

فحص إيجابية مصل الهليكوباكتر بيلوري في حالات القئ المستعصي بالسيدات الحوامل

رسالة

توطئة للحصول علي درجة الماجستير
في التوليد وأمراض النساء

مقدمة من

طبيبة\ ايمان محمد حملي

بكالوريوس الطب والجراحة (٢٠٠٩)

جامعة عين شمس

طبيب مقيم التوليد وأمراض النساء

مستشفى غمرة العسكري للعائلات

تحت إشراف

دكتورة / فكرية احمد سلامة

أستاذ التوليد وأمراض النساء

كلية طب - جامعة عين شمس

دكتور / احمد عادل ثروت

أستاذ مساعد التوليد وأمراض النساء

كلية طب - جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٤

Screening for H.pylori Serum IgG Seropositivity in Hyperemesis Gravidarum Pregnant Ladies

Thesis

**Submitted for Partial Fulfillment of the Master
Degree in Obstetrics and Gynecology**

By

Eman Mohamad Hemally

M.B.B.CH (2009)

Ain Shams University

Resident of Obstetrics & Gynecology

Ghamra Military Hospital

Under supervision of

Dr. Fekrya Ahmad Salama

Professor of Obstetrics & Gynecology

Faculty of medicine - Ain Shams University

Dr. Ahmed Adel Tharwat

Assistant professor of Obstetrics & Gynecology

Faculty of medicine - Ain Shams University

Faculty of medicine

Ain shams university

2014

Acknowledgement

First of all I thank **Allah** for his great mercy and help to complete this work.

I would like to express my deepest gratitude and sincere appreciation to **Prof. Dr. Fekrya Ahmad Salama** professor of obstetrics and gynecology Faculty of Medicine Ain Shams University for her continuous encouragement and valuable advice to bring this work to light.

Many thanks should be expressed to **Dr. Ahmed Adel Tharwat** assistant professor of obstetrics and gynecology Faculty of Medicine Ain Shams University for his tremendous effort he has done in the meticulous revision of this work.

I would like to thank **Dr. Nashwa El Khazragy** consultant of clinical pathology, head of research department Faculty of Medicine Ain Shams University for her sincere help in the laboratory work.

At last, I am indebted for my family

✍ Eman Mohamad Kemally

Contents

Subjects	Page
• List of Abbreviations	I
• List of Tables	II
• List of Figures	IV
• Protocol	
• Introduction	1
• Aim of the Work	4
• Review of literature	
- Chapter One: Maternal gastrointestinal tract adaptation to pregnancy	5
- Chapter Two: Emesis & Hyperemesis gravidarum	10
- Chapter Three: Helicobacter pylori infection & Relation between Helicobacter pylori and emesis gravidarum	63
• Patients and Methods	85
• Results	90
• Discussion	107
• Summary	121
• Conclusion & Recommendations	127
• References	128
• Arabic Summary	

List of Abbreviations

ACG	American College of Gastroenterology
ACTH	Adrenocorticotrophic Hormone
AUC	Area Under the ROC Curve
AU/ml	Absorbance units per milliliter
b.d	Bis in die ‘twice daily’
Cag	Cytotoxin Associated Gene Protein
CI	Confidence interval
COPD	Chronic Obstructive Pulmonary Disease
C-UBT	Carbon Urea Breath Test
ELISA	Enzyme Linked Immuno-sorbant Assay
FDA	Food and Drug Administration
FMIA	Flow Microparticle Immunofluorescence Assay
GERD	Gastroesophageal Reflux Disease
HCG	Human Chorionic Gonadotropin
HG	Hyperemesis Gravidarum
HP	H.pylori /Helicobacter Pylori
HS	Highly Significant
IL	Interleukin
IM	intestinal metaplasia
ITP	Idiopathic Thrombocytopenic Purpura
MALT	Mucosal associated lymphoid tissue
NSAID	Non-Steroidal Anti-Inflammatory Drugs
NVP	Nausea and Vomiting of Pregnancy
PCR	Polymerase Chain Reaction
PPI	Proton Pump Inhibitors
S	Significant
TB	Toluidine blue
Th	T Helper Cell
TNF- α	Tumor Necrosis Factor
Vac A	Virulence Factors Toxin
+PV	Positive Predictive Value
-PV	Negative Predictive Value

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page</i>
Table (01):	Differential diagnosis for hyperemesis gravidarum.	33
Table (02):	Maternal complications of hyperemesis gravidarum.	35
Table (03):	Diatery instructions for nausea and vomiting with pregnancy (NVP).	42
Table (04):	United States FDA Pharmaceutical Pregnancy Categories.	46
Table (05):	FDA classification of drugs for treatment of NVP.	47
Table (06):	Summary of drugs used to treat nausea and vomiting of pregnancy.	57
Table (07):	Mehanism for Helicobacter pylori mucosal injury.	65
Table (08):	Diagnostic tests for helicobacter pylori	78
Table (09):	ACG recommendations for first-line therapy of H. pylori.	81
Table (10):	Patients characteristics in both groups.	90
Table (11):	Obstetric history in both groups.	92
Table (12):	Hematocrit level in both groups.	95
Table (13):	Ketone body analysis in both groups.	96
Table (14):	Biochemical results in cases.	97

