

## Association of Helicobacter Pylori Seropositivity with Emesis and Hyperemesis Gravidarum: Comparative Cross Sectional Study

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**Received:**

**Accepted:**

### Abstract

**Background:** Hyperemesis gravidarum (HG) is characterized by persistent nausea and vomiting accompanied by ketosis and loss of weight. The Helicobacter pylori (H. pylori) are considered as an important cause of gastritis in human beings and as an essential factor in the pathogenesis of peptic ulcer. **This study aimed to** investigate the association of Helicobacter Pylori infection in pregnant women with Emesis and Hyperemesis Gravidarum. **Methods:** This comparative cross-sectional study included 90 pregnant women in the Obstetrics and Gynecology Department of Benha University Hospitals & Health Insurance Hospital. Patients were divided into three groups. Group A: included 30 pregnant women complicated with HG, Group B: included 30 pregnant women complicated with emesis gravidarum and Group C: included 30 healthy pregnant women having neither emesis nor hyperemesis gravidarum of matched age as control group. All studied cases were subjected to general examination, complete physical and cardiac, abdominal examination, trans-abdominal or Transvaginal pelvic ultrasound and routine laboratory investigations. **Results:** The incidence of H. pylori was significantly higher in group A and B compared to group C (P=0.016). IgG antibody titer was significantly higher among group A and B compared to group C (P=0.001). **Conclusion** Our results suggest that there was a strong association between H pylori and hyperemesis gravidarum, allowing us to conclude that when a pregnant patient is complaining of hyperemesis gravidarum, we should do a test for H pylori seropositivity.

**Keywords:** Helicobacter pylori; Seropositivity; Emesis; Hyperemesis Gravidarum

## Introduction

Nausea and vomiting during pregnancy, which is also known as 'Emesis gravidarum', affects between 50–80% of all pregnancies in the first trimester. It is a common symptom experienced up to approximately 16 weeks without having any adverse effects on growing fetus as well as mother (1). However, in few women, it is severe and causes deleterious effects on maternal health and incapacitates her day-to-day activities. This severe nausea and vomiting are considered pathological and known as hyperemesis gravidarum. It occurs in 0.3-2% of pregnancies, and it is unresponsive to simple dietary modification and anti-emetics (2).

Hyperemesis gravidarum (HG) is characterized by persistent nausea and vomiting accompanied by ketosis and loss of weight (>5% of the weight before pregnancy). It may cause hypovolemia, electrolytes disturbance and acid-base imbalance, nutritional deficiencies, and even, in severe cases, death. Severe cases with hyperemesis require hospitalization in 0.3-2% of pregnancies. It is the most common cause of hospitalization in the first half of pregnancy and second only after preterm labor for pregnancy overall (3). It can be associated with serious maternal morbidity such as Wernicke's encephalopathy and fetal morbidity such as intrauterine growth retardation, and in severe cases maternal and fetal death may happen (4).

The exact etiology of hyperemesis gravidarum is not well-known and is probably multifactorial in which psychological factors, disturbance of gastrointestinal motility, hormonal changes, infections, immunological, metabolic and anatomical factors appear to intervene (5).

*Helicobacter pylori* (*H. pylori*), which is also named *Campylobacter pylori*, is a gram-negative, microaerophilic bacterium found in the stomach, and may be in other parts of the body, such as the eye. *H. pylori* are considered as an important cause of gastritis in human beings and as an essential factor in the pathogenesis of peptic ulcer (4).

It was proposed that HG may be triggered due to chronic infection with *Helicobacter pylori*. On the other hand, some researchers failed to assign a relation between the onset and the chronicity of the infection and the occurrence and the severity of HG (6)

The aim of this work was to assess association of *Helicobacter Pylori* infection in pregnant women with Emesis and Hyperemesis Gravidarum.

## Patients and methods

This comparative cross-sectional study included 90 pregnant women in the Obstetrics and Gynecology Department of Benha University Hospitals & Health Insurance Hospital during the period from February 2023 till February 2024.

An informed written consent was obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University (MS 34-2-2023).

