

Upper Gastrointestinal Disorders in Children with End-Stage Renal Disease

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Abstract: This study was undertaken to define the prevalence of the upper Gastrointestinal (GI) lesions, dyspeptic symptoms, *H.pylori* infection, and the impact of duration of dialysis on upper GI symptoms and lesions of children with End-stage renal disease. We studied 69 children with ESRD who were under regular hemodialysis therapy in our department. The age of the patients were between 4-18 years (mean: 11.3). 57(82.6%) of 69 patients had GI symptoms and 12(17.4%) were symptom free, the prevalence of each symptom in 57 symptomatic children was as follows: anorexia 48(84.2%), nausea/vomiting 39 (68.4%), belching/heartburn 20(35%), abdominal distention 15(26.3%), and epigastric pain 8(14%). 65(92.4%) of 69 patients with ESRD had pathologic lesions and the most common lesion was gastritis. There was no case of gastric angiodysplasia in our patients. 15(21.7%) of 69 patients had *H. pylori* infection. The prevalence of *H.pylori* infection in non-uremic children with upper GI symptoms is about 27% in our pediatric gastroenterology department, so there was no significant difference in prevalence of *H.pylori* infection between uremic and non-uremic children in our study (p value = 0.4735). There was no significant relationship between duration of dialysis and dyspeptic symptoms or upper GI lesions (p values were 0.8775 and 0.7435, respectively). **Conclusions:** Upper GI disorders are very common in children with ESRD, even when they have no upper GI symptoms, the most common lesion is gastritis. The prevalence of *H.pylori* infection is not different between children with ESRD and non-uremic children with upper GI symptoms, and duration of hemodialysis therapy has no significant effect on prevalence of GI symptoms and lesions.

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Key words: Upper gastrointestinal tract, End-Stage Renal Disease, chronic renal failure, hemodialysis, children, *H.pylori* infection

Introduction

Upper gastrointestinal (GI) disorders like esophagitis, gastritis, duodenitis and gastro-esophageal reflux are common in patients with end-stage renal disease (ESRD) and there are many articles regarding incidence, pathophysiology and symptoms of upper GI disorders in adult patients with ESRD, but few studies are available in children (1-3). Because upper GI disorders can lead to feeding problems, undernutrition and failure to thrive in children, their importance in children is more than adults. So the present study was undertaken to define the prevalence of upper GI disorders, dyspeptic symptom, *H.pylori* infection, and the impact of duration of dialysis on upper GI symptoms and lesions of children with ESRD.

Patients and Methods

69 children with ESRD who were under regular hemodialysis therapy in our department underwent upper GI endoscopies as a part of routine evaluation for renal transplantation. Based on interviews and questionnaires, data on symptoms of GI tract disorders were acquired. With informed consent of the parents and discussion of procedure for the children and their parents, upper GI endoscopies were performed by an expert pediatric gastroenterologist using a videogastroscope (PENTAX EG-2731, JAPAN). The endoscopic appearance of esophagus, stomach and duodenum were recorded and during endoscopies, biopsy specimens were obtained from esophagus, gastric antrum and, in case of abnormal appearance of

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duodenum, from duodenum and sent for pathologic evaluation. For detection of *H.Pylori* infection, modified Giemsa staining on biopsy specimens and Urease test were done.

In order to evaluate the impact of the duration of hemodialysis on prevalence of GI symptoms and pathological lesions, patients were divided into the 6 following groups: lower than 6 months under hemodialysis, 6-12, 12-24, 24-36, 36-48, and over 48 months and the prevalence of GI symptoms and lesions were compared among them.

All analyses were performed using Instant software program and comparisons were made using Fisher's exact test and Mann-Whitney test. *p values* lower than 0.05 and Odd's ratio more than 1 were considered significant.

Results

The ages of our patients were between 4-18 years of age (mean 11.3 years). 39(56.5%) were girls and 30 (43.5%) were boys, and most of the children were between 10-12 years of age. Minimum interval between the start of hemodialysis and endoscopic evaluation was 4 months and maximum was 58 months (mean 27 months).

57(82.6%) of 69 patients had GI symptoms and 12(17.4%) were symptom free. The prevalence of symptoms in 57 symptomatic children is seen in table 1.

