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Original Article

Helicobacter Pylori Screening in pregnant women with and without Hyperemesis Gravidarum

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Abstract

Aim: to evaluate the prevalence of H. pylori infection among pregnant women with HG in comparison to pregnant women without HG.

Methods: A cross-sectional trial was carried out on 113 pregnant women (<16 weeks) that were divided into a positive HG group (n=63) and a negative HG group (n=50). Fresh stool samples were in airtight containers until the stool antigen tests were done on all patients.

Results: Age was significantly lower in the positive HG group than the negative HG group (P<0.05). Gestational age and crown-rump length were significantly lower in the positive HG group than the negative HG group (P<0.05). The number of vomits was significantly higher in the positive HG group than the negative HG group (P<0.00001). Complete blood count, direct bilirubin, indirect bilirubin, and total bilirubin were significantly higher in the positive HG group than in the negative HG group (P<0.001). Potassium (K^+) and sodium (Na^+) were significantly lower in the positive HG group than in the negative HG group (P<0.001). Ketonuria was significantly higher in the positive HG group than the negative HG group (P<0.001) and finally, H pylori testing was not significantly different in both studied groups (P=0.560).

Conclusions: The present study demonstrated that the occurrence of H. pylori infection was comparable in pregnant women with and without hyperemesis gravidarum (HG). Additionally, HG was linked to several physiological and biochemical alterations, such as elevated hematological parameters (hemoglobin, hematocrit, and platelets), bilirubin levels, electrolyte imbalances (K+, Na+), and the presence of ketonuria.

Trial registration: The study was registered prospectively on ClinicalTrials.gov with trial registration number (NCT05835076).

Keywords: Antigen Test, Early Pregnancy, Helicobacter Pylori, Hyperemesis Gravidarum, Stool Analysis.

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Background:

Hyperemesis gravidarum (HG) is an extreme form of pregnancy-related vomiting and nausea, which often necessitates hospitalization and medical attention to prevent potentially fatal complications, such as losing weight, nutritional deficiencies, as well as metabolic disturbances like acidosis from hypokalemia, starvation, and transient hepatic dysfunction. [1]

Although HG is a complex condition that complicates 0.3–3.6% of pregnancies, little is known about its origin. However, a number of mechanisms, including immunologic factors, endocrine hormones like progesterone, estradiol, and human chorionic gonadotropin (HCG), and personal issues like increasing weight, which is suggested as a potential underpinning reason and may contribute to this disorder. [2]

Helicobacter pylori (H. pylori) is known as one of the significant etiological agents of gastritis in humans and a crucial contributor to the pathophysiology of peptic ulcers, gastric lymphoma, and cancer. [3]

In underdeveloped nations, 70%- 90% of the residents are contaminated with bacteria, whereas in developed nations, the frequency is lower, ranging from 25% to 50%. [4] Gram-negative spiral bacterium H. pylori colonizes the stomach and lays the groundwork for the pathophysiology of gastric diseases, such as mucosa-associated lymphoid tissue lymphoma, duodenal and gastric ulcers, gastric adenocarcinoma, and chronic gastritis. [5-7]

The serological diagnosis of H. pylori infection is possible through testing patients' sera for having antibodies of anti–H pylori IgG. These tests cannot differentiate between ongoing infection and prior experience of H. pylori. Various commercial diagnostic kits have differing degrees of accuracy, ranging from 68% to 82%. [5]

The stool antigen test is an enzyme immunoassay that identifies the active H. pylori antigen in human feces. Stool tests may be advised for preliminary diagnosis in sick cases, exhibiting an initial sensitivity and specificity ranging from 63% to 100%. [6]

Concerning the detection methods utilized for pregnant mothers, serum and fecal samples were obtained with HG to examine specific antibodies for Helicobacter pylori (immunoglobulin IgG, IgA) and stool antigens. The stool antigen test indicated a significant relationship between HG and H. pylori infection, whereas serological evaluation did not demonstrate this correlation (40% vs 12.4%, $P < 0.001$). Therefore, there was no correlation between the symptoms of H. pylori and HG positivity using the H. pylori IgG/IgM antibody test . [7]

This research was conducted to evaluate the prevalence of H. pylori infection among pregnant women with HG in comparison to pregnant women without HG.

