Gastrin level in patients with Helicobacter pylori dyspepsia

Thesis
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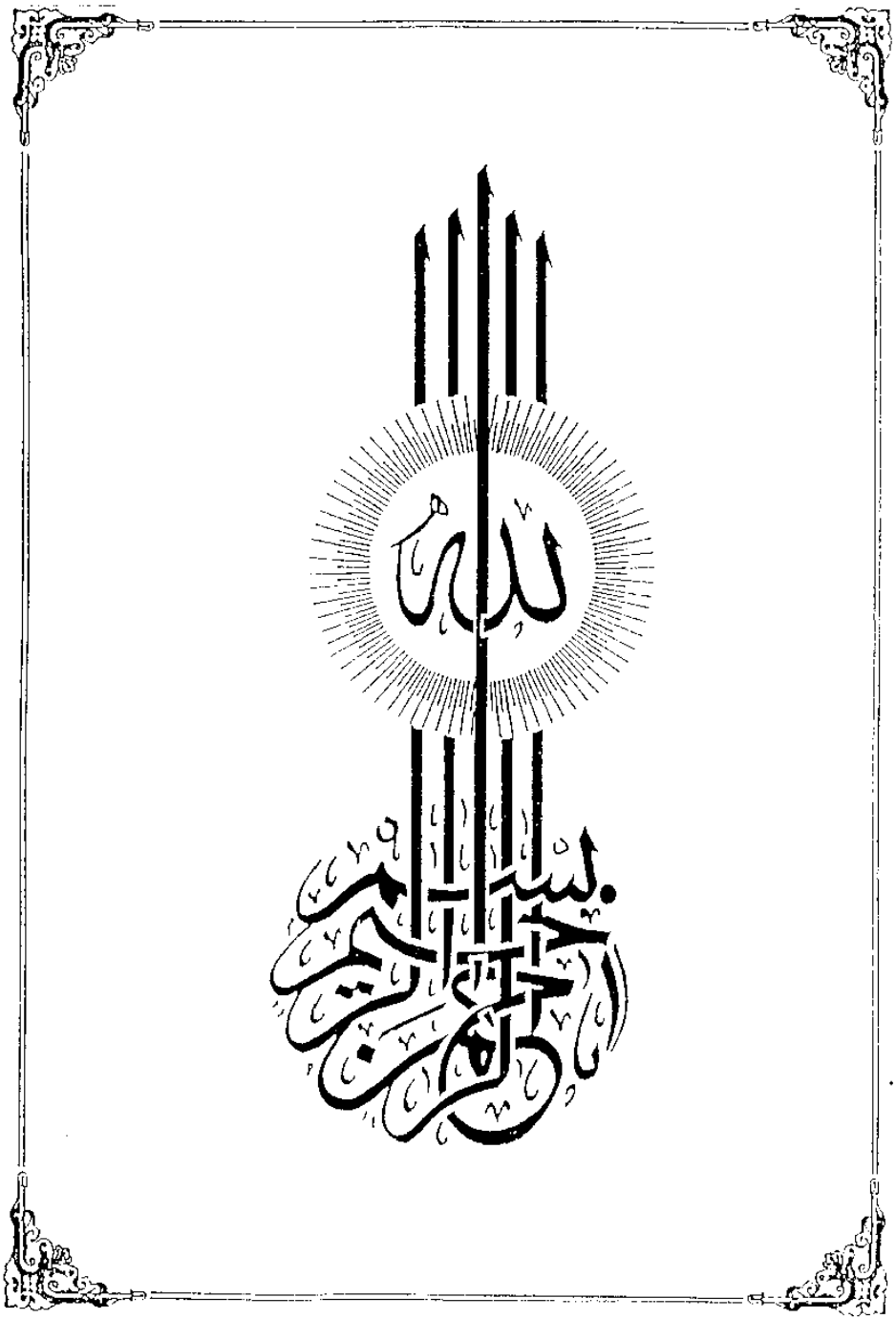

