Role of different types of Helicobacter organisms in hepato gastro-intestinal diseases and malignancies

Essay
Submitted for partial fulfillment of the master degree in Internal Medicine

By Noha Abd Elhamid Elmahdy M.B.B.CH

Under Supervision of

Prof. Dr.Mohsen Moustafa Maher

Professor of Internal Medicine Faculty of Medicine Ain Shams University

Prof. Dr.Emad Ahmed Awad

Professor of Internal Medicine Faculty of Medicine Ain Shams University

Dr. Manal Sabry

Lecturer of Internal Medicine Faculty of Medicine Ain Shams University

Ain Shams University Faculty of Medicine

2009

List of Contents:

Acnowledgment	II
Table of Contents	III
List of Tables	IV
List of Figures	${f V}$
Abbreviations	\mathbf{VI}

Chapter 1:

- Introduction.
- Aim of work.

Chapter 2:

- Helicobacter species.
- Campylobacter species.

Chapter 3:

Bacteriology of Helicobacter pylori, Helicobacter hepaticus and Campylobacter jejuni:

- -Bacteriology of Helicobacter pylori.
- -Bacteriology of Helicobacter hepaticus.
- -Bacteriology of Campylobacter jejuni.

Chapter 4:

Management of Helicobacter Pylori:

- -Diseases caused by Helicobacter Pylori.
- -Diagnosis of Helicobacter Pylori.
- -Treatment of Helicobacter Pylori.

Chapter 5:

Managemen tof Helicobacter hepaticus:

- -Diseases caused by Helicobacter hepaticus.
- -Diagnosis of Helicobacter hepaticus.
- -Treatment of Helicobacter hepaticus.

Chapter 6:

Management of Campylobacter jejuni:

- -Diseases caused by Campylobacter jejuni.
- -Diagnosis of Campylobacter jejuni.
- -Treatment of Campylobacter jejuni.

Chapter 7: Conclusion.

References.

List of abbreviations:

ALT Alanine aminotransferase.

BabA Blood group antigen binding adhesion.

C.jejuni Campylobacter jejuni.

CagA Cytotoxin-Associated Antigen A.

CDT Cytolethal distending toxin.

13C Carbon-13.
DU Duodenal ulcer.

ELISA Enzyme-linked immunoassay. ESR Erythrocyte sedimentation rate.

GBS Guillain-Barré syndrome. H&E. Haematoxylin & Eosin H.pylori Helicobacter pylori.

HIV Human immunodeficiency virus. HLA-B27 Human lymphocyte antigen- B27. HpSA Helicobacter pylori stool antigen. IBD Inflammatory bowel disease.

IgA Immuno globulin A.
IgG Immuno globulin G.
IgM Immuno globulin M.

IL Interleukin.

INOS Inducible nitric oxide synthase.

Leb antigen Lewis b antigen.

LPS Lipopoly saccharides.

MALT Mucosa-associated Lymphoid Tissue

Lymphoma.

NUD Non ulcer dyspepsia.

PCR Polymerase Chain Reaction.
PPIs Proton pump inhibitors.

PUD Peptic ulcer disease.
TD Travelers' diarrhea.
TLR Toll-like receptors.

Vac Vacuolating cytotoxin antigen.

List of figures:

