

## The Impact Of Thyroid Dysfunction And TSH On The Pathogenesis Of Gallstone And Its Composition

تأثير الهرمون المحفز للغدة الدرقية TSH واختلال الغدة الدرقية في أمراضية حصوة المرارة وتركيبها

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### الخلاصة:

**الأهداف:** لمعرفة تأثير مستويات الهرمون المحفز للغدة الدرقية TSH واختلال الغدة الدرقية في أمراضية **منهجية البحث:** أجريت دراسة تطبيقية شملت قياس مستوى TSH ( ) مع الأخذ بالنظر للاختلافات بين الجنسين وسيادة نوع sonographically ( نيسان - نيسان ) المريض. واستخدم الباحثون التحليل الإحصائي Chi X<sup>2</sup> test للبيانات المأخوذة. **النتائج:** أظهرت نتائج البحث ارتفاع معدل انتشار الإصابة في الإناث بينما كانت مستويات TSH عالية في الذكور أكثر من الإناث (p<0.001). وسيادة نوع حصوة (p<0.0001). هكذا نتائج الحالية تبين الخلل في الغدة الدرقية لها دور في تشكيل

**الاستنتاج:** هناك علاقة معنوية بين حصوة المرارة وبين الخلل في الغدة الدرقية. **التوصيات:** بمعالجة الخلل في الغدة الدرقية والاختلال الهرموني وخاصة هرمون TSH.

### Abstract:

**Objectives:** to study the impact of thyroid stimulating hormone (TSH) levels and thyroid dysfunction on the pathogenesis of gallstones and their compositions.

**Methodology:** a study is applied including measuring of TSH levels in serum blood of (100) patients with gallstones diagnosed by sonographically or current cholecystectomy ( from April 2009 – April 2011 )with regarded to the differences between sex of patients and predominated of gallstone type with age . The researcher used statistical analysis( Chi X<sup>2</sup> test) to the data.

**Results:** the search results showed significant increase in the rate of pathogenesis in female, but TSH levels is higher in male than female (p < 0.001). And cholesterol gallstone type is predominated (p < 0.0001). Current results were stated that the thyroid dysfunction had a role in the formation of gallstones.

**Conclusion :** there is a significant association between the gallstones and thyroid dysfunction

**Recommendations:** the study recommends that must handling and treatment the thyroid dysfunction and hormonal dysfunction especially TSH.

**Keywords:** gallstones, TSH, thyroid dysfunction.

## INTRODUCTION

Gallstone disease is consider a major health problem in the world since it is remain one of the most common medical conditions in general. Gallstones form when liquid stored in the gallbladder hardens into pieces of stone-like material which develop in the gallbladder. It is composed mainly of cholesterol, bile pigment, and calcium salts with small amounts of protein and other materials. The major driving forces in litho genesis of gallstones are cholesterol saturation of the bile and haemolysis<sup>(1)</sup>. The low solubility of cholesterol and unconjugated bilirubin induces its precipitation into the gallstones. Thus, any supersaturation of the bile by cholesterol relative to the bile salts and any increase in the unconjugated bilirubin content are lithogenic, however, the stones were classified into cholesterol, pigment, and mixed stones<sup>(2)</sup>. The pathogenesis of gallstone disease is suggested to be multifactorial and probably develops from complex interactions between many genetic and environmental factors<sup>(3)</sup>.The role for thyroid dysfunction in the

pathogenesis of gallstones is not indicated in prior studies that the purpose of this study was to investigate the frequency of diagnosed hypothyroidism in patients with Cholelithiasis.

