

ORIGINAL PAPER

## ***Helicobacter pylori* – associated gastritis in different forms of functional dyspepsia**

### **The infection of *Helicobacter pylori* in functional dyspepsia**

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#### **Abstract**

**Introduction:** “Functional dyspepsia” defines gastroduodenal symptoms not explained by any organic disease. Moreover, two clinical forms of this disease have been distinguished: postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). The role of *H. pylori* infection still remains under debate. **The aim of the study** was to determine whether the density of *H. pylori* colonization and the immune response to the infection are similar in different forms of functional dyspepsia. **Material and methods:** the study involved 30 subjects without dyspeptic ailments (K), 30 with PDS and 30 with EPS. The diagnosis was based on Rome Criteria III. The subjects were selected randomly after earlier detection of anti- *H. pylori* antibodies in serum with serological method. *H. pylori* infection was confirmed with urea breath test. **Results:** mean serum concentration of anti- *H. pylori* antibodies in subjects with asymptomatic infection was  $89.90 \pm 48.16$  U/L. These values were similar in PDS group and they were:  $71.53 \pm 36.13$  U/L ( $p > 0.05$ ). Statistically significantly higher values of this concentration were found in EPS group and they were:  $264.55 \pm 98.20$  ( $p < 0.01$ ). Similar differences were observed in the values of urea breath test. In the groups of patients with asymptomatic infection and dyspepsia in the form of PDS the results were similar:  $14.77 \pm 5.13\%$  and  $15.10 \pm 5.75\%$ , respectively ( $p > 0.05$ ). In patients with EPS the values of breath test were significantly higher -  $26.44 \pm 14.01\%$  ( $p < 0.001$ ). **Conclusions:** 1. The results of urea test and the serum concentration of anti- *H. pylori* antibodies are different in different forms of functional dyspepsia. 2. Density of *H. pylori* colonization and immune response to the infection affect the clinical picture of functional dyspepsia. (*Clin Exp Med Lett* 2009; 50(3):131-135)

**Keywords:** *Helicobacter pylori*, density of colonization, functional dyspepsia;

#### **Introduction**

Introduction of fiberoscopy in 1960s into the diagnostics of digestive diseases was a great progress in gastroenterology. Elimination of inaccuracy of radiological diagnostics and determination that in quite a few cases there are no organic changes in stomach despite persistent gastric complaints are the important aspects of this progress. These were the cause of introduction of the term “functional dyspepsia” into medical nomenclature. Within several dozen years the definition of this disease has changed many times [1-3]. Experts from all over the world worked on its formulation and they worked out successively the Rome Criteria I, II and III (1988, 1999 and 2006). According to current consensus “functional dyspepsia defines gastroduodenal symptoms not explained by any organic, systemic or metabolic disease”. Moreover, two clinical forms of this disease have been distinguished: postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). However, these terms do not explain the cause of chronic dyspepsia ailments. Alterations in gastric secretion and motility are most frequently listed among its pathogenic factors. The role of *H. pylori* infection still remains under

debate. Within the first few years after detection of this bacterium by Marshal and Warren (40, it was generally believed that it was the cause of dyspeptic ailments. It resulted from the first publications that *H. pylori* eradication removed dyspeptic symptoms in majority of subjects [5-7]. Unfortunately, the results of further studies were not so optimistic and they encouraged to further observations [8]. It results from multicentre analysis that the effectiveness of eradication therapy in functional dyspepsia oscillates from 30 to 45% of the treated patients and it is only slightly better than placebo effect [9-11]. However, doubts arose as to the reliability of the methods estimating this infection, particularly serological methods. Doubts disappeared after introduction of objective tests – especially urea breath test [12,13]. Nevertheless, a lot of questions remain unanswered. It is not known whether the nature of dyspeptic ailments depends on the infection and on the intensification of immune response.

**The aim of the study** was to determine whether the density of *H. pylori* colonization and the immune response to the infection are similar in different clinical forms of functional dyspepsia.