Materials and Methods:

Study population and eligibility criteria

This cross-sectional trial included 113 pregnant women, 18-40 years in age, gestational age <16 weeks, where 63 cases of them were suffering from HG and the remaining 50 cases were not suffering from HG. All patients were presented to the Emergency Unit, Department of Obstetrics and Gynecology, Sohag University Hospital (an Egyptian tertiary referral hospital) between April 1st 2023 and April 30th 2024. Furthermore, all patients with gastrointestinal disorders, renal and hepatic disorders, surgical disorders, gestational trophoblastic diseases and psychological disorders, and pregnant women (>16wks) were not included.

Ethical considerations

This research received the approval of the Ethical Committee, Faculty of Medicine, Sohag University (Soh-Med-23-04-03MS). The research was registered with clinicaltrials.gov (NCT05835076).

The accompanying doctor elucidated the study's nature, and all participating cases were requested to provide informed consent.

All patients were subjected to full history, clinical examinations, transvaginal or transabdominal pelvic ultrasonography, laboratory analysis [complete blood count (CBC), complete urine analysis, serum electrolytes, and tests of renal and liver functions], as well as certain laboratory tests [stool antigen test by using H. pylori antigen enzyme-linked immunosorbent assay (ELISA) quantitative test kit]. The participants supplied fresh stool samples in sealed containers until the stool antigen assays were conducted.

Principle of the test:
The H. pylori Antigen ELISA test kit is an immunoassay of the solid phase enzymes designed to detect H. pylori antigen in human stool both qualitatively and quantitatively. It is based on the sandwich principle. Anti-H. pylori antibodies are deposited onto the microwell plate. To conduct the test, the antigens were removed from the specimen using an extraction solution; then, they were combined with enzyme-conjugated H. pylori antibodies on a microwell plate covered with antibodies. After that, the plate was incubated. If there were H. pylori antigens within the specimens, attachment to the conjugate and fixation to the coated antibodies on the microwell plate would occur, which led to immobilized antibody-H. pylori antigen-conjugate complexes. The complexes did not form specimens lacking H. pylori antigens. The microwell plate was cleaned to get rid of any loose components after the first implantation. After adding substrates A and B, the specimens were incubated to create a blue color that indicated the concentration of H. pylori antigens. To inhibit the reaction that was causing the microwell plate's color to change from blue to yellow, sulfuric acid solution was applied. A microplate reader was used to measure the intensity of colors related to the quantity of H. pylori antigens in the specimen at 450/630-700 nm or 450 nm.

Specimen collection:
This H. pylori antigen ELISA Test was conducted exclusively on human stool samples that were gathered in clean containers, and patients were required to collect the specimens, taking into consideration to avoid any potential contact with water or urine. Patients were instructed to avoid antibiotics and anti-bacterial treatments that are known to affect H. pylori, which might lead to false interpretations. Samples were kept in the refrigerator at (2-8 °C) from one to two days before assessment. To store the specimens longer, they were stored frozen at -20ºC. At that time, samples were completely thawed and equilibrated to room temperature prior to conducting the test.

