

CLINICAL-EPIDEMIOLOGICAL CONSIDERATIONS REGARDING PRIMARY PEPTIC ULCER IN CHILDREN – 5 YEARS RETROSPECTIVE STUDY

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ABSTRACT

Primary peptic ulcer still remains highly quoted in children from developing countries, the infection with *H. pylori* having a high incidence among this cases. Between 2007 and 2012 a retrospective study was performed, involving 84 children who were hospitalized in our clinic, ulcer disease being the main diagnosis. The study's inclusion criteria were suggestive clinical symptoms and positive endoscopy. The studied group consisted by 79 children with primary ulcer and 5 with secondary ulcer. Reporting data for 1,400,000 children population in North – Eastern Romania an incidence of 5.64/100.000 of primitive ulcer disease has been found, the frequency being 2.58% compared with the overall 3052 upper digestive endoscopies done in the years mentioned above. Male to female ratio was 1.46:1. 77.41% of the patients originated in urban areas. The onset was by functional digestive syndrome in 70,89% of the cases or by complications in 29.11% of the cases. By upper digestive endoscopy 62 duodenal ulcers (DU) and 10 gastric ulcers (GU) were identified. Perforation allowed intraoperative diagnosis of ulcerative lesions in 7 children. 70.89% were *H. pylori* infection – related ulcers. The contributing factors for developing this condition were unproper diet (63.16%), smoking (57.89), alcohol consumption (15.78), psychological stress (27.27%). We obtained a significant correlation between the high number of a family members, ($r = 0.63\%$; $p = 0.002$), the low socio-economical status ($r = 0.87$, $p = 0.0003$) and *H. pylori* infection. We used the standard triple therapy on 73.33% of the patients, the quadruple therapy, based on bismuth on 16.66% of the children, and the sequential therapy in 10% of the cases. The global eradication rate was 66.66% therefore we considered this as being an indirect proof for the high claritromycine resistance in children from our region.

Keywords: primary ulcer disease, child, *H. pylori*

INTRODUCTION

Peptic ulcer represents a gastric or duodenal mucosa discontinuity, along with muscularis mucosa penetration and submucosal exposure (1).

In the last two centuries, the peptic ulcer was a major threat for the population, having a high mortality and morbidity. The epidemiological data for the peptic ulcer and its complications revealed major geographical variation regarding the incidence and prevalence. (2). Discovering the antisecretory therapy, along with *Helicobacter pylori* infection have been associated with a decrease of peptic ulcer's rate; thus, the causes, the pathogenesis and the treatment of this disease have been reconsidered.

Peptic ulcer is classified in primary and secondary ulcer, depending on the subjacent pathology.

The ulcer disease still remains frequent in children from developing countries that have a high incidence of *H. pylori* infection, with a high percentage of the people having a deficitary socio-economical status. The disease's ethyology also involves an impaired balance between defence and aggression factors, heredity, familial history and psychological factors.

AIMS

The aims of this study is to investigate the prevalence, the clinical characteristics and risk factors regarding the ulcer disease in hospitalized children from the 5th Clinics of Pediatric Gastroenterology from „Sf. Maria“ Hospital, Iasi, between 2007-2012.

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MATERIAL AND METHOD

We retrospectively examined all the endoscopic records and observation sheets on a 5 years period (2007-2012). 84 children with peptic ulcer were included in the study. From the observation sheets we considered the following data: patient's sex and gender, environmental factors, patient's medical history (emphasizing the eso-gastro-duodenal pathology); family medical history (ulcer disease on Ist and IInd degree relatives, confirmed *H. pylori* infection in the certain family); socio-economical status; the presence of psychological factors as scholar stress, familial and entourage conflicts, chronic drugs intake, smoking, alcohol consumption. We insisted on disease history, the way the symptoms appeared, the duration, (self) drugs administration and their effect.

In all the patients upper digestive endoscopy was performed, and gastric mucosa biopsy was taken in order to assess the *H. pylori* infection (urease rapid test and microscopy). One day before the endoscopy, the children were explained about the technique, and informed consent was requested and obtained from their parents. General antesthesia was used in children under 10 year of age, and conscious sedation with midazolam was preferred for older children. Indications for endoscopy were: active or persistent/relapsing haematemesis/melena; upper abdominal pain and/or dispeptic disorders, especially associated with anorexia, weight loss, school classes missing, as symptoms that showed an organic pathology, persistent vomiting, iron deficiency anemia of unknown ethiology, inconclusive radiological image. In order to check the ulcer lesions, their evolution under the treatment and *H.*

pylori infection eradication, we also performed upper digestive endoscopy.

