ACTA FAC MED NAISS

UDK 613.24:579.8:616.61-78

Original article

ACTA FAC MED NAISS 2006; 23 (3): 129-133

Hamid Nasri

Shahrekord University of Medical Sciences,
Hajar Medical, Educational and Therapeutic Center,
Department of Internal Medicine
Shahrekord, Iran

STRONG INVERSE CORRELATION BETWEEN HELICOBACTER PYLORI INFECTION WITH BODY MASS INDEX IN MALE HEMODIALYSIS PATIENTS

SUMMARY

In dialysis patients, chronic infections induce overproduction of pro-inflammatory substances and inflammation has been associated with cachexia and anorexia. Infection with *Helicobacter pylori (H.pylori)* is also associated with anorexia, inflammation, and malnutrition in dialysis patients. The aim of the study was to conduct a research on the association of body mass index (BMI) in hemodialysis (HD) patients with *H. pylori* IgG antibodies in order to find the effects of *H.pylori* infection on the development of malnutrition. The patients with an end-stage renal disease undergoing maintenance HD treatment who had had various upper gastrointestinal complaints such as epigastric pain, epigastric burning, postprandial fullness, early satiety, bloating and belching were investigated. Serum *H. pylori* specific IgG antibodytiters, serum Leptin serum post and predialysis blood urea nitrogen (BUN), albumin (Alb) ,C-reactive protein (CRP) were measured. BMI was also calculated. In the study, no significant difference of serum *H.Pylori* specific IgG antibody titer, serum Alb, serum leptin and BMI between males and females were found, as well as between diabetics and non-diabetic HD patients. In all patients and in females, 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 URR) was registered. It is possible that inflammation and activity in antrum in *H. pylori* infection may be higher in men with an end-stage renal disease on hemodialysis treatment, although this susceptibility needs more investigation with larger groups of patients.

Keywords: **Hemodialysis, Helicobacter pylori infection. End-stage renal failure, Helicobacter pylori IgG Specific Antibodies, Body Mass Index**

INTRODUCTION

Helicobacter pylori (H. pylori) was cultivated first from human gastric mucosa in 1983 (1) and since than 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

Corresponding author. Tel. 0098/ 912-143-95-84 • E-mail address: hamidnasri@yahoo.com

divided by the square of their height in meters (kg/m^2). BMI correlates, better than body weight alone, with direct measures of body 'fatness' or 'density' HD-treated patients. A 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). 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 hemodialysis treatment (8). Studies concerning the association of *H.pylori* infection with malnutrition in hemodialysis population showed different results. Previously, we had showed the inverse association of *H.pylori* infection with serum albumin of HD patients (9). The aim of the study was to conduct a study on the association of BMI of HD patients with *H. pylori* IgG antibodies to find the effects of *H.pylori* infection on the development of malnutrition.

MATERIAL AND METHODS

This is a cross-sectional study comprising patients with end-stage renal disease undergoing maintenance HD treatment with acetate basis dialysate and polysulfone membranes. All patients had various upper gastrointestinal complaints including epigastric pain, epigastric burning, postprandial fullness, early satiety, bloating and belching. Exclusion criteria for patients were using H_2 blocators, proton pump inhibitors, antibiotics and aluminium hydroxide jells 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) were measured by enzyme-linked immunosorbent assay (ELISA) method using Trinity Biotech Kits (USA). Serum Leptin (normal range of values for males is 3.84 (±1.79) and for females is 7.36(±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); Chol, albumin (Alb), C-reactive protein (CRP) were measured using standard methods. Also, complete blood count containing hemoglobin (Hgb) and hematocrit (Hct) was measured using Sysmex-KX-21N Cell counter. For the efficacy of HD, the urea reduction rate (URR) was calculated from pre- and post-blood urea nitrogen (BUN) data (11). BMI was calculated using the standard formula (postdialyzed weight in kilograms/height in square meters; kg/m^2). Duration and doses of HD treatment were calculated from the patients' records. Duration of each HD session was four hours. For statistical analysis, the data are expressed as the Mean ± 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 1, 2 and 3* summarize patients' data. Mean age of patients was 46 (±18) years. The time patients spent on HD was 30± (35) months (median: 18 months). The value of serum *H.pylori* specific IgG antibody titers of all patients was 7.6 (±9.9) u/ml (median: 2 u/ml). The values of serum *H.pylori* specific IgG antibody titers in the female and male groups were 5.9 (±8) u/ml (median :2 u/ml) and 8.7 (±10.9) u/ml (median :2 u/ml)

Table 1. Mean ±SD, minimum and maximum of age, duration and dosage HD and also laboratory results of all HD patients

