

Journal of Nephrology

Association between helicobacter pylori infection and body mass index, before and after eradication of infection in hemodialysis patients

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ARTICLE INFO

Article type:
Original Article

Article history:
Received: 21 May 2012
Revised: 30 May 2012
Accepted: 2 June 2012
Published online:
1 October 2012
DOI: 10.5812/nephropathol.8115

Keywords:
Hemodialysis
H. pylori infection
Body Mass Index

ABSTRACT

Background: In dialysis patients, chronic infections have been associated with cachexia and anorexia.

Objectives: This study was carried out to determine the association between Helicobacter pylori (HP) infection and body mass index (BMI) in hemodialysis (HD) patients.

Patients and Methods: Ninety eight patients were divided into two groups of negative (group 1) and positive (group 2), for HP. BMI of all patients was measured at the beginning and in group 2 after six months following eradication of HP. Before dialysis, various paraclinical parameters were checked at the same intervals.

Results: Fifty-nine patients were enrolled in group 1 and 39 patients in group 2. The means of BMI in groups 1 and 2 were 23.4 ± 3.7 and 25.8 ± 4.4 kg/m², respectively. Prior to the study, there was no significant difference for BMI, duration of HD and paraclinic data between two groups. Group 2 took anti HP therapy and eradication occurred in 30 of them. In this group six months after eradication of HP, the BMI was significantly decreased from 25.02 ± 4.4 to 24.4 ± 4.0 kg/m² (P = 0.001). Also six months following the eradication of HP, the mean of serum albumin level was significantly declined from 4.2 to 3.7 g/L (P < 0.001). There was also significant decrease in cholesterol (P = 0.001), blood urea nitrogen (P = 0.005) and calcium (P = 0.02). However, significant increase in hemoglobin level was also seen (P = 0.03).

Conclusions: The results of this study show that eradication of HP has an impact on BMI. The results need to be investigated with larger cases.

Implication for health policy/practice/research/medical education:

In dialysis patients, chronic infections have been associated with cachexia and anorexia. To determine the association between Helicobacter pylori (HP) infection and body mass index (BMI) in hemodialysis (HD) patients, this study was conducted on 98 HD patients. We found that eradication of HP was accompanied by decrease of BMI, a finding which needs to retest with large sample populations.

Please cite this paper as: Jalalzadeh M, Ghadiani MH, Mousavinasab N. Association between Helicobacter Pylori infection and body mass index, before and after eradication of infection in hemodialysis patients. J Nephrology. 2012; 1(3): 170-176. DOI: 10.5812/nephropathol.8115

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1. Background

Malnutrition is common among patients with chronic kidney disease (CKD) (1), which is strongly correlated with morbidity and mortality in this population (2). Appropriate dialysis, nutritional support and treatment of gastrointestinal disorders may reverse this condition (3).

In dialysis patients, chronic infections induce overproduction of pro-inflammatory substances and inflammation, which have been associated with cachexia and anorexia (4). Infection with *Helicobacter pylori* (HP) is also associated with anorexia, inflammation and malnutrition in dialysis patients (5).

Body mass index (BMI) is used as an indicator of nutritional status (6). In HD patients, a lower BMI is consistently found to be a strong predictor of an increased mortality risk (7).

2. Objectives

Considering the association between HP infection and nutritional parameters (4,8), we aimed to determine the association between HP infection and the status of BMI in HD patients and to found out the link between HP infection and development of malnutrition (8).

3. Patients and Methods

This study was conducted between 2008 and 2009 in two HD centers (Vali-e-asr & Beheshti hospitals) in Zanjan province, Zanjan, Iran. We determined the presence of HP infection in 98 HD patients using serum anti-HP IgG, HP stool antigen (HpSAg) and Urease Breath Test (UBT) (9).