„STATISTICA” programme was used for the statistical data processing.

RESULTS

From the 84 studied children, 79 were diagnosed with primary ulcer disease (94.5%) and 5 with secondary ulcer (5.95%), thus, an incidence of 5.64/100.000 children with primary peptic ulcer was recorded, with a frequency of 2.58%.

The 79 children with primary ulcer disease were 7 to 18 years. An incidence peak was situated between 14 and 16 years of age (49.36% of the cases).

The studied lot includes 47 boys and 32 girls, sex ratio de M/F = 1.46. The age of the male patients being diagnosed with primary ulcer was significant different from the one of the female patients. The signification level was calculated using the ANOVA test ($p = 0.000114$, $p \ll 0.05$), which support this conclusion.

The environmental factors may influence the primary ulcer, thus the incidence of ulcer in urban children being higher (78.48%) that the one in rural children (21.52%). We can appreciate that the environmental factors prognostic for the 7 to 18 years patients with primary ulcer is 77.41% for the urban.

The familial history was positive in 55.33% of the children with duodenal ulcer; in this group, we found the 0(I) blood group in 55.56% of the cases.

The direct correlation found between the personal medical history and ulcer disease ($r = 0.788$) proves that these conditions promote the primary ulcer. The statement was made on a 95% confidence interval.

The contingency test sustains the conclusion affirming that the personal medical history influences

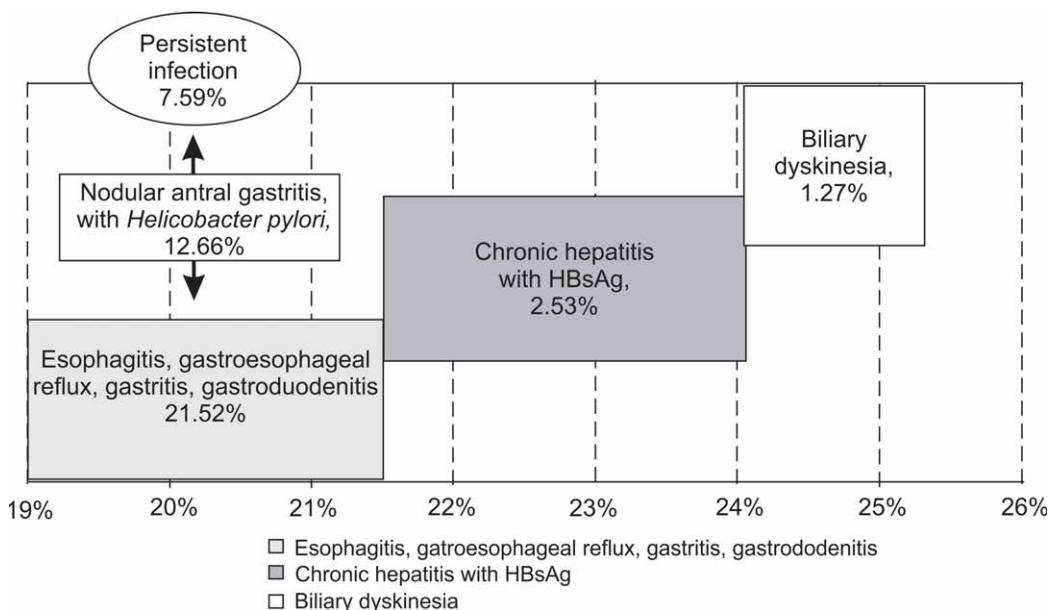


FIGURE 1. Personal medical history in children with primary ulcer

the disease to appear. Chi-square = 70.90 is greater than the reference value, corresponding to the 4 freedom degrees ($\chi^2 = 9.49$) (Fig. 1).

Analyzing the data referring to the socio-economical status (the number of the family siblings, family budget, type of accommodation), we got a multiple significantly correlation between the high number of family members ($r = 0.63$, $p = 0.002$) respectively poor economical status ($r = 0.87$, $p = 0.0003$) and the presence of *H. pylori* infection.

Of the exogenous factors that influence the ulcer epidemiology, we indentified an unproper diet in 63.16% cases, smoking in 57.89% cases and alcohol consumption in 15,78%, these percentage being registered in urban children.

The correlation coefficient value ($r = 0.6283948$) indicates the influence that the psychological elements have in the start of the ulcer disease in children, especially in teens. Thus, the scholar stress was revealed in 27.27% of the cases, the familial conflicts in 22.73% of the cases, and entourage conflicts in 13.64% of the cases (Fig. 2).

