

Prevalence of hypothyroidism in patients with gallstone disease

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الخلاصة

أثبتت بعض الدراسات بوجود علاقة تصاعدية بخمول الغدة الدرقية لدى المرضى المصابين بحصاة المرارة وبالعلاقة بين خمول الغدة الدرقية وببطء تفريغ المادة الصفراوية لدى هؤلاء المرضى والتي يمكن تفسيرها بغياب تأثير هرمون الثايروكسين (هرمون الغدة الدرقية) على إرخاء معصرة قناة الصفراء (معصرة أودي). التفسير الآخر لهذه العلاقة هي اضطراب أيض الدهون مما يؤدي إلى تغيير بتركيب المادة الصفراوية وترسب حصاة المرارة لقياس درجة شيوع وتشخيص خمول الغدة الدرقية لدى المرضى المصابين بحصى المرارة. تم أخذ ٢٢٥ عينة عشوائية من مرضى مستشفى الصدر التعليمي في النجف من الخامس عشر من شباط ٢٠٠٨ إلى الأول من تشرين الثاني ٢٠٠٨ لغرض إجراء هذه الدراسة. لكل مريض بحصى المرارة تم إجراء الفحص السريري وواخذ تاريخ المرض بدقة ثم اجري لهم سونار الرقبة وعينة دم لفحص وظائف الغدة الدرقية. من أصل ٢٢٥ مريض ١٩٨ كانوا نساء و ٢٧ كانوا رجال. وجد عدد المصابين بخمول الغدة الدرقية ٢٤ مريض (١٠,٦٪)، من هذه النسبة ٢٢ (٩,٧٪) كانوا نساء منهم ١٨ (٨٪) كن لايبدين اعراض المرض و ٤ (١,٧٪) باعراض كاملة للمرض ومريضان من الرجال وكانوا لايبدون اعراض المرض (٠,٩٪). من أصل ٢٢٥ مريض ٢٢ (٩,٧٪) كانوا يعانون من تضخم الغدة الدرقية. وكان أعلى مستوى إصابة بين عمر ٥١-٦٠ سنة. استنتج انه لا توجد هناك علاقة هامة بين مرضى حصاة المرارة وخمول الغدة الدرقية في كلا الجنسين. يجب قياس وظيفة الغدة الدرقية للمرضى المصابين بحصى المرارة بين الفئة العمرية ٥١-٦٠ سنة بسبب ارتفاع الإصابة بخمول الغدة الدرقية في هذه الفئة.

Abstract

Back ground: Earlier, the studies had been shown an increased prevalence of previously diagnosed hypothyroidism in gallstone patient and a delayed emptying of the biliary tract in hypothyroidism, explained partly by the missing prorelaxing effect of thyroxine on the sphincter of oddi contractility .

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Other explanations include the known link between thyroid failure and disturbances of lipid metabolism that may consecutively lead to change of the composition of the bile and motility of biliary tract.

Aim:To show the prevalence of previously undiagnosed hypothyroidism in patients with gallstones .

Patient and method:A cross sectional study was done in Al-Sader Teaching Hospital in Al-Najaf city between 15th of February 2008 and 1st of November 2009 of 225 cases were taken to show relation between gallstone and hypothyroidism. For every patient with diagnosed gallstone, full history and clinical examination was taken and sent for ultrasound of neck for goitre detection and laboratory blood test for T3, T4 and TSH.

Results:Out of 225 patients with gallstone 198 (88%) were females and 27 (12%) males. Thyroid disorder in form of hypothyroidism was found in 24 (10.6%), (from this percentage 22 (9.7%) were females and from this 18 (8.0%) were subclinical and 4 (1.7%) were clinical hypothyroidism and males were 2 (0.9%) with subclinical cases. From 225 cases with gallstones, 22(9.7%) cases complaining from goitre. Peak age between 51-60 years.

Conclusion and recommendation:There is no significant association between hypothyroidism and gallstones in both genders. Gallstone patients between 51-60 years should be checked for serum TSH, T3 and T4 because of high incidence of hypothyroidism among this age group.

Key words:

- 1- Thyroid hormonal assay.
- 2- Gallstone.
- 3- Goitre.

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^[1,2].

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^[2,3].

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].

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%^[5].

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^[6].

Recent studies also demonstrated low bile flow in hypothyroid subjects. Further more, the sphincter of oddi expresses thyroid hormone receptors and thyroxine has a direct prorelaxing effect on the sphincter^[6,7]. Both low bile flow and sphincter of oddi dysfunction are regarded as important functional mechanisms that may promote gallstone formation^[7]. 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 ^[8].

In western countries 10-12% of adults develop gallstones ^[9,10]. The prevalence of common bile duct (CBD) stones in patients with gallstones varies from 8 to 16% ^[11].

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 ^[12], which may be caused for examples by sphincter of oddi stenosis, dyskinesia, or bile duct strictures ^[13].

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 ^[14].

Hypothyroidism is the most common cause of secondary hypercholesterolaemia, 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 ^[15].

Patients and Methods

A cross sectional study was done in Al-Sader Teaching Hospital in Al-Najaf city between 15th of February 2008 and 1st of November 2009 in which 225 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 were included, neck ultrasound and level of serum T3, T4, and TSH and ECG changes.

Patients were divided according to history, clinical examination, ultrasound of the neck and laboratory test (T₃, T₄, TSH) into 3 groups:

1. Subclinical hypothyroidism includes the symptom free-patients with TSH concentrations above the upper limit of normal range and T₄ and / or T₃ decrease below normal limit. (According to our laboratory readings)
2. Clinical hypothyroidism in which there are symptoms of hypothyroidism with TSH level above the upper limit and T₄ and / or T₃ decrease below the normal limit.
3. Euthyroid group where clinical and laboratory tests were normal.

