

Thyroid Disorders and It's relation with some infectious factor studying on Iraqi Patients

Abdulwahid B. Al-Shaibani ^{#1} , Sarah T. Al-Mofarji ^{#2} and Sanad B. Al-A'araji ^{#3}

#1College of Applied Biotechnology/Al Nahrain University

#2Forensic DNA research and training center/Al Nahrain Unieversity

#3College of Science for Women, University of Baghdad

Abstract:

This study was aimed to investigate the association between thyroid disorder and *Helicobacter pylori* infection in 122 patients (100 females and 22 males)and for comparison, 60 healthy individuals (31females and 29 males),who had no thyroid disorder, were also included in the study. Blood samples were collected from both patients and the healthier individuals. Enzyme Linked Fluorescent Assay (ELFA) technique through using Vitek Immuno Diagnostic Assay System (VIDAS) was applied to measure levels of the thyroid hormones (tri-iodothyronine T3, tetra-iodothyroxine T4) and thyroid stimulating hormone (TSH). From the results obtained, patients were classified into three groups: 40 were considered as belonging to the controlled group (26 females and 14 males), 57 to the hypothyroidism group (52 females and 5 males) and25 belonged to hyperthyroidism group (22 females and 3 males). On the other hand, highest incidence rate of thyroidism was recorded in the age group of (30-39)yrs. 19.67% , followed by (40-49)yrs. with 24.59% and(50-59)yrs. with 18.03%. When concentration and presence of anti -*Helicobacter pylori* IgG antibodies in the human blood samples were detected and measured by Enzyme Linked Immuno Sorrbent Assay (ELISA) technique , the results were showed high prevalence rates of *H. pylori* infection were detected in the hypothyroidism patients (94.07%), while the lowest prevalence rates were recorded in the healthy individuals (66.7%).Statistical analysis of anti –*Helicobacter pylori* IgG antibodies distribution among both healthy and thyroidism patients showed that highly significant differences at $p < 0.01$ were found between thyroid disorders patients groups.

Key words: *H. pylori*, thyroidism , Hypothyroidism , Hyperthyroidism

Corresponding Author: Sarah T. AL- Mofarji

Introduction:

Thyroid gland is one of the important organ in the human body that produces important hormones: triiodothyronineT3 and tetraiodothyroxine T4 which have an important role in regulation of metabolic functions, development and growth thus thyroid dysfunction affecting various vital activities; those resulting from hypo or hyper thyroid gland activity leading to

increase or decrease thyroid hormones T3 and T4[1]. Hypothyroidism(Hashimotos' thyroiditis) and hyperthyroidism (Graves' disease) are the most common autoimmune thyroid disorders as one of most complications of thyroid dysfunctions as well autoimmune diseases occur when immune system begins to attack its own self antigens, so, that the best feature of autoimmune thyroid disease is the presence of auto- antibodies against thyroid antigens , such diseases are triggered by factors including infectious agents ,just like as infection with *Helicobacter pylori* [2,3].

Many researchers found that a high percentage of individuals who have been diagnosed as thyroid patients were also infected with *H. pylori* which means that these bacteria plays an important role in the pathogenesis of such diseases.[4,5]. *Helicobacter pylori* is one of the most common bacterial pathogens that infects human around the worldwide, which acquired in the early childhood and is carried throughout lifetime if not treated with antimicrobial agents[6].

In order to link *H. pylori* infection with the development of autoimmune thyroid diseases, a sensitive assay and careful population studies are required . Due to the important role of *H. pylori* in developing of autoimmune thyroid diseases and malfunctions of human in Iraq as well in other parts of the world , studies are needed in this aspect especially those correlating dysfunction of thyroid gland and ulcer caused bacteria *H. pylori* so , this study was suggested to fulfill the aims of :Investigating the amounts of T3,T4 and thyroid stimulating hormone TSH secreted by patients suffering from hyperthyroidism and hypothyroidism and investigating the association between occurrence of thyroidism and *H. pylori* .

