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# **Levels of Liver Enzymes and Some Changes in Renal Functions in Iraqi Hypothyroid Patients Women**

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## **Summary**

The present study aimed to investigate physiological disorders in some liver and kidney functions in hypothyroid Iraqi women .The study was carried on 120 subjects in the Specialist Center of Endocrine and Diabetic diseases at Rusafa region, near AL-Kindeg Hospital . That study began on 20/10/2013 to 25/1/2014

The subjects were divided into 4 groups (control, euthyroid ,subclinical and overt hypothyroid).Each group included 30 females ,their ages ranged ( $39.45 \pm 1.79$ ) years.

The results showed a significant( $P < 0.05$ ) increase in the level of TSH in subclinical ( $18.23 \pm 2.34 \mu\text{u/l}$ ) and overt hypothyroid patients ( $41.37 \pm 3.75 \mu\text{u/l}$ ) in comparison with control ( $2.09 \pm 0.23 \mu\text{u/l}$ ) and euthyroid groups ( $2.89 \pm 0.20 \mu\text{u/l}$ ). The levels of T4 and T3 were within the normal limits in control ( $79.73 \pm 2.11 \text{ nmol/L}$ ); ( $1.70 \pm 0.07 \text{ nmol/L}$ ), euthyroid ( $87.10 \pm 2.16 \text{ nmol/L}$ ) ; ( $1.58 \pm 0.05 \text{ nmol/L}$ ) and subclinical ( $77.76 \pm 2.31 \text{ nmol/L}$ ) ; ( $1.52 \pm 0.08 \text{ nmol/L}$ ) respectively. While overt hypothyroid group showed a significant ( $P < 0.05$ ) decrease in T4 level ( $46.36 \pm 2.32 \text{ nmol/L}$ ) with normal T3( $1.30 \pm 0.11 \text{ nmol/L}$ ).

The changes in liver function tests in overt hypothyroid group showed a significant ( $P < 0.05$ ) increase in the levels of SGOT ( $23.05 \pm 2.67 \text{ U/L}$ ), SGPT( $21.89 \pm 2.35 \text{ U/L}$ ) and ALP( $99.98 \pm 7.47 \text{ U/L}$ ) in comparison with SGOT in control ( $8.80 \pm 0.88 \text{ U/L}$ ) , euthyroid ( $11.36 \pm 0.85 \text{ U/L}$ ) and subclinical ( $11.88 \pm 1.42 \text{ U/L}$ ) and SGPT in control ( $13.46 \pm 0.75 \text{ U/L}$ ) euthyroid ( $10.93 \pm 1.03 \text{ U/L}$ ), and subclinical ( $14.08 \pm 1.87 \text{ U/L}$ ) and in the level of ALP in control( $50.27 \pm 2.65 \text{ U/L}$ ), euthyroid ( $65.27 \pm 2.87 \text{ U/L}$ ) and subclinical( $71.58 \pm 4.90 \text{ U/L}$ ) respectively.

Total serum protein( $7.49 \pm 0.16 \text{ g/dl}$ ) and bilirubin ( $1.23 \pm 0.11 \text{ mg/dl}$ ) were increased significantly ( $P < 0.05$ ) in overt hypothyroid patients in comparable with control ( $6.82 \pm 0.04 \text{ gm/dl}$ ) ; ( $0.613 \pm 0.04$

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mg/dl), euthyroid ( $6.93 \pm 0.07$  gm/dl); ( $0.653 \pm 0.04$  mg/dl), and subclinical ( $6.91 \pm 0.08$  gm/dl); ( $0.883 \pm 0.08$  mg/dl) respectively.

Creatinine level was increased significantly ( $P < 0.05$ ) in subclinical and overt hypothyroid groups ( $1.07 \pm 0.07$  mg/dl); ( $1.26 \pm 0.06$  mg/dl), in comparable with control and euthyroid groups ( $0.846 \pm 0.03$ ), ( $0.836 \pm 0.02$ ) respectively. The level of uric acid was increased significantly ( $P < 0.05$ ) in the overt group ( $7.11 \pm 0.11$  mg/dl) in comparable with control, euthyroid and subclinical ( $3.78 \pm 0.18$  mg/dl), ( $3.66 \pm 0.16$  mg/dl), ( $4.42 \pm 0.28$  mg/dl) respectively.

We concluded from this study that the overt hypothyroidism had effected the liver function tests by increasing liver enzymes SGOT, SGPT, and ALP. Also we found that total plasma protein and bilirubin levels were increased in overt hypothyroid group. The renal function test showed an increase in the levels of creatinine in subclinical and overt hypothyroid groups while uric acid increased in overt hypothyroid.

Euthyroid group showed normal levels for the above studied parameters which means that the levels of these parameters returned to the normal values in treated hypothyroid group (euthyroid patients) with Levodroxine -L at a dose 50mg or 100 mg orally.

### Introduction:

Thyroid gland is one of the largest endocrine gland, it weights 20-25 grams (1). It is regarded as the master gland to control the body metabolism, growth, development and maintenance at the internal environment. It works under the control of thyroid stimulating hormone (TSH) which in turn is under the control of (TRH). It secretes 93% thyroxine (T4) and 7% tri-iodothyronine T3 (2). Thyroid disorders are commonly separated into two major categories hyperthyroidism (over active thyroid gland) and hypothyroidism (under active thyroid gland). Depending on whether serum thyroid hormones levels (T4, T3) are increased or decreased. (3,4,5,6). Primary hypothyroidism is indicated when TSH level high  $> 10$  mu/l with decreased T3 and T4 levels, secondary hypothyroidism is diagnosed when TSH is low  $< 0.4$  mu/l with decreased T3 and T4 levels, whereas the diagnosed of subclinical hypothyroidism is mainly based on increased TSH level between 4.5 -10 mu/l while T3 and T4 with in normal range. (7,8). Subclinical hypothyroidism may progress to overt hypothyroidism in approximately 2.5% of cases annually (9,10).

Thyroid hormones regulate the Basal Metabolic Rate (BMR) of all cells including hepatocytes and there by modulate hepatic function (11). Hypothyroidism may have features that mimic liver disease and

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muscle cramps in the presence of elevated of AST(SGOT) enzyme from myopathy (12). Pandey *et al.* (13) had been reported that the alterations in liver enzymes occurred in hypo and hyperthyroidism patients in pokhara. More over total serum protein and bilirubin levels were also affected in hypothyroid patients(14,15,16). It was found that serum creatinine and uric acid levels were increased in hypothyroid patients and could be affected due to a decrease in the levels of T4 and T3 hormones (14,15,17,18)

### Aims of the study:-

To investigate the physiological disorders in some liver and renal functions in females hypothyroid patients through the following items:

- 1- Thyroid hormones (TSH,T4,T3) assay among control and hypothyroid groups.
- 2-Biochemical measurements for liver functions :
  - a-Liver enzymes(AST,ALT and ALP u/l).
  - b-Bilirubin levels mg/dl.
  - c-Total serum protein levels (TSP) gm/L.
- 3-Biochemical parameters for renal function test:
  - a-Serum creatinine (mg/dl).
  - b-Uric acid (mg/dl).

### Materials and Methods:

#### Collection of Information

A questionnaire form was used for recording the necessary information that concerning with subject groups which included name, age, sex, length, body weight, blood arterial pressure, duration of the disease, type of medical treatment beside marital status.

