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**Title:** Age-specific causes of upper gastrointestinal bleeding in children

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Dear Editors and Reviewers,

We appreciate the time and effort you put into reviewing our manuscript. We have read your insightful comments and have revised the manuscript.

All revisions are highlighted in yellow in the updated version of the manuscript.

We respond below to your comments item-by-item.

**Response to Editorial comments:**

**COMMENT 1:** Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

**Response:** We have provided the tables according to the Editor’s instructions in the revised version of the manuscript.

**COMMENT 2:** Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial

intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision.

**Response:** We thank the Editor for addressing us to this useful tool. We have used it to find some high-impact articles.

### **Responses to Reviewer #1's comments**

**COMMENT 1:** Please provide the references for Table 1 and Table 2.

**Response:** We have provided the references for all tables in the revised version of the manuscript.

**COMMENT 2:** Table 1 can be classified and summarized according to different age groups and different regions (such as North America and Europe, the Middle East and Asia, etc.) and attach the corresponding references in the table.

**Response:** We have reorganized Tabel 1 into four Tables according to different age groups and attached the corresponding references. Unfortunately, comparison according to the various geographic regions is possible only regarding specific causes such as „esophageal varices“. On the other hand, a lot of the UGIB causes mentioned in this manuscript do not have different geographic distributions or there is not enough valuable epidemiological data to prove otherwise. Besides, the incidence of the most common UGIB causes in countries within select regions and continents is often inconsistent. In recent years, the most common causes in some Middle Eastern and Far Eastern countries are becoming similar to those in Western countries. Therefore, the differences in the incidence of UGIB causes between various countries and regions are described using the results of different studies throughout the manuscript text, and it would be hardly possible to make a comprehensive Table.

**COMMENT 3:** Please provide a diagnostic flow chart for UGIB classified according to different age groups.

**Response:** We have created a comprehensive diagnostic-therapeutic flow chart that, combined with the information provided in the Tables of this article, may help clinicians in the initial management of the child with UGIB. The chart is based on the information regarding anamnestic data, clinical findings, previous diseases and estimated amount of bleeding. Tables 1-5 are intended to be hyperlinked with this flow-chart, this way providing all the necessary information regarding common UGIB casues at different ages, unusual UGIB causes, and subsequent steps for their differentiation, at the same place.

**COMMENT 4:** The part "UNUSUAL CAUSES OF UGIB" is too verbose and does not require an introduction to each special disease. It can be simplified and summarized.

**Response:** We have shortened and reorganized the part "UNUSUAL CAUSES OF UGIB" to make it more concise and readable. Now, the unusual causes are summarized into four subsections according to bleeding location (esophagus, stomach, duodenum, and distinct locations). Wherever possible, the introduction to each special disease is shortened. However, some disorders like Dieulafoy's lesions or Zollinger-Ellison syndrome should contain a few sentences regarding their etiology to make them more readable and understandable for non-pediatricians or other readers. Besides, writing this type of epidemiological review considers the use of a lot of numerical and statistical data that helps explain the rarity of specific diseases and make them comparable. Wherever possible, we have reduced the use of numerical data, but, on the other hand, more deletion would lead to valuable data loss.

**COMMENT 5:** If possible, an anatomical picture of the upper gastrointestinal tract (i.e. esophagus, stomach, duodenum, etc.) and the corresponding causes can be annotated to make the article more readable and interesting for non-pediatricians or other readers.

**Response:** The anatomical picture of the upper gastrointestinal tract with corresponding causes is added to the revised version of the manuscript.

**COMMENT 6:** Although it is a review of the cause of the disease, it is recommended to mention the clinical approach appropriately, such as giving a clinical approach flow chart or a summary of treatment according to different age groups or according to the amount of bleeding, etc., to make the article more clinically practical.

**Response:** We thank the reviewer for this useful advice that, indeed, makes this article more clinically practical. We have created a comprehensive diagnostic-therapeutic flow chart that, combined with the information provided in the Tables of this article, may help clinicians in the initial management of the child with UGIB. The chart is based on the information regarding anamnestic data, clinical findings, previous diseases and estimated amount of bleeding. Tables 1-5 are intended to be hyperlinked with this flow-chart, this way providing all the necessary information regarding common UGIB cases at different ages, unusual UGIB causes, and subsequent steps for their differentiation, at the same place. This flow-chart describes the basics of the UGIB treatment. A more thorough therapeutic protocols with drug dosages, explanation of different endoscopic and surgical procedures etc. demand a more extensive discussion that is not primarily subject of this article.

**COMMENT 7:** There are too many references in this review, I recommend deleting some unnecessary references and simplifying some paragraphs and sentences.

**Response:** We have reduced the number of references and simplified some sentences in the revised version of the manuscript.

**Reviewer #2** had no questions regarding the manuscript.

**Responses to Reviewer #3's comments**

**COMMENT 1:** It would be better the authors provided some representative images (endoscopic, radiographical...) to show the common caused of UGIB.

**Response:** We have added the representative images of UGIB causes in children to the revised version of the manuscript.

**COMMENT 2:** The whole manuscript should be more concised.

**Response:** We understand the reviewer's concerns. Unfortunately, writing this type of epidemiological review considers the use of a lot of numerical and statistical data that helps explain the epidemiological distribution of specific diseases and makes them comparable. This might make an article appear too long.

We have shortened and completely reorganized the longest section of the manuscript, a section regarding the unusual causes of UGIB in children. This section was too long and verbose, therefore we made the rearangment to make it more concise and readable. Wherever possible, the introduction to each special disease is shortened.

**COMMENT 3:** It would be better the authors provided a diagnostic flow chart for UGIB in children.

**Response:** We have created a comprehensive diagnostic-therapeutic flow chart that, combined with the information provided in the Tables of this article, may help clinicians in the initial management of the child with UGIB. Tables 1-5 are intended to be hyperlinked with this flow-chart, this way providing all the necessary information regarding common UGIB casues in different ages, unusual UGIB causes, and subsequent steps for their differentiation, at the same place.

**ADDITIONAL MINOR CHANGES:** Several minor improvements were made in the manuscript.

We thank the Editors and Reviewers for their helpful comments and suggestions to improve our manuscript.

We would highly appreciate your time and effort in reevaluating our manuscript.

Please do not hesitate to contact us for any questions or concerns.

Best regards,

Petar Rasic