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## **Relationship of anti-thyroid peroxidase antibody enzyme to antioxidant and lipid level in women with thyroid diseases**

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**Abstract**--The research involved study the relation between thyroid peroxidase (TPO) and some of the measured biochemical parameters reduced glutathione (GSH), arylesterase (ARE), ceruloplasmin, malondialdehyde, cholesterol, triglyceride, LDL, VLDL, HDL, atherogenic index) in serum blood patients compared with control group, the result demonstration is a significant increase in the activity of TPO enzyme ( $112.63 \pm 69.5$  Iu/ml), ( $273.9 \pm 235.1$  Iu/ml) in hyperthyroidism and hypothyroidism patient respectively compared with activity in control group was ( $33.9 \pm 18.99$  Iu/ml), also the results showed the significant increase in the concentration of (HDL), significant decrease in (GSH, ARE enzymes, cholesterol, LDL, atherogenic index) and while a non significant increase in (ceruloplasmin, malondialdehyde), non significant decrease in (triglyceride, VLDL) in hyperthyroidism, also the results had been shown a significant increase in (malondialdehyde, triglyceride, VLDL), and a significant decrease in (GSH, ARE enzymes) while a non significant increase in (ceruloplasmin, cholesterol, LDL, atherogenic index) and a non significant decrease in (HDL) in hypothyroidism, Correlation coefficient of TPO enzyme with these clinical parameters showed a positive significant correlation with (GSH enzyme) in control group and with (HDL) in hyperthyroidism while the results showed that there is no significant correlation between TPO enzyme with the rest of biochemical parameters (GSH enzyme) in control group and with (HDL) in hyperthyroidism while the results showed that there is no significant correlation between TPO enzyme with the rest of biochemical parameters.

**Keywords**---TPO enzyme, dyslipidemia, antioxidant, BMI, thyroid disease.

## Introduction

The thyroid gland secretes two hormones –thyroxine and triiodothyronine ,these hormones T4 and T3 are derivatives of tyrosine ,there are controlled by the hypothalamic thyrotropin –releasing hormone (TRH) which it stimulates the synthesis of thyrotropin stimulating hormone (TSH)from the anterior pituitary ,then the secretion of thyroid hormones [1] hypothyroidism is defined a decrease in thyroid hormones secretion and action ,while hyperthyroidism due to increase secretion of thyroid hormones from thyroid gland or extra thyroidal tissues which may be divided into primary and secondary varieties.[2]

Oxidative stress is described imbalance between the production of reactive oxygen species(ROS)and the antioxidant defense system of cells and tissues,the overproduction of free radicals damages all components of the cell and their physiological functions.[3] also ,any imbalance due to an excess oxidant formation or lowered antioxidants leads to an oxidative stress damaging lipids ,proteins and nucleic acids which lead to inflammation and cell death,[2] thyroid diseases are increased with oxidative stress,thyroid dysfunction was induce metabolic disorders,including obesity which is a metabolic disease involving mitochondrial dysfunction and chronic oxidative stress as in several metabolic disorders since the thyroid diseases are increased in individuals with increased body weight[4] also Thyroid hormones play an important role in the metabolism of lipids ,like lipid digestion ,transport ,biosynthesis and catabolism[1,5] thyroid peroxidase enzyme (TPO,EC 1.11.1.1-14)is participates in the formation of thyroid hormones,the gene for it is located on the chromosome 2p25,it consists of 933 amino acid in the form homodimer ,its molecular weight ( 107 KD), the oxidation of iodide to iodine is catalyzed by the thyroid peroxidase (TPO) in the presence of hydrogen peroxide ,tyrosin is iodized in thyroglobulin, then the enzyme works on the formation of thyroid hormones by conjugating pro-tyrosine molecules with the persence of NADPH molecules as energy .[6,7,8] obesity was associated with increased risk of hypothyroidism and thyroid peroxidase antibody TPO Ab ,and there is positive related between TPO Ab and body mass index BMI [9],while there is inverse correlation were seen between TPO Ab and GSH enzyme in Hashimotos thyroiditis HT [10]

## Aim of researed

Since there were a little previous studies In Iraq about the relation TPO enzyme with antioxidant and lipid profile in the body ,especially in patients with hyperthyroidism and hypothyroidism disease ,so it was proposed to study its mechansium of action in patients and its relationship with the measured biochemical parameters.

## Experimental

(60) blood samples were collected from thyroid patients ,(30)samples for both hyperthyroidism and hypothyroidism , their ages between (15-75)year ,also (30)

blood samples were collected from healthy people from Ibn-Sina Teaching Hospital ,After the blood serum was isolated from the samples ,it was used to estimate the following some biochemical parameters.