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## Material and methods

The study involved 30 subjects without dyspeptic ailments (K), 30 with postprandial distress syndrome (PDS) and 30 with epigastric pain syndrome (EPS) at the age 19-37 years (mean 28,3 years). The diagnosis of functional dyspepsia was based on Rome Criteria III. The subjects were selected randomly after earlier quantitative determination of concentration anti- *H. pylori* antibodies in serum with serological method with the use of Cobas Core II – Roche. *Helicobacter pylori* infection was confirmed with urea breath test. The test was performed with 75 µg of urea labelled with carbon 13 (UBT-13C) and mass spectrometer FanCi-2 (Fisher Analyzer Instruments). The examined patients swallowed a capsule with urea, drank 100 ml of orange juice and remained in supine position for 30 min. Initially and after 30 min. the exhaled breath was collected into containers and after computer analysis the result demonstrated the difference between the initial and the final activity measured in per mil (‰) of the content of carbon isotope in the exhaled breath.

All patients were subjected to upper digestive tract endoscopy, ultrasonography, biochemical investigations to exclude organic diseases. Habitual smokers and subjects taking gastrototoxic drugs were excluded from the study. Seven days prior to the examination the patients were prohibited from using any medication and from performing any diagnostic tests.

Written consent was obtained from all the subjects and the study protocol was approved by the Bioethical Committee of the Medical University in Lodz (NO. RNN 266/04/KB).

Kruskal-Wallis test, U-Mann-Whitney test and Spearman's rank correlation test were used for statistical analysis.

## Results

Mean serum concentration of anti- *H. pylori* antibodies in subjects with asymptomatic infection with this bacterium was  $89.90 \pm 48.16$  U/L.

These values were similar in PDS group and they were:  $71.53 \pm 36.13$  U/L ( $p > 0.05$ ).

Statistically significantly higher values of this concentration were found in EPS group and they were:  $264.55 \pm 98.20$  ( $p < 0.01$ ).

Similar differences were observed in the values of urea breath test. In the groups of patients with asymptomatic infection and dyspepsia in the form of postprandial distress syndrome the results were similar:  $14.77 \pm 5.13\%$  and  $15.10 \pm 5.75\%$ , respectively ( $p > 0.05$ ). In patients with epigastric pain syndrome the values of breath test were significantly higher, and they were:  $26.44 \pm 14.01\%$  ( $p < 0.001$ ).

Different results were obtained when the coefficients of correlation between the values of breath test and the concentration of anti- *H. pylori* antibodies were compared. In the groups of patients with asymptomatic infection and with EPS the values of correlation coefficient

were respectively:  $r = 0.7927$  and  $r = 0.7954$  ( $p < 0.001$ ). No significant correlation was found between the results of UBT and IgG in subjects with dyspepsia in the form of postprandial distress syndrome ( $r = 0.0864$ ).

## Discussion

Association of functional dyspepsia and *H. pylori* infection is still not clear. On the one hand, it has been accepted that this bacterium always leads to inflammatory changes in gastric mucosa of different intensification and progression. Taking this into consideration, some clinicians suggest excluding cases of *H. pylori* infection from the group of functional dyspepsia. On the other hand, there are no clinical symptoms in majority of infected subjects. Of course, lack of the symptoms does not exclude organic changes of different aetiology in the upper digestive tract. Buckley et al. [14] did not find differences in microscopic picture of gastric mucosa in subjects with symptomatic and asymptomatic infection.

It results from a multicentre study that from 1% to 8% of peptic ulcers do not manifest subjective symptoms or they are imperceptible in their course. These observations include mainly cases of ulcers after non-steroidal anti-inflammatory drugs, but they also concern patients not taking any medications. In their programme study including 1010 blood donors, Vairo et al. [15] diagnosed *H. pylori* infection in 42%; in 15% of them they detected duodenal ulcer and in 55% gastric ulcer. Similarly, Anand et al. [16] among 470 healthy volunteers with asymptomatic *H. pylori* infection diagnosed duodenal ulcer. Thus, *H. pylori* infection can present different clinical manifestation – from asymptomatic form to chronic dyspepsia. Jaakkimainen et al. [17] in their metaanalysis of multicentre studies demonstrated that subjects with symptoms of functional dyspepsia are infected significantly more frequently than healthy subjects. Armstrong et al. carried out similar analysis [18] demonstrating that

*H. pylori* infection in patients with functional dyspepsia occurs 1.8-2.3 times more frequently than in healthy subjects.

