

SCREENING FOR H. PYLORI SERUM IGG SEROPOSITIVITY IN HYPEREMESIS GRAVIDARUM

By

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ABSTRACT

BACKGROUND: Nausea and vomiting associated with pregnancy commonly occurs in 80% of all pregnancies. They begin usually at 9th-10th weeks of gestation, reaching the peak at 11th – 13th weeks and disappear at 16th – 18th weeks. Its severity varies from mild (not affecting general condition of the patients) to severe (causing intractable vomiting, electrolyte imbalance, weight loss >5%, impairment of liver and kidney functions and dehydration). It may cause even maternal and fetal deaths. Hyperemesis gravidarum (HG) is defined as persistent and excessive vomiting starting before the end of the 22nd week of gestation. HG affects approximately 0.3%–2.0% of pregnancies. Helicobacter pylori is one of the most common bacterium 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 affects young children. Acute infection manifests as acute gastritis and stomach pain, whereas chronic infection causes chronic gastritis and peptic ulcer, 2% of which may develop into stomach cancer.

OBJECTIVE: Assessing the seropositivity for helicobacter pylori IgG in hyperemesis gravidarum patients versus normal pregnant women.

SUBJECT AND METHODS: A case control study was done on 100 pregnant women, divided into two equal groups; Group (I): Pregnant women complaining of hyperemesis gravidarum, while Group (II): Normal pregnant women. Both groups underwent routine clinical and laboratory examination, and H. Pylori infection assessment by qualitative and quantitative determination of H. pylori IgG in serum by ELISA.

RESULTS: There was no significant difference between both groups as regards age or gestational age. No significant association between groups and H. Pylori IgG Seropositivity. The IgG antibody titers was higher in pregnant women with emesis gravidarum than in normal pregnant “control” women. The cutoff point for IgG titer in pregnant women with HG was 34 AU/ml. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 82%, 97.9%, 97.6%, 83.6% and 89.6% respectively.

CONCLUSION: There was a significant correlation between Helicobacter pylori infection and occurrence of emesis gravidarum. It is recommended to add Helicobacter pylori serum IgG as a screening test to the investigations for all women who are complaining of emesis gravidarum.

Keywords: Nausea; Vomiting; Hyperemesis gravidarum; Helicobacter pylori.

INTRODUCTION

Nausea and vomiting associated with pregnancy and has a pervasive detrimental

impact on women’s family, social and professional life. It commonly occurs in 80% of all pregnancies (Sheehan, 2007).

They begin usually at 9th-10th weeks of gestation, reaching the peak at 11th – 13th weeks and disappear at 16th – 18th weeks (Ebrahimi *et al.*, 2010). Its severity varies from mild (not affecting general condition of the patients) to severe (causing intractable vomiting, electrolyte imbalance, weight loss >5%, impairment of liver and kidney functions and dehydration) it may cause even maternal and fetal deaths. In 1-10% of pregnancies, symptoms may continue beyond 20-22 weeks (Shirin *et al.*, 2004).

Hyperemesis gravidarum (HG) is defined as persistent and excessive vomiting starting before the end of the 22nd week of gestation. HG affects approximately 0.3–2.0% of pregnancies (Dodds *et al.*, 2006). It is characterized by the occurrence of >3 episodes of vomiting per day with ketonuria and >3 kg or 5% weight loss, may cause volume depletion, dehydration, electrolytes and acid-base imbalances, nutritional deficiencies, and even death. Severe hyperemesis requiring hospital admission (Goodwin, 2008).

The exact cause of HG is not well known and is probably multifactorial in which psychological factors, alteration of gastrointestinal motility, hormonal changes, infections, immunological, metabolic and anatomical factors appear to intervene (Kazemzadeh *et al.*, 2014).

It is the most common cause of hospitalization in the first half of pregnancy and second only to preterm labor for pregnancy overall (Gazmararian *et al.*, 2002). It can be associated with serious maternal and fetal morbidity such as Wernicke's encephalopathy, fetal growth restriction, and even maternal and fetal death (Testerman and Morris, 2014).

