

**Research Article**

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# Could *Helicobacter Pylori* Infection Be A Risk Factor for Hyperemesis Gravidarum

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**Background:** Hyperemesis gravidarum may be severe enough to affect the patient physically and psychologically. Previous studies indicated a relationship between *Helicobacter pylori* and hyperemesis gravidarum. The aim of this study is to evaluate if *Helicobacter pylori* infection has a possible etiological role in hyperemesis gravidarum.

**Methods:** The study was a case control study which was conducted at the obstetrics and gynecology department, Al Saily hospitals Makka and included 120 patients pregnant between 7 and 16 weeks and presented with hyperemesis gravidarum. Patients underwent a stool analysis for detecting *Helicobacter pylori* antigen and according to the test results were included in either case group (antigen positive, 60 patients) or control group (antigen negative, 60 patients).

**Results:** The cases group showed ketonuria in 22 (36.7%) patients, proteinuria in 34 (56.7%) patients and urinary tract infection in 26 (43.3%) patients. The control group showed ketonuria in 4 (6.67%) patients, proteinuria in 18 (30%) patients and urinary tract infection in 8 (13.3%) patients and these differences were all significant statistically.

**Conclusions:** *Helicobacter pylori* infection possibly contributes to the etiology of hyperemesis gravidarum. Also, the severity of the disease seems strongly related to *Helicobacter pylori* infection.

**Keywords:** Hyperemesis gravidarum; Nausea; Vomiting; Morning sickness; *Helicobacter pylori*

**Background**

Nausea and vomiting during pregnancy are the most common conditions affecting pregnancy, occurring in about 80% of all pregnancies and commonly disappears by 16 to 18 weeks of gestation. Hyperemesis gravidarum is the most severe form of nausea and vomiting in pregnancy, it is accompanied by starvation, dehydration, acidosis, alkalosis from hydrochloric acid loss in the vomits, hypokalemia, weight loss and transient hepatic dysfunction [1]. Many hypotheses have been published to explain the etiology and pathophysiology of hyperemesis gravidarum including infections, gastrointestinal tract dysfunctions, endocrinal changes, anatomical, metabolic and immunological factors. However, no

single theory is enough to give an adequate explanation for all the properties of hyperemesis gravidarum. Some studies done on patients with hyperemesis gravidarum indicated a relationship between *Helicobacter pylori* and hyperemesis gravidarum, in addition multiple gastrointestinal and extra digestive pathologies may be associated with *Helicobacter pylori* infection [2].

*Helicobacter pylori* is one of the most common bacteria affecting humans. It is a gram-negative helix-shaped microaerophilic bacterium transmitted by the oro oral or feco oral route. It is more prevalent in developing countries and young children. Types of diagnostic methods currently used include invasive and non-

invasive methods for detection of *Helicobacter pylori* bacteria. The more widely accepted methods by the patients are the non-invasive methods, such as stool antigen detection, serum antibody detection and carbon labeled urea breath test. The investigation of choice for *Helicobacter pylori* in pregnancy is the stool antigen detection test [3].

The consequences of activated latent *Helicobacter pylori* could have an impact not only on the mother's health (organ injury and nutritional deficiency), but also on her infant (malformations and in-utero growth restriction). Gastrointestinal manifestations during pregnancy, maternal anemia and fetal neural tube defect due to decreased iron and vitamin B12, are indications for investigation for *Helicobacter pylori* infection [4].

Most studies conducted on the correlation between pregnancy related disorders of gastrointestinal tract and *Helicobacter pylori* infection was cross sectional investigations in which the pregnant female was detected to be *Helicobacter pylori* positive during pregnancy or soon after delivery. However, there is no follow up study was conducted to explain the complete immune response against *Helicobacter pylori*. One prospective study tested the presence of *Helicobacter pylori* infection before conception and showed that early pregnancy loss was associated with the presence of positive *Helicobacter pylori* before intra-cytoplasm sperm injection [5].

The aim of this study is to evaluate if *Helicobacter pylori* infection has a possible etiological role in hyperemesis gravidarum.

## Methods

This study was a case control study which was conducted at the obstetrics and gynecology department, Al saidy hospitals Makka during the period from July 2017 to April 2019. The study was approved by the medical ethical committee and an informed verbal and written consent was obtained from all patients before inclusion.