All these groups may present with or without goiter.

Results

In this cross-sectional study a 225 patients with gallstones were randomly selected. 198(88%) were females and 27(12%) were males with median age was 40 yrs (range 24-65) yrs and 37yrs (30-43) yrs respectively.

Thyroid disorder in form of hypothyroidism was found in 24(10.6%) patients, 22(9.7%) were females and 2(0.9%) males.

Among the 22 females with hypothyroidism, 18(8.0%) diagnosed as subclinical hypothyroidism and 4(1.7%) as clinical hypothyroidism while both males were subclinical hypothyroidism as shown in table 1.

Table 1. The distribution of 225 patients with gallstones according to gender, age and hypothyroidism.

Gender	Age		Hypothyroidism			
	No.	%	Mean	Range	Clinical	subclinical
Male	27	12	37 yrs	30-43 yrs	0	2 (0.88)
Female	198	88	40 yrs	24-65 yrs	4 (1.76%)	18 (8%)
P = >0.06			Fisher's exact probability=0.69			

Peak age of our patients in this study was between (51-60) years as shown in table 2.

Table 2. The prevalence of subclinical and subclinical hypothyroidism and euthyroid in 225 patients with gallstones in different age groups and in total.

Total Age(yrs)	clinical hypothyroidism		subclinical hypothyroidism		total hypothyroidism		euthyroid		Total	
	n	%	n	%	n	%	n	%	n	%
21-30	0	0	1	0.4	1	0.4	11	4.9	12	5.3
31-40	0	0	2	0.9	2	0.9	34	15.1	36	16
41-50	2	0.9	2	0.9	4	1.8	71	31.6	75	33.4
51-60	2	0.9	13	5.7	15	6.7	77	34.2	92	40.9
61-70	0	0	2	0.9	2	0.9	8	3.6	10	4.4
Total	4	1.8	20	8.8	24	10.5	201	89.4	225	100

$X^2= 7.28$ $df=4$ $P=0.12$ N.S

In laboratory investigation we found that 20 cases recorded with high TSH and low T₃, T₄ , 3 cases with high TSH and low T₄ and 1 case with high TSH and low T₃ as shown in table 3.

Table 3. The levels of T₃, T₄ and TSH of 24 hypothyroid patients with gallstones.

	No. of patients	High TSH	Low T ₃	Low T ₄	Low T ₃ &T ₄
Gallstones with low T ₃ &T ₄	20	20	0	0	20
Gallstones with low T ₄	3	3	0	3	0
Gallstones with low T ₃	1	1	1	0	0
Total	24	24	1	3	20

From 225 cases, 22(9.7%) were found with goitre, 20(8.9%) (according to the laboratory investigation) they were euthyroid, and other 2(0.8%) where 1(0.4%) with clinical hypothyroidism female and another 1(0.4%) with subclinical hypothyroidism female as shown in table 4.

* From total number of hypothyroidism 2 were males and 22 were females F/M ratio 22/2.

Table 4. Relationship between thyroid enlargement and hypothyroidism in 225 patients with gallstones.

Gender	Total cases No (%)	Goitre		Non goitre	
		Euthyroid No (%)	hypothyroid No (%)	Euthyroid No (%)	hypothyroid No (%)
Female	198(88%)	19 (8.4%)	2 (0.88%)	157(69.7%)	20 (8.9%)
Male	27(12%)	1(.44%)	0	24(10.6%)	2 (0.88%)
Total	225	22(9.7%)		203(90.3%)	
P value		0.74 N.S		0.58 N.S	

N.S : not significant

Discussion

Earlier, an association between gallstone and diagnosed hypothyroidism and delayed emptying of the biliary tract in experimental and clinical hypothyroidism have been shown , explained at least partly by the lack of prorelaxing effect of T4 on the sphincter of oddi contractility ^[7, 17].

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 TSH concentration. ^[18].

In the subclinical form, an increased TSH level is accompanied by a normal T4 and T3 level, and the patient is asymptomatic ^[19].

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

In this study the majority of patients age was between (51-60) years, while in study done by Johanna L, Gediminas K (2007) it was in women older than 60 years while in other study by Honore LH, and Inkinen were conducted of a high gallstones prevalence in women were > 65 years old, this probably contributed to the sex hormonal imbalance at this age [7].

In study done by Johanna L, Gediminas K (2007), the prevalence of subclinical hypothyroidism was 11.4% in gallstones and none of the patients was clinically hypothyroidism [20] but in this study the prevalence of thyroid disorder in form of hypothyroidism was found in (10.6%), subclinical hypothyroidism was (8.0%) and (1.7%) was clinical in female and (0.9%) was subclinical hypothyroidism in males with no clinically significant association between hypothyroidism and gallstones (P=0.12 N.S).

In a study done by Henry Volzke in 2005 [21] there were (10.3%) with low TSH which is the same as in this study (10.6%) and (88.6%) with normal TSH which is approximately the same as this study (89.7%). In this study, among males there was an independent relation between high serum TSH and cholelithiasis and there was a tendency towards an elevated risk of cholelithiasis in persons with low serum TSH, in females no such relations was found. In our study no such relation was found for both genders.

Conclusion and recommendation

There is no significant relation between gallstones and hypothyroidism in this study (P=0.12 N.S) and it needs further study and more sampling in the future.

- 1- The prevalence in this study was the same as other studies (10.6% vs 10.3%) in the world which is low.
- 2- Among hypothyroid patients the incidence was highest among 51- 60 years of age (62.5 %) so we recommend that TSH level

should be measured for every patient with gallstone disease in this age range.

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