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Endoscopic Findings and *Helicobacter pylori* in Children on Long-Term Hemodialysis

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Abstract: The aim of this study is to evaluate the prevalence of GI symptoms, endoscopic abnormalities, histologic gastritis and *Helicobacter pylori* infection in children with End Stage Renal Disease (ESRD) undergoing maintenance hemodialysis. Upper endoscopy and gastric biopsy were performed in 31 consecutive ESRD children from 2002-2007, before renal transplantation. *H. pylori* status was determined by urease test and histology. The mean age of patients was 11±3.3 years (4-16 year). The mean duration of dialysis was 12.4±11 months (1.5-54 months). Seventeen patients (54.8%) were symptomatic. Twenty patients (64.5%) had endoscopic abnormalities. Antral erythema, esophagitis, antral nodularity and diffuse gastritis were common endoscopic findings. Endoscopic abnormalities were more common in symptomatic patients than asymptomatic patients ($p<0.05$). Twenty patients (64.5%) were *H. pylori* positive. There was no statistical correlation between age, sex, serum creatinine level, presence of any symptoms and endoscopic abnormalities with *H. pylori* positivity. The mean duration of dialysis in *H. pylori* negative patients was significantly longer in comparison with *H. pylori* positive patients. High prevalence of eodoscopic abnormalities and *H. pylori* infection in both symptomatic and asymptomatic patients emphasize the necessity of upper GI evaluation in ESRD children before renal transplantation.

Key words: End stage renal failure, *Helicobacter pylori*, gastroduodenal lesions

INTRODUCTION

Gastrointestinal (GI) disorders are common in patients with end stage renal disease (ESRD). Upper endoscopy in stable adult dialysis patients reveals abnormalities in up to 51%. Gastritis, duodenitis and mucosal erosions are the most common findings (Lew *et al*., 2001). The pathogenesis of uremic GI lesions is not understood. Multiple factors may be involved in development of GI lesions including uremia, multiple drug taking, dietary restrictions, hypergastrinemia and *Helicobacter pylori* infection. Current evidences strongly suggest that *H. pylori* is a major factor in pathogenesis of peptic diseases in general population (Gur *et al*., 1999). It has been estimated that approximately 60% of the world population is colonized with this organism (Aydemir *et al*., 2005). It is suggested that increased gastric urea concentration in renal failure and high urease activity of the bacterium, converting urea to ammonia, provides protection against the low pH of the gastric juice (Watanabe *et al*., 2003). However the relationship between *H. pylori* and peptic disease in patients with renal failure is not documented. Prevalence of *H. pylori* in Iranian adult patients with ESRD has been reported as high as 58.8 and 63% (Sotoudemanesh *et al*., 2003; Khedmat *et al*., 2007). Although there are many studies on gastroduodenal lesions and *H. pylori* in adult ESRD patients, data concerning children with ESRD is insufficient. The aim of this study is to assess the prevalence of GI symptoms, endoscopic abnormalities and *H. pylori* infection in children undergoing maintenance hemodialysis and determine the value of upper GI assessment in children awaiting renal transplantation.

MATERIALS AND METHODS

In this descriptive-analytic study performed from January 2002 to December 2007 in Children's Hospital of Tabriz, all children with ESRD on chronic hemodialysis that waiting for renal transplantation were investigated. A questionnaire was completed for each patient including history of renal disease and GI symptoms. Upper GI endoscopy performed in all patients by an experienced pediatric endoscopist with an Olympus GLF XP20 device, under appropriate sedation. Two gastric antral biopsies were taken for urease test and histologic assessment. Two other samples, one from duodenum and one from esophagus, were taken for histologic examination.

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Formalin fixed biopsy samples were stained with hematoxylin and eosine. Histological examination was done by one pathologist as recommended by Sydney working group report on gastritis (Price, 1991). *Helicobacter pylori* positivity was defined as the presence of histologically proven micro-organism and positive urease test. Patients who had received antibiotics, nonsteroidal anti inflammatory drugs, H_2 receptor blockers and proton pump inhibitors for 4 weeks prior to endoscopy were excluded. We treated *H. pylori* positive patients with omeprazol 20 mg once daily, amoxicillin 50 mg/kg/day and metronidazol 20 mg/kg/day for 14 days. Drug dosages were adjusted for glomerular filtration rate. Urease breath test was performed 2 weeks after termination of treatment to evaluate the eradication of *H. pylori*. The research ethics committee of Tabriz University of Medical Sciences approved the study and informed consent was obtained from all parents. Statistical analysis was performed using the SPSS 14 software for windows. Chi square and independent t-test were used to compare the groups. Pearson test was used for correlations. p-value less than 0.05 was considered significant.

RESULTS

Thirty one children (20 boys and 11 girls) were investigated during 6 years. The mean age of patients was 11±3.3 years (range: 4-16 year). The mean duration of hemodialysis was 12.4±11 months (range: 1.5- 54 months). Mean serum creatinine prior to hemodialysis session was 7±1.9 mg dL^{-1} (range: 3.9-9.7 mg dL^{-1}). Etiology of ESRD has been shown in Table 1. Seventeen patients (54.8%) had GI symptoms (Table 2). Mean age of symptomatic patients (13±1.7 year) was significantly higher than mean age of asymptomatic patients (8.3±3.1 year) ($p<0.05$). Twenty patients (64.5%) had one or more abnormal endoscopic findings (Table 3). Sixteen of symptomatic patients (16/17 = 94%) had abnormal endoscopic findings while only 4 of asymptomatic patients (4/14 = 29%) had endoscopic abnormalities ($p<0.05$). Epigastric pain was the most common symptom and antral erythema was the most common endoscopic finding. There was no statistical correlation between the age, sex, duration of dialysis and creatinine level with the presence of endoscopic abnormalities.

