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Full Length Research Paper

Helicobacter pylori Infection and Its Impact on Peptic Ulcer Disease Among Children in Albania

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Aim: To evaluate the role of H pylori in peptic ulcer disease in albanian children according to clinical findings, histological data and eradication rate. Methods and patients: We have enrolled in this study all the patients who underwent to FGS for gastrointestinal symptoms during three years. We found 22 patients with peptic ulcer disease 20 of them with duodenal ulcer and 2 with gastric ulcer. For each patient we performed two biopsies (antrum and corpus) and one more antral biopsy for urease rapid test. After completing the data for 22 patients we have started eradication therapy for Hp positive group. Two months after therapy we have evaluated the eradication rate. For each patient we have included clinical, endoscopic and histological findings. Results: Of the 22 patients with peptic ulcer disease we found 17 patients infected by H pylori and 5 patients negative for H pylori. Range was from 8 years old to 14 years old (mean age was 11,3 years old). In this study with 22 patients there are 18 boys and 4 girls. Hp positive group had 14 boys and 3 girls while Hp negative group had 4 boys and 1 girl. Abdominal pain was equal with GI bleeding while the most frequent histological finding was chronic active gastritis. Of the 17 patients Hp positive 15 of them were negative for Hp two months after triple therapy. Conclusion: H. pylori play an important role in peptic ulcer disease in albanian children . His incidence is approximately 77 %. Male predomination was another interesting finding in our study. Eradication rate of H pylori was 88.2 %

Keywords: helicobacter pylori, peptic ulcer disease , fibrogastroduodenoscopy.

Background

Helicobacter pylori (Hp) is a gram-negative bacillus responsible for one of the most common infections found in humans worldwide (Blecker 1997). Warren and Marshall first cultured and identified the organism as *Campylobacter pylori* in 1982. By 1989, it was renamed and recognized to be associated closely with antral gastritis (gastric and duodenal ulcers in adults and children). In recognition of this crucial discovery, they were awarded the Nobel Prize for medicine in 2005.

Peptic ulcer disease (PUD) affects up to 10 % of the general population (Bernersen et al., 1990; Wenger et al., 1985). Ulcer disease has been classified into primary and secondary ulcer. Today there are a lot of studies that confirm the link between primary ulcer and H. pylori infection. In Albania we have not an epidemiological study to evaluate the prevalence of H. pylori in general

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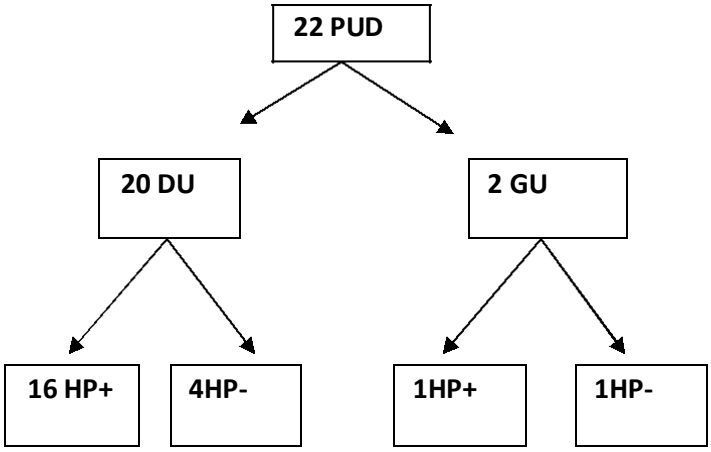

Figure 1. Flow chart of patients according to endoscopic findings and HP infection.
PUD:peptic ulcer disease; DU:duodenal ulcer;GU:gastric ulcer;HP:helicobacter pilory

population. Knowing that our country is a developing country we hypothesized that incidence of H. pylori in our population will be high. This is the first study in Albania that shows eradication rate of H pylori in children with peptic ulcer disease.

According the most recent ESPGHAN and NASPGHAN guidelines is recommended eradication of the organism in children with peptic ulcer disease (Koletzko et al., 2011). Besides treatment studies on children are limited by the small number of infected children in each individual center (Francavilla et al., 2005; Odertda et al., 2007; Lionetti et al., 2010), we would like to give our opinion about the role of H pilory in children with peptic ulcer disease.