**Inclusion criteria** were age (18 – 40) years old, gestational age less than 16 weeks confirmed by US, diagnosis of HG according to her foundation (hyperemesis education & research foundation) was based on: excessive pregnancy-related nausea and/or vomiting that prevents adequate intake of food and fluid, measuring weight loss (>5% of pre-pregnancy weight), signs of dehydration (feeling thirsty, tired, dizzy or lightheaded, not peeing very much and having dark yellow and stony smelling pee, dry mouth, lips, and eyes), ketonuria (+1 or more) and hemoconcentration: hematocrit value was more than 48%.

**Exclusion criteria** were multiple gestation pregnancy, hydatidiform molar pregnancy, patients refused to participate in the study, hepatobiliary disorders and peptic ulcers or any intestinal disease, patient with thyroid diseases and patient with psychological disorders.

**Grouping:** all patients were divided into three groups: Group A: included 30 pregnant women complicated with HG, Group B: included 30 pregnant women complicated with emesis gravidarum and Group c: included 30 healthy pregnant

women having neither emesis nor hyperemesis gravidarum of matched age as control group.

**All comparative cross sectional study cases were subjected to the following:**

**Detailed history taking, including:** (personal history: maternal age, weight, height, special habits as smoking, obstetric history: gravidity, parity, accidental hemorrhage. any associated complication during pregnancy, menstrual history: first day of last menstrual period, family history and past medical history and drug taking].

**General examination including** examination of vital signs as:- blood pressure, temperature, heart rate and respiratory rate, oxygen saturations, **Signs of Pallor, Cyanosis, Jaundice and Lymph node enlargement, Complete physical and cardiac examination**

including weight, signs of dehydration Signs of muscle wasting. **Abdominal examination:** The abdomen is characteristically lax with no tenderness rigidity or rebound tenderness. **Trans-abdominal or Transvaginal pelvic ultrasound:**

An ultrasound examination was performed to assess fetal viability and confirm the gestational age, biometry and amniotic fluid and exclude gestational trophoblastic diseases and multiple gestations. **Routine laboratory investigations including** [complete blood count: (RBCs, WBCs, platelet count, Hb%, hemoglobin concentration), complete urine analysis: for protein, ketone bodies, bile salts, and sample sent for culture to exclude urinary tract infection which might be the cause of the

vomiting, serum electrolytes (sodium, potassium) for detection of electrolyte disturbance, renal function tests (serum creatinine, creatinine clearance), liver function tests: (SGOT and SGPT), thyroid function tests: (TSH, free T3, free T4), fasting and 2 hours post prandial sugar].

Under completely aseptic precaution & with informed written consent 3ml venous blood sample was collected to test the serum for Helicobacter pylori IgG seropositivity by Enzyme Linked Immunoassay (ELISA).

#### **Outcome measures:**

Prevalence of Helicobacter pylori IgG-Seropositivity level among cases and control groups and Classification of the severity of cases according to Helicobacter pylori IgG seropositivity

#### **Sample size:**

This study is based on a study carried out by Shaban, et al (7), Epi Info STATCALC we calculated the sample size by considering the following assumptions: - 95% two-sided confidence level, with a power of 80%. & error of 5% odds ratio calculated= 1.115. The final maximum sample size taken from the Epi- Info output was 82. The expected drop-out incidence will be 10%; thus, the sample size was increased to 90 subjects to assume any drop out cases during follow-up.

#### **Statistical analysis:**

The collected data were organized, tabulated and statistically analyzed using statistical package social sciences (SPSS) version 21 (SPSS Inc, Chicago, USA). For qualitative data, frequency and percentage distributions were calculated. For quantitative data, mean, standard deviation (SD), minimum and maximum were calculated. For comparison between groups, the independent samples (t) test was used. For all tests p value <0.05 were considered significant. For all tests p value >0.05 were considered insignificant.