#### samples collection:

The study was conducted on( 120 ) females divided into four groups (control ,euthyroid ,sub clinical and overt hypothyroid patients),each group included 30 subjects. Their ages ranged between 20-60 years with average  $(39.45 \pm 1.79)$  who visited to the Center Specialist Endocrine and Diabetes Diseases, at Al-Rusafa region adjacent to the AL-kindy hospital, the study was begun at (20/10/2013-25/1/2014). Ten milliliter of blood via veni puncture was drawn from each fasting individual between 8:30 to 10:30 AM, by using disposable syringes and placed in sterile tubes and left at room temperature for 15-30 minutes and then centrifuged at a rate of 5000 rpm for ten minutes. Sera were separated and kept in Apendrof tubes, stored in deep freeze, at  $-20^{\circ}\text{C}$  till examination for biochemical assay.

#### Experimental design

The study included four groups :

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- 1- First group(control group) included (30) subjects, their age ranged between 20-30 years by mean ( $34.17 \pm 1.63$ ).
- 2- Second group (Euthyroid) included (30) subjects, their age ranged between 21-60 years with mean ( $41.03 \pm 2.21$ ).
- 3- Third group (subclinical) included (30) subjects, their age ranged between 23-60 years with mean ( $41.70 \pm 1.63$ ).
- 4- Fourth group (overt hypothyroidism) included (30) subjects, their age ranged between 23-60 years with mean ( $40.93 \pm 1.69$ ).

### Samples collection for testing :

**1-Thyroid hormones assay:**(Thyroid stimulating hormone (TSH)( $\mu\text{u/l}$ ), Thyroxine hormone (T4) ( $\text{nmol/l}$ ) and Tri-iodothyronine (T3) ( $\text{nmol/l}$ ))

### 2-Biochemical parameters for liver functions:

- a- Liver enzyme (Alanine Aminotransferase (ALT),Aspartate Aminotransferase (AST) and Alkaline phosphatase (ALP))
- b- Bilirubin ( $\text{mg/dl}$ ).
- c- Total serum protein (TSP)  $\text{gm/l}$ .

### 3-Biochemical parameters for renal function test:

- a-Serum creatinine ( $\text{mg/dl}$ ).
- b-Uric acid ( $\text{mg/dl}$ ):.

### Measurement of Thyroid Hormones Levels (TSH,T4,T3) in Blood Serum:

**TSH,T4,T3** hormone concentrations were measured in the serum by using Biomerieux kits according to the vidas method.

At the end of assay results are automatically calculated by instrument in relation to the calibration curve stored in memory ,and then printed out.

### Reference Range:

**TSH**=0.25 - 5.3  $\mu\text{u/l}$  , **T4** =60 - 120  $\text{nmol/l}$  , **T3** = 0.4 - 2.3  $\text{nmol/l}$

### Liver Enzymes Test:

**Alanine Aminotransferase (ALT):**ALT was measured in sera for subjects using Randox kits,by colorimetric method Reitman and Frankel(19)

**Principle:-** $\alpha$ -oxoglutarate + L -alanine  $\xrightarrow{\text{ALT}}$  L- glutamate + pyruvate  
Alanine Aminotransferase was measured by monitoring in the concentration of pyruvate

**Normal range :** Men 4-31  $\text{u/l}$  , Women 4-21  $\text{u/l}$

### Aspartate Aminotransferase (AST)

Concentration of AST was measured in the sera for subjects using Randox kit by colorimetric method Reitman and frankel (19)

**Principle:-**

$\alpha$ -oxoglutarate + L-aspartate  $\xrightarrow{\text{GOT}}$  L-glutamate + oxaloacetate

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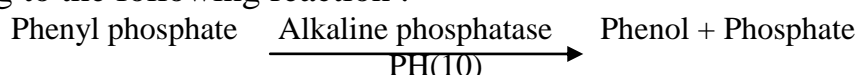
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- 1- Mix and read the absorbance of sample (A sample) against the reagent blank after 5 minutes by spectrophotometer at a wave length 546 nm

**Normal range :** Men 4-26 u/l Women 4-21 u/l

**Phosphatase alkaline:** The Phosphatase alkaline was measured in serum by using Biomerieux method according to method of kit.

**Principle:-**Colorimetric determination of alkaline phosphatase activity according to the following reaction :



The liberated phenol is measured in the presence of 4-aminoatipyrine and potassium ferricyanide .The presence of sodium arsenate in the reagent stops the enzymatic reaction . Kind and King(20) , Befield and Goldberg(21)

**Range of expected values in serum:**

**Children:** 10-20 kind and king U/100 ml ; 71-142 u/l

**Adults:** 3-13 kind and king U/100 ml ; 21-92 U/l

One kind and king u/100ml:n =20 ; **Note :** U/l : n =14

**Total Serum Protein :** The total protein was measured by using Biuret method according to of kit. Koller *et al.*(24)

**Principle: -** Protein gives an intensive violet – blue complex with copper salts in an alkaline medium .Iodide is included as an antioxidant .The intensity of the color formed is proportional to the total protein concentration in sample.Koller *et al.*(24), Burtis *et al.*(23).

**Reference values: Adult :** 6.6- 8.3 g/dl **New born :** 5.2 – 9.1 g/dl.

**Bilirubin :**The Bilirubin was measured in serum by using Randox method according to method of kit.

**Principle:-**Direct (conjugated) bilirubin reacts with diazotized sulphanilic acid in alkaline medium to form a blue coloured complex .Total bilirubin is determined in the presence of caffeine ,which releases albumin bound bilirubin ,by the reaction with diazotized.

**Normal values in serum:**

**Total Bilirubin** up to 17  $\mu$  mol/l , up to 1mg/dl

**Direct Bilirubin** up to 4.3  $\mu$  mol/l

**Kidney Functions Test:**

**Measurement of Serum Creatinine**

The creatinine was measured by using jaffe colorimetric test according to method of kit.

**Reference values:** serum or plasma

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**Male :** 0.7 – 1.4 mg/dl = 61.8 – 123.7  $\mu$  mol/l

**Female:** 0.6 – 1.1 mg/dl = 53.0 – 97.2  $\mu$  mol/l

## Measurement of serum uric acid:

Uric acid was measured in serum by using biosystems kit method

**Principle:-** Uric acid in the sample originates by means of coupled reaction is

described below and a coloured complex that can be measured by spectrophotometer .(Barham and Trinder, (24), Fossati *et al.*(25)

Uric acid + O<sub>2</sub> + 2H<sub>2</sub>O  $\xrightarrow{\text{uricase}}$  Alantion + CO<sub>2</sub> + H<sub>2</sub>O

2H<sub>2</sub>O<sub>2</sub> + 4-Aminoantipyrine + DcFs  $\xrightarrow{\text{peroxidase}}$  Quinoneimine + 4H<sub>2</sub>O

**Reference values:** Serum and plasma

**Men :** 3.5 – 7.2 mg/dl = 210 - 420  $\mu$  mol/l

**Women :** 2.6 – 6.0 mg/dl = 150 - 350  $\mu$  mol/l

## Statistical Analysis

Statistical analysis was performed using “The statistical Analysis System-SAS (2010)” .Analysis of variance one way (ANOVA) was done to assess the significance among the groups and between groups respectively.

Least significant difference ,LSD under probability (p < 0.05 ; P < 0.01)was used to significant comparison between means of the groups Pearson correlation coefficient between parameters was estimated.

