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Helicobacter pylori infection in pregnant women and it's correlation with the alterations of some trace elements levels in the serum at Maternity Teaching Hospital in Erbil City

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Abstract:

Helicobacter pylori (H. pylori) is a spiral-shaped pathogenic bacterium found on the human gastric mucosa, Warren and Marshall isolated H pylori for the first time in 1982. It is one of the most common worldwide human infections [1]. H. pylori play a vital role in the development of chronic gastritis, gastric ulcer, duodenal ulcer, gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue lymphoma [2]. The current study included (120) pregnant women, (50) positive anti -H. Pylori Ig and (70) negative anti- H. Pylori Ig with pregnancy for first, second and third semester at mean age/ years 28.36 for the positive anti-H. Pylori and 26.17 for the negative anti-H. Pylori appeared that an alteration of zinc level in serum of positive anti- H. Pylori Ig groups was (48.904 ± 18.3486) (µg/dl) comparing with the negative groups (90.757 ± 9.2727) with the highly significant difference ($P < 0.01$). While serum copper levels of positive anti-H. Pylori Ig group was (µg/dl), (100.412 ± 23.8234), documented as normal highly significant ($P < 0.01$) compared to the negative anti- H. Pylori Ig group (114.971 ± 20.4995).In this study, the GIT disorder with anti-H. Pylori Ig positive groups were (32, 64%) and anti-H. Pylori Ig negative groups were (32, 45.7%), with significant difference ($P < 0.05$).

Key words: H. pylori, Pregnancy, Trace elements, Copper, Zinc

في النساء الحوامل وارتباطها بالتغييرات *Helicobacter pylori* عدوى جرثومة التهاب المعدة ببعض مستويات العناصر الذرية في مصل الدم في مستشفى الولادة بمدينة أربيل

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الخلاصة:

هيليكوباكتر بيلوري (H. pylori) هي بكتيريا ممرضة شكلها حلزوني وجدت على الغشاء المخاطي في المعدة، عزل وارين ومارشال هيليكوباكتر بيلوري (H. pylori) لأول مرة في عام 1982. وهي واحدة من أكثر أنواع العدوى البشرية شيوعًا في العالم . هيليكوباكتر بيلوري (H. Pylori) تلعب دورا حيويا في تطور التهاب المعدة المزمن ، وقرحة المعدة ، وقرحة الاثني عشر ، وسرطان الغدد المعويه ، والغدد اللمفاوية المرتبطه بالغشاء المخاطي المعوي.شملت الدراسة الحالية (120) امرأة حامل ، (50) امراة منهم كانوا مصابات بالجرثومه ويحملون اجسام مضاده لـ H. Pylori Ig Positive و (70) منهم كانو غير مصابات بالجرثومة Negative H. Pylori Igوشملوا فصول الحمل الأولى و الثانيه والثالثة و كانت متوسط اعمارهم 28.36 للمجموعه الموجبه (المصابه بالجرثومه) بينما كانت 26.17 للمجموعه الغير مصابه Negative H. Pylori Ig، ظهر أن تغيير مستوى الزنك في مصل الدم للمجموعه الموجبه كانت (48.904 ± 18.3486) (ميكروغرام / ديسيلتر) مقارنة مع المجموعة السالبه والتي كانت (90.757 ± 9.2727) مع فرق احصائي كبير للغاية ($P <0.01$). في حين كانت مستويات النحاس في مصل الدم للمجموعه المصابه بالجرثومه (100.412 ± 23.8234) (ميكروغرام / ديسيلتر) موثقة بفرق احصائي كبير للغاية ($P <0.01$) بالمقارنة مع المجموعة السالبة (Negative H. Pylori Ig (114.971 ± 20.4995. اظهرت هذه الدراسه انه نسبه اضطراب الجهاز الهضمي بسبب

الاصابه بالجرثومه المسببه لالتهاب المعدة (H. Pylori). كانت (32 ، 64 ٪) في النساء الحوامل بينما كانت (32، 45.7٪) للمجموعه السالبة مع فرق احصائي (P <0.05).
مفاتيح الكلمات : هيليكوباكتر بيلوري، حمل، العناصر النزرة، الزنك، النحاس.

