

THE ROLE OF *HELICOBACTER PYLORI* IN PATHOGENESIS OF HYPEREMESIS GRAVIDARUM

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ABSTRACT

OBJECTIVE

To evaluate the role of Helicobacter pylori in the pathogenesis of HG and the value of adding a non-teratogenic regimen for its treatment in intractable cases.

PATIENTS & METHODS

Sixty pregnant women with hyperemesis gravidarum (HG) were matched with 60 control pregnant women with no history of HG. The study was conducted at Basrah Maternity and Child Hospital. A full history was obtained including medical disorder and drug usage. Serum H.pylori IgG antibody titres were estimated by using commercial ELIZA method for all patients and control. The pregnant women with positive H.pylori test were subdivided into 2 groups for the purpose of treatment. The first group was received traditional treatment of HG which include I/V fluid, antiemetic, antacid and vitamin supplement. The second group was received H.pylori treatment include proton pump inhibitor, amoxicillin and metronidazole. Then, both groups were followed up for the number of vomiting, duration of hospitalization and pregnancy outcome.

RESULTS

Fifty three out of 60 women with HG were seropositive for H.pylori (85%) and 34 out of 60 control group were seropositive (55%). It is highly significant in regard to primigravida and level of education between the seropositive and seronegative in the studied group. There is significant clinical improvement in patients who received H.pylori regimen than the group who received traditional therapy regard duration of admission to hospital and decrease number and frequency of vomiting in the studied group.

CONCLUSIONS

Helicobacter pylori should be considered as one of the causes of HG and screening for it should be added for investigation. H.pylori regimen may be considered in intractable cases.

KEYWORDS: *Helicobacter pylori, Hyperemesis, Pathogenesis & Pregnancy*

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INTRODUCTION

Hyperemesis gravidarum (HG) is a condition of intractable vomiting during pregnancy, leading to fluid, electrolyte and acid-base imbalance, nutrition deficiency and weight loss often severe enough to require hospital admission. It occurs between 4th and 10th week of gestation and it resolute by 20 week of gestation⁽¹⁾. Symptoms will persist among 10% of patients throughout pregnancy⁽²⁾.

There are numerous theories regarding the cause of HG including hormonal, placental serum marker, immunology and *Helicobacter pylori* infection⁽³⁾. An increased incidence of *H.pylori* infection has been observed in gastric antrum and corpus in HG patients. A small portion of *H.pylori* infected subjects develop peptic ulcers and gastric carcinoma, usually during adulthood⁽⁴⁾.

Adhesion, such as outer inflammatory protein binding adhesion, facilitate bacterial attachments to host epithelium leading to inflammatory response^(5, 6).

The aim of the study is to evaluate the role of *H.pylori* in the pathogenesis of HG and the value of adding a non-teratogenic regimen for its treatment in intractable cases.

Patients and Methods

This is a prospective case control study which was conducted at Basrah Maternity and Child Hospital during the period from May 2014 till October 2015. Sixty pregnant women with a history of hyperemesis gravidarum were enrolled in the study. The criteria for diagnosis of HG included severe vomiting (more than 3 times/day) which interfere with ordinary life of the patient and need admission to the hospital with or without ketonuria. Exclusion was done for women with hyperthyroidism, psychological disorders, hepatic disorders, urinary tract infection or intra cranial disorders.

The control group involved 60 pregnant women without HG, matched for age, parity and gestational age. Serum *H.pylori* IgG antibody titre was estimated by using commercial ELISA method for all patients and control group. The pregnant women with positive IgG test were subdivided into 2 groups for the purpose of treatment.

The first group was received traditional treatment for HG which include I/V fluid and antiemetic drug (metoclopramide 5-10mg/day, antacid and vitamin supplement). The second group was received *H.pylori* treatment according to guideline recommendation which included triple therapy: proton pump inhibitor omeprazole 20mg/2days, amoxicillin 2g/days, metronidazole 500mg/2times daily rectally or I/V for 5 days.

Statistical analysis: X2 test was used for nominal values and paired t-test by using SPSS. Value <0.05 considered statistically significant.

RESULTS

The demographic data of both groups were summarized in Table (1). There were no statistical differences between the patients and control groups in terms of age, gestational period and parity. Positive serum *H.pylori* IgG antibody was detected in 53 out of 60 pregnant women with HG (88%) in comparison to 34 out of 60 control women (57%) with P value <0.05 (Table 2). Among patients group, the seropositive was not significantly different from the seronegative in relation to age, multiparity, gestational age at time symptoms onset, duration of symptoms and rate of abortion (Table 3). Never the less, there was high significant relationship in regard to primigravidae and education level which was significantly high in seropositive patients than in seronegative patients (Table 3). No significant difference was observed between the patients and control group in regard to number need admission to the hospital and severity of vomiting (Table 4). But there was significant difference in relation to duration of staying in the hospital and dehydration status.

