Relationship Between Serum Levels of TSH and Cholesterol with Types of Gallstones

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ABSTRACT :

BACKGROUND :

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 the known link between thyroid failure and disturbances of lipid metabolism that may consecutively lead to a change of the composition of the bile , motility of biliary tract and it's effect on sphincter of Oddi .

OBJECTIVE:

To show the relation between serum levels of thyroid stimulating hormone (TSH) and cholesterol and types of gallstone .

PATIENT AND METHOD :

A prospective analysis of 150 cases with cholecystectomy , were studied in Al – Sadar teaching hospital in AL – Najaf goverment between 1st of January 2008 till end of December 2008 , for each studied patient with gall stone serum was taken for measuring the levels of TSH and cholesterol , stone was taken after cholecystectomy and sent for chemical analysis.

RESULTS :

There was a remarkable gender difference with predominance of female gender as it constitutes 132 (88%) versus 18 (12%) males . Abnormal high levels of serum TSH and cholesterol were reported in 12 cases (8%) and in 15 cases (10%) respectively . Types of gallstones , were cholesterol stones in 95 cases (63%) , pigmented stone in 33 cases (22 %) and mixed stone in 22 cases (15%) .

CONCLUSION :

There was relationship between high serum levels of TSH and cholesterol with types of gallstones .

KEYWORDS :TSH , gallstone , cholesterol .

INTRODUCTION :

Gallstones are the most common biliray pathology and are classified into cholesterol , pigmented and mixed stones . Cholesterol or mixed stones are the most common type and constitute 80% . Black pigmented stones are largely composed of an insoluble bilirubin pigment polymer mixed with calcium phosphate and carbonate and brown pigmented stones contain calcium bilirubinate, calcium palmitate and calicum stearate ,as well as cholesterol .

Brown stones are rare in gall bladder . The major elements involved in the formation of gallstones are cholesterol , bile pigment and calcium , other constituents include iron , phosphorus , carbonate , protein , carbohydrate , mucus and cellular debris . Formation of gallstones occurred as a result of solid settling out of solution and solubility of cholesterol depend on concentration of conjugated bile salts , phospholipids and cholesterol in bile . [1, 2, 3]

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 due to a disorder of the physico-chemical equilibrium which normally maintains cholesterol in micellar form in bile . 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 .[4, 5, 6]

The increasing freguency of biliary stone with it's different epidemiological factors and diseases , prompted us to carry out a chemical analysis of gallstones. Rate of lipid synthesis in general and of cholesterol in particular be different in patient with mixed stones than in patient with pigmented stones.[7, 8, 9]

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Hypothyroidism is a common secondary cause of hypercholesterolemia , patients with hypothyroidism have serum level of cholesterol a pproximately 50% higher than level in euthyroid and 90 % of all hypothyroid patients have elevated cholesterol level .[10]

Stone growth is dependent on cyclical changes in biliary substance , this may explain the permissive or causal role of endogenous hormones in gallstones formation , that mean gallstones disease has a multifactorial causations , including gall bladder Infection , decreased gall bladder motility after surgery for obesity and/or weight loss , ileal disease or resection , hemolytic disease , familial hypercholestereamia and metabolic defect in hepatic bilirubin glucuronidation .[5 ,6, 7]

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 the known link between thyroid failure and disturbances of lipid metabolism may consecutively lead to a change of the composition of bile .[11]

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 .[12 , 13 , 14]

The usage of thyroxine was even suspected to dissolve gallstones , however a spontaneous passage of the stone to the duodenum could not be excluded in this case report .[15 , 16]

In an animal model of rabbits in whom a fatty diet induced gallstone formation, administering thyroxine was associated with a low gallstone weight , but did not dissolve the gallstones .[17]

PATIENT AND METHOD :

A prospective study was done in AL – Sadar teaching hospital in AL – Najaf goverment for randomized 150 cases . For every patient with gallstone we took serum for measuring serum levels of TSH and cholesterol (standered levels were 3mIU/l and 200 mg / dl respectively) and the stone was sent for biochemical analysis . Gallstone was taken after cholecystectomy , placed on sterile gauze for dryness , then sent for chemical analysis to show the type of stone with name , age , sex of the patient and number of stones . The first collection of stones from 69 patients (46%) sent to the laboratory in Al – Diwaniya teaching hospital and a second collection of stones from 81 patients (54%) to biochemistry department in AL–Kufa college of medicine for biochemical analysis .