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List of abbreviations

Abbreviation	Full name
AP	Aminopyrine uptake
APUD	Amino precursor uptake and decarboxylation
BBG	Big big gastrin
C. jejuni	Cambylobacter jejuni
CCK	Cholecystokinin
CFA	Colonization factor antigens
DNA	Deoxyribo-nuclic acid
DU	Duodenal ulcer
ELISA	Enzyme linked immunosorbent assay
G-cells	Gastrin cells
GU	Gastric ulcer
H. pylori	Helicobacter pylori
IMX	Isobutyl methyl xanthin
NSAIDs	Non steroidal anti-inflammatory drugs
PPU	Pre-pyloric ulcer
RIA	Radioimmunoassay
RNA	Ribo-nucleic acid
SGV	Selective gastric vagotomy

Introduction and Aim of work

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Introduction :-

Despite extensive research, the cause of peptic ulceration is still not known. It is generally accepted that peptic ulcers result from an imbalance between aggressive factors and intimate mucosal protective mechanisms ***(Levi et al., 1989).***

Investigations are paying increasing attention to factors that might weaken the defense of gastric and duodenal epithelium. In the last 7 years, attention has been directed at the organism H. pylori, that inhabits the area between the mucus layer and the underlying gastric epithelium in virtually all patients with active, chronic gastritis, and duodenal ulcer disease ***(McKinlay et al., 1990).***

The pathogenicity of the bacteria is multifactorial, of these factors, hypergastrinemia is now an important factor especially in the pathogenesis of peptic ulceration. Thus, patients positive for H. pylori have abnormalities in the regulation of gastrin release that may be the link between H. pylori and duodenal ulcer, as gastrin stimulated acid secretion is increased in patients positive for H. pylori with or without duodenal ulcer, but more so in duodenal ulcer patients, and eradication of H. pylori leads to a reduction in gastrin-mediated acid secretion ***(McColl et al., 1989 & El-Omar et al., 1993).***

Aim of the Work :-

The aim of this work is to correlate between serum gastrin level and H. pylori infection in patients with dyspepsia.

Review of Literature

Review of Literature

Helicobacter Pylori

Hisiorical Background :-

In *(1893) Bizzozero* described the microscopic appearance of gastrointestinal epithelium in a number of animals, which included lizards, frogs, and dogs. He described spiral organisms within the dog stomach, seen mainly in the mucous layer,, but also invading the lumen of the pyloric glands.

In *(1896) Salomon* confirmed Bizzozero's work and showed that spiral organisms were also present in cats and rats.

Spiral bacteria were first reported in humans by *Krientz* in *(1906)*, who isolated "spirochaetes" from the stomach of a patient with gastric carcinoma. Until this time, the organism has been considered to be a commensal.

Kasai and Kobayashi, (1919) transmitted canine spirochaetes to a series of animals and were able to induce hemorrhagic erosions in rabbits and guinea pigs. They also showed that the organisms could be eliminated by Salvarsan (an arsenical compound used to treat syphilis and other spirochaetal infections).

In *(1938)* ***Doenges*** found spirochaetes in 43% of 242 human stomach's in post-mortem. He also found spiral bacteria in all of a series of 43 monkeys.

Two years later, ***Freedbourg and Barron, (1940)*** associated the organism with gastric cancer and peptic ulcer, but they concluded that they were merely natural inhabitants of normal human gastric mucosa, becoming more prominent when gastric pathology was present, presumably as a secondary effect.

In *(1954)* ***Palmer*** extensively examined human gastric section biopsies and suggested that the previously recognized spirochaete like structures were oral flora only colonizing the gastric ulcer or in post-mortem specimens

Using the fiber-optic techniques, ***Stear and Collin-Jones, (1975)*** observed Gram-negative bacilli under the mucous layer in 80% of their patients with gastric ulcer, but not on normal mucosa. They noticed that these bacteria cause ultrastrucural changes within the cell and were seen to be phagocytosed by polymorphnuclear leukocytes. It was only, recently however, that the significance of gastric spiral organisms was recognized by ***Warren and Marshall*** in *(1983)* who identified the previously detected curved bacilli on the gastric epithelium of the majority of patients with active chronic gastritis by Warthin starry silver stain.