PATIENTS AND METHODS

From January 2011 to January 2014 we enrolled all children who underwent to fibrogastroduodenoscopy for gastrointestinal symptoms. We have selected all children with peptic ulcer disease excluding medicaments ulcers, crohn ulcers etc. For each patient we performed standard techniques of endoscopy prescribing macroscopic findings (for example erythema, gastric nodularity, place of ulcer etc). We have taken two biopsies (antrum, corpus) and one more for urease rapid test (Pyloryset Urease–Orion diagnostica) .Histological analyses are performed at our department of Histopathology at Mother Teresa Hospital. Biopsies were stained with hematoxilin –eosin. H pylori presence, neutrophil infiltration, mononuclear infiltration, gastric atrophy or intestinal metaplasia were recorded according to Updated Sydney grading system. A patient was considered infected by H pylori if biopsy result was positive . It was considered also infected by H pylori a child whose biopsy was negative but rapid urease test was strongly positive . We have considered “strongly positive” when rapid urease test is turned red in 15-30 minutes while interval of positivity for this test go to three hours .We divided patients in two groups Hp positive and Hp negative. Children Hp positive are treated with standard therapy for eradication of H pilory according to the last recommendation of ESPGHAN and NAPSGHAN .Our approved protocol of treatment was : PPI (1-2 mg/kg/d) q.d 4 weeks+ amoxicillin 50-70 mg/d b.i.d for one week + clarythromycine 15-20 mg/kg/d b.i.d for one week. One patient was treated with Metronidazole in place of amoxiciline because of previous penicillin side effects. Children Hp negative are treated only with PPI (1-2 mg/kg/d) for 4 weeks. We have evaluated eradication rate in Hp positive group two months after therapy performing again upper endoscopy with biopsy for histopatology and one more for rapid urease test .

RESULTS

We enrolled all children that underwent to upper digestive endoscopy for gastrointestinal symptoms. We found in total 22 patients with peptic ulcer disease. Interval of age was from 8 years old to 14 years old (mean age was 11,3 year). We had 20 patients with duodenal ulcer and two patients with gastric ulcer (see Figure 1). Of 22 patients diagnosed with peptic ulcer disease 18 of them were boys and 4 were girls (see Figure 2). After diagnostic test for H pylori (biopsies and rapid urease test) we confirmed 17 patients Hp positive and 5 patients Hp negative (figure.1) .Incidence of H pylori in our group of patients was 77%. All Hp positive children were under standard triple therapy. As we

