

COMPARATIVE STUDY BETWEEN INCIDENCE OF HELICOBACTER PYLORI INFECTION IN WOMEN WITH HYPEREMESIS GRAVIDARUM AND NORMAL PREGNANCY

By

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ABSTRACT

Background: Nausea and vomiting in early pregnancy is so common that it can be considered a normal part of pregnancy. It is referred to as "morning sickness" although this is a misnomer because symptoms will often persist throughout the day. Nausea and vomiting occurs significantly more often in primigravidas and women who were less educated younger-nonsmokers, obese or those with a history of nausea and vomiting in previous pregnancy.

Objective: This work aimed at assessing the possible relation between H. Pylori infection and hyperemesis gravidarum (HG).

Patient and Methods: Study setting: Al Azhar University Hospitals (Al_ Hussein and Sayed Galal), **Duration of study:** November 2018 to May 2019. The Study included two groups Group (A): (Thirty) pregnant women with hyperemesis gravidarum in the first trimester attending at antenatal clinics and admitted in the ward in addition to Group (B): (Thirty) normal pregnant women with antenatal care. The pregnant women with hyperemesis gravidarum, aged 18-40 years old and less than 16 weeks gestation.

Results: The current study found significant difference between two groups regarding positivity of HPSA. Positive stool antigen were found in 26 out of 30 of hyperemesis gravidarum (86.7%) compared with 11 out of 30 controls (36.7%) and highly statistical significant difference between studied groups as regard H pylori antibodies.

Conclusion: There was a significant association between Helicobacter Pylori infection and pathogenesis of hyperemesis gravidarum.

Keywords: Hyperemesis gravidarum.

INTRODUCTION

Nausea and vomiting in early pregnancy is so common that it can be considered a normal part of pregnancy. It is referred to as "morning sickness" although this is a misnomer because symptoms will often persist through the day. Symptoms usually begin between the

fourth and seventh week after the last menstrual period and resolve in many women by the twelfth week and in most women by twentieth week of pregnancy (Niebyl, 2010).

The condition is usually self-limiting and peaks at around 9th gestational week. However, in up to 20% of cases nausea

and vomiting may continue until delivery. Nausea and vomiting occurs significantly more often in primigravidas and women who were less educated younger-nonsmokers, obese or those with a history of nausea and vomiting in previous pregnancy (*Jueckstock et al., 2010*).

Symptoms including nausea, gagging, retching and vomiting may persist 'round the clock despite the common term morning sickness (*Clark et al., 2014*).

A smaller number of pregnant women (approximately 0.3–1%) have a more severe form of nausea and vomiting – hyperemesis gravidarum which is characterised by persistent vomiting, weight loss of more than 5%, ketouria, electrolyte abnormalities (hypo-kalaemia) and dehydration (*O'Carroll et al., 2011*).

H.pylori has been recognized to play a role in disease of gastrointestinal tract. It has been hypothesized that H.pylori may increase the risk of hyperemesis gravidarum (*Irene Sanddven et al., 2009*).

Helicobacter pylori is a spiral-shaped, gram-negative bacterium that is found in the gastric mucous layer or is adherent to the epithelial lining of the stomach. Most people who are infected by H. pylori never suffer any symptoms related to the infection; however, H pylori is associated with chronic gastritis, gastroduodenal ulcers, duodenal structural and functional abnormalities, and gastric malignancies (*Guyen et al., 2011*).

Hyperemesis gravidarum is an intractable nausea and vomiting sign of delay duration such as ketonuria, high urine specific gravity, electrolyte imbalances, and weight loss of at least 5%

of pre-pregnancy weight ketosis and need for admission to hospital (*Mella, 2011*).

This work aimed to assess the possible relation between H. Pylori infection and hyperemesis gravidarum.

PATIENTS AND METHODS

Study setting: Al_Azhar university hospitals (Al_Hussein and Sayed Galal).

Duration of study: November2018 to May2019.

Study design: Case control study.

This work contained 2groups:

1. Group (A): (30patient) pregnant women with hyperemesis gravidarum who have vomiting sufficiently enough to produce weight loss, dehydration and hypokalemia and admitted in hospital.

2. Group (B): (30patient) Control patients which have been selected from pregnant women presenting to the outpatient clinics for routine antenatal care at the same gestational age. Some age range and some socioeconomic standard as cases.

All controls have no gastro-intestinal symptoms and had the same exclusion criteria of the cases.

All women were subjected to:

1. Full history taking.
2. Clinical examination (general and abdominal).
3. Investigations.
 - Complete blood count.
 - Complete urine analysis.
 - Liver and kidney function test.
 - Coagulation profile (PT, PTT and INR).