Test procedure: To create the functioning wash buffer, fill the wash buffer bottle included in the kit with deionized or distilled water until it holds one liter. At 15–30°C, the working wash buffer remained steady for two weeks. One mL of the extracted solutions was distributed into the extraction tube of the specimen. Regarding the solid stool specimen, the cap of the extraction tube was taken to get about 30 mg of the specimen (about 1/4 of a pea), and a specimen collecting stick was stabbed into the stool specimen at least three times at random. Scooping the stool sample was avoided. The specimen extraction tube was transferred. On the contrary, regarding liquid stool specimens, a liquid specimen dropper was held in a vertical position. After that, 2 drops (approximately 50 µL) were dispensed and aspirated into the tube of the extraction solution. They were screwed on, and the cap was closed tightly. A specimen extraction tube was forcefully quaked to blend the specimen, and the extraction solution, A1, was left as a blank well. Moreover, 50 µL of calibrator 1 was dispensed in B1 and C1 wells (yellow reagent). An equal amount was allotted in D1 and E1 wells (blue reagent). Moreover, 50 µL of calibrator 3 was distributed in F1 and G1 wells (blue reagent), and an equal amount was distributed in H1 and A2 wells (blue reagent). The specimen extraction tube was grasped upright, and the tip was detached. The designated wells were filled beginning at B2 with two drops of the specimen extraction solution (about 50 µL). The yellow reagent was flipped. 50 µL of conjugate was dispensed to each well, excluding the blank well. (red reagent) and was mixed slightly through the swirl of the microwell plate on a flat bench for 30 s. After that, the microwell plate was covered with a sealer and incubated at (15-30°C) in an incubator, water bath, or room for 60 m. ± 5 m. Then, the sealer was detached. Each well was washed five times with 350 µL of working wash buffer per well, and then the liquid was removed. The microwell plate upside was turned down on absorbent tissue for seconds. 50 µL of substrate A was dispensed in each well (clear reagent). A similar amount of B was dispensed in each well (clear reagent). After that, a blue color developed in those wells with the positive specimens mixed gently. Besides, the microwell plate was covered with a sealer and incubated at (15-30°C) in an incubator, water bath, or room for 10 m ± 1 m. The sealer was removed.

Additionally, 50 µL of stop solution was dispensed in each well. (clear reagent). Then, a yellow color developed in those wells with positive specimens and was read at 450/630-700 nm within 30 minutes.

Data processing:

The microplate reader was set, and the absorbance of each well was read using a dual wavelength of 450nm/630nm. A four-parameter fitting method was used, and a standard curve and calculation of the H.P antigen content of the sample were established. The blank absorbance was subtracted from the mean absorbance of each calibrator. After that, it was plotted on the Y-axis against the Log10 of the corresponding concentration in µg/mL on the X-axis on a linear graph paper. Finally, the calibration curve was drawn.

Statistical analysis:

Statistical analysis was conducted using SPSS version 26 (IBM Inc., Chicago, Illinois, USA). Quantitative data were expressed in the form of mean and standard deviation (SD) with comparisons between both groups using an unpaired Student's t-test. Moreover, the qualitative variables were expressed in the form of percentage (%) and frequency and evaluated using the Chi-square or Fisher's exact tests, as applicable. A two-tailed P <0.05 was deemed to have statistical significance.

Results:

Age exhibited less significant values in the positive hyperemesis (HG) group than in the negative HG group (P<0.05). Residence showed no significant differences between both groups. Table 1

Table 1: Demographic data of the participants

		Positive HG group (n=63)	Negative HG group (n=50)	P value
Age (years)	Mean ± SD	25.87 ± 4.11	28.12 ± 4.11	0.005*
	Range	18 - 36	19 - 37	
Residence	Sohag district	46 (73%)	24 (48%)	
	Tema	2 (3.17%)	5 (10%)	0.101
	Tahta	2 (3.17%)	5 (10%)	
	Gerga	7 (11.11%)	7 (14%)	
	Akhmim	3 (4.76%)	4 (8%)	
	Elmonshaa	1 (1.59%)	0 (0%)	
	Gehena	0 (0%)	2 (4%)	
	Elbalyana	1 (1.59%)	3 (6%)	
	Sagulta	1 (1.59%)	0 (0%)	

Mean ± SD or frequency (%) were used to represent data.

* Significant P value < 0.05. HG: Hyperemesis gravidarum.

The gestational age (GA) and crown rump length (CRL) showed less significant values in the positive HG group than in the negative HG group (P<0.05). The number of feti exhibited no significant
difference between the groups. The number of vomits illustrated higher significant values in the positive HG group than in the negative HG group (P<0.05). (**Table 2)**

Table 2: Number of feti, GA, CRL, number of vomits and signs of dehydration of the studied women

	Positive HG group (n=63)	Negative HG group (n=50)	P value
Number of feti	1.19±0.59	1.06±0.24	0.146
GA (weeks)	9.97±2.42	11.94±2.84	<0.001*
CRL (weeks)	10.4±4.07	11.94±2.84	0.025*
Number of vomit (times)	14.27±1.35	0.32±0.47	<0.00001*

Mean ± SD or frequency (%) were used to represent data.
* Significant P value < 0.05. GA: Gestational age
CRL: Crown-rump length, HG: Hyperemesis gravidarum.

