Saudi J Kidney Dis Transpl 2009;20(6):969-974

Saudi Journal of Kidney Diseases and Transplantation

Review Article

Current Knowledge on Helicobacter Pylori Infection in End Stage Renal Disease Patients

Hossein Khedmat[1,2], Saeed Taheri[3]

[1]Baqiyatallah Research Center for Gastroenterology and Liver Diseases, [2]Baqiyatallah University of Medical Sciences, [3]Dr. Taheri Medical Research Group, Tehran, Iran

ABSTRACT. Gastric infection with *Helicobacter Pylori* in end-stage renal disease patients is of relevance because of its potential impact on the quality of life as well as morbidity and mortality of patients. Existed data on the issue are controversial, and we attempt in this article to evaluate the available data to approach extended perception of the current knowledge on the epidemiology, relevance, and optimum therapeutic strategies.

Introduction

Helicobacter Pylori (*H. pylori*) is a gram-negative spiral flagellate bacillus that resides usually in the gastric mucosa and can cause chronic active gastritis and peptic ulcer disease.[1] In addition, chronic *H. pylori* infection has close associations with gastric hyperplastic polyps, gastric adenoma, gastric cancer, and gastric mucosa associated lymphoid tissue lymphoma.[2-6] Recently, increasing evidence suggests that some extra-gastrointestinal disorders including chronic idiopathic urticaria, iron deficiency anemia and idiopathic thrombocytopenic purpura (ITP) are also related to *H. pylori* infection.[7-9]

Correspondence to:

Dr. Hossein Khedmat
Baqiyatallah Research Center for Gastroenterology and Liver Disease
Baqiyatallah Hospital, Mullasadra St.
P.O. Box 14155-6437, Tehran, Iran
E-mail: Khedmat.h@gmail.com

Uremia triggers considerable clinical symptoms as well as pathological changes in the gastrointestinal (GI) system.[10,11] Dyspepsia defined as discomfort in the upper part of the abdomen is a common complication in chronic renal disease (CKD) patients, especially in regular dialysis patients, and it affects the quality of life in these patients.[12-14] *H. Pylori* infection is the single most reported responsible factor for dyspepsia by the studies that investigated the causes of this complaint in end-stage renal disease (ESRD) patients.[1]

Epidemiology

H. pylori infection is the most common chronic bacterial infection in humans. Estimates indicate that approximately 60% of the world population is colonized with this agent.[15] However; the epidemiological data concerning *H. pylori* infection in ESRD patients are controversial. The reported frequency of anti *H. pylori* antibody in patients with renal failure ranges from 21-64%.[16-26]

These conflicting results may be related to various factors including the methods of detecting *H. pylori* infection, the size of the study population, the local prevalence of the organism in the general population, and the various features of the study population. Several studies of the epidemiological features of *H. pylori* infection have revealed similar findings in ESRD and non-uremic patients.[15] However, higher or lower prevalence rates of *H pylori* infection in ESRD patients than the general population have been reported by other investigations.[1,27-33] There are different explanations for the variable prevalence. In a previous study on hemodialysis (HD) and renal transplant patients in comparison with healthy controls, we found a significantly higher prevalence of *H. pylori* infection in the HD patients than that in the other two groups.[1] Investigators who detected similar results to ours have mostly related it to the impaired immune system function.[15,27,28] Some investigators focused on the higher concentration of urea in the gastric juice of renal failure patients raising the local gastric pH and providing abundant substrate for *H. pylori.*[1,20] On the other hand, other investigators concluded that the higher levels of urea in the mucus of stomach in ESRD patients may result in a lower prevalence of *H. pylori* colonization in these patients.[29] Furthermore, fluctuations in the gastric blood supply,[1] low gastric motility, and hypo[15] as well as hyperchlohydria[30] have also been proposed for the higher the prevalence of *H. pylori* infection in the uremic patients.[31] Schoonjans et al[28] reported that positive *H. pylori* antibodies by serological tests may not be related to dyspepsia or gastroparesis in uremic patients.

Leffeld et al,[18] Luzza et al,[19] Fabrizi et al,[15] and Hosseini et al[32] found no difference of prevalence of *H. pylori* infection between patients on HD and healthy controls. They concluded that the levels of urea in ESRD patients do not represent a risk factor for acquiring *H. pylori* infection in this patient population. Altay et al[33] reported a 26.6% prevalence rate of *H. pylori* infection among chronic ambulatory peritoneal dialysis (CAPD) patients complaining of dyspepsia. Although they did not compare their finding with healthy individuals, one may observe that peritoneal dialysis patients have lower rate of *H. pylori* infection than the general population.