As far as treatment is concerned, there was clear observation for patients with *H.pylori* regime in regard to staying in the hospital, dehydration status, improvement in the frequency of vomiting which was statistically significant (Table 5).

Table 1: Characteristic Features of Patients and Control Groups

Variable	Hyperemesis Gravidarum N=60	Control N=60	P Value
Age (years)	25 ± 3.6	24 ± 3.3	N/S
Primigravida	53 (88.3%)	55 (91.7%)	N/S
Multigravida	7 (11.7%)	5 (8.3%)	N/S
Gestational weeks at time of blood sample.	9.2 ± 1.2	10 ± 1.6	N/S

Table 2: Seropositivity of *H.Pylori* in Patients and Control Groups

Group	Patients with HG	Control	P Value
Positive	53 (85%)	34 (55%)	0.05
Negative	7 (15%)	26 (45%)	0.05
Total	60 (100%)	60 (100%)	

Table 3: Characteristics of Patients in Regard to *H.Pylori* seropositive.

	Seropositive N=53	Seronegative N=7	P Value
Age (years)*	26 ± 3.0	24 ± 4.0	N/S
Primigravida	46 (86.8%)	7 (85.7%)	0.001
Multigravida	6 (13.2%)	1 (14.3%)	N/S
Education			
Primary school	15 (28.3%)	2 (28.6%)	0.05
Higher school	38 (71.7%)	5 (71.4%)	0.05
Symptoms onset (Gestational week)	7.66 ± 0.7	7.37 ± 0.8	N/S
Symptoms duration (weeks) *	9.52 ± 1.2	8.63 ± 1.6	N/S
Abortion	3 (6.3%)	1 (14.3%)	N/S

*= mean ± S.D

Table 4: The Response to Traditional Treatment Measure in Sero positive Group to HG

Criteria	Seropositive N=53	Seronegative N=7	P value
Admission to hospital	34 (64%)	3 (42%)	0.05
Duration of staying hospital	3-5 days	2-3 days	0.05
Ketonuria			
Positive	29 (54.7%)	1 (14.3%)	0.05
Negative	24 (45.3%)	6 (85.7%)	0.05
Number of vomiting			
> 3 times/day	30 (56.6%)	2 (28.6%)	0.05
< 3 times/day	23 (43.4%)	5 (71.4%)	0.05

Table 5: Comparison between the 2 Types of Treatment Regime in the Seropositive *H.Pylori* in HG Pregnant Women

Criteria	Traditional Regime Group N=17	<i>H.Pylori</i> regime Group N=17	P Value
Days of hospitalization more than 3 days.	16 (94%)	5 (29.4%)	0.01
Persistence of ketonuria.	14 (82.6%)	5 (29.5%)	0.01
Number of vomiting attacks/day.	7 (41.2%)	12 (70.6%)	>0.07
Decrease vomiting attack <3/day.	10 (58.8%)	5 (29.4%)	>0.05
Attack of >3/day.			

DISCUSSIONS

Helicobacter pylori is one of the commonest bacterial infection worldwide and accepted as a cause of chronic active gastritis, most patients continue through life with chronic superficial gastritis while others develop either duodenal or gastric ulcer⁽⁷⁾. The present study revealed higher *H.pylori* seropositivity in pregnant women with HG. However, the prevalence rate for this organism is higher in developing countries than developed countries (Soll, 1996). The overall prevalence of seropositivity was 65-91% in pregnant women with HG^(8,9).

The high rate of *H.pylori* in pregnant women during the early pregnancy due to increased accumulation of fluid and the displacement of intracellular and extracellular volume caused by the increase in the steroid hormone result in a change of pH in gastrointestinal tract⁽¹⁰⁾. In addition, the altered humoral and cell mediated immunity also contribute to the manifestation of a latent *H.pylori* infection⁽¹¹⁾.

The present study indicates that the gastrointestinal symptoms during pregnancy were more common in young educated primigravida (25 years of age) which is in contrast to other study who agreed with occurrence of HG in young primigravida but less educated⁽¹²⁾.

The results of this study could not demonstrate any correlation between the onset and duration of symptoms and seropositivity in HG group. These findings may reflect either the existence of underlying mechanism other than HG in the exacerbation of HG or the complex nature of the *H.pylori* infection related symptoms. It has been suggested that oral antibiotics give a good treatment response for *H.pylori* in HG⁽¹³⁾. Thus, in relation to days of hospitalization, persistence ketonuria and vomiting attack, *H.pylori* treatment regime is recommended.

In conclusion, *H.pylori* should be considered as one of the causes of HG. Also non teratogenic regimen for treatment of *H.pylori* may be considered in intractable cases.

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