Introduction:

Helicobacter pylori (*H. pylori*) infection affects around 50% of the world population and it is more predominant in developing countries. The infection of *H pylori* persists for years once acquired and it is may be obtained at any age [1-3]. The worse socioeconomic group of developing countries has a higher age-specific dominance of *H pylori* infection [4].

H. pylori infection usually causes both acute and chronic inflammatory cell infiltration, leading to an increase in reactive oxygen species (ROS) which have been shown to accumulate in *H pylori* gastritis [5]. In addition, numerous reports showed an association between *H. pylori* infection and various extra-gastric disorders during the past decades. Such as manifestations include ischemic heart disease, diabetes mellitus, idiopathic thrombocytopenia, urticaria, and sideropenic anemia [6].

Trace elements are broadly disseminated in variable proportions and they play a crucial role in the growth, health, and preserves of the human body. Alterations of these elements' levels may damage cellular and physiological functions or cause infection, through the alteration of metalloenzymes activities that need a minor and constant number of atoms of metal per mole to achieve full activity [7,8]. Furthermore, deficiencies in micro-nutrients such as trace elements and minerals, caused by *H. pylori* infection could affect the digestion and absorption of dietary nutrients by disrupting gastric secretion and acidification functions. Consequently, this may trigger impairments in biological and immunological functions [9]. Numerous studies are revealed that the deficiencies in copper, vitamin B12, folic acid, and vitamin A, C, and E is associated to the *H. pylori* infection.These shortages may be occurred as a result of anorexia that caused by dyspeptic symptoms or from malabsorption secondary to intestinal bacterial infections, which is due to hypo-achlorhydria in the stomach in the presence of *H. pylori* [6]. In *H. pylori* endemic population, pregnant women may be harboring asymptomatic *H. Pylori* infection, with its attendant shortages of crucial micronutrients which may affect the course and outcomes of pregnancy as evidenced in [10].

Aims of study

1. The Current study aimed to investigate the levels of some Trace elements (Copper and Zinc) of infected pregnant women with *H pylori* for the first, second and third semester in some population of Erbil City at Maternity Teaching Hospital .

2. To note the frequency of GIT disorder for both positive and negative anti-*H. Pylori* Ig groups.

Materials and Methods

This study was carried out on pregnant women that attended antenatal unit at Hawler Teaching Maternity hospital who's diagnosed as gastrointestinal tract (GIT) disorder from15 September 2017 to 15 February 2018. One hundred and twenty pregnant women were included in this study, all are in the age group of 20-40 years in the first, second and third semester in both positive and negative Anti-*H. pylori* Ig selection was based on using (Systematic random probability). A 50 positive anti-*H. Pylori* Ig pregnant women were selected in this study their mean age / Years ± standard deviation was (28.36 ± 5.649), in the first semester (N = 10), second semester (N = 10) and the third semester (N = 30). Whereas, seventy negative anti-*H. Pylori* Ig group mean age/ Years ± standard deviation was (26.17 ± 5.905), in the first semester (N = 6), second semester (N = 10) and the third semester (N = 54) Fig (1).

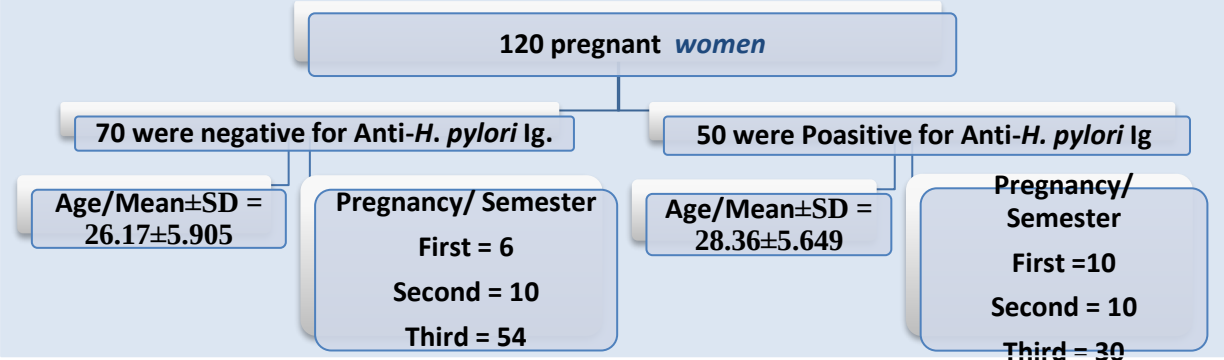

Figure (1): Distribution of *H pylori* in pregnant women.

