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Article in *Transplantation Proceedings* · December 2011

DOI: 10.1016/j.transproceed.2011.08.112 · Source: PubMed

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The Seroprevalence of *Helicobacter pylori* Infection in Renal Transplant Recipients

Z.R. Khameneh, N. Sepehrvand, S. Hatami, and A.T. Afshari

ABSTRACT

Background. *Helicobacter pylori* (HP), a small gram-negative spiral bacillus living in the mucus layer of the human stomach, mediates some gastrointestinal disorders. Considering the immunocompromised nature of transplant recipients due to immunosuppression, they are generally prone to viral and bacterial infectious diseases. In this study we sought to investigate the seroprevalence of HP infection among Iranian kidney transplant recipients.

Methods. We selected randomly 91 kidney transplant patients who were examined for anti-HP Immunoglobulin G (IgG) using an enzyme-linked immunosorbent assay method (Lake Success, NY, USA).

Results. Forty-three subjects (47.3%) were seropositive for anti-HEV IgG. There was no difference by age ($P = .49$), sex ($P = .22$), blood transfusion history ($P = .19$), or hemodialysis history ($P = .46$) between seropositive and seronegative groups, but there was a significant difference regarding the educational status of the subjects ($P = .03$). The difference was not confirmed by considering diploma as the cut point to categorize subjects ($P > .05$). Comparing age groups, Pearson chi-square analysis revealed no significant correlation between HP seropositivity and increasing age ($P = .963$), even when controlled for sex, educational status, history of blood transfusion, or hemodialysis.

Conclusion. The frequency of transplant recipients with anti-HP IgG antibodies in our institution (47.3%) was not higher than that in the general population (almost 60% in Urmia). This rate was lower than reports from developing countries possibly due to better health and sanitation.

HELICOBACTER PYLORI (HP), a small gram-negative spiral bacillus living in the mucus layer of the human stomach,¹ produces asymptomatic infections in most cases (70%).² During the last 25 years since its discovery, numerous studies have focused on HP infections.

Renal transplantation is the treatment of choice among renal replacement therapies.³ Gastrointestinal complications are frequent, occurring among almost 20% of recipients.^{4,5} Although peptic ulcer and related complications are more rare among transplant recipients than in the past,⁵ its frequency increases after renal transplantation.⁶ Due to their immunocompromised nature from immunosuppressive therapy these patients are susceptible to viral and bacterial infections.^{7,8} Considering the strong body of evidence supporting causal effects of HP infections on the development of peptic ulcers and gastric malignancies, the argued rate of gastrointestinal complaints may be attributed to increased HP infection rate among this pop-

ulation. Of course HP infections have been demonstrated to show negligible effects on the outcomes of patients who have undergone renal transplantation.⁹

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The authors would like to thank Students' Research Committee of Urmia University of Medical sciences for the grants provided for our study.

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A few studies have investigated the prevalence of HP infection; about 30% to 40% of renal transplant recipients shown HP colonization of the stomach.⁹⁻¹¹ In this study, we sought to investigate the seroprevalence of HP infection among Iranian kidney transplant recipients.

MATERIALS AND METHODS

This study was conducted with the approval of our Scientific and Ethical Review Board. We selected randomly 91 kidney transplant patients who were grafted from 1991 to 2010. Informed consent was obtained from each patient prior to participation in the study. Blood samples (2 mL) were obtained via venipuncture for serological study. Samples were centrifuged and sera separated without delay for storage at -30° C, and subsequent analysis using the anti-HP immunoglobulin G (IgG) by an enzyme-linked immunosorbent assay (ELISA; E-Z-EM, Lake Success, NY, USA). The presence of anti-HP IgG antibody was considered to be evidence of prior exposure and infection by HP.

Data were collected regarding the following variables: age, sex, educational status, marital status, etiology of end-stage renal disease (ESRD), ESRD duration, hemodialysis history, blood transfusion history, and immunosuppressive therapy.

All collected data were analyzed using SPSS software ver16 (Chicago, Ill, USA). Descriptive statistics were reported as mean values ± standard deviations for continuous variables and as frequencies (%) for dichotomous variables. To evaluate the relationship between factors we performed chi-square analysis. Quantitative variables were compared using independent student *t* test. *P* values lower than .05 were considered significant.

RESULTS

The etiology of renal failure among patients were glomerulonephritis (*n* = 30; 33%), HTN (*n* = 28; 30.8%), polycystic kidney disease (*n* = 12; 13.2%), Renal atrophy (*n* = 3), nephrolithiasis and focal-segmental glomerulosclerosis (*n* = 2), and diabetes mellitus, Alport syndrome, neurogenic bladder, or urinary infection each in one participant (1.1%).

Mean anti-HP titer was 13.94 ± 9.79 among 43 (47.3%) kidney graft recipients who were seropositive for HP. Eight patients (8.8%) were within the indeterminate range of IgG titers and 40 (44%) were seronegative. For the purposes of analysis, sera with HP-specific IgG values within the indeterminate range were considered seronegative, consisting of 48 cases (52.7%). Antiparvovirus B19 IgG titer was 21.2 ± 9.1 in the seropositive and 7.4 ± 4.0 in the seronegative group (*P* = .000).

We compared patient characteristics of age, sex, educational level, history of hemodialysis, and history of blood transfusion between the seropositive and seronegative groups in the Table 1. There was no significant difference by age (*P* = .49), sex (*P* = .22), blood transfusion history (*P* = .19), or hemodialysis history (*P* = .46) but there was a significant difference regarding educational status (*P* = .03). However, by considering diploma as the cut point to categorize subjects based on their educational status, there was no such relationship (*P* > .05).