In the studied lot, there have been 23 primary ulcers that onset with a complication (16 cases of upper haemorrhage and 7 cases of perforation) and 56 cases in which the onset was with a digestive functional syndrome, corresponding to 29.11% and 70,89% respectively.

The onset of the abdominal pain was acute in 16 cases (“acute” meaning a period up to 3 weeks) (20,25%) and chronic in 40 % of the cases (50,64%) (Fig. 3).

The accompanying symptomatology was: nausea (21,52%), pirosis (18,99%), flatulence (11,39%), postprandial plenitude (10,13%), early satiety (8,86%), regurgitation (7,59%), belching (6,33%).

Vomiting was present in 36 patients (45,57%). Most of the patients had food vomiting (19 cases), food and bile (8 cases). 9 children had haematemesis as first sign of the upper digestive haemorrhage (Fig. 4).

Upper digestive endoscopy was performed in 72 cases from all 79 cases, excepting the perforative lesions. We underline that this technique revealed without any doubt the localization of the ulcer lesions in absolutely all the cases.

In 70.89% of the cases, the ulcer disease was associated with a *H. pylori* infection, of which 77.42% being duodenal ulcers. The ulcer disease without a *H. pylori* infection was found in 29.11% of the cases (Fig. 5).

The first line treatment in *H. pylori* infection eradication was represented by the triple therapy which included a proton pump inhibitor (PPI) (1-2 mg/kg/day), clarithromycin (20 mg/kg/day) and amoxicillin (50 mg/kg/day) for 7-10 days. We used the standard triple therapy on 73.33% of the patients. The quadruple therapy – the combination of PPI (1-2 mg/kg/day), bismuth subcitrate (8 mg/kg/day), metronidazole (20 mg/kg/day) and amoxicillin (50 mg/kg/day) – was used in 16.66% of the cases, and the sequential therapy – 5 days PPI (1-2 mg/kg/day) and amoxicillin (50 mg/kg/day) followed by 5 days of PPI (1-2 mg/kg/day), clarithromycin (20 mg/kg/day) and metronidazole (20mg/kg/day) – in 10% of cases. The global eradication rate was 66.66%. We mention that we did not have any technical facilities for testing the bacterial antibiotal resistance. Previous studies have reported a 33% clarithromycin resistance in Romania (3).

Complicated ulcers were endoscopically treated (upper digestive haemorrhage) and surgically (perforations), respectively.

