis.5 ml fresh venous sample is collected from patients for estimation of thyroid profile which included serum T3, serum T4 and serum TSH & serum lipid profile which included Total cholesterol, Total triglyceride, HDL-cholesterol and LCL-cholesterol. Following is the normal range of parameter for thyroid and lipid profile. Patient is diagnosed as having hypothyroidism if TSH ≥ 5μIU/ml and euthyroid if TSH<5 μIU/ml. Patients having only raised TSH are denoted as having primary hypothyroidism & those with low TSH as having primary hyperthyroidism. Patients having only high TSH are denoted as having subclinical hypothyroidism. Patients having any of the lipid profile parameter is denoted as having dyslipidaemia. Statistical analysis was done on the collected data by applying Fisher's exact probability test, student 't' test & X^2-square test and p value was calculated. P value <0.05 was considered statistically significant. Patients with low T3 & T4 with raised TSH were denoted as having clinical hypothyroidism.

RESULT

Male to female ratio was 1:3.54, showing females have more prevalence of gallstone disease than males. The overall majority of patient age was between 46-60 years, in males majority of age was 61-75 years (10%) while in females it was 46-60 years (34%).In this study, the most common diagnosis was cholelithiasis (72%) followed by acute calculus cholecystitis (16%) patients, chronic cholecystitis (6%), mucocele (2%), choledocholitihasis (2%) and cholelithiasis with choledocholithiasis (2%). Thyroid disorder in the form of hypothyroidism was found in 3(6%) patients, in which 3(6%) were females and no male was hypothyroid in this study. Hence, in this study prevalence of hypothyroidism in gallstone disease was 6%.Among 3 females with hypothyroidism, 2(4%) were having normal serum T3 and T4 while female (2%) had low serum T3 and T4 (2%) has low serum T4 with higher TSH levels. There was no statistically significant association with abnormal thyroid profile and gallstone disease patients (p value 1.000). It needs further study and more sampling in the future. Amongst 3 females with hypothyroidism 2 belonged to age group of 46-60 years and 1 belonged to age group of 61-75 years. Hence, prevalence was highest among 46-60 years age group. In this study, out of 50 gallstone disease patients, 21 (42%) had LDL-C≥100mg/dl. Females had higher LDL-C than males. Most of the patients having high LDL-C were in the age group of 46-60 year. In males, higher LDL-C was common in 61-75 year age group. Association of higher LDL-C with gallstone disease patient was statistically significant (p value <0.0001). Out of the 50 patients, 28(56%) had HDL-C <40mg/dl. Amongst those with low HDL, 23(46%) were females and 5 (10%) were males. Most commonly deranged lipid profile parameter. No. of females having lower HDL-

C were more than no. of males. Most of the patients having low HDL-C values were in the 46-60 years. However, in males, low HDL-C was common in 61-75 years age group. Association of low HDL-C and gallstone disease in statistically significant. (p value <0.0001). Serum total cholesterol was raised in 15(30%) of the patients of gallstone disease. Amongst those with higher total cholesterol, 2(4%) were males and 13(26%) were females. More no of females had higher total cholesterol values than males. Most of the males were in the age group of 61-75 year while most of the females were in the age group of 46-60 year having higher total cholesterol values. There is statistically significant association between higher total cholesterol and gallstone disease. Serum triglyceride was increased in 19(38%) patients of gallstone disease more no. of males had higher triglyceride values as compared to females. Most of the males having higher value were in age group of 61-75 year and most of the females were in the age group of 46-60 years. There exists statistically significant to association with increased serum triglyceride and gallstone disease. Overall, 30(60%) patients with gallstone disease had dyslipidaemia showing statistically significant association between deranged lipid profile and gallstone disease (p value <0.002). This also shows that females tend to have dyslipidaemia in younger age group than males in our study. When BMI was studied in there so patients, 24(48%) had BMI in the ≥25 kg/m2. Amongst those having higher BMI, 3(6%) were categorized as having obesity and rest (42%) as overweight. 20 females (40%) had higher BMI and 4(8%) males tend to have higher BMI. Association of BMI with gallstone disease in clinically significant (p value <0.0001). When the 3 parameters were assessed in combination, it was seen that, dyslipidaemia with higher BMI had most significant association with gallstone disease (p value <0.0004) as compared to different combinations.