Total patients n=39	Mean±SD	Median
Age years	46± 18	42
DH* months	30± 35	18
Dialysis dose sessions	279± 381	156
BMI kg/m^2	21.6±4.3	21
H.Pylri-IgG u/ml	7.6±9.9	2
Leptin ng/ml	10 ±14	6.8
Chol mg/dl	116± 38	110
Hgb g/dl	8.9± 2	9
Alb g/l	3.8± 0.5	4
Hct %	28± 6	29
URR%	58± 8	58
CRP mg/l	8.8± 6.7	6

respectively. The BMI of all patients was 21.6 (±4.3) kg/m^2 (median: 21 kg/m^2). The BMI in the female and male groups was 22(±4.6) kg/m^2 (median: 22 kg/m^2) and 21.5 (±4.2) kg/m^2 (median: 20 kg/m^2)

Table 2. Mean ±SD, minimum and maximum of age, duration and dosage HD and also laboratory results of male HD patients

Male group n=24	Mean±SD	Median
Age years	47±19	41
DH* months	29±32	18
Dialysis dose sessions	314±409	159
BMI kg/ m^2	21.5±4.2	20
H.Pylri-IgG u/ml	8.7±10.9	2
Leptin ng/ ml	10.4±15	5.8
CHOL Mg/ dl	108±35	104
Hgb g/dl	9±2	9
Alb g/l	3.8±0.6	3.9
Hct %	28.9±6	29.5
URR%	56.6±5.8	56.5
CRP mg/l	10±8	10

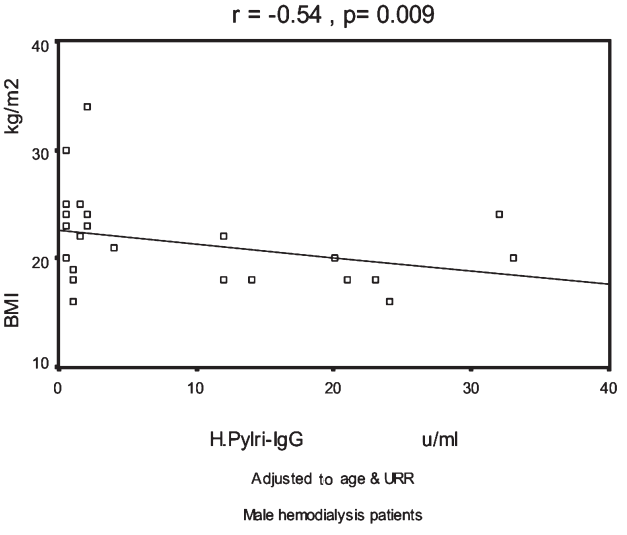
respectively. The value of serum leptin of all patients was 10 (±14) ng/ml (median : 6.8 ng/ml) . The values of serum leptin in the female and male groups were 9.3 (± 12.7) ng/ml (median: 8.3 ng/ml) 10.4 (±15) ng/ml (median: 5.8 ng/ml), respectively. In this study, no significant difference of serum H.Pylori specific IgG antibody titer, serum Alb and serum leptin and BMI between males and females and also between diabetics and non- diabetic HD patients

Table 3. Mean ±SD, minimum and maximum of age, duration and dosage HD and also laboratory results of female HD patients

Female group n=15	Mean±SD	Median
Age years	44±15	44
DH* months	32±40	20
Dialysis dose sessions	223±337	108
BMI kg/ m^2	22±4.6	22
H.Pylri-IgG u/ml	5.9±8	2
Leptin ng/ ml	9.3± 12.7	8.3
CHOL Mg/ dl	128±41	124
Hgb g/dl	8.5±2	9
Alb g/l	3.9±0.4	4
Hct %	25±6	29
URR%	62±11	62
CRP mg/l	6.7±2.9	6

were found. In all patients, as well as in females, non -diabetic and diabetic groups, no significant correlation of *H.pylori* IgG antibody titer with BMI was seen, while in male population a significant

Figure 1. Significant inverse correlation of H. pylori IgG antibody titer with BMI of male HD patients (r= -0.54 P= 0.009) (adjusted to age and URR)



inverse correlation of H.pylori -IgG antibody titer with BMI (r= - 0.54, p= 0.009; *Figure 1*) (adjusted to age and URR) was registered.

