Upper gastrointestinal bleeding in children: an 11-year retrospective endoscopic investigation

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Background: **Upper gastrointestinal bleeding (UGIB) may present as hematemesis, coffee-ground emesis, or melena requiring esophagogastroduodenoscopy (EGD) for diagnosis and/or therapy. Worldwide, differences exist for the etiology of UGIB reflecting geographical differences in common disease states. In the past 25 years, there have been improvements in endoscopic optics. This study was undertaken to determine: 1) if identifying a bleeding source in UGIB have improved with better endoscopic optics, 2) geographic differences in causes of UGIB, 3) differences in severity of UGIB based on clinical factors, and 4) the likelihood of finding a bleeding source based on symptom duration and time to endoscopy.**

Methods: **A retrospective chart review was made on children having EGD for evaluation of UGIB. Data collected included type, etiology, and degree of bleeding.**

Results: **Of 2569 diagnostic procedures, 167 (6.5%) were performed for UGIB. The most common presentation was hematemesis (73.4%). Melena was associated with lower hemoglobin levels and higher transfusion rates. A source of UGIB was found in 57.0%, no cause in 11.4% and a questionable cause in 29.7%. A source was found less commonly in children with a history of UGIB less than one month and in those undergoing endoscopy over 48 hours after a bleeding episode.**

Conclusions: **Improved endoscopic optics has not changed diagnostic ability for UGIB. Etiologic differences for UGIB in children from varying geographic areas are related to indication for endoscopy, patient selection, and co-morbid conditions. Duration of bleeding and time to endoscopy after a bleeding episode may help predict when endoscopy should be performed to determine a bleeding source.**

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Introduction

Upper gastrointestinal bleeding (UGIB) varies greatly in presentations. It is not uncommon in children and may provoke anxiety in the child, care-givers, and health-care providers.

Esophagogastroduodenoscopy (EGD) is established as a safe method for the diagnosis and treatment of UGIB. Establishing an etiology is important for determining the risk of re-bleeding, yet timing of endoscopy is dictated by the severity of bleeding and need for therapeutic intervention. Endoscopy may be delayed in hemodynamically stable children with UGIB, decreasing the diagnostic success.

The etiology of UGIB differs throughout the world, reflecting geographical differences in common disease states.[1-10] There is a paucity of data available from studies of UGIB in the pediatric population from the United States; the most recent data derived from studies reported over 25 years ago.[11-14] During this time, there has been marked improvement in the optics of endoscopes providing better diagnostic ability. The purpose of this study was to determine the etiology of UGIB in a pediatric population within the United States, and compare them to previous US studies and recent studies from different geographic regions. The study also aimed to compare clinical features that may improve the diagnostic success for endoscopy.

Methods

A retrospective chart review of children between birth and 17 years of age who presented with an UGIB and underwent EGD was conducted. UGIB was defined

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as coffee-ground emesis (CGE), hematemesis, or melena. A database of all EGDs performed by the Division of Pediatric Gastroenterology at the University of Mississippi Medical Center between September 1998 and October 2009 was reviewed to identify all diagnostic procedures and therapeutic procedures to control bleeding. Data collected from records included age, gender, type of UGIB, duration of UGIB, time to EGD from presentation, hemoglobin, need for transfusion, endoscopic findings, and histological diagnoses. EGDs performed on the same child within 3 months were not included, as they represented persistence of the initial underlying pathology in all cases.

Statistical analysis

Descriptive analyses were performed using frequency distribution, means, standard deviations, proportions, and 95% confidence intervals. After testing for normality of the data using Kolmogorov-Smirnov test, one way analysis of variance was used to perform group comparisons. Levene statistics was used to test the homogeneity of variance, and post-hoc comparisons were performed using Bonferroni correction. Crosstab analysis was used for categorical variables and the Chi-square test was done to test the association between independent and dependent variables. All analyses were performed using SPSS 15.0 (SPSS Inc. Chicago, IL), and significance level was set at 0.05.

Results

Totally 2800 children underwent 3372 EGDs, 2705 (80.2%) were diagnostic procedures. Among them 2569 charts (95.0%) were reviewed, of which 167 (6.5%) were performed for UGIB. Nine EGDs were performed on the same child within 3 months of a previous endoscopy and were excluded. Ten EGDs were performed on the same child greater than 3 months from a previous endoscopy and were included. Thus, the study population included 158 cases of UGIB in 148 children. Demographic data of the children showed a mean ± SD (median) age of 9.3 ± 5.7 years (10.1 years), a male to female ratio of 1.1:1, and a racial make-up of white (53.4%), African American (43.2%), and all others (3.4%).