Dyspeptic symptoms can depend on numerous factors including duration of the infection. Rosenstock et al. [19] observed for 5 years nearly three thousand *H. pylori*-positive subjects and they found out that the risk of the development of dyspepsia was significantly higher than in uninfected subjects. However, it was not established what factors conditioned the occurrence of dyspepsia. It is known that at the beginning of the infection acute dyspeptic symptoms are often observed particularly in young subjects and they are diagnosed as "food poisoning" or "intestinal influenza". Then, the infection becomes asymptomatic in majority of patients. Most probably the intensification of colonization results in the recurrence of the ailments. The results of own study can in part confirm this conception, because the intensification of the colonization was significantly higher in patients with epigastric pain syndrome. The

results of the urea breath test in patients with postprandial distress syndrome were similar to those in the group with asymptomatic infection. Similarly, the results of immune response (IgG antibodies) in these groups did not differ significantly.

Numerous researchers found correlation between serum IgG level and the density of *H. pylori* colonization on gastric mucosa [19,20]. However, the results of the concentration of antibodies in IgG class should be considered critically due to their individual high changeability over time. Nevertheless, their very high level in EPS group may prove that inflammatory/immunologic changes in gastric mucosa are responsible for epigastric pain. The reports of other authors are also worth mentioning and they indicate that in subjects with gastric cancer the concentration of anti- *H. pylori* antibodies both in class G and A are lower than in superficial and atrophic gastritis [21]. This remark should be related to the well known fact that gastric cancer is very common in *H. pylori*-positive patients and it is usually diagnosed at the advanced stage of the disease. The initial phase of the cancer is asymptomatic or with mild symptoms in the form of postprandial distress syndrome.

Everything that has been mentioned here indicates that the effects of *H. pylori* infection are very complex and individually differentiated. Very dense colonization of this bacterium in gastric mucosa triggers dyspeptic complaints similar to the symptoms in duodenal ulcer disease. Such a condition is, according to international (Maastricht III) and Polish (from the year 2008) con-

sensus, an indication for *H. pylori* eradication. Unfortunately, it results from many studies in different regions of the world that in the cases in which the results of urea breath test (UBT-13C) are high, the resistance to antibiotic therapy is also high [22-24].

In the mentioned consensuses no clinical forms of functional dyspepsia were distinguished and eradication was recommended in any dyspeptic complaints. The results of own studies confirm rightness of such management because in both forms of dyspepsia the intensity of the infection significantly exceeds the accepted standard. Moreover, it results from numerous studies performed in our academic centre that even in asymptomatic infections there comes to destructive changes in gastric mucosa including gastrocyte DNA damage which may contribute to the development of neoplastic processes [25]. *H. pylori* infection still remains an important medical problem due to the frequency of its occurrence and numerous unbeneficial consequences.

## Conclusions

1. The results of urea test and the serum concentration of anti- *H. pylori* antibodies are different in different forms of functional dyspepsia.
2. Density of *H. pylori* colonization and immune response to the infection affect the clinical picture of functional dyspepsia.

