

Peer Review File

Article Information: <https://dx.doi.org/10.21037/apm-22-783>

Reviewer A

The study design is suitable for the the purpose of the study. The sample size is relatively small but adequate for the conclusions drawn. The inclusion and exclusion criteria are clearly stated and locate those patients with diagnostic endoscopy for peptic esophagitis and classify them as cases, neurological patients, and healthy controls. The diagnosis of gastroesophageal reflux disease is based on the clinic and it might have been correct to have had the pH-metry records if they existed.

Reply: we added a clarification that the diagnosis of GERD was made clinically, based on the patient record reviewed. There were no medical indications for pH-metry in the group that presented with upper gastrointestinal bleeding. (see Page 7, line 145)
Changes in the text: page 5, line 104

Reviewer B

The authors have done a nice job in reviewing a lengthy clinical experience on a difficult topic. They have chosen to highlight differences in their “neurologically impaired” vs “non neurologically impaired” populations who have also been diagnosed with erosive esophagitis. They have made an important association which will have clinical value for other gastroenterologists, the correlation of EE with GI bleeding. They have correctly pointed out that documentation of GI bleeding is a valuable marker that can be employed when caring for this population.

However, some of the assumptions that they make are not conclusively demonstrated by the data they present. Recognizing that the chart review is only as robust as the material that has been documented will need to be addressed as there is little that the authors could do regarding that situation.

The presence of minor GI bleeding, which is not significant enough to cause a statistically different hematocrit value, is likely most associated with the length of time and severity that the reflux has been occurring. EE similarly is also most closely associated with these variables. Incorporating any data available that would be relevant to the variables of severity of reflux would enable their central argument to be strengthened.

Reply: We added in the limitations that due to the nature of a retrospective study, length of symptom was not documented or available. All the neurologically impaired patients in this study were non-verbal which prohibit this subgroup their ability to communicate discomfort. (see page 10, line 197). The severity of esophagitis was analyzed and weight were added.

Changes in the text: page 6, line 109; page 7, line 134; page 11, line 240; and page 8, line 160

Were pH probes and or motility studies, or imaging performed, and were there significant differences between the two groups which could provide insights into variance in severity? Similarly, can the authors compare the severity of the histologic findings between the two groups?

Reply: We added the assessment of macroscopic findings of erosive esophagitis: “The severity of esophagitis was determined using the Hetzel-Dent classification for peptic esophagitis in children”.

The most common reason for EGD in neurologically impaired children is upper gastrointestinal bleeding in the study group. We added it in the limitations to clarify. There were no medical indications for pH-metry. (see Page 7, line 145).

Changes in the text: page 6, line 109; page 8, line 160 and page 11, line 241.

On the other hand, are there any data that could address the length of time that the two respective cohorts had GERD symptoms? The authors correctly point out that neurologically impaired patients are less able to communicate verbally to their care providers. However, impaired intake of feeds, potentially leading to weight loss or diminished rate of weight gain, more aggressive or more subdued behavior, coughing, choking gagging with feeds are all potential markers of esophageal pain and dysfunction. Perhaps there is data regarding these features, especially weight data, that the authors could review. Alternatively, the authors could discuss the value of developing tools that care providers could employ to yield earlier recognition of pathology in the future.

However, their observations have validity and are worthwhile for publication.

Reply: The severity of esophagitis was analyzed and weight was added. The NIC patients are usually underweight compared to the general population.

There is a lack of objective measurement including the timeline and the symptoms in such vulnerable populations because of their inability to communicate their symptoms (see page 10, line 197). We added it in the limitations to clarify. Also, the symptoms of Erosive esophagitis vary widely as they are not specific. Other subtle signs of

erosive esophagitis can lead to being a confounder factor, as the neurologically impaired patients can present with coughing, choking, or food avoidant from other non-GI causes (not limited to pneumonia, seizures, behavioral, or any acute infections), which is out of the scope of the research.

Changes in the text: page 7, line 134; page 11, line 241; page 6, line 109, and page 8, line 160.

Reviewer C

Suggestions for modifications:

- 1. define GERD in methods (how a patient was labelled as GERD patient?). If the diagnosis was based on the patient record as defined by his/her attending physician, it should be stated. Maybe, it should be re-worded as "previous clinical diagnosis of GERD".**
- 2. In results, 26.9% of NIC and 42.9% of non NIC had erosive esophagitis and NO GERD, what was the cause? Were there biopsies? If so, it should be mentioned, as the other alternative diagnosis.**

Reply1: We added to the methods “previous clinical diagnosis of GERD”
Changes in the text: page 5, line 104

Reply 2: We clarified by adding “clinical diagnosis of GERD”. Patients with a diagnosis other than gastroesophageal reflux disease (GERD) as the cause of EE were excluded, including caustic ingestions, Crohn’s disease, and fungal infections (see page 6, line 119).

Changes in the text: page 11, line 241; page 6, line 109; page 8, line 160; page 9, line 191