## Results and Discussion

**Results:** Table (1) is presented the levels of thyroid hormones in all study groups:

**Table (1) comparison between TSH, T4 & T3 values (M  $\pm$  SE) in control , Euthyroid, Subclinical and Overt hypothyroid subjects.**

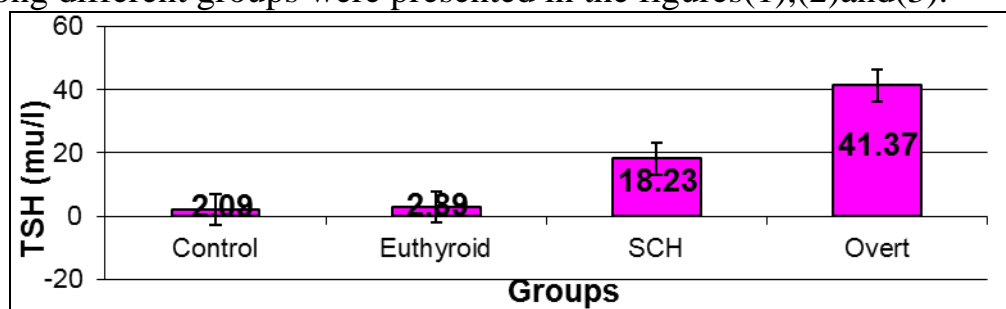
Parameters	TSH	T4	T3
Groups	(0.25-5.3)	(60-120)	(0.4-2.3)
N. values	(mu/l)	(n mol/l)	(n mol/l)
Control	2.09 $\pm$ 0.23 c	79.73 $\pm$ 2.11 b	1.70 $\pm$ 0.07 a
Euthyroid	2.89 $\pm$ 0.20 c	87.10 $\pm$ 2.16 a	1.58 $\pm$ 0.05 a
Subclinical	18.23 $\pm$ 2.34 b	77.76 $\pm$ 2.31 b	1.52 $\pm$ 0.08 ab
Overt	41.37 $\pm$ 3.75 a	46.36 $\pm$ 2.32 c	1.30 $\pm$ 0.11 b
LSD Value	6.12 *	6.250 *	0.225 *
* (P<0.05).			

A significant (P< 0.05) increase was observed in the levels of serum TSH in the subclinical (18.23 $\pm$  2.34 mu/L) and overt (41. 37 $\pm$  3.75 mu/L) groups in comparison with the control (2.09  $\pm$  0.23 mu/L) and euthyroid (2.89 $\pm$  0.20 mu/L) groups. There was a significant (P< 0.05) decrease in the levels of T4 hormone (46.36 $\pm$ 2.32 nmol/l) in the overt hypothyroid

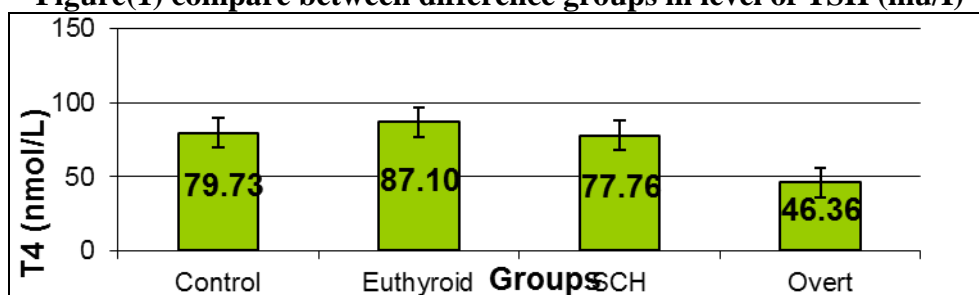
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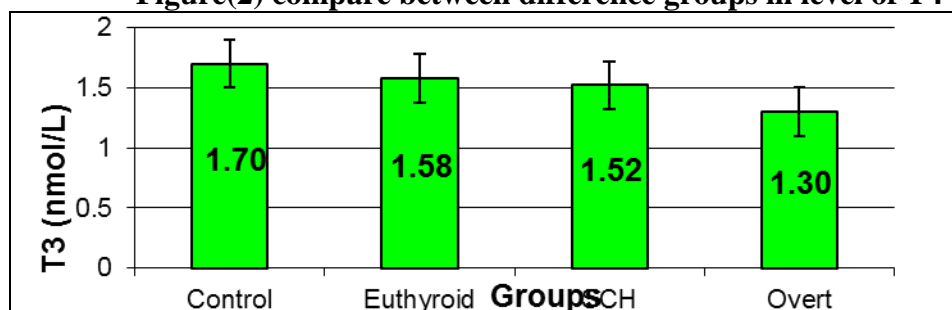
group in comparison with control ( $79.73 \pm 2.11$  nmol/l), euthyroid ( $87.10 \pm 2.16$  nmol/l) and subclinical ( $77.76 \pm 2.31$  nmol/l) groups. Although there was a significant ( $P < 0.05$ ) increase in the levels of T4 ( $87.10 \pm 2.16$  nmol/l) in the euthyroid group but the value was within normal limits (60-120 nmol/l). The subclinical and overt groups showed a significant ( $P < 0.05$ ) decrease in the level of T3 ( $1.52 \pm 0.08$  nmol/l); ( $1.30 \pm 0.11$  nmol/l) respectively in comparison with euthyroid and control ( $1.58 \pm 0.05$  nmol/l); ( $1.70 \pm 0.07$  nmol/l) groups. But the values were within normal range (0.4-2.3 nmol/l) so the subclinical group showed high TSH with normal levels of T4 and T3 hormones, while the overt group showed highly increase of TSH ( $41.37 \pm 3.75$  nmol/l) with low level of T4 ( $46.36 \pm 2.32$  nmol/l) and normal level of T3. The levels of thyroid hormones among different groups were presented in the figures (1), (2) and (3).



Figure(1) compare between difference groups in level of TSH (mu/l)



Figure(2) compare between difference groups in level of T4



Figure(3) compare between difference groups in level of T3 (nmol/l)

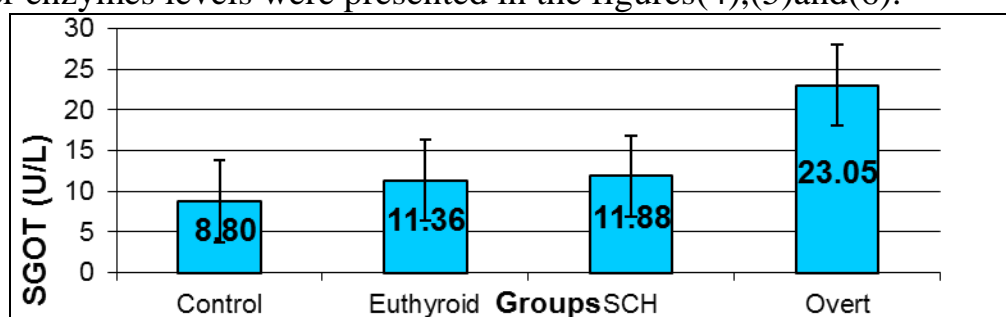
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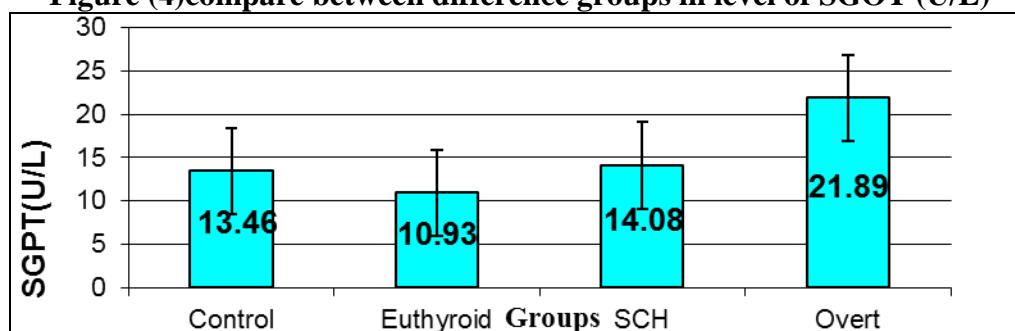
**Table(2) showed the levels of liver enzymes among study groups.**

