NTU Journal of Pure Sciences (2023) 2 (3) : 19-24
DOI: https://doi.org/10.56286/ntujps.v2i3

IRAQI Academic Scientific Journals

ISSN: 2789-1089 EISSN: 2789-1097
NTU Journal of Pure Sciences
Available online at: https://journals.ntu.edu.iq/index.php/NTU-JPS/index

Effect of H. *pylori* infection on incidence of hyperthyroidism and hypothyroidism in men and women

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Article Informations

Received: 28-07- 2022,
Accepted: 15-11-2022,
Published online: 30-09-2023

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Key Words:
H.pylori ,
Hyperthyroidism,
hypothyroidism,
Euthyroidism.

A B S T R A C T

There are some controversial studies that associate Helicobacter pylori infection with autoimmune thyroid disease (AITD). The study aimed to evaluate the effect of H. pylori infection on the development of thyroid diseases, so the study was carried out on 90 patients (male and female) with thyroid disorders, and 50 healthy individuals as a control group. Biochemical and immunological assays including estimation of anti-*H. pylori* IgG and Anti-cag-A IgG titer by ELISA method, while assessment of Tri-iodothyronine (T3), tetra iodothyroixine (T4), and thyroid Stimulating Hormone (TSH) by (e601 Cobas) automated immunoassay analyzer. The result recorded a significant decrease in TSH concentration ($P < 0.05$) in the hyperthyroidism group and a significant increase in TSH concentration ($P < 0.05$) in hypothyroidism patients whereas the concentration of T4 and T3 recorded a significant increase ($P < 0.05$) in hyperthyroidism group while a significant decrease in T4 and T3 concentrations ($P < 0.05$) occur in hypothyroidism patients when compared with control (Euthyroidism) group. On the other hand, there is a significant increase ($p < 0.05$)in the titer of *H.pylori* IgG and the titer of anti-cag IgG in both females and males of hyperthyroidism and hypothyroidism groups in comparison to control Euthyroidism group. The highest prevalence of *H.pylori* IgG positive (74.5%) occurs hypothyroidism group followed by (71.4%) for hyperthyroidism patients while (56%) occurs in the control group (Euthyroidism).
In conclusion, our findings indicated that *H.pylori* infection is more susceptible in thyroid disorder patients, and anti –Helicobacter pylori IgG antibodies distribution among hypothyroidism is greater than in other groups.

Introduction

Helicobacter pylori is a gram-negative bacteria that resides in stomach and can cause peptic ulcers, chronic gastroenteritis, and mucosa-associated lymphoid tissue lymphoma, and may cause gastric carcinoma [1]**.** The prevalence of this pathogen is reported to be over 50% worldwide. However, there are differences in the reported infection rates between different regions, with developing nations having a higher incidence than developed nations [2,3]**.** A complex interplay between host, environmental, and bacterial virulence determinants mediates *Helicobacter pylori* pathogenesis and disease consequences, four phases are essential for bacteria to achieve effective colonization, persistent infection, and disease pathogenesis after *H. pylori* enters the stomach of the host: living in an acidic stomach, the ability to move toward epithelial cells through flagella-mediated motility; the ability to adhere to host cells by the interaction of adhesions and receptors; and the ability to release toxins to cause tissue damage [4]**.** One other hand one of the biggest and most significant endocrine glands is the thyroid [5]**.** The most common type of endocrine disorders worldwide are thyroid diseases [6]**.** Thyroid hormones may be the cause of numerous gastrointestinal (GI) symptoms, the risk of several distinct pathogenesis in the GI system can be increased by thyroid disorders, Triiodothyronine (T3) and thyroxine (T4), which the thyroid gland secretes and which are controlled by thyroid-stimulating hormone (TSH), thyroid may have an impact on the GI tract, skin, cardiovascular system, and nervous system [7]**.** The two main categories of thyroid disorders are hypothyroidism and hyperthyroidism. A common endocrine disorder called hypothyroidism results in insufficient thyroid hormone production (T3 and T4) or inadequate thyroid hormone action on the target tissues[8]**.** While patients with hyperthyroidism may have hyper metabolic status due to an excessive concentration of thyroid hormones carried on by increased synthesis of the thyroid hormones T3 and T4, or from an endogenous or exogenous extra thyroidal source [9]**.**

