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Strong inverse correlation between *Helicobacter pylori* infection and body mass index in male haemodialysis patients

Wyrażna ujemna korelacja między zakażeniem *Helicobacter pylori* a wskaźnikiem masy ciała u mężczyzn poddanych hemodializie

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Abstract

Introduction and Aim of study: In dialysis patients chronic infections induce overproduction of pro-inflammatory substances. Inflammation has been associated with cachexia and anorexia. Infection with *H. pylori* is also associated with anorexia, inflammation, and malnutrition in dialysis patients. This study aimed to evaluate the association of body mass index (BMI) of haemodialysis (HD) patients with *Helicobacter pylori* IgG antibodies to find the effects of *H. pylori* infection on the development of malnutrition.

Material and methods: Patients with end-stage renal disease undergoing maintenance haemodialysis treatment who had had various upper gastrointestinal complaints consisting of epigastric pain, epigastric burning, postprandial fullness, early satiety, bloating and belching were studied. Serum *Helicobacter pylori* specific IgG antibody titers, serum Leptin, serum post and predialysis blood urea nitrogen, albumin, C-reactive protein were measured. Body mass index was calculated.

Results: In this study no significant difference of serum *H. pylori* specific IgG antibody titer, serum Alb, serum leptin and BMI between males and females and also between diabetics and non diabetic HD patients were found. In all patients and in female non diabetic and diabetic groups no significant correlation of *H. pylori* IgG antibody titer with BMI was seen, while in male population a significant inverse correlation of *H. pylori* IgG antibody titer with BMI ($r=-0.54$; $P=0.009$) (adjusted for age and urea reduction rate) was found.

Conclusions: It is possible that inflammation and activity in antrum with *H. pylori* infection may be higher in men with end-stage renal disease on haemodialysis treatment, although this susceptibility needs more investigation with larger groups of patients. (**Gastroenterol. Pol., 2006, Vol. 13, No. 6, p. 437-440**)

Key words: haemodialysis, *Helicobacter pylori* infection, end-stage renal failure, *Helicobacter pylori* IgG specific antibodies, body mass index

Streszczenie

Wprowadzenie i Cel pracy: U pacjentów poddawanych dializie przewlekłe zakażenia powodują nadprodukcję substancji zapalnych. Zapalenie jest związane z kacheksją i anoreksją. Zakażenie *Helicobacter pylori* (*H. pylori*) jest również związane z anoreksją, zapaleniem i złym odżywianiem u chorych poddanych dializie. W niniejszej pracy poddano ocenie związek wskaźnika masy ciała (*body mass index* – BMI) u pacjentów poddanych hemodializie z przeciwciałami IgG przeciw *H. pylori* w celu określenia wpływu infekcji *H. pylori* na rozwój niedożywienia.

Materiał i metody: Badano pacjentów będących w końcowym stadium choroby nerkowej poddanych hemodializie podtrzymującej, którzy wcześniej skarżyli się na różne dolegliwości żołądkowo-jelitowe, takie jak: ból nadbrzuszy, palenie w okolicy nadbrzusza, poposiłkowe uczucie pełności w żołądku, uczucie wczesnej sytości, wzdęcia oraz odbijanie. Zmierzono miana przeciwciał IgG przeciw *H. pylori* w surowicy, leptynę w surowicy, azot mocznikowy w surowicy przed i po dializie, albuminę, białko C-reaktywne. Obliczono BMI.

Wyniki: W badaniu nie stwierdzono istotnej różnicy mian przeciwciał IgG przeciw *H. pylori* w surowicy między kobietami i mężczyznami, jak również między poddanymi hemodializie diabetykami a niediabetykami. U wszystkich pacjentów oraz w grupach diabetyków i niediabetyków płci żeńskiej nie zaobserwowano istotnej ujemnej korelacji między mianem przeciwciał IgG przeciw *H. pylori* a BMI, podczas gdy wśród męskiej populacji zanotowano znaczącą ujemną korelację między mianem przeciwciał IgG przeciw *H. pylori* a BMI ($r=-0,54$; $P=0,009$) (dopasowane pod kątem wieku i stopnia redukcji mocznika).

Wnioski: Istnieje możliwość, że zapalenie i aktywność zakażenia *H. pylori* w antrum mogą być większe u mężczyzn w końcowym stadium choroby nerek poddanych hemodializie niż u kobiet, choć to przypuszczenie wymaga dalszych badań większych grup pacjentów.