Parameters	SGOT	SGPT	ALP
Groups	(4-21)	(4-24)	(21-92)
N. values	(U/L)	(U/L)	(U/L)
Control	8.80 ± 0.88 b	13.46 ± 0.75 b	50.27 ± 2.65 c
Euthyroid	11.36 ± 0.85 b	10.93 ± 1.03 b	65.27 ± 2.87 b
Subclinical	11.88 ± 1.42 b	14.08 ± 1.87 b	71.58 ± 4.90 b
Overt	23.05 ± 2.67 a	21.89 ± 2.35 a	99.98 ± 7.47 a
LSD Value	4.575 *	4.581 *	13.669 *
* (P<0.05).			

The level of SGOT ( $23.05 \pm 2.67$ u/L) was increased significantly ( $P < 0.05$ ) in the overt group when compared with control ( $8.80 \pm 0.88$  u/L); euthyroid ( $11.36 \pm 0.85$  u/L) and subclinical ( $11.88 \pm 1.92$  u/L) there was a significant ( $P < 0.05$ ) increase in the level of SGPT ( $21.89 \pm 2.35$ u/L) in the overt group. In comparison with control ( $13.46 \pm 0.75$ ) euthyroid ( $10.93 \pm 1.03$  u/L) and subclinical ( $14.08 \pm 1.87$  u/L) but the levels of SGPT in overt group ( $21.89 \pm 2.75$ u/L) was within normal range (4-24 u/L). The overt group showed a significant ( $P < 0.05$ ) increase in the levels of ALP ( $99.98 \pm 7.47$ u/L) in comparison with control ( $50.27 \pm 7.65$ u/L), euthyroid ( $65.27 \pm 2.87$ u/L) and subclinical ( $71.58 \pm 4.90$  u/L). Although there was a significant increase ( $P < 0.05$ ) in the ALP levels in euthyroid ( $65.27 \pm 2.87$  u/L) and subclinical ( $71.58 \pm 4.90$  u/L) but the values were within normal range (21-92 u/L). The all differences among liver enzymes levels were presented in the figures(4),(5)and(6).



**Figure (4) compare between difference groups in level of SGOT (U/L)**



**Figure (5) compare between difference groups in level of SGPT (U/L)**



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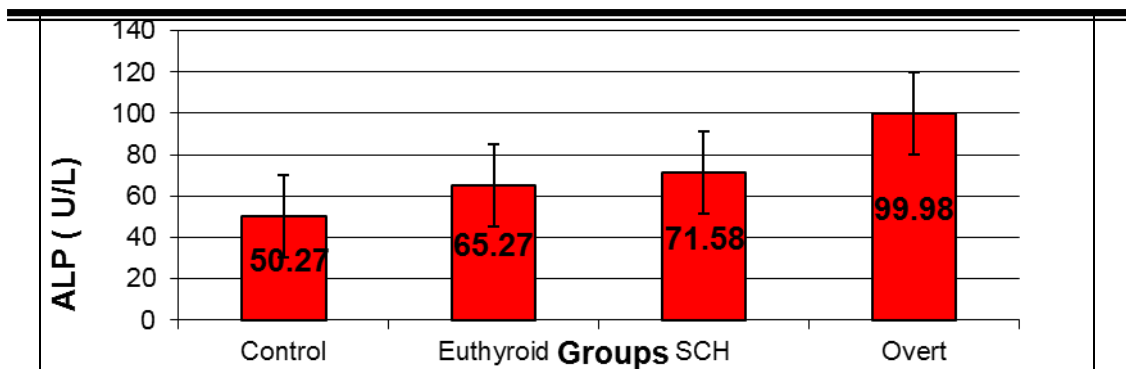


Figure (6) compare between difference groups in level of ALP (U/L)

Table (3) levels of total serum protein , Bilirubin and (M ± SE) in the study groups

Parameters	Protein	Bilirubin
Groups	(6.6-8.3)	(1-1.1)
N. values	(g/dl)	(mg/dl)
Control	6.82 ± 0.04 b	0.613 ± 0.04 c
Euthyroid	6.93 ± 0.07 b	0.653 ± 0.04 c
Subclinical	6.91 ± 0.08 b	0.883 ± 0.08 b
Overt	7.49 ± 0.16 a	1.23 ± 0.11 a
LSD Value	0.283 *	0.208 *
* (P<0.05).		

A significant ( $P < 0.05$ ) increase was observed in the level of total serum protein ( $7.49 \pm 0.16$  gm/dl) ,when compared with the control( $6.82 \pm 0.04$ ) g/dl,euthyroid( $6.93 \pm 0.07$ )g/dl and subclinical ( $6.91 \pm 0.08$ )g/dl respectively, the overt group was within normal values (6.6-8.3)g/dl.The serum bilirubin level increased ( $P < 0.05$ ) significantly ( $1.23 \pm 0.11$  mg/dl) in the overt group when compared with control ( $0.61 \pm 0.04$  mg/dl),euthyroid ( $0.65 \pm 0.04$  mg/dl) and subclinical ( $0.88 \pm 0.08$  mg/dl) ,respectively. figure(7) and (8).

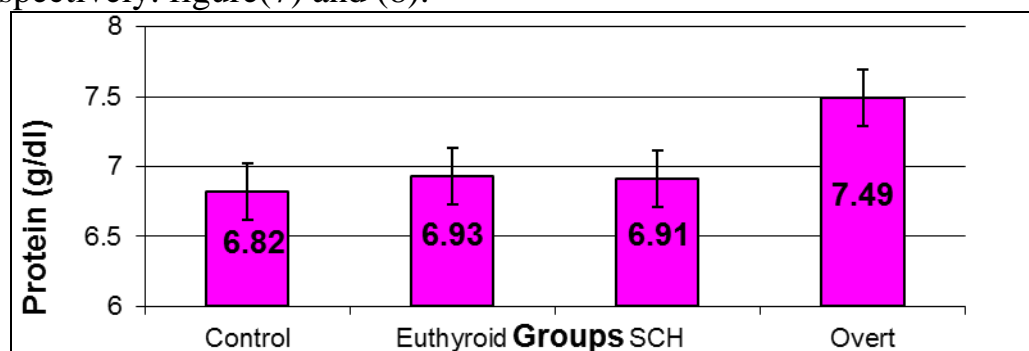


Figure (7) Compare between difference groups in level of Protein (g/dl)

