Prevalence of Helicobacter Pylori Infection in Pregnant Women with Hyperemesis Gravidarum

Mohammad AM Ahmed[a*], Abd–Elnaser Abd-Elgaber Ali[a], Zyad Adel Mohamed[a], Esraa Abbas Abdallah[b]

[a]Obstetrics and Gynecology Department, Faculty of Medicine, South Valley University, Qena, Egypt.
[b]Clinical Pathology Department, Faculty of Medicine, South Valley University, Qena, Egypt

Abstract

Background: Hyperemesis gravidarum (HG) is a severe form of vomiting that occurs in 0.3-2% of all pregnant women. There is geographic difference in the prevalence of Helicobacter Pylori (H. Pylori). The exact prevalence in Egypt is not well-studied.
Objectives: To detect prevalence and risk factors for H. Pylori in pregnant women with HG.
Patients and Methods: This was a cross-sectional study. The study was conducted at the Department of Obstetrics and Gynecology, South Valley University hospitals.
Results: The study included 100 pregnant women with HG. In this study, the H. Pylori stool antigen testing was positive in 44 cases out of 100 cases, making a prevalence of 44%. Risk factors of H. Pylori was rural residence (adjusted OR: 3.45; CI:1.12-10.94; and P value: 0.03), recurrence of vomiting in the current pregnancy (adjusted OR was 3.85; CI:1.15-12.91; and P value: 0.03), and anemia (adjusted OR: 0.74; CI: 0.55-0.98; and P value: 0.04)
Conclusion: H. Pylori affects 44% of women with HG. There was significant association between H. pylori and the rural residence, the recurrence of vomiting in the same pregnancy, and the presence of anemia.

Keywords: Helicobacter; Pylori; Hyperemesis; Gravidarum; Pregnancy

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Introduction

Nausea and vomiting during pregnancy are common, with an incidence of 80%. Hyperemesis gravidarum (HG) is a severe form of this disorder affects 0.3-2% of pregnant women (**Abramowitz et al., 2017**). Associated symptoms include weight loss, ketonemia, and ketonuria. HG may cause electrolyte imbalance, dehydration, possible hepatic damage, renal impairment, and compromised fetal growth (**McCarthy et al., 2014; Cardaropoli et al., 2014**).

The exact etiology of HG is not known (**McCarthy et al., 2014**) H. pylori, a gram-negative spiral bacterium, inhabit the stomach, can lead to nausea and vomiting, and in rare but severe cases, ulcers and cancer (**Diaconu et al., 2017**).

Many studies showed the causal relationship between H pylori and HG, A meta-analysis of 32 studies on 4113 pregnant women was published. This meta-analysis included 29 studies with control group (these were pregnant women without HG). The H. pylori infection rate was 69.6% in women with HG and 46.2% in control group. The Odds ratio for H. Pylori infection in women with HG when compared to women in the control group was 3.34 (95% CI: 2.32–4.81, $P < 0.001$). Also, this study found a significant geographic variation in the incidence of HG. (**Li et al., 2015**) The exact prevalence in Egypt is not well established. Furthermore, the evidence for many studies showed that the eradication of H. Pylori in pregnancy led to improvement of HG (**Nguyen et al., 2019; Ahmed et al., 2017**).

The aim of the study was to detect prevalence and risk factors for H. pylori in pregnant women with HG.

Patients and methods

This was a cross-sectional study performed from May 2019 to May 2020. Cases included women admitted in the Department of Obstetrics and Gynecology, South Valley university hospitals. Ethical approval from the local ethical committee in faculty of medicine, South Valley University was taken. All women had informed consent before participation in the research. Women were assessed as regards the number of vomiting and a Pregnancy-Unique Quantification of Emesis (PUQE-24) scoring was used to quantify the severity of HG at time of admission. PUQE-24 scoring is generated to be specific for vomiting during pregnancy and simpler than the non-specific Rhodes index score (**Rhodes et al., 1999; Ebrahimi et al., 2009**). The total score is sum of replies to each of the three questions: Mild ≤ 6; Moderate = 7–12; Severe = 13–15 (**Table. 1**).

Patient had been enrolled in this study if she was pregnant and had HG before gestational age 12 weeks. For the purpose of the research, vomiting was considered HG if she had any of the following: (a) vomiting more than 3 times per day; (b) weight loss more than 3kg; (c) ketonuria; (d) PUQE-24 score > 3 (Table 1) (**Ebrahimi et al., 2009**), and co-existence of any of the complications related to HG as dehydration, VTE, electrolyte disturbance, renal impairment, or elevated liver enzymes. (**Nelson-Piercy 1998; McCarthy et al., 2014**). Patients were excluded if they had any of the following: (a) History of peptic ulcer disease; (b) Multiple pregnancy; (c) Gestational trophoblastic disease; (d) Thyrotoxicosis; (e) Diabetes mellitus; (f) Psychiatric disease; or (g) Clinically evident infection including urinary tract infection.