Słowa kluczowe: hemodializa, zakażenie *Helicobacter pylori*, końcowe stadium niewydolności nerek, IgG specyficzne przeciwciała przeciw *Helicobacter pylori*, wskaźnik masy ciała

Introduction

Helicobacter pylori (*H. pylori*) was cultivated first from human gastric mucosa in 1983 (1) and since then has emerged as one of the most common chronic bacterial infections in the

world, affecting about 40% and 80% of the general population in developed and developing countries, respectively (2). Infection with this bacterium induces gastric inflammation in most subjects and has been associated with an increased production of cytokines such as tumor necrosis factor, interferon, and interleukins (3). End-stage renal failure patients often have dyspeptic symptoms and may develop peptic disease or digestive disorders leading to severe gastrointestinal complications (4-6). Body mass index (BMI) is a standardized measure calculated from an individual's weight in kilograms divided by the square of their height in meters (kg/m^2). Body mass index correlates, better than body weight alone, with direct measures of body 'fatness' or 'density' in haemodialysis (HD)-treated pa-

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tients. Lower BMI is consistently found to be a strong predictor of an elevated mortality risk. In contrast, a higher BMI, either overweight or obesity, has generally not been associated with any increase in mortality risk (7). Haemodialysis (HD) patients with lower BMI have a higher relative mortality risk, irrespective of race. We hypothesized that an increased mortality risk might be associated with high BMI in a variety of other 'healthier' subgroups of HD patients (7). In dialysis patients chronic infections induce overproduction of pro-inflammatory substances, and inflammation has been associated with cachexia and anorexia. Infection with *H. pylori* is also associated with anorexia, inflammation, and malnutrition in dialysis patients (4). Malnutrition is a relevant risk factor for mortality for patients on maintenance haemodialysis treatment (8). Studies concerning the association of *H. pylori* infection with malnutrition in haemodialysis population showed different results. Previously we showed the inverse association of *H. pylori* infection with serum albumin of haemodialysis patients (9). In this study we aimed to conduct a study on the association of BMI of haemodialysis patients with *H. pylori* IgG antibodies to better find the effects of *H. pylori* infection on the development of malnutrition.

Material and methods

This is a cross-sectional study that was conducted on patients with end-stage renal disease undergoing maintenance haemodialysis treatment with acetate basis dialysate and polysulfone membranes. All patients had various upper gastrointestinal complaints consisting of epigastric pain, epigastric burning, postprandial fullness, early satiety, bloating and belching. Exclusion criteria for patients were using H2 proton pump inhibitors, antibiotics and aluminum hydroxide gels as well as active or chronic infection before the study. Serum *H. pylori* specific IgG antibody titers (titer >10 U/ml was interpreted as positive according to the manufacturer's instructions) was measured by enzyme-linked immunosorbent assay (ELISA) method using Trinity Biotech Kits (USA). Serum Leptin (normal range of values for males is 3.84 (\pm 1.79) and for females 7.36 (\pm 3.73) ng/ml) was measured by ELISA method using DRG kits of Germany. Also peripheral venous blood samples were collected for biochemical analysis including serum post and predialysis blood urea nitrogen (BUN), cholesterol (Chol), albumin (Alb), C-reactive protein (CRP) which were measured using standard methods. For patients also complete blood count containing hemoglobin (Hgb) and hematocrit (Hct) was measured using Sysmex-KX-21N Cell counter. For the efficacy of haemodialysis the urea reduction rate (URR) was calculated from pre- and post-BUN data (10). Body mass index was calculated using the standard formula (postdialyzed weight in kilograms/height in square meters; kg/m²). Duration and doses of haemodialysis treatment were calculated from patients' records. The duration of each haemodialysis session was four hours. For statistical analysis, the data are expressed as the mean \pm SD and median values. Statistical correlations were assessed using the partial correlation test. All statistical analyses were performed using SPSS (version 11.5.00). Statistical significance was determined at a *p*-value <0.05.

Results

The study was carried out on 39 (F=15; M=24) stable HD (diabetic - 12; non-diabetics - 27) patients with upper gastrointestinal symptoms as mentioned above. Tables I-III summarize patients' data. Mean ages of patients were 46 (\pm 18) years. The length of the time patients had been on haemodialysis was 30 (\pm 35) months (median: 18 months). The value of

serum *H. pylori* specific IgG antibody titers of all patients was 7.6 (\pm 9.9) u/ml (median: 2 u/ml). The value of serum *H. pylori* specific IgG antibody titers in the female and male groups were 5.9 (\pm 8) u/ml (median: 2 u/ml) and 8.7 (\pm 10.9) u/ml (median: 2 u/ml), respectively. The BMI of all patients was 21.6 (\pm 4.3) kg/m² (median: 21 kg/m²). The BMI in female and male groups were 22 (\pm 4.6) kg/m² (median: 22 kg/m²) and 21.5 (\pm 4.2) kg/m² (median: 20 kg/m²), respectively. The value of serum leptin in all patients was 10 (\pm 14) ng/ml (median: 6.8 ng/ml). The values of serum leptin in the female and male group were 9.3 (\pm 12.7) ng/ml (median: 8.3 ng/ml) and 10.4 (\pm 15) ng/ml (median: 5.8 ng/ml), respectively. In this study no significant difference of serum *H. pylori* specific IgG antibody titer, serum Alb and serum leptin and BMI between males and