Materials and Methods:

Sample collection

A total of 182 samples were collected from Iraqi individuals who attended to the Specialized Center for Endocrinology and Diabetes at Al Kindy teaching Hospital in Baghdad during the period from October 2012 to January 2013. Samples included 60 healthy individuals (31 females and 29 males) and 122 thyroid patients (100 females and 22 males) .Thyroid patients were divided into three subgroups: 40 patients were considered as a controlled group(individuals who have been under thyroid drug treatment either thyroxine or carbimazole) contains 40 patients (26 females and 14 males) , 57 patients belong to hypothyroid group (52 females and 5 males) and 25 patients hyperthyroid group (22 females and 3 males). All of them were subjected to a personal interview to fill specialized designed questionnaire form with a personal and medical history aspect. Measurement of Tri-iodothyronine (T3) ,tetra iodothyroxine (T4) and Thyroid Stimulating Hormone (TSH) by Enzyme Linked Fluorescent assay (ELFA) using BioMérieux kit (France) [7] and detection of Anti – *Helicobacter pylori* IgG Antibody by ELISA method using NovaTec kit(Germany) [8].Lipid profile assay using (cholesterol , triglycerides and HDL) kits, linear chemicals (Spain) [9,10].LDL and VLDL estimation [11, 12]. All the Statistical Analysis and Findings results were Supervised by Bio-Statistician Prof. (Dr.) Abdulkhalik Al-Naqeeb, College of Health and Medical Technology, Baghdad – Iraq.

Results and Discussion:

Distribution of healthy and thyroid disorder patients according to gender.

A total of 122 samples were belonged to patients suffering from thyroid disorders, and 60 others were considered as healthy individuals. Thyroid disorder was found to be more abundant

in females (100, 81.96 %) than in males (22, 18.03%) as shown in table (1) . Moreover, females constructed the vast majority of groups of hypothyroidism (52, 42.62%), hyperthyroidism (22,18.03%) and controlled (26, 21.31%) groups .Adversely, males showed lowest incidences of hypothyroid(5, 4.09%) hyperthyroid (3,2.45%) and controlled (14 , 11.47%) groups . These results were closely related to a study performed in Egypt by Hamad *et al.*, [13] who found that thyroid disorders of patients infected with *Helicobacter pylori* were more common in females than males . In another studies by Vander [14] in London and Darwish *et al.*, [15] in Al Bahrain , thyroid disorders were found to be higher in females than in males with ratios of 10:1 and 3:1 ,respectively . While these results were disagreed with a study performed by Mansoor *et al.*, [16] in Pakistan who found that thyroid disorders were more pronounced greater in males than in females . Mahadevan [17] stated that thyroid disorders are more prevalent in females (with an incidence of roughly 8 to 10 times) more than in males ,which may be due to that female reproductive activity stresses the thyroid gland .

Table (1) Distribution of healthy and thyroid disorder patients according to gender .

Gender	Healthy (60)		Patients Group (122)						Total	
			Controlled		Hypothyroid		Hyperthyroid			
	No.	%	No.	%	No.	%	No.	%	N o.	%
Females	31	51.7	26	21.31	52	42.62	22	18.03	100	81.96
Males	29	48.3	14	11.47	5	4.09	3	2.45	22	18.03

Distribution of healthy and thyroid disorders patients according to age .

It can be observed from table (2) that opportunity of thyroid disorders was increased with the age. Highest occurrence of thyroid disorders were recorded in the ages between (40- 49) yrs with a total number of 30 (24.59%) which are distributed as; 11 (9.01%), 14 (11.47%) and 5(4.09%) in the controlled, hypothyroid and hyperthyroid groups, respectively. Followed by ages between (30- 39) yrs with a total number of 24 (19.67%) distributed as; 4 (3.27%), 14 (11.47%) and 6 (4.91%) in the controlled, hypothyroid and hyperthyroid groups, respectively. While the lowest percentages of thyroid disorders were recorded in ages of less than 5 yrs and those between (5 – 9) yrs with a total number of 4 (3.27%) for each. However, no hypothyroid disorder was recorded in any patient of less than 5 yrs old. According to the age of healthy and patients included in the study, statistical analysis showed there were significant differences at ($p < 0.01$) between each of the (healthy and controlled) group and the (healthy and hypothyroid) group. These results were closely related to a study performed by Aboud [18] in Iraq who found high significant differences among age groups of patients with peptic ulcer caused by *Helicobacter pylori* ,and studies performed by Pedersen *et al.*, [19] in Cobenhagen / Danemark and Vadiveloo *et al.*, [20] in Scotland who found that thyroid disorders incidence rates increased with patients ages. On the other side Ahmed *et al.*, [21] in their study performed in Pakistan when they found that thyroid hormones levels increased in the first decade of patients life and decreased in the second and third decades , while remained unaffected beyond the fourth decade of life .