No cause for UGIB was found in 18 cases (11.4%), non-gastrointestinal causes in 3 (1.9%), and questionable causes in 47 (29.7%). The latter group consisted of endoscopic and/or histological evidence of esophagitis, gastritis, or duodenitis without evidence of a recent bleeding. The most commonly found source of bleeding was prolapse gastropathy syndrome (PGS; 12.7%), followed closely by gastric erosions/ulcers (10.8%), erosive esophagitis (9.5%), and duodenal erosions/ulcers (8.2%). Less common diagnoses included esophageal varices (6.3%) and Mallory-Weiss tears (MWT, 3.8%). Multiple etiologies were found in 5.7% including esophagitis and PGS (2), gastric ulcer and PGS (1), gastric ulcer and MWT (1), gastric ulcer and duodenal ulcer (1), gastric ulcer and ulcerative esophagitis (1), duodenal ulcer and PGS (1), duodenal ulcer and ulcerative esophagitis (1), and duodenal erosion and PGS (1).

Presentations of UGIB are summarized in Table 1. The most common presentation of UGIB in our study was hematemesis (73.4%), followed by melena (20.8%) and CGE (5.7%). Melena led to more significant bleeding as indicated by lower mean hemoglobin level (8.4 ± 2.6 g/dL) and higher transfusion rate (60.6%) than hematemesis (11.4 ± 2.5 g/dL and 13.1%, respectively) and CGE (13.9 ± 2.1 g/dL and 0%, respectively; $P<0.001$). A bleeding source was more often found in children presenting with melena (80.6%) than hematemesis (54.8%) or CGE (33.3%; $P= 0.01$). A bleeding source was found more commonly in children requiring transfusion (82.4%) than those not requiring a transfusion (53.2%; $P= 0.002$).

Hemoglobin levels (mean ± SD) according to the endoscopic diagnosis are shown in Fig. 1. No significant difference was seen among normal (12.0 ± 2.3 g/dL), questionable etiology (11.6 ± 2.3 g/dL), vomiting-induced bleeding (PGS and Mallory-Weiss tears, 11.8 ± 1.8 g/dL), erosive esophagitis (12.4 ± 2.3 g/dL), and gastric erosion/ulceration (10.8 ± 3.2 g/dL, $P>0.05$) groups. Significantly lower hemoglobin levels were found in children with duodenal erosion/ulcerations (8.3 ± 2.8 g/dL) and varices (7.7 ± 2.3 g/dL).

The percentage of cases in which a source was found versus the duration of bleeding is shown in Fig. 2. No differences were seen between children with a history of bleeding for less than a day, less than a week,

Table 1. Presentation of upper gastrointestinal bleeding

Variables	Coffee-ground emesis	Hematemesis	Melena
Number (%)	9 (5.7)	116 (73.4)	33 (20.8)
Hemoglobin (g/L)	13.9 ± 2.1	11.4 ± 2.5	8.4 ± 2.6*
MCV† (fL)	84.1 ± 7.9	83.0 ± 7.5	82.8 ± 8.2
Transfused‡ (%)	0.0	13.1	60.6
Source found (%)	33.3	54.8	80.6§

Hemoglobin and mean corpuscular volume (MCV) are expressed as mean ± SD. *: $P<0.001$, the mean hemoglobin level was significantly lower in the melena group than in the other two groups; †: no significant difference between the groups; ‡: $P<0.001$, the need for transfusion was significantly higher in the melena group than in the other two groups; §: $P=0.01$, a source of bleeding was more commonly found in the melena group than in the other two groups.