DISCUSSION

Earlier, an association between gallstone and diagnosed hypothyroidism has been shown. Delayed emptying of the biliary tract in experimental animals in hypothyroidism has been shown, explained partly by the lack of pro-relaxing effect of thyroxine on sphincter of Oddi contractility. In this study, we further investigated the prevalence of previously undiagnosed hypothyroid abnormalities in gallstone patients. The laboratory hallmark of primary hypothyroidism and the most sensitive test for detecting early thyroid failure is an increased serum TSH concentration. The pathogenesis of gallstone formation is a complex process involving factor affecting bile content and bile flow. The genesis of cholesterol gallstone involves cholesterol saturation of bile, formation & growth of cholesterol monohydrate crystals, and the absorptive, secretory and motor functions of the gall bladder. Pigment stones are formed secondary to biliary stasis, which is the major factor leading to anaerobic bacterial degradation and precipitation of biliary lipids. In the current study, we did not analyze the composition of the diagnosed gallstones, which is why the association of hypothyroidism with certain type of gallstones remains unverified.

An ultrasound is the initial investigation of any patient suspected of disease of the biliary tree. It is noninvasive painless, does not submit the patient to radiation and can be performed in a critically ill patients. USG will show stones in the gallbladder with sensitivity and specificity of >90%, stones are acoustically dense and reflect the ultrasound waves back to USG transducer. Thyroid hormones are known to have number of effect on cholesterol metabolism. When serum cholesterol values rise in hypothyroidism bile may also become supersaturated with cholesterol, leading to gallbladder hypomotility, depressed contractility and impaired filling, giving rise to prolonged residence of bile in the gallbladder. This may contribute to the retention of cholesterol crystals thereby allowing sufficient time for nucleation and continual growth into mature gallstones. In addition, the rate of bile secretion may be decreased, physically impairing clearance of precipitates from the bile ducts and gallbladder. Obesity and dyslipidaemia, similarly has been considered as strong risk factors for gallstone disease. Some investigators have reported that gallstones patients have hyperlipidaemia, cholesterol gallstones results from secretion by liver of bile supersaturated with cholesterol. This results in crystallization.

This occurs in association with high calorie and cholesterol rich diet or from increased activity of HMG-CoA reductase[11]. Similarly, large body size was suggested to be associated with higher risk of gallstone[12]. Also a large clinical study showed that being even moderately over weight increased the risk for developing gallstones. Since, BMI correlates with body fat than body weight it has been included in the study. In our study conducted in 50 patients, only 3(6%) had hypothyroidism and all of them were females. Most common age group having hypothyroidism was 45-60 years. None of the male was hypothyroid, there is no statistically significant relation between hypothyroidism and cholelithiasis as in study conducted by Sumer Singh MS 2013, this non significance can be due to the fact that those patients who were already diagnosed as having thyroid disorders were not included in the study. Even in those patients having hypothyroidism with gallstone disease, it couldn't be solely attributed to deranged thyroid profile because all patients had associated higher BMI and dyslipidaemia.