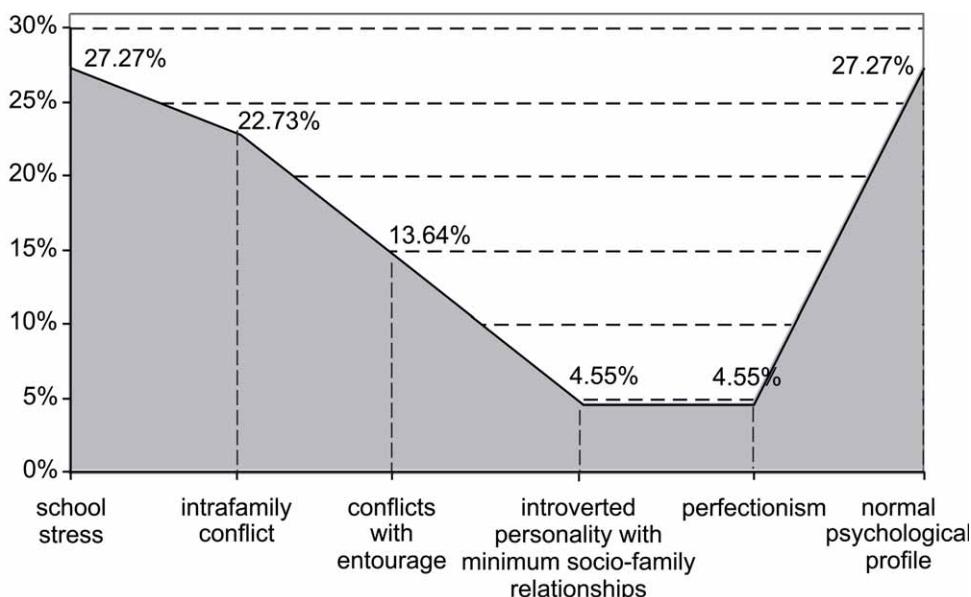


FIGURE 2. Incidence of the cases correlated with the psychological factors

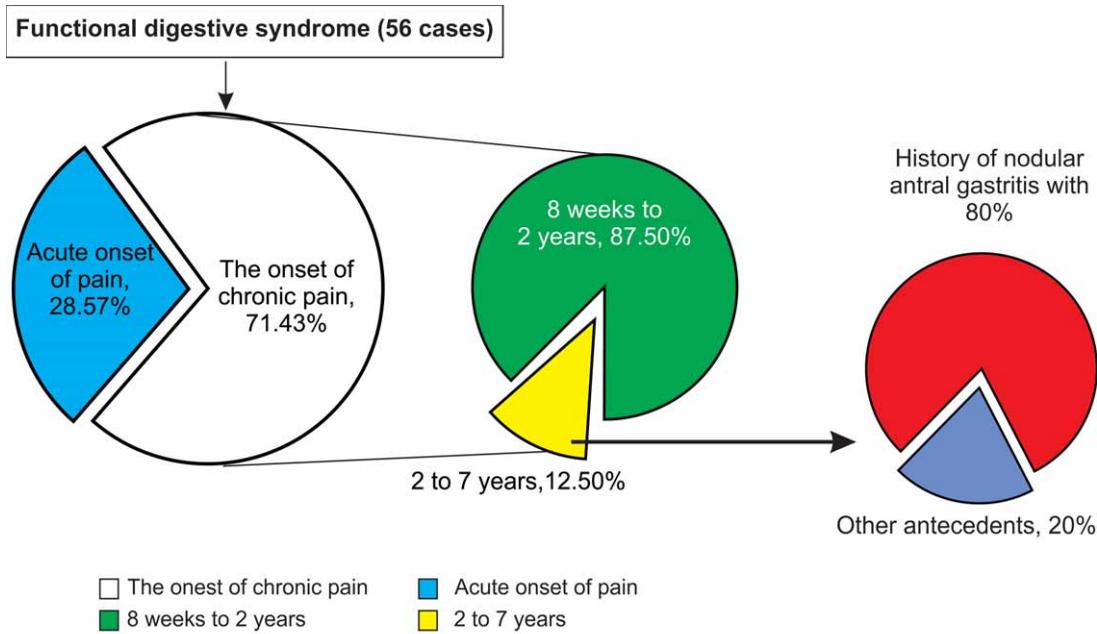


FIGURE 3. Incidence of the cases correlated with the type of onset of the disease