H. pylori was detected in 20 patients (64.5%). There was no significant difference in *H. pylori* positivity between symptomatic and asymptomatic patients (70.6% versus 57%) ($p>0.05$). The mean duration of hemodialysis in *H. pylori* negative patients (21.2±13.9 months) was longer than duration of dialysis in *H. pylori* positive ones (7.6±4.9 months) ($p<0.05$). Rate of *H. pylori* positivity in patients with endoscopic abnormalities (15/20 = 75 %) was higher than its rate in patients with normal endoscopy (5/11 = 45.4%), however the difference was not significant ($p>0.05$). There was no statistical correlation between the age, sex, and creatinine level with *H. pylori* positivity.

Table 1: Causes of ESRD in 31 children on maintenance hemodialysis

Etiology of ESRD	No. (%)
Acquired glomerular disease	14 (45.2)
Vesicourethral reflux	7 (22.6)
Hereditary renal disease	5 (16)
Obstructive uropathy	2 (6.5)
Unknown	3 (9.7)
Total	31

Table 2: Frequency of gastrointestinal symptoms

Symptoms	No. (%)
Asymptomatic	14 (45.2)
Symptomatic	17 (54.8)
Epigastric pain	9
Dyspepsia	6
Anorexia	5
Abdominal pain	4
Nausea/Vomiting	1

Table 3: Results of upper endoscopic examination

Endoscopic findings	No. (%)
Normal	11 (35.5)
Abnormal	20 (64.5)
Antral erythema	16
Esophagitis	11
Antral nodularity	11
Diffuse gastritis	8
Duodenal nodularity	2
Gastric ulcer	1
Duodenitis	1

Table 4: Results of histopathologic evaluation

Histopathology	No.
Chronic gastritis	21
Esophagitis	12
Duodenitis	6
Acute gastritis	1
Peptic ulcer	1

In histopathologic study, chronic gastritis followed by esophagitis and duodenitis were the most common findings (Table 4). Urea breath test after treatment in *H. pylori* positive patients revealed eradication of *H. pylori* in 14 (14/20 = 70%) patients. The 6 patients who didn't respond to first line therapy were treated with clarithromycin and amoxicillin.

DISCUSSION

GI symptoms are said to be common in patients with ESRD. Some studies on adults have reported the prevalence of GI symptoms as high as 77 and 79% (Cano *et al*., 2007). Cano *et al*. (2007) observed that the frequency of abdominal pain was 70% in uremics, 21% in

medical outpatients and 16% in healthy control group. Emir *et al.* (2000) studied 37 children with ESRD and showed that 40% of patients had GI symptoms before endoscopy and 80% of symptomatic and 23% of the asymptomatic patients had GI lesions on upper endoscopy. In this study 54.8% of patients were symptomatic and similar to Emir's study symptomatic patients had significantly higher rate of endoscopic abnormalities than asymptomatic patients. These findings indicate that most GI complaints in children with ESRD have an organic origin. However 29% of our asymptomatic patients also had abnormal findings on endoscopy which if not detected, may increase the risk of post transplant complications.

In most studies in adults and children mucosal erosions are the predominant finding in endoscopy and ulcers are uncommon (Emir *et al.*, 2000). In this study 64.5% of patients had endoscopic abnormalities and mucosal lesions were the most common finding and ulcer was found only in one patient. So the results of endoscopy in this study are similar to other studies.

It has been shown that *H. pylori* is closely involved in the development of peptic diseases. However there are conflicting reports about its real role in pathogenesis of uremic GI lesions in ESRD patients. In some studies in adults and children there was no difference in the prevalence of *H. pylori* in ESRD and control group (Abou Saif *et al.*, 2000; Olmos *et al.*, 2003; Al-Mueilo, 2004). Even in some studies on adults the prevalence of *H. pylori* in dialysis patients was significantly lower than nondialysed CRF patients and nonuremic group (Kang *et al.*, 1999; Nakajima *et al.*, 2004; Tsukada *et al.*, 2003). Nardone *et al.* (2005) observed high frequency of peptic lesions and *H. pylori* in uremics in comparison with dyspeptic nonuremic patients (2005). In this study rate of *H. pylori* positivity was 64.5%. Although the prevalence of *H. pylori* positivity in children of our area is not detected, in our recent study on children who underwent upper GI endoscopy for abdominal pain, its rate was 46% (Rafeey *et al.*, 2004). The relatively high incidence of *H. pylori* in ESRD patients may be due to their low socioeconomic condition. In this study the mean duration of dialysis in *H. pylori* negative patients was significantly longer than duration of dialysis in *H. pylori* positive patients. This finding has also been reported by Nakajima *et al.* (2002). It seems that long term dialysis decreases the prevalence of *H. pylori*. The reduction of gastric acid secretion related to chronic gastritis, or frequent antibiotic consumption may be involved in this rate reduction. In conclusion this study shows a high frequency of endoscopic abnormalities and *H. pylori* positivity in both symptomatic and asymptomatic ESRD children. So, clinical symptoms are not adequately reliable for prediction of GI lesions. Pretransplant detection and treatment of upper GI lesions is crucial for prevention of serious complications after transplantation.

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