The study included 120 pregnant women between 7- and 16-weeks gestational age with singleton pregnancy and presented with severe intractable vomiting more than 3 times per day and subjective weight loss as described by the patient and / or her relatives. The exclusion criteria were: 1) history of vomiting not related to pregnancy, 2) history of gastric troubles not related to pregnancy, 3) cases suspected to have acute condition which may be associated with vomiting e.g. appendicitis, intestinal obstruction, 4) multiple gestation, 5) associated disease e.g. hepatobiliary disorders, diabetes and 6) psychological disorders.

After consenting, patients underwent stool analysis for detecting *Helicobacter pylori* antigen in stool (specific test) and according to the test results they were included in either the study group which included 60 patients with positive *Helicobacter pylori* antigen or the control group which included 60 patients with negative *Helicobacter pylori* antigen.

Then all patients underwent full history taking, thorough clinical examination and an ultrasound assessment to confirm dating, viability and placental formation. Laboratory investigations included: 1) Urinary sample to test for ketonuria, proteinuria and urinary tract infection. 2) Blood sample for routine laboratory investigations including complete blood picture to see (hemoglobin levels, total leukocytic count, platelet count), blood creatinine, aspartate transaminase (AST), alanine transaminase (ALT) and electrolytes (Na and K).

## Sample size calculation

Sample size was calculated using G\* power program and a sample size of 120 patients in both groups will achieve 90% power with 95% confidence interval for frequency of *Helicobacter pylori* of 88% in pregnant patients with HG as previously reported [6].

## Statistical analysis

Data was collected throughout history, basic clinical examination, laboratory investigations and then it was coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean  $\pm$  SD, the following tests were used to test differences for significance; Differences between frequencies (qualitative variables) and percentages in groups were compared by Chi-square test. Differences between parametric quantitative independent groups by t test. P value was set at <0.05 for significant results & <0.001 for high significant result.

## Results

This study included 120 pregnant females between 7- and 16-weeks gestational age presented with hyperemesis gravidarum who were equally divided into two groups according to presence of *Helicobacter pylori* antigen in stool. The age of the included patients ranged between 20-35 years and there was no statistically significant difference between both groups. The body mass index in the study group ranged from 21 to 29.1 with a mean value of  $25.29 \pm 2.34$  and in the control group it ranged from 21.1 to 29.8 with a mean value of  $25.27 \pm 2.90$  which was not significant. Gestational age in study group ranged from 7 to 16 weeks with a mean value of  $12.33 \pm 4.32$  weeks while in the control group gestational age ranged from 7 to 15 weeks with a mean value of  $12.07 \pm 4.05$  weeks.

Thirty patients (50%) in the study group were rural residents compared to 24 patients (40%) in the control group and this difference was not significant ( $p > 0.05$ ). Table 1 shows comparison between the two studied groups regarding occupation and the difference between both groups was also not significant.

Routine laboratory investigations included hemoglobin levels, total leukocytic count, platelet count, blood creatinine, AST, ALT and serum electrolytes (Na and K) and the difference in these tests was not significant between the study and control groups.

Regarding urine analysis (Table 2), ketonuria was found in 22 (36.7%) patients in the study group compared to 8 (13.3%) patients in the control group which was significant ( $p = 0.037$ ). proteinuria was found in 34 (56.7%) patients in the study group versus 18

(30%) patients in the control group which was also significant ( $p = 0.037$ ). urinary tract infection was diagnosed in 26 (43.3%) patients in the study group compared to 8 (13.3%) patients among controls ( $p = 0.01$ ).

