

# Clinical presentations of erosive esophagitis found at endoscopy in neurologically impaired children: a historical study

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**Background:** Data is lacking as to the clinical presentation of erosive esophagitis (EE) in neurologically impaired children compared to non-neurologically impaired children (non-NIC). To determinate the clinical presentation, associations, management, and outcomes of EE in neurologically impaired children compared to children without neurologic impairment.

**Methods:** Retrospective chart review of all esophagogastroduodenoscopies performed in pediatric patients at the University of Mississippi Medical Center from 1998 to 2020 with the diagnosis of EE. Fisher's exact test was used to compare results from neurologically impaired children group and non-NIC. A probability <0.05 was considered statistically significant.

**Results:** Forty-seven patients were diagnosed with EE and met study criteria. Twenty-six patients were neurologically impaired children, and 21 were non-neurologically impaired children. No significant difference was seen between age at diagnosis, sex, or hematologic markers of anemia. The most common indication for esophagogastroduodenoscopies in neurologically impaired children was hematemesis (65.4%), whereas abdominal pain (33.3%) was the most common in non-NIC. Neurologically impaired children were more likely to be treated with acid-blockade. Nine neurologically impaired children had gastrostomy tubes prior to diagnosis as opposed to 0 non-neurologically impaired children. After diagnosis, 8 neurologically impaired children underwent gastrostomy tube placement compared to 0 non-neurologically impaired children as compared to 1 non-NIC. The sensitivity of fecal occult blood test for detecting EE was higher for neurologically impaired children (91.7%) than for non-NIC (33.3%).

**Conclusions:** EE in neurologically impaired children presents differently than in non-neurologically impaired children with blood loss being the most common presentation in neurologically impaired children. Neurologically impaired children are more likely to be treated with acid-blockade prior to diagnosis, likely due to heightened risk for gastroesophageal reflux disease (GERD). Additionally, they are more likely to undergo surgical management of EE than non-neurologically impaired children.

Keywords: Gastroesophageal reflux disease (GERD); erosive esophagitis (EE); neurologically impaired children

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### Introduction

Gastroesophageal reflux disease (GERD) is defined as the passage of gastric contents into the esophagus with or without regurgitation or vomiting that might lead to esophagitis or structuring (1). GERD symptoms are a relatively common complaint in the Pediatric age group, occurring in 2–8% of children aged 3–17 years and increasing with age (2). One of the more significant manifestations of GERD is erosive esophagitis (EE), reported in 12% of children presenting with GERD symptoms (3).

EE most commonly presents with epigastric pain, regurgitation, food refusal, nausea, or vomiting (4,5). Risk factors include age, hiatal hernia and duration of GERD (1,3). Another well described risk factor for EE is neurological impairment, including Down Syndrome (6,7), cerebral palsy (3,7,8), and muscular dystrophy, due in part to esophageal motor abnormalities (8), and increased intraabdominal pressure secondary to spasticity and scoliosis (7-9). EE requires esophagogastroduodenoscopy (EGD) assessment for proper grading and diagnosis (1,10). EE is diagnosed by the presence of patchy, striated, or circular and confluent breaks in the mucosa of the esophagus (1,11). Current medical treatment of EE consists of initial treatment with proton pump inhibitors (PPI) for 8 to 12 weeks, withdrawal of treatment as tolerated, then the extension of the treatment with a PPI if necessary (1).

Data is lacking as to the clinical presentation of EE in neurological impaired children (NIC) compared to nonneurologically impaired children (non-NIC). The nature of the NIC makes it difficult to assess symptoms of EE prior to EGD diagnosis, often relying on the observations of the parents. We undertook this study to compare clinical presentation of the two groups of children to better understand the presentation and outcomes of EE in NIC compared to non-NIC. Specific aims were: (I) to determine if there is a difference in the clinical presentation of NIC diagnosed with EE by EGD compared to non NIC, and (II) to determine the outcomes of children with NIC compared to those non-NIC following diagnosis and treatment. We present the following article in accordance with the STROBE reporting checklist (available at https://apm. amegroups.com/article/view/10.21037/apm-22-783/rc).