LIST O	i figures:	
Figure	subject	page
1	Scanning electron micrograph of	
	Helicobacter bacteria.	
2	Campylobacter bacteria.	
3	Electron micrograph of H. pylori shows	
	spiral-shaped bacterium. The organism has	
	2 to 6 unipolar, sheathed flagella.	
4	Map showing percentages of population	
	infected with H. pylori as determined by	
	epidemiological studies. Within national	
	populations, rates of infection vary across	
	subsets and can be attributed	
	socioeconomic conditions in childhood.	
5	Prevalence of H pylori infection by age in	
	developing and developed countries.	
6	Campylobacter jejuni is a species of	
	curved, rod-shaped, gram-negative	
	microaerophilic bacteria.	
7	Scanning electron micrograph of	
	Helicobacter hepaticus.	
8	Transmission electron micrograph of H.	
	hepaticus grown in pure culture (A).	
	scanning electron micrograph of an	
	organism with typical H. hepaticus	
	ultrastructure in the intestine of a mouse	
	(B) transmission electron micrograph of H.	
	hepaticus in the liver of a mouse (C).	
	Neutrophilic and mono nuclear cells	
9	infiltration in acute gastritis.	
10	Acute Gastritis (Pangastritis). Gastritis is	
	defined as the presence of mucosal	
	inflammatory changes leading eventually	
	to mucosal atrophy and intestinal	
	metaplasia.	
	•	

Figure	Subject ॄ	Page
11	Infiltration of lymphocytes and plasma	
	cells in chronic gastritis.	
12	Peptic ulcer is a mucosal defect which	
	penetrates the muscularis mucosae and	
	muscularis propria.	
13	Gastric ulcers are most often localized on	
	the lesser curvature of the stomach. The	
	ulcer is a round to oval parietal defect	
	(hole), 2 to 4 cm diameter.	
14	Acute peptic ulcer which has a smooth	
	base and perpendicular borders. These	
	borders are not elevated or irregular.	
	regular but with elevated borders and	
	inflammatory surrounding in the chronic	
	form.	
15	Squamous cell carcinoma of the stomach.	
	suspicious stomach ulass that was	
16	suspicious stomach ulcer that was diagnosed adenocarcinoma of the resected	
	stomach.	
177		
17	Hepatocellular carcinoma, Tumor nodules	
10	are round to oval, grey or green	
18	Hepatocellular carcinoma, poorly	
	differentiated, developed on liver cirrhosis.	
19		
19		
	regenerativeepithelium.Helicobacter pylori.	
20	H.pylori bacteria as seen on Giemsa stain	
20	of stomach biopsy.	
	of stomach blopsy.	

Figure	Subject	page
21	Scanning EM photo of <i>H. hepaticus</i>	
	within cecal crypts.	
22	(a) Characteristic lesions associated	
	with chronic typhlocolitis due to	
	helicobacter hepaticus including	
	extensive infiltration of the lamina	
	propria with mononuclear cells,	
	epithelial cell hyperplasia, and	
	dysplasia (b) Normal cecal-colic	
	junction from a helicobacter-free	
	mouse.	
23	Immunohistochemistry showing <i>H</i> .	
	hepaticus in bile canaliculi (between	
	hepatocytes) of mouse liver	
24	a) Characteristic lesions associated	
	with chronic active hepatitis due to H.	
	hepaticus infection in A/J mice	
	including cholangiohepatitis (upper	
	left white arrow), interface hepatitis	
	(lower right black arrow),	
	hepatocellular dysplasia (black	
	arrowhead), and lobular inflammation	
	(central upper white arrow). b) Inset	
	depicts Warthin-Starry positive	
	organisms	
	Colon section from a pregnant female	
25	SCID/NCr mouse. Warthin-Starry	
	stain reveals many spiral	
	H. hepaticus-like organisms within a	
•	crypt.	
26	Scanning electron microscope image	
	of Campylobacter jejuni, illustrating	
	its corkscrew appearance and bipolar	
	flagella.	

List of Tables:

Table	subject	Page
1	Gastric Helicobacter taxa.	
2	Enterohepatic Helicobacter Taxa.	
3	Association between the presence of	
	H.pylori in the liver and	
	Hepatocellular carcinoma.	
4	Selected Long-Duration Regimens	
	for Helicobacter pylori Eradication.	



Introduction & Aim of the Work

Introduction

Helicobacter pylori organism is a-gram negative spirally curved motile rods. It is associated with an increased risk of peptic ulcer disease development & recurrence, ulcer healing is dependent upon angiogenesis, requiring endothelial cell proliferation & chemotaxis. Helicobacter pylori & jejuni have the ability to inhibit one of the key stages of angiogenesis which have implications in peptic ulcer disease (**Pearce** *et al.*, **2004**).