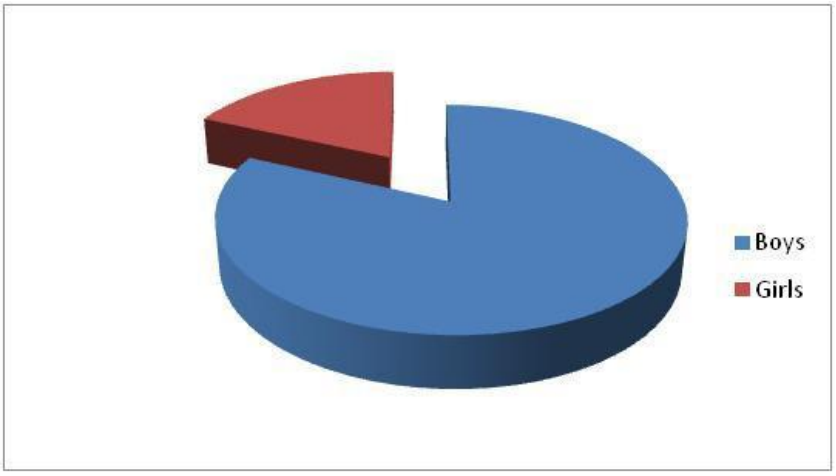

Figure 2. Sex difference in our group of children

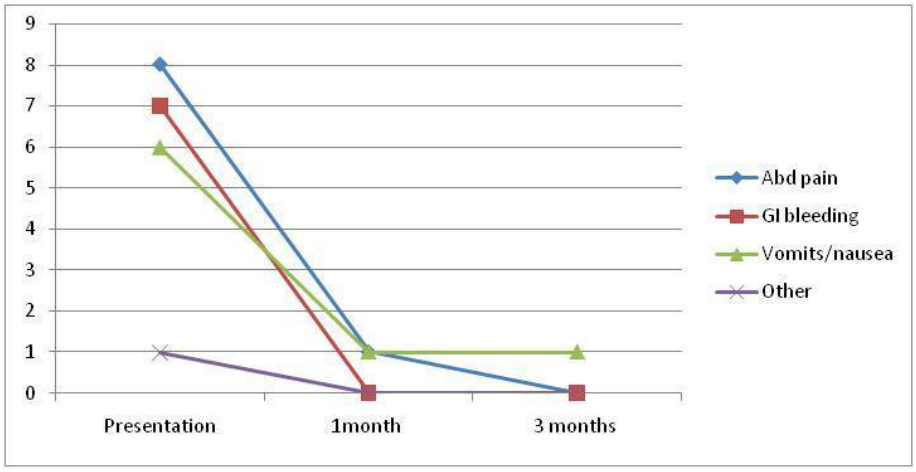

Figure 3. Clinical findings at presentation, one month and 3 months after

mentioned before we have evaluated the eradication rate one month after triple therapy by upper digestive endoscopy taking again three biopsies. Two biopsies (corpus and antrum) for histopathology and one more in antrum for rapid urease test. Of 17 patients Hp positive only two patients were positive for H pylori. Eradication rate was 88.2%.

We evaluated clinical data at presentation, one month and three months later (see Figure 3). Of the 22 patients with peptic ulcer disease 11 of them presented abdominal pain as the first symptom (38%). 10 of them has presented symptoms of gastrointestinal bleeding (hematemesis or melena)(35%); 8 children presented vomits or nausea as the first symptom and one child(3%) has presented a syncopal episode as a result of severe anemia and hypotension (see Figure 4).

Histological data are evaluated according to Updated Sydney system. Of 17 patients HP positive the most frequent histopathological finding was Active chronic gastritis (11/17). 6 patients had chronic gastritis but low activity. Interesting was the fact that after eradication therapy histopathological view has changed dramatically. Histopathological images of 15 patients in Hp positive groupe didn`t show neutrophil infiltration two months after therapy. Only two patients had the persistence of Hp infection with neutrophil and lymphoplasmacytic infiltration.

DISCUSSION

The discovery of H pylori by Marshall and Warren (Marshall and Warren 1984), has changed the

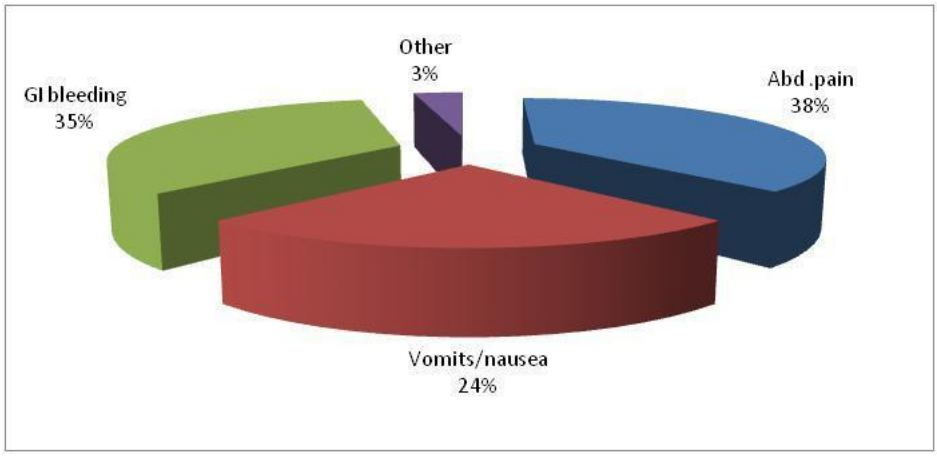

Figure 4. Chart that shows symptoms of our children at presentation

management for peptic ulcers. H pylori infection is now considered to be the most important cause for primary peptic ulcers in both adults and children, and eradication of bacteria is effective in decreasing the ulcer relapse(Sherman et al., 2002; Malfertheiner et al., 1997).

However, contrary to most of previous reports that abdominal pain was the most common presentation (Drumm et al., 1988; Roma et al., 2001; Goggin et al., 1998), acute GI bleeding occurred as the primary presentation in 35% of our patients. An earlier study conducted in China, reviewing patients from 1975 to 1988, also found that acute GI bleeding to be the most common presentation (Chan et al., 1997). In our study we have quite the same number of children that presented gastrointestinal bleeding (10) compared with abdominal pain (11). Improvement of symptoms was very significant after therapy in both groups.