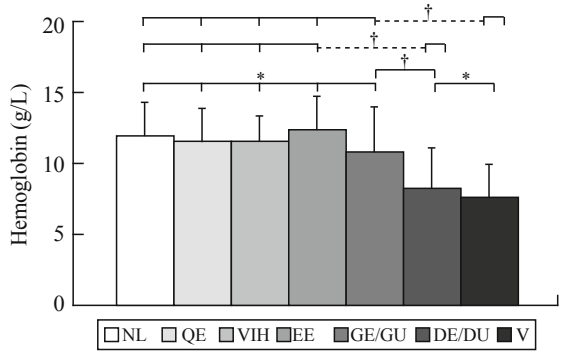

Fig. 1. Hemoglobin levels (mean ± SD) according to the endoscopic diagnosis. *: $P>0.05$; †: $P<0.01$. NL: normal; QE: questionable etiology; VIH: vomiting-induced hematemesis; EE: erosive esophagitis; GE/GU: gastric erosion or ulceration; DE/DU: duodenal erosion or ulceration; V: varices.

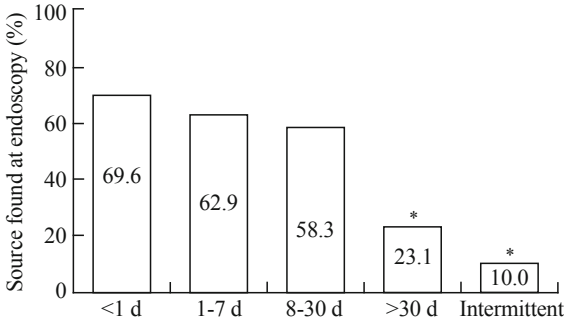

Fig. 2. Correlation between duration of upper gastrointestinal bleeding and identification of a source. *: $P<0.01$, a bleeding source was less likely to be found in children with a history suggestive upper gastrointestinal bleeding for >30 d or intermittent bleeding compared to children with symptoms <30 d.

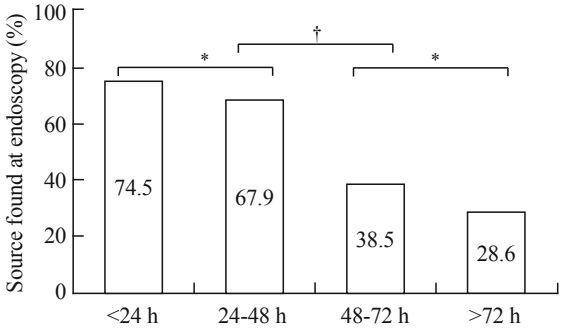

Fig. 3. Correlation between time to endoscopy and identification of a source. *: $P>0.05$; †: $P<0.01$, a significant difference was seen for finding a bleeding source for endoscopy done <48 h and endoscopy done >48 h.

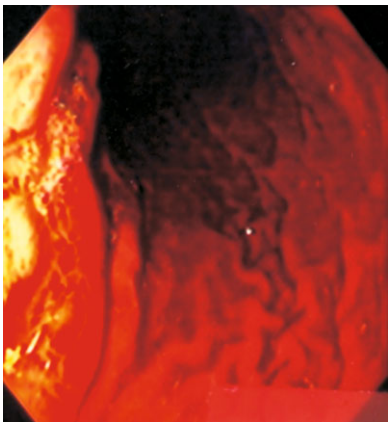

Fig. 4. Endoscopic picture of prolapse gastropathysyndrome (PGS). Upon entering the gastric lumen a discrete area of erythema is seen on the mucosa of the lesser curvature of the stomach. Biopsy showed submucosal hemorrhage supporting a diagnosis of PGS.

Table 2. Comparison of etiology of upper gastrointestinal bleeding by geographic areas*

Areas	Varices	EE	VIH	PUD	Questionable	Other	None	Multiple
Eastern hemisphere	23.4%	0.2%	0.2%	23.6%	34.3%	0.0%	18.4%	0.0%
Western hemisphere	10.6%	0.6%	1.2%	43.5%	27.3%	4.3%	12.4%	0.0%
Present study	7.1%	10.0%	17.0%	17.1%	30.6%	1.2%	11.8%	5.3%

*: Data from the Eastern hemisphere derived from studies in the Middle East[1,2] and Asia[3-9]. Data from the Western hemisphere derived from studies in South America[10] and North America.[11-14] EE: erosive esophagitis; VIH: vomiting-induced hematemesis; PUD: peptic ulcer disease.

or less than a month. A source was less likely to be found in children with a history of UGIB for greater than one month and those with intermittent bleeding (P=0.001).

