



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 76166

Title: Prevalence and factors associated with vitamin C deficiency in inflammatory bowel disease

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06101020

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Portugal

Author's Country/Territory: United States

Manuscript submission date: 2022-03-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-04-04 12:28

Reviewer performed review: 2022-04-07 12:48

Review time: 3 Days

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This study aims to report the prevalence of vitamin C deficiency in Inflammatory Bowel Disease (IBD). The authors discuss relevant results that could eventually be of interest in the IBD consultation. The manuscript is well written, cohesively and coherently organized, with a detailed description of the methods and results. The authors also present limitations to their study, adding to the strengthening of the manuscript. However, the authors should clarify some aspects regarding the Methods and Discussion sections. Major revisions: 1. Although the Methods section is written with detail, the authors do not mention if the manuscript was prepared according to the STROBE statement. If it was, this should be stated in the text, and a STROBE checklist should be provided as an Additional File. 2. In the “Patients Population” section, the authors state that “In patients with multiple plasma vitamin C levels, the lowest value and associated visit were utilized.”. What is the reasoning behind this? Why did the authors not use a mean of all values that were below 11.4 μ mol/L? If there is a reasonable reason, it should be stated in the text. 3. As the authors stated, in IBD patients, vitamin C deficiency can be originated from insufficient consumption or malabsorption. As so, results on vitamin C deficiency should depend on the diet profile of each patient. However, the authors do not mention whether the blood was collected after a fasting period, neither do they mention if the composition of the last meal of each patient was assessed. How would one know if the results observed are in fact, a consequence of IBD etiopathology, or a consequence of the patient’s diet? If the blood was collected without any of these concerns, this should be a limitation of this study and stated in the text. 4. Throughout the manuscript (Abstract-conclusion; Results;



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Discussion), it is mentioned that vitamin C deficiency is more prevalent in CD than UC. This is not true, since the numerical difference was not statistically significant. The text should be revised so that this numerical difference is not misleading to the readers. For example, in Discussion, line 3, “(...) with elevated rates in CD patients (24.4%).” is not accurate. 5. It is mentioned in the Introduction that TNF-alpha downregulates transcription of transporters necessary for vitamin C uptake. The authors assessed the prevalence of vitamin C in patients under therapy with biologics (that includes drugs anti-TNF-alpha), but failed to discuss these results. How do the authors explain that biologic medication use is associated with increased rates of vitamin C deficiency? A subgroup of patients under therapy with anti-TNF-alpha biologics (infliximab, adalimumab, golimumab, and certolizumab pegol) should be created and analyzed. Minor revisions: 1. Throughout the manuscript, “umol/L” should be changed to “ $\mu\text{mol/L}$ ”.



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Reviewer's code: 04163041

Position: Editorial Board

Academic degree: FACS, MBBS, MNAMS

Professional title: Professor

Reviewer's Country/Territory: India

Author's Country/Territory: United States

Manuscript submission date: 2022-03-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-04-10 17:15

Reviewer performed review: 2022-04-21 17:50

Review time: 11 Days

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

There being limited data available on deficiency of micro nutrients like Vitamin A, C and E and selenium in IBD patients, this study is significant. This is a significantly large study on the prevalence of vitamin C deficiency in IBD patients but to say that a larger portion of IBD patients suffer this deficiency is over statement wherein only 21.6% of patients have this. One of the limitation of the study is that the study population of IBD is not specifically screened for vitamin C level but retrospectively included. And hence there is no data on other micro-nutrient deficiencies which may have bearing on IBD management. There is no data on marginal or significant deficiency. (Studies variously quote that 11 to 40 umol/L ,or 11 to 28 umol/L as marginal deficiency). Also the general risk factors for vitamin C deficiency are not analyzed in this study (Smoking is included in the table not in the text). There is no discussion on the pathophysiology of Vitamin C deficiency in UC, compared to CD which affects the absorptive areas of the micronutrients. The described clinical features of vitamin C deficiency, except scurvy, are mostly non-specific and are multifactorial as quoted by the authors. Though this study is claimed to be the first one to report, “vitamin C deficiency and endoscopic activity relationship” the number of patients who had endoscopy report available are only about one third of the study population. In the discussion, the role of Vitamin C as an antioxidant may be added and also studies describing the role of antioxidant supplementation in IBD may be included in the references.