TPOenzyme- was estimated by using BT LAB Bioassay Technology Laboratory kit(China)by enzyme linked immunoassay ELISA technique [11]

Glutathione reductase enzyme –was determined by using Elman's reagent by modified method for researchers(Sedlak and Lindsay ;1968) [12]

Ceruloplasmin –was determined by using (para-phenylenediamine) by modified method for researchers(Menden et.al.;1977) [13]

Aryl esterase enzyme –was determined by analyzing the substrate phenylacetate to phenol and acetic acid.[14]

Malondialdehyde –was determined by using Thiobarbituric acid (TBA) by modified method for researchers(Guidet and Shah,1989)[15]

Cholesterol-was determined by using BIOLABO kit (France).[16]

Triglyceride- was determined by using BIOLABO Kit (France).[17]

LDL-C - was determined by using BIOLABO Kit (France).[18]

VLDL-C-was determined relying on the method of researchers [19]

HDL-C- was determined by using BIOLABO Kit (France).[20]

### **Data analysis**

The obtained data were analysed by using test for normality (shapiri-wilk),test for hypotheses (kruskal test and dunst) to found the mean and standard deviation, when the p-Value $\leq$  0.05 was assumed statistically significant also the relationship between the thyroid peroxidase (TPO) enzyme and the measured parameters was determined by finding the linear correlation coefficient [21].

### **Results and Discussion**

#### **The activity of TPO enzyme in hyperthyroidism and hypothyroidism disease patients compared with control group**

Fig.(1) shows a significant increase in TPO enzyme activity in both hypothyroidism and hyperthyroidism ,which were(  $273.9 \pm 235.1$  Iu/ml), ( $112.63 \pm 69.5$  Iu/ml)respectively compared to the TPOenzyme activity in the healthy group where it was (  $33.9 \pm 18.9$  Iu/ml),these results are in agreement with the findings of a study done on patients with thyroid disorders[22],that there the study has shown elevated thyroid antibodies among patients with thyroid dysfunction and females or that thyroid autoimmunity is common among thyroid patients .

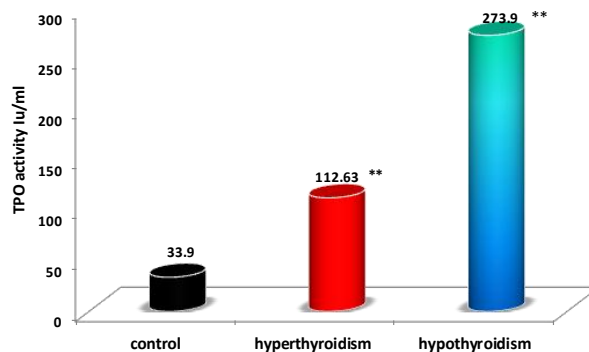


Fig. 1: Thyroid peroxidase (TPO) activity in hyperthyroidism and hypothyroidism compared with control group

### Some clinical parameter concentration in hyperthyroidism, hypothyroidism compared with control group

table (1) was showed a significant increase in HDL and significant decrease in (cholesterol, LDL, atherogenic index) while a non decrease significant with the (triglycerid, VLDL)in hyperthyroidism this may due to increase thyroid hormones which stimulate the enzymes in the lipid metabolism such as hepatic lipase ,lecithin cholesterol acyl transferase (LCAT)and cholesterol ester transfer protein (CETP)also,the thyroid hormones stimulates the hepatic cholesterol synthesis by inducing the HMG-COA reductase that catalyzes the conversion of HMG-COA to mevalonate ,also thyroid hormones increases the Basal Metabolism Rate (BMR) then decreasing serum lipid[1] the result also showed a significant decrease in ( GSH and ARE enzymes)in hyperthyroidism and hypothyroidism and a significant increase in malondialdehyde in hypothyroidism these results are in agreement with the finding researchers[2,7]that there arylesterase is decreased in autoimmune thyroid disease (AITD)patients and it is positively correlated with levels of the antioxidant and elevated MDA levels were observed in subclinical hypothyroidism, while the table (1) has been showed a significant increase in (triglyceride, VLDL)and a non significant increase in (cholesterol, LDL, athrogenic index ), non significant decrease in (HDL) in hypothyroidism ,these result may due to hypothyroidism slows down the rate of metabolism leading increase lipid level[1]also there is correlation between dyslipidemia and TPO antibody in subclinical hypothyroidism [23].

