

# Serum Leptin Level in Patients with Duodenal Ulcer

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## Abstract

**Background:** Leptin and its receptors have been found in the human gastric mucosa. Its secretion by gastric mucosa has generated interest in its probable role in the gastrointestinal tract and pathophysiology of diseases.

**Objective:** To determine any possible correlation between serum leptin level and pathological findings in patients with duodenal ulcer (DU).

**Methods:** In a cross-sectional study, 22 patients diagnosed as DU were randomly selected and compared with 22 healthy controls. From each participant a fasting blood sample for measurement of serum leptin level and anti-*H. pylori* antibody IgG was taken. Two antral biopsies for evaluating the intensity of gastritis and *H. pylori* infection were also taken from patients with DU.

**Results:** Compared to the control group, serum leptin level was significantly ( $p < 0.05$ ) higher in patients with DU. Leptin level also significantly ( $p < 0.05$ ) correlated with the presence of gastritis and *H. pylori* infection.

**Conclusion:** An increase in serum leptin in patients with DU may be a defense mechanism. There is a possibility that leptin accelerates ulcer healing.

**Iran J Med Sci 2004; 29(1):5-8.**

**Keywords** • Leptin • Duodenal ulcer • *H. pylori* • gastritis

## Introduction

**L**eptin, a 16-kDa product of *ob* gene, is a pleiotropic hormone that is involved in the regulation of food intake, body weight and energy expenditure.<sup>1</sup> It signals nutritional status to the central nervous system and peripheral organs.<sup>1</sup> Since its discovery,<sup>2</sup> leptin has been implicated in many functions both in health and disease states.<sup>2</sup> Recently, leptin expression has been detected in gastric epithelium. However, the physiologic role of gastric leptin remains unknown.<sup>3</sup>

Secretion of leptin by gastric mucosa has provoked interest in its role in gastrointestinal tract. In animal models gastroprotective effect of this hormone has been demonstrated.<sup>4</sup> On the other hand, changes in gastric and serum leptin levels in *Helicobacter* infected patients have been the subject of several investigations with controversial results.<sup>3,5,6</sup>

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	Duodenal ulcer	Control
Mean±SD age (yrs)	35.45±12.11	35.71±11.24
Sex (M/F)	10/12	10/12
BMI* (kg/m <sup>2</sup> )	22.50±4.10	22.85±3.35
Serum leptin** (ng/ml)	11.60±8.69	3.97±1.90
<i>H. pylori</i> OD***	1.90	1.85

\*Body mass index

\*\**P*<0.001

\*\*\*Optical Density Value

In some reports, *H. pylori* infection significantly increased gastric leptin expression.<sup>3</sup> Cure of infection significantly reduced this over-expression with a concomitant increase in body mass index.<sup>3</sup> However, the latter has been debated in more recent reports that indicated serum leptin level did not change significantly after curing *Helicobacter* infection.<sup>6</sup> The role of leptin in the inflammatory response is further strengthened by the findings that in interleukin-1 $\beta$  deficient mice no increase in leptin production was found after an inflammatory stimulus<sup>7</sup>.

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. The aim of this study was to determine any possible correlation between leptin and duodenal ulcer (DU).

### Patients and Method

In a cross-sectional study, from April 2001 to April 2003, all patients referred to our center for upper endoscopy were treated as our sampling frame. Twenty-two patients with endoscopically-proven DU were randomly selected. During endoscopy two biopsies were taken from the antrum and sent to the laboratory for histological evaluation. Twenty-two age- and sex-matched healthy individuals who had referred for check-up and had no gastrointestinal complaints were also selected as comparison group. An informed written consent was obtained from each participant. Excluded from the study were those on NSAIDs, those who had used proton pump inhibitors or antibiotics in the previous month, any patient with concomitant systemic diseases including diabetes mellitus, asthma, renal or liver failure, patients with a body mass index (BMI) >30 kg/m<sup>2</sup>, patients with diagnosis of major depression, psychosis, anorexia nervosa, bulimia nervosa, those on regular antipsychotic or antidepressant drugs, patients with heartburn as their predominant complaint and/or endoscopic findings of erosive esophagitis, patients with typical history of biliary colic and/or gall-stone on their abdominal sonography, patients with prior

Variable	n	Serum leptin (ng/ml)
Sex	22	
Male	10	12.26±6.90
Female	12	10.64±6.80
<i>H. pylori</i>	22	
Absent	3	9.70±1.52
Present	19	12.16±7.47
Gastritis	22	
Absent	1	4
Present	21	11.96±8.93

history of gastroduodenal surgery and pregnant or lactating women.

