



## Is there a Relationship between *Helicobacter pylori* and Urotensin-II in Peptic Ulcer Patients?

Ahmet Uyanikoglu<sup>1\*</sup>, Çiğdem Cindoglu<sup>2</sup>, Umut Sert<sup>2</sup>, İsmail Koyuncu<sup>3</sup> and Necati Yenice<sup>1</sup>

<sup>1</sup>Gastroenterology, Medical Faculty, Harran University, Sanliurfa, Turkey

<sup>2</sup>Internal Medicine, Medical Faculty, Harran University, Sanliurfa, Turkey

<sup>3</sup>Biochemistry, Medical Faculty, Harran University, Sanliurfa, Turkey

\*Corresponding Author: Ahmet Uyanikoglu, Associate Professor, Gastroenterology, Medical Faculty, Harran University, Sanliurfa, Turkey.

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### Abstract

**Objective:** The aim of this study was to detect the relationship between serum urotensin-II (U-II) levels and *Helicobacter pylori* (*H. pylori*) positive peptic ulcer.

**Materials and Methods:** Between March 2014 and August 2015, peptic ulcer patients (group 1) who had at least two positive tests for *H. pylori* from histopathology, urea-breath test or *H. pylori* stool antigen test and no previous eradication treatment, were compared with the *H. pylori* negative control group (group 2). One tube of blood sample was taken from each patient and stored at -85°C degrees for measurement.

**Results:** The mean age of 76 patients, 36% of whom was female was  $38.0 \pm 13.1$  years in group 1. Group 2 had 33 subjects, 38% of whom was female and their mean age was  $39.0 \pm 15.6$  years in this group. The mean serum U-II level was higher in group 1 than in group 2 ( $5.31 \pm 2.1$  vs.  $2.05 \pm 0.8$  ng/ml,  $p < 0.001$ ).

**Conclusion:** U-II level was significantly higher in *H. pylori* positive peptic ulcer patients than in *H. pylori* negative subjects. We suggest that serum U-II levels might have an importance in the pathogenesis of *H. pylori* positive-peptic ulcer and may be a useful marker in the diagnosis.

**Keywords:** *Helicobacter pylori*; Urotensin-II

### Introduction

*Helicobacter pylori* (*H. pylori*) infection is a common worldwide infection which may lead to peptic ulcer disease and gastric cancer [1]. Gastric colonization with *H. pylori* causes pathologies such as human superficial gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric adenocarcinoma [2]. It was reported that 90% of duodenal ulcers and 70% of gastric ulcers were associated with *H. pylori* infection [3].

Urotensin-II (U-II) is a vascular peptide with potent vasoconstrictor effect, which plays an important role in hypertension, coronary artery disease and vascular remodeling [4,5]. U-II has been found to have angiogenic and prethrotic properties [6]. Recently, strong evidence has shown that U-II and its receptors played a role in the initiation and progression of different epithelial cancers [7].

### Aim of the Study

The aim of this study was to compare serum U-II levels between *H. pylori* positive peptic ulcer patients and *H. pylori* negative control subjects.

### Materials and Methods

#### Demographic characteristics

Between March 2014 and August 2015, 76 peptic ulcer patients (group 1) who had at least two positive tests for *H. pylori* (histopathology, urea-breath test or *H. pylori* stool antigen test) and did not receive previous eradication treatment, were compared with *H. pylori* negative control group who had no peptic ulcer (group 2). One tube of blood sample was taken from each subjects and stored at -85°C degrees for measurement.

We obtained local ethic committee approval and patients' written informed consent. Patients with other inflammatory disorders such as diabetes mellitus, hepatic or renal dysfunction, autoimmunity, and malignancy were excluded.

### Human Urotensin II (U-II) ELISA Kit

Human U-II level was measured in serum with commercially available kits (Elabscience) by using a via microplate reader (Spectra max M5, USA), absorbance was read at 450 nm. Urotensin II levels were expressed as ng/ml.

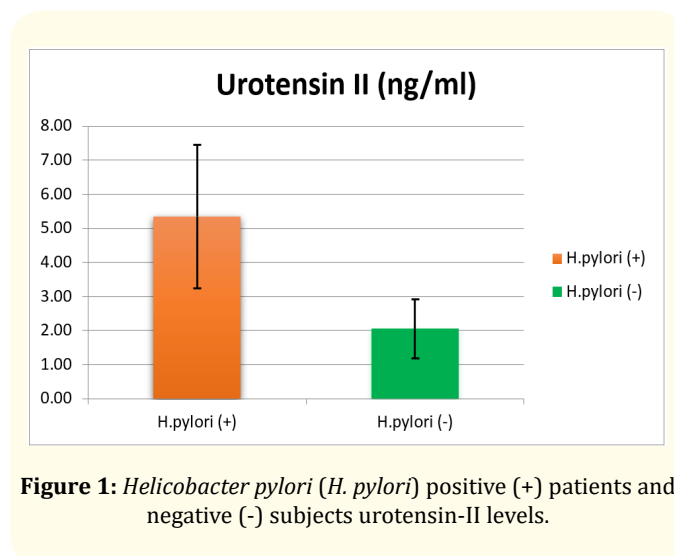
### Statistics

We used student's t-test to compare parametric values between the groups using SPSS 18 analysis programme.  $p < 0.05$  was considered as statistically significant.

