

STUDY OF THE ROLE OF
CAMPYLOBACTER PYLORI IN PATIENTS
WITH NON ULCER DYSPEPSIA

السيد اغد

Thesis

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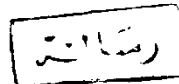
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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

“يَقُولُ يَا عِيسَى ابْنُ مَرْيَمَ تَهَمِّسُ

“صَلِّ عَلَى أَسْمَاءَ الْعَظِيمِ”



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
~~~~~

إلى أستاذي الجليل، الأستاذ الدكتور

محمد حوضي الدين سلام

هذه قطرة من فيض علمكم الغزير .. ارتشفها التردى ظمئاً  
إلى العلم والمعرفة ، ولتكون خطوة في طريق أسير فيه  
بتوفيق من بهد - طريق البحث في موضوع هام سيظل في  
حاجة إلى المزيد استجابة لقول ربنا عز وجل :  
" وَخَفْ أَنْفُسَكُمْ أَفَلَا تُبْصِرُونَ "

وإلى جانب ما استفدته من علمكم لا أنسى الإرشادة  
بأخلاقكم الكريمة .. أخلاق العلماء التي فيها القدوة لكل  
طالب علم ... نفعتنا به بعلمكم وجزاكم خير الجزاء ..

حاتم عبد اللطيف محمد عبد السلام

***To my Father and my Mother  
The earliest teacher in my life  
and to whom who supported me  
all through this work.***

***Hatem Abd El-Latif***

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# ***INTRODUCTION AND AIM OF THE WORK***



## Introduction and Aim of The Work

Since the discovery of the genus *Helicobacter* by Bizzazero in 1893 and the detection of the organism by Krienitze in the human stomach in 1906, many studies have been done to detect the ability of the organism to produce various pathological changes in the gastrointestinal tract, including inflammatory changes of the mucosa, peptic ulcer disease and malignant changes of the stomach.

This study is concerned with the effect of *Helicobacter pylori* in pathogenesis of non ulcer dyspepsia.

## ***REVIEW OF THE LITERATURE***

## **A- Helicobacter Pylori**

### **Historical Background About Helicobacter Pylori:**

The earliest description of an organism present in the stomach was that done by *Bizzazero* in 1893 when he studied the mucosa of the stomach of some animals including dogs, frogs and others. He described the presence of spiral organisms within the mucus membrane of the pyloric glands.

In another study done in 1896 by Salmon the spiral organisms were found in the stomach of cats and rats confirming the work of Bizzazero. Until that time the organism was not studied in the human stomach, when Krienitize studied the stomach of the patients with gastric cancer in 1906 and reported the presence of spiral organisms in these patients. In 1924, *Luck and Seth* found the enzyme urease in gastric mucosa of some animals specially cats but this study was of little importance because the biochemical activity of the organism was not studied properly.

In 1940 *Fredbery and Barron* found an association between the organism and both gastric cancer and peptic ulcer disease, but they concluded that the organism is a normal inhab-

itant of the stomach that becomes more prevalent in cases of gastric cancer and peptic ulcer disease. In 1988, *Collin - Jones* did a study on the mucosa of patients with gastric ulcer and they found out the association of gastric ulcer and these organisms in 80% of cases. Furthermore, they studied the histopathological changes and they found that the organisms were phagocytosed by polymorphnuclear leucocytes.

In 1987 *Graham et al* documented the association between *Helicobacter pylori* and the occurrence of peptic ulcer disease.

## Bacteriological Aspects of Helicobacter Pylori

### I- Morphology of H.P.

The outer cell membrane of *Helicobacter pylori* is double layered which is loosely fitted to the cell and has wavy morphology. The cytoplasmic membrane is thick at both polar regions (*Slubert 1984*).

*Helicobacter pylori* has been studied by electron microscopy in 1988 by *Kang et al* and it was found to be curved and sometimes U shaped organism with gram negative staining. It is 2.2 to 3  $\mu\text{m}$  in length and 0.5  $\mu\text{m}$  in diameter. It has unipolar

3-5 sheathed flagellae. This is in contrast to *Helicobacter* *Jejuni* which is 1.4-3  $\mu\text{m}$  long and 0.5  $\mu\text{m}$  in diameter and has bipolar unsheathed flagellae.

