Endoscopic diagnosis in a Tunisian paediatric population with upper gastrointestinal bleeding (UGIB)

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L'endoscopie diagnostique dans une population pédiatrique Tunisienne présentant une hémorragie digestive haute

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R É S U M É

Prérequis : L'endoscopie digestive haute est l'examen de première ligne pour explorer l'hémorragie digestive haute.
But : Préciser l'apport diagnostic de l'endoscopie digestive haute chez l'enfant présentant une hémorragie digestive haute selon l'âge et voir si les étiologies sont différentes de celles des pays développés.
Méthodes : Une étude rétrospective a été réalisée à partir de dossiers d'enfants adressés pour hémorragie digestive haute à l'unité de gastroentérologie au service de pédiatrie C à l'Hôpital d'Enfants de Tunis entre Janvier 1998 et Décembre 2006. Les patients ont été classés en trois groupes ; G1: nouveau nés, G2 : nourrissons, G3 : enfants et adolescents.
Résultats : 614 endoscopies ont été retenues. L'étiologie n'a pas été retrouvée dans 20,68 % des cas. Le G1 comprenait 125 nouveaux nés dont 97 avaient des lésions muqueuses ,24 n'en avaient pas, deux avaient un ulcère et deux autres une tumeur gastrique. La prise de médicaments gastro agressifs a été rapportée chez140/489 enfants. L'endoscopie était normale chez 101sur489 patients. L'œsophagite peptique a été répertoriée chez 57/205 (27,8%) des enfants du G2 versus 52/284 (18.3%) du G3 (P = 0,0015).La gastrite a été rapportée chez 164/284 (57,77%) des enfants du G2 versus 86/205 (41,9%) du G3 (P < 0,001). L'ulcère peptique a été trouvé chez 10 garçons. Le syndrome de Malory Weiss, les varices œsophagiennes ont été isolés chez respectivement 11et 10 enfants
Conclusion : Les étiologies de l'hémorragie digestive haute différaient selon l'âge et l'origine géographique des pays.

M o t s - c l é s

Endoscopie digestive haute - Hémorragie digestive haute – Etiologies - Enfant.

S U M M A R Y

Background: Esophagogastroduodenoscopy (EGD) is currently considered the first line diagnostic procedure chosen for Upper Gastrointestinal Bleeding (UGIB) since 1970. However, studies are still limited in our country.
Aim: Finding out the most common causes of UGIB in children and whether the causes differed according to age in developing and developed countries.
Methods: A retrospective review of the medical records of children referred to the Paediatric Gastroenterology Department of The Tunis Hospital of Children between January 1998 and December 2006 for upper gastrointestinal bleeding. The children were divided into three groups; G1: neonates; G2: infants; G 3: children and adolescents.
Results: The study involved 614 endoscopies. The aetiology was not ascertained in 20.68%of cases. G1 included 125 newborns: 24 with no identified causes, 97 mucosal lesions (isolated or associated); two ulcers and two tumours. G2 and G3 included respectively 205 infants and 289 children. Toxic drug intake was recorded in 140 out of 489 patients. Endoscopy was normal in 101 cases. Peptic oesophagitis was recorded in 57/205 (27.8%) of G2 infants versus 52/284 (10%) of G3 children (p=0.015). Gastritis was recorded in 164/284 (55.6%) of G2 infants versus 86/205 (41.9%) of G3 children (p≤0.001). Peptic ulcers were reported in ten boys. Mallory Weiss tears and Variceal lesions were found in respectively eleven and ten cases.
Conclusion: Aetiologies of UGIB in children in Tunisia varied according to age and geographic areas.

K e y - w o r d s

Children, endoscopic diagnosis, upper gastrointestinal bleeding.

Esophagogastroduodenoscopy (EGD) is currently considered the first line diagnostic procedure chosen for upper gastrointestinal bleeding (UGIB) since 1970 [1].However, studies are still limited in our country.

The aetiology of acute UGIB in paediatrics can be broadly divided into, two main groups [2]: variceal (extra hepatic portal vein obstruction (EHPVO) and chronic liver disease) and nonvariceal (ulcers and erosions secondary to drug intake and infections, vascular malformations and miscellaneous).