Table 1. Pregnancy-Unique Quantification of Emesis (PUQE) index20

In the last 24 hours, for how long have you felt nauseated or sick to your stomach?	Not at all (1)	≤1 hour (2)	2–3 hours (3)	4–6 hours (4)	> 6 hours (5)
In the last 24 hours have you vomited or thrown up?	≥7 times (5)	5–6 times (4)	3–4 times (3)	1–2 times (2)	I did not throw up (1)
In the last 24 hours how many times have you had retching or dry heaves without bringing anything up?	No time (1)	1–2 times (2)	3–4 times (3)	5–6 times (4)	≥7 times (5)

Methods

All cases of HG included in this study had been subjected to detailed history, and examination. All women had routine investigations in the form of ultrasound, complete blood count (CBC), random blood sugar (RBS), complete urine analysis (including testing for ketonuria), SGOT & SGPT, serum Urea & creatinine, and TSH. All cases were tested for the presence or absence of H. Pylori in stool based on Ig M antibody titre using ELISA method. Test procedure: 5 ml stool samples were collected, stored at temperature -20^{o} C and then collectively tested for H. Pylori Ig M using ELISA technique (Abon Biopharm, Co., Ltd, Hangzhou, China).

Statistical Analysis

Data were subjected to revision and validation then description and analysis by using SPSS (version 24; IBM-SPSS, Chicago, IL). Descriptive statistics were performed for all studied parameters and were presented in the form of mean and standard deviation (SD) for continuous data and number and percentage for categorical data.

Analytical comparison between different groups was done by using student t test to compare means and Chi square test for qualitative data. Wilcoxon-Mann-Whitney test was used to compare ordinal data. To find a causal relationship between the patients' characteristics and the H. Pylori infection regression analysis was done to generate the crude odds ratio. Adjusted Odds ratio were calculated for significant predictors to control for confounders by multiple logistic regression. P value was considered significant at < 0.05 and highly significant at < 0.001

Results

The study included 100 pregnant women with HG. In this study the H. Pylori stool antigen testing was positive in 44 cases out of 100 cases, making a prevalence of 44%.

(**Table 2, Fig.1**) showed comparison between the group of women with negative H. Pylori test and those with positive H. Pylori test. There was significantly higher percentage of women with severe and moderate vomiting according to the PUQE score than women with negative H. Pylori test. Women with H. Pylori positive test had significantly higher percentage of women with recurrence of vomiting in the current pregnancy. Other demographic and clinical data were not statistically different.

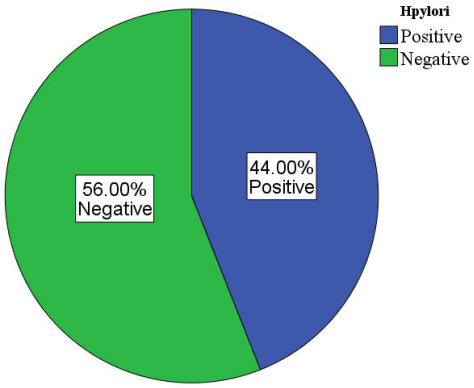

Fig.1. Distribution of the HG cases according to testing for H. Pylori

(**Table 3**) showed that women from rural areas had more than 3 times the risk of having H. Pylori even after control for confounders (adjusted OR was 3.45; CI was 1.12-10.94; and P value was 0.03). Moderate and severe PUQE score increased the risk of H. Pylori by more than 5 when compared to women with mild score, but this effect disappeared when multiple regression analysis was done. The recurrence of vomiting in the current pregnancy increased the risk of H. Pylori by more than 3 times even after controlling the confounders (adjusted OR was 3.85; CI was 1.15-12.91; and P value was 0.03). H. Pylori was significantly associated with lower blood haemoglobin. Each 1-gram increase in the blood haemoglobin was associated with decrease risk of H. Pylori by 26% (OR 0.74; CI: 0.55-0.98; and P value 0.04).