Table(2):Distribution of healthy and thyroid disorders patients group according to age

Age group (year)	Healthy (60)		Patients Group (122)						Total	
			Controlled		Hypothyroid		Hyperthyroid			
	No.	%	No.	%	No.	%	No.	%	N o.	%
< 5	7	11.7	3	2.45	0	0.00	1	0.81	4	3.27
5 – 9	4	6.70	2	1.63	2	1.63	0	0.00	4	3.27
10 – 19	15	25.0	6	4.91	8	6.55	3	2.45	17	13.93
20 -29	11	18.3	3	2.45	6	4.91	6	4.91	15	12.29
30- 39	5	8.30	4	3.27	14	11.47	6	4.91	24	19.67
40-49	10	16.7	11	9.01	14	11.47	5	4.09	30	24.59
50 – 59	7	11.7	7	5.73	11	9.01	4	3.27	22	18.03
60-70	1	1.70	4	3.27	2	1.63	0	0.00	6	4.91

Distribution of healthy and thyroid patients according to Body Mass Index

From the body weight and square of the height, body mass index (BMI) was calculated for each of the healthy individuals and thyroid disorders patients. Results declared that thyroid disorder patients can be classified to: underweight (16.00 – 17.00 kg/m²) , normal weight (18.50 – 25 kg /m²) , over weight (25 – 30 kg / m²) and obese (>30 kg/ m²) . It can be observed from table (3) that highest percentages of overweight patients were recorded in the controlled (13, 10.65%) and hypothyroidism (16,13.11%) groups , while in the obese patients , the highest occurrences were in both controlled (13,10.65%) and hypothyroidism (22,18.03%) groups. Koritschon *et al.*, [22] declared that most important causes of obesity are unhealthy life style and hypothyroidism . Thyroid hormones are the major regulators of energy metabolism, so that any change in the thyroid status is associated with body weight change . Adversely, Mittal *et al.*, [23] pointed out that there was no correlation between thyroid hormones status and body weight .

Table (3) :Distribution of healthy and thyroid patients according to Body Mass Index (BMI) .

B.M.I	Healthy (60)		Patient Group (122)						Total	
			Controlled		Hypothyroid		Hyperthyroid			
	No.	%	No.	%	No.	%	No.	%	N o.	%
Under weight	5	8.30	4	3.27	1	0.81	1	0.81	6	4.91
Normal weight	19	31.7	10	8.19	18	14.75	8	6.55	22	18.03
Over weight	16	26.7	13	10.65	16	13.11	8	6.55	37	30.32
Obese	20	33.3	13	10.65	22	18.03	8	6.55	43	35.24

Lipid profile in healthy and thyroidism patients.

The results in figure (1) declared that normal levels of cholesterol were recorded in healthy , controlled and hypothyroidism groups mean value (180.7 mg/dl) , (188.7 mg/dl) and (190.4 mg/dl) respectively, while lower cholesterol levels were recorded in hyperthyroidism group mean value (157.3 mg/dl).

Normal triglycerides levels were recorded in both healthy and thyroid patients with mean value (173.5 mg/dl) in healthy group , (176.3 mg/dl) in controlled group , (166.6 mg/ dl) in hypothyroidism group and (149.4 mg/dl) in hyperthyroidism group.

High density lipoprotein (HDL) results showed that the normal mean values were recorded in healthy (55.8 mg/dl) and controlled (51.2 mg/dl) groups higher than that were recorded in hypothyroidism (44.9 mg/dl) and (41.2 mg/dl) in hyperthyroid groups.