Blood collection was performed during the dialysis and the patients were asked to take a stool sample for the study. Both sera and feces were immediately frozen until analysis. Sera were test-

ed for H. pylori antibodies by a commercial enzyme linked immunosorbent assay in accordance with the manufacturer's instructions. Patients with an antibody titer of 1.8 or more values were regarded as positive for H pylori. An enzyme-linked immunosorbent assay (ELISA) using polyclonal antibodies Premier Platinum HPSA was performed in accordance with the manufacturer's specifications (Astra SRL, Via Ciro Menotti, Milano, Italy). Readings were made at 450/630 nm. Samples with absorbance higher than 0.12 were considered as positive; those with less than 0.1, as negative, and those between 0.1 and 0.12, as undetermined. The ¹³C-UBT was also performed using the modified European protocol.

Patients who had dyspepsia and showed two positive results from the three mentioned diagnostic tests were considered as HP positive. Patients who had a history of treatment for HP during the preceding six months and those who did not cooperate in undergoing UBT were excluded from the study. All the patients gave informed consent before they were assigned into two groups: group 1 negative for HP infection and group 2 positive. All the patients in group 2 received triple therapy regimen of Omeprazole 20 mg, Amoxicillin 500 mg and Clarithromycin 250 mg or Azithromycin 250 mg twice a day for 14 days. In addition, administration of Omeprazole (20 mg) continued for two more weeks. Eradication of HP in group 2 was confirmed by UBT and HPSA two months after treatment.

At the beginning, BMI of all patients [defined as the weight in kilograms divided by the square of the height in meter (kg/m²)], were measured. BMI was also determined at six months following the eradication of HP in group 2. To assess the relationship between clinical factors and metabolic or nutritional metrics; serum pre-dialysis blood urea nitrogen (BUN), creatinine (Cr),

hemoglobin (Hb), albumin (Alb), cholesterol (Chol), triglyceride (TG), calcium (Ca) and phosphorous (P) were checked before eradication of HP and six months after. The data was compared between the groups. Duration of dialysis, age and gender were extracted from the patients' records. The HD protocol for all the patients was 4 h by using hemophane membranes and an average blood flow rate of 300 to 350 mL/min and with bicarbonate basis dialysate. All exams were made and laboratory values collected when patients got their dry weight six months after the start of chronic maintenance dialysis. Patients with serum ferritin level of greater than 350 ng/mL and transferrin saturation (TSAT) more than 20% were administered recombinant erythropoietin (rEPO) at a dose of 360 U/kg/wk. Statistical analysis was performed using SPSS for windows (version 17) software, employing Student's t-test for comparing continues variables in two groups and paired t-test for before and after data. Mann-Whitney U-test and Wilcoxon sign rank test were used for non-normal variables. All of the statistical tests were two-sided. P-values of less than 0.05 were considered significant.

4. Results

Out of the 98 HD patients, 59 (26 female and 33 male, with mean age of 51.1 ± 16.4) were tested negative, thus they were placed in group 1. Thirty-nine patients (18 female and 21 male, with mean age of 59.0 ± 16.2) were infected with HP and were placed in group 2. There was not any statistically significant difference between the two groups in terms of gender, duration of HD, serum levels of BUN, Cr, Hgb, Alb, Chol, TG, Ca and P ($p > 0.05$). However, there was significant difference for age between two groups ($P = 0.02$) (Table 1). The mean of BMI was 23.4 ± 3.7 kg/m² in group 1 and 25.8 ± 4.4 kg/m² in group 2,

and there was no significantly difference between the two groups as shown in Table 1 ($P = 0.07$). The BMI in the female and male groups was 23.5 ± 4.7 kg/m² and 24.5 ± 3.5 kg/m², respectively ($P = 0.26$).