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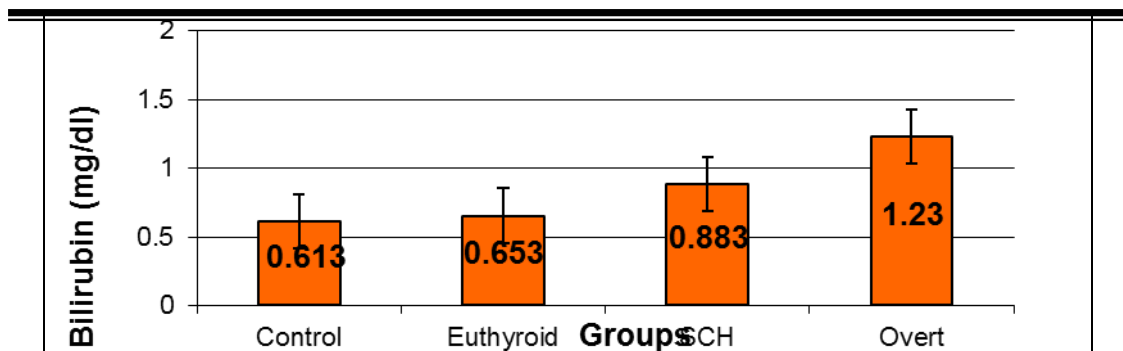


Figure (8) Compare between difference groups in level of Bilirubin (mg/dl)

Table (4) Levels of Creatinine and Uric acid ( $M \pm SE$ ) in study groups

Parameters	Creatinine	Uric acid
Groups	(0.6-1)	(2.5-6.8)
N. values	(mg/dl)	(mg/dl)
Control	$0.846 \pm 0.03$ c	$3.78 \pm 0.18$ c
Euthyroid	$0.836 \pm 0.02$ c	$3.66 \pm 0.16$ c
Subclinical	$1.07 \pm 0.07$ b	$4.42 \pm 0.28$ b
Overt	$1.26 \pm 0.06$ a	$7.11 \pm 0.11$ a
LSD Value	0.140 *	0.555 *
* ( $P < 0.05$ ).		

A significant ( $P < 0.05$ ) increase in the level of serum creatinine was noticed in the subclinical ( $1.07 \pm 0.07$  mg/dl) and overt groups ( $1.26 \pm 0.06$  mg/dl) in comparison with euthyroid ( $0.83 \pm 0.02$  mg/dl) and control ( $0.84 \pm 0.03$  mg/dl) groups. The level of uric acid increased significantly ( $P < 0.05$ ) in the overt group ( $7.11 \pm 0.11$  mg/dl). When compared with control ( $3.78 \pm 0.18$  mg/dl) euthyroid ( $3.66 \pm 0.16$  mg/dl) and subclinical group ( $4.42 \pm 0.28$  mg/dl) respectively. The values presented in the figure (9) and (10).

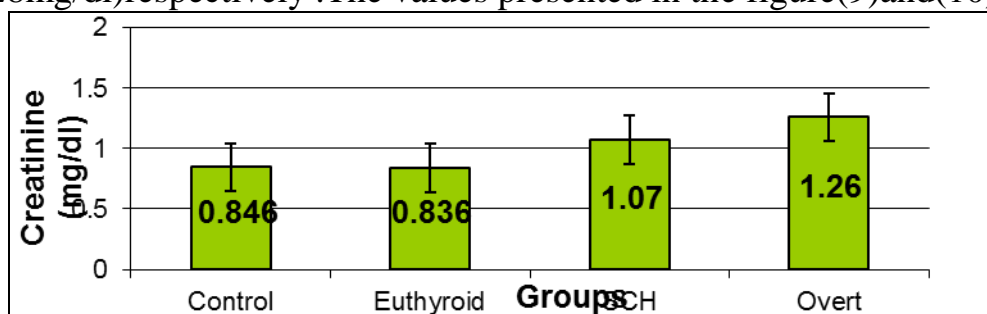


Figure (9) Compare between difference groups in level of Creatinine (mg/dl)

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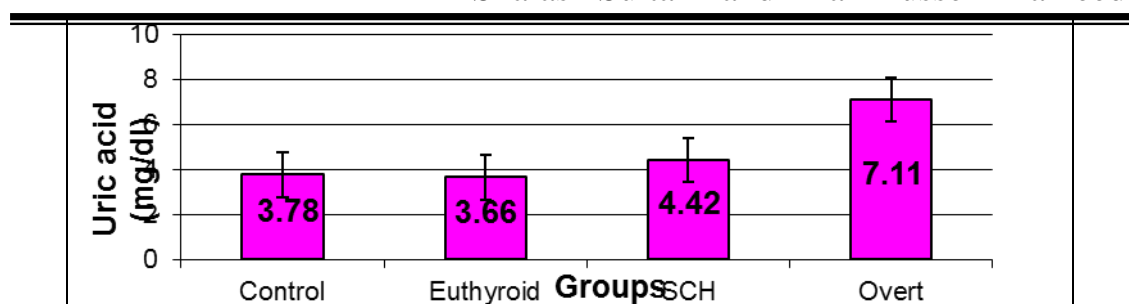


Figure (10) Compare between difference groups in level of Uric acid(mg/dl)

### Discussion:

Hypothyroidism is the disease state caused by insufficient production of thyroid hormones by the thyroid gland. Thyroid hormones are essential for normal organ growth, development and function nearly of all tissues (26,2). Subclinical hypothyroidism (SCH) is defined as an elevated serum thyroid stimulating hormone (TSH) level with normal serum thyroxine (T4) and serum tri-iodothyrodine (T3) level. Our findings in table(1) were in agreement with that reported by (27,28). Subclinical hypothyroidism has been suggested as a risk factor, for hypothyroid complications there is a need to identify and treat patients with SCH before they convert to overt hypothyroidism and develop complications (29,30). Khandelwal and Tandon, (10) reported that serum TSH raised concentrations identify primary hypothyroidism irrespective of the cause or severity. If the TSH level is high, further measurement of the free T4 should be carried out. A low serum free T4 in conjunction with an elevated serum TSH level establishes a diagnosis of overt hypothyroidism, while in subclinical hypothyroidism the serum free T4 concentration is, by definition normal so our results were comparable with that findings in table(1) so patients with overt hypothyroidism, whether symptomatic or not, showed being treated as hypothyroidism is the majority of patients is permanent and require life long treatment. The data presented in table (2) clearly indicate how biochemical markers of liver may be affected by alteration in thyroid hormones levels in the body. In the present study significant difference was seen in the liver function tests when subjects in hypothyroid group were compared with control and euthyroid subjects. Hypothyroidism may have features that mimic liver disease (pseudo-liver disease): examples include myalgias, fatigue and muscle cramps (31), and in the presence of elevated SGOT from myopathy (11). The liver enzyme (AST/SGOT) showed a significant positive correlation ( $P < 0.05$ ) with serum TSH levels in the overt hypothyroidism ( $r = 0.30$ ) and negative correlation ( $r = -0.032$ ) in T3 when compared with control, euthyroid and subclinical hypothyroid groups in our present study. That may be due to myopathy associated

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with hypothyroidism. Our data was in agreement with that reported by Ahmad *et al.* (32) who found an elevation in the levels of SGOT ( $34.7 \pm 1.87$  u/l) and SGPT ( $47.6 \pm 2.21$  u/l) in diagnosed hypothyroidism 55 subjects (24 males and 31 females).