## Methods

We performed a case-controlled retrospective review of children with a previous EGD and proven clinical diagnosis of EE identified by reviewing all EGD performed at the University of Mississippi Medical Center from 1998 to 2020. Patients identified with EE underwent a structured chart review and the following data collected: patient age and weight at the time of EE diagnosis, presence or absence of neurological impairment, presence or absence of gastroesophageal reflux (GER), symptoms prompting EGD, hemoglobin and mean corpuscular volume at time of EGD, presence of fundoplication prior to and post EGD, severity of esophagitis, use of acid-blockade prior to EGD, and fecal occult blood testing (FOBT) results. The severity of esophagitis was determined using the Hetzel-Dent classification for peptic esophagitis in children (12). This classification grades the degree of inflammation on a 5-point scale with a score of "0" for normal-appearing mucosa and "4" for the most severely ulcerated mucosa (12). The score for each patient was determined by the description of the degree of inflammation in the endoscopy report or review of the images taken at endoscopy. We combined occult fecal blood, melena, shock, anemia, and hematemesis to note all forms of blood loss.

Inclusion criteria included children (ages 2 to 18 years) with an endoscopic diagnosis of EE. Exclusion criteria included children under 2 years of age and older than 18 years of age and children with a diagnosis other than GERD as the cause of EE, including caustic ingestions, Crohn's disease, and fungal infections.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of the University of Mississippi Medical Center (No. UMMC-IRB-20210653) and individual consent for this retrospective analysis was waived.

#### Statistical analysis

Fisher's exact test, *t*-test, and odds ratio were used to compare results from the NIC and non-NIC. A probability <0.05 was considered statistically significant. Analysis was performed in R (ver. 4.1.1).

Table 1 Clinical indication prompting endoscopy

Indication for EGD	NIC (n=26)	Non-NIC (n=21)
Abdominal pain	0 (0%)	7 (33.3%)
Blood loss <sup>†</sup>	22 (84.6%)	6 (28.6%)
Hematemesis	15 (65.4%)	5 (23.8%)
Dysphagia	2 (7.7%)	5 (23.8%)
GER	1 (3.8%)	2 (9.5%)
Anemia	2 (7.7%)	0 (0%)
Other	4 (15.4%) <sup>‡</sup>	2 (9.5%) <sup>§</sup>

<sup>†</sup>, "Blood loss" data combining occult fecal blood, melena, shock, anemia, and hematemesis; <sup>‡</sup>, 1 each (incidental, occult fecal blood, melena, shock); <sup>§</sup>, 1 each (meat bolus impaction). EGD, esophagogastroduodenoscopy; NIC, neurologically impaired children; GER, gastroesophageal reflux.

#### **Results**

Review of the database of 3,286 diagnostic EGD revealed 49 (1.5%) children with EE. Two patients less than 2-year of age were excluded from the review leaving 47 children, of which 26 (55.3%) were NIC and 21 (44.7%) were non-NIC. The diagnoses in NIC included cerebral palsy (69.2%), various genetic syndromes (11.5%), structural brain malformations (7.7%), severe intellectual disability (7.7%), and chromosomal abnormalities (3.8%). No difference was seen between the NIC and non-NIC for age (9.4±4.4 vs. 10.2±4.9 years, P=0.59), sex (male, 61.5% vs. 57.1%, P=0.76), hemoglobin (10.6±4.8 vs. 12.3±2.4 g/dL, P=0.33), or mean corpuscular volume (81.7±8.5 vs. 80.8±5.5 fl, P=0.77). The mean for weight of NIC was significantly lower than the mean of non-NIC (P=0.006). No difference between the NIC and non-NIC was seen for presence of clinical diagnosis of GERD (73.1% vs. 57.1%, P=0.36). There was a difference between NIC and non-NIC receiving an acid-blocker for GERD (89.4% vs. 46.2%, P=0.015). No difference between the NIC and non-NIC was seen for treatment with a PPI (38.5% vs. 19.0%, P=0.21) or a histamine-2 receptor antagonist (H2RA) (26.9% vs. 9.5%, P=0.16). At the time of diagnosis of EE, a gastrostomy tube was present in 9 (34.6%) NIC, but none of the non-NIC. Following the diagnosis of EE, 8 (47.1%) of the 17 NIC without a gastrostomy tube had one placed, no non-NIC required a gastrostomy. No child in either group had undergone fundoplication prior to the diagnosis of EE. Following the diagnosis of EE, fundoplication was performed in 11 (42.3%) NIC and in 1 (4.8%) non-NIC.