Morphologically and in respect to their atmospheric requirements and DNA base composition, these organisms were most closely related to the genus Campylobacter ***(Marshall and Warrens, 1984).***

The new organisms were originally called Campylobacter-like organisms (CLOS), later Campylobacter pyloridis (C. pyloridis), while more recently, they were named Helicobacter pylori (H. pylori) ***(Maddocks, 1990).***

Graham et al., (1987) documented the association between H. pylori and gastric ulcer, duodenal ulcer, non-ulcer dyspepsia, gastritis, and gastric carcinoma.

The microbiology of Helicobacter pylori :-

• Morphology :-

H. pylori organisms are small, curved or spiral shaped, Gram-negative bacteria that are found only on the luminal surface of the gastric mucosa and within the gastric pits, but rarely invade the underlying tissues ***(Rollason et al., 1984).*** It is mainly inhabitating the antrum and body of the human stomach. It is especially adapted for life in the environment of overlying gastric epithelial cells, where it is protected from gastric acid by a combination of overlying mucus and secretions of bicarbonate. The single flagellum enables it to inhabit within this zone, where it has a predilection for the space overlying the intercellular junctions, a

microenvironment where it probably gains nutrition from metabolites and growth factors which diffuse from the host *(Axon, 1988)*.

The organism is not associated with any other type of epithelial cells, being absent from areas of intestinal metaplasia and goblet cells. When found in the duodenum, it occurs only in areas of gastric metaplasia *(Rollason et al., 1984)*. This may suggest the presence of specific receptors for H. pylori in gastric cells that are absent from cells of small intestine, although the existence of these receptors has to be documented *(Tytgat, 1988)*.

It is to be noted that, H. pylori appears as slender, curved, spiral or S-shaped gram-negative organisms in fresh specimens of gastric mucus *(Marshall et al., 1984)*.

• Strains of H. pylori :-

Burnie et al., (1988) studied different strains of H. pylori and using immunological techniques, divided the isolates into nine types. Two groups comprised 2/3 of all the isolates. Type (1) being formed in cases of mild, moderate, or severe gastritis, whilst type (2) was also isolated from patients with normal mucosa, 82% of type (1) compared to 59% of type (2) came from patients with moderate or severe gastritis, which suggest that not every strains of H. pylori is equally virulent.

• Virulence of H. pylori :-

The virulence factors of H. pylori are currently under study, but the organisms are ideally suited to survive in the hostile environment of the stomach and duodenum ***(Bode et al., (1988)*** Alterations in the surface mucous cells associated with H. pylori attachment include a reduction in mucus content, and increase in lumax flavus agglutinin binding, suggesting that contact with H. pylori "demask" glycoproteins on the surface mucosal cells, resulting in a decrease in neutral carbohydrates and an increase in sialic acid rich glycoproteins.

Helicopacter pylori cells are surrounded by two nm diameter flexible fibrillar structures. ***Graham, (1989)*** postulated that these fibrillar structures contain the colonization factor antigens (CFA) that allowed H. pylori to attach to the epithelium. Antibodies to the CFA are also found in the serum of individuals with H. pylori infection.

Helicobacter pylori urease is another virulent factor. It has been postulated that ammonia (or ammonium ions) produced by ureas might injure duodenal epithelium. Other virulent factors derived from media in or on which H. pylori have been grown have been described. One of these factors appears to be a protein that causes non-lethal vaculation of a number of tissue culture cell lines ***(Leunk et al., 1988).*** The other factor is a protease that partially degrades mucus glycoproteins ***(Slomiany et al., 1992)..***

Table (1);

Helicobacter pylori virulence factors

1- Motility

2- Ability to withstand acid

3- Urease

4- Fimbirial adhesions

5- Soluble product (toxins)

a- Chemotaxis

b- Protease

C- Others

Tytgat, (1988)

• Culture media :-

Helicobacter pylori can be cultured from gastric biopsy specimens using both selective ***(Goodwin et al., 1985b)*** and also non-selective media ***(Jones et al., 1986).***

Non-selective media such as blood agar or chocolate agar were commonly used in the past in an attempt to isolate this organism which could explain some of the low detection rates. Isolation has now been simplified by using selective media such as Marshall's selective brain heart infusion (BHI) blood agar medium ***(Tytgat, 1989).***