Table1: Comparing the HP seronegative (Group-1) and positive (Group-2) patients.

variables	Group 1 (n:59)	Group 2 (n:39)	P value
Age (years)	51.1 ± 16.4	59.0 ± 16.2	0.02
Gender (F/M)	26/33	18/21	0.84
Duration of dialysis (Hour)	33.8 ± 33.8	43.1 ± 35.4	0.10*
BMI (kg/m ²)	23.4 ± 3.7	25.8 ± 4.4	0.07
Alb (mg/dL)	4.2 ± 0.8	4.2 ± 0.6	0.96
TG (mg/dL)	158.0 ± 107	158.8 ± 115.1	0.31*
Chol (mg/dL)	174.5 ± 45.9	175 ± 4.4	0.89
BUN (mg/dL)	76.7 ± 33.0	94.2 ± 47.9	0.10*
Cr (mg/dL)	9.7 ± 3.5	10.0 ± 2.9	0.68
Hgb (g/dL)	10.1 ± 1.9	10.4 ± 2.2	0.48
Ca (mg/dL)	9.4 ± 1.1	9.6 ± 1.1	0.44
P (mg/dL)	6.2 ± 3.08	5.7 ± 1.7	0.95*

BMI: Body Mass Index, TG: Triglyceride, Chol: Cholesterol, Cr: Creatinine, P: phosphorus

*Mann Whitney U test

The causes of ESRD among the patients were as follows: diabetic mellitus 19.6%, hypertension 33.3%, glomerulonephritis 3.9%, urologic problem 2%, polycystic kidney disease 3.9%, poisoning 2%, lupus nephritis 2% and unknown etiology 33.3% of cases. The mean of kt/v for patients was 1.21 ± 0.14 . The BMI of infected group before eradication and six months after was 25.02 ± 4.4 and 24.4 ± 4.4 , respectively (Table 2) ($P = 0.001$). Thirty-nine patients took anti HP drug regimen and 37 of them completed the treatment period. Two patients died before the start of treatment and were excluded from the study. A few number of patients complained of gastro-intestinal symptoms but there was no severe enough to compel them to drop out of the study. Eradication was successful in 30 patients

(81.1%), while seven patients (18.9%) remained positive. In group 2, six months after eradication of HP, the BMI was significantly decreased from 25.02 ± 4.4 to 24.4 ± 4.0 ($P=0.001$) and the mean of serum Alb level was significantly decreased from 4.2 to 3.7 ($P<0.001$). Significant decrease of BMI (from 25.02 ± 4.4 to 24.4 ± 4.0 , $P=0.001$) and serum Alb (from 4.2 to 3.7, $P<0.001$) after eradication of HP in group 2 was also seen. In addition, there was significant decrease in serum Chol ($P=0.001$), BUN ($P=0.005$) and Ca ($P=0.02$) and significant increase in Hgb ($P=0.03$). However, there was no significant difference in serum Alb, Chol, TG, BUN, Cr and BMI between male and female patients, as well as between diabetics and non-diabetic HD patients.

Table 2: Association of anti HP treatment on BMI and nutritional factors of HP positive patients (Group 2).

variables	Before treatment	After 6 months treatment	P value
BMI(kg/m ²)	25.02 ± 4.4	24.4 ± 4.4	0.001**
Alb(mg/dL)	4.2 ± 0.6	3.7 ± 0.5	<0.001
TG(g/ dL)	140.1 ± 76.4	155.7 ± 99.3	0.2*
Chol(mg/ dL)	179.7 ± 41.8	159.9 ± 36.2	0.001
BUN(mg/ dL)	90 ± 45.1	67.5 ± 16.4	0.005*
Cr(mg/ dL)	10.1 ± 3.2	9.6 ± 2.8	0.32
Hb(g/ dL)	10.7 ± 2.2	11.6 ± 1.7	0.03
Ca(mg/ dL)	9.7 ± 1.1	9.2 ± 0.9	0.02
P(mg/ dL)	6.2 ± 3.1	5.8 ± 1.7	0.48

*Wilcoxon signed test **repeated measure test

5. Discussion

The major aim of this study was to determine the association between HP infection and BMI or nutritional markers in HD patients.

Malnutrition is common among patients with CKD and is a risk factor for mortality among patients on maintenance HD treatment (10). Several factors may contribute to this problem, including age, nausea and vomiting due to ure-

mic toxins, gastroparesis, inadequate dialysis, loss of nutrients in the dialysate, inadequate protein intake, protein degradation and amino acid oxidation, as well as catabolic processes that occur during dialysis with bioincompatible membranes (8). In addition, malnutrition may be related to inflammatory and infectious complications (11). There is also the possibility that HP infection would have adverse nutritional effects (12).