Tools of the Study

Methods of data collections provided by face to face interview with patients using

1- Questionnaire: Questionnaire that constructed for the purpose of the study which composed of Socio-demographic data that included Age and pregnancy semester.

2- Serological and Biochemical tests.

Serological tests: *H. pylori* infection has been diagnosed by using Antigen Cassette test (Linear chemicals, S. Barcelona, Spain) followed the instruction of the procedure [11]. ELIZA test (indirect biokitLQ300+I) was used to detect Anti-*H. pylori* IgG, IgM antibodies.

Biochemical tests:

A- Complete blood count (CBC) test was done for all samples to indicate anemia, CBC analyzer (Coulter Medonic) was used to count WBC and platelets [12]. Followed the instructions of applying the test.

B- Investigation of the concentrations of trace elements (copper and zinc) of pregnant women were achieved using flame atomic absorption spectrometry (PYE UNICAM SP9) [6,13-14]. Followed the instructions of applying the test.

Statistical Analysis

The statistical analysis was performed using the statistical package for social sciences (SPSS), version 23 and (Excel 2010). Qualitative data were existed using number and percentage. Quantitative data were presented using mean and standard deviation. ($P < 0.05$) was chosen as Significance for results.

We used the following statistical tests:

A. Chi-square test: in categorical variables

B. T-test: in normally quantitative variables. Statistical significance was achieved at $p < 0.05$.

Results

The distribution of age group per years for positive and negative (anti-*H. pylori Ig* pregnancy women group) was achieved. In addition to the Semester of pregnancy of both groups**.**

The predominant age group per years, for positive anti-*H. pylori* Ig group was (20-30) years, represented as 40 with 80% frequency, followed by (31-40) years, represented as 10 with 20% frequency. While negative anti-*H. pylori* Ig group was (20-30) years, represented as 54 with 77.1% frequency followed by (31-40) years, represented as 16 with 22.9 % frequency, the Non-significant difference between positive and negative groups, ($P > 0.05$), table (1).

Table (1): Distribution of age group per years for positive and negative anti- *H. Pylori* Ig pregnancy women group.

Age groups/ Years		Anti- *H. pylori* Ab.		Pearson Chi-Square (P-value)
		Positive	Negative	
20-30	N	40	54	P=0.708 Non-sign. (P>0.05)
	%	80	77.1	
31-40	N	10	16	
	%	20	22.9	
Total	N	50	70	
	%	100	100	

Distribution of semester pregnancy for positive Anti- *H. pylori* Ig group was 10 with 20% frequency for the first and second semester and 30 with 60% frequency for the third semester. While the distribution of semester for negative Anti-*H. pylori* Ab group was 6 with 8.6% frequency for the first semester, 10 with 14.3% frequency for the second semester and 54 with 77.1% frequency for the third semester, a non-significant difference (P>0.05). table (2)

Table (2): Distribution of semester pregnancy for positive and negative (anti-*H. Pylori* Ig groups*).*

Pregnancy Semester		Anti- *H. pylori* Ab.		Pearson Chi-Square (P-value)
		Positive	Negative	
First	N	10	6	P=0.098 Non-sign. (P>0.05)
	%	20	8.6	
Second	N	10	10	
	%	20	14.3	
Third	N	30	54	
	%	60	77.1	

The frequency of GIT disorder for positive and negative anti-*H. Pylori* Ig groups were done depending on patients answer (32, 64%), answered yes (18, 36%), answered no for the positive group, whereas (32, 45.7%) answered with Yes, (38, 54.3%) answered with No for the negative group. Significant differences between the positive and negative group were observed (P < 0.05), table (3).

Table (3): The frequency of GIT disorder for (positive& negative anti- *H. pylori Ig* pregnant women groups).