TABLE I: Mean \pm SD of age, duration and dosage haemodialysis and also laboratory results of all haemodialysis patients

Total patients n=39	Mean \pm SD	Median
Age (years)	46 \pm 18	42
DH* months	30 \pm 35	18
Dialysis dose sessions	279 \pm 381	156
Body mass index (BMI) [kg/m ²]	21.6 \pm 4.3	21
<i>H. pylori</i> IgG [u/ml]	7.6 \pm 9.9	2
Leptin [ng/ml]	10 \pm 14	6.8
Cholesterol [mg/dl]	116 \pm 38	110
Hemoglobin [g/dl]	8.9 \pm 2	9
Albumin [g/l]	3.8 \pm 0.5	4
Hematocrit [%]	28 \pm 6	29
Urea reduction rate (URR) [%]	58 \pm 8	58
C-reactive protein (CRP) [mg/l]	8.8 \pm 6.7	6

DH - dosage haemodialysis

TABLE II: Mean \pm SD of age, duration and dosage haemodialysis and also laboratory results of male haemodialysis patients

Male group n=24	Mean \pm SD	Median
Age (years)	47 \pm 19	41
DH* months	29 \pm 32	18
Dialysis dose sessions	314 \pm 409	159
Body mass index (BMI) [kg/m ²]	21.5 \pm 4.2	20
<i>H. pylori</i> IgG [u/ml]	8.7 \pm 10.9	2
Leptin [ng/ml]	10.4 \pm 15	5.8
Cholesterol [mg/dl]	108 \pm 35	104
Hemoglobin [g/dl]	9 \pm 2	9
Albumin [g/l]	3.8 \pm 0.6	3.9
Hematocrit [%]	28.9 \pm 6	29.5
Urea reduction rate (URR) [%]	56.6 \pm 5.8	56.5
C-reactive protein (CRP) [mg/l]	10 \pm 8	10

DH - dosage haemodialysis

TABLE III: Mean \pm SD of age, duration and dosage haemodialysis and also laboratory results of female haemodialysis patients

Female group n=15	Mean \pm SD	Median
Age (years)	44 \pm 15	44
DH* months	32 \pm 40	20
Dialysis dose sessions	223 \pm 337	108
Body mass index (BMI) [kg/m ²]	22 \pm 4.6	22
<i>H. pylori</i> IgG [u/ml]	5.9 \pm 8	2
Leptin [ng/ml]	9.3 \pm 12.7	8.3
Cholesterol [mg/dl]	128 \pm 41	124
Hemoglobin [g/dl]	8.5 \pm 2	9
Albumin [g/l]	3.9 \pm 0.4	4
Hematocrit [%]	25 \pm 6	29
Urea reduction rate (URR) [%]	62 \pm 11	62
C-reactive protein (CRP) [mg/l]	6.7 \pm 2.9	6

DH - dosage haemodialysis

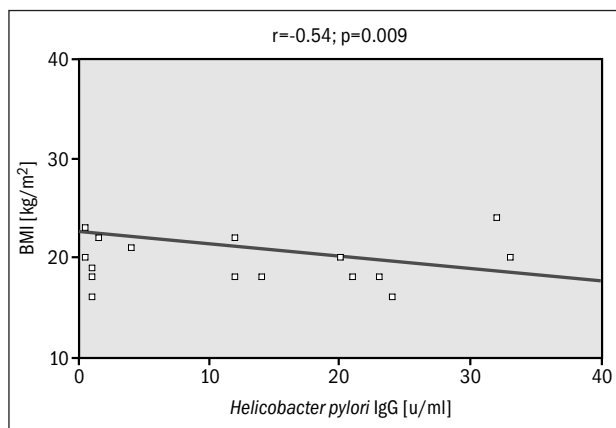


FIGURE 1. Significant inverse correlation of *Helicobacter pylori* IgG antibody titer with BMI of male haemodialysis patients ($r=-0.54$; $P=0.009$) (adjusted for age and URR)

BMI - body mass index; URR - urea reduction rate

females as well as between diabetics and non diabetic HD patients were found (P N.S.). In all patients as well as in female non diabetic and diabetic groups no significant correlation of *H. pylori* IgG antibody titer with BMI was seen (P N.S.), while in male population a significant inverse correlation of *H. pylori* IgG antibody titer with BMI ($r=-0.54$; $P=0.009$; fig. 1) (adjusted for age and URR) was found.