## II- Taxonomy of *Helicobacter pylori*

Five different species of *Helicobacter* are listed in Bergeys manual 1974, *H. Fetus*, *H. Jejuni*, *H. coli*, *H. Sputorum* and *H. Consisus*.

*H. fetus* is divided into two subspecies, *H. fetus* subspecies *fetus* and *H. fetus* subspecies *venerealis*.

*H. coli* and *H. jejuni* were previously considered as subspecies of *H. fetus* but DNA studies proved that they are separate species. *H. coli* and *H. jejuni* are identical except in the ability to hydrolyse hippurat, *H. coli* is hippurate negative while *H. jejuni* is hippurate positive. *H. sputorum* is divided into three subspecies. *H. sputorum* subspecies *sputorum*, *H. Sputorum* subspecies *bubulus* and *H. sputorum* *mucosalis* (*Simbert*, 1984). Other newly discovered species include *H. Fecalis*, *H. Laridis*, *H. Cinoedi*, *H. Fennelliae*, *H. Pylori* and *H. Hypointestinalis* (*Weiss feld and Kaplan*, 1987).

**Phenotypic Characteristics of H.P and Other Related Species of Helicobacter**

|                                     | H. pylori | H. coli | H. jejuni<br>biotype I | H. jejuni<br>biotype II | H. nitro-<br>fragilis |
|-------------------------------------|-----------|---------|------------------------|-------------------------|-----------------------|
| Growth at 25°C-28°C                 | -ve       | -ve     | -ve                    | -ve                     | +ve                   |
| Growth at 42°C                      | -ve       | +ve     | +ve                    | -ve                     | -ve                   |
| Nitrate reduction                   | -ve       | +ve     | +ve                    | -ve                     | +ve                   |
| Alkaline phosphatase<br>activity    | +ve       | -ve     | ???                    | -ve                     | -ve                   |
| Glutamyl amino<br>peptidase         | +ve       | -ve     | -ve                    | +ve                     | +ve                   |
| Urease activity                     | +ve       | -ve     | -ve                    | -ve                     | +ve                   |
| Susceptability to<br>nalidixic acid | Resist    | Suscept | Suscept                | Suscept                 | Suscept               |

**III- Ecology of Helicobacter Pylori**

It is well known that Helicobacter pylori prefers to settle in the mucosal layer of the stomach specially the pyloric antrum (*Rollason et al*, 1984).

An important factor in the survival of H.P in the acidic medium of the stomach is the presence of flagellae which enable the bacterium to travel within the mucosa where it has a predilection to the space overlying the intercellular junction. A microenvironment where it gains nutrition from metabolites

and growth factors which diffuse from the host (*Axon*, 1988). Another important factor in the protection of H.P from the acidic medium is the overlying mucus and the secretion of bicarbonate by the underlying cells (*Axon*, 1988). It was noted by *Rollason et al*, 1984 that H.P does not exist except in areas of gastric epithelial cells and areas of gastric metaplasia in the duodenum but never in areas of intestinal epithelium or intestinal metaplasia in the stomach so there may be specific receptors for H.P in the gastric epithelium. However the presence of these receptors has not been established yet (*Tytgat*, 1988).

In 1987, *Marshall and Goodwin* studied the effect of PH on the survival of H.P and reported that the organism can survive well in PH of 4-4.5 but survival is reduced at PH of 3.5 and the addition of 5 mmol of urea protected H.P at PH values down to 1.5. It is well known that the organism protects itself by a cloud of ammonia thus creating microenvironment which has a relatively high PH (*Axon*, 1988).

In a study done in 1987 by *Tompkin and West* H.P and H.J have been cultured on blood agar plate containing beef bile for 72 hour in proper condition. H.J had survived in bile concentration up to 10% but H.P was inhibited at bile concentration of