GIT disorder		Anti- *H. pylori* Ab.		Pearson Chi-Square (P-value)
		Positive	Negative	
Yes	N	32	32	P=0.048 Sign. (P<0.05)
	%	64%	45.7%	
NO	N	18	38	
	%	36%	54.3%	

Hematological assay used to determination of (Platelet count 10^9/L, WBC count (White blood cell count) 10^3/L and Hb (Hemoglobin) level g/dL), all results have represented as (mean ± standard deviation), non-significant difference appeared at ($P > 0.05$), Platelet count 10^9/L were (224.72 ± 60.597), (230.51 ± 86.318), WBC count (White blood cell count) 10^3/L were (10.37 ± 3.132), (10.54 ± 3.019) respectively for positive and negative groups. These results showed slight increases in WBC count for both group with normal platelet count, while Hb (Hemoglobin) level g/dL was (11.52 ± 1.411) in positive group, (11.79 ± 1.884) in the negative group which shows Slightly decreases in both groups, table (4).

Table (4): A hematological assay for pregnant women (positive and negative anti –*H. pylori* groups).

Hematological assay	anti-*H. pylori Ig*	Mean	Std. Deviation	Std. Error	t-test (P-value)
Platelet 10^9 / L	Positive	224.72	60.597	8.569	P=0.684 Non-sign. (P>0.05)
	Negative	230.51	86.318	10.316	
WBC 10^3 /L	Positive	10.37	3.132	0.443	P=0.772 Non-sign. (P>0.05)
	Negative	10.54	3.019	0.361	
Hb g/dL	Positive	11.52	1.411	0.199	P=0.389 Non-sign. (P>0.05)
	Negative	11.79	1.884	0.225	

In this study the assessment of the trace element concentration (zinc and Copper) (µg/dL) in the serum of both positive and negative anti-*H. pylori* Ig groups represented as (mean ± standard deviation), Serum zinc concentration (µg/ dL) in pregnant women of the positive group was (48.904 ± 18.348). Which showed decreasing the level of zinc compared with the level of zinc in the negative group which was (90.757 ± 9.2727) with highly significant differences ($P<0.01$). While serum copper concentration (µg/ dL) in the positive group was (100.412 ± 23.8234) which showed highly significant differences ($P<0.01$) comparing with the normal levels of copper in the negative group which was (114.971 ± 20.4995), table (5).

Table (5): Trace element levels in sera of positive and negative anti-*H. Pylori* Ig. pregnant women group

Trace elements in serum	Anti-*H. pylori* Ab.	Mean	Std. Deviation	Std. Error	t-test (P-value)
Zinc µg/dL	Positive	48.904	18.3486	2.5949	P=0.00 Highly sign. (P<0.01)
	Negative	90.757	9.2727	1.1083	
Copper µg/dL	Positive	100.412	23.8234	3.3691	P=0.00 Highly sign. (P<0.01)
	Negative	114.971	20.4995	2.4502	

