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SCHOOL OF MEDICINE

DIVISION OF GASTROENTEROLOGY AND HEPATOLOGY
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Dear Editor,

Thank you very much for your e-mail of August 9, 2023, regarding the review of our manuscript. The reviewers' comments were very helpful, and we have revised our manuscript as described below.

Responses to reviewers' comments:

Reviewer #1:
Specific Comments to Authors: Serum leucine-rich alpha-2 glycoprotein (LRG) is a novel monitoring biomarker for the assessment of disease activity in IBD. And this manuscript established an appropriate LRG cut-off values that haven't be studied to predict endoscopic and histological remission in patients with UC, which performed excellent application value. However, as a single-center study, the results was limited by the number of patients.

REPLY: Thank you for your comment. As the reviewer pointed out, this study is a single-center study and the results were limited out and involved a limited number of patients. We added the sentence in Discussion section (Page 13, lines 10-11). Also, this study is a preliminary study and further studies are being conducted in future prospective studies

Reviewer #2:
Specific Comments to Authors: The authors submit a manuscript describing that serum leucine-rich alpha-2 glycoprotein may be a marker for endoscopic activity of ulcerative

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colitis (UC). The results seem to be good. However, I don't think there's anything unique about these findings, and there's nothing surprising about them for clinicians. I have several comments/suggestions for consideration: 1. In the results, only 30 patients were examined the correlations between clinical, endoscopically assessed, or histological activity and biomarkers in 30 patients. Therefore, why not just list the baseline demographic characteristics of 30 patients. 2. Several papers have reported that the serum levels of LRG are correlated with endoscopically assessed activity in patients with UC. Moreover, the conclusions of this study are consistent with those of previous studies. 3. The quality of English needs improving.

REPLY: Thank you for your comment. We have replaced the data in the original Table 1 with the baseline demographic characteristics of the 30 patients. As the reviewer pointed out, the conclusions of this study are consistent with those of previous studies. Also, we have had the revised manuscript edited by a native English speaker from a professional manuscript editing service.

Reviewer #3:
Specific Comments to Authors: The article has some merits on a relatively new biomarker for disease activity in IBD. The important part of analysis is done on only 30 patients. We are not informed about the extent of the disease in these patients. As the low correlation with proctitis has been reported in past, this could be important in the analysis. There are larger reports prospectively from Japan for instance: https://doi.org/10.3390/jcm11216366 These reports also have introduced cut off levels for this biomarker . This could be a weaker evidence for the use of leucine-rich alpha-2 glycoprotein (LRG) and the cut off here probably would be more close to the larger studies. It would be very informative to know whether there were any patients with

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normal CRP and normal FC with abnormal LRG in whom disease was active and vice versa.

REPLY: Thank you for your comment. The sample size of patients with the proctitis type of ulcerative colitis is small, and the usefulness of LRG as a biomarker in those patients could not be determined. In this study, 5 patients had normal C-reactive protein (CRP) levels and abnormal LRG levels. Two of those 5 patients had Mayo scores of 6 or higher, 3 had Mayo endoscopic subscores (MES) of 2 or higher, and 4 had an ulcerative colitis endoscopic severity index (UCEIS) of 4 or higher. The relationship between LRG and CRP is shown in the table below. LRG is useful in assessing the clinical and endoscopic activity of ulcerative colitis, because clinical and endoscopically active cases with normal CRP levels and abnormal LRG levels are seen. The association between LRG and FC was not examined, and this point was added to the content in the Discussion section. (Page 11, lines 12-13).

	LRG <13.4	LRG ≧13.4
CRP ≦0.3	17	5
CRP > 0.3	0	8

Your kind continued consideration of our paper for publication in ***World Journal of Clinical Cases*** is greatly appreciated.

Sincerely yours,

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