Also Helicobacter pylori & other Helicobacter organisms present in gall bladder & liver of patients with chronic cholecystitis detected by immunological & molecular methods (**Apostolov** *et al.*, **2007**).

Helicobacter pylori is prevelance in patients with liver cirrhosis and HCC (Leone et al., 2003).

Helicobacter pylori can be detected in association with colorectal neoplasia (Jones et al., 2007).

Campylobacter jejuni is an infrequent cause of self limiting acute diarrhea in adults & occurrence of a-lifethreating diarrhea (**Ryan** *et al.*,2004).

Campylobacter jejuni can cause immunoproliferative small intestinal diseases (in a form of lymphoma) that arises in small intestinl mucosa (Lecuit *et al.*, 2004).

H.hepaticus has a cytolethal distending toxin activity which is a potential virulence of H.hepaticus that may play a role in its pathogenesis of hepatitis & enterocolitis (**Youg** *et al.*, **2000**).

H.hepaticus might be the no. 1 for the gall stone formation that ultimately leads to malignancy or itself acts as a risk factor for pathogenesis of gall bladder carcinoma (**Pradhan** *et al.*, 2004).

Its cytolethal distending toxin (CDTS) containing DNase-like activity can induce dysplastic changes in infected mice livers (Ge et al., 2007).

Aim of work

The aim of this work is to evaluate the role of Helicobacter pylori, Helicobacter hepaticus & Campylobacter jejuni in Hepato gastro-intestinal diseases and malignancies.

List of abbreviations:

ALT Alanine aminotransferase.

BabA Blood group antigen binding adhesion.

C.jejuni Campylobacter jejuni.

CagA Cytotoxin-Associated Antigen A.

CDT Cytolethal distending toxin.

13C Carbon-13.
DU Duodenal ulcer.

ELISA Enzyme-linked immunoassay. ESR Erythrocyte sedimentation rate.

GBS Guillain-Barré syndrome.

H&E. Hematoxin & eosin.H.pylori Helicobacter pylori.

HIV Human immunodeficiency syndrome. HLA-B27 Human lymphocyte antigen B27.

HpSA H. pylori stool antigen.

IBD Inflammatory bowel disease.

IgA Immuno globulin A.
IgG Immuno globulin G.
IgM Immuno globulin M.

IL Interleukin.

INOS Inducible nitric oxide synthase.

Leb antigen Lewis b antigen.
LPS Lipopolysaccharides.

MALT Mucosa-associated Lymphoid Tissue

Lymphoma.

NUD Non ulcer dyspepsia.

PCR Polymerase Chain Reaction.

PPIs proton pump inhibitors.
PUD Peptic ulcer disease .
TD Travelers' diarrhea.
TLR Toll-like receptors.

Vac Vacuolating cytotoxin antigen.



Review of Literature



Genus Helicobacter and Campylobacter

Genus Helicobacter and Campylobacter:

I-Helicobacter Species:

Helicobacter is a genus of Gram-negative bacteria possessing a characteristic helix shape (**Figure 1**) They were initially considered to be members of the campylobacter genus, but since 1989 they have been grouped in their own genus, some species have been found living in the lining of the upper gastrointestinal tract, as well as the liver of mammals and some birds (**Ryan** *et al.*,2004).

Helicobacter organisms are gram –ve curved or spiral shaped, strictly microaerophilic bacilli and motile by means of sheathed flagella. Helicobacter species had several Campylobacter like characters they were separated from the genus Campylobacter on the basis of their unique profile, specific fatty acid specific ultra-structure. quinines, respiratory growth requirements, characteristics and a very different RNA sequence. There are at least 14 species within the genus Helicobacter (Glupenzynski, 1998).