Pandey *et al.* (13) found an increase in the levels of SGOT, SGPT and ALP enzymes, in 30 overt hyperthyroid and 30 hypothyroid patients visited Manipal teaching hospital in pokhara. The increase was higher in hyperthyroid in comparison with hypothyroid group. The age range of participants was 20-60 years. They concluded that thyroid dysfunction may disturb liver, muscle and other organs function and vice versa.

Our results for liver enzymes SGOT, SGPT, ALP were in agreement with their elevation with Yadav *et al.* (16) who found an increase in these enzymes, in 124 women were found to be hypothyroid, (77 subclinical hypothyroid and 47 overt hypothyroid) and 120 were euthyroid (control). The increase in the liver enzymes was significant in overt hypothyroid group in our study. A significant change was observed in serum ALP levels which showed a positive correlation ( $r=0.11$  NS) with serum TSH levels in overt hypothyroid subjects. While Arora *et al.* (15) found ( $r=-0.018$ ) in ALP levels in 80 subclinical hypothyroid patients. These observations may be explained on the basis that in hypothyroidism there is an increase in membrane cholesterol phospholipids ratio and diminished membrane fluidity, which affect a number of canalicular membrane transporters and enzymes, including the  $\text{Na}^+, \text{K}^+$ -ATPase resulting in the changes ALP enzymes (33). Serum ALP levels can rise as a result of either intra hepatic or extra hepatic obstruction due to bile acids accumulation in hepatocytes rather than impairment bile secretion (34) so when bile acids accumulation intracellular solubilization of the hepatic plasma membrane ensues, leading to ALP release (35). Serum total protein demonstrated a statistically significant increase in overt hypothyroid subjects table (3) as compared with control, euthyroid and subclinical groups. The increase in the level of TSP may be related to low grade of inflammation associated with even mild degrees of hypothyroidism may lead to a resultant increase in inflammatory proteins and immunoglobulins (36). Yadav *et al.* (16) recorded a statistically significant increased value of TSP in subclinical and overt hypothyroid cases. As the liver extracts 5-10% of plasma T4 during a single passage indicating that subclinical amount of protein-bound T4 is available for up take (31). An active stereo specific transport mechanism has been identified for transporting T4 and T3 across the hepatocyte membrane. The intracellular concentrations of the free hormones (T3, T4) are higher than the plasma levels and the process is energy dependent

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(37) So this may lead to an increase in the levels of TSP in hypothyroid patients. The bilirubin levels in our study was higher in the overt hypothyroid groups ( $1.23 \pm 0.11$  mg/dl), this increase may be associated with cholestatic jaundice attributed to reduced bile excretion (38).

As Umesono *et al.* (39) reported a reduced bile excretion in experimental hypothyroidism due to decreased in the activity of bilirubin UDP – glucuronyl transferase. Arora *et al.* (15) reported an increase in bilirubin ( $1.14 \pm 0.59$  mg/dl) in the 80 hypothyroid patients. Yadav *et al.* (16) found a higher level of bilirubin in overt hypo- thyroid group but the values were not found to be statistically significant, but bilirubin level was in agreement with that reported in our study in subclinical hypothyroid group which was found not to be statistically significant. Table (4) showed an increase in the creatinine and uric acid levels in overt hypothyroidism group, our results were in agreement with Tayal *et al.* (14) who found an increase of creatinine levels in 98 subclinical and 89 overhypothyroid patients and the uric acid increased in the overt hypothyroid subjects in comparison with 198 euthyroid, based on their findings suggested that serum creatinine was influenced by a decrease in T3 and /or T4 with an increase with TSH levels. The increase in uric acid in the overt hypothyroid in our study may be result from either increased production due to myopathy associated with hypothyroidism or due to decreased renal clearance of uric acid (40).

Arora *et al.* (15) found an increase in the level of serum creatinine and uric acid in 80 hypothyroid patients. Our findings was comparable with that reported by Saini *et al.* (41) who reported a significant increase in creatinine and uric acid levels in 47 patients with overt hypothyroid (TSH  $\geq 10.0$  mIU/L) and 77 patients with subclinical hypothyroidism (TSH 6.0-9.9 mIU/L) when compared with 120 euthyroid control. Our results were in agreement with that recorded by Wedaatalla and Abdella (42) who found a significant (P < 0.05) increase in the levels of uric acid in both hypothyroidism and hyperthyroidism in Sudanese women ( $6.7 \pm 1.69$  mg/dl) and ( $6.5 \pm 1.66$  mg/dl) respectively when compared with control ( $4.0 \pm 0.87$  mg/dl). Kumar (17) found in 30 patients newly diagnosed primary hypothyroidism an increase in the serum creatinine and uric acid compared to euthyroid patients. The study confirms association of hypothyroidism with elevated uric acid and creatinine which may be due to a decrease in GFR levels and alteration in Renin- angiotension – aldosterone system (RAAS), rennin reduced in the hypothyroid and leading to increased vascular resistance and a decrease in GFR as thyroid hormones act on systemic vascular resistance (SVR) and vascular smooth

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muscle cell (VSMC) (43). Our results were also in accordance with that reported by Khan *et al* . (18) in clinically and biochemically diagnosed 80 overt hypothyroid patients divided in 3 groups A,B,C of both sexes, age 20-60 years , with history of no thyroxine treatment in the last 3 month and 31 euthyroid subjects . That the TSH was between 0.5 -5.0 mlu/L in group A 50 -100 mlu/L in group B and > 100 mlu/L in group C .The serum creatinine and uric acid levels were  $1.38 \pm 0.53$  mg/dl and  $7.00 \pm 2.54$  mg/dl respectively in the overt hypothyroid patients .The serum creatinine values were found gradually increased in the group A to group C .

**Conclusions:** We concluded from our present study that the overt hypothyroidism had been affected liver function through :

- 1- Increasing levels of liver enzymes (AST,AIT,ALP) , bilirubin ,total serum protein.
- 2- Renal function was affected through increasing level of serum creatinine in subclinical and overt hypothyroid group ,while uric acid increased in overt hypothyroid group only .
- 3- Treated hypothyroid (euthyroid patients) showed normal values for thyroid hormones and others parameters,suggesting that treatment of hypothyroid patients had adverse effects on impaired parameters in the liver and Kidney function.

### Recommendations:

Our recommendations include the following :

- 1- Evaluating the level of thyroid peroxidase (TPO)enzyme among hypothyroid and find it' s correlation with level of TSH,T4and T3.
- 2- Evaluating the level of parathyroid hormone and calcitriol among hypothyroid patients and their correlation with level of calcium ( $Ca^{+2}$ ).
- 3- More study about the levels of Zinc ,Selenium and some antioxidants among hypothyroid groups.
- 4- Evaluation or estimation of leptin level among different hypothyroid subjects and it' s correlation with BMI.
- 5- Evaluation of levels of different protein ,albumin, $\alpha 1$ , $\alpha 2$ ,  $\beta$  and Gamma globulins with C-reactive protein to evaluate hypothyroid affects on total serum protein.

### References

- 1- **Saladin,K.S. and Miller,L.**(2003).Anatomy and physiology the unity of form and function.3<sup>th</sup> ed.McGraw-Hill Co. London.pp.1192.
- 2- **Lynn, WR .and Lynn, JA.**(2007). Hypothyroidism is easily over looked. Practioner.22(4):224-231
- 3- **Guyton.A.C. and Hall,JE.**(2006).Medical physiology text book .11<sup>th</sup> ed.Elsevier Saunders,Philadelphia. 0-7216-0240-1.

