Author's response to reviews

Title: Factors associated with growth disturbance at celiac disease diagnosis in children: a retrospective cohort study

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Version: 2 Date: 25 August 2015

Author's response to reviews: see over
Dear Editor,
Thank you for the opportunity to revise our manuscript "Factors associated with growth disturbance at celiac disease diagnosis in children: a retrospective cohort study". We have now made changes to the manuscript according to the valuable comments of the reviewers. All changes are highlighted in red and responses to reviewer's comments are shown item by item below. We hope that the revised manuscript would be acceptable to the BMC Gastroenterology.

Yours sincerely,
Kalle Kurppa, corresponding author

Associate editors´ comment:
The Associate Editor himself has no additional suggestion, but an improvement of the English form.

Response: The manuscript has been edited by a native English speaking linguistic (Robert McGilleon, M.A.).

Reviewers’ comments:
Reviewer: Christina Meazza
In this study Nurminen et al. investigated the association of impaired growth with celiac disease (CD) in children. They showed that growth failure in CD children is associated with young age and severe presentation at diagnosis. Furthermore, they demonstrated that CD children who present with sole poor growth are clinically different from children with other symptoms. The study is interesting for paediatricians who usually face with short statured children and the design is commendable.

1) There are many studies about the association of CD and growth hormone deficiency which sometimes is the cause of short stature in these children. Therefore, when a catch-up growth is not shown after at least one year of gluten free diet, an endocrinological evaluation is mandatory. The authors should discuss this issue in the discussion.

Response: We thank the reviewer for this valuable comment and have now further discussed this issue as requested. See Discussion, page 10, paragraph 2, lines 219 – 221.

2) In table 1, patients are grouped according the presence or absence of growth failure at diagnosis. Growth failure patients are 182, but in only 45 data about height are available. How were the authors able to classify patients with growth failure without having height data?
Response: In most cases the presence of growth failure was defined (using nationwide guidelines) already by the physician referring the patient for endoscopic investigations. Next, if there was a clear CD suspicion, the children entered the gastroscopy any many cases without actual height measurement, and the height was measured again only during the first control visit to while already on a GFD. To make the results more comparable, we decided to accept in the Table 1 only measurements made by a pediatrician at the time of endoscopy. Nevertheless, the presence of growth failure was defined equally in all
cases. This issue is now further clarified; See M&M, page 6, paragraph 2, lines 119-120 and Table 1, footnote.

**Reviewer: Bruno Bonaz**

This is an interesting and well done study. I am convinced by the results. I have only minor comments.

1) **In the liver blood samples, it seems that the authors did not evaluate ASAT and ALAT as well as gamma-GT.**

Response: The AFOS value was given in the original text since it is often measured in children with growth problems. We now added also ALT as suggested; see Abstract, page 2, line 24; M&M, page 5, line 99; Table 1 and Results, page 7, lines 142-143. Interestingly, there indeed was a significant difference between the groups in ALT, which is now briefly discussed; see Discussion, page 9, paragraph 1, lines 184-186. In contrast, since AST rarely provides additional information in children if ALT is taken, we do not evaluate it routinely in our clinical practice. Similarly, gamma-GT values were available from too low number of patients for any meaningful statistical analyses.

2) **Page 9, line 197: it’s possible that these adult patients had microscopic colitis which is known to be associated to celiac disease and to induce secretory diarrhea.**

Response: It is true that microscopic colitis is overrepresented in celiac disease, which was not mentioned in the referred paper by Abu Daya and colleagues. This sentence is now reformulated; see Discussion, pages 9-10, lines 202-205.