DISCUSSION

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 females, 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 was registered. 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 (10). Thus, while a high BMI is associated with mortality in the general population, the obesity is suggested to confer a survival advantage in HD patients(11). The study conducted by Aguilera et al. on 1313 peritoneal dialysis patients showed that infection with *H.pylori* is associated with anorexia, inflammation, and malnutrition in their patients. Eradication of *H.pylori* significantly improves this syndrome. They concluded that residual renal function has a protective effect on appetite preservation (12). In our previous study, the association of *H.pylori* infection with serum albumin was shown (9). The relationship between *H.pylori* infection and BMI is controversial. It is possible that *H. pylori* infection decreases serum ghrelin and increase gastric leptin levels, which may,

in turn, decrease BMI (13). To determine whether H. pylori seropositivity is associated with BMI, 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 (1988-91) during a study by Ioannou et al. They evaluated the association between *H. pylori*/CagA antibody status [both negative (-/-), *H. pylori*-positive/CagA-negative (+/-), or both positive (+/+)] and BMI, adjusting to sociodemographic factors. They found that *H. pylori* seropositivity and CagA antibody status are not associated with BMI or fasting serum leptin (14). With the conception that *H. pylori* may play a role in regulating body weight, Cho et al. 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 > or = 20 years who had had *H. pylori* testing performed and BMI 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 (15). On a nine-hundred and thirty-two employees of an industrial corporation, Azuma et al. carried out a study 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. BMI, 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 the 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 the 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 (16). Diseases associated with *H. pylori* infection, such as peptic ulcer disease and gastric cancer, afflict men more frequently than women. Replogle et al. conducted a study on a group of healthy population undergoing multiphase health evaluations in 1992-1993 as members of the Kaiser Permanente Medical Care Program of Northern California, adults aged 20-39 years to screen 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 (17). Is it possible that there is a sex differences 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 the diagnosis of benign disease of the stomach, it was shown that inflammation and activity in antrum with *H. pylori* infection were higher in men (18). 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 (19-21). As we showed, infection with *H. pylori* had an inverse correlation with the BMI of male hemodialysis patients. It is possible that inflammation and activity in antrum with *H. pylori* infection may be higher in men with an end-stage renal disease undergoing maintenance HD treatment. In the meantime, more investigation on the association of *H. pylori* with BMI with large study groups needs to better find more susceptibility of male HD patients to weight reduction during infection *H. pylori*.

REFERENCES

1. Warren JR, Marshall B. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. Lancet 1983; I:1273-1275.

2. Blaser MJ. Helicobacter pylori: its role in disease. Clin Infect Dis 1992; 15:386-393.

3. Genta RM. The immunobiology of Helicobacter pylori gastritis. Semin Gastroenterol Dis. 1997; 8:2-11.

4. Nardone G, Rocco A, Fiorillo M, Del Pezzo M, Autiero G, Cuomo R, Sarnelli G, Lambiase A, Budillon G, Cianciaruso B.Gastroduodenal lesions and Helicobacter pylori infection in dyspeptic patients with and without chronic renal failure Helicobacter, 2005;10 (1):53-8.

5. Baradaran A, Nasri H. Helicobacter pylori IgG antibodies in association with secondary hyperparathyroidism in end-stage renal failure patients undergoing regular hemodialysis. Arch Med Sci 2005, vol. 1, issue 4.

6. Nasri.H. Baradaran A. Relationship of Helicobacter Pylori Specific IgG Antibodies with Serum Magnesium in Patients on Maintenance Hemodialysis. The Journal of Applied Research 2005; 5 (3) : 438-443.

7. Bouchard C. Genetics of Obesity. CRC Press, Boca Raton, FL, 1994 .

8. Leavy SF, McCullough K, Hecking E, Goodkin D, Port FK, Young EW.Body mass index and mortality in 'healthier'

as compared with 'sicker' haemodialysis patients: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant. 2001;16 (12):2386-94.

9. Wiesholzer M, Harm F, Schuster K, Putz D, Neuhauser C, Fiedler F, Balcke P.Initial body mass indexes have contrary effects on change in body weight and mortality of patients on maintenance hemodialysis treatment. J Ren Nutr 2003 ;13 (3):174-85.

10. Baradaran A. Nasri H.Helicobacter Pylori IgG Specific Antibodies in Association with Serum Albumin in Maintenance Hemodialysis Patients. Pakistan Journal of Nutrition 2005; 4 (4): 265-269.

11. Heitmann BL, Erikson H, Ellsinger BM, et al. Mortality associated with body fat, fat-free mass and body mass index among 60-year-old swedish men: A 22-year follow-up. The study of men born in 1913. Int J Obes Relat Metab 2000;24:33-37.

12. Kahraman S, Yilmaz R, Akinici D, Arici M, Altum B, Erdem Y, Yasavul U, Turgan C.U-shaped association of body mass index with inflammation and atherosclerosis in hemodialysis patients. J Ren Nutr. 2005 ;15 (4):377-86.