CBC, D.bilirubin, Ind.bilirubin, and T.bilirubin exhibited more significant results in the positive HG group than in the negative HG group (P<0.001).
ALT, AST, and S.creatinine illustrated the lack of a significant difference between the groups. (**Table 3)**

Table 3: CBC, liver, and kidney function tests of the studied women

		Positive HG group (n=63)	Negative HG group (n=50)	P
CBC	HB (g/dl)	12.07±1.08	10.9±0.91	<0.001*
	HCT (%)	35.44±2.59	33.72±2.53	<0.001*
	PLT (×109/L)	263.02±72.34	203.28±29.16	<0.001*
Liver Function test	ALT (U/L)	29.43±29.6	28.94±10.08	0.911
	AST (U/L)	27.68±16.02	28.2±10.19	0.843
	D.bilirubin	0.48±0.21	0.37±0.09	<0.001*
	Ind.bilirubin	0.39±0.24	0.29±0.09	0.007*
	T.bilirubin	0.87±0.41	0.66±0.13	<0.001*
Kidney function test	S.creatinine	0.53 ± 0.13	0.56 ± 0.1	0.190

Mean ± SD or frequency (%) were used to represent data. * Significant P value < 0.05. HG: Hyperemesis gravidarum, CBC: Complete blood count, HB: Hemoglobin, HCT: Hematocrit, PLT: Platelet, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, D.bilirubin: Direct bilirubin, Ind.bilirubin: Indirect bilirubin, T.bilirubin: Total bilirubin, S.creatinine: Serum creatinine.

The serum electrolytes K+ and Na+ exhibited less significant values in the positive HG group than in the negative HG group (P<0.001). Ketonuria exhibited better results in the positive HG group
than in the negative HG group (P<0.001). Serum Ca+ and H. pylori testing illustrated the lack of significant differences between both groups (P= 0.560). (**Table 4)**

Table 4: Minerals, urine analysis, and H.pylori test of the studied women

			Positive HG group (n=63)	Negative HG group (n=50)	P value
Minerals	Ca+ (mmol/L)		1.05±0.1	1.03±0.11	0.508
	K+ (mmol/L)		2.9±0.27	3.93±0.26	<0.001*
	Na+ (mmol/L)		142.51±10.78	151.22±6.51	<0.001*
Urine analysis	Ketonuria	0	0(0.0%)	50(100.0%)	<0.001*
		+1	7(11.11%)	0(0.0%)	
		+2	30(47.62%)	0(0.0%)	
		+3	24(38.1%)	0(0.0%)	
		+4	2(3.17%)	0(0.0%)	
H. Pylori test	Positive		46(73.02%)	34(68.0%)	0.560
	Negative		17(26.98%)	16(32.0%)	

Mean ± SD or frequency (%) were used to represent data.
* Significant P value < 0.05. HG: Hyperemesis gravidarum, K+: Potassium, Na+: Sodium, Ca+: Calcium.

Discussion:

The current research adopted this design as the most appropriate to answer the question of the relationship between H. pylori infection and HG patients.

Nausea and vomiting of pregnancy (NVP), called "morning sickness," has effects on about 70%- 80% of pregnancies during the earliest three months . [8,9]

In the present study, parity was insignificantly different between both groups. In agreement with our results, Albeltagy et al. [10] found that the parity and age were insignificantly different between both groups. Consistently, Albeltagy et al. [10] reported that the comparison between the HG and control groups concerning maternal age illustrated the lack of significant differences between them. In contrast, Wu, Tseng et al. [11] reported that women experiencing regular vomits in the early three months of pregnancy and testing positive for H. pylori were substantially older than those testing negative for H. pylori.

In our study, the number of feti exhibited the lack of significant differences between the groups. GA and CRL illustrated that the low significant results in the positive HG group than the negative HG group (P value <0.05).