RESULTS:

Out of 150 cases , 132 patients were females (88%) and 18 were males (12%) with gallstones . The level of TSH was high in 12 cases (8%) more than 3 mIU/l and the level of cholesterol was high in 15 cases (10%) more than 200 mg / dl in fasting state according to our laboratory as shown in table no. 1 .

Table.1: Showed gender incidence of patients in relation to serum levels of TSH and cholesterol were high mostly in female patients .

Gender	No, of patients	%	Serum level of TSH		% of high TSH related to all patients	Serum level of cholesterol		% of high cholesterol related to all patients
			Normal	High		Normal	High	
Female	132	88	121	1\	7.4	121	11	7.3
Male	18	12	17	1	0.6	14	4	2.7
Total	150	100	138	12	8	125	15	10
P.value	0.683 was not significant					0.065 was not significant		

Age of our patients ranged from between 20—70 years , but the majority between 40—49 years old , and the lowest between 20—29 years old as shown in table no. 2 .

Table 2: Showed different age groups in relation to serum levels of TSH and cholesterol were high mostly in age group (40—49) years old .

AGE OF PATIENTS (YEARS)	NO. OF PATIENTS	SERUM LEVEL OF TSH		SERUM LEVEL OF CHOLESTEROL	
		Normal	High	Normal	High
20___29	12	12	0	12	0
30___39	28	26	2	28	0
40___49	55	51	4	50	5
50___59	37	33	4	30	7
> 60	18	16	2	15	3
Total	150	138	12	135	15
p. value	0.78 was not significant			0.07 was not significant	

Types of gallstones in our study usually of cholesterol were (63%) and single in 37 cases were (38.9%) of cholesterol type , but of no single stone detected in other types of stones as shown in table no . 3 .

Table 3: Showed different types of gallstones in relation to gender of patients where high in female patients for all types of stones .

Types of gallstones	No. of patients	Gender of patients		%
		Femal	Male	
Cholesterol	95	90	5	63
Pigmented	33	22	11	22
Mixed	22	20	2	15
Total	150	132	18	100
P . value	0.0001 was significant			

Table 4: Showed different types of gallstones in relation to serum levels of TSH and cholesterol were cholesterol stone more in patients with high levels .

Types of gallstones	Serum level of TSH		Serum level of cholesterol	
Cholesterol	Normal	High	Normal	High
	87	8	85	10
Pigmented	31	2	32	1
Mixed	20	2	18	4
Total	138	12	135	15
P . value	0.007 was not significant		0.178 was not significant	

Table 5: Showed different types of gallstone in relation to number of stones were no single stone detected in pigmented and mixed stones .

Types of gallstones	No . of stones	
	Single	Multiple
Cholesterol	37	58
Pigmented	0	33
Mixed	0	22
Total	37	113
P . value	o.ooo1 was significant	

We divided our patients into 6 main groups according to serum levels of TSH and cholesterol .
Group 1 those with normal serum level of TSH = 138
Group 2 those with normal serum level of cholesterol = 135
Group 3 those with normal serum level of both TSH and cholesterol =133
Group 4 those with high serum level of TSH = 12
Group 5 those with high serum level of cholesterol = 15
Group 6 those with high serum level of both TSH and cholesterol = 10

We found high level of serum cholesterol in patients with high serum TSH , and level of cholesterol in stone was high in patients with high serum levels of TSH and cholesterol . The percentage of cholesterol in gallstone types as such , in cholesterol stone (90 % – 96%) , in pigmented stone (10% - 12%) and in mixed stone (51% - 56%) .

