# Clinical study of Hyperthyroidism with Diabetes Mellitus patients and relationship with Liver function tests in Nassiriayh city

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#### Abstract

This study planned to assess liver function in patients with hyperthyroidism and diabetes mellitus .The study conclude measure the concentrations of liver enzymes such as aspartate aminotransfererase (AST), alanine aminotransfererase (ALT) and alkaline phosphates (ALP) and tests of thyroid function tests (T3),(T4) and (TSH) hormones, concentration of blood sugar (FBS) .The study take place in city of Nasiriyah in Dhi Qar. The study included 40 volunteer healthy (9 male and 31 female), 40 patients with hyperthyroidism (9 male and 31 female), 40 patients with diabetes mellitus (9 male and 31 female),40 patients with [hyperthyroidism & diabetes mellitus] together (9 male and 31 female), ages ranged from 20 - 55 years. 40 healthy volunteers were taken as a standard .In this study, the average values of the enzymes (AST),(ALT) and (ALP) significantly higher in patients compared to control group. Average values of serum glucose concentration in patients revealed a significant difference compared with the control group. Although the differences were statistically significant . Overall 35 patients (87.5%) infected with [hyperthyroidism & diabetes mellitus] together they had at least two or more abnormalities of the enzymes in liver function tests.

**Keywords** : Hyperthyroidism, Diabetes Mellitus, Alkaline phosphatise, Alanine amino transferase, Aspartate amino transferase.

# Introduction

Hyperthyroidism(**Thyrotoxicosis**) is one of the most common endocrine disorder characterised by increased secretion of thyroid hormones T3 and T4. It my be associated with diffuse goitre and ocular signs it is known as Grave's disease. It accounts for 60– 80% of all the thyrotoxic cases with the highest incidence in women between the ages of 20–40 years Grave's disease<sup>[1]</sup>. Thyroid hormones are essential for normal growth. The liver in turn metabolises thyroid hormones and regulates their systemic endocrine effects. Therefore thyroid dysfunction may disturb liver functions and liver diseases modulate thyroid hormones metabolism<sup>[2]</sup>.

Thyrotoxicosis is associated with a variety of abnormalities of liver function. The pathogenesis of hepatic dysfunction in Hyperthyroidism (**Thyrotoxicosis**) is unknown, but has been attributed to mitochondrial dysfunction and hepatic tissue hypoxia <sup>[1]</sup>. Liver has a key role in thyroid hormones metabolism and their serum

level is very important for normal function and hepatic bilirubin metabolism<sup>[3]</sup>. Besides the associations between thyroid and liver diseases of an autoimmune nature, such as primary biliary cirrhosis and Hyperthyroidism (Thyrotoxicosis) thyroid diseases are frequently associated with liver injuries and biochemical test abnormalities<sup>[2]</sup>, elevation of ALT, AST, and ALP. The liver's capacity to transport organic anions and to metabolize drugs- Serum bilirubin, urine bilirubin, urobilinogen. The Liver's biosynthetic capacity-Serum proteins, albumin, prealbumin, ceruloplasmin, procollagen serum peptide, antitrypsin, a feto protein, prothrombin time <sup>[4]</sup>. These thyroids liver associations may cause diagnostic confusions and neglect of these facts may result in over or under diagnosis of associated liver diseases and thyroid diseases. Therefore it is suggested to measure free T4 and TSH level to rule out coexistent possibility of thyroid dysfunction in any patient with unexplained liver biochemical test abnormalities. All the studies carried out reflect a strong relationship between thyroid and liver in health and disease <sup>[1]</sup>. In diabetes mellitus over there, that a strong link exists between certain liver enzymes such as g-glutamyltranspeptid (GGT), and alanine transaminase (ALT), and diabetes. These liver enzymes may be involved in several critical processes that affect the risk of developing conditions such as diabetes. In conclusion, elevations of concentrations of GGT and ALT translated into an increase in the incidence of diabetes .Although the mechanisms for these associations along with possible avenues of interventions require further the investigation, considerable knowledge base at present seriously merits considering elevations of GGT and possibly those of ALT as pointing