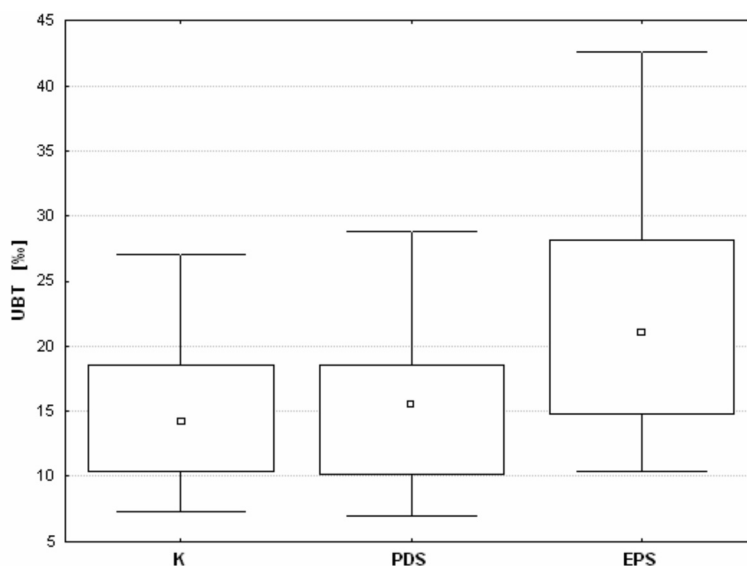


Figure 1. Concentration of anti- *H. pylori* antibodies in serum in subjects with *H. pylori* infected asymptomatic (K) and with postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS); K: PDS –  $p < 0,01$

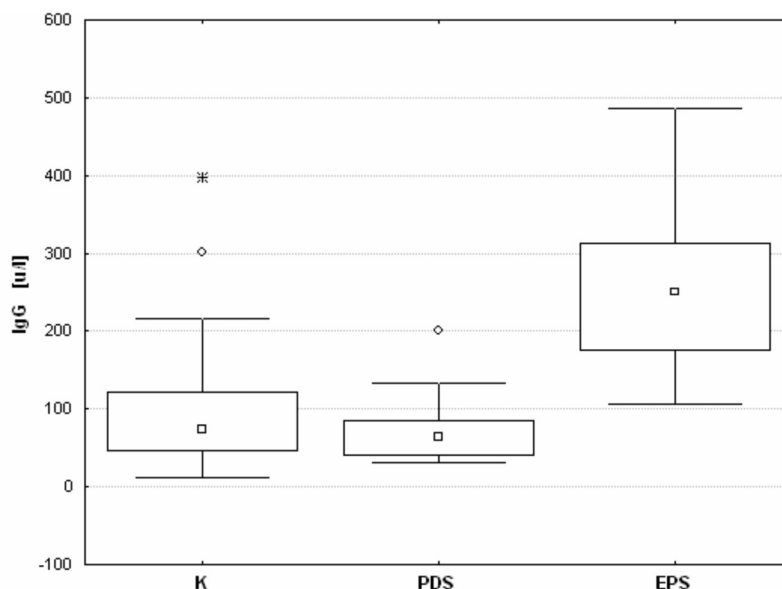


Figure 2. Value of breath test in subjects with *H. pylori* infected asymptomatic (K) and with postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS); K: PDS –  $p > 0.05$ , K: EPS –  $p < 0.01$

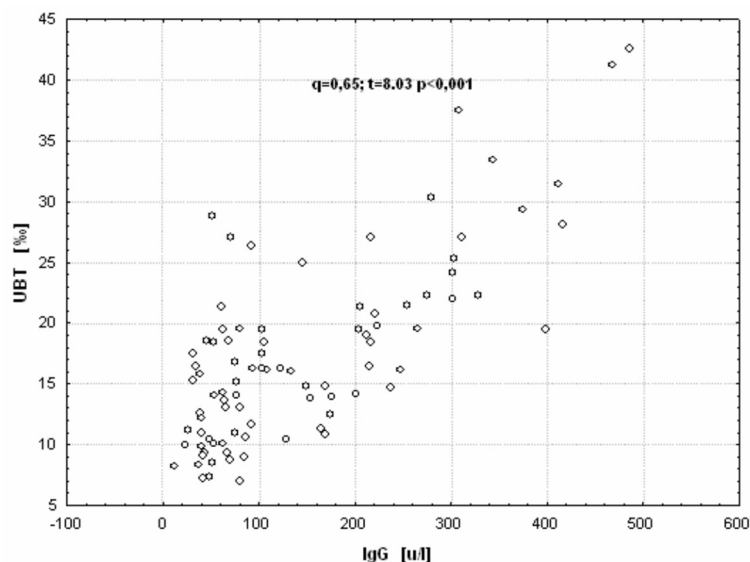


Figure 3. Dispersion of breath test value relatively to concentration of anti – *H. pylori* antibodies in patients with epigastric pain syndrome

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