Low density lipoprotein (LDL) results recorded normal value in both healthy (88.8 mg/dl) group and thyroid patients groups : (101.7 mg/dl) in controlled , (112.7 mg/dl) in hypothyroidism and (87.3 mg/dl) in hyperthyroidism .

Very low density lipoprotein (VLDL) results were recorded normal values in healthy (34.72 mg/dl) group and in thyroid patients groups : (34.80 mg/dl) in controlled ,(33.40 mg/dl) in hypothyroidism and (29.11 mg/dl) in hyperthyroidism.

Cholesterol and triglycerides are the major circulating lipids which are water insoluble, so that they can not be transferred throughout blood stream as individuals molecules; a large spherical particles called lipoproteins package them into a core surrounded by a shell of water -soluble proteins and phospholipids so that , lipoproteins serve as vehicles to transport cholesterol and triglycerides from one part to another in human body[24].

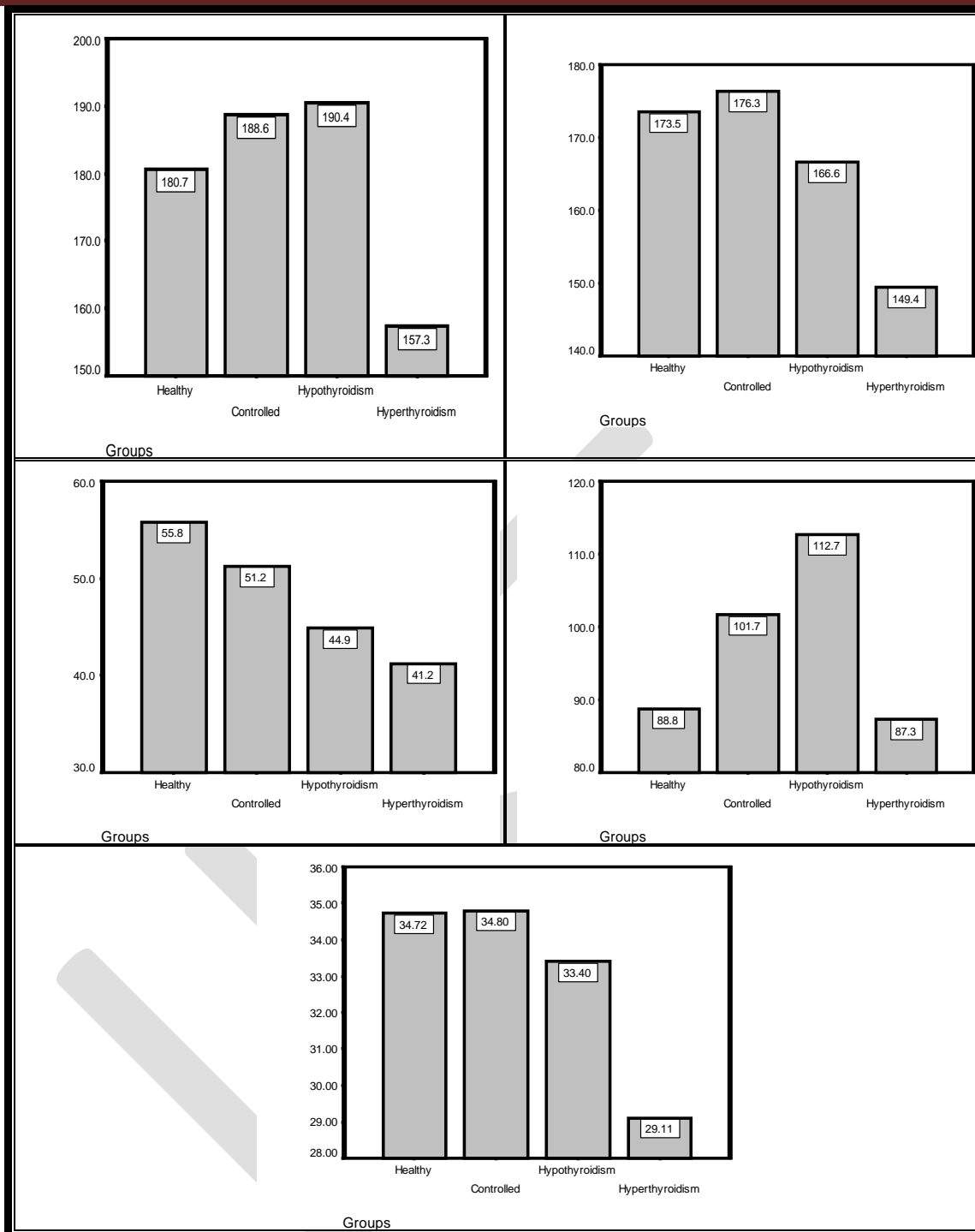


Fig. (1):Mean value of lipid profile among healthy and thyroid patients

According to the lipid profile of healthy and patients included in the study , statistical analysis showed in table (4) that were significant differences at $p < 0.01$ between (controlled and hyperthyroidism), (hyperthyroidism and hypothyroidism) and significant differences at $p < 0.05$ between (healthy and hyperthyroidism) according to cholesterol levels. As well as significant differences at $p < 0.01$ between (healthy and hypothyroidism), (healthy and hyperthyroidism)and significant differences at $p < 0.05$ between (controlled and hyperthyroidism)according to HDL levels and there were significant differences at $p < 0.01$ between (healthy and hypothyroidism) , (hypothyroidism and hyperthyroidism) according to LDL levels .

**Table (4) : Multiple Comparison (LSD) among all pairs of Lipid Profile parameters
According to different treated samples**

(I) Group	(J) Group	Cholesterol	Triglycerides	HDL	LDL	VLDL
		P-value ^(*)	P-value ^(*)	P-value ^(*)	P-value ^(*)	P-value ^(*)