The aim of this study is to find out the most common causes of UGIB in children and whether the causes of UGIB are different between developing and developed countries.

METHODS

This retrospective study was carried out on 614 consecutive children aged less than 20 years, who were referred to the paediatric gastroenterology department of Tunis Children's Hospital for UGIB during the period between January 1998 and 31 December 2006.

Inclusion criteria: Cases of children aged less than 20 years were included. The first endoscopy was retained for analysis.

Exclusion criteria: cases of patients with haematemesis caused by swallowing caustic agents and foreign bodies and children with ear, nose, throat disorder and coagulopathy were excluded.

Esogastroesophageal endoscopy (Olympus GIF-XP20 – Olympus GIF P30) was performed without sedation. Time of endoscopy after the onset of bleeding was recorded in hours. We considered that the EGD was done on emergency, if it was carried out within the first 48 hours after the bleeding episode.

Data Collection:

Data were collected by reviewing the health chart of each patient. Patient's history included age, gender, appearance of vomiting (red bloody, coffee ground striated with blood), appearance of stool (red, melena), presence of dyspepsia or abdominal pain, underlying cirrhosis, history of previous variceal or nonvariceal bleeding, co-morbid disease and medication used within a week as non steroidal anti-inflammatory drugs(NSAIDs) and Corticosteroid.

The management of gastrointestinal bleeding was also recorded hemodynamic resuscitation and use of pharmacological therapy.

We divided the children into 3 groups according to their age: group 1 (G1): neonates aged less than 28 days; group 2 (G2): infants aged between 29 days and 3 years; and group 3 (G3): children older than 3 years.

Endoscopic lesions were recorded as follows: for esophagus, normal, inflammatory esophagitis (grade I), ulcerative esophagitis (grade II,III,IV, endobrachyesophagus), mycotic esophagitis and esophageal varices; for gastric lesions, normal, gastritis (congestive,petechial, erosive,hemorragic ,ulcerative, necrotic ,atrophic and nodular) and ulcer; for bulbar lesions, normal, bulbitis (congestive,petechial,ulcerative,nodular and atrophic), and bulbar ulcer; for duodenal lesions, normal, duodenitis (congestive, petechial, ulcerative, nodular and atrophic), and duodenal ulcer.

Data of anatomic biopsy sites and histological results were recorded. The importance of blood loss was defined subjectively as mild, if the vomiting was striated with blood and average if the child vomited blood without consequences neither on the level of the haemoglobin nor in the hemodynamic status. The blood loss was considered severe, if the children needed blood transfusion or if they had substantial fall in haemoglobin concentration after their admission.

Statistical analysis:

Statistical analysis was conducted using SPSS 11. Descriptive statistics of the subjects' characteristics were reported as mean and standard deviation or median with ranges depending on the variable distribution. Krushal-Wallis tests for abnormally distributed variables and X2 test for dichotomous outcome variables were used. All of the tests were considered significant at the $p < 0.05$ levels.

The study was approved by the ethics committee of the Tunis Hospital of Children.

RESULTS

Epidemiological results

Out of 2814diagnostic procedures, 614 was performed for UGIB (317 girls, 293 boys and in four cases the gender was not available) with a mean (+/-SD) 49.15 months old +/- 50.12 (range 6 days – 240 months).

G1 included 125 newborns. G2 included 205 infants and toddlers. G3 included 284 children and adolescents. 538 endoscopies were undertaken on emergency within 48 hours, 35 up to 48 hours. 409 endoscopies were undertaken within less than 24 hours. These data weren't available in 41 cases.

Haematemesis was isolated in 538 cases (87. 3%), associated to melena in 35 cases (5.7%), to red blood stools in one case and to both melena and red blood stools in one case. Melena was isolated in 27 cases (4.4%) and was associated to red blood stools in one case. These data were not available in 11 cases.

The importance of blood loss varied from low in 54.3% cases, average in 20.4% cases and severe in 3.3%. These data weren't available in 21.5% of the cases.

A NSAIDs history intake was recorded in 140 cases (23%) and the data weren't available in 80 cases (13%).

The endoscopy was normal in 125cases.