On the other hand, lower prevalence of *H. pylori* in HD patients has repeatedly been reported.[1,18,24,25,29,34] Patients with renal dysfunction may be partially protected against *H. pylori*; the reasons include increased prescription of antibiotics[24] and aluminum-containing anti-acids[35] in addition to uremia that can change bacterial colonization of the upper gastrointestinal tract with reduced *H. pylori* and overgrowth of other bacteria.[36] In a recent long-term prospective study by Sugimoto et al[29] on 539 Japanese HD patients, the prevalence of *H. pylori* infection was significantly lower than the general population, but it increased with the increased duration on HD. With respect to this finding, they presented three explanations: 1) blood urea levels as well as urea nitrogen levels in gastric secretions are higher in dialysis patients than in patients with normal renal function as high urea levels inhibit *H. pylori* growth in the stomach;[20] 2) *H. pylori* might be eradicated upon antibiotic treatment because antibiotics are commonly used or their concentrations are higher in patients with renal failure; 3) Patients receiving dialysis have higher levels of proinflammatory cytokines, including interleukin-1b, -6, -8, and tumor necrosis factor from activated inflammatory cells infiltrating the gastric mucosa.[37] As a result, gastric atrophy progresses with increased pH, and finally *H. pylori* cannot live in the gastric mucosa.[38]

Children with ESRD and Helicobacter Pylori

Gastrointestinal symptoms are quite common in children with ESRD, and under nutrition resulting from these symptoms contributes to their poor growth.[39] Several studies have investigated gastric *H. pylori* infection in adult HD patients, but scarce data exist regarding the above mentioned issue in infancy and childhood.[40-44]

The role of *H. pylori* in the pathogenesis of gastric diseases is well known in both adults and children.[45-48] However, there are several important differences in pediatric *H. pylori* infec-

tion compared to adults;[49-53] evidence suggests a lower incidence of *H. pylori* infection in children undergoing endoscopy.[45,48,49,54-56]

In a study on 37 chronic HD pediatric patients of whom 40% had gastrointestinal complaints, Emir et al detected *H. pylori* infection in 27%; 80% of *H. pylori*-positive patients were symptomatic, while only 14% of asymptomatic patients revealed *H. pylori* infection in their gastric tissues. In addition, *H. pylori* were detected in 62.5% of the patients with gastroduodenal lesions. Moreover, *H. pylori* positivity was associated with endoscopic abnormalities. Emir et al also reported comparable results for *H. pylori* infection among ESRD children with gastritis to children with normal kidney function.[49,55,57-59] With regard to all their findings, they recommended that upper gastrointestinal examination should be considered for symptomatic pediatric ESRD patients most notably in areas where *H. pylori* is known to be endemic.

Mortazavi et al,[60] in a study on 31 HD children, found that 17 (55%) had gastrointestinal symptoms and 20 (65%) were positive for *H. pylori* antibody, and children with longer duration on dialysis were more likely to be negative for *H. pylori* infection. These investigators, as other studies,[57] recommended gastrointestinal evaluations for all ESRD children, emphasizing the unreliability of symptoms in these patients.

Relevance of Helicobacter Pylori Infection in ESRD Patients and Impact of Treatment

H. pylori have a notable relationship with CRF and HD in several ways: 1) HP contributes to the development of peptic ulcer disease, esophagogastro-duodenal erosions, and anemia due to gastro-duodenal blood loss, which is common in HD patients. 2) HP produces gastric mucosal inflammation and, hence, may contribute to dyspepsia, anorexia, malignancies, and malnutrition in HD patients.[27,61] 3) HP may have an independent role in anemia of HD patients.[62]

An increased concentration of fasting serum gastrin is observed in patients with impaired renal function.[63,64] The mechanisms for the hypergastrinemia revealed in such patients are believed to be the declined renal clearance of gastrin and the increase in gastric G cell density.[63,64] It has been shown that *H. pylori* in the stomach plays a crucial role in the elevation of serum gastrin concentration.[65,66] However, scientific reports regarding the influence of *H. pylori* infection on the serum gastrin concentration in patients with ESRD have been limited and the results are conflicting. Luzza et al[19] and Tokushima[67] reported that dialysis patients with *H. pylori* infection had significantly higher serum gastrin levels than those who were not infected, while other studies did not find such differences.[68,69] Furthermore, Tokushima et al reported in two other studies that successful eradication of *H. pylori* using a combination therapy of amoxicillin, lansoprazole and plaunotol in patients on dialysis would induce a significant reduction in the serum gastrin concentrations.[70,71] The serum gastrin level was normalized in over 90% of patients who became *H. pylori* negative after treatment. The restoration of normal gastrin levels was associated with a marked reduction in the gastric juice ammonia levels and pH. Regarding these findings, Tokushima et al suggested that *H. pylori* infection might be responsible, at least in part, for the hypergastrinemia observed frequently in patients on dialysis. The same findings were reported in a study by Gur et al.[72]

In conclusion, in the context of the current knowledge, we suggest that eradication of *H. pylori* in uremic patients should be considered in all patients with upper GI symptoms, and the efficacy of this approach should be further evaluated in controlled prospective clinical trials. Moreover, although routine evaluation of asymptomatic adult ESRD patients for *H. pylori* infection does not seem warranted, it should be considered for all pediatric ESRD patients irrespective of symptoms.

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