### *H. pylori* serology, leptin, and pepsinogen I determination:

Overnight fasting blood samples were obtained from all patients and the comparison group at 8:00 am. The specimens were stored at -20 °C. Anti *H. pylori* IgG antibody was determined semi-quantitatively by enzyme-linked immunoassay (ELISA, Diagnostic system laboratories, USA) according to the manufacturer's instruction. The sample was considered positive when the ratio between the average optical density (OD) of the sample and that of the cut off value was above 1.1.

The serum leptin levels were determined using sandwich leptin solid phase ELISA (DRG-instrument GmbH-Germany).

### Histopathology:

Endoscopically obtained biopsies were stained with hematoxylline and eosin and were reported by a pathologist who was blinded to clinical and endoscopic findings. Severity of inflammation was graded according to modified Sydney classification and *H. pylori* density in antrum was scored according to Sheu's classification.<sup>8,9</sup>

### Statistical Analysis:

All data were analyzed SPSS (Chicago, IL) software, version 10.0, and MS Excel (Microsoft, Redmond, WA) software. Student t-test, one-way and two-ways ANOVA, Kolmogorov-Smirnov test was used for statistical analyses, when appropriate. Values were expressed as mean±SD. *P* values of less than 0.05 were considered significant.

### Results

Twenty-two patients (10 males and 12 females) with a mean age of 35 years, and 22 controls (10 males and 12 females) participated in the study. The characteristics of patients and the comparison group are shown in Table 1. There was no difference in prevalence of *H. pylori* infection between the two

groups. Serum leptin level was significantly ( $p < 0.001$ ) higher in patients with DU ( $11.60 \pm 8.69$  ng/ml) than normal group ( $3.97 \pm 1.90$  ng/ml) (Table 1). Correlation between serum leptin level, sex, presence of gastritis and *H. pylori* infection in DU patients are shown in Table 2.

## Discussion

Leptin has been shown to exhibit similar effects to cholecystokinin (CCK) cytoprotective activity against acute gastric lesions.<sup>10-12</sup> It is released endogenously by CCK or meal and depending on vagal activity, exerts a potent gastroprotective action.<sup>11,12</sup> However, the physiological significance of leptin in the stomach and its contribution to gastric mucosal integrity remains unknown. The possible mechanisms may be firstly, inducing hyperemia probably mediated by increasing the production of NO due to up-regulation of constitutive and inducible NO synthase and secondly, through up-regulating tissue growth factor alpha.<sup>10-12</sup> These effects are probably unrelated to endogenous prostaglandins<sup>10-12</sup>

In this study, there was no correlation between serum leptin level in DU patients and sex, presence of *H. pylori* infection and gastritis (Table 2). This study showed that during active DU, 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.

In addition to its critical role in energy expenditure, leptin is a strong regulator of T cells.<sup>16</sup> The higher serum leptin level in patients with DU 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 induces DU in some individuals.<sup>17</sup> Besides the role of the chemokines such as interleukin 8,<sup>17-18</sup> leptin, through regulating T cells response to *H. pylori* may play a role in clinical outcome of infection. Further investigations are needed to confirm this hypothesis.

We conclude that in addition to almost proven gastroprotective characteristics of leptin, it may also exert some duodeno-protective effects in particular, and it might have a healing effect on ulcer of any kind, in general. Alternatively leptin may have a role in the regulation of immune response to *H. pylori* infection and consequently its clinical outcome. Our findings may help in better understanding of the pathogenesis of DU which may lead to development of more effective treatments.

## Acknowledgement

This work was partly supported by a grant from Research Council Shiraz University of Medical Sciences.

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