Discussion

In the general population, an increased BMI is associated with higher mortality; more properly, total mortality is a linear increasing function of high fat mass and low fat free mass. On the contrary, an inverse BMI-mortality relationship has been reported in HD (11). Thus, while a high body mass index (BMI) is associated with mortality in the general population, the obesity is suggested to confer a survival advantage in HD patients (10). A study conducted by Aguilera et al. (12) on 1313 peritoneal dialysis patients showed that infection with HP is associated with anorexia, inflammation and malnutrition in their patients. Eradication of HP significantly improves this syndrome. They concluded that residual renal function have a protective effect on appetite preservation (12). In our previous study association of *H. pylori* infection with serum albumin was shown (9). The relationship between *H. pylori* infection and body mass indices is controversial. It is possible that *H. pylori* infection decreases serum ghrelin and increases gastric leptin levels, which may, in turn, decrease body mass index (13). To determine whether *H. pylori* seropositivity is associated with body mass index, serum *H. pylori* and cytotoxin-associated gene product A (CagA) antibody levels were measured on 6724 adult participants of the third National Health and Nutrition Examination Survey (1988-1991) during a study by Ioannou et al. (13). They evaluated the association between *H. pylori*/CagA antibody status [both negative (-/-), *H. pylori*-positive/CagA-negative (+/-), or both positive (+/+)] and body mass index, adjusting for sociodemographic factors. They found that *H. pylori* seropositivity and CagA antibody status are not associated with body mass index or fasting serum leptin (13). With the conception that *H. pylori* may play a role in regulating body weight, Cho et al. (14) examined the association between *H. pylori* colonization and overweight status. Non-pregnant participants in the Third National Health and Nutrition Examination Survey (1988-1994) aged ≥ 20 years who had had *H. pylori* testing performed and body mass index measured were studied. Serum leptin levels did not differ significantly between the three *H. pylori* groups. In this US population-based study, there

was no significant association between *H. pylori* colonization, cagA+ strains of *H. pylori*, and being overweight (14). Azuma et al. (15) carried out a study on nine-hundred and thirty-two employees of an industrial corporation to investigate the relationship between *H. pylori* infection and body indices and to examine the effect of *H. pylori* eradication therapy on body indices. Three hundred and two *H. pylori*-positive cases diagnosed with chronic gastritis by upper gastrointestinal endoscopy or radiography underwent eradication therapy. Body mass indices, serum total cholesterol levels and symptom scores were obtained before and at 12 months after eradication therapy. They found that there was no significant difference in body weight, BMI or serum total cholesterol level between the *H. pylori*-positive and *H. pylori*-negative groups. However, body weight and BMI increased significantly 12 months after eradication of *H. pylori* infection. In contrast, there was no significant difference in body weight and BMI 12 months after eradication therapy in the non-eradication group. Serum total cholesterol levels did not change after eradication therapy in either the eradication or non-eradication groups. They concluded that eradication of *H. pylori* infection induced an increase in BMI in industrial workers with chronic gastritis in Japan (15). As the diseases associated with *H. pylori* infection, such as peptic ulcer disease and gastric cancer, afflict men more frequently than women, Replogle et al. (16) conducted a study on a group of healthy population undergoing multiphasic health evaluations in 1992-1993 as members of the Kaiser Permanente Medical Care Program of Northern California. Adults aged 20-39 years were screened for antibodies to *H. pylori* infection and were surveyed with regard to their demographic characteristics and health practices. Among 556 African-American, Hispanic, and white men and women, male sex was a significant risk factor for infection (16). It is possible that there is a sex difference in mucosal response to *H. pylori* infection in the stomach. In this regard in an age-, sex-, *H. pylori* status- and disease-matched case-control study on 574 *H. pylori*-positive and 225 *H. pylori*-negative patients selected from 4125 patients with a diagnosis of benign disease of the stomach, it was shown that inflammation and activity in antrum with *H. pylori* infection were higher in men (17). Taken together, in dialysis patients malnutrition is an independent factor causing morbidity and mortality. Both inadequate alimentation and metabolic alterations, which involve nitrogen and energy metabolism, contribute to malnutrition (18-20). As we could show, infection with *H. pylori* had an inverse correlation with the BMI of male haemodialysis patients. It is possible that inflammation and activity in antrum with *H. pylori* infection may be higher in men with end-stage renal disease undergoing maintenance haemodialysis treatment. In the meantime more investigation on the association of *H. pylori* with BMI in large study groups needs to better clarify higher susceptibility of male HD patients to weight reduction during infection with *H. pylori*.

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