

Reviewer #1:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** The authors discussed uncommon pathological and clinical entity that is difficult to diagnose and treat. The work is interesting, but as a gastroenterologist, I will be happy to see some important points in this review: 1- It may be valuable to insert a briefing of search methods adapted to extract the data of this narrative review e.g. search terms and the searched databases. 2- I think this narrative review needs subheadings that better to present the topic e.g. pathogenesis, pathology, types, presentations, diagnosis, prognosis ...etc. 3- Supporting this review with some figures may be beneficial e.g. biopsy pictures, CT pictures, endoscopic pictures....etc. 4- I wish to see a clear differentiation between local and systemic GIT amyloidosis e.g. in a table 5- I failed to characterize localized GIT amyloidosis in this article 6- Previous studies e.g. that by Yen et al., failed to diagnose 45% of cases of GIT amyloidosis with the biopsies, how these patients were diagnosed? And what recommendations for clinicians in such cases? 7- The biopsy is the gold standard in diagnosis of GIT amyloids, and I recommend the authors to discuss in details the characteristics of adequate biopsy regarding the methods to obtain, sufficient quantity, handling, examination ....etc. under a separate heading. 8- If it is possible, suggest a management algorithm for GIT amyloidosis based on the available literature. I think it would be beneficial for clinicians. 9- I am not a native English speaker, but I think the article needs proofreading.

**Team Response:** We would like to thank you for a review of the manuscript. The following remarks have been addressed:

1. Thank you for your suggestion. An additional section on the search methods has been added.
2. Thank you for your suggestion. You are right, a better way of presentation is bound to increase reader interest and hence the manuscript has been changed to include the appropriate sections.
3. Thank you for your suggestion. Figures have been included in the manuscript.
4. Thank you for your suggestion. An additional table has been added to differentiate systemic and localised amyloidosis.
5. Thank you. Localized GI amyloidosis is an uncommon disease entity with a low prevalence. In literature, the data available on localised GI amyloidosis is mainly only through case reports. We have made additional changes to the manuscript to include more literature on localized GI amyloidosis.
6. Thank you for pointing that out. According to the study by Yen et al, 55% of the patients with symptoms of amyloidosis had a negative result on the biopsy. In the study, a specific attempt to diagnose these patients was not made. However, they report that only 23.2% of these patients underwent diagnostic studies for functional assessment of the luminal gastrointestinal tract (such as esophageal or anorectal manometry, capsule endoscopy, or gastric emptying study) as they met the Rome IV criteria for several functional bowel disorders. In the discussion section, Yen et al recommend additional diagnostic studies for motility disorders in these patients with negative biopsy results. Similarly, the authors also recommend additional motility studies for these patients. Additional changes have been made in the manuscript to include this part of the literature.
7. Thank you for your suggestion. On EGD or colonoscopy, the site of highest diagnostic yield from biopsy specimens was found to be the duodenum, followed by the stomach, colon, and rectum, and the esophagus. Liver biopsy, through a transjugular route, may also be performed to confirm hepatic infiltration. They are included in the manuscript. Additionally, staining methods and the appearance of amyloid proteins have also been included in the manuscript.
8. Thank you for your suggestion. An additional table has been added to the manuscript for the management of GI amyloidosis based on the subtype of deposition.

9. Thank you for your input. The manuscript has been revised again.

Reviewer #2:

**Scientific Quality:** Grade A (Excellent)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** Dear Sir, I report on a review entitled "Gastrointestinal Amyloidosis: A Focused Review" I want to congratulate the authors on this very clear and well readable review. I have two suggestions: 1. Even if the incidence and prevalence is accurately described in the discussion sector, the readability of the introduction sector could be improved by adding a number for the general incidence of this disease. (Page 3, Line 4) 2. The authors state " ... on the US population and its burden on the healthcare system." I believe that this disease not only affects US citizens and the US healthcare system. As the readership of the journal is an international readership one should generalize this statement. (Page 3, Line 20; Page 7, Line 20)

**Team Response:** We would like to thank you for a review of the manuscript. The following remarks have been addressed:

1. Thank you so much for your suggestion. We have added the incidence rate in the introduction section of the manuscript.

2. Thank you for pointing that out. The statement has been corrected.

Reviewer #3:

**Scientific Quality:** Grade D (Fair)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Rejection

**Specific Comments to Authors:** The authors have scrutinized the literature and summarized the sparse level of today's knowledge regarding GI Amyloidosis. However, a review includes a method section. The reader wants to know which studies have been performed concluding the treatment strategies of today. Any ongoing studies (clinical [trials.gov](https://clinicaltrials.gov))? I can read the whole conclusion text in the introduction section (and in abstract). In the introduction we need to know why this manuscript is needed, and a review should collect the current data/knowledge and summarize in conclusion. Is there any news found by this literature-search that affect current assessment of AL and AA? Would like to know the authors own ideas of what to do next in the conclusion.