<i>Table No.</i>	<i>Title</i>	<i>Page</i>
Table (15):	Quantitative assay of serum H pylori in both groups.	99
Table (16):	Qualitative assay of serum H pylori IgG level in both groups.	100
Table (17):	Receiver-operating characteristic (ROC) curve analysis for classification of patients into those with or without hyperemesis using serum H pylori IgG level.	101
Table (18):	Simple binary logistic regression model for prediction of hyperemesis using an H pylori IgG level >8.85 AU/ml.	102
Table (19):	Simple binary logistic regression model for prediction of hyperemesis using an H pylori IgG level >5.5 AU/ml.	103
Table (20):	Comparison of the areas under the receiver-operating characteristic (ROC) curves derived from the simple binary logistic regression models for prediction of hyperemesis using an H pylori IgG level >8.85 or >5.5 AU/ml.	104
Table (21):	Incidence of hyperemesis-related complications.	105
Table (22):	Study characteristics.	110

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page</i>
Figure (01):	Acupressure point P6 (Neiguan).	44
Figure (02):	Mechanism of action of antiemetics used to treat nausea and vomiting in pregnancy.	48
Figure (03):	Pharmacologic treatment of nausea and vomiting of pregnancy algorithm.	62
Figure (04):	False-color transmission electron micrograph (TEM) of bacterium helicopacter pylori.	63
Figure (05):	Sequential therapy regimens.	82
Figure (06):	Mean age in both study groups.	90
Figure (07):	Mean gestational age in both study groups.	91
Figure (08):	Box plot showing parity in both study groups.	92
Figure (09):	Box plot showing number of previous cesarean sections (CS) in both study groups	93
Figure (10):	Box plot showing number of previous miscarriages in both study groups.	94
Figure (11):	Mean hematocrit level in both study groups.	95

<i>Figure No.</i>	<i>Title</i>	<i>Page</i>
Figure (12):	Result of ketone body analysis in both study groups.	96
Figure (13):	Mean serum sodium (Na ⁺) level in cases.	97
Figure (14):	Mean serum potassium (K ⁺) level in cases.	98
Figure (15):	Mean serum ALT and AST level in cases.	98
Figure (16):	Mean serum H pylori IgG level in both study groups.	99
Figure (17):	Qualitative assay of serum H pylori IgG level in both study groups.	100
Figure (18):	Receiver-operating characteristic (ROC) curve for classification of patients into those with or without hyperemesis using serum H pylori IgG level.	101
Figure (19):	Receiver-operating characteristic (ROC) curve derived from the simple binary logistic regression model for prediction of hyperemesis using an H pylori IgG level >8.85 AU/ml.	102

<i>Figure No.</i>	<i>Title</i>	<i>Page</i>
Figure (20):	Receiver-operating characteristic (ROC) curve derived from the simple binary logistic regression model for prediction of hyperemesis using an H pylori IgG level >5.5 AU/ml.	103
Figure (21):	Comparison of the areas under the receiver-operating characteristic (ROC) curves derived from the simple binary logistic regression models for prediction of hyperemesis using an H pylori IgG level >8.85 or >5.5 AU/ml.	104
Figure (22):	Incidence of hyperemesis-related complications.	106

Introduction

The nausea and vomiting associated with pregnancy usually begins by 9-10 weeks of gestation, peaks at 11-13 weeks, and resolves in most cases by 12-14 weeks. Studies estimate that nausea and vomiting occurs in 50-90% of pregnancies. In 1-10% of pregnancies, symptoms may continue beyond 20-22 weeks (*Bailit, 2005*).

Hyperemesis gravidarum (HG) is characterized by persistent nausea and vomiting associated with ketosis and weight loss (>5% of prepregnancy weight). It may cause volume depletion, electrolytes and acid-base imbalances, nutritional deficiencies, and even death. Severe hyperemesis requiring hospital admission occurs in 0.3-2% of pregnancies (*Goodwin, 2008*).

Prevalence of HG varies from 0.3 to 1.5% of all live births (*Sheehan, 2007*). 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 (*Verberg et al., 2005*). It is the most common cause of hospitalization in the first half of pregnancy and second only to preterm labor for pregnancy overall. It can

be associated with serious maternal and fetal morbidity such as Wernicke's encephalopathy, fetal growth restriction, and even maternal and fetal death (*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 (*Dunn et al., 1997*). Various findings suggest that this organism is also involved in the pathogenesis of cancer and lymphoma of the stomach (*Versalovic et al., 1998*).

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% (*Dunn et al., 1997*).

The action of *H. Pylori* is widely studied in literature and some studies now focus specifically on its association with nausea and vomiting (*Kenneth, 2010*). A possible association between *H. pylori* infection and HG has been the focus of researching for some studies (*Kazerooni et al., 2002*).

Several ways of testing exist. One can test noninvasively for *H. pylori* infection with a blood antibody test, stool antigen test, or with the carbon urea breath test (in which the patient drinks ^{14}C or ^{13}C labelled urea, which the bacterium

metabolizes, producing labelled carbon dioxide that can be detected in the breath). Another method for detecting H. pylori infection is a biopsy check during endoscopy with a rapid urease test, histological examination, and microbial culture (*Stenström et al., 2008*).

In essence, serology samples the entire stomach whereas biopsy only samples a small region, and the inflammatory process may be patchy, so serologic analysis may be more sensitive than diagnostic methods involving biopsy (*Blaser, 2000*). The development of H. pylori-specific fluorescent serum antibody test allows for suitable screening for H. pylori infection and with the ease of his simple, cheap and non-invasive testing, it is possible to detect H. pylori infection in pregnant women (*Kocak et al., 1999*).

Aim of Work

To assess the value of screening for helicobacter pylori seropositivity in hyperemesis gravidarum for better evaluating the condition and improving the cure rate especially in resistant cases of hyperemesis gravidarum.

Question:

In women suffering from hyperemesis ravidarum is the level of H.pylori IgG higher than normal pregnant women?