



Role of Helicobacter pylori in childhood dyspepsia

Thesis

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By

Yosra Mohamed Mohsen

M.B.B.Ch. (2006) M.Sc (2011)

Faculty of Medicine, Ain Shams University

Supervisors

Prof.Dr. Mohsen Saleh El Alfy

Professor of Pediatrics

Faculty of medicine- Ain Shams University

Prof. Dr. Mostafa Abd Al Aziz El Hodhod

Professor of Pediatrics

Faculty of medicine- Ain Shams University

Prof. Dr. Hanaa Ahmed Amer

Professor of Clinical Pathology

Faculty of medicine- Ain Shams University

Dr. Ahmad Mohamed Hamdy

Assistant Professor of Pediatrics

Faculty of Medicine – Ain Shams University

**Faculty of medicine
Ain Shams University**

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ABSTRACT

Introduction: *Helicobacter pylori* infects more than half of the world's population, and it has been linked to several diseases, whether gastric or extragastric. The effect of *H pylori* eradication on functional dyspepsia, had been a matter of debate for a long time, as well as the predictors to the response of eradication.

Aim of the study: To assess the frequency of *H pylori* infection among children with dyspepsia, and to assess the impact of *H pylori* eradication on this disturbance, also to find out a correlation between both the virulence factors of *H pylori* together with host susceptible phenotypes as regarding the blood group antigens, the clinical presentation of the disease and response to eradication therapy.

Patients and methods: a prospective cohort study was conducted in Ain Shams University Children's hospital in the period from July 2012 till July 2014, included 154 patients presenting with dyspepsia. Their ages ranged from 5-17 years, with mean age of 9.09 years (+/-2.01), 72 males (46.7%), and 82 females (53.3%). All patients were subjected to thorough medical history and clinical examination. Modified Glasgow dyspepsia symptom score was used to assess severity of dyspepsia symptoms. Laboratory workup included CBC, iron profile (serum iron, serum ferritin and total iron binding capacity), Blood groups (ABO, Lewis A and Lewis B) and fecal antigen of *H pylori*. All patients underwent upper gastro-intestinal endoscopy, 4 gastric biopsies were taken, one for the rapid urease test, one from the antrum, one from the corpus for histopathology, and another antral biopsy for genotyping of *H pylori* (CagA, VacAs1m1, BabA2 and iceA).

Patients were divided into four groups, organic non H pylori, organic H pylori, functional non H pylori and functional H pylori. Those who had H pylori infection all received eradication therapy and the success of eradication was confirmed by fecal antigen testing. Organic non H pylori group received their specific treatment according to cause, while functional non H pylori group received prokinetics, antacids and psychotherapy in selected cases. All patients were followed up at 6 weeks, 3 months, 6 months and 12 months, and dyspepsia symptom score was applied every follow up visit. CBC and iron profile were repeated at the 3 months follow up visit. By the end of the 12 months, H pylori positive patients were re-classified into totally cured children, controlled with minimal relapses, controlled with stormy bouts, and uncontrolled patients.

Results: *Helicobacter pylori* infection was present in 61 patients (39.6%), 14 of them (23%) showed no evidence of inflammation in endoscopy and histopathology, thus diagnosed as functional dyspepsia, the rest of them (77%), showed various endoscopic and histopathologic findings consistent with organic dyspepsia. The outcome H pylori positive group (organic and functional) was 47% total cure, 38% partial control (control with minimal relapses and control with stormy bouts), and 15% uncontrolled. Those with partial control were considered mixed organic and functional pathology. Genotyping of H pylori for 26 patients with dyspepsia (42.6%) showed: CagA (53.8%), VacAs1m1 (42.3%), BabA2 (57.7%) and iceA1 (30.8%). There was no statistically significant difference between genotypes among organic and functional dyspepsia. Iron deficiency anemia was significantly higher in the H pylori positive group, versus H pylori negative group, Although TIBC and transferrin saturation improved after 3 months, but this happened simultaneously in both groups. Blood group AB was significantly higher, and blood group B was significantly lower in the H

pylori positive patients, than H pylori negative patients. Proportion of Lewis a,b positive (weak secretors) was high in our study population(45%) of dyspeptic patients, and Lewis negative (a-b-) was significantly higher in H pylori negative patients.

