

Original article

Helicobacter Pylori Infection and Peptic Ulcer Disease in Children and Adolescents from the Age Range of 6 to 18 Years Old in Yaounde (Cameroon)

Infection à H pylori et maladie ulcéreuse peptique chez l'enfant et l'adolescent à Yaoundé (Cameroun)

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ABSTRACT

BACKGROUND: A high prevalence of Helicobacter pylori (H pylori) infection is observed in the pediatric age in developing countries. Thus, in these countries with a high prevalence of H pylori infection, peptic ulcer disease (PUD) is still common in the pediatric age. This study aimed to describe the prevalence, clinical manifestations and complications of PUD in the pediatric age in Cameroon.

MATERIAL AND METHODS: This was a 9-year retrospective study. Data of children and adolescents admitted to the “Centre Médical la Cathédrale” of Yaounde, for upper GI tract endoscopy between January 2006 and December 2014 were reviewed. A group of 115 patients with PUD (84 boys [73.0%], 31 girls [27.0%]; 24 children [20.9%], 91 adolescents [79.1%]; mean age 14.7 ± 3.0 years) were compared with a control group of 99 patients without ulcer (49 boys [49.5%], 50 girls [50.5%]; 35 children [35.4%], 64 Adolescents [64.6%]; mean age 14.1 ± 3.4 years). H pylori was diagnosed when the rapid urease test and histology were both positive.

RESULTS: PUD was found in 33.1% (115/347) of patients. The overall prevalence of H pylori was 68.3%. Peptic ulcers were mostly duodenal ulcers (75.7%) and Helicobacter pylori-positive ulcers (77.4%). The prevalence of Helicobacter pylori in gastric ulcer and in duodenal ulcer was 61.9% and 79.3%, respectively. H pylori was more frequent in patients with PUD than in control patients (77.4% vs. 52.4%; p=0.0001). H pylori was more frequently detected in girls than in boys (90.3% vs. 72.6%; p= 0.07), in adolescents than in children (78.0% vs. 75.0%, p= 0.75). Most of patients were admitted due to abdominal pain (80.9%). There was no significant association between abdominal pain and Helicobacter pylori infection (p= 0.99). Peptic ulcer hemorrhage accounted for 20% of PUD and was mostly duodenal ulcer in children. Stenosis complicated 13% of PUD and this was more frequent in male adolescents.

CONCLUSION: PUD is common in the pediatric age in Cameroon. H pylori-related PUD is the most frequent variety and is more common among boys and in the duodenum. Measures to improve the hygienic and the social conditions are necessary to protect children against H pylori infection.

KEYWORDS: Helicobacter pylori, Peptic ulcer disease, Children, Adolescent, Cameroon

RÉSUMÉ

OBJECTIF : Évaluer la prévalence de l'infection à H pylori, déterminer les manifestations cliniques et les complications dans la maladie ulcéreuse peptique chez l'enfant et l'adolescent camerounais.

MATÉRIELS ET MÉTHODES: Il s'agit d'une étude rétrospective sur 9 ans chez des patients issus de la cohorte du Centre Médical la Cathédrale de Yaoundé, qui effectue des endoscopies digestives. Un groupe de 115 patients avec un ulcère peptique (84 garçons [73,0%], 31 filles [27,0%] ; 24 enfants [20,9%], 91 adolescents [79,1%] ; moyenne d'âge 14,7±3,0 ans) a été comparé à un groupe contrôle de 99 sujets sans ulcère (49 garçons [49,5%], 50 filles [50,5%] ; 35 enfants [35,4%], 64 adolescents [64,6%] ; moyenne d'âge 14,1±3,4 ans). Tous ont bénéficié d'une endoscopie digestive haute à la même période pour des symptômes digestifs. L'infection à H pylori était diagnostiquée quand le test rapide à l'uréase et l'histologie étaient tous les deux positifs.