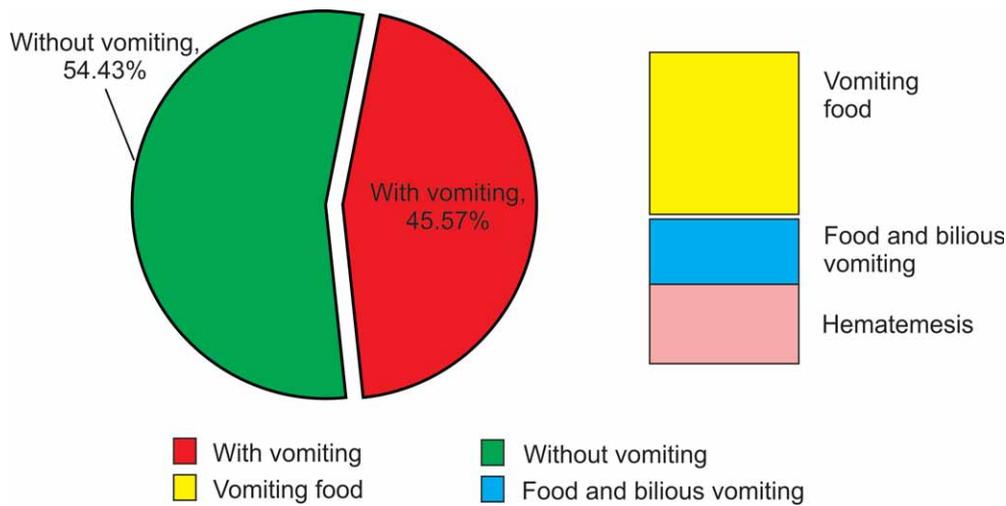


FIGURE 4. Vomiting in primary ulcer disease

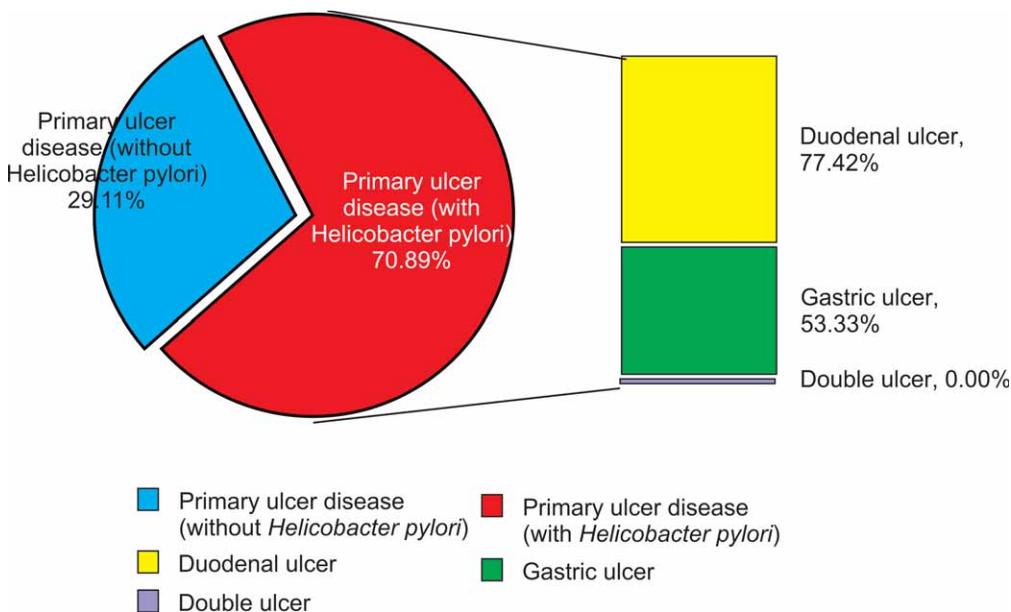


FIGURE 5. *Helicobacter pylori* infection in primary ulcer disease

DISCUSSIONS

A multicentric European study (4) reported a frequency of 8.1% for peptic ulcer in children. The main indications for upper digestive endoscopy were abdominal pain and gastroesophageal reflux presumption. Epigastric pain, haematemesis, melena and stationary weight gain were significantly associated with existence of ulcers.

In Turkey, the authors reported the presence of the ulcer disease in 13.2% of the children to whom an upper digestive endoscopy was performed. In the evaluated population, gastric ulcer and *H. pylori* infection were the most frequent, and the most children were hospitalized for abdominal pain (5). Our study demonstrates that the duodenal ulcer was more frequent and the presence of *H. pylori* infection and the onset symptoms were according with the literature.

Other researchers from Israel (6) found similar data. The study was performed on 651 endoscopies on a period of 4 years. The ulcer disease was recorded in 6.8% patients, with a higher frequency in children over 10 years, gastric ulcer being present in smaller ages. *H. pylori* was present in 66.3% of the patients.

Nowadays, the *H. pylori* infection is the most frequent cause of peptic ulcer in children, interfering with the diagnosis, evolution and treatment of this disease (7,8). *H. pylori* infection is acquired in the childhood and is frequent in developing countries (5).

High treatment-failure rates of *H. pylori* infection are being recorded. This is why more efficient treatment schemes are needed (9). We obtained a global eradication rate of 66.66%, using the recommended first line therapies (10). Although we didn't have any technical facilities for testing the antibio-

tical bacterial resistance, we considered the moderate eradication rate as an indirect proof for the high clarithromycin resistance in Romanian children, because of the wide-spread empirical antibiotics usage in our country.

It has been proven that the prophylactic treatment with PPI noticeably decreased the risk for gastric and duodenal ulcer (11). The antisecretory treatment during an entire year is indicated for the high-risk patients (recurrent, complicated, giant ulcers) (12).

Peptic ulcer cases, apparently without any risk factor, are reported in the literature (9).

CONCLUSIONS

In the North-Eastern of Romania, the primitive ulcer disease affects first of all the urban teens, coming from large families with low socio-economic status and a great incidence of *H. pylori* infection. Duodenal ulcer was more frequent associated with 0(I) blood group and with positive medical family history. The associated risk factors for the disease are: diet, smoking, alcohol, stress. A moderate eradication rate obtained using the recommended first line therapy regimens was considered as being an indirect proof of high clarithromycin resistance in Romanian children, statement that must be proven by further studies.

ACKNOWLEDGMENTS

We thank to Endoscopy Department and Microbiology Laboratory of „Sf. Maria“ Children's Emergency Hospital.

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