## OBJECTIVES :

The materials of the current prospective study were one hundred gallstones patients, 53 females and 47 males , ages were  $48.89 \pm 7.21$  ,  $48.45 \pm 9.84$  for females and males. These patients have diagnosed with gallbladder stones (Cholelithiasis ) by previous history of cholecystectomy or current, sonographically diagnosed gallstones( from April 2009 – April 2011 ). In both groups of males and females there were pigment, mixed and cholesterol stones. Detailed history including age, sex, were taken. After the morphological study, gallstones were washed, dried and grinded to a powder. Powder was weighed and was taken for chemical analysis using conversional methods for chemical analysis<sup>(4)</sup>. TSH level was determined<sup>(5)</sup>. In the analysis of serum TSH, patients classified by the results obtained during analysis for serum TSH among 100 patients 10 with low TSH, 52 who had high TSH and 38 who had normal serum TSH. All TSH measurements were performed in one central laboratory. The functional sensitivity of the TSH assay was 0.03 mIU/L. The reference range was 0.3-3 mIU/L. The three groups consisted of persons with low (<0.3 mIU/L), normal (0.3-3 mIU/L) and high (>3 mIU/L) serum TSH levels.

## Statistical analysis

Data on the quantitative characteristics are expressed as mean  $\pm$ SD. Categorical data are expressed as a number of cases and percentages. Chi  $X^2$  test was used to compare the effect of sex, age and the data between the patients distributed in different groups,  $P < 0.05$  was considered statistically significant.

## RESULTS:

The impact of TSH on the gallstone composition was studied. In the current study, there were 10 (0.1%), 38( 38%), and 52(52%) patients for low, normal and high levels of TSH respectively. Also the current result was demonstrated the prevalence of gallstone between male and female , it showed a high proportion of females (53%) compared to the males (47%) .

Females were demonstrated high prevalence of normal TSH (71.69%) , 13.20% and 15 for both high and low levels TSH respectively. while male demonstrated high prevalence (95.47%) of high levels of TSH and (4.53%) of low levels of TSH.

However, Compared between the current results of gallstone types, individuals with high serum TSH levels were more often of male gender, the results appeared to be significant association( $X^2 = 19.02$ ,  $df = 4$ ,  $p < 0.001$ : $X^2 = 69.76$ ,  $df = 2$ ,  $p < 0.0001$ ) between high TSH level and predominated cholesterol gallstone (table 1 and table 2). On the other hand, hypothyroidism has been associated to the older age more than 45 year ( $X^2 = 8.47$ ,  $df = 2$ ,  $p < 0.05$ .), in which the disturbance in the lipid metabolism and encourage the gallstone formation was involved ( table3). However, age was studied to be effect on the predominant cholesterol gallstone with old age patients ( $X^2 = 12.81$ ,  $df = 2$ ,  $p < 0.001$ , table 4). The relation between gallstone type and sex that was found a significant ( $X^2 = 8.72$ ,  $df = 2$ ,  $p < 0.05$ , table 5) relationship between sex and predominated gallstone, for relevant cholesterol gallstone for females patients.

**Table 1: TSH effect on the predominance of gallstone type.**

Gallstone type	Distribution of TSH level			Total
	low	normal	high	
Pigment	8	6	11	25
Mixed	0	7	12	19
Cholesterol	2	25	29	56
Total	10	38	52	100

$X^2 = 19.0$ ,  $df = 4$ ,  $p < 0.001$ .

Table (1) shows that significant association between high TSH level and predominated cholesterol gallstone.

**Table 2: The relationship between disturbance of serum TSH and sex of patients.**

Sex of patients	Distribution of TSH level			Total
	low	normal	high	
females	8	38	7	53
males	2	0	45	47
Total	10	38	52	100

$X^2 = 69.26$   $df = 2$ ,  $p < 0.0001$ .

Table (2) reveals that high serum TSH levels were more often of male gender, while females were demonstrated high prevalence of normal TSH.

**Table 3: Association between TSH disturbance and age of patients.**

Age (years)	Distribution of TSH level			Total
	low	normal	high	
> 45	6	36	45	87
< 45	4	2	7	13
Total	10	38	52	100

$X^2 = 8.47$ ,  $df = 2$ ,  $p < 0.05$ .

Table (3) presents thyroid dysfunction has been associated to the older age more than 45 year where encourage the gallstone formation was involved.

**Table 4: The relationship between gallstone type and age of patients.**

Age (years)	Gallstone type			Total
	Cholesterol Mixed	pigment		
> 45	58	13	16	87
< 45	2	4	7	13
Total	60	17	23	100

$X^2 = 12.81$ ,  $df = 2$ ,  $p < 0.0001$ .