The mean IgG titer compared among men and women showed no significant difference: 14.66 ± 10.6 versus 12.5 ±

Table 1. Patient Characteristics Among Two Different Groups with Positive or Negative anti-Helicobacter Pylori (HP) IgG

Characteristic	Anti-HP-Positive (n = 43)	Anti-HP-Negative (n = 48)	<i>P</i> Value
Age	36.5 ± 14.4	34.4 ± 14.6	.49
Sex			
Male	31 (72.0%)	36 (66.6%)	.22
Female	12 (27.9%)	18 (33.3%)	
Education			
Illiterate	4 (9.3%)	15 (31.2%)	.03*
Lower than diploma	23 (53.4%)	17 (35.4%)	
Diploma & higher	16 (37.2%)	16 (33.3%)	
History of blood transfusion			
+	20 (54.0%)	23 (42.5%)	.19
-	17 (45.9%)	31 (57.4%)	
History of HD			
+	30 (69.7%)	35 (72.9%)	.46
-	13 (30.2%)	13 (27.0%)	
Anti-HP IgG titer	21.2 ± 9.1	7.4 ± 4.0	.00

* Significant; HP, Helicobacter pylori; IgG, immunoglobulin G; HD, hemodialyses.

7.7 (*P* = .33). Also the mean IgG titer in patients who underwent hemodialysis before transplantation was 13.6 ± 9.1, and 14.7 ± 11.3 in those without a history of hemodialysis (*P* = .63).

Twenty patients (22%) were younger than 20 years old, including 9 seropositive and 11 seronegative. Thirty-two patients (35.2%) were aged between 20 and 39 years with 15 seronegative but 17 were seronegative for HP infection. Finally, 39 patients (42.9%) were older than 40 years old with 19 seropositive and 20 seronegative. Comparing the age groups, Pearson chi-square analysis revealed no significant correlation between HP seropositivity and increasing age (*P* = .963). Multinomial logistic regression revealed no correlation among HP seropositivity and increasing age, even when controlled for sex, educational status, history of blood transfusion, or hemodialysis (*P* = .34; odds ratio = -0.03; 95% confidence interval: -0.11-0.03).

DISCUSSION

The frequency of transplant recipients with anti-HP IgG antibodies was 47.3% in our institution: whereas it has been reported to be 23% by Teenan et al,¹⁰ 29% by Davenport et al,¹² 31% by Sarkio et al,⁹ 38.5% by Yildiz et al,¹¹ 70% by Ozgür et al,¹³ and finally 60.5% by Abu Farsakh et al.¹⁴ Most reports are from developed countries, in which the prevalence of HP among the adult population is almost 30%.² The rate of seropositivity in our study was lower than the study of Ozgür et al in Turkey, another developing country in the Middle East region,¹³ which may be attributed to better health and sanitation status.

Comparing the age groups, Pearson chi-square revealed no significant correlation between HP seropositivity and increasing age (*P* = .963), consistent with the findings of Yildiz et al,¹¹ contrasts with the findings of Sarkio et al and Ozgür et al.^{9,13}

Several diagnostic methods have been suggested to diagnose HP infections. In the current study, we used an ELISA to determine previous or recent exposure to HP. Considering the patchy involvement of the stomach, all biopsy-based methods, including histology, culture, or urease test are subject to sampling errors. Consensus guidelines recommended multiple biopsies to overcome this shortcoming; moreover, these methods are invasive. HP can attack the lining of the stomach inhomogeneously.¹¹ Detecting anti-HP IgG using an ELISA is a reliable method (sensitivity 95.6%, specificity 85%). It represents the whole gastric mucosa and is more sensitive than other pathological methods. It is simple, reproducible, inexpensive, and noninvasive. Unfortunately, there is no reliable immunoglobulin M assay to indicate the recent acquisition of an HP infection or to identify acute infections and possible routes of transmission.

An unpublished study, which is conducted by Rabiepoor et al in our institution¹⁵ demonstrated an 58.3% seroprevalence of HP among healthy controls. The lower infection rate among renal transplant recipients compared with healthy controls may be explained by decreased humoral responses due to immunosuppression in the transplantation group. It may not represent a decreased infection rate. These findings are consistent with the findings of Yildiz et al¹¹ and Korzonek et al,¹⁶ who noted a lower prevalence of HP infections among renal transplant recipients than that in patients with normal renal function.

The mean age of subjects in the study of Rabiepoor et al was 42.9 ± 18.6 years old. Since the prevalence of HP infection has been demonstrated to be higher among older age groups in both developed and developing countries,^{9,13,17} the lower prevalence of HP infection in our study may have been due to a lower mean age in our study.

There is a controversy around the seroprevalence of HP infection among hemodialysis patients and transplant recipients. Some studies indicated higher rates of HP infection in uremic patients including hemodialysis patients compared with renal transplant recipients (63% vs 40%; $P < .001$).⁴ They have attributed the greater rate to higher levels of serum urea and anemia, as well as to fluctuations in gastric blood supply of uremic patients. On the other hand, Özgür et al failed to observe a significant difference in the seroprevalence of HP infections between hemodialysis patients and transplant recipients.¹³

Considering the controversy, it is suggested to perform a similar study among the hemodialysis patients at the same institution to compare HP infection seroprevalence.

Because of its retrospective design, our patients were not asked for their symptoms. Although most infected people

are asymptomatic,² the current study lacks information in this regard.

In conclusion, the prevalence rate of anti-HP IgG was 47.3% among Iranian transplant recipients, which was almost similar to that of the general population.

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