Healthy	Controlled	0.358	0.841	0.258	0.113	0.979
	Hypothyroidism	0.214	0.598	0.003	0.001	0.612
	Hyperthyroidism	0.021	0.151	0.002	0.878	0.092
Controlled	Hypothyroidism	0.837	0.502	0.117	0.179	0.628
	Hyperthyroidism	0.004	0.133	0.045	0.155	0.109
Hypothyroidism	Hyperthyroidism	0.001	0.307	0.440	0.008	0.201

Thyroid diseases are associated with various metabolic abnormalities due to the effect of thyroid hormones on the major metabolic pathways [25]. The explanation of thyroid hormones affected on lipid metabolism is that thyroid hormone regulates the activity of some key enzymes in lipoproteins transport and ,therefore, alter the lipoprotein levels in hypothyroid patients [26]. As well as there was an association between *Helicobacter pylori* and lipid abnormalities so, these results were closely related to Ansari *et al* .,[27] when they found that there was an association between *H. pylori* infection and increased level of cholesterol and decreased level of HDL thus they suggested that *H. pylori* infection can be caused a lipid metabolism disorders. Results of the present study were closed to those of Peppa *et al*., [25] and Kim *et al*.,[28] who recorded significant differences among the low density lipoprotein (LDL) levels in both hyperthyroidism and hypothyroidism groups of patients .

Thyroid status in healthy and thyroidism patients

Regarding to the thyroid hormones (tri-iodothyronine T3 and tetra-iodothyroxine T4) and thyroid stimulating hormone (TSH), results as shown in figure (2), high level of T3 and T4 hormones and TSH hormone were recorded in hyperthyroidism group ,while low level of T3 and T4 hormones and high level of TSH hormone were recorded in hypothyroidism group when compared with healthy and controlled groups. Tomer [29] mentioned that many genetic and environmental factors played role in developing of thyroidism (hypothyroidism or hyperthyroidism), while Cappa *etal*.,[30] listed age, gender, pregnancy,bacterial infection and socioeconomic level as the most affected factors on thyroidism

