

Increase serum leptin level in *Helicobacter pylori* infection in Iraqi gastritis patients

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Abstract

Background: *H.pylori* colonized gastric mucosal epithelium will virtually develop gastritis and had the capacity to persist for decades. Pathogenesis is dependent upon strain, virulence host genetic susceptibility, and environmental cofactors. Leptin is a member of the class 1 cytokine family so altered leptin production during infection and inflammation that leptin part of the cytokine cascade, which orchestrates the defense mechanism.

Objective: Examine the effect of *H.pylori* infection on serum leptin level.

Methods: One hundred and thirty(130) Patients attending the Endoscopic Unit at "Gastroenterology and Hepatology Teaching Hospital/ Baghdad Medical City" were included in this study with ages range from 18 years to 65 years are the source of specimens to undergo oesophageal gastroduodenoscopy (OGD)

compared with twenty healthy control the study began from April 2009 to the end of March 2010 were eligible for this study. Two types of samples were taken, biopsy for rapid urease test and histopathological examination to detect *H.pylori* and blood sample for estimation of serum leptin by ELISA test.

Results: The results show significant increase in serum leptin concentration ($P < 0.001$) in gastritis patients caused by *H.pylori* compared with patients control and healthy control.

Conclusion: Increase of serum leptin concentration explained the role of leptin in the immune response to *H.pylori* infection that leptin consider as member of cytokine.

Keywords: Leptin, *H.pylori*, gastritis.

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Introduction:

Helicobacter pylori infection was usually acquired in childhood by feco-oral or oral-oral transmission and humans represent the natural hosts for infection⁽¹⁾. The clinical manifestations usually occur later in life when patients present with (gastritis, peptic ulcer, or gastric cancer) *H. pylori* infection is associated also with the development of a chronic active gastritis⁽²⁾. The development of these abnormalities is dependent on the virulence of the infecting strains and the host's genetic predisposition. This is clinically relevant to the development of different disease entities (ulcers or carcinoma)⁽³⁾.

Leptin, the *ob* gene product, its identification in 1994, it is a 16-kD protein synthesized mainly by the adipose tissue (adipocytes)⁽⁴⁾. Leptin is a pleiotropic bioactive molecule^(5,6). Contrary to initial reports, leptin production is not restricted to adipocyte, It is also detected in human placenta, muscles and gastric chief cells.

Leptin is a member of the cytokine family, its receptor is a member of the gp130 group of cytokine receptors its receptors has been found in the human gastric mucosa⁽⁷⁾ and it has been reported to activate the peripheral immune system⁽⁸⁾.

Leptin expression has been detected in gastric epithelium. However the physiologic role of gastric leptin remains unknown⁽⁶⁾. Secretion of leptin by gastric mucosa has provoked interest in its role in gastrointestinal tract. On the other hand, changes in gastric and serum leptin levels in *Helicobacter pylori* infected patients have been the subject of several investigations with controversial results⁽⁷⁾. Since the leptin receptors are present ubiquitously in the stomach, most studies on leptin level and its correlation with healing have been done on gastric ulcers. Leptin has been shown to exhibit similar effects to cholecystokinin (CCK) cytoprotective activity against acute gastric lesions⁽¹⁰⁾. It is released endogenously and exerts a potent gastro protective action⁽¹¹⁾. However the physiological significance of leptin in the stomach and its

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contribution to gastric mucosal integrity remains unknown, leptin is a strong regulator of T cell⁽¹²⁾. The higher serum leptin level in patients with gastritis as compared to normal individuals may indicate a role of leptin in the immune response to *H. pylori* infection. It is not known why *H. pylori* infection induced DU in some individuals⁽¹³⁾. Besides the role of the chemokines such as interleukin-8(IL-8) leptin, through regulating T cells response to *H. pylori* may play a role in clinical outcome of infection. In addition to almost proven gastroprotective characteristics of leptin it may also exert some duodenoprotective effects in particular, and it might have a healing effect on ulcer of any kind. Alternatively leptin might had a role in the regulation of immune response to *H. pylori* infection and consequently its clinical outcome⁽¹⁴⁾.

Methods:

Study Groups: Two groups were studied:

1- Patients Groups: 130 Patients attending the Endoscopic Unit at "Gastroenterology and Hepatology Teaching Hospital/ Baghdad Medical City" were included in this study with ages range from 18 years to 65 years are the source of specimens to undergo oesophageal gastroduodenoscopy (OGD) from April 2009 to end of March 2010 were eligible for this study. They were all suffering from clinical manifestation of gastritis. The diagnosis was based on the clinical and endoscopy examination under supervision of physicians or surgeon specialists.

The exclusion criteria were patients taking a proton pump inhibitors, H2-blockers, within past 2 weeks had received bismuth compounds, antibiotics, eradication therapy for *H. pylori* and administration of non-steroidal anti inflammatory drugs (NSAID).

2-Control healthy group: 20 healthy individuals were included in the study. They were 11 males and 9 females with mean age range 18-65 years. Samples were collected from healthy subjects only if they were not receiving any medications. They have no previous history

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of any complain of gastrointestinal trac(GIT) disease and clinically no signs, and gave no smoking or alcohol history.