an increased potential for to developing diabetes<sup>[5]</sup>. In type 2 diabetes have a higher incidence of liver function test abnormalities than who do not have diabetes. Determine whether hepatic enzyme elevations could be linked to the development of type 2 diabetes. At baseline, ALT, AST, and GGT were related to percent body fat. After adjustment for age, sex, fat. whole body body insulin sensitivity, and acute insulin response, only elevated ALT at baseline was associated with an increase in hepatic glucose output. Prospectively, increasing ALT concentrations were associated with a decline in hepatic insulin sensitivity and risk of type 2 diabetes. The authors concluded that higher ALT is a risk factor for type 2 diabetes and indicates a potential role of increased hepatic gluconeogenesis and/or inflammation in the pathogenesis of type 2 diabetes <sup>[6]</sup>. Aims of this study:- To find The abnormalities of in liver function test in patients with combined diabetes mellitus and hyperthyroidism, and to find relationship the between [hyperthyroidism& diabetes mellitus] and liver function tests .

## Materials and methods:

Blood samples were collected from 160 samples included four groups: Samples for 40 volunteers' healthy (9 male and 31 female) control (C), Samples for 40 patients with Diabetes Mellitus (D), Samples for 40 patients with Hyperthyroidism (H) and 40 patients Samples for with Hyperthyroidism with Diabetes Mellitus (H&D) .We determines all groups serum levels blood sugar (Fasting Blood Sugar) by manual, thyroid function tests T3,T4 and TSH mnividas Supplier, (by Vidas Company, France) and liver function tests (enzymes) AST,ALT and ALP

(by Reflotron Supplier .Roche Company Germany).In center of Diabetic Endocrine and Gland specialization in Thi Qar patients with diabetes mellitus (DM) for period Nov. 2011 to john. 2012 .The patients were composed of 93 females (77.5%) and 27 males (22.5%).

#### **Statistical Analysis:-**

All data were expressed as mean  $\pm$  SD of the number of experiments. The statistical significance was evaluated by Student's t-test using SPSS version 10.0. Values are given as mean  $\pm$  SD (\*p<0.01).

**Results:-**Three variables were measured for all the cases and controls, i.e., plasma level of liver specific enzymes ALT, AST and ALP. Reports of serum levels of thyroid hormones

T3, T4 and TSH were available with however, they the cases; were measured in the controls. The data were analyzed to compare the mean values between cases and controls and to find out correlation between thyroid hormones profile and liver enzymes profile in the cases and controls <sup>[4]</sup>. The Table [1] demonstrated the level of Thyroid Hormones of the patients in all . The level of Thyroid group Hormones of the patients are different from group to another. The highest level of Thyroxine (T4) and Triiodothyronine (T3) hormones are for the value's with hyperthyroidism & Diabetes Mellitus followed by the patient's. The lowest level of Thyroid-Stimulating Hormone (thyrotropin) (TSH) was for the value's with hyperthyroidism followed by the patient's.

Groups	Number	TSH	T4	Т3
Control	40	2.4713 <u>+</u> 1.2899	98.8500 <u>+</u> 14.2919	2.1513 <u>+</u> 0.5160
Diabetes Mellitus	40	2.465 <u>+</u> 1.1059	95.8428 <u>+</u> 15.5871	1.8240 <u>+</u> 0.4258
Hyperthyroidism	40	0.0600 <u>+</u> 0.0184	224.9248 <u>+</u> 54.557	5.4838 <u>+</u> 1.3946
Diabetes Mellitus & Hyperthyroidism	40	0.0735 <u>+</u> 0.0296	234.2125 <u>+</u> 48.551	5.6050 <u>+</u> 1.3913
Normal Value	_	0.25-5.0 n.mol/l	60-120 n.mol/l	0.92-5.0 n.mol/l

Table [1]: Thyroid profile of the cases and controls (n.mol/l) (Mean + Std. Deviation).

T3:Tri-iodothyronine T4:Thyroxin

TSH: Thyroid-Stimulating Hormone

The Table [2] explained the level of the sugar (Glucose) in blood of the patients are different from group to another . The highest level of sugar was for the value's with Diabetes Mellitus followed by the patient's with (Hyperglycemia). The level of sugar was for the value's increase with hyperthyroidism & Diabetes Mellitus followed by the patient's, while the value's with hyperthyroidism was normal.

Table [2]:Diabetes Mellitus of the all groups (mg/dl) (Mean + Std. Deviation).