We concluded from this study that Eradication of H pylori, totally or partially improves the symptoms of dyspepsia in most of the patients, whether it was causing organic changes on endoscopy or not, which necessities that H pylori dyspepsia would be classified as a different category. No predictors were found for good outcome of dyspepsia except for being organic in nature, a higher dyspepsia symptom score at presentation and drop of dyspepsia symptom score more or equal to 23.08% at 6 weeks, more or equal to 36.36 % at 3 months and more or equal to 41.18 %, at 6 months.



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الطبيبة / يسرا محمد محسن

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تحت إشراف

الأستاذ الدكتور / محسن صالح الألفى

أستاذ طب الأطفال

كلية الطب - جامعة عين شمس

الأستاذ الدكتور / مصطفى عبد العزيز الهدهد

أستاذ طب الأطفال

كلية الطب - جامعة عين شمس

الأستاذة الدكتورة / هناء أحمد عامر

أستاذ الباثولوجيا الإكلينيكية

كلية الطب - جامعة عين شمس

الدكتور / أحمد محمد حمدى

أستاذ مساعد طب الأطفال

كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس

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LIST OF ABBREVIATIONS

¹³C	13 Carbon
5HT1A	5 hydroxytryptamine 1A
ALT	Alanine transaminase
ASA	American Society of Anesthesiologists
AST	Aspartate transaminase
BabA	Blood group antigen binding adhesion
bp	Base pair
CagA	Cytotoxin associated gene A
CagAT4SS	Cag type 4 secretion system
CagPAI	Cag pathogenicity island
CBC	Complete blood count
CCR2	Chemokine C receptor 2
Co₂	Carbon dioxide
CT	Computed tomography
DSS	Dyspepsia symptom score
DU	Duodenal ulcer
EGD	Esophago-gastro-Duodenoscopy
ESPAGHAN	European society for Pediatric Gastroenterology Hepatology and Nutrition
FD	Functional dyspepsia
FGID	Functional gastrointestinal disorders
Fig	Figure
fMRI	Functional magnetic resonance imaging
FUT	Fucosyl transferase

GERD	Gastro-eosophageal reflux disease
GHSR	Growth hormone secretagogue receptor
GI	Gastro-intestinal
GU	Gastric ulcer
H pylori	Helicobacter pylori
H2 receptor	Histamine 2 receptor
Hb	Hemoglobin
HopQ	Helicobacter pylori outer membrane protein HopQ
HopZ	Helicobacter pylori outer membrane protein HopZ
Hp	Helicobacter pylori
Hp D	Helicobacter pylori dyspepsia
HPI	Helicobacter pylori infection
IBS	Irritable bowel syndrome
iceA	Induced by contact with epithelium
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IQR	Interquartile range
ITP	Idiopathic thrombocytopenic purpura
Le	Lewis
Le b	Lewis b
Leb	Lewis B
MALT	Mucosa associated lymphoid tissue
MCP	Monocyte chemoattractant protein
Mgcl2	Magnesium chloride
NASPGHAN	North America Society for Pediatric Gastroenterology Hepatology and nutrition

NPV	Negative predictive value
OD	Organic dyspepsia
OMP	Outer membrane protien
pbp	Penicillin binding protien
PCR	Polymerase chain reaction
PET	Positron emission tomography
PPI	Proton pump inhibitor
PPV	Positive predictive value
QOL	Quality of life
RAP	Recurrent abdominal pain
SabA	Sialic acid binding adhesion
SD	Standard deviation
Sew	Weak secretor
SF	Serum ferritin
TIBC	Total iron binding capacity
UIBC	Unsaturated iron binding capacity
UK	United Kingdom
USA	United States of America
Vac	Vaculating cytotoxin A
Ver	Version
vs	versus
wk	week

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