The percentage of cases in which a source was found compared to the time to endoscopy from presentation is shown in Fig. 3. No difference was seen in children having endoscopy in less than 24 hours (74.5%) and those having endoscopy between 24 and 48 hours (67.9%, $P>0.05$). A significant difference was seen between those children having endoscopy within 48 hours and those having endoscopy greater than 48 hours (P=0.001). No difference was seen between children having endoscopy between 48 and 72 hours (38.5%) and those having endoscopy at greater than 72 hours (28.6%, $P>0.05$).

Discussion

UGIB is a concerning and sometimes life-threatening problem affecting children of all ages. In the past 25 years, improvements have been made in the optics of endoscopes. We performed a retrospective analysis of

EGDs in children with UGIB to determine if there have been improvements in identifying a bleeding source and to compare causes of UGIB in children from different geographic regions. We found 14 previous studies that addressed the causes of UGIB in children: nine were from the Eastern Hemisphere (2 Middle East,[1,2] 7 Asia[3-9]) and five from the Western Hemisphere (1 South America,[10] 4 North America[11-14]). Data from these studies are summarized in Table 2.

We compared our data with those from other Western Hemisphere (WH) countries to determine if there have been any changes in etiology of UGIB over the past 25 years, as these studies were all performed before 1983. We also compared our data with recent data from Eastern Hemisphere (EH) countries to determine geographic differences in the etiology of UGIB in children.

In the present study, no difference was seen in the percentage of non-diagnostic endoscopies (11.8%) compared to the WH countries (12.4%); the percentage of non-diagnostic endoscopy was higher in EH countries (18.4%). Mucosal inflammation (esophagitis, gastritis, and/or duodenitis) detected by endoscopy was similar in our study (30.6%) in comparison with the WH (27.3%) and EH countries (34.3%). We consider the presence of mucosal inflammation a questionable cause for UGIB as the findings are usually not evident for UGIB.

The incidence of varices (7.1%) in our population was similar to that of historic controls from the WH countries (10.6%), while it was more common in the EH countries (23.4%). This finding may be related to the underlying geographic disease states resulting in UGIB.[7,9] An alternative explanation may be patient selection bias. UGIB caused by varices is more common in studies from centers with active hepatology services than from those centers providing mostly gastrointestinal services.[1] We deal with children with both gastrointestinal and hepatic diseases, but do not have an active liver transplant program. However, we do follow patients after liver transplant in conjunction with regional transplant centers, offering treatment of esophageal varices if it is required emergently. Thus, the rate of varices in the present study might be expected to be lower than the centers specializing in treatment of chronic liver disease.[1]

Differences were seen for peptic ulcer disease (PUD), vomiting-induced hematemesis (VIH), including MWT and PGS, and erosive esophagitis between our series and the other two groups.

PUD was more common in the WH group (43.5%) and EH group (23.6%) than in the present study (17.1%). The decreased incidence of PUD in the WH group may be explained in part by better acid-suppressing medications than they were available 25 years ago. Also, identification of *Helicobacter pylori* as a causative factor for PUD and the development of effective therapy have improved treatment outcomes of children with PUD. The reason for the increased incidence of PUD in the EH group may be related to the higher prevalence of *Helicobacter pylori* in these populations.

VIH was less common in the WH (1.2%) and EH (0.2%) groups compared with our series (17.0%). Overall, MWT accounted for all VIH in the EH group (0.2%) and half (0.6%) in the WH group; in our series it accounted for 3.8% of UGIBs. PGS was not seen in the EH group and accounted for 0.6% in the WH group; in our series it accounted for 12.7% of UGIBs. In the present study, the rate of PGS was three times higher than that of MWT, accounting for the higher rate of VIH compared to previous reports. PGS was first described in adults in 1975,[15] PGS in pediatrics was reported as "submucosal hemorrhage caused by retching" due to UGIB in 1977 by Ament and Christie.[11] But it was not mentioned in other series.[1-10,12-14] Difference in the role of VIH in UGIB may be explained by under recognition and/or reporting of PGS as an etiologic factor. Endoscopically, PGS is characterized by a well-demarcated, focal area of erythematous, congested mucosa, which sometimes is associated with a reticulated-mosaic pattern reminiscent of hypertensive gastropathy (Fig. 4).[16] Prolapse gastropathy is typically seen in the upper stomach, just distal to the esophagogastric junction, most commonly on the greater curvature.[15,17,18] Biopsy specimens of PGS may show acute inflammation, chronic inflammation, submucosal hemorrhage, and superficial ulceration, either alone or in combination.[16,17]