Groups	Number	FBS	Male / Female
Control	40	94.0250 <u>+</u> 14.2622	9 / 31
Diabetes Mellitus	40	223.2750 <u>+</u> 63.6485	9 /31
Hyperthyroidism	40	98.3000 <u>+</u> 12.8506	9 /31
Diabetes Mellitus & Hyperthyroidism	40	217.0500 <u>+</u> 54.3483	9 / 31
Normal Value		70-120 mg/dl	

The Table [3] showed the level of liver enzymes in Females, Aspartate amino transferase (AST), Alanine amino transferase (ALT) and Alkaline Phosphates (ALP) of the patients are significant difference from groups to another compared with control group. The highest level of Aspartate amino transferase (AST), Alanine amino transferase (ALT) and Alkaline Phosphates (ALP) are for the value's with hyperthyroidism & Diabetes Mellitus followed by the patient's

Table [3]:Liver enzymes profile of the Female (U/L) (Mean + Std. Deviation)

Groups	Number	AST	ALT	ALP
Control	31	26.745±11.25	14.307±8.50	61.181±24.73
Diabetes Mellitus	31	25.981±9.01	20.735±10.98	81.265±18.08
Hyperthyroidism	31	29.303±11.52	17.742±7.59	85.790±58.82
Diabetes Mellitus & Hyperthyroidism	31	36.692±5.38	36.445±6.38	140.790±32.47
Normal value to Female by Reflotron Supplier		Up to 33 U/L	Up to 32 U/L	35-104 U/L

The Table [4] showed the level of liver enzymes in Males, Aspartate amino transferase (AST), Alanine amino transferase (ALT) and Alkaline Phosphates (ALP) of the patients are significant difference from groups to another compared with control group. The highest level of Aspartate amino transferase (AST) was for the value's with hyperthyroidism. The highest level of alanine amino transferase (ALT) and Alkaline Phosphates (ALP) are for the value's with hyperthyroidism & Diabetes Mellitus followed by the patient's.

Table [4]:Liver enzymes profile of the Male (U/L) (Mean + Std. Deviation)

	Number	AST	ALT	ALP
Control	9	21.122±8.43	18.078±6.02	77.156±29.55
Diabetes Mellitus	9	28.078±11.25	22.822±12.32	70.289±19.78
Hyperthyroidism	9	40.800±20.63	19.078±6.33	91.744±45.24
Diabetes Mellitus &	9	38.633±6.21	38.078±6.88	139.356±22.45
Normal value to		Up to 41 U/L	Up to 40 U/L	40-129 U/L

#### DISCUSSION

Liver function test it's a toll of the test to identification the

dysfunction or the damage of liver tissue. It reflex the effect that happened on the liver, for by some reasons like the age, sex, environmental factors, various diseases and drugs <sup>[1]</sup>. The liver made many functions, so that we need more test to know or prognosis and diagnosis to liver function. The masseur of the concentration of liver enzymes refer to diagnosis in injury or damage on liver tissue. The rising of liver enzyme for long period and without diagnosis or care of the case, lead to develop for chronic liver disease. That give the values and high level enzyme that cause less than injury or damage in the liver tissue . We get the results on high level Std. Deviation and that cause high range width and dispersed value. Table (1) shown the values of hormone concentrations for all groups , the group with diabetes mellitus is normal value, while the values of two groups (hyperthyroidism & hyperthyroidism with diabetes mellitus) are very high T4 and T3 hormones and very low in TSH, comparison with the control group.

Table (2) explain the values of blood sugar concentrations (fasting blood sugar) to all groups, the group effected with hyperthyroidism is normal value while the values of two mellitus groups (diabetes & hyperthyroidism with diabetes mellitus) are very high comparative with the control group. Table (3) values of enzyme explain the concentrations AST, ALT and ALP for female while the table (4) explain this values for male, we notice the values of enzyme concentrations in the group at effected with diabetes mellitus one from three enzyme is abnormal ( high values ) for male and female