- Electrolytes (serum Na⁺, K⁺).
- Abdominal ultrasound.
- The investigator was ensured that all persons assisting with the trial were adequately informed about the protocol.
- Before begin admitted to the clinical study. Written consent was taken from every woman in the study. After proper conselling and explanation of the study in a form understandable to her.

a. Fetal assessment:

Trans-abdominal ultrasound including fetal viability and gestational age.

b. H. pylori infection assessment:

One step H.pylori stool antigen test.

All pregnant women (cases and controls) were asked to bring a stool sample in a clean container; collected sample was tested in a laboratory.

Stool sample was tested by using one step H.pylori stool antigen test (CER test Biotec) Pol. Industrial Rio Gallego II Calle J. No. 1-5. No 1. 50840 for detection of H.pylro antigen.

Inclusion criteria:

- Age of patients between 18-40 years old.
- Fetal single viable fetus in ultrasound.
- Gestational age less than 16 wks confirmed by pelvic ultrasound and LMP.

Exclusion criteria:

- Multiple pregnancies.
- Hydatidiform molar pregnancy.
- Other causes of vomiting:
 - Gastroenteritis.
 - Cholecystitis.
 - Pyelonephritis.
 - Liver dysfunction.
 - Hyperthyroidism.

Statistical analysis:

Data were analyzed using Statistical package for Social Science (SPSS) version 15.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

Independent-samples t-test of significance: was used when comparing between two means.

Chi-square test: was used when comparing between qualitative data.

- P-value < 0.05 was considered significant.
- Mann-Whitney-U test was used to compare mean scores of continued variables between two groups in abnormally distributed samples. P value of less than 0.05 was considered as statistically significant.

RESULTS

Thirty pregnant women with hyperemesis gravidarum and gestational age-matched 30 control subject were enrolled in the study.

There were no statistically significant differences between the study groups with

hyperemesis gravidarum and control groups in terms of age, gestational week, parity, educational level and socio-economic state (**Table 1**).

Table (1): Comparison between studied groups as regard demographic data

Variables		Groups	Group A (N = 30)	Group B (N = 30)	P-value
Age (years)	Mean		28.5	31.7	0.122
	±SD		8.4	7.4	
Gestational Age (weeks)	Mean		9.5	8.9	0.191
	±SD		1.6	1.9	
Parity	Para 0		18 (60%)	17 (56.7%)	0.793
	Para 1		6 (20%)	8 (26.7%)	0.541
	Para 2		6 (20%)	5 (16.7%)	0.738
Socioeconomic state	Low		24 (80%)	22 (73.3%)	0.541
	Intermed.		6 (20%)	8 (26.7%)	
Educational level	Not educated		20 (66.7%)	22 (73.3%)	0.573
	Primary school		10 (33.3%)	8 (26.7%)	

They were statistically significant differences between studied groups as regard kidney function tests (urea and Creat) and liver enzymes (SGPT and

SGOT), and Na, K, coagulation profile, acetone. No statistical significant differences between studied groups as regard Hb, WBCS and PLT (Table 2).

Table (2): Comparison between studied groups as regard kidney function tests, liver enzymes , Na , K , coagulation profile , acetone and blood picture

Variables		Groups	Group A (N = 30)	Group B (N = 30)	P-value
Urea (mg/dl)	Mean		21.1	24.56	0.005
	±SD		8.3	5.30	
Creat (mg/dl)	Mean		0.71	0.79	0.022
	±SD		0.23	0.16	
SGPT (U/L)	Mean		56.03	35.32	< 0.001
	±SD		22.34	7.20	
SGOP (U/L)	Mean		43.97	26.64	< 0.001
	±SD		18.73	4.82	
Na (mEq/L)	Mean		132.86	142.17	< 0.001
	±SD		4.2	5.01	
K (mEq/L)	Mean		3.3	4.00	< 0.001
	±SD		0.6	0.69	
Prothrombin concentration (%)	Mean		90.19	82.18	< 0.001
	±SD		9.57	6.93	
INR	Mean		1.23	1.44	< 0.01
	±SD		0.27	0.37	
APTT (Sec)	Mean		34.97	32.40	< 0.03
	±SD		3.49	5.31	
Acetone	Negative		0 (0%)	9 (30%)	< 0.001
	Positive		30 (100%)	21 (70%)	
Hb (g/dl)	Mean		9.2	11.60	> 0.188
	±SD		1.3	1.98	
WBCs (x10 ³ /ul)	Mean		10.2	7.57	> 0.135
	±SD		7.6	2.34	
PLT (x10 ³ /ul)	Mean		244.97	251.94	> 0.399
	±SD		87.37	80.82	

They were shows statistically significant difference between studied groups as regard H pylori Ag in stool and H pylori antibodies (Table 3).