RÉSULTATS: L'ulcère peptique a été retrouvé chez 33,1% (115/347) des patients ayant bénéficiés d'une endoscopie. La prévalence globale de H. pylori était de 68,3%. La majorité des ulcères étaient duodénaux (75,7%) et H pylori positif (77,4%). La prévalence de H pylori dans l'ulcère gastrique et dans l'ulcère duodénale était de 61,9% et 79,3%, respectivement. H pylori était plus fréquent chez les patients avec un ulcère que chez les sujets contrôles (77, 4% vs. 52,4% ; p=0,0001). H pylori était détecté plus fréquemment chez les filles que chez les garçons (90, 3% vs. 72,6% ; p=0,07), chez les adolescents que chez les enfants (78,0% vs. 75,0% ; p=0,75). La majorité des patients étaient admis pour les douleurs abdominales (80,9%) et les hématomésés (23,5%). Il n'y avait pas d'association significative entre la douleur abdominale et l'infection à H pylori (p=0,99). L'ulcère peptique hémorragique représentait 20% des ulcères et était plus fréquent dans le duodénum et chez l'enfant. La sténose compliquait 13% des ulcères et plus fréquemment chez les adolescents de sexe masculin.

CONCLUSION: La maladie ulcéreuse est très fréquente parmi les enfants et adolescents camerounais, il s'agit souvent des ulcères compliqués duodénaux et H pylori positif.

MOTS CLÉS : Helicobacter pylori, maladie ulcéreuse, enfant, adolescent, Cameroun

INTRODUCTION

A high prevalence of *Helicobacter pylori* (*H. pylori*) infection is observed in the pediatric age in developing countries [1-4]. Usually, more than two thirds of children are infected before the age of 2 years, and the prevalence of *H. pylori* infection in these children reached 80 to 100% [3]. Among the risk factors of infection, the most common are poor socioeconomic circumstances and poor hygienic conditions, including overcrowding in developing countries [1-7].

Generally, only a small proportion of children infected with *H. pylori* develop clinical manifestations and peptic ulcer disease (PUD) [1, 8]. PUD is relatively rare in children as compared with adults, but it is frequently associated with *H. pylori* infection [9, 10]. Thus, in developing countries with a high prevalence of *H. pylori* infection, PUD is still common in the pediatric age [9, 11, 12].

Primary *H. pylori*-related PUD is most frequently located in the duodenal bulb [9]. The main clinical manifestations are: recurrent abdominal pain, vomiting, hematemesis and melena. *H. pylori* related gastrointestinal (GI) symptoms are generally aspecific [12, 13]. The relation of cause and effect between the clinical manifestations and the infection remains discussed except in the case of duodenal ulcer [3, 8].

The role of *H. pylori* infection in the primary PUD in the pediatric age has never been studied in Cameroon.

The aim of this 9-year retrospective study at the "Centre Médical la Cathédrale" was to assess the prevalence of *H. pylori* infection in Cameroonian children and adolescents suffering from PUD proven by upper GI tract endoscopy. Also, clinical manifestations, mainly abdominal pain and complications at the time of endoscopy were analyzed in relation to their possible association with *H. pylori* infection.

MATERIAL AND METHODS

Study Design and Study Population

Data of children and adolescents admitted to the "Centre Médical la Cathédrale" of Yaounde, for upper GI tract endoscopy between January 2006 and December 2014 were reviewed retrospectively. The child was defined as a human subject between 6 and 12 years, while the adolescent was defined as a human subject between 13 and 18 years [14].

Yaounde is located in the Central Region. It covers 304 km² and is home to a cosmopolitan population estimated in 2005 during the third census of population and housing in March 2010 to 1,817,524 inhabitants, the population in over half the cases is less than 20 years. The socioeconomic conditions of the population are poor and the hygiene conditions are often deplorable because of the shortage of

drinking water and the grouping of several individuals in cramped homes.

