

Peer Review File

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Reviewer Comments

This is a brief study about the usefulness of RDW in celiac disease children patients. I have both minor and major revisions:

Minor revisions:

Comment 1. Page 3, line 89, the CBC abbreviation is not explained when first used.

Reply 1: we have modified our text as advised (see Page 3, line 89)

Comment 2. Page 3, line 97, perhaps the behaviour of RDW in case of iron deficiency anemia could be also explained here.

Reply 2: added comment and reference (see page 3, lines 98-101). Further explained on page 6.

Comment 3. Page 3, lines 102-104, " In a study of adult patients with CD, Brusco et al 8 found RDW to be the most frequent abnormality from a hematologic standpoint (58%) with the next most frequent being anemia (31%) and iron deficiency (29%)." should it be " In a study of adult patients with CD, Brusco et al 8 102 found increased RDW to be the most frequent abnormality from a hematologic standpoint (58%) with the next most frequent being anemia (31%) and iron deficiency (29%)."

Reply 3: we have modified our text as advised (see Page 3, lines 103-105)

Comment 4. Page 4, lines 110-112, " Our study aims to determine if RDW is a reliable marker of compliance in children treated for CD, similar to that of the adult counterpart studies". The authors do not name adult studies where RDW would have been used in determination of compliance here, references needed here, not only in the discussion, where also a more extensive discussion in needed of the references 5, 9 and 10.

Reply 4: added reference to adult studies in which RDW was used to assess response to GFD, (see page 3, lines 108-110)

Comment 5. Page 4, lines 123-125, the abbreviations should be opened.

Reply 5: opened the abbreviations, (see page 4, line 129-130)

Comment 6. It seems like RDW 12.7 is used as a cut-off in the results, maybe this and the RDW reference values should be explained also in the M&M.

Reply 6: added explanation in M&M section, "Exploratory secondary outcomes consisted of analyzing RDW values and determining if a cut-off level led to a significant difference between the presence or absence of atrophy." (See page 5 lines 158-159)

Comment 7. Page 4, lines 128-129, how was the villous atrophy determined and CD diagnosis made (serology and histology)? Did also those without atrophy receive a diagnosis. If so, it should be explained.

Reply 7: added statement to clarify that atrophy and CD diagnosis was made by histology and serology (Page 4, lines 135-136). Also added sentence stating that CD was considered in patients with Marsh 2 (page 4, lines 135-139).

Comment 8. Page 5, lines 160-165, why are both means and medians documented? Maybe rather to determine the skewness of the data and present only other?

Reply 8: This was done to show any skewed data. I have removed median results to ensure no confusion. (See page 5, lines 174-178)

Comment 9. Page 5, lines 169-170, "Mean initial RDW was 13.4 ± 0.93 in patients with atrophy which was slightly higher than patients with no atrophy (13.2 ± 0.80); $p=0.11$." No statistical difference and SDs overlap.

Reply 9: Added clarification statement that RDW in patients with or without atrophy was not found to be statistically different (See page 5, lines 182-184). This was further clarified in our discussion section (see page 6, lines 243-244).

Comment 10. Page 5, lines 175-176, "Further, there was also a statistically significant association among patients having a follow-up RDW >12.9 and presence of atrophy." Should it be "no atrophy at the time of diagnosis" etc?

Reply 10: We have modified our text as advised. (See Page 5, lines 189.)

Comment 11. Page 5, lines 168-183, the sentences could be simplified by deleting the proportional differences and the numbers presented in the Table 2 are unnecessary to be repeated.

Reply 11: Deleted proportional differences and removed excessive data that was already reflected in Table 2. (See page 5, line 186-190)

Comment 12. Page 5, lines 179-180, "Median difference in initial values of tTG-IgA was 83.0 in patients without atrophy and significantly higher in patients with atrophy 129.0. T" Should it be only "Median tTG-Iga" and are units missing? The whole start of the paragraph could be written "There was a significant difference in the tTG-IgA values obtained at the time of diagnosis between patients with and without villous atrophy (129.0 vs 83.0 U/L, $p=0.010$)." Same kind of simplifying is also needed in other paragraphs of the Results.

Reply 12: Rewrote sentence using style recommended. Included units for values. (See page 5 Line 191-194)

Comment 13. Table 1, why are the differences between patients with or without atrophy presented in age, gender, race and weight?

Reply 13: To show that there was not bias in age/gender/race between two groups.

Comment 14. The results of differences between the atrophy and no atrophy groups are not discussed in the Results.

Reply 14: It was discussed but labeled as follow up and not labeled with pre and post GFD. Corrected. (See page 5, lines 186-190)

Comment 15. Page 5-6, lines 187-189, " The relationship with iron deficiency anemia and CD has been well established. It has been shown that patients with CD can present with iron deficiency due to malabsorption, and this improves with proper dietary modification." Indeed, anemia, most of the due iron deficiency is one of the most common extra-intestinal manifestations of CD, but actually the relationship between these entities is rather poorly understood as also patients without villous atrophy present with anemia. Additionally, anemia does not cure in all patients even with more than two years in strict GFD.

Reply 15: Added recommended suggestion that anemia can be present without atrophy and that GFD does not always improve anemia in CD patients (See page 6, lines 262-264).

Comment 16. Page 6, lines 200-202, " While our patient population did demonstrate a clear mean decrease in mean RDW value from diagnosis to follow up on GFD, this was not found to be statistically significant ($p=0.585$). " Was the decrease in fact that clear? Additionally, both of median values were in the references.

Reply 16: Agreed, changed sentence to remove any confusion or misstatements (See page 6, lines 276-277)

Major revisions:

Comment 1. There are a number of sentences in the manuscript that lack references and only 10 are found in the reference list. For example " This may not be accurate given that ferritin may be falsely elevated as it is an inflammatory marker. MCV is also potentially not reliable in CD since this condition can cause anemia of chronic disease. RDW may be a more accurate marker, which is inexpensive and easy to obtain." Each of the sentences could use references.

Reply 1: Added references throughout paper. See reference page.