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Original article

Prevalence of Helicobacter pylori infection in pregnant women with hyperemesis gravidarum

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Abstract

Background: Hyperemesis Gravidarum (HEG) is the most frequent reason for hospitalization in early pregnancy. The exact etiology is unknown and likely multifactorial. The Helicobacter pylori (H.pylori) infection is linked to peptic ulcers and possibly other gastric disorders. **Aim**: to determine the prevalence of Helicobacter Pylori infection in pregnant women with hyperemesis gravidarum. **Methods:** This is a cross-sectional study of 143 women with HEG. They were subjected to clinical assessment and the Pregnancy Unique Quantification of Emesis (PUQE) questionnaire. Routine ultrasonographic and laboratory evaluations were done, and stool testing for H. pyri infection was performed using the IgM ELISA technique. **Results:** 20 patients (14%) had PUQE scores ≥13, consistent with severe disease. H.pylori was positive in 69 patients (48%), including 75% of those with severe disease (p=0.031). Those with positive H.pylori results had younger ages and were more frequently primigravidae. **Conclusion:** Helicobacter pylori infection is common in

pregnant women with HEG, particularly those with severe disease.

1. Introduction:

Nausea and vomiting during pregnancy, also termed morning sickness, affect between 50% and 90% of pregnant women. Symptoms usually begin between 5-8 weeks gestation and generally continue up to 16-18 weeks [1]. The condition may rarely (1-10% of pregnancies) persist beyond 20-22 weeks [2].

Although it is usually benign and self-limited, Hyperemesis gravidarum (HEG) is the protracted severe form of the condition. It may lead to ketosis, weight loss (>5%), hypovolemia, disturbances in electrolytes and acid-base status, malnutrition, or even death. Fetal loss and morbidity, including growth restriction and Wernicke's encephalopathy, may complicate the disease as well. [3].

Severe HEG is the most common reason for hospitalization in early pregnancy, occurring in between 0.3-2% of pregnancies [4].

The etiology of HEG is likely multifactorial and not precisely known. Psychological, hormonal, metabolic, and immunological factors may be implicated, as well as GI motility disturbance and anatomical factors [5].

The Pregnancy Unique Quantification of Emesis (PUQE) tool is a scoring system based on a simple three-item patient questionnaire. It provides a simpler and more specific assessment of vomiting during pregnancy than the Rhodes index [6].

Helicobacter pylori (H. pylori) is known to be associated with peptic ulcers. In addition, it has been suggested to be linked to gastric carcinoma and lymphoma cancer and lymphoma [7]. H.pylori infection is common, particularly in developing countries where it can affect up to 70-90% of the population [8].

The gold standard for diagnosis is endoscopic biopsy, with histological and microbiological studies. Several non-invasive methods have been described, including serum antibody testing and radioactive carbon urea breath test [9]. The H. pylori antigen test in stool based on a monoclonal antibody is rapid and non-invasive. It has been reported to be sensitive and specific (94% and 98%, respectively). It yields positive results during the early stage of infection [10]. This research

attempts to establish the prevalence of Helicobacter Pylori infection in pregnant women experiencing hyperemesis gravidarum.

2. Subjects and Methods:

Cross-sectional research was conducted in the obstetrics and gynecology department of Beni-Suef University Hospital from November 2021 to May 2022. It involved 143 pregnant women diagnosed with hyperemesis gravidarum.

Inclusion criteria: We enrolled patients between the ages of 17 and 38 with gestational ages ranging from 5 to 18 weeks. Pregnant women with a weight within 20% of the average weight for their height at the beginning of pregnancy [11] were eligible. Hyperemesis gravidarum (HEG) was defined as (a) vomiting more than three times per day, (b) weight loss greater than 3 kg, and/or (c) ketonuria. [3].

Exclusion criteria: We have excluded participants who have multiple pregnancies, medical disorders associated with pregnancy such as DM, HTN, thyroid, and renal disease, gastrointestinal disease, infection, or history of GI bleeding, psychosocial disorders, received H pylori treatment before and during pregnancy, and those who received recent treatment with antibiotics, PPI, and N-acetylcysteine.