Whether one develops PGS or MWT is related to the tonicity of the lower esophageal sphincter. A lax lower esophageal sphincter favors the development of PGS, while MWT occurs in the setting of high intragastric pressure and a tight lower esophageal sphincter.[19-21] It has been proposed that children other than adults are protected from MWT by a greater tensile strength of the gastrointestinal tract.[22]

Erosive esophagitis was less common in the WH (0.6%) and EH (0.2%) groups compared to the present study (10.0%). Most children with erosive esophagitis (83%) in our study had cerebral palsy and severe developmental delay. Their conditions were associated with a higher frequency of gastroesophageal reflux.[23,24] Of mentally retarded adults admitted to the hospital with UGIB, 70% had erosive esophagitis as the underlying cause.[24] In the past 25 years, the survival of extremely premature infants accompanied with cerebral palsy has been improved. This trend may help explain the difference in erosive esophagitis as

an etiology in UGIB between our series and the WH group. Differences between our series and the EH group are more difficult to explain. While studies have shown that in adults gastroesophageal reflux disease is more common in the West than in the East[25,26] but no such studies in children. A more plausible explanation for the high rate of erosive esophagitis in the present study is the criteria used for performing endoscopy. In non-conversant, developmentally delayed children, symptoms could not be relayed, prompting us to proceed with endoscopy more quickly than in those with the ability to provide a history of symptoms.

Our results must be interpreted with the understanding that there was no consistent method for data collection among the various studies. Several general concepts have been proposed to explain differences in causes of UGIB in geographically diverse areas, including endoscopist experience, criteria for performing endoscopy, selection bias, and confounding comorbidities.[1,2,5] The endoscopists in the present study have been performing endoscopic procedures for more than 15 years. In our study, children with evidence of UGIB of any degree were included. Despite inclusion of lesser degrees of UGIB, the rate of non-diagnostic procedures was not significantly different from that reported previously. We consider that a selection bias was not a significant factor in our patients as the institution is the only children's hospital in the state caring for children with both gastrointestinal and hepatic diseases. The role of co-morbidity is realized in the group with erosive esophagitis, most of them had cerebral palsy.

In the present study, UGIB presenting as melena resulted in bleeding more significantly than UGIB presenting with hematemesis or CGE, as determined by hemoglobin level and need for transfusion. Passage of melanotic stool is less dramatic than vomiting blood and may go unrecognized as abnormal by the patient causing a delay in seeking medical attention. Conversely, vomiting blood of any amount is easily recognized as abnormal, prompting immediate evaluation.

The two conditions associated with the most significant UGIBs are duodenal ulcers and esophageal varices.[4,7,9] Duodenal ulcers may bleed for a prolonged time prior to recognition of melena. Children with esophageal varices had the most severe bleeding in the hematemesis group. Varices tend to bleed profusely because of a high pressure gradient related to portal hypertension.

We determined if the duration of bleeding based on patient recollection had an effect on the ability to identify a bleeding source. Although there was a decreasing trend, a bleeding source was found in similar percentages of patients reporting a history of UGIB for less than a day, less than a week, and less than a month. However, bleeding lasting for more than a month or intermittent in nature was less likely to yield an identifiable source.

We also determined if the time between the most recent bleeding episode and endoscopy had an effect on the ability to identify a bleeding source. There was no difference in the percentage of patients with a bleeding source identified for children having EGD at less than 24 hours or later than 48 hours. There was a decreased chance of identifying a bleeding source if the endoscopy was postponed more than 48 hours. Although EGD should be performed as quickly as possible, delay for up to 48 hours due to hemodynamic instability does not aversely affect the ability to identify a bleeding source.

In conclusion, despite improvements in endoscopic equipment the rate of non-diagnostic endoscopy after UGIB has not changed in the past 25 years. We found a decrease in the rate of PUD compared with the reported results from both WH and EH groups, mostly because of the presence of PGS and a relatively new and underreported contributor to UGIB. More significant bleeding was seen in children with melena than in those with hematemesis or coffee-ground emesis. Conditions which are most likely to result in anemia include esophageal varices and duodenal ulcers. Factors affecting the chance of finding a source of UGIB in children include criteria for endoscopy, patient selection, and co-morbid conditions. The duration of bleeding and time of endoscopy from the most recent bleeding episode may help to predict patients who warrant endoscopy to determine a source of bleeding.

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