The most common reason for EGD (Table 1) in NIC was hematemesis (65.4%) followed by anemia (7.7%), dysphagia (7.7%), and GER (3.8%). In contrast, the most common indication for EGD in non-NIC was abdominal pain (33.3%), followed by dysphagia (23.8%), hematemesis (23.8%), and GER (9.5%). A statistically significant difference was seen between NIC and non-NIC for abdominal pain (P=0.002), any gastrointestinal bleeding (P<0.001), and hematemesis (P=0.003). The odds of any bleeding (anemia, hematemesis, FOBT positive or melena) in the NIC group was 7.2 times higher than the non-NIC group. FOBT was performed in 28 of 47 (59.6%) of the patients, in only 13 (50%) of NIC, but 15 (71.4%) of non-NIC. The sensitivity of FOBT for detecting EE was higher for NIC (91.7%) than for non-NIC (33.3%). These differences may be related to the concern for upper gastrointestinal bleeding (UGIB) as the reason for EGD. In NIC, UGIB was the most common reason for EGD, and accounted for 12 of 13 patients who had FOBT performed; 11 patients with known UGIB were positive. In the non-NIC, UGIB was the reason for EGD in 5 of 15 patients who had FOBT performed; only the 5 patients with known bleeding were positive. It was elected not to perform FOBT in patients with known UGIB when the decision to perform EGD had already be made.

Using the Hetzel-Dent classification for peptic esophagitis (12), the severity of esophagitis had adequate documentation for determining a score in 19 (73%) of NIC group and 17 (81%) of the non-NIC group. The data was evaluated by determining the percentage with mild (grade 1 or 2) or severe (grade 3 or 4) EE and the overall average score for each group. Severe EE was found more often in the NIC group (79%) than in the non-NIC group (59%). Also, the average Hetzel-Dent score was higher in the NIC group (3.3±0.8) than the non-NIC group (2.5±0.9), but did not reach statistical significance (P=0.28).

In the present study 20 of 26 (77%) of NIC had GER, in this group of patients with GER: 2 (10%) were not receiving acid-blockade, 7 (35%) were receiving a H2RA, and 11 (55%) were on a PPI. No NIC had undergone fundoplication prior to the diagnosis of EE, while a gastrostomy tube was present in 9 (35%). In NIC with a gastrostomy tube at the time EE diagnosis, 2 of 9 (22%) underwent fundoplication following diagnosis. In NIC without a gastrostomy tube at the time of EE diagnosis, 8 of 17 (47%) underwent fundoplication with gastrostomy tube placement, one (6%) underwent fundoplication alone, and one (6%) had a gastrostomy tube placed without fundoplication.

#### Discussion

EE is a relatively common finding at endoscopy in children, with the prevalence varying depending on the reason EGD was performed. The prevalence of EE in children in a retrospective study of nearly 7,200 EGDs was 12.4% (3). In two smaller, retrospective studies looking at causes of UGIB in children, EE was identified as the etiology in 1.7% and 9.5%; in one of the studies NIC accounted for 83% of those with EE (13,14). In a highly selected study of children with non-cardiac chest pain, EE was found at EGD in 42% (4).

Although our study did not show an increase in EE with increasing age or a gender difference, previous studies have shown that EE increases with age, is more common in males, and is more likely to be associated with a hiatus hernia (1,3); there is incongruent data about racial differences in EE (3).

Symptoms of EE vary widely and are non-specific, common complaints include GER, vomiting, abdominal pain, cough, heartburn, chest pain, dysphagia, gastrointestinal bleeding, and food refusal (4,5,13,14). Gupta *et al.*, compared children with EE to children with non-EE, there was no difference in reported symptoms including regurgitation, abdominal pain, cough, or heartburn; the only symptom that was statistically different was food refusal (5).