Endoscopic findings according to age were as follow:

In G1, specific risk factors of bleeding were recorded in 20 cases: eight maternal infections; four respiratory distress; four vomiting; and four acute foetal disability. The endoscopy was normal in 24 cases and abnormal in 101 cases: we recorded 97 cases of mucosal lesion (oesogastroduodenitis), isolated or associated in the oesogastric tract (the endoscopic features are summarised in table 1), two cases of ulcer and two cases of tumour. One of the newborns with gastric ulcer was ten days old. He had a history of acute respiratory distress and was hospitalised in the intensive care unit. The other neonate, three days old, free of underlying diseases had bulbous ulcer associated to ulcerated hemorrhagic gastric mucosal lesion.

The gastric tumours (one on the fundus and the other on the

antrum) were recorded in two-day-old neonate boys who had an important loss of blood (subsequent fall of haemoglobin). An endoscopic check-up was done in one of the cases after a month. It had shown the healing of the tumour but the ulcerated, haemorrhagic mucosal lesion in the stomach persisted.

In G2 and G3, the endoscopy was normal in 101 cases. The toxic drug intake was recorded in our study in 140 out of 489 children (28%). The lesions were divided into two types: variceal and nonvariceal. Variceal lesions were found in ten children: five girls and five boys with a mean age of 247.5months +/- 54.59 [range 8 months – 390months]. The portal hypertension signs were evident in four cases: two had cirrhosis and three had extra hepatic portal vein hypertension. The haematemesis was average in five cases and important in two cases. The data weren't available in three cases. Oesophageal varices were classified in grade I in one case, grade II in six cases, and grade III in three cases. Variceal ligation was undertaken in five children after one or two months of the bleeding episode.

Table 1 : Endoscopic aspects of oesogastroduodenitis (n=97) in G1 (number s are not exclusive)

Site of injury	Aspect of the Mucosa	Number (%)
Oesophagus	Erodated	24(24.74)
	Ulcerated	24(24.74)
	Hemorrhagic	6(6.2)
	False membranes	7 (7.2)
Stomach	Erythematous	85 (87.63)
	Petechial	30(31)
	Erodated	9(9.3)
	Ulcerated	7(7.14)
	Hemorrhagic	7(7.14)
	Atrophic	1(1)
Duodenum	Erythematous	10(10.3)
	Petechial	9(9.8)
Bulbous	Erythematous	18(18.55)
	Petechial	9(9.27)
	Hemorrhagic	1(1)
	Ulcerated	1(1)

As for non variceal lesions, a peptic oesophagitis was recorded in 109 cases in 57 girls and 51 boys; the gender was not available in one case. Age at diagnosis was 54.33 months +/- 50.7 months (range 1.5 months and 216 months).

A pathological history was reported in 68 cases as gastrooesophageal reflux disease in 30 children, failure to thrive, abdominal pain, anaemia in eleven cases, encephalopathy in six cases, asthma and chronic obstructive bronchopathy in three cases, miscellaneous causes in 18 cases. In G2, 57 out of 205 infants (27.8%) had oesophagitis versus 52 out of 284 children of G3 (p=0.015). The peptic oesophagitis was associated to hypotonic cardia in 28 cases and to hiatal hernia in 17 cases. Oesophagitis was classified in 52cases (48%) in grade I, 34(31%) grade II, 20(18%) grade III, 2(2%) grade IV, 1(1%) grade V.

The second main aetiology of UGIB in G2 and G3was gastritis recorded in 139 girls and in 111 boys. In G3, 164 out of 284 children (55.6%) and 86 out of 205 infants (41.9%) had gastritis (p≤0.001). The gastrointestinal history recorded in gastritis was summarized in figure 1.The mucosal aspects of gastritis were summarized in table 2. Gastric biopsies were undertaken in 90 out of 250 cases (36%): 26 were normal, 56 were abnormal and in eight cases, the findings were not available. Histological findings were as follow: chronic gastritis in 53 cases; atrophic gastritis in 5 cases; and metaplasic gastritis in one case. Helicobacter Pylori was isolated in 39 biopsy samples.