Discussion

This 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%. A recent systematic review of H. Pylori epidemiology containing 184 studies from 62 countries found that the prevalence of H. Pylori was highest in Africa (79.1%) and lowest in Oceania (24.4%). (**Hooi et al., 2017**) A lower overall global prevalence of 44.3% was found in a more recent meta-analysis. (**Zamani et al., 2018**) This geographic difference may be explained in part by the variation in virulence factors of the H. Pylori, especially CagA, VacA and OipA. (**Yamaoka 2010**)

This study used stool antigen testing for H. Pylori. Metanalysis of 38 studies found that serologic and stool antigen testing were comparable in the ability to detect H. Pylori. (**Ng et al., 2018**) However stool antigen testing is cheap and does not require high laboratory technology. Furthermore, the current kits for stool antigen test have comparable accuracy for urea breath test. (**Miftahussurur et al., 2016**)

Table 2. Characteristics of the studied group

Variables	H. Pylori Positive (n=44)	H. Pylori Negative (n=56)	P value
Age: Mean ± SD	23 ± 4.1	22.7 ± 3.7	0.7
Residence: number (%)			0.059
• Rural	27/44 (61.4%)	24/56 (42.8%)	
• Urban	17/44 (38.6%)	32/56 (51.2%)	
Education			0.8
• Non-Educated	19/44 (43.2%)	25/56	
• Educated	25/44 (56.8%)	31/56	
SES			0.9
• High	19/44 (43.2%)	25/56 (44.6%)	
• Mid	12/44 (27.3%)	15/56 (26.8%)	
• Low	13/44 (29.5%)	16/56 (28.6%)	
BMI	21.5 ± 3.4	22.3 ± 3.4	0.2
Gestational age: mean ± SD	9.6 ± 2.1	10.2 ± 2.4	0.2
Vomiting per day: Number (%)			0.4
• ≤ 2	10/44 (22.7%)	8/56 (14.3%)	
• 3 -4	11/44 (25%)	12/56 (21.4%)	
• 5-6	23/44 (52.3%)	36/56 (64.3%)	
• ≥ 7			

PUQE Score: Number (%)			**0.03**
• **Mild (≤6)**	10/44 (22.7%)	3/56 (5.3%)	
• **Moderate (7-12)**	11/44 (25%)	18/56 (32.2)	
• **Severe ≥13**	23/44 (52.3%)	35/56 (62.5%)	
Ketonuria: degree (%)			0.9
• +	14/44 (31.8%)	21/56 (37.5%)	
• + +	15/44 (34.1%)	16/56 (28.6%)	
• +++	8/44 (18.2%)	9/56 (10.1%)	
• ++++	7/44 (15.9%)	10/56 (17.8%)	
Previous HG: number (%)			0.4
• No	35/44 (79.5%)	41/56 (73.2%)	
• Yes	9/44 (20.5)	15/56 (26.8%)	
Recurrence of vomiting in same pregnancy: number (%)			**0.005**
• No	36/44 (81.2%)	31/56 (55.3%)	
• Yes	8/44 (18.2%)	25/56 (44.7%)	
Hemoglobin (g/dl): Mean ± SD	**11.05 ± 1.36**	**10.44 ± 1.46**	**0.03**
Albumin (g/dl): Mean ± SD	4 ±0.5	3.9 ± 0.7	0.3
Total bilirubin (mg/dl): Mean ± SD	0.70 ± 0.13	0.73 ± 0.15	0.3
Creatinine(mg/dl): Mean ± SD	0.68 ± 0.1	0.66 ± 0.1	0.5
ALT (mg/dl): Mean ± SD	33.1 ± 29	38.7 ± 40	0.4
AST(mg/dl): Mean ± SD	31.4 ± 26	32.6 ± 34	0.8
Na (mmoI/L): Mean ± SD	138.7 ± 6	137.3 ± 6.5	0.2
K (mmoI/L): Mean ± SD	3 ± 0.6	3.2 ± 0.5	0.1
Calcium(mg/dl): Mean ± SD	7.9 ± 0.9	8.2 ± 0.7	0.1

Table 3. Binary logistic regression for the patients' characteristics in relation to the H. Pylori test status

Variables	Crude OR (CI)	P value	Adjusted OR (CI)	P value
Age: in years	0.98 (0.88-1.08)	0.7		
Residence:				
• **Urban**	**1**		**1**	
• **Rural**	**2.11 (0.94-4.74)**	**0.07**	**3.45 (1.12-10.94)**	**0.03**
Education:				
• Educated	1			
• Non-Educated	1.06 (0.48-2.35)	0.8		
SEC		0.9		
• High	1			
• Mid	0.95 (0.36-2.49)	0.9		
• Low	0.93 (0.36-2.40)	0.9		
BMI: in Kg/m^2	1.07 (0.95-1.20)	0.2		
Gestational age: in weeks	1.11 (0.93-1.34)	0.2		
Vomiting per day: Number		0.4		
• 3 -4	1			
• 5-6	1.36 (0.39-4.70)	0.6		
• ≥ 7	1.96 (0.67-5.68)	0.2		
PUQE-24 score		**0.05**		**0.09**
• **Mild (≤6)**	**1**		**1**	