### Results

Group 1 comprised 76 *H. pylori* positive patients with peptic ulcer, 27 (36%) of whom were female, and 49 (64%) male and their mean age was  $38.0 \pm 13.1$  years. Group 2 had 33 non-ulcer cases with an *H. pylori*-negative test, 12 (38%) of whom were female, and 21 (62%) male and their mean age was  $39.0 \pm 15.6$  years. There were no significant differences between two groups interms of age and sex.

The mean serum U-II level was higher in group 1 than in group 2 ( $5.34 \pm 2.1$  vs.  $2.05 \pm 0.86$  ng/ml,  $p < 0.001$ ) (Figure 1).



**Figure 1:** *Helicobacter pylori* (*H. pylori*) positive (+) patients and negative (-) subjects urotensin-II levels.

### Discussion

*H. pylori* is an important human pathogen causing malignant and non-malignant diseases. This bacteria is the third most common cause of cancer death in the world and is a human carcinogenic bacterium strongly associated with gastric cancer. It is also associated with common diseases such as dyspepsia and peptic ulcer [8]. *H. pylori* infection has been found to be associated with 90% of duodenal ulcers and 70% of gastric ulcers [3]. Our patient group had a gastric and/or duodenal ulcer detected by endoscopy and an *H. pylori* positivity detected by at least two different methods. Control group cases had no peptic ulcer and *H. pylori* in endoscopy and other diagnostic tests. There was a significant difference between the patient and control groups in terms of serum U-II level. To the best of our knowledge, no previous study has investigated the serum level of U-II in *H. pylori* positive patients with peptic ulcer. Therefore, our study firstly showed the possible role of U-II in *H. pylori*-positive peptic ulcer.

Variations in the concentration of U-II have been found at various intervals and in various pathologies. It has been reported that this range may be  $2.055 \pm 0.588$  ng/ml, although it was not possible to define the normal range [9]. In our study, U-II level was found to be  $2.05 \pm 1.8$  ng/ml in *H. pylori*-negative control group. This result was consistent with the normal range indicated in the literature.

Urotensin II is a new peptide demonstrating angiogenic and profibrotic properties as well as vasoconstrictive effect. Onat, *et al.* reported that U-II might play a role in chronic inflammation [6]. Smolka, *et al.* remarked that bacterial virulence factors, inflammatory cytokines, and atrophy cause decreased acid secretion in many patients with pangastritis developing *H. pylori* chronic infection. These patients are at risk for developing gastric adenocancer (approximately 1%) [10]. In our study, we thought that U-II might lead to the inflammation in patients with peptic ulcer induced by *H. pylori*. Moreover, *H. pylori*-positive peptic ulcer patients had the level of U-II about 2 times higher than the control group. This suggested that *H. pylori* may be involved in the pathway leading to inflammation as well as adenocancer, and thus U-II could be examined in peptic ulcer patients.

Again, strong evidence has recently shown that U-II and its receptors play a role in the initiation and progression of different epithelial cancers. The growth, motility and invasion of breast, bladder, prostate, colorectal and glioblastoma cancer cells have been

reported to be regulated by U-II and U-II receptors [7]. Gastrointestinal cancers are the most deadly cancers in the world and have a strong association with chronic inflammation. In the last decade, these malignancies have unacceptably poor survey via current surgery, chemotherapy and/or radiotherapy, despite advances in the understanding of the etiology, both in terms of host and environmental factors. For this reason, it has been reported that new molecular targets need to be determined to develop new generation treatment strategies to treat patients and new biomarkers are needed to diagnose diseases early [11]. Despite studies on other system and colorectal cancers related to U-II and its receptors, no such study has been found in the literature related to gastric cancer. Our finding of high U-II levels in patients with *H. pylori*-positive peptic ulcer suggested that stomach cancer may be one of the cancers requiring biomarkers in terms of diagnosis and treatment strategies, and thus there is a need for well planned studies relevant to this subject.

### Conclusion

Serum U-II level was significantly higher in *H. pylori*-positive peptic ulcer patients than in *H. pylori*-negative control group. We suggest that serum U-II levels may be usefull marker in peptic ulcer diagnosis and its increase might have an importance in the pathogenesis of *H. pylori*-positive peptic ulcer and other associated diseases such as gastric adenocarcinoma.

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