## Levels of Liver Enzymes and Some Changes in Renal Functions in Iraqi Hypothyroid Patients Women .....

Ali Shalash Sultan and Ban Hussein Hameedi

- 4- **Dunn,J.T.**(2001).Biosynthesis and secretion of thyroid hormones. Endocrinology DeGroot . Philadelphia.pp.1290-1298.
- 5- **Dillmann,W.H.**(2004).The Thyroid cecil textbook of Medicine. Goldman , L. and Aursello saunders,Philadelphia,pp.1391-1411.
- 6- **Jameson,J.L.and Weetman,A.P.** (2010). Disorders of the thyroid gland in harrison' sEndocrinology.McGraw-Hill companies,pp.(62-69).
- 7- **Surks , MI. ; Ortiz , E. ; Daniels , GH. ; Sawin , CT. ; Col , NF. ; Cobi RH.; Franklyn , JA.; Hershman, JM.; Bucman , KD.; Denke, MA.; Gorman, C.; Cooper, RS. and Weissman ,NJ.**(2004).Subclinical thyroid disease:Scientific review and guidelines for diagnosis and management .J AMA.291(2):228-238.
- 8- **Biondi,B. and Klein,I.**(2004).Hypothyroidism as a risk factor cardio vascular disease.Endocrine .24(1):1-13.
- 9- **Vanderpump , MP. ; Tunbridge ,WM. and French, JM.**(1995).The incidence of thyroid disorders in the community: a twenty year follow-up of the whickhan . survey.Clin.Endocrinol . oxf.43(1):55-68.
- 10- **Khandelwal,D. and Tandon,N.**(2012).Overt and subclinical hypothyroidism who to treat and how.Drugs .72(1):17-33.
- 11- **Malik,R. and Hodgson,H.** (2002).Review: the relationships between the thyroid gland and the liver.Q .J. Med.95:559-569.
- 12- **Laycock , MA. and Passcuzzi , RM.**(1991).The neuromuscular effects of hypothyroidism.semin Neurol .11:288-294.
- 13- **Pandey , R. ; Jaiswal , S. ; Sah , J.P.; Bastola,K.and Dulal,S.**(2013). Assessment of serum Enzymes level in patients with thyroid Alteration attending manipal teaching hospital pokhara .J of life sci.3(1):2249-2256.
- 14- **Tayal,D.; Chawla,R.; Arora,S.; Gupta,V.; Sohi,J. and Mallika ,V.**(2009). Dynamic changes in Biochemical markers of renal function with thyroid status-a study in Indian population.Int. J . Med .4(2):36-41.
- 15- **Arora,S.;Chawla , R.; Tayal , D.;Gupta,V.K.;Sohi , J.S. and Mallika ,V.** (2009).Biochemical Markers of liver and Kidney function are influenced by thyroid function .A case-controlled follow up study in Indian hypothyroid subjects.Indian. J. Clin. Biochemistry .24(4):370-374.
- 16- **Yadav, A.; Arora, M.S.; Saini, M.V.; Arora, M.M.K.; Singh, M.R. and Bhattacharjee. J.**(2013).Influence of thyroid hormones on biochemical parameters of liver function: a case control study in north Indian population. Int. J. Med . 8(1):4-8.
- 17- **Kumar,A.N.**(2013).The effect of L-Throxine on metabolic parameters in newly diagnosed Primary hypothyroidism.J. Clin. Exp Pharmacol.3(3):1000128.
- 18- **Khan,A.H.;Majumder,I.;Hoque,M.; Fariduddin.Mollah,F.H. and Arslan , I.**(2013b).Serum creatinine and uric acid levels in hypothyroid patients:A cross sectional study .J of Enam Medical college.3(2):84-87.

## Levels of Liver Enzymes and Some Changes in Renal Functions in Iraqi Hypothyroid Patients Women .....

Ali Shalash Sultan and Ban Hussein Hameedi

- 19- **Reitman,S. and Frankel,S.**(1957). A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. Am. J. Clin. Pathol.28:56-63.
- 20- **Kind,P.R.N.;King,E.J.**(1954).Estimation of plasma phosphatase by determination of hydrolysed phenol with amino –antipyrine. J.Clin.Path.7(4):322-236.
- 21- **Belfield,A.and Goldberg,D.M.**(1971).Revised assay for serum phenyl phosphatase activity using 4- amino-antipyrine- enzyme.12:561-573.
- 22- **Koller,A.Total serum protein.Kaplan, A. et al.**(1984).Clin Chem The C.V.Mosby Co .1316-1316 and 418.
- 23- **Burtis,A. et al.**(1999).Tietz Text Book of Clinical Lab.3<sup>rd</sup> ed AACC.
- 24- **Braham,D. and Trinder ,P.**(1972).An improved colour reagent for the determination of blood glucose by oxidase system.Analyst .27:142-145.
- 25- **Fossati,P.;Prencipel,L.and Berti,G.**(1980).Use of 3,5-dichloro 2-hydroxybenzene sulfoni acid /4-aminophenazone chromogenic system in direct enzymic assay of uric acid in serum and urine .Clin.Chem .26:227 231.
- 26- **Rubio, G.R; Mellinger, R.C.; Zafar, M.S. et al .**(1976).Evaluation of thyroid function during growth hormone therapy .Metabolism.25:15-21.
- 27- **Woerber,K.A.**(1997).Subclinical thyroid dysfunction. Arch.Inter. Med.157:1065-1068.
- 28- **Ringel,MD. and Mazzafem.**(2005). Subclinical thyroid dysfunction – can there be a consensus about the consensus?.J. Clin. Endocrinal .Metab. 90:588-559.
- 29- **Smallridge, R.C. and Disclosing, SCTD.**(2000). Anapproach to mild laboratory abnormalities and or absent sympatoms. postgrad. Med.107:143-152
- 30- **Hashim,S.**(2004).Subclinicalhypothyroidism.Med.Todey.2:132-135.
- 31- **Mendel,C.M.;Cavalieri,R.R.and Weisiger,R.A.**(1988).Uptake of thyroxine by the perfused rat liver .implication for the free hormone hypothesis. Am. J. Physiol.255:110-19.
- 32- **Ahmed,M.;Alam,S.M.; Habib,S.; Mehjabeen and Jahan,N .**(2013). Effect of thyroid dysfunction on systolic or diastolic blood pressure, pulse rate, serum creatinine and liver enzymes. Int. Res. J. pharm. 4(8):117-119.
- 33- **Inkinen,J.;Sand,J.and Nordback,I.**(2000).Association between common bile duct stones and treated hypothyroidism. Hepatogastroenterology.47:919-21.
- 34- **Pratt,D.S. and Kaplan,M.M.** (2000). Evaluation of abnormal liver enzyme results in a symptomatic patient.New Engl .J Med. 342 (17):1266-1271.
- 35- **Seetharam, S.; Sussman, NL.; Komoda,T. et al .**(1986).The mechanism of elevated alkaline phosphatase activity after bile duct ligation in the rate.J Hepatology.6:374-380.