Table (3): Comparison between studied groups as regard H pylori Ag in stool and H pylori antibodies

Variables		Groups	Group A (N = 30)	Group B (N = 30)	P-value
H pylori Ag in stool	Negative		4 (13.3%)	19 (63.3%)	< 0.001
	Positive		26 (86.7%)	11 (36.7%)	
H pylori Abs	Mean		58.97	31.23	< 0.001
	±SD		25.91	28.66	

DISCUSSION

The study included 30 pt with HG patients were confirmed with H pylori infection implied that the rate of Hpylori infection was much greater in HG patients than that in non HG patients after adjusting for cofounding variables

There was no significant difference between the two groups regarding demographic data (age, gestational age and socioeconomic status).

There was statistically significant difference between studied groups as regard kidney function tests (urea and Creat) as they found decrease in urea in group A than group B. Mean creat decrease in group A than group B. and this study was agreed with study carried out by *Rasha (2015)*.

And there was statistical significant difference between studied groups as regard liver enzymes (SGPT and SGOT). They found increase in group A than group B. Mean SGOT increase in group A than in group B and this study was agreed with study carried out by *Rasha (2015)*.

And there was statistical significant difference between studied groups as regard Na and K they found decrease in group A than group B. Mean K they found decrease in group A than group B.

No statistical significant difference between studied groups as regard Hb, WBCs & PLT.

The current study found significant difference between two groups regarding positivity of HPSA. Positive stool antigen were found in 26 out of 30 of hyperemesis gravid arum (86.7%) compared with 11 out of 30 controls (36.7%) This study

found that the rate of H. pylori infection was higher in HG patients than that in non-HG patients and this was agreed with study carried out by Guven and colleagues which investigated the relationship between H. pylori infection and HG in early pregnancy through serologic and stool antigen tests in a prospective cross-sectional study on 40 women with HG and 40 controls at 7–12 weeks of pregnancy. They found that the rate of serology-specific H. pylori IgG positivity was 80% in subjects with HG and 35% in controls-a significant difference. There was also a significant difference in the rate of H. pylori stool antigen test positivity, with a rate of 87.5% in subjects with HG and 62.5% in controls (*Guven et al., 2011*).

In the other study a serum anti-Helicobacter pylori IgG antibody by ELISA > 1.1 was associated with hyperemesis gravidarum at a sensitivity of 86.67%, a specificity of 65.91%, a positive predictive value of 72.22 %, a negative predictive value of 82.86 (*Mansour and Nashaat, 2011*).

Also, *Abdl Alwahed et al.* found that Hyperemesis gravid arum patients were found to have a significantly higher Helicobacter Pylori prevalence compared to control subjects (69% vs. 15%; $p < 0.05$) especially in intractable cases where the Helicobacter Pylori prevalence is 80%. The hyperemesis gravid arum patients were found to have a significantly higher HpSA positivity compared to control group ($p < 0.05$) (*Abdl Alwahed et al., 2014*).

Study also carried out by *Ahmed et al.* Shows significantly high prevalence of H. pylori among pregnant with hyperemesis gravid arum compared to control group

(80% vs. 15 %). Patients with hyperemesis gravid arum were found to have significantly higher in HPSA positive compared to control group (Ahmed *et al.* 2014).

Also, AlBasam & Obaid reported that the rates of H pylori stool antigen test positivity were 52% (26 out of 50) among patients with HG and 18% (9 out of 50) in control group. The difference between the two groups was statistically significant. P value < 0.05 (AlBasam & Obaid, 2013).

Cases and controls in this study were recruited from the clinics of Al_Hussein and Sayed Galal Hospital where medical service is almost free. This explains the same socioeconomic level of all women participated in this study.

In this study, it was mentioned that all the study participants were from areas of low socioeconomic status; this situation was designated only by the education level. The prevalence of H pylori in our region was 86.7 by stool antigen test, which indicates active infection in HG cases, and this rate is higher than those in other control studies 36.7.

Patients' education for food safety was important. Careful food handling and hand washing were important to prevent transmission of foodborne pathogens to the diet of pregnant women. Patients' education for food safety should be considered to prevent the increasing numbers of infected cases especially in developing countries with low socioeconomic levels.