Definition of patients and collected variables

In this study, 115 patients with PUD and 99 control subjects with normal upper GI tract endoscopy were included. Gastroduodenal erosions were not included in PUD. The data collected included: the sex, age, and gender of the patient, the result of *H. pylori* infection, the reasons for upper GI tract endoscopy, the macroscopic appearance in upper GI tract endoscopy and the microscopic appearance to histology.

In all patients an upper GI tract endoscopy was performed and gastric mucosal biopsies collected to research *H. pylori* infection (rapid urease test and microscopy) and to research gastritis according to the modified Sydney gastritis classification system [15]. *H. pylori* infection status was positive when the rapid urease test and histology were both positive.

Upper GI tract endoscopy was performed when informed consent was obtained from patients' families. The children benefited from sedation by diazepam 10 mg and local oropharyngeal anesthesia by lidocaine 20% oral gel was preferred for adolescents.

Taking of nonsteroidal anti-inflammatory drugs (NSAIDs) was not found among patients. The past medical history of the patients was unknown.

The first line recommended treatment for *H. pylori*-related PUD in the reports was represented by the standard triple therapy with proton pump inhibitor (1-2mg /kg/day), clarithromycin (20 mg /kg /day) and ampicillin (50 mg /kg /day) from 7 to 10 days. We have not found the effectiveness of this treatment nor the patients' outcome.

Statistical analysis

Data were entered and analyzed using SPSS Statistics 20.0 software (IBM Corp., Chicago, USA). For quantitative variables, the mean and standard deviations were calculated. The proportions were established for qualitative variables with their 95% confidence interval (95% CI).

Comparisons of proportions and means were performed using Chi² or Student test. Relative risks (RR) were calculated to assess the association between variables. The Yates correction and the Fisher exact test were used for small numbers. The significance level was set at 5%.

Ethical Considerations

The study was approved by the Ethics Committee of the Faculty of medicine and biomedical sciences of the University of Yaoundé 1.

RESULTS

During the study period, 347 upper GI tract endoscopy were performed in children and adolescents. PUD was detected in 115 (33.1%) (84 boys [73.0%], 31 girls [27.0%]; 24 children [20.9%], 91 adolescents [79.1%]; mean age 14.7 ± 3.0 years). They were compared to 99 control subjects with normal upper GI tract endoscopy (49 boys [49.5%], 50 girls [50.5%]; 35 children [35.4%], 64 adolescents [64.6%]; mean age 14.1 ± 3.4 years). Table 1

Table 1: Demographic characteristic of patients

Variables	Patients with PUD N (%)	Control subjects N (%)*
Mean age \pm SD	14.7 \pm 3.0 years	14.1 \pm 3.4 years
Pediatric Age		
Children	24(20.9)	35(35.4)
Adolescents	91(79.1)	64(64.6)
Gender		
Female	31(27.0)	50(50.5)
Male	84(73.0)	49(49.5)
Total	115	99

PUD: peptic ulcer disease,* Subjects with normal upper GI tract endoscopy, n: number of cases, %: percentage, SD: standard deviation

The overall prevalence of *H pylori* was 68.3% (233/341). Nearly 89% of patients with PUD and 68.2% of control subjects had gastritis ($p < 0.0001$). Among patients with PUD, 87 had duodenal ulcer (75.7%), 21 had gastric ulcer (18.3%) and 7 had a double gastric and duodenal location (6.1%).

The prevalence of *H pylori* was significantly higher in patients with PUD 77.4% (89/115) than in control subjects 52.4% (52/99); the relative risk (RR) was 1.47 (95%CI: 1.19-1.82; $p = 0.0001$) for patients with PUD compared to control subjects. *H pylori* was more frequently detected in girls 90.3% (28/31) than in boys 72.6% (61/84); the RR was 1.24 (95%CI: 1.04-1.48%; $p = 0.07$) for girls compared to boys. Besides, *H pylori* was more frequently detected in adolescents 78.0% (71/91) than in children 75.0% (18/24); the RR was 1.04 (95%CI: 0.82-1.31%; $p = 0.75$) for adolescents compared to children. Among the 21 patients with gastric ulcer, 13 were *H pylori*-positive (61.9%) and 8 were *H pylori*-negative (38.1%). Of the 87 patients with duodenal ulcer, 69 were *H pylori*-positive (79.3%) and 18 were *H pylori* negative (20.7%). The 7 patients with double gastric and duodenal ulcer location were 100% *H pylori*-positive. *H pylori*-negative ulcers were found in 26 patients (22.6%) (20 adolescents and 6 children, 23 boys and 3 girls). Table 2

