The Egyptian Society for Pediatric Nephrology and Transplantation (ESPNT)

Original Article

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

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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

Helicobacter Pylori (H. pylori) is a gram-negative bacillus that resides usually in the gastric mucosa 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. It is highly prevalent in low-income countries and colonization usually happens early in life. Upper gastro-intestinal (GI) abnormalities are common in end stage renal disease (ESRD). 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.
can convert the urea to ammonia, thus providing protection against the low gastric pH.

There are various methods for the diagnosis of H. pylori. Urea breath test 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 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 and gives a rapid result.

The prevalence database of H. pylori infection in children with ESRD is very scant.

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 accordance with the University by laws for 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 (mean ± 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.

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 (2.01 ± 0.43).

Laboratory investigations were done including complete blood count, pre-dialysis urea, serum iron, total iron binding capacity (TIBC), transferrin 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 II M test:** 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 immuno-assay 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” 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 to 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 standard deviation 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 *H. pylori* positive patients was 6-17 years (1 1.5 + 3.12) versus 4-18 years (11.825 ± 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 *H. pylori* positive group (4/18 = 22.2%) and nine (9/20 == 45%) were in the *H 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 + 0.81 in the *H. pylori* positive cases and - 2.335 ± 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 transferriner saturation index (p 0.033) but not in the hemoglobin, iron. TIBC or ferritin.

The weight SDS in *H 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 \( (r = 0.774, p = 0.000) \), transferrin saturation index \( (r = 0.533, p = 0.016) \) and with serum albumin \( (r = 0.711, p = 0.000) \).

The influence of the presence of \( f_1. pylori \) 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.

<table>
<thead>
<tr>
<th></th>
<th>( H. pylori ) positive</th>
<th>( H. pylori ) negative</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>10.88 ± 1.88</td>
<td>10.59 ± 1.57</td>
<td>0.604</td>
</tr>
<tr>
<td>Iron</td>
<td>71.22 ± 49.26</td>
<td>87.45 ± 43.54</td>
<td>0.288</td>
</tr>
<tr>
<td>TIBC**</td>
<td>296.0 ± 99.65</td>
<td>242.65 ± 89.91</td>
<td>0.091</td>
</tr>
<tr>
<td>Transferrin saturation index</td>
<td>25.72 ± 18.54</td>
<td>39.39 ± 19.43</td>
<td>0.033*</td>
</tr>
<tr>
<td>Ferritin</td>
<td>1037.89 ± 730.17</td>
<td>1016.45 ± 568.55</td>
<td>0.920</td>
</tr>
</tbody>
</table>

* Significant  ** Total iron binding capacity

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

<table>
<thead>
<tr>
<th></th>
<th>( H. pylori ) positive</th>
<th>( H. pylori ) negative</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>67.17 ± 16.69</td>
<td>65.57 ± 20.87</td>
<td>0.797</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.76 ± 0.53</td>
<td>3.57 ± 0.36</td>
<td>0.214</td>
</tr>
<tr>
<td>Calcium</td>
<td>8.57 ± 0.94</td>
<td>9.08 ± 1.66</td>
<td>0.260</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>4.74 ± 1.97</td>
<td>5.29 ± 1.58</td>
<td>0.346</td>
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</tbody>
</table>
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%\(^{10}\) to around 65% in other studies\(^{6,14}\).

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* infection with uremia\(^{15,16}\). However, some authors found lower frequency of *H. pylori* infection with uremia due to inhibition of *H. pylori* by other bacterial colonization or by the toxic waste product accumulation in severe uremia\(^{18}\).

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\(^{14,22}\). However, male predominance was noticed among apparently healthy children in urban Kampala\(^{8}\). Higher prevalence of *H. pylori* was noticed, as the age gets older, in ESRD patients\(^{4,10}\).

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 ESRD patients; with non-significant difference between colonized and non-colonized cases (p = 0.256) in our study as well as in other studies\(^ {6,1,14}\). 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 uremic 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 according to The European Pediatric Task/Force\(^ {23}\) and no need to screen children with recurrent abdominal pain to all children with upper GI 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 GI 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\(^ {26}\). *H. Pylori* is associated with short stature; indeed, the incidence of *H. pylori* infection in malnourished children...