• **Moderate (7-12)**	**5.45 (1.22-24.26)**	**0.02**	**6.70 (0.96-46.57)**	**0.054**
• **Severe ≥13**	**5.07 (1.26-20.43)**	**0.02**	**4.03 (0.28-58.27)**	**0.3**
Ketonuria		0.8		
• +	1			
• + +	0.71 (0.26- 1.88)	0.5		
• +++	0.75 (0.23-2.41)	0.6		
• ++++	0.95 (0.29-3.09)	0.9		
Recurrence of HG (HG in previous pregnancies)				
• No	1			
• Yes	1.42 (0.55- 3.65)	0.5		
Recurrence of HG in the current pregnancy				
• **No**	**1**		**1**	
• **Yes**	**3.63 (1.43-9.19)**	**0.007**	**3.85 (1.15-12.91)**	**0.03**
Hemoglobin (g/dl)	**0.65 (0.34-0.92)**	**0.02**	**0.74 (0.55-0.98)**	**0.04**
Albumin (g/dl)	0.72 (0.37-1.40)	0.3		
Total bilirubin (mg/dl)	3.31 (0.22-49.57)	0.3		
Creatinine(mg/dl)	0.47 (0.04-5.66)	0.5		
ALT (mg/dl)	1.01 (0.99-1.02)	0.4		
AST(mg/dl)	1.01 (0.98-1.02)	0.8		
Na (mmoI/L)	0.96 (0.90-1.03)	0.2		
K (mmoI/L)	1.85 (0.86-3.98)	0.1		
Calcium(mg/dl)	1.41 (0.85-2.34)	0.2		

The current study found that there was no association between age of the patient and H. Pylori. The relationship between H. Pylori and age is controversial. Some studies found that older women had higher risk of H. Pylori (**Miernyk et al., 2018; Logan et al., 2001**), while other studies found that age was not a risk factor for H. Pylori. (**Eshraghian, 2014**)

This study found the rural residence of women increased the risk of H. Pylori by more than double in our study. The urban-rural disparity was also found by other studies. (**Wen et al., 2017**) The route of infection by H. Pylori may partly explain the association between H. Pylori and the rural residence in our study or the low SES in other studies. Oral-oral, feco-oral, and drinking poorly treated water in villages may partially explain this association. (**Goh et al., 2011**) Also, storage of food in refrigerator was found to protect against H. Pylori. (**Yamaoka, 2010**). In our study, the socioeconomic status was not a risk factor for H. Pylori. Contrary to this, other studies found that low socioeconomic status, crowded areas, inadequate sanitation practices, and poor hygiene as a risk factor for H. Pylori. (**Brown, 2000**)

The number of vomiting was not predictor for H. Pylori in our study, but the PUQE-24 score showed that women with severe and moderate score were had significantly higher risk of having H. Pylori. However, after multiple logistic regression analysis, the severity was shown to be a confounder. Other studies found that H. Pylori is a predictor of the severity of vomiting in women with HG (adjusted Odds ratio was 1.44; CI: 1.16-1.78). (**Grooten et al., 2017**) Also, there is indirect evidence of association between H. Pylori and severe vomiting is that HG, which is a severe form of vomiting by definition, is associated with HG. (**Ng et al., 2018**)

Recurrence of vomiting was significantly associated with H. Pylori. This may be

partially explained by the possibility of recurrence of the infection by H. Pylori found in other studies. (**Sjomina et al., 2018**) History of HG in previous pregnancy was no a risk factor for H. Pylori in this study. Contrary to this, other researchers found that H. Pylori is associated with recurrence in subsequent pregnancy. (**Fan et al., 2010**)

Low haemoglobin increased risk of H. Pylori in our study. A meta-analysis of 14 studies found the association between H. Pylori and iron deficiency anemia. (**Hudak et al., 2017**) The cause of anemia in patients with H. Pylori is not clear, but may be due to decreased absorption of iron secondary to achlorhydria, occult blood loss, or consumption of iron by the H. Pylori (**Xu et al., 2017**)

Data from this study found that there was no significant difference as regards the levels of electrolytes (Na, K, Ca), serum creatinine, serum albumin, or liver enzymes. Some studies found a significant association between H. Pylori and elevated liver enzymes, (**Hussein, 2020**) and eradication resulted in drop of liver enzymes. (**Salehi et al., 2014**)

Conclusion

44% of HG-afflicted women have H. Pylori. The rural residence, the recurrence of vomiting during the same pregnancy, and the presence of anaemia were all significantly associated with H. pylori.

Limitation of the study

The current study could not find if there was a causal relationship between H. Pylori and HG. However, many studies were done to answer this question. A metanalysis of 38 studies containing a control group of women without HG proved that H. Pylori increased the risk of HG by 35%. (**Ng et al., 2018**). Also, data on diet, lifestyle, and smoking were missed from this study. Lower consumption of vegetables, fruits, honey, and yoghurt, higher consumption of fried food, lower frequency of hand washing, and smoking was associated with H. Pylori. (**Sjomina et al., 2018**).

Conflict of Interest

The authors report no conflict of interest.

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