Table 2: Frequency of *H pylori* infection in patients with PUD

Variables	n	Mean age \pm SD	<i>H pylori</i> + N (%)	<i>H pylori</i> - N (%)	p value
All patients	115	14.7 \pm 3.0	89 (77.4)	26 (22.6)	<0.0001
Gender					
Female	31	14.3 \pm 3.1	28 (90.3)	3 (9.7)	
Male	84	14.8 \pm 3.0	61 (72.6)	23 (27.4)	0.07
Pediatric age					
Adolescents	91	15.8 \pm 1.9	71 (78.0)	20 (22.0)	
Children	24	10.1 \pm 1.9	18 (75.0)	6 (25.0)	0.753
Location of the ulcer					
Gastric	21	14.6 \pm 3.0	13 (61.9)	8 (38.1)	
Duodenal	87	14.6 \pm 3.1	69 (79.3)	18 (20.7)	
Both	7	15.0 \pm 2.0	7 (100)	0	0.07
Pain					
Yes	93	15.1 \pm 2.7	72 (77.4)	21 (22.6)	
No	22	12.9 \pm 3.7	17 (77.3)	5 (22.7)	0.988

PUD: peptic ulcer disease, n: number of cases, SD: standard deviation,%:percentage

The main symptoms among patients with PUD were: abdominal pain (80.9%), hematemesis (23.5%), vomiting (19.1%) and melena (5.2%). Abdominal pain was also the most common symptom in control subjects, observed in 82.8%.

There was no significant association between abdominal pain and PUD; the RR was 0.98 (95%CI: 0.86-1.11%; $p = 0.71$) for patients with PUD compared to control subjects. Similarly, there was no significant association between abdominal pain and *H pylori* infection; the RR was 0.99 (95%CI: 0.87-1.13%; $p = 0.99$) for infected patients as compared to uninfected patients.

Out of 115 patients with PUD, 39 patients had complications (32.0%). GI bleeding occurred in 23 patients (20.0%) and stenosis in 16 patients (13.9%). Out of 23 cases of peptic ulcer hemorrhage, 19 were located in the duodenum (82.6%), 3 in the stomach (13.0%), and one was not found. There was no significant association between the infection and the hemorrhage, the RR was 1.08 (95%CI: 0.71-1.62%; $p = 0.72$) for infected patients compared to uninfected patients. About 72% of complications occurred in adolescents against 28% in children ($p = 0.07$), bleeding was the most common complication in children compared with adolescents; the RR was 0.61 (95%CI: 0.38-0.97%; $p = 0.07$) for the adolescents compared to children.

DISCUSSION

This study conducted in Yaounde, including children and adolescents from all socioeconomic background revealed a high prevalence of PUD (33.1%) and of *H pylori* infection (68.7%). It also showed a significant association between *H pylori* infection and PUD, particularly duodenal ulcer. In this study, the great

majority of patients with PUD were adolescents and male subjects.

Frequency of PUD in the pediatric age in Cameroon

The frequency of PUD in children is geographically variable [10]. A recent European multicenter study reported a frequency of 56 cases of ulcers and/or erosions in 694 (8.5%) children [13]. Similarly, in a retrospective study conducted in Taiwan, Huang et al. [16] reported a frequency of 67 cases of PUD in 1234 (5.4%) children who underwent an upper GI tract endoscopy. On the contrary, in Turkey and Japan the frequency is high. Uğraş et al. [9] reported a frequency of 47 cases of PUD in 357 (13.2%) children aged 9-14 years in eastern Turkey, while Kato et al. [11] reported a frequency of 143 cases of PUD in 732 (19.5%) children with gastritis or peptic ulcer disease in Japan. Other published studies have reported frequencies near 2% [8, 17]. In our study, PUD was very common as compared to published series. One hundred fifteen pediatric age patients out of 347 (33.1%) had PUD. This high frequency is compatible with the prevalence of H pylori infection in our environment, and also explained on the one hand by the high mean age of our patients, and on the other, by the male predominance in our series.