The *Helicobacter pylori* (*H. pylori*) are recognized as a significant causative agent of gastritis in humans and as an essential factor in the pathogenesis of peptic ulcer (Wu *et al.*, 2000). Various findings suggest that this organism is also involved in the pathogenesis of cancer and lymphoma of the stomach (Li *et al.*, 2015)

In developing countries, 70% to 90% of the population is infected by the bacteria, while in industrialized countries the prevalence is smaller, ranging between 25% and 50% (Wu *et al.*, 2000).

The action of *H. Pylori* is widely studied in literature and some studies now focus specifically on its association with nausea and vomiting (Shirin *et al.*, 2004). A possible association between *H. pylori* infection and HG has been the focus of researching for some studies (Shaban *et al.*, 2014).

SUBJECTS AND METHODS

This a case-control study that had been carried out in collaboration between the Obstetrics & Gynecology, Radiology and Clinical pathology Departments, Bab Al-Sha'aria University Hospital, Faculty of Medicine, Al Azhar University and Al-Ahrar general Hospital – ministry of health, during the period between July 2015 and April 2016.

Before the start of the study, permission was obtained from Ethical Committee in the faculty of medicine, Al-Azhar University. Also informed written consents from patients included in the study were obtained.

- ◆ **Subjects:** A total number of 100 pregnant women were included and classified into two equal groups:

1. **Group I:** Pregnant women with hyperemesis gravidarum with age ranged from **19-36** years with mean \pm SD **26.26 \pm 5.74** years.
 2. **Group II:** Normal pregnant women of matched age, parity and gestational age as control with age ranged from **19-37** years with mean \pm SD **27.9 \pm 5.89** years.
- * **Inclusion Criteria:** The study group included pregnant women aged **18-40** years, gestation age less than 16 weeks confirmed by U/S, hyperemesis gravidarium that was diagnosed according to H.E.R. Foundation (Hyperemesis Education & Research Foundation) is based on:
- Excessive pregnancy-related nausea and/or vomiting that prevents adequate intake of food and fluids.
 - Signs of dehydration “Ketonuria (+1 or more) and Hemoconcentration (normal Female haematocrit value: 36.1 - 44.3%)”.
- * **Exclusion criteria:** Other causes of vomiting such as gastroenteritis, cholecystitis, pyelonephritis, liver dysfunction and hyperthyroidism. Pregnant women with multiple gestation pregnancy, Hydatiform molar pregnancy and Urinary tract infection were also excluded.
- ♦ **Methods:** All subjects of the study were subjected to the following:-
- A) Full history and thorough clinical examination:
 - B) Routine investigations:
 - a) Fetal assessment by transabdominal pelvic ultrasound.
 - b) Maternal assessment by:
 - i. Complete blood count.
 - ii. Complete urine analysis.
 - iii. Liver and kidney function tests.
 - iv. Abdominal ultrasound.
 - v. Urine analysis to detect Ketones bodies “indicator for starvation ketosis”.
 - c) HP infection assessment: A venous blood sample was collected from the mothers to be examined for seropositivity, qualitative and quantitative determination of H. Pylori by ELISA.
- Statistical Analysis:** Data were analyzed with SPSS version 15.0 (statistical package for the Social Science, Chicago, IL). Quantitative data were expressed as mean \pm standard deviation (SD) or standard error (SE). $SE=SD/\text{square root of patients number}$ which was used in case of big SD, data were analyzed by independent sample, paired t test. While qualitative data were expressed as number and percentage and were analyzed by Chi square (X²) test. The receiver operating characteristic (ROC) curve and 95% confidence interval (CI) was performed to determine cutoff values for the studied test. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were determined. P-value was considered significant if <0.05 and highly significant if <0.001 .

RESULTS

The maternal age in the study “HG” group was **27.9 \pm 5.89** years (range: **19-36**), while in the control group was

26.26 ± 5.74 years (range: **19-37**) with no statistical significant difference between both group (*P-value: 0.16*).

Regarding the gestational age, it was **8.64 ± 2.27** (range: 5-12 weeks) in the study group, and **8.52 ± 2.1** (range: 5-12 weeks). There was no statistical significant difference between both groups (*P-value: 0.79*).