BMI is often used as an indicator of nutritional status (13). According to WHO (14), BMI is an index commonly used to determine weight status: underweight, overweight and obesity.

In HD patients, a BMI of less than 19 kg/m² is considered as an indicator of increased mortality risk (15-22). It has been shown that weight loss in the HD patients is linked with elevated risk of cardiovascular and other causes of death (19). Since most of low BMI, patients show symptoms of chronic inflammation, the increased mortality risk of low BMI in the HD population has been associated with the malnutrition-inflammation cachexia syndrome (16, 18).

Individual metabolic syndrome risk factors, such as blood pressure, body mass index and serum cholesterol concentration, have been shown to have a paradoxical, and even opposite association with mortality rate in dialysis population, a phenomenon labeled as 'reverse epidemiology' (23).

However, Torun and Majchrzak reported that an increased BMI was not a reliable marker of good nutrition in HD patients. They further asserted that obesity was linked with higher C-reactive protein and lower serum albumin level in HD patients (23, 24). In addition, other reports have shown that HD patients with a high BMI may have elevated risk of coronary heart disease due to atherogenic role in fat tissue (19, 26).

In our study, after eradication of HP, the level

of albumin serum was significantly decreased. There was not any statistically significant difference in BMI between HP positive and negative patients prior to treatment. However, in HP positive group, BMI was influenced by treatment and BMI significantly decreased from 25.02 ± 4.4 to 24.4 ± 4.0 .

One study has shown that non-uremic HP infected patients had higher hypo-proteinemia compared with a HP negative group; and after HP eradication body weight ($p < 0.001$) and serum levels of total cholesterol ($p < 0.001$), total protein ($p = 0.001$) and albumin increased ($p < 0.001$), significantly (27).

Studies on the association of HP infection with malnutrition in HD patients have shown different results. A previous study has reported that HP infection induced inflammation and low serum albumin level in HD patients, due to various bacterial and host-dependent cytotoxic substances (28). Moreover, another study reported that eradication of HP, significantly improved the nutritional status [albumin level increased from 3.8 ± 0.3 to 4.0 ± 0.6 g/dL, ($P < .03$)] in HD population. Hence, all HD patients with malnutrition should be examined for HP infection (8). However, there are some researchers who believe that HP eradication has no effect on metabolic parameters (29-31).

However, the results of HP eradication were contradictory and no significant effect on metabolic parameters was even shown (29-31).

6. Conclusions

We detected HP infection in 39 out of 98 HD patients. We found that there was not any statistically significant difference between HP positive and negative patients in terms of BMI before eradication of HP. However, in HP positive group, BMI was influenced by treatment and

decreased significantly.

At the beginning of our study, the HP positive as well as negative groups did not show any difference in nutritional markers such as serum albumin, creatinine, BUN, hemoglobin, calcium, triglyceride and cholesterol. In group 2 six months after eradication, BMI and other Para-clinical factors were compared. We observed significant decreases in serum albumin, cholesterol, calcium and BUN levels (Table 2). We do not have an explanation for such a reduction in nutritional factors after eradication of HP. A significant increase in hemoglobin level was also observed in the group that underwent HP eradication therapy. Perhaps, reducing inflammation was induced by the increase in hemoglobin level following eradication of HP.

In the meantime, we believe that further studies, with large sample population (cases), should be conducted to ascertain any association between HP and BMI.

Limitation of study: Inflammatory elements were not checked.

Authors' contributions

MJ and NM designed and performed the research. NM and MHG analyzed data and wrote some parts of paper. MHD provided extensive intellectual contribution and reviewed the manuscript. MJ and NM reviewed the draft too. MJ prepared the manuscript.

Conflict of interest

The author declared no competing interests.

Funding/Support

This study was supported by a grant from Zanjan University of Medical Sciences.

Acknowledgments

The authors wish to thank staffs of Hemodialysis ward of Zanjan University of Medical Sciences.

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