**Team Response:** We would like to thank you for a review of the manuscript. The following remarks have been addressed.

1. Thank you for your suggestion. An additional method section has been included in the manuscript.

2. Thank you for your suggestion. The articles are referenced in the treatment section. Additionally, changes have been made in the manuscript to give the readers one click access to all the clinical trials on amyloidosis from [clinicaltrials.gov](https://clinicaltrials.gov).

3. Thank you for pointing that out. Changes have been made to the conclusion section and the abstract and introduction.

4. Thank you for your suggestion. We have included all the information available to us through the literature search in the manuscript.

5. Thank you for your suggestion. We have made the changes to the conclusion.

Reviewer #4:

**Scientific Quality:** Grade A (Excellent)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (High priority)

**Specific Comments to Authors:** To Authors I congratulate the authors for Gastrointestinal Amyloidosis: A Focused Review name's article. Best regards.

**Team Response:** We would like to thank you for a review of the manuscript.

Reviewer #5:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** This is a review article about the gastrointestinal (GI) amyloidosis. The authors summarized the causes, types and GI manifestations of amyloidosis well; therefore, I am sure that this review will give clinicians a good information on how to diagnose and how to treat GI amyloidosis, (Minor comments) 1. Endoscopic and histopathologic pictures about GI amyloidosis should be included in this article for readers to understand. 2. It is recommended that a table on the treatment according to the amyloidosis types would be included. 3. The format of this article is corrected, and some errors such as misuse of abbreviation should be corrected.

**Team Response:** We would like to thank you for a review of the manuscript. The following remarks have been addressed:

1. Thank you for your suggestion. Unfortunately, after a thorough search of our database for many weeks we were unable to find clear pictures on GI amyloidosis.
2. Thank you for your suggestion. A table on the management of GI amyloidosis based on the specific type of protein has been included.
3. Thank you for pointing that out. The appropriate changes have been made in the manuscript.

#### EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

**(1) Science editor:** 1 Scientific quality: The manuscript describes a minireview of the gastrointestinal amyloidosis. The topic is within the scope of the WJGE. (1) Classification: Grade A, Grade D, Grade C, Grade A and Grade B; (2) Summary of the Peer-Review Report: It is a clear and well readable review, providing useful information to clinicians on how to diagnose and treat gastrointestinal amyloidosis. However, a method section should be used to present the studies that lead to the treatment strategies today, and a briefing of the search methods adapted to extract the data should be included. The authors should summarize any ongoing studies/trials. The authors should discuss gastrointestinal amyloidosis in a more general way, not limiting to the United States. The manuscript can be improved by using proper subheadings and by incorporating more figures and tables as suggested. The questions raised by the reviewers should be answered; and (3) Format: There is 1 table. A total of 64 references are cited, including 9 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade A, Grade A, Grade B, Grade A and Grade B. 3 Academic norms and rules: The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The topic has not previously been published in the WJGE. The corresponding author has not published articles in the BPG. 5 Issues raised: (1) I have changed the manuscript type "Review" to "Minireviews"; (2) the author should number the references in Arabic numerals according to the citation order in the text. The reference numbers need to be superscripted in square brackets and positioned before the punctuation or after the cited author's name, with no spaces; (3) please provide the audio core tip file where the core tip content is recorded; and (4) please provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. 6 Re-Review: Required. 7 Recommendation: Conditionally accepted.

**Team Response:** We would like to thank you for a review of the manuscript. The following remarks for the manuscript have been addressed:

1. Thank you for changing the type for us. We appreciate it.

2. All the referencing has been changed according to the required format.
3. An audio file with the core tip content of the of the manuscript has been provided with this submission.
4. A signed Conflict-of-Interest Disclosure Form and Copyright License Agreement has been provided with this submission.

(2) *Editorial office director:* I have checked and revised the comments written by the science editor.

**Team Response:** We would like to thank you for a review of the manuscript.

(3) *Company editor-in-chief:* I have reviewed the Peer-Review Report and the full text of the manuscript, all of which have met the basic publishing requirements, and the manuscript is conditionally accepted with major revisions. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report and the Criteria for Manuscript Revision by Authors. Before final acceptance, authors need to correct the issues raised by the editor to meet the publishing requirements.

**Team Response:** We would like to thank you for a review of the manuscript.