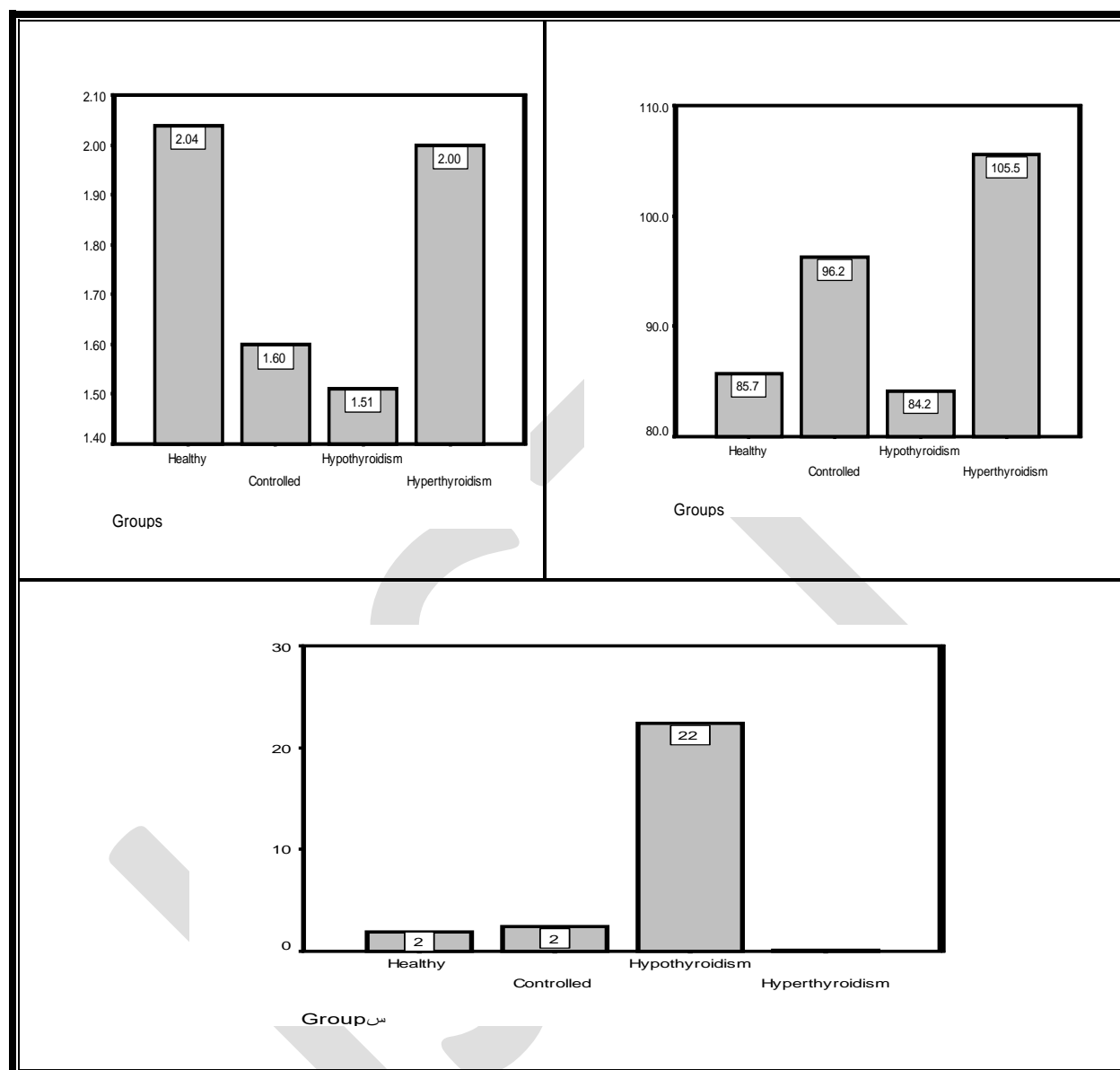


Fig. (2): Mean value of thyroid hormones (T3 and T4) and TSH hormone among healthy and thyroid patient groups.

Person's Correlation Coefficients between (Age, BMI, T3, T4, and TSH) Parameters at the studied samples with comparison significant.