Full history and examination were completed for each patient. The PUQE system was used to quantify the severity of HEG at the time of assessment, as described by Koren et al..[6] as shown in table 1. HEG-related complications were reported, including dehydration, ketonuria, electrolyte disturbances, and hepatic or renal involvement [12].

Routine investigations included Trans-vaginal ultrasonography using a Toshiba Xario 200 machine with a 6 - 9 MHz transducer to ascertain the date of pregnancy and viability and identify any abnormalities. A blood count, serum electrolytes, liver and kidney function tests, urine analysis, and thyroid functions were performed.

Stool samples were obtained for all patients, stored at -20^{o} C, and collectively tested for H. Pylori using the IgM ELISA technique (Abon Biopharm, Co., Ltd, Hangzhou, China).

Table (1) Elements of the Pregnancy Unique Quantification of Emesis (PUQE) scoring system.

3 Questions	**Assign a score for each question**				
On average in a day:	5	4	3	2	1
1. How long do you feel nauseated?	>6h	4-6h	2-3h	≤1h	0
2. How many times do you vomit?	≥7	5-6	3-4	1-2	0
3. How often have you had retching/ dry hives without vomiting?	≥7	5-6	3-4	1-2	0
	Total score of the 3 items: Nausea/ vomiting of pregnancy mild (≤6), moderate (7-12) or severe (≥13)				

(modified from Koren et al., 2002)

Ethical considerations:

The research protocol received approval from the Ethical Committee of the Faculty of Medicine at Beni-Suef University. (approval number FMRECBSU01112021/Ali). All participants provided informed permission after receiving an explanation of the research. Participants chose to take part voluntarily, and the confidentiality of information was maintained.

Statistical Analysis:

The sample size was calculated with a power of 0.8 and a significance level of 0.05 using the G Power sample size calculator. The data were evaluated using statistical metrics like mean, range, standard deviation, frequency, and relative frequency. Quantitative variables were assessed using a Student t-test, while categorical data was examined using a Chi-square test. A p-value below 0.05 was deemed significant. Statistical computations were conducted using SPSS version 27.

3. Results:

Regarding the 143 patients included in this study, the mean age was 23.4±3.8 years (range 17-32). Seventy-five (52.4%) were primigravidae and 68(47.6%) multigravida. Severe nausea and vomiting (PUQE score >12) were present in 20 cases (14%), as shown in Table 2.

H.pylori antigen was positive in 69 patients and negative in 74 (Fig 1). As presented in Table 3, the presence of H.pylori was significantly associated with younger age and was more common in primigravidae.

Table 4 shows that 75% of patients with PUQE in the "severe" range were positive for H.pylori, compared to 44% and 41% of mild and moderate cases, respectively. H. Pylori antigen was more prevalent in those with PUQE scores of more than 12.

Table (2) Age, gravidity, and NVP severity of the studied participants

Age (years) *Mean ± SD* *Range*	23.4±3.8 17-32	
	Frequency (n=143)	*Percentage*
Gravidity		
Primigravida	75	52.4
Multigravida	68	47.6
Severity (PUQE score)		
Mild (≤6)	81	56.6%
Moderate (7-12)	42	29.4%
Severe (13-15)	20	14%