**Table 1:** Comparison between the study and control groups regarding occupation.

Occupation	Study group	Control group	X <sup>2</sup>	p value
Professional	8 (13.3%)	14 (23.3%)	4.532	0.476
Service	2 (3.3%)	2 (3.3%)		
Skilled worker	12 (20%)	2 (3.3%)		
Unskilled worker	10 (16.7%)	10 (16.7%)		
Retired	2 (3.3%)	2 (3.3%)		
No work	26 (43.3%)	30 (50%)		

**Table 2:** Comparison between the study and control groups regarding findings of urine analysis.

Urine analysis	Study group	Control group	X <sup>2</sup>	p value
Ketonuria	22 (36.7%)	8 (13.3%)	4.356	0.037
Protienuria	34 (56.7%)	18 (30%)	4.344	0.037
Urinary tract infection	26 (43.3%)	8 (13.3%)	6.648	0.01

## Discussion

It is well known that nausea and vomiting is associated with changes in endocrine levels following gestation, but the pathogenesis of hyperemesis gravidarum is still unclear. Different etiologic factors have been suggested for hyperemesis gravidarum, of which the most recent is the association with *Helicobacter pylori* infection [7]. It has been reported that *Helicobacter pylori* infection is associated with more cases of hyperemesis gravidarum in a dose response manner [8]. Jacobson, et al. also reported 5 cases of women with hyperemesis gravidarum who did not respond to standard treatment but were receptive to *Helicobacter pylori* treatment, which resulted in a complete relief of symptoms [9]. In the present study we aimed to evaluate the relationship between *Helicobacter pylori* infection and hyperemesis gravidarum.

This relation has been shown in many studies demonstrating the high prevalence of *Helicobacter pylori* infection among cases suffering from hyperemesis gravidarum. Mansour and Nashaat [6] reported *Helicobacter pylori* seropistivity in 88% of hyperemesis gravidarum patients. Elmahdy, et al. [10] reported that *Helicobacter pylori* seropostivity was 77.5% (31 of 40 patients) while *Helicobacter pylori* antigens in stool samples were positive in 75% (31 of 40 patients) among cases with hyperemesis gravidarum. Al Ghazali and Hussein [11] reported that *Helicobacter pylori* serum antibody test was positive in 38 out of 45 (84.44 %) patients with hyperemesis gravidarum. Alwahed, et al. [12] reported that sixty-nine (69%) women had *Helicobacter pylori* antigens in the stool. More recent studies reported a frequency of *Helicobacter pylori* infection in patients with hyperemesis gravidarum ranging between 88 and 92% [13-15].

In this study, we found that the frequency of ketonuria, proteinuria as well as urinary tract infection is significantly more

frequent among cases in the study group compared to the control group. In agreement with our study, it was previously reported that there were statistically significant differences between patients and control groups regarding ketonuria, protinuria and urinary tract infection in cases presenting with HG and h pylori infection compared to controls with no infection [16].

Our results show that more severe cases of hyperemesis gravidarum is related to *Helicobacter Pylori* infection. This is in agreement with previous studies which indicated that relation. In a previous study which investigated the association between *Helicobacter Pylori* infection and hyperemesis gravidarum, it was reported that there is a marked statistical difference between both groups in terms of *Helicobacter Pylori* seropositivity and the frequency of vomiting [16]. It was also reported that more cases of *Helicobacter Pylori* infection among the more severe cases of pregnancy vomiting although this correlation could not be detected in less severe cases of nausea and vomiting of pregnancy and the researchers concluded that *Helicobacter Pylori* probably potentiates the progression of mild nausea and vomiting to more severe one [17].

In disagreement with the present study, a previous study failed to show more *Helicobacter Pylori* sero-positive cases in the pregnant women with hyperemesis gravidarum than no hyperemesis gravidarum cases [18]. In another study, it was also reported that more seropositive cases for *Helicobacter pylori* were detected in hyperemesis gravidarum patients than in pregnant women without hyperemesis gravidarum, but the study could not show any correlation between *Helicobacter pylori* seropositivity and the duration of hyperemesis gravidarum or the time of its beginning. Therefore, the researchers concluded that *Helicobacter pylori* probably increases the severity of hyperemesis gravidarum

but is not a sole factor [19].

Based on our results, we recommend further studies to investigate the impact of *Helicobacter pylori* infection in triggering the onset of hyperemesis gravidarum and to assess whether pregnancy screening and eradication would reduce the incidence of hyperemesis gravidarum or moderate the severity of its clinical presentation

## Conclusion

*Helicobacter pylori* infection possibly contributes to the etiology of hyperemesis gravidarum. Also, the severity of the disease seems strongly related to *Helicobacter pylori* infection

## Acknowledgment

None.

## Conflict of Interest

Author declares no conflict of interest.

## Ethics Approval

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Ain Shams University.

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