percentage 15% ,15% and 5% respectively from (40 patients) with diabetes mellitus comparative with the control group, the reason come back to a long period of disease and the treatment with drug or the end of Insulin degradation in the liver tissue cause secretion of this enzymes, this elevation in enzymes comprise two types of diabetes mellitus <sup>[6,7]</sup> surrogate markers of liver dysfunction and nonalcoholic fatty liver. This is considered as part of metabolic syndrome and related diabetes mellitus <sup>[8]</sup>. The patients with diabetes have an increased incidence of severe fibrosis and when the patient was being treated with insulin <sup>[9]</sup>, or progress of this disease ,we notice the enzyme concentrations in the group of the effected with hyperthyroidism one or two from three enzymes are abnormal (high value )at male and female in percentage 30%,15% and 15% respectively from 40 patients effected with hyperthyroidism comparative with control group this result agree with <sup>[10,11]</sup>, the reason come back to long period of disease and treatment with drugs such as (methimazole, carbimazole and agree propylthiouracil), this with <sup>[2,12,13,14]</sup>. The end place of hormones degradation in the liver and the excess of this hormones cause damage in this tissue, this agree with [2,11,12]. The hyperthyroidism effected on the liver lead to elevation of liver enzymes secretion, this result agree with<sup>[13,14,15]</sup>. All this reasons are effected on the liver lead to elevation of liver enzymes secretion.

In the group effected with (hyperthyroidism & diabetes mellitus), we notice two from three enzymes are abnormal in percentage 75%,80% and 60% respectively from 40 patients, in the female the percentage of abnormal enzymes 100% from 31 patients, whether in the male the percentage were 77.7% from 9 patients ( two from three enzymes are abnormal), the reasons come back to the sickness of patients with two cases and the long of period, treatment of the drug its effect on the liver functions the reason come back to use treatment by antithyroid and antidiabetic, this result agree with <sup>[16,17]</sup>. The end place of hormones degradation in the liver and the excess of this hormones cause damage in this tissue, this agree with [2,13]. The hyperthyroidism effected on diabetes mellitus and the two cases effected on liver, this conduce elevation of liver enzymes secretion. The relationship between hyperthyroidism and diabetes mellitus ( two types) is reverse and the two cases effected on liver function , this result agree with <sup>[14,18,19]</sup>. The carelessness of continuation this cases may be conduce to chronic liver disease .The hyperthyroidism and diabetes mellitus effected on the liver lead to elevation of liver enzymes secretion, this result agree with<sup>[18,19]</sup>. All this reasons are effected on the liver lead to elevation of liver enzymes secretion.

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#### الخلاصة

تم اجراء هذه الدراسة لتقييم وظيفة الكبد في المرضى المصابين بحالتي فرط افراز الغدة الدرقية وداء السكّري معاً بقياس تراكيز انزيمات الكبد مثل اسبارتات ترانس اميينيز (AST) والانيين ترانس اميينيز (ALT) والفوسفاتيز القاعدي ( ALP) ، وفحوصات هرمونات الغدة الدرقية (T3) و(T4) و (TSH) , وفحص قياس تركيز السكر بالدم حال الصيام (FBS). الدراسة تمت في مدينة الناصرية في محافظة ذي قار تضمنت 40متطوّع اصحاء (9 ذكر آ و 11 أنثى)، و 40 مريضاً مصابآبفرط افراز الغدة الدرقية (9 ذكر آ و 31 أنثى) ، و 40 مريضاً مصابآ بداء السكّري (9 ذكر آ و 11 أنثى) ، و 40 مريضاً مصابآ بحالتي فرط افراز الدرقية وداء السكّري معاً (9 ذكر آ و 31 أنثى) ، و 40 مريضاً مصابآ بحالتي فرط افراز الدرقية وداء السكّري معاً (9 ذكر آ و 31 أنثى) ، أو 40 مريضاً مصابآ بحالتي فرط افراز الدرقية وداء السكّري معاً (9 ذكر آ و 31 أنثى) ، أعمار همّراوحت و 31 أنثى فرط افراز الدرقية وداء السكّري معاً (9 ذكر آ و 31 أنثى) ، أعمار مماراً بحالتي أنتى القيم للانزيمات (AST) و (ALT) أعلى جداً في المرضى مُقَارَنِة إلى المجموعة القياسية. اما متوسط قيم تركيز الكلوكوز في المصل المرضى يبين 21 معاد معا القياسية. اما متوسط قيم تركيز الكلوكوز في المصل المرضى يبين إختلاف مصاب بفرط افراز الدرقية ورات الاختلافات واضحة احصائيا . عموماً 35 مريض (7.5 %) مصاب بفرط افراز الدرقية وارتفاع تركيز السكر بالدم معلكان لديهم على الأقل اثنان او اكثر من إنزيمات فحوصات وظيفة الكبر غير طبيعية.