Table (4) shows that age was studied to be effect on the predominant cholesterol gallstone with old age patients.

**Table 5: The relationship between gallstone type and sex of patients.**

Sex of patients	Gallstone type			Total
	Cholesterol	pigment	Mixed	
females	37	10	6	53
males	23	7	17	47
Total	60	17	23	100

$\chi^2 = 8.73$ ,  $df = 2$ ,  $p < 0.01$ .

Table (5) reveals The relation between gallstone type and sex that was found a significant and cholesterol gallstone in females patients has a high rate.

## DISCUSSION

Because the pathogenesis of gallstone disease is still not well clear and strategies for prevention and efficient non-surgical therapies are missing, many studies are related to the gallstone, these research have shown that gallstone disease is related to age, sex, and metabolic disorders, such as obesity, dyslipidemia<sup>(6)</sup>. However, the current findings concerning metabolic disorder of TSH and gallstone disease are studied in relation to sex, age and it is effect of the prevalence of gallstone type. It was investigated possible associations between serum TSH levels and gallstone disease. There was an independent relation of high serum TSH levels with cholelithiasis among males. However, the potential mechanism by which elevated serum TSH levels as an independent risk factor for cholelithiasis confirm previous research<sup>(7-8)</sup>. From all 100 current cases, we examined the effects of high TSH levels in males on the gallstone formation. Excess levels of TSH can lead to the disturbances of lipid metabolism<sup>(1)</sup> that may consecutively lead to a change of the composition of the bile, and mostly involved in the pathogenesis of gallstone. Recent studies<sup>(9)</sup> also demonstrated low bile flow in hypothyroid subjects. Also, for more than 45 years, increased serum concentrations of cholesterol have been implicated in the cholelithiasis disease<sup>(10)</sup>. In this study, most of the cholesterol gallstones were found to be more commonly involved in females than males. Conflicting data exist about low level of TSH levels in females. Although several studied have implicated the role of low levels of TSH in the progression of gallstones to the females<sup>(11,12)</sup>. Therefore, in this study we have analyzed and examined the role low TSH in female because females in the studied population were had a known thyroid disorder which had diagnosed and treated because female gallstones were became symptomatic that lead to the earlier detection and treatment of hypothyroidism. The study by Henry<sup>(7)</sup> et al, demonstrated the prevalence proportions of cholelithiasis among males with low, normal and high serum TSH levels were 22.5%, 13.3% and 30.8%, respectively. In addition, The prevalence proportions of cholelithiasis among females with low, normal and high serum TSH levels were 31.7%, 24.7% and 26.7%, respectively<sup>(7)</sup>. During which (47) cases of the male population, also an association between low serum TSH levels and cholelithiasis. 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<sup>(13)</sup>. However, Previous studies that were conducted in a neighborhood region identified a high cholelithiasis prevalence proportion of greater than 22.5% in men

who was low levels of TSH, This prevalence is in good agreement with the results of our study. Also in accordance with other studies<sup>(14,15)</sup>. In their prospective approach of obvious studies could demonstrate a high proportions between males with low serum TSH levels. Including them had a higher risk of previous cholecystectomy. Which was cholelithiasis became symptomatic in an earlier state in hyperthyroid persons suggesting that part of the effect of thyroid disorder on the prevalence of gallstones was limited with patients with known thyroid disease and the thyroid function status may change dramatically over time mainly due to the effects of treatment.

### CONCLUSION:

there is a significant association between the gallstones and previously diagnosed hypothyroidism. Sex differences relation between hypothyroidism and cholelithiasis. The cholelithiasis may become symptomatic in an earlier state in hyperthyroid persons. and, the role of hyperthyroidism with respect to gallstone formation in human beings is not clear and further research is needed.

### RECOMMENDATIONS:

Since there is a significant association between the gallstones and previously diagnosed hypothyroidism , the study recommends that must handling and treatment the thyroid dysfunction and hormonal dysfunction especially TSH.

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