Further case reports described that there was significant improvement in patients with hyperemesis gravid arum and a positive Helicobacter pylori serum

titer after treatment with clarithromycin and/or amoxicillin and a proton pump inhibitor (lansoprazole or omeprazole) or H2-antagonists (famotidine or ranitidine).

The advantages of the antibody tests were their low cost, widespread availability, and rapid results.

Early detection for Helicobacter pylori and proof of eradication are the keys for preventing severe consequences of infection. And stool antigen test which detect active infection and it is noninvasive, cheap and easy test. Although serologic testing is the most common noninvasive diagnostic method for Hp and is relatively inexpensive and convenient, in our opinion a test that shows an active gastrointestinal colonization will be more appropriate in diagnosis of patients with HG.

LIMITATION OF THE STUDY

1. Small sample size as statistical normally required larger sample size to ensure and preventative distribution of the population.
2. Study demonstrated the pathogenesis of H. pylori in hyperemesis gravid arum but not treated it.

CONCLUSION

A significant association between Helicobacter Pylori infection and pathogenesis of hyperemesis gravid arum.

RECOMMENDATION

- It is recommended to add Helicobacter Pylori stool antigen test as a screening test to investigations for all women who are complaining of hyperemesis gravid arum as it is noninvasive, cheap and easy test.

- It is highly recommended to exclude Helicobacter Pylori infection in resistant cases of hyperemesis gravid arum to routine treatment or deteriorating cases of hyperemesis gravid arum.
- Finally, when Helicobacter Pylori infection is discovered before pregnancy, it is recommended to receive treatment for Helicobacter Pylori before pregnancy

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دراسة مقارنة بين الإصابة بالجرثومة الحلزونية في النساء اللاتي تعانين من القيئ المستعصي مقارنة بالحمل الطبيعي فهد عبدالعال العمدة، أشرف حمدي محمد- محمود عبداللطيف حشيش، محمد عبدالله بدير عبدالله

قسمى النساء والتوليد والباثولوجيا الاكلينيكية، كلية طب الازهر

خلفية البحث: الغثيان والقيء في الحمل المبكر أمر شائع لدرجة أنه يمكن اعتباره جزءاً طبيعياً من الحمل يشار إليها باسم "غثيان الصباح" على الرغم من أن هذا هو تسمية خاطئة لأن الأعراض سوف تمر في كثير من الأحيان طوال اليوم وتبدأ الأعراض عادة بين الأسبوع الرابع والسابع بعد فترة الحيض الأخير وتزول في كثير من النساء في الأسبوع الثاني عشر وفي معظم النساء بحلول الأسبوع العشرين من الحمل.

الهدف من البحث: تقييم المقارنة بين الإصابة بالجرثومة الحلزونية في النساء اللاتي تعانين من القيئ المستعصي مقارنة بالحمل الطبيعي.

المريضات وطرق البحث: تم إجراء الدراسة بمستشفيات جامعة الأزهر القاهرة (الحسين وسيد جلال).

وقد شملت الدراسة ٦٠ سيدة من السيدات الحوامل الأقل من الأسبوع السادس عشر من الحمل حيث تم تقسيمهن إلى مجموعتين :

• **المجموعة الأولى:** الحالات وهن النساء الحوامل اللاتي تعانين من قيئ مستعصي مع الحمل وتم حجزهن بالقسم الداخل بالمستشفى.

• **المجموعة الثانية:** مجموعته المقارنه واللاتى تم إختيارهن عشوائياً من بين الحوامل اللاتي تترددن لمتابعة الحمل بعيادة الحوامل بمستشفى الحسين والسيد جلال واللاتي في نفس عمر الحمل وفي نفس سن الحالات .

وقد امتدت مدة الدراسة من نوفمبر ٢٠١٨ – مايو ٢٠١٩

النتائج : وجدت الدراسة الحالية فرق كبير بين مجموعتين فيما يتعلق بإيجابية HPSA وقد تم العثور على مستضد البراز الإيجابي بنسبة ٨٦,٧% في النساء اللاتي تعانين من القئ المستعصي مقارنة مع مجموعة المقارنة بنسبة ٣٦,٧% والفرق كبير إحصائياً بين المجموعات المدروسة فيما يتعلق الأجسام المضادة بالبكتريا الحلزونية، ولم يكن هناك فرق كبير بين القئ المستعصي ومجموعة التحكم من حيث العمر، وأسبوع الحمل، والتكافؤ، والمستوى التعليمي، والحالة الاجتماعية والاقتصادية والتدخين.

الاستنتاج: يوجد ارتباط مهم بين العدوى هيكلوباكتريلور والقئ المستعصي مع الحمل.