The results shows that the shaded cells of each contrasts of two parameters at the table (5) illustrated the meaningful /or significant correlation in at least $P < 0.05$, while the leftover of were reported no significant correlation coefficients at $P > 0.05$, and as follows : Regarding to the subjects of the Age parameter, there was a significant reversed correlation had been reported with (T3, and T4) in the Healthy sample, then followed significant correlation with (BMI) in

the Controlled sample, then significant correlation with (BMI) in the Hypothyroidism and Hyperthyroidism samples.

Table (5): Person's Correlation Coefficients between (Age, BMI, T3, T4, and TSH) Parameters at the studied samples with comparison significant

Contrast	Correlation Coefficient & P-vale	Parameters	BMI	T3	T4	TSH
Healthy	Correlation	Age (Per year)	0.314	-0.432	-0.351	-0.095
		BMI		-0.182	-0.245	0.038
		T3			0.321	0.054
		T4				0.075
	Sig. (1-tailed)	Age (Per year)	0.052	0.011	0.034	0.315
		BMI		0.177	0.104	0.423
		T3			0.048	0.392
		T4				0.352
Controlled	Correlation	Age (Per year)	0.417	-0.056	-0.070	0.090
		BMI		-0.010	-0.019	-0.268
		T3			0.410	-0.077
		T4				-0.196
	Sig. (1-tailed)	Age (Per year)	0.017	0.392	0.367	0.331
		BMI		0.481	0.463	0.093
		T3			0.019	0.355
		T4				0.169
Hypothyroidism	Correlation	Age (Per year)	0.505	-0.095	0.142	-0.247
		BMI		-0.239	-0.100	-0.097
		T3			0.300	-0.330
		T4				-0.659
	Sig. (1-tailed)	Age (Per year)	0.001	0.300	0.215	0.083
		BMI		0.091	0.289	0.296
		T3			0.045	0.030
		T4				0.000
Hyperthyroidism	Correlation	Age (Per year)	0.855	-0.238	-0.073	-0.277
		BMI		-0.127	-0.014	-0.075
		T3			0.607	0.170
		T4				0.260
	Sig. (1-tailed)	Age (Per year)	0.000	0.216	0.407	0.180
		BMI		0.340	0.482	0.404
		T3			0.014	0.290
		T4				0.195

With respects to the subjects of T3 parameter, there was a significant correlation had been reported with T4 in the studied samples, as well as reversed correlation with TSH parameter in the Hyperthyroidism sample. Finally, T4 parameter was reported reversed significant correlation with TSH parameter in the Hypothyroidism sample.

Distribution of *Helicobacter pylori* among healthy and thyroidism patients.

Results of anti –*H. pylori* IgG antibodies (table 6) showed that highest percentages of *H. pylori* infections were detected in both hypothyroid (94.7%) and hyperthyroid (72 %) groups, while the lowest percentage was recorded in the healthy group; this could be related to the fact that *H. pylori* infection incidence increased in thyroid patients groups who have abnormal levels of T3,T4 and TSH hormones. In the controlled group, the percentage of *H. pylori* infection occurrence was (77.5%), which falls between those results of healthy individuals and the thyroidism patients group . Statistical analysis has been showed that by comparison between (healthy and controlled) groups an odd ration showed that negative outcomes of *H. pylori* infection increased 1.7 times in healthy group when compared with controlled group, that is mean positive outcomes in controlled group increased in the same ration when compared with healthy but when compared (healthy and hypothyroid) groups the odd ratio showed that negative outcomes increased 9 times in healthy than hypothyroid group as well as the positive outcomes increased at the same ratio in hypothyroid group when compared with healthy group but by comparison between (healthy and hyperthyroid) groups odd ration showed that positive outcomes increased 1.3 times in hyperthyroid than healthy .