As regard Parity, the study group was consisted of **27 “54.0%”** multigravida and **23 “46.0%”** primigravida, while the control group was consisted of **23 “46.0%”** multigravida and **27 “54.0%”** primigravida. There was no statistical significant difference between both groups (*P-value: 0.42*).

Regarding the *H. pylori* IgG seropositivity, all the pregnant women in the study group “**100.0%**” were positive for *H. pylori* IgG, while in the control group **47 “94.0%”** pregnant women were positive for *H. pylori* IgG and only **3 “6.0%”** were negative for *H. pylori* IgG with no significant difference between both groups (*P-value: 0.08*).

Table (1): Helicobacter pylori IgG Seropositivity.

			HG	Control	Total	t	p
H-Pylori	-VE	N	0	3	3	3.09	0.08
		%	0.0%	6%	3%		
	+VE	N	50	47	97		
		%	100%	94%	97%		
Total	N	50	50	100			
	%	100%	100%	100%			

The *H. pylori* IgG titer in the study group was **60.84±23.7** (range: **20-95**) was higher than the titer in the control group **21.82±9.4** (range: **5-45**), with a statistical significant difference between both group (*P-value: <0.001*).

Table (2): Helicobacter pylori IgG titer in study groups (mean±SD).

Group	HG	Control	T	P
Parameter				
Titer	60.84±23.7 20-95	21.82±9.4 5-45	10.49	0.001

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 82%, 97.9%, 97.6%, 83.6% and 89.6% respectively. The area under the ROC curve (AUC) was 0.906 (95% CI =0.00** to 0.966, P-value: <0.001).

Table (3): sensitivity and specificity of for detection of IgG titer for Emesis Gravid-arum.

- Sensitivity	82%
- Specificity	97.9%
- Positive Predictive value	97.6%
- Negative Predictive value	83.6%
- Accuracy	89.6%

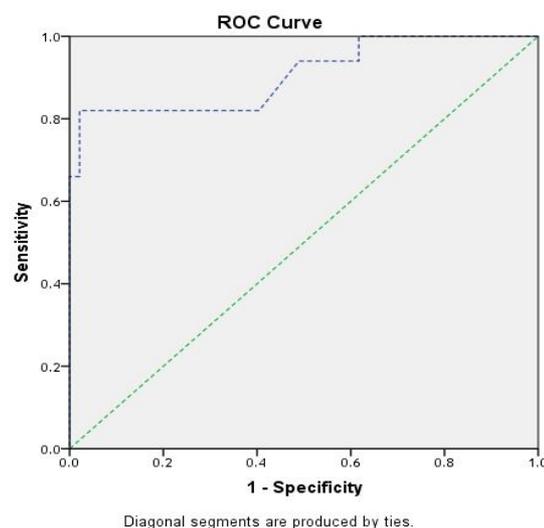


Figure (3): ROC curve for detect IgG titer cut off for Emesis Gravid-arum.

DISCUSSION

Nausea and vomiting are the most common disorders affecting pregnant women in the first trimester. It varies from mild (emesis gravidarum), which does not interfere with a patient's physical activity, to severe (hyperemesis gravidarum) (Wegrzyniak et al., 2012).

H pylori is one of the most common infectious diseases on earth. Its prevalence varies among different populations. More prevalent rates are found in developing countries, with lower prevalence rates in developed countries (Sheehan, 2007).

The Helicobacter pylori (H. pylori) are recognized as a significant causative agent of gastritis in humans and as an essential factor in the pathogenesis of peptic ulcer (Wu, et al. 2000). Various findings suggest that this organism is also involved in the pathogenesis of cancer and lymphoma of the stomach (Li, et al., 2015).