#### **Results**

There is no significant difference between the groups regarding age, BMI and parity. **Table 1**

There is no significant difference between the three studied groups regarding studied CBC parameters and kidney and liver parameters. **Table 2**

The incidence of H. pylori was significantly higher in group A and B compared to group C (P=0.016). IgG antibody titer was significantly higher among group A and B compared to group C (P=0.001). **Table 3**

There is no significant difference between the groups regarding neonatal outcome. **Table 4**

**Table 1:** Demographic characteristics and parity distribution among the three studied groups

	<b>Group A (n=30)</b>	<b>Group B (n=30)</b>	<b>Group C (n=30)</b>	<b>F/ <math>\chi^2</math></b>	<b>p</b>
<b>Age (years)</b> Mean $\pm$ SD	28.33 $\pm$ 4.28	29.15 $\pm$ 5.29	27.49 $\pm$ 4.54	.927	.399
<b>BMI (kg/m<sup>2</sup>)</b> Mean $\pm$ SD	27.14 $\pm$ 3.1	27.23 $\pm$ 2.43	26.53 $\pm$ 2.61	.585	.559
<b>Parity</b>					
<b>Primi</b>	11 (36.7%)	12 (40%)	9 (30%)	0.679	.712
<b>Multi</b>	19 (63.3%)	18 (60%)	21 (70%)		

BMI: body mass index.

**Table 2:** Laboratory investigations of the studied groups

	<b>Group A (n=30)</b>	<b>Group B (n=30)</b>	<b>Group C (n=30)</b>	<b>F/ <math>\chi^2</math></b>	<b>p</b>
<b>Hb (g/dL)</b> Mean $\pm$ SD	11.49 $\pm$ 1.21	11.05 $\pm$ 1.73	11.68 $\pm$ 1.17	1.61	.205
<b>TLC (x 10<sup>3</sup>/L)</b> Mean $\pm$ SD	8.15 $\pm$ 2.32	8.23 $\pm$ 2.29	8.41 $\pm$ 2.53	.094	.911
<b>PLT (x 10<sup>3</sup>/L)</b> Mean $\pm$ SD	287.54 $\pm$ 50.76	282.17 $\pm$ 61.22	292.31 $\pm$ 45.14	.277	.759
<b>ALT (U/L)</b> Mean $\pm$ SD	30.22 $\pm$ 9.34	28.25 $\pm$ 9.11	26.31 $\pm$ 7.76	1.49	.231
<b>AST (U/L)</b> Mean $\pm$ SD	27.37 $\pm$ 7.85	28.53 $\pm$ 7.41	25.47 $\pm$ 8.33	1.16	.320
<b>RBS (mg/dl)</b> Mean $\pm$ SD	129.75 $\pm$ 22.41	131.96 $\pm$ 26.75	128.63 $\pm$ 24.88	.141	.869
<b>Creatinine (mg/dl)</b> Median (Range)	0.77 (0.7 - 1.2)	0.79 (0.7 - 1.2)	0.78 (0.7 - 1.1)	.137	.641
<b>Urea (mg/dL)</b> Mean $\pm$ SD	13.25 $\pm$ 3.83	14.38 $\pm$ 3.71	12.47 $\pm$ 3.6	2.01	.141
<b>INR</b> Mean $\pm$ SD	1.03 $\pm$ 0.076	1.03 $\pm$ 0.041	1.05 $\pm$ 0.085	.817	.445

Hb: hemoglobin, TLC: total leucocyte count PLT: platelets, ALT: alanine aminotransferase, AST: aspartate aminotransferase, RBS: random blood sugar, INR: international normalized ratio.

**Table 3:** Incidence of H. Pylori and H. pylori antibody titer distribution between the three studied groups

	<b>Group A (n=30)</b>	<b>Group B (n=30)</b>	<b>Group C (n=30)</b>	<b><math>\chi^2</math>/F</b>	<b>P</b>
<b>Positive</b>	21 (70%)	20 (66.7%)	11 (36.7%)	8.29	<b>.016</b>
<b>Negative</b>	9 (30%)	10 (33.3%)	19 (63.3%)		
<b>IgG antibody titer (U/ml)</b> Mean $\pm$ SD	45.97 $\pm$ 25.31	45.23 $\pm$ 22.91	24.18 $\pm$ 16.54	<b>9.8</b>	<b>.001</b>

