Geget (2011) 11 (1) : 11 - 18
O The Egyptian Society for Pediatric Nephrology and Transplantation (ESPNT)

Original Article

Helicobacter Pylori in End Stage Renal Disease Paediatric Patients; Where Do We Stand?

Rania H. Tomerak; Samar M. Sabry and Mafia M. Gaafar *

Departments of Pediatrics and Clinical Pathology, Faculty of Medicine, Cairo University.*

ABSTRACT

Background: H. Pylori infection in end stage renal disease (ESRD) patients can have a potential impact on morbidity and mortality of these patients.

Objectives: This work is done to know the frequency of H. pylori infection in ESRD paediatric patients in comparison with healthy-matched children and to assess the impact of H. pylori on the disease status of these patients.

Patients and Methods: A cross-sectional study in which H. pylori stool antigen test was assessed in 38 ESRD pediatric patients on hemodialysis and in 50 healthy age and sex matched children to compare the prevalence of **H. pylori. Gastrointestinal** symptoms, hematological and biochemical parameters (including iron indices) were recorded in the patients together with hepatitis C virus co-infection. Comparison of these variables were done among H. pylori positive and negative ESRD patients.

Results: Among the 38 ESRD patients 18 (47.4%) had H. pylori versus nine (18%) of the 50 healthy children (p ° 0.0064). There was no significant difference between H. pylori positive and H. pylori negative patients as regards age, duration of dialysis, gastrointestinal symptoms, weight standard deviations and hepatitis C co-infection. Transferrin saturation index was significantly lower in H. pylori positive patients compared to H. pylori negative patients.

Conclusions: The prevalence of H. pylori infection is higher in ESRD children than in healthy children. Although this seems to have minimal effect on their current disease status, a definite protocol for the diagnosis and treatment of H. pylori is required being classified as group 1 carcinogen by the WHO - in already compromised patients.

INTRODUCTION

Helicobăcter Pylori (H. pylori) is a gram-negative bacillus that resides usually in the gastric mriucosa and represents the most common chronic bacterial infection'). Although *H. pylori* is widely seen, it is accepted as an etiologic factor in peptic ulcers, chronic gastritis, dyspepsia, gastric cancer, and mucosal-associated lymphoid tissue lymphomaa[2] . It is highly prevalent in low-income countries and colonization usually happens early in lifet[3].

Upper gastro-intestinal (GI) abnormalities are common in end stage renal disease (ESRD)[41]. Gastric infection with *H. pylori* in ESRD patients is of relevance because of its potential impact on their morbidity and mortality"[ ]. *H pylori* neutralizes gastric acid by urease, penetrates the mucus layer by the flagella and mucolytic enzymes, and attaches to the gastric epithelium by specific receptorst[5]. Since ESRD patients have increased gastric urea, they may be more susceptible to *H. pylori* colonization, which

can convert the urea to ammonia, thus providing protection against the low gastric pH[6].

There are various methods for the diagnosis of H. pylori. Urea breath test[1] or invasive methods, such as gastroscopy with biopsies and/or urease tests used to be the "gold standard" for detection of H. pylori. These are technically advanced and time consuming methods. Serological tests are also available but in children they often show lower specificity [8] and does not discriminate between current and past infections. The H. pylori stool antigen test (HPSA) has a high sensitivity, specificity and accuracy in children, 91-96%, 95-96% and 94-96% respectively[9] and gives a rapid result[3].

The prevalence database of *H. pylori* infection in children with ESRD is very scanty[10].

AIM OF THE WORK

This study was designed to know the frequency of occurrence of *H. pylori* infection in ESRD children in comparison with healthy-matched children, identify the relationship between *H. pylori* infection and the gastrointestinal symptoms in ESRD, to study the relationship between *H. pylori* infection and the iron status and to know the association between Hepatitis C virus (HCV) and *H. pylori* infection in these patients.

PATIENTS AND METHODS

This is a cross-sectional study conducted in the hemodialysis unit of the Center of Pediatric Nephrology and Transplantation of the Cairo University Children's Hospital. This study was approved by the ethical and scientific committees and was conducted in accoidance with the University by_1aws tor human research. All caretakers have given their informed consent. Thirty-eight patients having ESRD on maintenance hemodialysis were recruited. This included 18 males and 20 females aged between 4 and 18 years (mean + SD of 11.67 + 3.68).