Infection of *H. pylori* has been linked to some extra-digestive conditions, including diabetes mellitus, autoimmune thyroid diseases, autoimmune atrophic thyroiditis, Hashimoto thyroiditis, dyslipidemia, obesity, primary hyperparathyroidism and osteoporosis; moreover, there is conflicting evidence regarding the relationship between *H. pylori* infection and these diseases [10,11]**.** Based on established research that there is a significant positive relationship between *H. pylori* infection and autoimmune thyroid diseases, thyroid disorders have been linked to Helicobacter pylori infection [12,13]**.** Because *H. pylori* might play an important role in the development of thyroid dysfunction, we thought it necessary to carry out this study to investigate the association and incidence of thyroid gland dysfunction with *H. pylori* infection.

Materials and methods:

Our study involved 140 men and women: patient groups included (90 male and female) with thyroid disease and (50 healthy people) serving as control group (Euthyroidism). patients group were confirmed by specialist physician in many Doctors' private clinic in Kirkuk city .Five ml of venous blood samples were drawn from each patients and control group , and left to clot at R.T. the serum was taken after centrifugation, and then stored in the deep freeze (-20°C) till biochemical and immunological analysis, included :Detection of Anti – *Helicobacter pylori* IgG Antibody titer by enzyme-linked immunosorbent assay (ELISA) method using AccuBindmonobind Inc. ELISA Kit (USA) for anti *H.pylori* IgG. Assessment of thyroid disorder by measurement the levels of Tri-iodothyronine (T3) ,tetra iodothyroixine (T4) and Thyroid Stimulating Hormone (TSH) by the electrochemiluminescence immunoassay "ECLIA" is intended for use on(Roche Cobas 6000-e602; Roche Diagnostics, Germany) automated immunoassay analyzer. A total of 90 subjects with thyroid disorders in the study, were grouped into two categories: hypothyroidism(55 subjects) and hyperthyroidism (35 subjects) according to the normal values mentioned in instruction of TSH,T4,and T3 cobas e601 kits. On the other hand the control group (50 subjects) without thyroid disturbances (Euthyroid). Results of anti *H.pylori* IgG concentration of more than 20 IU/L confirmed the presence of IgG antibody according to the cut-off point as mentioned in the manufacturer's instructions, and the titer of anti- cytotoxin associated gene IgG (Anti-cag-A IgG) was measured in pg/ml unit.

Statistical analysis

Statistical analysis was performed using IBM SPSS statistical software. the differences between groups were statistically analyzed by one-way analysis at variance (ANOVA).

Result

Table (1) showed results of the study according to thyroid hormones status were recorded a significant increase in TSH concentration ($P < 0.05$) in hypothyroidism group, whereas there is a significance decrease in TSH concentration ($P < 0.05$) in hyperthyroidism patients when this two group compared with control (Euthyroidism) group. The level of T4 and T3 recorded a significant increase ($P < 0.05$) in hyperthyroidism group as compared to control group. Also there was significance decrease in T4 and T3 concentrations ($P < 0.05$) in hypothyroidism patients in comparison to control (Euthyroidism) group.