DISCUSSION :

The study showed a relation between serum levels of TSH , cholesterol and gallstone disease , but in study done by Ros E et al , who investigated possible associations between serum TSH and cholesterol levels and gallstone disease,[4] there was an independent relation of high serum TSH and cholesterol levels with cholelithiasis among males , predominantly among those who had sonographically detected gallstones , in female population , no such associations were identified . At least in the male population , the finding of high serum TSH and cholesterol levels as an independent risk factor for cholelithiasis confirmed other studies were done by Rose et al and Kleinero et al [5, 6] , also similar to other studies were done by Lapidus A et al and Duvaldestin et al [7, 8] , but these findings were dissimilar to this result , absence of such an association among females might be explained by firstly , the studied population only comprised persons with as yet undiagnosed thyroid disorders and females were more often excluded due to a known thyroid disorder than males .

Thus , there might be earlier diagnosis and treatment of hypothyroidism (regarding high TSH and cholesterol levels) in women compared to men , reflected by a longer and more intense exposure in males . Likewise , the higher proportion of cholelithiasis in women compared to men was mainly due to the higher proportion of previous history of cholecystectomy in females . Thus , in women gallstones may become symptomatic earlier than in men and the consecutive diagnostic procedures may further lead to an earlier detection and treatment of hypothyroidism , but in study done by Hatsushika et al and Laukkarinen J et al supported this result by the fact that the association between high serum TSH and cholesterol levels and cholelithiasis was mainly found in males with sonographically detected gallstones .[9, 10] Secondly, there are also gender differences with respect to the type of gallstones . In study done by Bergman F and Van der Linden W , that males had less often cholesterol stones than women may assume that , if hypothyroidism would indeed be a causal factor for gallstone disease , then this may lead to a specific type of stone other than cholesterol stones [(11)], these result similar to this study in regarding gender differences with respect to the type of gallstone but dissimilar in regarding that

hypothyroidism may lead to a specific type of stone other than cholesterol , in study done by Inkinen J et al , there was no association between thyroid function and the stone type and in male population, also an association between low serum TSH levels and cholelithiasis bordered statistical significance in the full model , this was not expected , because experimental evidence suggested a direct association between thyroid function and the bile flow to the duodenum , while the flow was reduced in hypothyroidism , it was enhanced in hyperthyroidism [12] , however, this study was performed in rats without gall bladder .

In study was done by Cicala M et al in hamsters , extremely high doses of thyroxine may induce the formation of gallbladder stones [13] , but in study done by Vassilakis JS et al showed dissolution of gallstones following thyroxine administration [16] , in general the role of hyperthyroidism with respect to gallstone formation in human beings is currently not well investigated and further research is needed.

In this study the incidence of gallstone types were , cholesterol stone in 95 cases (63%) , pigmented stone in 33 cases (22%) and mixed stone in 20 cases (15%) which was dissimilar to other study done by Russel RCG , Williams NS showed the result of gallstone types in the USA and Europe , 80% were cholesterol or mixed stones , while in Asia , 80% were pigmented stones and this may be related to variation in nutritional habbits and life style among population .

In this study the age majority of patients between (30—59) years , while in study done by Honore LH and Inkinen J et al showed high gallstone incidence in patients older than 65 years old . [14 ,15]

In this study the level of serum cholesterol was high in patient with high serum level of TSH (wither clinical or subclinical hypothyroidism)which was similar to study done by Alfan H and Stenman U. [18,19,20]

In study done by Volzke H et al showed variation of cholesterol level in stone as variation in composition of gallstone were (51% -- 99%) , [1 , 17] but in this study the percentage of cholesterol level in stone of different types as such , in cholesterol stone around (90% --96%) , in pigmented stone around (10% --12%) and in mixed stone around (51% --56%) .

CONCLUSION :

There was a relation between high serum levels of TSH and cholesterol and types of gallstones , and high serum levels are associated with cholesterol or mixed stone and with high cholesterol level in stone . Especialy for middle aged patients with gallstones so better send them for measuring serum levels of TSH and cholesterol for early detection of abnormal levels and treatment .

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