In order to study the association between H. pylori infection and HG in pregnant women our case-control study was conducted in collaboration between the Obstetrics & Gynecology, Radiology and Clinical pathology Departments, Bab Al-Sha'aria University Hospital, Faculty of Medicine, Al Azhar University and Al-Ahrar General Hospital, Ministry of Health, during the period between July 2015 and April 2016 on 100 pregnant females who were divided into 2 groups: group A (study group) composed of 50 pregnant women who had hyperemesis gravidarum and group B (control group) made up of 50 normal pregnant women having no vomiting or normal nausea and vomiting with pregnancy

Comparison between both groups of the study as regard maternal age showed that there was no significant difference between the study "HG" group and the control group. In comparison between both groups regarding the gestational age, there was no statistical significant difference between both groups. These results agreed with results reported by Abbasalizadeh, et al. (2011) who showed no statistical significant difference was found regarding maternal age and gestational age between cases and controls. In contrast, Shirin et al. (2014) found that the women who were complaining of frequent vomiting in the first trimester and were positive for H pylori were significantly older than those who were negative for H pylori.

Comparison between the both groups as regard Parity, showed that there was no statistical significant difference between both groups. These results agreed with those reported by Wu et al. (2000). However, Brousard and Richter (1998) noted that there is an increased incidence of hyperemesis in multipara women, and ACOG (2004) found that there is an increased incidence of hyperemesis gravidarum in primipara women.

In comparing seropositivity for H. pylori IgG, all the study "HG" group "100%" was positive for H. pylori IgG. In the control group 94.0% pregnant women were positive for H. pylori IgG and only 6.0% were negative for H. pylori IgG with no significant difference between both groups.

In order for more differentiation and clarifying the association between HG and H.pylori IgG we measured the serum H. pylori IgG and there was a statistical

significant difference between both groups of the study. These results agreed with conclusion reported by *Kazemzadeh et al. (2014)* that HP infection was higher in HEG cases in this study, and may be considered as its risk factor. Also, there went in agree with *Shaban et al. (2014)* who reported 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, a test for H pylori seropositivity should be done.

CONCLUSION

There was a significant correlation between Helicobacter pylori infection and occurrence of emesis gravidarum.

REFERENCES

1. **Abbasalizadeh F, Abbasalizadeh S, Bastani P and RezaBonyadi M. (2011):** Helicobacter pylori and Cag A antibodies in Hyperemesis gravidarum (HG). African Journal of Microbiology Research. 5(15): 2100-2102.
2. **ACOG (American College of Obstetrics and Gynecology) (2004):** Practice bulletin: nausea and vomiting of pregnancy. Obstet Gynecol., 103:803-14.
3. **Broussard C and Richter J. (1998):** Nausea and vomiting of pregnancy. Gastroenterol Clin North Am., 27:123-51.
4. **Ebrahimi N, Maltepe C and Einarson A. (2010):** Optimal management of nausea and vomiting of pregnancy. Int J Womens Health, 2:241-8.
5. **Goodwin TM. (2008):** Hyperemesis gravidarum. Obstet Gynecol Clin North Am., 35(3):401-17.
6. **Kazemzadeh M, Kashanian M, Baha B and Sheikhsari N. (2014):** Evaluation of the relationship between Helicobacter Pylori infection and Hyperemesis Gravidarum. Med J Islam Repub Iran,72: 21-28.
7. **Lee NM and Saha S (2011):** Nausea and Vomiting of Pregnancy Gastroenterol Clin North Am., 40(2): 309.
8. **Li L, Li L, Zhou X, Xiao S, Gu H, Zhang G. (2015):** Helicobacter pylori Infection Is Associated with an Increased Risk of Hyperemesis Gravidarum: A Meta-Analysis. Gastroenterol Res Pract., 2015; 278905.
9. **Mansour GM and Nashaat EH. (2011):** Role of Helicobacter pylori in the pathogenesis of hyperemesis gravidarum. Arch Gynecol Obstet., 284(4):843-7.
10. **Mylonas I, Gingelmaier A and Kainer F. (2007):** Nausea and vomiting in pregnancy. Dtsch Arztebl., 104:A1821-6.
11. **Shaban MM, Kandil HO and Elshafei AH. (2014):** Helicobacter pylori seropositivity in patients with hyperemesis gravidarum. The American Journal of the Medical Sciences, 347 (2); 101-105.
12. **Sheehan, P. (2007):** Hyperemesis gravidarum assessment and management. Aust Fam Physician., 36(9):698-701.
13. **Tamay AG and Kuşçu NK. (2011):** Hyperemesis gravidarum: current aspect. J Obstet Gynaecol., 31(8):708-12.
14. **Testerman TL and Morris J. (2014):** Beyond the stomach: an updated view of Helicobacter pylori pathogenesis, diagnosis, and treatment. World J Gastroenterol., 28;20(36):12781-808.
15. **Wegrzyniak LJ, Repke JT and Ural SH. (2012):** Treatment of Hyperemesis Gravidarum. Rev Obstet Gynecol., 5(2): 78-84.
16. **Wu CY, Tseng JJ and Chou MM. (2000):** Correlation between Helicobacter pylori infection and gastrointestinal symptoms in pregnancy. Adv Ther., 17:152-8.