Table 1. Thyroid hormones concentrations according to study groups

Groups	No	Gender	TSH (μIU/mL)		T4 (nmol/L)		T3 (nmol/L)	
			Mean ± S.D	**P. value**	**Mean ± S.D**	**P. value**	**Mean ± S.D**	**P. value**
Hypothyroidism	13	Male	37.41 ± 34.65 a		67.20 ± 17.6 d		0.87 ± 0.30 d	
	42	Female	32.88 ± 29.59 a		66.22 ± 18.1 d		1.29 ± 0.85 cd	
Hyperthyroidism	9	Male	0.021 ± 0.027 b	**0.0006**	155.60 ± 27.0 b	**0.0008**	2.98 ± 1.26 ab	**0.0006**
	26	Female	0.026 ± 0.054 b		181.30 ± 23.2 a		3.55 ± 1.97 a	
Euthyroidism (control)	14	Male	2.12 ± 0.77 b		110.72 ± 26.45 c		2.03 ± 0.45 bc	
	36	Female	2.05 ± 0.91 b		111.19 ± 21.80 c		1.90 ± 0.38 c	

a, b, ab, bc : small letters refers to present significant differences ($P < 0.05$) between groups at the vertical column.

($P < 0.05$) = significant, ($P \leq 0.01$)= Highly significant, ($P > 0.05$) = Non-significant

Table (2) showed the results of the study with significant increase ($p < 0.05$)in titer of *H.pylori* IgG in both female and male of hyperthyroidism and hypothyroidism groups respectively in comparison to control group. On other hand the results revealed there was significant increase ($p < 0.05$)in titer of anti-cag IgG in hypothyroidism and hyperthyroidism group when compared to hyperthyroidism and control group.

Table 2. Concentration of *H.pylori* IgG and cag-A IgG among study groups

Groups	No.	Gender	H.pylori IgG (IU/L)	P.value	Anti-cag-A IgG (pg/ml)	P.value
			Mean ± S.D		Mean ± S.D	
Hypothyroidism	13	Male	54.29 ± 35.34 c	0.026	22.72 ± 4.93 a	0.005
	42	Female	74.38 ± 52.54 b		24.86 ± 3.68 a	
Hyperthyroidism	9	Male	91.0 ± 66.2 a		23.41 ± 3.96 a	
	26	Female	74.60 ± 53.3 b		24.35 ± 3.65 a	
Euthyroidism (control)	14	Male	48.89 ± 34.90 c		15.59 ± 2.69 b	
	36	Female	53.25 ± 43.54 c		17.25 ± 2.07 b	

a, b, ab, bc : small letters refers to present significant differences ($P \leq 0.05$) between groups at the vertical column.

($P \leq 0.05$) = significant, ($P \leq 0.01$)= Highly significant, ($P > 0.05$) = Non-significant

Results of anti –*H. pylori* IgG antibodies in (table 3) showed that the highest percentages of *H. pylori* infections were detected in both hypothyroid (74.5%)and hyperthyroid (71.4%) groups, while the lowest percentage (56%) was recorded in the healthy group which are summarized in fig. **1**. However, The incidence of *H.pylori* IgG in female 69 (73%) was greater than male 25 (27%) among total 140 subjects which are showed in Table3.

Table(3): Distribution of *H.pylori* among patient and control groups

Groups		Helicobacter pylori IgG		Total
		Positive No. (%)	Negative No. (%)	
Hypothyroidism	T	41 (74.5%)	14 (25.5%)	55
	M	10 (24%)	3 (21%)	13
	F	31 (76%)	11 (79%)	42
Hyperthyroidism	T	25 (71.4%)	10(28.6%)	35
	M	7 (28%)	2 (20%)	9
	F	18 (72%)	8 (80%)	26
Euthyroidism (control)	T	28 (56%)	22 (44%)	50
	M	8 (29%)	6 (27%)	14
	F	20 (71%)	16 (73%)	36
Total	T	94	46	140
	M	25 (27%)	11 (24%)	36
	F	69 (73%)	35 (76%)	104