None of the patients had taken antibiotic and/or antacid therapy within 4 weeks of the study. Patients were given IV iron guided by their iron indices parameters done every 3 months. Doses were adjusted according to the National Kidney Foundation - Kidney Disease outcomes Quality Initiative (NKF-KDOQI) anemia treatment guidelines". A control group was chosen to compare the rate of *H. pylori* infection between children having ESRD and healthy children. This included 50 children, 24 males and 26 females aged between 3.5 and 18 years (meant SD of 13.65 + 4.76).

General information of the patients was recorded including age, gender, duration of dialysis, GI symptoms and administered drugs. In addition, weight measurements and Standard Deviation Scores (SDS) for the patients' weights were obtained using *Tanner et al.* curves [2].

Dialysis duration in the patients ranged between 9 months to 8 years (3.58 . 2.38 years). Their Kt/v ranged between 1.2 and 3 (2.01t 0.43 3).

Laboratory investigations were done including complete blood count, pre-dialysis urea, serum iron, total iron binding capacity (TIBC), transferiin saturation index (iron/ TIBC), ferritin, albumin, calcium and phosphorus. HCV antibody was measured using

ELISA; as part of the routine investigations done to our ESRD patients.

The IIM lest: A stool sample was collected in air tight containers and transferred in a cool box - within two hours of collection - to the microbiology laboratory and stored at - 20°C till analyzed. DIA.PRO (Diagnostic Bioprobes SrL Columella поз 1-20128 Milano-Italy) was used to analyze the stool samples. It is an enzyme immunoassay for the qualitative determination of *H. pylori* antigen in human stools. The test utilizes microplates, which are coated with a cocktail of affinity purified mouse monoclonal antibodies directed • to the most specific *H. pylori* antigens. In the 1" incubation, the solid phase was treated with the sample, previously prepared from stool, and simultaneously with a mixture of monoclonal antibodies to *H. pylori,* conjugated with Horseradish Peroxidase (HRP). After washing out all the other components of the sample, in the 2"ᵈ incubation, the bound-enzyme specifically present on the solid phase generates • an optical signal that is proportional to the amount of *H. pylori* antigens present in the sample. The results were reported as positive or negative according t the manufacturer's cut-off values.

Statistical methods: Patients' data were tabulated and processed using SPSS (10.0) statistical package for Windows XP. Quantitative variables were expressed by means and standardrdeviation and were analyzed using student's unpaired t-test. Qualitative data will be expressed by frequency and percent and were analyzed using Chi-square. Pearson correlation co-efficient test was used to rank different variables against each other's positively or inversely. P value was considered significant if less than 0.05.

RESULTS

Among the 38 ESRD patients 18 (47.4%) had *H pylori* versus nine (18%) of the 50 healthy children (p 0.0064).

The age range (mean + SD) of the !f. *pylori* positive patients was 6-17 years (1 1.5 + 3.12) versus 4-18 years (11.825 Нь. 4.203) in the *H. pylori* negative patients (p 0.790). The duration of dialysis (mean + SD) in the *H. pylori* positive patients ranged between 9 months and 7 years (4.11 + 2.34 years) versus 11 month and 8 years (3.12 › 2.308 years) in the *H. pylori* negative patients (p = 0.204). No gender related differences were found between the two groups (p 1.000).

Dyspepsia was present in 13 (34.2%) ESRD patients; 4 of them were in the *II. pylori* positive group (4/18 ¨ 22.2%) and nine (9/20 == 45%) were in the *II pylori* negative group (p = 0.256).

The SDS for the patients' weights ranged between - 4.70 and 0.00 with a mean + SD of -2.352 + 0.932; -2.372 A: 0.81 in the *II. pylori* positive cases and - 2.335 1 1.025 in the *H. pylori* negative cases (p 0.903).

'the influence of *H. pylori* on the iron status of ESRD patients is shown in Table 1.

A significant difference between the two groups was found in the transferrer saturation index (p - 0.033) but not in the hemoglobin, iron. TIBC or ferritin.

The weight SDS in *II pylori* positive cases correlated positively with serum iron (r = 0.479, p 0.044) and transferring saturation index (r 0.544. p = 0.02) but

not with serum albumin (r = 0.323, p __: 0.192). The weight SDS in *H. pylori* negative cases correlated positively with serum iron (r = 0.774, p = 0.000), transferring saturation index (r = 0.533, p 0.016) and with serum albumin (r = 0.711, p = 0.000).