Prevalence of H pylori infection

The geographical distribution of H pylori infection varies in different regions of the world and within the same country [1]. Thus, Kato et al. [18] reported prevalence between 7.6% and 19.5% among asymptomatic children in Japan. In Turkey, the frequencies of 53% and 64% were reported, respectively in the West and East of Turkey [19, 20]. The Belgian authors reported that the prevalence of H pylori was related to the country of origin of parents of children. Thus, it was 3.2% among children of parents born in Belgium and 60% for children of parents from countries with high prevalence of H pylori [21]. In developed countries, the prevalence of H pylori infection is only 10% in children and decreases with the improvement of hygiene conditions and the socioeconomic environment. On the contrary, in developing countries where there are poor socioeconomic and hygienic conditions, the prevalence of H pylori infection remains high and increases with the age of children. For example, in Kampala, Uganda, the overall prevalence of H pylori was 44.3% and according to age it was 28.7% in children under 1 year and 40% in children 9 -12 [22]. In our study, the overall prevalence of H pylori infection was high (68.3%), and according to age it was 75% in children and 78% in adolescents. This high prevalence of H pylori is compatible with a disadvantaged socio-economic background and poor hygiene in some populations of Yaounde. Indeed, many families are grouped into several individuals in cramped housing and lack of drinking water is

common. Therefore, gastroenteritis epidemics, during which vomiting and diarrhea are common, are regular among children. It is accepted that the acquisition of H pylori occur with the waning of outbreaks of gastroenteritis [23, 24]. In a study previously conducted in 2013 in Yaounde, we already found a frequency of 83.1% for H pylori in patients under 40 [25].

PUD and H pylori infection

In this study, H pylori-related PUD was more frequent (77.4%) than H pylori-negative PUD (22.6%). In children, H pylori-related PUD has particularities. Thus, it is more common in aged children and in boys [9]. Therefore, the H pylori-related PUD is usually located in the duodenal bulb. Our study found similar results, 71 H pylori-related PUD patients out of 89 (79.8%) were adolescents between 12-18 years and 61 H pylori-related PUD patients out of 89 (68.5%) were boys and the male / female sex ratio was 2.2. Other published series have found similar results. Tam et al. [26] in a retrospective study in China showed that H pylori-related PUD was more common among boys and aged children. Similarly, the frequent location of H pylori-related PUD in the duodenal bulb was reported by Kato et al. [11] in Japan and Egbaria et al. [27] in Israel. A few studies, such as that of Uğraş et al. [9] reported a frequent location of PUD in the stomach. H pylori-negative ulcers were relatively frequent in this study as compared to the literature, they were found in 22.6% of patients, mainly in adolescents and boys, the sex ratio between male and female was 7.7. H pylori-negative ulcers are usually reported in children with a female predominance [9]. The male predominance in this study may reflect the fact that our population of PUD patients was dominated by male adolescents. In the literature, H pylori-negative ulcers are often secondary to systemic diseases including chronic kidney diseases, chronic neurological diseases, and chronic arthritis [27, 28]. Some ulcers have an idiopathic cause [9, 27]. Other causes of ulcers in children, other than systemic causes, namely active smoking and NSAIDs were not found in endoscopy reports.