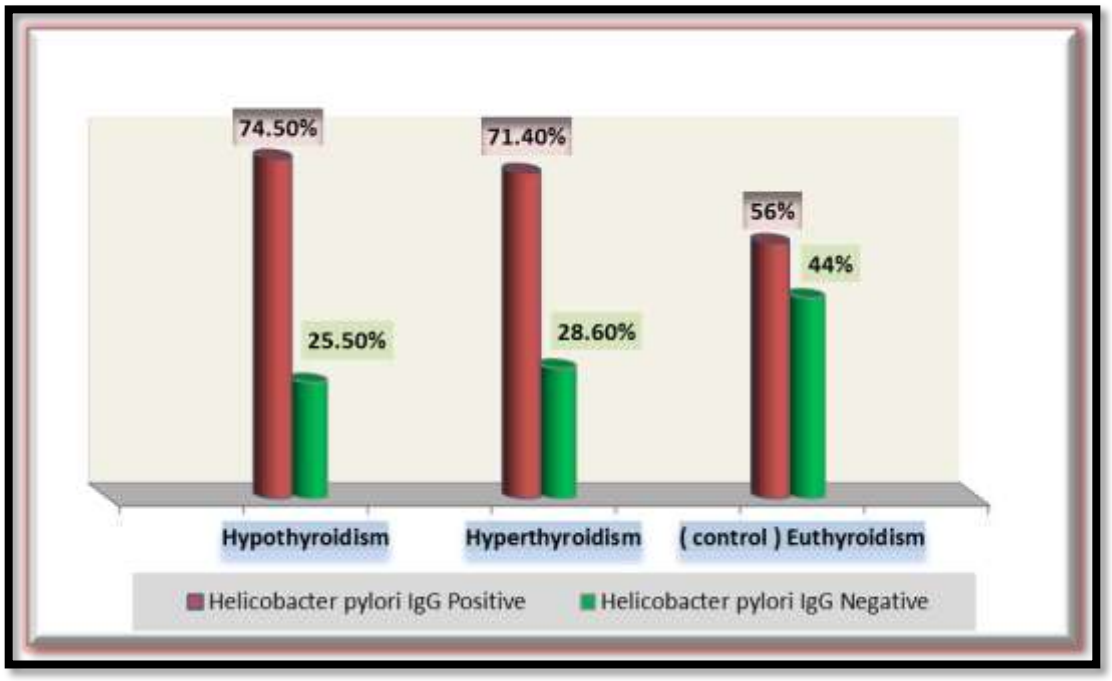

Figure 1. prevalence of H.pylori IgG among Hypothyroidism , Hyperthyroidism and Euthyroidism

Discussion

In our study we recorded a significant decrease in TSH concentration ($P < 0.05$) in hyperthyroidism group and a significant increase in TSH concentration ($P < 0.05$) in hypothyroidism patients whereas the concentration of T4 and T3 recorded a significant increase ($P < 0.05$) in hyperthyroidism group while a significance decrease in T4 and T3 concentrations ($P < 0.05$) occur in hyporthyroidism patients when compared with control (Euthyroidism) group, these finding was compatible with [14]**.**

The results recorded a significant increase ($p < 0.05$)in titer of *H.pylori* IgG in both female and male of hyperthyroidism and hypothyroidism groups so findings of present study, are in line with other study represented that *H.pylori* IgG positivity was more prevalent among patient group than in control group [12]**.**

Cytotoxin-associated gene A (CagA) is one of the most critical virulence determinants of *H.pylori* infection, in results of the our study we found a significant increase ($p < 0.05$) in the level of anti-cag IgG in both hypothyroidism and hyperthyroidism patients as compared to Euthyroidism (control group) this result was in agreement with [15]**.** The result of current study showed that the highest percentages of *H. pylori* infections were detected in hypothyroid (74.5%)followed by (71.4%) in hyperthyroid groups when compared with Euthyroidism healthy individuals, this finding is compatible with[14,11]**.** Also Prevalence of female patients with *H.pylori* IgG positive (73%) was greater than male (27%), this result was in agreement with [11,16]**.**

Conclusion

We concluded that thyroid disorders patients were more susceptible for *Helicobacter pylori* infection, and the incidence rate of *H.pylori* infection in hypothyroidism patients is more than hyperthyroidism patients, so the virulence factor cag A may play a role in this relationship.

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