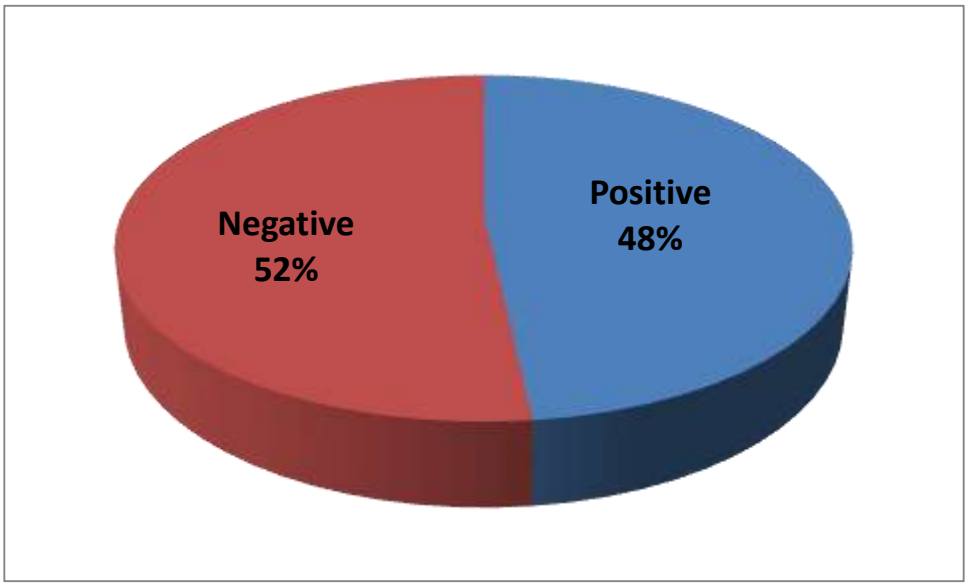

Fig (1) Prevalence of H.pylori among the studied patients

H. pylori antigen in stool was present in 69 patients (48.3%).

Table (3) Association between H.pylori and age, gestational age and parity in the studied participants:

Items	Absent *(n=74)*	Present *(n=69)*	P-value
Age (yr); *mean±SD*	24.5±3.8	22.2±3.364	<0.001*
Gestational age (wk); *mean±SD*	10.1±2.3	10.2±2.3	0.781
Gravidity:			
Primigravida	32(43.2%)	**43(62.3%)**	0.031*
Multigravida	42(56.8%)	26(37.7%)	

P-value is significant

Table (4) Relation between H.pylori and PUQE score of the studied participants:

PUQE	Negative (no=74)	Positive (no=69)	P-value
Mild ≤6	44(59.5%)	37(53.6%)	
Moderate 7-12	25(33.8%)	17(24.6%)	0.031*
Severe 13-15	5(6.8%)	**15(21.7%)**	

P-value is significant

Table (5) Association between H.pylori and HEG-related complications

	All cases (n=143)	H.pylori positive (n=69)	H. pylori Negative (n=74)	P value
Dehydration	44 (30.8%)	28 (40.6%)	16 (21.6%)	0.014*
Ketonuria	61 (42.7%)	36 (52.2%)	25 (33.8%)	0.026*
Hyponatremia	20 (14.0%)	13 (18.8%)	7 (9.5%)	0.11
Hypokalemia	12 (8.4%)	8 (11.6%)	4 (5.4%)	0.18
Renal affection	23 (16.1%	14 (20.3%)	9 (12.2%)	0.18
Hepatic affection	6 (4.2%)	4 (5.8%)	2	0.35

P-value is significant

4. Discussion:

Pregnancy-induced nausea and vomiting are quite prevalent. Hyperemesis gravidarum (HEG) is the most intense manifestation of nausea and vomiting during pregnancy. A continuum of nausea and vomiting intensity varies from common symptoms in pregnancies to the severe condition of hyperemesis gravidarum [1]. Nausea and vomiting are estimated to occur in 50-90% of pregnancies, according to studies. Pregnancy-related nausea and vomiting often start at 9-10 weeks of gestation, reach their highest point around 11-13 weeks, and normally subside by 12-14 weeks. Symptoms may persist beyond 20-22 weeks in 1-10% of pregnancies. [2].

Hyperemesis gravidarum is defined by continual feelings of nausea and vomiting linked with ketosis and loss of weight. (>5% of pre-pregnancy weight) [4].

Helicobacter pylori (H. pylori) infection impacts almost 50% of the global population and is more common in poorer nations. This bacterium colonizes the stomach. [7].

The occurrence of H. pylori infection in pregnant women differs according to geographical location, socioeconomic status, and detection technique. [8].

The research included 143 pregnant women diagnosed with hyperemesis gravidarum between 5 and 18 weeks of pregnancy. The mean age of the women with HEG was 23.4±3.8 years and ranged from 17 to 32 years with a median of 23 years. These results agree with the previous work done by Owe et al. [13], who reported that hyperemesis gravidarum is more common in younger patients. Additionally, it was found that the mean gestational age of the studied women was 10.1±2.3 weeks and ranged from 5 to 16 weeks with a median of 10 weeks.