Figure 1 : Gastritis according to digestive history

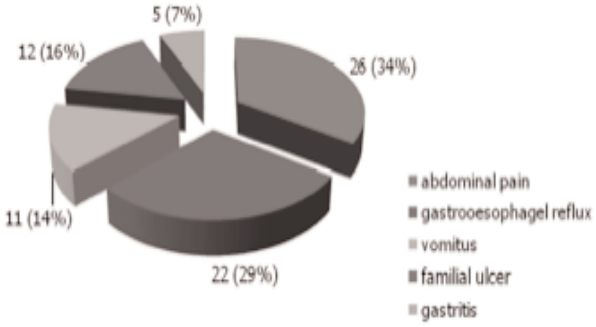

Table 2: Mucosal endoscopic aspect of gastritis (n=250)in G2andG3 (numbers are not exclusive)

Mucosal aspect	Number	%
Erythematous	145	(58)
Petechial	75	(30)
Erodated	48	(19,2)
Ulcerated	14	(5,6)
Hemorragic	12	(4,8)
Necrotic	4	(1,6)
Nodular	32	(12,8)
Atrophic	20	(8)

Mallory Weiss tears were reported in 11 patients. Peptic ulcers were recorded in ten boys.

There were six gastric ulcers in respectively a 6-month-, 30-month-, 6-year-, 12-year-, 13-year-, and 10 -year old children. In the later case, gastric ulcer was associated with a duodenum ulcer secondary to Helicobacter Pylori infection diagnosed by histological examination. NSAIDs intake was reported in the first gastric ulcers cases. Bulbous ulcers were recorded in three cases: in a 7 month-old toddler who had a respiratory distress, in a 4-year- and in a 9-year-old boys.

Bulbous lesions were recorded in 33 cases: 20 were erythematous; six were petechial; two were ulcerated; and there were five cases of lymphoid nodular hyperplasia. Duodenum lesions were recorded in 27 cases: 11 were erythematous; six were ulcerated; and five were described as having nodular lymphoid hyperplasia. One case of duodenal polyp was described in an eight old boy with recurrent abdominal pain.

DISCUSSION

During this period of study, UGIB was a clinical purpose for endoscopy in 21.8% of cases. This percentage was higher than in western countries where this indication has declined from 34.2% in 1985 to 4.8% in 2005[1]. In our study, the cause of bleeding was not identified in 20.5% of cases. This may be due to some delay in performing the endoscopy or to some cases of oesophageal or gastric erosions that got healed up spontaneously or after a proton pump inhibitor treatment. The same results were found in different studies (table 3) [3, 4, 5, 6], however, the proportion of non indentified causes was lower (9.8%),(11.8%) in a study conducted respectively in Taiwan [7] and in USA[8].

The UGIB aetiologies differed according to age. In GI, ulcerative and/or hemorrhagic lesions of the oesophagus and the stomach have been widely reported in our study as in the literature. The risk factors of these lesions were studied in a case control multicenter study. Antacid drug used during pregnancy was associated with oesophageal and gastric lesions. Breast feeding may play a protective role against severe lesions in neonates [9]. We also recorded two cases of vascular tumours. The histological examination wasn't carried out but according to literature, the main causes of gastric tumour in neonates were gastric teratoma [10] and severe blue rubber bleb nevus syndrome [11].

Ulcers were rare in neonates. Only few case reports were recorded, for example, a gastric antral ulcer was described in a full-term, seven-day-old neonate who showed an episode of haematemesis and in a 13-day-old who presented an episode of apparent life-threatening event secondary to the increase in gastrin secretion [12]. UGIB is not the only clinical symptom that could reveal ulcer in neonates. We should also consider apnoea which was reported in a full-term neonate [13]. Although ulcer is a rare phenomenon in the neonatal period, a case-control study reported 18 ulcers (17 gastric ulcers and one duodenal ulcer) out of 53 healthy full-term infants [14]. Other uncommon causes were reported, like cow-milk allergy. The diagnosis relies on clinical suspicion helped by endoscopy and gastric biopsies [15].