From each fasting patient 5 ml of venous blood was collected. All fasting blood was taken before endoscopy. Serum samples were obtained for detection leptin by DRG leptin enzyme immunoassay Kit provides materials for the quantitative determination of leptin in serum.

Multiple antral biopsies (3-5) specimens were collected; the one tested by rapid urease test and the other was used for histological examination was placed in 10% formalin and sent for standard histopathologic examination for detection *H. pylori*.

Statistical analysis:

Data were translated into a computerized database structure. An expert Statistical advice is sought for Statistical analysis was done using SPSS version 17 computer software (Statistical package for social sciences).

Results:

Age, and Gender distribution: Age and gender distribution of the studied groups were shown in table 1. A total 130 patients distributed as females 56(43.1%) and males 74(56.9%) with GIT symptoms distributed as (110) suffered from gastritis caused by *H. pylori* termed as HP+ve and twenty patients termed as HP-ve compared with twenty healthy controls distributed as females 9(45.0%) and males 11(55.0%), there was significant differences between females and males according to chi-square test. Age ranged from >20 to ≥ 60 years that distributed as >20 years represented 4(3.1%), 20-29 represented 26(20%), 30-39 represented 29(22.3%), 40-49 represented 24(18.5%), 50-59 represented as 25(19.2%) and ≥ 60 as 22(16.2%), while the healthy control group distributed as <20 represented 1 (5.0%), 20-29 represented 5(25.0%), 30-39 counted as 4(20.0%), 40-49 counted 7(35.0%), 50-59 represented 2(10.0%) and ≥ 60 counted 1(5.0%) there was significant differences (5.396) between age groups (table.1).

Table (1) Age and sex distribution in *H.pylori* infection

		Groups No.			
		GIT=130		Control No.=20	
Sex	Male	No.	%	No.	%
		Female	74	56.9%	11
Age (years)	(<20)	56	43.1%	9	45.0%
	(20—29)	4	3.1%	1	5.0%
	(30—39)	26	20.0%	5	25.0%
	(40—49)	29	22.3%	4	20.0%
	(50—59)	24	18.5%	7	35.0%
	(≥60)	25	19.2%	2	10.0%
Total		22	16.9%	1	5.0%
		130	100%	20	100%

Serum Leptin levels with *H.pylori* infection:

The results of serum leptin levels with *H.pylori* infection in correlation with age and sex are shown in Table 2. There was no difference in prevalence of *H.pylori* between age

and sex groups. Serum leptin levels was significantly higher ($p < 0.001$) in gastritis patients caused by *H.pylori* than in gastritis caused by another causes and in healthy control groups.

Table (2) Correlation between *H.pylori* infection , serum leptin level, ages and sex in patients with gastritis.

Age (years)	HP Positive				HP Negative				Control				
	Mean	SE	Min	Max	Mean	SE	Min	Max	Mean	SE	Min	Max	
	42.31	1.32	17.00	65.0	38.30	3.43	18.00	65.0	37.40	2.72	18.0	60.0	
Leptin (ng/ml)	male	17.38	1.53	0.08	68.25	2.61	0.3	0.3	6.36	3.37	0.48	0.39	1.68
	female	9.6	6.7	0.30	26.8	1.20	.043	0.20	1.32	2.32	0.233	0.23	1.23

Serum leptin level was significantly ($p < 0.001$) higher in patients with gastritis (11.60 ± 8.69

ng/ml) than normal group (3.97 ± 1.90 ng/ml) (Table 1).

Discussion:

Leptin is a member of the class 1 cytokine family so altered leptin production during infection and inflammation will alter defense mechanism. Leptin has been shown to exhibit similar effects to cholecystokinin (CCK) cytoprotective activity against acute gastric lesions^(10,12). It was released endogenously by cholecystokinin (CCK) or meal and depending on vagal activity, exerts a potent gastroprotective action.^(11,12) However, the physiological significance of leptin in the stomach and its contribution to

gastric mucosal integrity remains unknown. The study shows that there was no correlation between serum leptin level in gastritis patients and sex, presence of *H. pylori* infection and gastritis (Table 2). This study showed that during active gastritis, serum leptin is raised in humans (Table 1). This is probably a defense mechanism related to the release of gastric leptin both into the lumen and circulation⁽⁹⁾. In addition to its critical role in energy expenditure, leptin was a strong regulator of cells⁽¹⁶⁾. The higher serum leptin level in patients with

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gastritis as compared to normal individuals may indicate a role of leptin in the immune response to *H. pylori* infection. Such as interleukin 8, 17, 18 leptin through regulating T cells response to *H. pylori* may play a role in clinical outcome of infection. Further investigations needed to confirm this hypothesis⁽⁸⁾.

We concluded that in addition to almost proven gastroprotective characteristics of leptin, it might also exert some duodenoprotective effects and it might have a healing effect on ulcer of general. Leptin may have a role in the regulation of immune response to *H. pylori* infection and consequently its clinical outcome. Our findings help understanding of the of gastritis which may lead to development of more effective treatments.

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