The sex difference between the H pylori positive and the H pylori negative group is also of great interest. Studies have shown a male predominance in peptic ulcer disease in children. Epidemiological studies do not suggest any sex predilection in H pylori infection (Laine et al., 1998). We found that male predominance was only observed in the H pylori positive group. Of 17 patients Hp positive we found 14 boys and 3 girls. On the other hand we had only five patients Hp negative (4 boys and 1 girl) but the small number of patients in this group could not be conclusive. In another study performed in our center we have included 94 patients with dyspeptic symptoms. Among them we found 56 Hp positives patients but the ratio between girls and boys was equal.

Histological findings in H pylori –infected children have been extensively described elsewhere (Dixon et al., 1996; Guiraldes et al., 2002; Rubin 1997). For clinical management purposes, the most important information is whether Helicobacter is present. Variation in H. pylori density may have a bearing on disease associations and have epidemiological importance. (Davies et al., 1994; Stolte et al., 1995; Trespi et al., 1994). The most frequent finding in our group Hp positive was chronic active gastritis (see Figure 5). In general, gastritis is classified into acute and chronic. Chronic gastritis is divided into nonatrophic chronic gastritis usually caused by Hp infection , and atrophic gastritis composed of autoimmune and multifocal atrophic gastritis caused by Hp or dietary factors , as well as special forms of gastritis composed of reactive (chemical ,reflux) ,radiation , lymphocytic ,non infectious granulomatous, eosinophylic and other infectious gastritis (Capella et al., 1999; Rugge and Genta 2005; Makristathis et al., 2004; O`Keffe and Moran 2008). However the presence of Hp in a biopsy specimen does not mean that is the sole etiological agent. In some cases there are multiple etiological agents(Duck et al., 2004; Franceschi et al., 2002; Graham et al., 2004; Graham 2000). In our study histological change was very significant after eradication therapy. Histological amelioration in Hp positive patients goes parallel with eradication rate. We didn`t find any child with gastric atrophy or intestinal metaplasia. Those findings are very rare in pediatric age group and may arrive after years if children are not treated.

In our study Hp eradication was achieved in 88.2% of patients. Two patients were offered to second line therapy

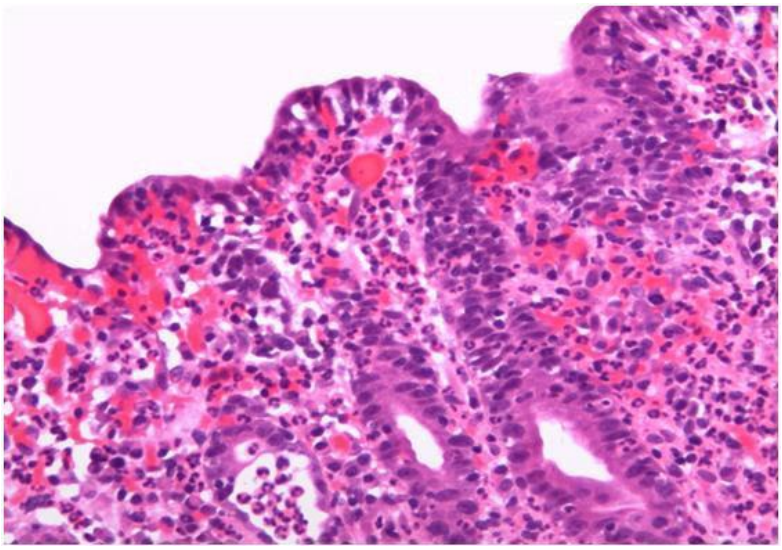

Figure 5. The most frequent histopathology image in our Hp positive group: chronic active gastritis

(PPI 1-2 mg/kg/d q.d +amoxicilin 50-70 mg/kg/d b.i.d and metronidazole 20 mg/kg/d b.i.d) according to ESPGHAN/NASPGHAN recommendation, confirming the possibility of a high resistance to clarithromycin. In fact we did not performed susceptibility test because is not available in our center.

CONCLUSION

In Albanian children male sex is predominant in Peptic ulcer disease. Our study has shown that abdominal pain is quite equal with gastrointestinal bleeding as presentation signs of PUD in children. We had a high eradication rate in our group of Hp positive children. The most frequent histopathological finding in this group was chronic active gastritis. We have seen a normal histopathological view in the most part of our patients after eradication therapy.

Competing interest

The authors declare that they have no competing interests.

Authors` contributions

VV designed the study and wrote the manuscript; GC has contributed for histopathological analysis; AC has performed a part of upper endoscopy and designed the study; ED provided data collection; PC gave the final approval of the version to be published. All authors read and approved the final manuscript.

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