فحص إيجابية مصل الهليكوباكتر بيلوري في حالات القيء المستعصي

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خلفية البحث: يحدث الغثيان والقيء المصاحب للحمل عادة في ٨٠٪ من جميع حالات الحمل. ويبدأ ذلك في الظهور عادة في الأسبوعين التاسع والعاشر من الحمل، وصولاً إلى أعلى معدلاتها في الأسابيع من الحادي عشر إلى الثالث عشر ثم تختفي في الأسابيع من السادس عشر إلى الثامن عشر من الحمل. وتختلف المدة بين بسيطة (لا تؤثر على الحالة العامة للمريض) إلى حادة (القيء المستعصي الذي يسبب خلل بكميائية الجسم، وفقدان أكثر من ٥٪ من الوزن، وخلل بوظائف الكبد والكلية، والجفاف، وقد يؤدي إلى وفاة الأم والجنين). ويعرف القيء المستعصي على أنه القيء المستمر والمفرط الذي يبدأ قبل نهاية الأسبوع الثاني والعشرين من الحمل، ويؤثر هذا النوع على ما يقرب من ٣،٠-٢٪ من حالات الحمل.

وبكتيريا الهليكوباكتر بيلوري هي واحدة من أكثر أنواع البكتيريا التي تصيب الإنسان شيوعاً، وتعتبر أكثر شيوعاً في البلدان النامية والأطفال الصغار، وتسبب التهابات حادة ومزمنة بالمعدة، وقد تسبب القرحة المعدية في حوالي ٢٪ من الحالات، وقد تتطور لتسبب سرطان المعدة.

الهدف من البحث: تقييم قيمة الكشف عن ايجابية مصل الهليكوباكتر بيلوري في القيء المستعصي بالحمل وذلك للوصول إلى تقييم أفضل للحالة مما يساعد على ارتفاع نسبة الشفاء لا سيما في الحالات الغير مستجيبة للطرق التقليدية من العلاج منها.

طرق البحث: إشتملت الدراسة على مائة من السيدات الحوامل خلال الشهور الثلاثة الأولى من الحمل واللاتي قمن بالتردد على كل من مستشفى الأحرار العام بمحافظة الشرقية ومستشفى باب الشعرية بجامعة الأزهر. وبعد الحصول على الموافقات المطلوبة، تم تقسيمهن إلى مجموعتين متساويتين: الأولى تتضمن السيدات الحوامل اللاتي يعانين من القيء المستعصي، والثانية هي المجموعة الضابطة وتتضمن السيدات الحوامل اللاتي لا يعانين من أى مشاكل بالحمل، أو تعانين من القيء الطبيعي المصاحب للحمل، وتم السؤال عن التاريخ المرضي الكامل، وتم عمل فحص سريري دقيق وكامل وإجراء الفحوصات المختبرية الروتينية ثم البحث عن الإصابة ببكتيريا الهليكوباكتر بيلوري باستخدام جهاز الإليزا .

نتائج البحث: لم يكن هناك فرق بين مجموعة الحالات والضوابط من ناحية عمر الأم وعمر الجنين و عدد مرات الحمل أو عدد مرات الإجهاض. وأظهرت النتائج أيضاً أن مستوى الأجسام المضادة المناعية بالدم للهليكوباكتر بيلوري في مجموعة الحالات أعلى من الذي يوجد في المجموعة الضابطة

الاستنتاج: أظهرت نتائج البحث أن هناك علاقة واضحة بين الإصابة ببكتيريا هليكوباكتر بيلوري والقيء المستعصي مع الحمل.