Discussion

In this study, the ages of the women in both groups ranged from 20 to 40 years. The mean age of this study was Age/Mean±SD = 28.36±5.649 for positive anti- *H. pylori* Ig group and Age/Mean ± SD = 26.17±5.905 for negative anti- *H. pylori* Ig group and this compatible with the previous study as in, forty or fifty normal pregnant females considered as (controls) while forty or fifty pregnant women complaining of hyperemesis gravidarum classified as (cases).The range of the age of the women in both groups were from 20 to 35 years, the mean age of the controls was 26.95±4.71 while that of patients was 27.50±4.66. Distribution of Pregnancy/ Semester for studying groups (anti-*H. pylori* Ig of the Positive group) were (10, 20%) for the First and Second semester, while the Third semester was (30, 60%). The non-significant difference appeared between positive and negative *H. pylori* pregnant groups (P > 0.05).The results of the current study were compatible to the results found in previous studies as in, who's showed that there is high percentage of incidence of *H. Pylori* infection symptom during the early gestational age (trimester),all pregnant women involved in the study were pregnant with gestational age from 5 to 15 weeks. The control group was pregnant women with the same gestational age but without indication of hyperemesis gravidarum HG, while the cases included in the study were complained from symptoms of severe vomiting (≥3 times a day) not responding to traditional treatments, weight loss (≥5% of body weight); hyperemesis gravidarum (HG) and presence of ketonuria. Both groups in the study were comparable as regards age, obstetric history, and gestational age [15]. The frequency of GIT disorder in pregnant women with Anti-*H. Pylori* Ig for both (Positive and Negative groups) in this study was (32, 64%), for positive *H. pylori* Ig. group and (32, 45.7%), for negative *H. pylori* Ig. group with significant difference (P<0.05). This agrees with previous studies, which targeted to determine the relation between *H. pylori* infection and (Hyperemesis gravidarum) HEG. The ratio of *H. pylori* sera positivity in hyperemesis patients was significantly higher (77.5%) compared to the control group (55.0%), p=0,058. The study of [16] Showed that 90.5% of female sufferings from HG were positive for *H. pylori* infection comparing to 46.5% of the normal pregnant group. Another study revealed that 92% of females with HG had positive serum *H. pylori* Ig and it was 45% in the normal women group [17]. Although *H. Pylori* infection determined by the seropositivity for its antibodies is also, prevalent in asymptomatic population but this infection is considered one of the factors that cause GIT disturbance, vomiting, and nausea in general population as found by [18]. The HG may persist throughout gestation, but the onset of gastrointestinal symptoms is always during the first trimester. The etiology of HG, which still remains unknown, looks to be multifactorial and may be the final result of various unrelated conditions. Indeed, treatment is achieved on a symptomatic foundation [19]. In particular,There are many of pathologic mechanism underlying HG, such as psychological causes, gastrointestinal tract dysfunctions, endocrine factors (i.e., elevated human chorionic gonadotropin and estrogen), genetic incompatibility, immunological factors and nutritional deficiencies. However, no single theory seems to provide an adequate explanation for HG [20]. In our study the concentrations of all trace elements (µg/dL) in both positive and negative anti-*H. Pylori* Ig Pregnant represented as (mean ± standard deviation). Serum zinc concentration (µg/ dL) in pregnant with positive anti-*H. pylori* Ig Were, (48.904 ± 18.348) which was lower than the level of zinc in negative anti-*H. Pylori*Ig group, (90.757 ± 9.2727) with highly significant difference (P < 0.01). While the serum copper levels had no alterations between positive and

negative *H. pylori* groups with the highly significant difference ($P < 0.01$).

The results of the current study were comparable to the results found in previous studies which showed that there is an alteration in the levels of trace elements especially with the Zinc level in *H. pylori* infection. *pylori* infection may result in stomach inflammation. *H. pylori*, when having altered gastric secretion coupled with tissue injury, leads to peptic ulcer disease and gastritis, and maybe progresses to atrophy, intestinal metaplasia, and eventually gastric carcinoma. *H. pylori* also lead to hypochlorhydria in *H. pylori*-related gastritis [21]. The change of gastric environment may affect the absorption of trace elements. Copper is an essential mineral in the human body, which is required as a catalytic cofactor in different enzyme reactions, such as an allosteric enzyme component and a potent antioxidant with a critical role in the oxidant defense system [22]. For children, previous reports have shown that serum copper level was associated with gastric *H. pylori* infection [23]. For adults, previous reports have shown that serum copper level had no significant difference between gastric *H. pylori* infection and non-infection [24,25]. Even after *H. pylori* eradication therapy, the serum copper levels had no significant changes between successful and failed *H. pylori* eradication groups. Zinc is an important trace element in the organism, with catalytic, structural, and regulatory roles. Zinc is also related to some diseases, including Alzheimer's disease, cancer, aging, diabetes, depression, and Wilson's disease [26].

The role of zinc in adults seems to control the oxidative stress in gastric mucosa. Increased susceptibility to oxidative stress may happened as a result of zinc deficiency and this may cause higher risk of mucosal damage in inflammation [27]. It has been reported that serum zinc level was an indicator of protecting gastric mucosa against damage, and it seems to be significantly reduced in patients with gastritis, peptic ulcer, and gastric cancer [28]. The gastric tissue zinc concentration may be modulating the degree of inflammation in *H. pylori*-induced gastritis. The lower concentration of zinc in gastric mucosa is, the more severe of *H. pylori* infection is noted [29].

Conclusion

Conclusion, the most important finding of this study was that *H. Pylori* infected pregnant women showed a significantly ($P < 0.05$) higher risk of gastrointestinal disorder with chronic inflammation of gastric mucosa and peptic ulcer disease. In addition, *Helicobacter pylori* infection may influence the absorption of essential trace elements like zinc and copper which decreased in the case of the level of Zinc in serum significantly ($P < 0.01$) in this study. These Alterations of the levels of these trace elements may harm cellular and physiological functions or cause infection.

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