## Levels of Liver Enzymes and Some Changes in Renal Functions in Iraqi Hypothyroid Patients Women .....

Ali Shalash Sultan and Ban Hussein Hameedi

- 36- **Kventy,J.;Heldgaard,P.E.;Bladbjerg,E.M.et al.**(2004).Subclinical hypothyroidism associated with a low grade inflammation,increased triglyceride levels and predicts cardiovascular disease in males below 50 years.Clin Endocrinol (oxf). 61:232-8.
- 37- **Hennemann , G.; Docter ,R. and Friesema , E.C et al.**(2001).Plasma membrane transport of thyroid hormones and its role in thyroid hormone metabolism and bioavailability.Endocr Rev.22:451-76.
- 38- **Vanderpump , MP. ; Tunbridge ,WM. and French, JM.**(1995).The incidence of thyroid disorders in the community: a twenty year follow-up of the whickhan . survey.Clin.Endocrinol . oxf.43(1):55-68.
- 39- **Umesono, K.; Murakami , KK.; Thompson ,CC. and Evans ,RM.**(1991). Direct repeats as selective response elements for the thyroid hormone, retinoic acid ,and vitamin D3 receptors .cell.65:1255-66.
- 40- **Yokogoshi,Y. and Saito,S.**(1996). Abnormal serum uric acid level in endocrine disorders. J Nippon Rinsho.54(12):3360-3.
- 41- **Saini,v.;Yadav,A.;Arora,MK et al.**(2012).Correlation of creatinine with TSH levels over hypothyroidism-requirement for monitoring of renal function in hypothyroid patients .Clin Biochem. 45(3):212-214.
- 42- **Wedaatalla, M.A.and Abdella,A.**(2012). Assessment of plasma uric acid level among sudanese female with thyroid dysfunction. Sudanese J of public health. 7(3):89-92.
- 43-**Ojamaa,K;Klemperer, JD. and Klein, I.**(1996). Acute effect of thyroid hormone on vascular smooth muscle .Thyroid.6:505-512.

**مستويات انزيمات الكبد وبعض التغيرات في وظائف الكلية في النساء العراقيات المريضات بقصور الغدة الدرقية**

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### الخلاصة:-

هدفت الدراسة الحالية لبيان الاضطرابات الفسلجية في بعض وظائف الكبد والكلية لدى النساء العراقيات المصابات بقصور الغدة الدرقية. ولقد أجريت الدراسة على 120 امرأة في المركز التخصصي لإمراض الغدد الصم والسكري الواقع في منطقة الرصافة بالقرب من مستشفى الكندي . للفترة من 2013/10/20 و لغاية 2014/1/25. قسمت مجاميع الدراسة أربعة أقسام : (مجموعة السيطرة control و مصابات سابقا بقصور الغدة ومعالجات Euthyroid و قصور تحت السريري Subclinical و قصور الغدة العلني أو الواضح ( Overt hypothyroid). تضمنت كل مجموعة 30 امرأة تراوحت أعمارهن بين ( 1.79±39.45 ) سنة.

أظهرت النتائج زيادة معنوية ( $P<0.05$ ) في مستوى هرمون TSH في القصور تحت السريري  $18.23 \pm 2.09$  (2.34 mu/l) و القصور العلني ( $41.37 \pm 3.75$  mu/l) مقارنة مع مجموعة السيطرة  $0.23 \pm 0.09$  (mu/l) و القصور في المعالجات ( $2.89 \pm 0.20$  mu/l) . كانت مستويات T3,T4 ضمن المستويات الطبيعية

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(79.73 ± 2.11 nmol/l), (1.70 ± 0.07 nmol/l) و قصور المعالجات (1.58 ± 0.05 nmol/l), (87.10 ± 2.11 nmol/l) و القصور تحت السريري (77.76 ± 2.31 nmol/l), (1.52 ± 0.05 nmol/l) على التوالي . بينما أظهرت مجموعة القصور العنلي انخفاضا معنويا ( $P < 0.05$ ) في مستوى T4 (46.36 ± 2.32 nmol/l) ومستوى طبيعي لـ T3 (1.30 ± 0.11 nmol/l) .

أظهرت فحوصات الكبد ارتفاعا معنويا ( $P < 0.05$ ) في مستويات انزيمات الـ SGOT (23.05 ± 2.67 U/L) و SGPT (21.89 ± 2.35 U/L) و ALP (99.98 ± 7.47 U/L) في مجموعة مرضى القصور العنلي مقارنة مع مستويات الـ SGOT في مجموعة السيطرة (8.80 ± 0.88 U/L) و القصور المعالجات (11.36 ± 0.85 U/L) و القصور تحت السريري (11.88 ± 1.42 U/L) و كذلك مستوى الـ SGPT في السيطرة (13.46 ± 0.75 U/L) و القصور المعالجات (10.93 ± 1.03 U/L) و القصور تحت السريري (14.08 ± 1.87 U/L) و كذلك مستويات الـ ALP في السيطرة (65.27 ± 2.65 U/L) و القصور المعالجات (65.27 ± 2.87 U/L) و قصور تحت السريري (71.58 ± 4.90 U/L) .

ازدادت مستويات البروتين الكلي (7.49 ± 0.16 g/dl) و البليروبين (1.23 ± 0.11 mg/dl) بصورة معنوية ( $P < 0.05$ ) في مجموعة مرضى القصور العنلي مقارنة مع مجاميع السيطرة ( ) , (0.613 ± 0.04 mg/dl) و القصور المعالجات (6.82 ± 0.04 g/dl) و القصور المعالجات (6.93 ± 0.07 g/dl), (0.04 mg/dl) . و القصور تحت السريري

((6.91 ± 0.08 g/dl), (0.883 ± 0.08 mg /dl)) على التوالي . أظهرت النتائج زيادة معنوية في مستوى الكرياتينين ( $P < 0.05$ ) في مجموعة تحت السريري (1.07 ± 0.07 mg/dl) و في القصور العنلي (1.26 ± 0.06 mg/dl) مقارنة مع مجموعة السيطرة (0.846 ± 0.03 mg/dl) و كذلك مجموعة القصور المعالجات (0.836 ± 0.02 mg/dl) . ازداد مستوى حامض البوليك uric acid زيادة معنوية ( $p < 0.05$ ) في مجموعة مرضى قصور الغدة العنلي (7.11 ± 0.11 mg/dl) مقارنة مع مجموعة السيطرة و قصور المعالجات و كذلك تحت السريري (3.78 ± 0.18 mg/dl) , (3.66 ± 0.16 mg/dl), (4.42 ± 0.28 mg/dl) على التوالي .

نستنتج من الدراسة الحالية الى أن قصور الغدة الدرقية العنلي قد أثر على وظائف الكبد والكلية إذ أظهرت الدراسة زيادة معنوية في مستويات أنزيمات الكبد SGOT, SGPT, ALP و زيادة معنوية في مستويات البليروبين والبروتين الكلي في مجموعة قصور الغدة العنلي مقارنة مع مجاميع السيطرة والقصور المعالجات والقصور تحت السريري . ازداد مستوى الكرياتينين زيادة معنوية في مجموعتي القصور العنلي والتحت السريري بينما ازداد مستوى حامض البوليك زيادة معنوية في مرضى قصور الغدة العنلي مقارنة مع مجاميع السيطرة , القصور تحت السريري والقصور في المعالجات و العنلي . أوضحت القيم المدروسة أعلاه في (مرضى القصور في المعالجات) رجوعها إلى الحالة الطبيعية بعد تناولهم العلاج L-levothyroxine بجرعتي (50 ملغم) أو (100 ملغم) .