The most common causes of UGIB in children vary according to age and to the geographical setting (table 4).Our study has shown that the aetiologies were the same as in a western country like France, but different from another developed

Table 3 : comparison of results of the present study with others

Causes	[3]2004 El Mouzan Saudi Arabia n = 60 (%)	[4]1994 Mittal SK India n = 236 (%)	[7]2003 Huang IF Taiwan n = 112 (%)	[5]2009 Deehghani Iran n = 118 (%)	[6]2010 Bensouda France n = 141 (%)	[8] 2012 Cleveland USA n=167(%)	Our Study Tunisia n = 489 (%)G2and(
Oesophagitis and Mallory Weiss Syndrome Tear	(36)	(23,7)	(30.4)	(9.5)	42 (29,8)	(27)	120 (24,5)
Oesophageal varices	(4,3)	(39,4)	(10,7)	(16)	7 (4,78)	(7.1)	10(2)
Gastritis							250(51)
° Erosive	(44)	(7,2)	(44,6)	(28)	12 (8)		48(9,8)
° Other aspects							202(41.3)
Gastric Ulcer	(7)	(1,3)	(9,8)	(8,5)			6(12)
Bulbous							
° Erosive					12 (8,5)		
° Other					24 (17,2)		
° Ulcer							3(0.6)
Duodenum							
° Erosive			(2,7)	(10)			
° Other							
° Ulcer		(0,4)	(15,2)	(6,8)			1 (0,2)
Normal	(25)	(25)	(9,8)	(20,5)	24 (17)	(11.8)	101(20,5)

country like Taiwan an Asian country ,and in USA were variceal lesion were reported respectively in 10 percent [7] and in 7.1 percent of cases [8]. In our study, this aetiology was found in ten out of 489 children (2%). However, this cause was found in 39.4% in India were this aetiology was common [4]. Elastic variceal ligation, which is the best endoscopic management to reduce rebleeding, was done to our patients after one month. This procedure is common in our department [16].We should compare our results with neighborhood countries but data were not available.

The nonvariceal lesions were dominated by oesophagitis and gastritis. Oesophagitis was statistically more frequent in G2 (27. 8%) than in G3 (18. 3%). However, 55.5% of gastritis were diagnosed in G3 versus 41.9% in G2. This difference was statistically significant. Helicobacter pylori infection was recorded in 39 out of 90 children (43%). This association had already been examined in a previous study and this infection was probably underestimated because the investigation wasn't systematically made [17]. In the French children, primary gastritis was more frequent than helicobacter pylori gastritis [18].

The toxic drug intake was recorded in our study in 140 out of 489 children (28%). A recent crossover case study—whereby 89 out of 177 children (46.9%) had taken NSAIDs—confirmed that UGIB was more likely to occur in children of younger age and showed that it is attributable to the use of NSAIDs. Some of these cases might have been avoided by using alternative drugs such as paracetamol. A call for more caution in prescribing NSAIDs in children is essential [6].

A previous study conducted in our department had examined the effect of NSAIDs and of Helicobacter Pylori infection on the gastric mucosa in children with UGIB and had shown that gut mucosal severity is significantly correlated to NSAIDs [19]. The 2% prevalence of peptic ulcer disease (PUD) in our study is clearly within the range reported by Roma [20] but it was lower than that reported by El Mouzan [21] whereby, UGIB occurred in 13% of the children who had PUD. The predominance of PUD in males in his study goes hand in hand with the data reported in literature. This difference is due to the selection of patients. These studies were conducted retrospectively by analysing all cases of PUD diagnosed by endoscopy whatever the complaint was.

In our study, gastric ulcer was predominant but our findings were not similar to the patterns reported by most authors who found out a higher percentage of duodenal ulcers [19] [20].

Peptic ulcer disease in children has been classified as primary and secondary. In our study, PUD was primary in one case due to Helicobacter Pylori. The prevalence of HP infection in children with duodenal ulcer varies in the literature from 33% to 100%, while in children with gastric ulcer it ranges from 17% to 75% [21]. PUD was associated to NSAIDs intake in three cases and in one case to respiratory distress.

CONCLUSION

UGIB remains an important indication for EGD in our unit, whereas it is lowering in western countries. Aetiologies of UGIB in children in our unit vary according to age and are not different from developed country as France but different from other developed ones like Taiwan and USA. In 20.5% of the cases, no aetiology was found. A study during the five last years is being carried out to found out if aetiologies have changed.

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