Additionally, it also showed that 75(52.4%) of the studied participants were primigravida, and 68(47.6%) were multigravida. The findings are consistent with Brousard and Richter's observation of a higher hyperemesis gravidarum occurrence in pregnant first-time women [14]. Also, Salimi-Khayati et al [15] found that hyperemesis gravidarum is more prevalent in primigravida.

Furthermore, there was a significant association of younger maternal age (P-value < 0.001) with H.pylori, but there was no significant association between H.pylori antigen and gestational age (P-value 0.781). In contrast, multiple studies indicate that the occurrence of H. pylori infection increases with age, being less common in those under 20 years old [16]. Kouitcheu et al. discovered that the prevalence of H. pylori infection rose with age but leveled off by age 30. [17]. Zhou

et al. demonstrated no noticeable pattern concerning age. [18].

This study showed that the prevalence of H.pylori antigen in stool was 69(48.3%) in the studied participants. Furthermore, several case-control studies have shown a significant positive association between HG and H. pylori infection, as validated in a thorough review of 14 case-control studies. Golberg et al. found a higher incidence of hyperemesis gravidarum in pregnant women with H. pylori infection compared to those without, with an odds ratio of 4.45 and a 95% confidence range of 2.31-8.54. Most studies examining the link between H. pylori and dyspepsia did not discover a notable correlation between the clinical symptoms of the illness and H. pylori infection. Only two studies investigated the association between CagA-positive H. pylori strains and gastrointestinal problems in pregnant women. Park et al. discovered a notable link between CagA-seropositivity and dyspepsia during pregnancy. However, the frequency of H. pylori-seropositivity was somewhat greater in pregnant women with dyspeptic symptoms (74.6%) compared to the control group (63.8%), but the difference was not statistically significant. [19]. Karakus et al. [20] showed that the infection frequencies of H. pylori and CagA-positive strains are notably higher in HEG patients (88.9% and 78.1%, respectively) compared to asymptomatic pregnant women (45.0% and 31.3%, respectively) ($P < 0.01$ for both) [21]. There were 20(14.0%) of the participants with Severe PUQE scores, 42(29.4%) with moderate PUQE scores, and 81(56.6%) with mild scores. It revealed that there was a significant association between H. Pylori antigen and severe PUQE score. It was detected that the presence of H pylori antigen is the only factor affecting the probability of acquisition of severe hyperemesis (PUQE≥13). The presence of H pylori antigen in stool increases the likelihood of acquisition of severe hyperemesis 5 times compared to negative H pylori cases. Furthermore, the evidence from many studies showed that eradicating H. Pylori in pregnancy led to improved HEG. There was a cross-sectional study of 100 pregnant women with HG admitted to South Valley University hospitals. The study revealed that the prevalence of H. Pylori was 44% [22].

In addition, this study revealed that there was a significant association between H.pylori-positive cases and some HEG-related complications such as dehydration (p-value 0.014) and ketonuria (p-value 0.026). Still, there was no significant association between H.pylori-positive cases and hyponatremia (p-

value 0.11), hypokalemia (p-value 0.18), renal affection (p-value 0.18), or hepatic affection (p-value 0.35).

This study used stool antigen testing for H. Pylori. A meta-analysis of 38 studies found that serologic and stool antigen testing were comparable in the ability to detect H. Pylori [23].

5. Conclusion and Recommendations:

This research demonstrated a significant correlation between Helicobacter pylori infection and hyperemesis gravidarum.

From this study, it is recommended that Helicobacter pylori diagnostic testing should be included in investigations for hyperemesis gravidarum in patients who do not respond to standard medication and in women planning to conceive soon. It is particularly efficient, quick, and precise for screening hyperemesis gravidarum patients who are unresponsive to standard treatment and persist into the second trimester. When Helicobacter pylori is difficult to cure, a non-teratogenic therapy regimen may be an option. It is crucial to provide patients with information on food safety to reduce the rising incidence of infections, particularly in developing countries and those with lower socioeconomic status. H. pylori may be found in feces, sewage, and water. Still, it is effectively eliminated by regular chlorination.

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