In the comparison between (controlled and hypothyroidism) group the odd ratio showed that negative outcomes of *H. pylori* infection increased 5 times in controlled than in hypothyroidism group and vice versa the positive outcome increased at hypothyroidism group than controlled group while when compared the (controlled and hyperthyroidism) groups the odd ratio showed that the negative outcome of *H. pylori* infection increased 0.8 times in controlled than hyperthyroid. The odd ration showed that positive outcomes of *H. pylori* infection increased 6.99 times in hypothyroid when compared with hyperthyroid. These results showed that there were a high significant correlation between *H. pylori* infection and hypothyroid disorders among each of the healthy individuals , controlled and hyperthyroidism groups . This may be referred to the fact that the thyroid hormones may influence the gut motility modulation neurology and smooth muscles function. Hypothyroidism could be associated with decreasing frequency of rhythmic colonic activity and slowing oro-cecal transit time . The pathogenic link could be that intestinal motor dysfunction associated with hypothyroidism reduces ability of the small bowel to clear luminal bacteria [31,32]. Results of the present study are close to a study performed by Hamad *et al.*, [13] in Egypt who found a significant correlation between *H. pylori* infection and

hypothyroidism, and the study in Czech Republic by Sterzl *et al.*, [33] who found an association between *H. pylori* infection and autoimmune thyroid diseases (ATD). Adversely, Tomasi *et al.*, [34] in Italy found that there was no association between *H. pylori* infection and autoimmune thyroid diseases (ATD), as well as Bassi *et al.*, [35] in Italy who detected a high significant increase in the *H. pylori* prevalence in the Graves' diseases patients (hyperthyroidism) and Bassi *et al.*, [36] found a marked correlation between the presence of *H. pylori* and Graves' disease but not in the Hashimotos' thyroiditis (hypothyroidism). Bugdaci *et al.*, [37] in their study in Turkey found a high prevalence of *H. pylori* infection in the hypothyroidism patients, in addition the effect of *H. pylori* eradication was in adequate response to thyroxine therapy, while in a study performed by Soveid *et al.*, [38] in Shiraz, Iran a significant association of *H. pylori*

infection with both hypothyroidism and hyperthyroidism patients was reported. The fact of association between thyroidism patients and *H. pylori* infection was supported also by other studies; such as those performed by El-Ashmawy *et al.* [39] in Egypt who found that a correlation between *H. pylori* infection and the presence of autoantibodies against thyroid antigens, and highly significant prevalence of *H. pylori* infection in the ATD patients when compared with healthy individuals. Another studies were performed to improve the effect of some factors on development of autoimmune thyroid patients infected with *Helicobacter pylori* a study performed by Wei [40] in China to improve the association between *H. pylori* infection and autoimmune thyroid disease in addition the influence of geographical factor on opportunity of the development of such correlation.

Another study performed by Karaca *et al.* [41] in Istanbul, Turkey reported how the lower socioeconomic status is considered as an important risk factor for the development of *H. pylori* infection. As well as other study performed by Shi *et al.*, [42] in China when they found an association between *H. pylori* infection and autoimmune thyroid diseases, they suggested that *H. pylori* may play a role in the development of autoimmune thyroid diseases.

Table(6):distribution of H. pylori among healthy and thyroid patients .

Group	Freq. &Percentages	<i>Helicobacter pylori</i>		Total
		Neg.	Pos.	
Healthy	Freq.	20	40	60
	% Group	33.3%	66.7%	100%
	% <i>Helicobacter pylori</i>	51.3%	28%	33%
Controlled	Freq.	9	31	40
	% Group	22.5%	77.5%	100%
	% <i>Helicobacter pylori</i>	23.1%	21.7%	22%
Hypothyroidism	Freq.	3	54	57
	% Group	5.3%	94.7%	100%
	% <i>Helicobacter pylori</i>	7.7%	37.8%	31.3%
Hyperthyroidism	Freq.	7	18	25
	% Group	28%	72%	100%
	% <i>Helicobacter pylori</i>	17.9%	12.6%	13.7%
Total	Freq.	39	143	182
	% Group	21.4%	78.6%	100%
	% <i>Helicobacter pylori</i>	100%	100%	100%

Conclusions:

- Thyroid disorders were increased with age of patients and females more susceptible than males.
- There was a correlation between thyroid disorders and high body weight.
- Cholesterol was found to be related to the high density lipoprotein (HDL) levels in patients of thyroid disorders.

- Thyroid disorders patients were more susceptible for *Helicobacter pylori* infection.
- *Helicobacter pylori* incidence rate increased in the hypothyroidism patients more than in hyperthyroidism ones.

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