In the present study, GER was symptomatically present in 70.2% of the children, with no difference between NIC and non-NIC. However, the number of NIC receiving acid-blockade, either a H2RA or a PPI, was higher than non-NIC. While the majority of children in this study had a GER, it was rarely the reason for EGD. Symptoms prompting EGD that were significantly different between NIC and non-NIC were any gastrointestinal blood loss, hematemesis, and abdominal pain. Potential reasons for these differences are speculative. All NIC in this study were non-verbal prohibiting their ability to communicate discomfort, including abdominal pain. Similarly, inability to communicate may have led to a more prolonged exposure to acid-exposure due to GER, despite the use of acidsuppression (15).

Prolonged exposure of the esophageal mucosa to an acid milieu is the primary cause of EE, particularly in NIC who cannot expressive discomfort and thus experience treatment delay. Proposed predisposing factors for GER in NIC include scoliosis, spasticity, seizures, hiatus hernia, and oropharyngeal dysphagia (7,8,16-18). In a study looking at long-term use of PPI for GERD, 79% had a predisposing

condition, of which neurological impairment was the most common predisposing condition (66%) (15). In this study there was no difference in the rate of EE between those with a predisposing condition (67%) and those without a predisposing condition (60%), however, all the children were on PPI.

Making a diagnosis of GER can be more challenging in NIC than non-NIC for a variety of reasons. Often NIC cannot express symptoms, the symptoms of GER may be non-specific (irritability, oral aversion, hyper-salivation), or atypical (laryngospasm, seizures, increased dystonia, recurrent pulmonary infections, anemia) (1).

While many symptoms of GER are present in NIC and non-NIC, anemia is a sign more frequently seen in NIC. In a study assessing GER in NIC with or without gastrointestinal symptoms, GER was more commonly found in those without gastrointestinal symptoms (75%) than those with symptoms (37%). Similarly, anemia was more common in asymptomatic (50%) than symptomatic children (1%) with GER (17). Another previous study, 11% of severe NIC were found to have GER, with anemia being more common in those with GER (26%) than those without GER (3%). Esophagitis was found in 71% of those undergoing EGD, of which EE accounted for 43% (16). In a study of NIC undergoing fundoplication for GER, 20% had hematemesis and 16% were anemic (7). In the present study, there was no difference in the prevalence of anemia in NIC (38%) and non-NIC (40%); while statistical significance was not attained, mean hemoglobin levels in NIC were lower than those in non-NIC.

Treatment recommendations for NIC with EE have been made by the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) are for use of PPIs as first line therapy as they are superior to H2RAs (19). The panel recommended EGD to assess for the degree of esophageal injury and Barrett's esophagus, as well as determination of acid milieu in the esophagus by a pH study when long-term therapy for GER is required (20). In NIC where EGD cannot be safely performed, empiric treatment with a PPI is recommended (9). In NIC requiring Gastrostomy tube placement, anti-reflux surgery is not recommended as most studies do not show worsening of GER following placement (21-26). Other reasons cited for not routinely performing anti-reflux surgery include concerns about risks of surgery in medically frail children, post-surgical complications (gas bloat, dysphagia, dumping syndrome), no decrease in hospitalization for GER-associated symptoms (asthma, aspiration, pneumonia) (21-27), and a high rate of re-operation in NIC compared to non-NIC (21). The rate of NIC requiring anti-reflux surgery following gastrostomy tube placement has been reported at <10% (28). What these recommendations could not address is what to do with NIC with asymptomatic or "silent" reflux.

This study was limited due to the retrospective nature of the study and some subgroups were underrepresented due to the small sample size. There was also missing information in the database, including the time between the presentation of GERD and EE, in part due to the inability to communicate discomfort in the NIC group. Also, some of the GER severity was not able to be determined in the procedure report. Longitudinal and multicenter studies may be needed.

#### Conclusions

This study shows that EE in NIC presents differently than in non-NIC, with blood loss being the most common presentation in NIC. NIC are at increased risk for GER, which may present with minimal to no symptoms prior to the development of EE. NIC are more likely to undergo surgical management of EE than non-NIC. A high suspicion for GER should be maintained in these children and medical therapy initiated early for any symptoms or signs suggestive of GER to prevent development of EE. PPI should be first line treatment for suspected or proven GER in NIC. The threshold for EGD should be lower for NIC due to their heightened risk for EE and inability to properly convey discomfort.

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#### Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-783/rc

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of the University of Mississippi Medical Center (No. UMMC-IRB-20210653) and individual consent for this retrospective analysis was waived.

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