**Table 4:** Neonatal outcomes between the three studied groups

	Group A (n=30)	Group B (n=30)	Group C (n=30)	F/ $\chi^2$	p
<b>GA (weeks)</b> Mean $\pm$ SD	38.44 $\pm$ 0.927	38.58 $\pm$ 0.726	38.67 $\pm$ 0.629	.678	.510
<b>Birth weight (kg)</b> Mean $\pm$ SD	2.84 $\pm$ 0.435	2.92 $\pm$ 0.411	3.02 $\pm$ 0.314	1.6	.207
<b>Apgar at 1 min</b> Mean $\pm$ SD	7.03 $\pm$ 0.865	7.05 $\pm$ 0.805	7.11 $\pm$ 0.964	.067	.935
<b>GA (weeks)</b> Mean $\pm$ SD	38.44 $\pm$ 0.927	38.58 $\pm$ 0.726	38.67 $\pm$ 0.629	.678	.510

GA: gestational age

## Discussion

In the current study, there was no significant difference regarding age, BMI parity between three groups ( $P > 0.05$ ). In group A mean age was  $28.33 \pm 4.28$  years, mean BMI was  $27.14 \pm 3.1$  kg/m<sup>2</sup> and the mean of parity was 11 (36.7%), in group B mean age was  $29.15 \pm 5.29$  years, mean BMI was  $27.23 \pm 2.43$  kg/m<sup>2</sup> and the mean of parity was 12 (40%). While, in group C mean age was  $27.49 \pm 4.54$  years, mean BMI was  $26.53 \pm 2.61$  kg/m<sup>2</sup> and the mean of parity was 9 (30%).

In agreement with our study, it was reported that there was no significant difference in age and BMI between cases and control group (5). In another study done by a group of researchers (8), no statistical differences were determined among the groups in terms of age, BMI and parity. The mean BMI value of the pregnant women participating in the study was measured as 24.1 kg/m<sup>2</sup>. Having had a look at the BMI values of each group, it was calculated as 24.5

kg/m<sup>2</sup> in the mild symptomatic group, as 24.8 kg/m<sup>2</sup> in the moderate symptomatic group and as 22.4 kg/m<sup>2</sup> in the severe symptomatic group. There was no

statistical difference between the groups. When the parity conditions of the pregnant women were investigated, the average parity was measured as 0.85 in the mild symptomatic group, 0.98 in the moderate symptomatic group and 0.82 in the severe symptomatic group. No statistical difference was found among the groups with these values.

Our results showed that there were no significant differences between the three studied groups regarding studied CBC parameters (Hb, TLC and PLT) p-values were 0.205, 0.911 and 0.759 respectively.

In the same line it was noted that there were no statistical differences determined among the groups in terms of complete blood count, blood biochemistry (8).

In a case-control study done in 2014 it was found that anemia had a much higher prevalence in women with HG and HpSA than in those without HpSA or those in the control group (9).

Regarding the studied kidney and liver parameters (ALT, AST, RBS, Creatinine, Urea and INR) there were no significant difference between the three studied groups ( $P > 0.05$ ).

In another study it was reported that, there were significant elevations in ALT and AST activities in cases compared to those in controls ( $33.15 \pm 7.70$  and  $31.63 \pm 6.44$  U/l vs.  $19.30 \pm 6.64$  and  $18.70 \pm 7.47$  U/l,  $P = 0.001$ ). In contrast, urea and creatinine concentrations showed significantly decreased activities in cases compared to those in controls ( $17.30 \pm 6.17$  and  $0.65 \pm 0.16$  mg/dl vs.  $19.93 \pm 5.63$  and  $0.72 \pm 0.14$  mg/dl,  $P < 0.05$ ). (4)

The present findings observed that, incidence of *H. pylori* was significantly higher in group A and B compared to group C ( $p = 0.016$ ). Also, IgG antibody titers were significantly higher among group A ( $45.97 \pm 25.31$ ) and B ( $45.23 \pm 22.91$ ) compared to group C ( $24.18 \pm 16.54$ ) ( $p$ -value= 0.001).

Along with our results, a study reported that, serologically positive *H. pylori* infection was detected in 19 out of 40 pregnant women with HG (47.5%) whereas in control group, only 8 out of 42 asymptomatic pregnant women were found to have positive antibody titers

against *H. pylori*. The ratio of HP positivity in pregnant women with HG was significantly higher than asymptomatic control group ( $P=0.006$ ) (10).