This finding is concordant with the findings of study conducted by Henry Volzke, Damniel M Robinson and Ulrich John which showed high BMI and low serum HDL-Cholesterol level as independent risk factors for cholelithaisis in females and males, irrespective of thyroid profile status[16]. In our study, 60% of patients had dyslipidaemia, 42% patients had higher LDL-C, 56% had lower HDL-C, 30% had higher total cholesterol and 38% had raised total triglyceride, more number of females had abnormal parameter except in serum triglyceride level. Our study was concordant with that conducted by Saraya A, Irshad M, Gandhi DM, Tandon RK, 1995;16(4): 16-21 as results of the

study revealed that more than half of gallstone patients had dyslipidaemia[17]. The higher prevalence of gallstones in females between 45-60 years was found in our study similar to that observed in study of Harshi Thilankea, Weerakoon, Shirani Ranasinghe, Ayanthi Navarathne Ramaiah Sivakanesan et al on. This gender preponderance may be due to beneficial effect of reproductive hormones in younger females and also due to ageing related lipid profile changes which leads to increased secretion of biliary cholesterol in postmenopausal females[18]. Similary, lower HDL-Cholesterol has statistically significant association with gallstones disease as seen in study conducted by H.Volzke, Baumeister, Alted, Hoffmann W, Sehwahn C, Simon P, John U and Lerch MM on independent risk factors for gallstone formation which showed female sex, lower serum HDL and BMI to be independent risk factors for occurrence of gallstones[19].

In a study conducted by Shraddha Singh, Shipradwivedi, Abhijeet Chndra, Sunita Tiwari, S.N. Natu, Devendra Singh and Amit Modeshiya on serum oestrogen and lipid profile in gallstone and cancer, it was found that higher total cholesterol total triglyceride, LDL-C and lower HDL-C are associated with gallstone disease, a finding similar to our study[20]. Similarly a study on undisputable behaviour of lipid profile in cholelithiatic gallbladder by Dr. Nagaraj and Dr. Satish Kumar D revealed that serum total cholesterol, LDL cholesterol and triglyceride levels in increased in gallstone patients and HDL-Cholesterol level was decreased, which was as seen in our study. Our study also revealed BMI to be associated significantly with gallstone disease as is the conclusion in one of the study conducted by H. Kodama, S. Kona, I Todoroki, S Honjo, Y Sakurai, Kiwakabayshi & colleagues on gallstone disease risk in relation to BMI and waist hip ratio. Association of this obesity indicator with gallstone disease can be due to multiple factor but it is commonly attributed to increased saturation of bile with cholesterol in men and women. This in turn can be due to hyperinsulinemia, association with obesity, which may be responsible for cholesterol saturation in bile. Hyperinsullinemia also leads to increased activity of HMG-CoA reductese, the rate limiting enzyme for cholesterol synthesis in liver. It also activates LDL receptors in the liver, thereby, increasing cholesterol excretion in the bile. However, using only present value of BMI has limitations as current levels of obesity may not be relevant to prevalent gallstones as we are not aware of past BMI of patients, secondly, rapid weight loss also predisposes to gallstone formation, hence, patients with low BMI might have had higher BMI before occurrence of cholelithiasis[21].

Another study on body mass index (BMI), abdominal fatness and the risk of gallbladder disease revealed that even moderate increase in BMI may increase the risk of stones[22]. Similarly, study conducted by Vimal Bhandari, Surya Prakaksh Gora, H.G. Vyas, Charanjeet Kaur & Neelam Roy on relationship of serum lipid profile, Apo-lipoproteins, BMI & Waist hip ratio on occurrence of cholelithiasis supported our study[23]. As our study revealed BMI and dyslipidaemia to be associated with gallstone disease but it has limitation that gallstone disease can be caused by variety of other factors, the involvement of confounding factors in the study cannot by excluded completely. Another limitation is non inclusion of control patients which limits association assessment of combined factors.

CONCLUSION

Out study shows that, although a subgroup of patients with gallstone disease (females with age group of 46-60 years) had highest prevalence of hypothyroidism, there is no statistically significant correlation b/w deranged thyroid profile and gallstone disease. Dyslipidaemia (that is low HDL with higher total cholesterol/serum triglyceride/LDL-C) had statistically significant association with gallstone disease patients. Higher BMI (≥25kg/m2) patients had statistically significant correlation with gallstone disease.

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