According to our results, the number of vomits exhibited high significant values in the positive HG groups when compared to the negative HG group (P value <0.00001). In agreement with our results, Elshazly. [12] found that group A had a highly significant increase in H.pylori IgG titer compared to group B. Also, Karadeniz, Ozdegirmenci, et al. [13] reported that the average value of H.pylori IgG antibody titer in the emesis group scored 73.8, unlike in the control group, which scored 25.8 (p<0.01). Moreover, Tamamy, Rahman, et al. [14] reported that the average IgG antibody titer in the emesis group scored 25 in comparison with10.5 in the control group (P < 0.05).

In this study, HB, HCT, and PLT exhibited more significant values in the positive HG group than in the negative HG group (P value <0.001). This finding is in accordance with Ahmed, Ali et al. [15] reported that low hemoglobin increased the risk of H. Pylori. In contrary, Doğan, Erkan et al. [16] reported no significant differences in the HB and HCT between positive and negative H. Pylori groups.

In the current study, D.bilirubin, Ind.bilirubin, and T.bilirubin exhibited more significant values in the positive HG group than in the negative HG group (P value <0.001). ALT, AST, and S.creatinine showed no significant differences between both groups. In agreement with our evidence, Ahmed, Ali et al. [15] found that there was no significant difference in the levels of serum creatinine, serum albumin, or liver enzymes between positive and negative H. pylori groups. Some studies found statistically significant correlations between H. Pylori and elevated liver enzymes, [17] and eradication resulted in drop of liver enzymes . [18]

In this study, K+ and Na+ showed less significant values in the positive HG group than in the negative HG group (P value <0.001). Ketonuria showed better significant values in the positive HG group than in the negative HG group (P value <0.001). Ca+ illustrated the lack of a significant difference between both groups(P=0.508).

Consistent with this study's results, Albeltagy, et al. [10] showed that the HG group exhibited reduced serum sodium and potassium levels (2.92±0.36 and 131.12±2.3) in comparison with the control group (4.22±0.43 and 141.48±3.12), respectively. In contrast to our results, Ahmed, Ali et al. [15] demonstrated the lack of significant differences in electrolytes (Na, K, Ca).

In our study, H.pylori test was insignificantly different between both groups. In this regard, Albeltagy et al. [10] identified positive serum IgG concentrations in 44 out of 50 HG cases (88%) and such difference could be explained by the differences in the study eligibility criteria and also the technique of diagnosis of H pylori infection.

A limitation of the research is the short follow-up. Therefore, we recommend a longer follow-up time to understand the incidence and the risk factors for this condition. Moreover, the diagnosis of H.pylori infection was performed by ELISA testing which is less sensitive that PCR testing of the stool sample. The current study is not a randomized trial and

hence allocation bias is present and so further larger randomized clinical trials are needed to confirm the results of the study.

The current research added novel information to the current literature, as it detects the prevalence H. pylori infection in patients with HG in comparison to patients without HG.

Conclusion:

Finally, the occurrence of H. pylori infection was comparable in pregnant women with and without hyperemesis gravidarum. Additionally, HG was linked to several physiological and biochemical alterations, such as elevated hematological parameters (HB, HCT, and PLT), bilirubin levels, electrolyte imbalances (K+ and Na+), and the presence of ketonuria.

Abbreviations

ALT Alanine aminotransferase
AST Aspartate aminotransferase
CBC Complete blood count
CRL Crown-rump length
GA Gestational age
H. pylori Helicobacter pylori
HB Hemoglobin
HCT Hematocrit
HG Hyperemesis gravidarum
NPV Nause and vomiting of pregnancy
PLT Platelet

Authors' contributions

Every researcher contributed to the completion of the final paper.

M.A: Study design, protocol review, analysis of data, manuscript composition, and submission of the final manuscript.

A.H: Review of the literature, protocol composition, data collection, and analysis of data.

M.S: Study design, analysis of data, and revision of the final manuscript.

S.M: Study design, collection of data, analysis of data, and manuscript composition.

H.A: study design, protocol review, analysis of data, and revision of the final manuscript.

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Data and material availability

Data are available upon adequate requests from the authors.

Declaration:

Approval of ethics and consent to participate

The current research received the approval of the Ethical Committee, Sohag Faculty of Medicine. The subjects signed the informed consent prior to participation.

Publication consent

Null

Competing interests

Not applicable.

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