Out of 57 patients with GI symptoms only one had normal upper GI endoscopic appearance and pathologic findings, while 56 patients had upper GI lesions. The prevalence of pathologic lesions in symptomatic patients is illustrated in table 2.

12 (21%) of 57 symptomatic patients were infected with *H. Pylori*, of whom 8(66.7%) had gastritis, 3(25%) had gastroduodenitis, and 1(8.3%) had peptic ulcer

Of 57 symptomatic patients only 2 had previous history of drug usage which could affect GI tract. Of these 2 patients, both having taken steroids for systemic lupus erythematosus, one had gastroduodenitis and the other had esophagogastrroduodenitis, but both were negative for *H. Pylori* infection.

Minimal interval between the first session of hemodialysis and endoscopic evaluation was 4 months; maximum was 58 months with the mean of 13 months. Patients were divided into 6 groups according to duration of hemodialysis and the prevalence of GI symptoms was compared among them. Using Mann-Whitney test, the *p value* was 0.8775, so there was no significant relationship between duration of dialysis and prevalence of GI symptoms. Prevalence of histologic changes was also compared among these 6 groups, the *p value* being 0.7435, so again there was no significant relationship between duration of hemodialysis and GI lesions.

9(75%) of 12 asymptomatic patients had pathologic lesions, and 3 (25%) had normal endoscopy. The prevalence of lesions in asymptomatic patients is illustrated in table 2. Of 12 asymptomatic patients, 3 were infected with *H.Pylori*. All of these 3 patients with *H. Pylori* infection showed pathologic changes, 2 having gastritis and one having peptic ulcer.

Table 1. The prevalence of GI symptoms in symptomatic patients

	Number of patients (percent)	
	Number	Percent
Anorexia	48	(84.2)
Nausea / Vomiting	36	(68.4)
Belching, heartburn	20	(35)
Abdominal distention	15	(26.3)
Epigastric pain	8	(14)

Table 2. The prevalence of upper GI tract lesions in all of our patients

lesion	Symptomatic patients	Asymptomatic patients	Number and percent (%)
Gastritis	39	3	42(60.8)
Duodenitis	8	1	9(13)
Gastro- duodenitis	3	2	5(7.2)
Peptic ulcer	2	1	3(4.3)
Esophago- gastritis	2	1	3(4.3)
Esophagitis	1	1	2(3)
Esophago-gastroduodenitis	1	-	1(1.4)
Without lesion	1	3	4(6)
Total	57	12	69(100)

Of 12 Asymptomatic patients, 2 had previous history of drug usage which could impact GI tract; one had gastritis and one had normal biopsy and none had peptic ulcer or *H. Pylori* infection.

In summary, of 69 patients with ESRD 65 (94.2%) had a pathologic finding in endoscopy or biopsy of upper GI, whereas only 5.8% were without lesion. The most common lesion was gastritis(60.8%), 3 patients (4.3%) had peptic ulcer, of whom all had duodenal ulcer and two were infected with *H. Pylori* infection.

Of 69 patients, 15 had *H.pylori* infection (21.1%).The prevalence of *H.pylori* infection in our gastroenterology department in non-uremic children with upper GI symptoms is about 27% and there was no significant difference in prevalence of *H.pylori* infection between uremic and non-uremic children in our study (P= 0.4735).

None of our patients had angiodysplasia of upper GI tract.

Discussion

Upper GI tract disorders in patients with ESRD can be considered from two aspects:

- 1- Gastroesophageal dysmotility
- 2- Mucosal lesions

Gastroesophageal dysmotility in ESRD patients manifests as delayed gastric emptying and gastro esophageal reflux. These functional disorders are very common in adult patients (4, 5). The other aspect of GI disorders in uremia is mucosal lesions such as esophagitis, gastritis, duodenitis and peptic ulcer.