Table (1)

Some clinical parameters concentration in control and hyperthyroidism, hypothyroidism patients

Clinical Parameters	Control Group	Hyperthyroidism	Hypothyroidism
T3 Iu/L	0.91 ± 0.45	3.21** ± 0.8	0.52 ± 0.42
T4 Iu/L	6.74 ± 1.44	8.57 ± 2.9	3.003** ± 1.26
TSH Iu/L	2.43 ± 1.3	0.43** ± 0.79	5.6** ± 2.6

Glucose mg/dl	82.2 ± 9.0	123.48** ± 53.6	119.23** ± 32.9
Vit. D ng/dl	41.4 ± 11.96	29.11** ± 12.5	18.41** ± 10.6
Calcium mg/dl	9.08 ± 0.7	8.27** ± 1.62	8.17** ± 1.08
Uric acid mg/dl	6.45 ± 1.61	7.7 ± 1.89	8.03 ± 3.18
Albumin mg/dl	4.37 ± 0.5	4.31 ± 0.3	4.36 ± 0.69
ALP Iu/L	65.7 ± 67.1	158.2** ± 36.4	100.81** ± 41.8
GOT Iu/L	15.9 ± 3.2	39.37** ± 6.9	16.67 ± 3.03
GPT Iu/L	16.52 ± 2.07	47.56** ± 9.3	18.22 ± 3.84

Significant difference at \*\*p<0.01

### **Correlation between TPO activity and some clinical parameters in hyperthyroidism, hypothyroidism patient comparing to control group**

The result in table(2) showed that TPO activity had a positive significant correlation with GSH enzyme in control group this result is in agreement with the research findings[24]that there GSH is a major endogenous antioxidant present in all mammalian cells and peripheral blood ,plays an important role in protecting the cells from oxidative stress, also TPO enzyme had a positive significant correlation with HDL in hyperthyroidism this result may due to elevated thyroid antibodies is common among patients with thyroid dysfunction in females more than in males [4]while the result in table (2)showed that TPO activity had a non significant correlation with the rest of the biochemical parameters.

Table (2)

Correlation between TPO activity enzyme and some clinical parameters in hyperthyroidism, hypothyroidism patient compared with control group

Clinical parameters	Control Group r- value	Hyperthyroidism r- value	Hypothyroidism r- value
T3	- 0.138	0.038	0.086
T4	0.09	0.125	- 0.094
TSH	- 0.18	0.04	- 0.068
Glucose	- 0.04	- 0.177	0.261
Vit. D	- 0.004	0.152	- 0.441*
Calcium	0.033	0.086	- 0.363*
Uric acid	- 0.103	- 0.23	0.156
Albumin	0.046	0.08	- 0.186
ALP	0.097	0.019	0.195
GOT	- 0.038	- 0.255	0.096
GPT	- 0.128	- 0.364*	0.188

\* Correlation is significant at the 0.05 level

### **Effect of Body Mass Index (BMI) on TPO activity in patients and control groups**

The result in table (3)showed that there is increase in TPO activity with higher BMI in hypothyroidism patients group ,while the result was showed there is

decrease in TPO activity with higher BMI in hyperthyroidism patients , this result is in agreement with the research findings[25,26],that the obese group had a significantly higher of TPO Ab than the normal weight group in hypothyroidism this may due to dipocytes of obese increase of peripheral resistance to thyroid hormones due to lower expression of TSH receptors ,then leading to increased plasma TSH level and decrease in thyroid hormones ,in contrast with hyperthyroidism patients, TPO activity had significant lower values with increase BMI.

Table (3)

TPO activity in hyperthyroidism, hypothyroidism compared with control group according to BMI

BMI kg/m <sup>2</sup>	TPO activity lu/ml mean $\pm$ SD		
	Control	hyperthyroidism	hypothyroidism
18.5 - 24.9	*** 28.91 $\pm$ 14.81	129.71 $\pm$ 111.35	191.75 $\pm$ 119.95
25 - 29.9	*** 37.5 $\pm$ 20	114.55 $\pm$ 52.91	254.5 $\pm$ 240.37
30 - 39.9	*** 31.25 $\pm$ 20.41	*** 104.5 $\pm$ 51.67	*** 282.61 $\pm$ 273
$\geq$ 40	68 $\pm$ 11.31	93 $\pm$ 103.23	410.31 $\pm$ 164.46

\*\*\* significant at the 0.001 level

### Body mass index (BMI)

is defined as the product of dividing bod weight in kilograms by the square length in meters ,using the world health organization (WHO)body mass index (BMI) is divided into four groups : normal weight (18.5-24.9 K/M2) ,overweight(25-29.9 Kg/m2 ,obese(30-39.9 Kg/m2),and morbidly obese ( $\geq$ 40Kg/m2)[27]

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