Clinical manifestations and H pylori infection

The formal responsibility of H pylori infection in a clinical manifestation is often difficult to establish, and the link with recurrent abdominal pain is controversial [4, 8, 29, 30, 31]. Generally, only a small proportion of children infected with H pylori develop clinical symptoms [1, 13, 29, 31]. These symptoms are not specific [1, 4, 13]. Some studies have shown an improvement in symptoms after treatment of the infection. For example, Abu-Zekry et al. [32] assessed the prevalence of H pylori infection among Egyptian children from 5 to 15 years, with GI manifestations. The authors found a significant association between recurrent abdominal pain and

infection ($p= 0.023$). The great majority of other published studies have not found this association [3, 28, 29, 33]. In our study, there was no significant association between abdominal pain and H pylori infection ($p= 0.99$), so there was no difference in the frequency of pain between patients with PUD and control subjects with normal upper GI tract endoscopy ($p= 0.71$). This could be explained by the high frequency of histological gastritis among patients both the ones with PUD (89%) and the ones without (68.2%). Finally, it noted that patients with PUD with abdominal pain were relatively older than those with PUD without abdominal pain as symptom (15.1 ± 2.7 years vs. 12.9 ± 3.7 years, $p= 0.007$). Abdominal pain (80.9%) and hematemesis (23.5%) were the dominant clinical manifestations among our patients. This could be explained by the significantly high frequency of duodenal ulcer and gastritis in our series.

Complications of PUD in the pediatric age in Cameroon

The complications of PUD are rare in the child [30]. Peptic ulcer hemorrhage is the most frequently reported complication. The frequency of peptic ulcer hemorrhage is variously reported in the literature [12, 34]. Thus, Brown et al. [35] in a US multicenter retrospective study on national registries reported a frequency of 17.4%. Shu-Ching et al. [36] in a single-center, retrospective and prospective study of a 9-year experience in Taiwan and El Mouzan et al. [37] in a single-center, retrospective and prospective study in children and adolescents in Saudi Arabia reported a frequency of 64.2% and 21%, respectively. On the contrary, Egbaria et al. [27] in Israel reported a frequency of 2.4%. Our study found a rate of 20% for the peptic ulcer hemorrhage which is close to the result of El Mouzan et al. [36] in a similar population. H pylori infection does not explain these differences, since among those studies, the H pylori is more common in the study of Egbaria et al. [27] (66.3%) than in that of Shu-Ching et al. [36] (47.7%). Moreover, our study found no significant association between H pylori and upper GI tract bleeding. The high prevalence of duodenal ulcer and the presence of children from 6 to 12 years in our series would explain our results. The bleeding was more common in duodenal ulcer than in gastric ulcer and in children than in adolescents.

Stenosis complicated 13 % of PUD in this study, especially among adolescents and boys with a duodenal ulcer.

This study has limitations. Indeed, the study population mainly included children and adolescents from privileged backgrounds. The cost of the upper GI tract endoscopy is exorbitant in Yaounde. Thus, the prevalence of H pylori infection has been underestimated. Therefore, patients who underwent upper GI tract endoscopy were adolescent boys. This also had to influence the high prevalence of PUD and

the high prevalence of the H pylori-related PUD. Nevertheless, this is the first study dealing PUD of the pediatric age in Cameroon, and the number of cases is high enough to draw some conclusions.

CONCLUSION

This study shows that PUD is very common in the pediatric age in Cameroon. H pylori-related PUD are the most numerous and are more common among boys than among girls and in the duodenum than in the stomach. They are common in both adolescents and in children. Abdominal pain is the main symptom and peptic ulcer hemorrhage the most common complication. This is a public health problem. Measures to improve the hygienic and the social conditions are necessary to protect children against H pylori infection.

COMPETING INTERESTS

The authors declare no competing interest.

AUTHORS' CONTRIBUTIONS

FA: study conception and Design, data analysis; GN: performed endoscopy, acquisition of data; MTS: performed endoscopy, analysis and interpretation of data; IDB: performed endoscopy and contributed on statistical analyses; MBS: study conception, drafting of the manuscript, data interpretation and supervision; ECNN: final approval of the version to be published. All authors have read and approved the final manuscript

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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