13. Aguilera A, Codoceo R, Bajo MA, Diez JJ, del Peso G, Pavone M,Helicobacter pylori infection: a new cause of anorexia in peritoneal dialysis patients. Perit Dial Int 2001; 21 (suppl 3) : S152-6.

14. Ioannou GN, Weiss NS, Kearnev DJ.Is Helicobacter pylori seropositivity related to body mass index in the United States? Aliment Pharmacol Ther 2005 ;21 (6):765-72.

15. Cho T, Blaser MJ, Francois F, Mathew JP, Ye XY , Goldberg JD, Bini EJ.Helicobacter pylori and overweight status in the United States: data from the Third National Health and Nutrition Examination Survey. Am J Epidemiol 2005; 162 (6) : 579-84.

16. Azuma T, Suto H, Ito Y, Muramatsu A, Ohtani M, Dojo M, et al.Eradication of Helicobacter pylori infection induces an increase in body mass index. Aliment Pharmacol Ther 2002;16 (Suppl 2):240-4.

17. Replogle ML, Glaser SL, Hiatt RA, Parsonnet J.Biologic sex as a risk factor for Helicobacter pylori infection in healthy young adults. Am J Epidemiol, 1995 15;142(8):856-63.

18. Kato S,Matsukura N, Togashi A, Masuda G, Matsuda N, Yamada N, et al.Sex differences in mucosal response to Helicobacter pylori infection in the stomach and variations in interleukin-8, COX-2 and trefoil factor family 1 gene expression. Aliment Pharmacol Ther 2004 ;20 (Suppl 1):17-24.

19. Aparicio M, Cano N, Chauveau P et al. Nutritional status of haemodialysis patients: a French national cooperative study. French study group for nutrition in Dialysis. Nephrol Dial Transplant1999; 14: 1679–1686.

20. Bergström J. Nutrition and mortality in hemodialysis. J Am Soc Nephrol1995; 6: 1329–1341.

21. Bergström J. Why are dialysis patients malnourished? Am J Kidney Dis1995; 26: 229–241.

JAKA INVERZNA KORELACIJA IZMEĐU HELICOBACTER PYLORI INFEKCIJE I INDEKSA MASE KOD MUŠKIH PACIJENATA NA HEMODIJALIZI

Hamid Nasri

Medicinski fakultet Shahrekord Univerziteta
Medicinski, edukacioni i terapeutski Hajar centar, Odeljenje interne medicine,
Shahrekord, Iran

SAŽETAK

Kod pacijenata na dijalizi, hronične infekcije dovode do prekomernog lučenja proinflamatornih supstanci i inflamacija se dovodi u vezu sa kaheksijom i anoreksijom. Infekcije izazvane bakterijom *H. pylori* dovode se u vezu sa anoreksijom, inflamacijom i neuhranjenošću kod pacijenata na dijalizi. Cilj studije bio je ispitivanje veze između indeksa mase kod pacijenata na dijalizi sa IgG antitelima na *H. pylori* kako bi se odredili efekti *H. pylori* infekcije na razvoj neuhranjenosti. Ispitivani su pacijenti u završnoj fazi bubrežne bolesti na tretmanu dijalize, koji su imali različite smetnje gornjeg gastrointestinalnog trakta, kao što su epigastrični bol, epigastrično žarenje, osećaj punosti nakon uzimanja hrane, osećaj rane sitosti, nadutost i podrigivanje. Mereni su sledeći parametri: specifični IgG titar antitela na *H. Pylori*, serumski leptin, serumska koncentracija ureje pre i posle dijalize, albumin, C-reaktivni protein. Takođe je izračunat i indeks mase. U toku studije nije uočena značajna razlika u vrednostima specifičnih IgG titar antitela na *H. pylori*, serumskog albumina, serumskog leptina i indeksa mase između muškaraca i žena, kao i između dijabetičara i nedijabetičara na dijalizi. Kod svih pacijenata i žena, nedijabetičara i dijabetičara, nije uočena značajna korelacija između titar IgG antitela na *H. pylori* i indeksa mase, dok je kod muškaraca uočena značajna inverzna korelacija između titra IgG antitela i indeksa mase (r= -0.54 P=0.009) (prilagođeno starosnoj dobi i UUR). Moguće je da su upala i aktivnost u antrumu kod *H. pylori* infekcije pojačane kod muškaraca u terminalnoj fazi bubrežne bolesti na dijalizi, premda ovu podložnost treba ispitati na većim grupama pacijenata.

Ključne reči: **hemodijaliza, H. pylori infekcija, terminalna faza bubrežne insuficijencije, specifična IgG antitela na H. pylori, indeks mase**