The influence of the presence of f1. *pylori* on the routine laboratory tests done to ESRD patients is shown in Table 2. Predialysis urea, albumin, calcium and phosphorus showed non-significant difference between the *K pylori* positive cases and *H. pylori* negative cases.

A significant correlation was noticed between urea and serum iron in positive cases (r = 0.477, p = 0.045) and between urea and serum ferritin in negative cases. (r = -0.466. p = 0.038).

Screening for HCV revealed eleven positive cases among the ESRD patients (28.9%). 7/18 (38.9%) of the *H. pylori* positive cases had HCV versus 4/20 (20%) in *H. pylori* negative cases but this comparison was non-significant (p == 0.288).

Table 1: **Iron status in H. pylori positive and H. pylori negative ESRD patients.**

	H. pylori positive	**H. pylori negative**	p-value
Hemoglobin	10.88t **1.88**	**10.59 A, 1.57**	0.604
Iron	71.22+49.26	87.45+43.54	0.288
TlBC**	296.0 + 99.65	242.65 f **89.91**	**0.091**
Transferrin saturation index	25.72f 18.54	39.39+ 19.43	0.033*
Ferritin	1037.89+ 730.1 7	1016.4 + 568.55	0.920

* Significant ** Total iron binding capacity

Table 2: Routine laboratory tests in H. pylori positive and H. pylori negative ESRD patients.

	H. pylori positive	H. **pylori negative**	p-value
Urea	67.17 + 16.69	65.57+20.87	0.797
Albumin	3.76+0.53	3.57+0.36	0.214
Calcium	8.57 + 0.94	9.08 :f 1.66	0.260
Phosphorus	*4.74+1.97*	5,29+1.58	0.346

DISCUSSION

The current study showed that the prevalence of *H. pylori* was significantly higher in ESRD patients than in the healthy subjects. Despite this, it seems to have minimal impact on their current disease status as evidenced by the non-significant difference in the occurrence of GI symptoms, growth parameters, haematological status and biochemical data.

Worldwide, *H. pylori* prevalence in children ranges from under 10% to almost 80%, being high in developing countries [13]. In ESRD pediatric patients, the prevalence of *H. pylori* is variable among the different studies ranging from around 25%t [10] to around 65% in other studiest [6,14].

In our study, 47.4% of the ESRD patients harbored *H. pylori* compared to only 18% of normal children (p = 0.0064). In uremic patients, many reports suggested a higher frequency of *H. pylori* infectiont [15, 16]. However, some authors found lower frequency of *H. pylori* infection with uremia [17,19] due to inhibition of *H. pylori* by other bacterial colonizationt [18] or by the toxic waste product accumulation in severe uremia [19].

There was no age or gender related differences between the *H. pylori* positive and negative cases in our study as well as in other studies done on ESRD patients(14,2°). However, male predominance was noticed among apparently healthy children in urban Kampala°. Higher prevalence of *H. pylori* was noticed, as the age gets older, in ESRD patientst [4.10]

Non-significant differences in dialysis duration were noticed in our study as well as in other studies [10,20]. However, longer *dialysis duration* was associated with lower *H pylori* prevalence in some studies [14,21,22].

Dyspepsia was present in 34.2% of ËSRD patients; with non-significant difference between colonized and non-colonized cases (p = 0.256) in our study as well as in other studiest [6, 1°.14]. Although GI symptoms and dyspepsia can predict the possibility of' GI disorders in non-uremic patient, they are not a good predictor in children with ESRD. Lack of symptoms in iiremic patients may be due to factors such as severity, the stress level of the patients, duration of these lesions, and alkalizing supplementation [15].

The guidelines for screening of *H. pylori* in children contradict. Recommendations vary from no need to screen children with GI symptoms cording to The European Pediatric Task/Force [23] and no need to screen children Ьlith recurrent abdominal paint [24] to all children with upper 01 symptoms should be tested for H. pylori infection according to the Consensus Report of The European *Helicobacter* Study Group; (Maastricht III) [25]. These recommendations are based on the lack of proof that infection with H. pylori is a significant cause of (H symptoms.