These disorders in children with ESRD can produce symptoms such as anorexia, nausea, vomiting, regurgitation, bloating, early satiety and can lead to feeding problems, under-nutrition and failure to thrive. 82.6% of our patients had upper GI symptoms. While some of these symptoms like anorexia, nausea, and vomiting are nonspecific and can be seen in most children with uremia, but others including epigastric pain, bloating, heartburn, and early satiety are more specific to upper GI disorders. Moreover, 56 (98.3%) out of 57 symptomatic patients showed mucosal lesions in endoscopy of upper GI tract and only one had normal endoscopy. Therefore, upper GI disorders are common and in children with ESRD and must be considered in management of these children, especially when they are preparing for renal transplantation.

We studied pathologic changes of upper GI tract in our patients. Of 69 children with ESRD, 65(94%) had upper GI tract lesions. This is much higher than the

percentage reported by Emir² and coworkers which was about 48%. A reason might be the fact that they did not report esophageal lesions. In adult patients, the reported incidence is between 25-67%, (1) even Moustafa and coworkers reported that in asymptomatic adult patients 60% had mucosal lesions in endoscopy of upper GI tract, (6) in our 12 asymptomatic patients, 9(75%) had mucosal lesions.

The most common reported pathology of upper GI in uremic patients is gastritis (4, 7, 8). This was confirmed in our study (60%).The incidence of peptic ulcer in general pediatric population is about 4-5.3% (6,9,10). In our patients and other reported series (11, 12) the incidence of peptic ulcer was similar to general population. Some studies have reported an increased incidence of gastric angiodysplasia in adult population (12, 13). However, in our patients there was no case of gastric angiodysplasia.

The duration of dialysis did not have any influence on prevalence of GI symptoms or lesions.

H.pylori is considered the most common causative agent of antral gastritis and duodenal ulcer, (14, 15) and because *H.pylori* produces urease, the high gastric juice urea level in CRF might create a favorable environment for its growth and it was expected that *H.pylori* infection be more common in CRF patients, but in many reported series (16, 17,) along with our study, the prevalence of *H.pylori* infection did not differ between hemodialysed and normal children. Even in some studies the incidence of *H.pylori* infection in CRF patients has been lower the general population (5, 18).

The etiology of upper GI disorders in ESRD is multifactorial and some of its aspects are not clear, but known factors are:

- 1- Psychological stress (19- 20)
- 2- Endocrine disturbances of CRF
- 3- Autonomic nervous system disorders
- 4- Miscellaneous causes: acidosis, hypo- or hypercalcaemia, hyperkalemia, hyperparathyroidism, and uremia

Psychological stress is widely believed to play a major role in gastrointestinal dysfunction, especially in irritable bowel syndrome. Some evidence suggests that psychological stress can inhibit upper GI motor functions and produce dyspeptic symptoms (20).

Many peptides are cleared from circulation in kidneys, and in uremia the blood level of some peptide hormones including gastrin, cholecystokinin, and gastric inhibitory peptide (GIP) is increased. These hormones affect gastric motility and secretion. Gastrin increases gastric motility and acid secretion, but in spite

of high level of gastrin in blood of majority of uremic patients, many have decreased gastric motility (4, 5, 21-23,).

Furthermore, CRF patients are heterogeneous in respect to gastric acid secretion (24); some have acid hypersecretion (25) whereas others have normal, or low acid secretion (25- 28). Rantala and Paronen (29, 30) reported that parietal cells, chief cells, and G cells are increased in stomach of uremic patients. Because G cells secrete gastrin, Hypergastrinemia in uremia may have two reasons: increased production by G cells and decreased clearance by the kidney. Also Rantala (30) and Co-workers observed that the number of oxyntic enterochromaffin cells in the stomach of uremic patients is reduced. Such changes reflect the complex interplay between different endocrinological activities in the gastrointestinal tract of the uremic patients.

The pathogenesis of upper GI dysmotility in these patients is not clear and seems to be multifactorial. Hormonal changes of CRF such as increase in gastrin, cholecystokinin, and GIP affect gastric motility (1, 31, 32). Derangements of autonomic nervous systems (especially in diabetic CRF patients) have a major role^[4] but it seems that many other factors such as electrolyte disorders and hyperparathyroidism also work together to produce dysmotility.

In summary, GI disorders are common in children with ESRD and can give rise to feeding problem and failure to thrive. Therefore, they must be considered in management of these children.

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