On contrary, some studies showed no significant association between *Helicobacter pylori* infection and emesis gravidarum. This may be because these studies have small sample sizes, which may also have precluded discovery of an association. Another limitation is that the study relies on patient recall of symptoms during pregnancy, which may cause self-reporting bias (11).

In the current study, there were no significant differences between the studied groups regarding neonatal outcome (GA, Birth weight, Apgar at 1 min and Apgar at 5 min;  $p$ -values  $> 0.05$ ).

In agreement with our findings the results gained from a study done previously (7), proved that the mean gestational age in hyperemesis gravidarum cases (group A) was 8.4 6 1.06 weeks (range: 5–12) and that in the control group was 8.64 6 1.34 weeks (range: 5–11), with no statistically significant difference ( $P$  value 0.33).

On the other hand, it was noted that, mean gestational age of Group-A (cases) was 10.90 ( $\pm 2.58$ ) and Group-B (control) was 12.67 ( $\pm 3.00$ ) and there was statistically significant difference between two groups ( $p$  values 0.006) (10).

## Conclusion

Our results suggest that there was a strong association between H pylori and hyperemesis gravidarum, allowing us to conclude that when a pregnant patient is complaining of hyperemesis gravidarum, we should do a test for H pylori seropositivity. However, these findings require confirmation by larger, more-powered study with larger sample size.

## References

1. Singh D, Asokan V, Bhat Nv G, Jain P, HI K. Effects of Bilwa-Lajadi syrup in emesis gravidarum - an exploratory single arm open labeled trial. *J Ayurveda Integr Med.* 2022;13:100522.
2. Math SG, Jana P. A Case Study on Ayurvedic management of Garbhini Chardi wsr to Hyperemesis gravidarum. *J Ayurveda Integr Med Sci.* 2019;4:105-8.
3. Ahmed A. Fetomaternal Acid-Base Balance and Electrolytes during Pregnancy. *Indian J Crit Care Med.* 2021;25:S193-s9.
4. Hussein KS. Hyperemesis Gravidarum in First-Trimester Pregnant Saudi Women: Is Helicobacter pylori a Risk Factor? *Front Physiol.* 2020;11:575.
5. Elshazly OG. The association between Helicobacter pylori infection and hyperemesis gravidarum. *Al-Azhar Intern Med J.* 2020;1:32-6.
6. Saxena K, Chauhan N, Jain U. Advances in diagnosis of Helicobacter pylori through biosensors: Point of care devices. *Anal Biochem.* 2021;630:114325.
7. Shaban MM, Kandil HO, Elshafei AH. Helicobacter pylori seropositivity in patients with hyperemesis gravidarum. *Am J Med Sci.* 2014;347:101-5.
8. Güngören A, Bayramoğlu N, Duran N, Kurul M. Association of Helicobacter pylori positivity with the symptoms in patients with hyperemesis gravidarum. *Arch Gynecol Obstet.* 2013;288:1279-83.
9. Abd Alwahed A, Elsaadany H, Radwan A, Noureldin M, Kumar R. Role of helicobacter pylori eradication in the management of hyperemesis Gravidarum. *J Obstet Gynaecol Res.* 2014;7:6-13.
10. Yasmin N, Begum K, Saha SK, Naher K, Ghosh DK, Nandi ER, et al. Association between helicobacter pylori and hyperemesis gravidarum. *J Shaheed Suhrawardy Med Coll.* 2016;8:13-6.
11. Golberg D, Szilagyi A, Graves L. Hyperemesis gravidarum and Helicobacter pylori infection: a systematic review. *Obstet Gynecol.* 2007;110:695-703.

**To cite this article:** Ahmed W. Morad, Ahmed S. Abd El Azim, Mohamed A. El Gazzar, Ghada Y. Ghaly. Association of Helicobacter Pylori Seropositivity with Emesis and Hyperemesis Gravidarum: Comparative Cross Sectional Study. *BMFJ XXX*, DOI: 10.21608/bmfj.2025.306939.2148