The acquisition of *H. pylori* infection in early childhood can lead to malnutrition and growth failure. *H. pylori* infection is associated with hypochlorhydria, increasing the susceptibility to other enteropathogenic infections, which ultimately results in impaired growth and cognitive function caused by the co-morbidity associated with malnutrition, micronutrient deficiency, and diarrheal disease [12b]. *H. Pylori* is associated with short stature; indeed, the incidence of *H. pylori* infection in malnourished children

Elitsur, Y.; Hassall, E.; Macarthur, C.; Snyder, J. and Sherman, P. (2000): Helicobacter pylori infection in children: recommendations for diagnosis and treatment. J. Pediatr. Gastroenterol. Nutr.; 31 (5): 490-497.

25. Malfertheiner, P.; Megraud, F.; O'Morain, C.; **Bazzoli, F.; El-Omar, E.; Graham, D.; Hunt, R.; Rokkas, T.; Vakil, N. and Kuipers, E. (2007):** Current concepts in the management of Helicobacter pylori infection: the Maastricht III Consensus Report. Gut. 56 (6): 772--781.
26. Windle, **H.; Kelleher, D. and Crabtree, J. (2007):** Childhood Helicobacter pylori infection and growth impairment in developing countries: a vicious cycle? Pediatrics; 119 (3): 754-759.
27. Sullivan, P.; **Thomas, J.; Wight, D.; Neale, G.; Eastham, E.; Correh, T.; Lloyd-Evans, N. and Greenwood, B. (1990):** Helicobacter pylori in Gambian children with chronic diarrhoea and malnutrition. Arch Dis. Child.; 65: 189-191.
28. Thomas, **J.; Dale, A.; Bunn, J.; Harding, M.; Coward, W.; Cole, T. and Weaver, L. (2004):** Early Helicobacter pylori colonisation: the association with growth faltering in The Gambia. Arch Dis. Child.; 89: 1149-1154.
29. **Mena, R.; Correa, P.; Fontham, E.; Reina, J.; Pradilla, A.; Alzate, A. and Bravo, L. (2006):** Effects of a new Helicobacter pylons infection on height and weight in Colombian children. Ann. Epidemiol.; 16 (5): 347-351.
30. **Richter, T.; Richter, T.; List, S.; Muller, D.; Deutscher, J.; Uhlig, H.; Krumbiegel, P.; Herbarth, O.; Gutsmuths, F. and Kiess, W. (2001): Five- to** 7-year-old children with Helicobacter pylori infection are smaller than Helicobacter-negative children: a cross-sectional population-based study of 3,315 children. J. Pediatr. Gastroenterol. Nutr.; 33 (4): 472-475.
31. **Mohammad, M.; Hussein, L.; Coward, A. and Jackson, S. (2008):** Prevalence of Helicobacter pylori infection among Egyptian children: impact of social background and effect on growth. Public Health Nutr.; 11(3): 230-236.
32. **Yuan, W.; Li, Yumin; Yang, Kehu; Ma, Bin; Guan, Quanlin; Wang, D. and Yang, L. (2010):** Iron deficiency anemia in Helicobacter pylori infection: meta-analysis of randomized controlled trials. Scand. J. Gastroenterol.; 45 (6): 665-676.
33. **Muhsen, K. and Cohen, D. (2008):** Helicobacter pylon infection and iron stores: a systematic review and meta-analysis. Helicobacter.; 13 (5): 323-340.
34. **E1-Masry, S.; EI-Shahat,. M.; Badra, G.; Aboel-Nour, M. and Lotfy, M. (2010):** Helicobacter pylori and Hepatitis C Virus Co-infection in Egyptian Patients. J. Glob. Infect. Dis.; 2 (1): 4-9.
35. **Cammarota, G.; Cianci, R.; Grillo, R.; Martini, M.; Di Campli, C.; Pompili, M.; Pignataro, G.; Cuoco, L.; De Lorenzo, A.; Gasbarrini, G.; Pandolfi, F. and Larocca, L. (2002):** Relationship between gastric localization of hepatitis C virus and mucosa-associated lymphoid tissue in Helicobacter pylori infection. Scand. J. Gastroenterol.; 37 (10): 1126-1132.
36. Rowland, **M. and Drumm, B. (1998):** Clinical significance of Helicobacter infection in children. Br. Med. Bull.; 54 (1): 95-103.