Format for ANSWERING REVIEWERS

MARCH 31ST, 2015

Dear Editor,

Title: THE EVOLUTION OF NONSPECIFIC DUODENAL LYMPHOCYTOSIS: FACTORS AFFECTING THE OUTCOME OVER 2 YEARS OF FOLLOW-UP

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The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer n.1

1. When you clinically found the evolution of DL (duodenal lymphocytosis), how did you exclude other diseases?

In the "Materials and methods" section, we have clearly stated the diagnostic process by which other diseases were excluded. All subjects underwent serology for celiac disease, full blood count, folate, vitamin B12, serum protein electrophoresis with immunoglobulin subclasses and HLA genotyping, anti-thyroid antibodies and thyroid hormones (TSH, fT3 and fT4). Stool samples were used to detect intestinal infection and parasitic diseases (in particular Giardia lamblia), and to assess fecal occult blood FOBT and fecal calprotectin. For h. pylori, urea breath test and stool antigen test and, in case of positivity, a further endoscopic and histological examination of four biopsy samples, taken two from the body and two from the antrum. Glucose and lactose breath tests were carried out to exclude respectively SIBO and hypolactasia. Finally, wheat allergy was tested by skin-prick test and Radio Allergo Sorbent Test (RAST).

The repetition at 6 months intervals of such tests assured the exclusion of other diseases.

2. In Table1, 1) Did nobody develop overlapping diseases other than the diagnosed disease? 2) Were not there any patients who developed the diseases listed in the Table? 3) You should add the statistics processing.

Nobody developed overlapping diseases. None of the patients developed diseases other than those listed in the table. An additional column was added in the table, reporting p values.

3. You should create a diagram of the 85 patients reflecting the diagnosis and the diagnosed time after the initial DL evolution, for the purpose of clarifying a contribution of the 2-year follow up results.

An additional figure (Fig. 2) was enclosed in the revised manuscript with the purpose of illustrating diagnosis time after the initial DL evolution

4. Details of Table2 have not been described in the manuscript.

Table 2 has been better detailed in the body of revised manuscript.

5. The last paragraph of RESULTS, an additional table of univariate and multivariate analysis should be necessary.

We perfectly agree that a table summarizing univariate and multivariate analysis would make the paper more appealing. Therefore, in the revised manuscript, a further table (Tab. 3) has been enclosed with this purpose.

Reviewer n.2

A study concerning the evolution of non-specific duodenal lymphocytosis in 2-year follow up period is a difficult task to accomplish. The authors did tell us that follow up patients of DL with IELs in addition to other diagnostic tests or factors can differentiate the CD, GS or non-gluten-related disorders somehow. Though the study results are not definite, they are informative. The article is worth of reading for gastroenterogists.

We thank the reviewer for the gratifying comments.

Reviewer n.3

his paper investigates an intriguing field of gastrointestinal pathology, which is constituted by gluten-related conditions. Duodenal lymphocytosis (DL) is a variegate condition, enclosing disorders related and unrelated to gluten assumption. The possible evolution of DL into celiac disease may be secondary to genetic and histopathological factors. However, the best management of DL remains a watchful waiting with targeted examinations. There is little revision in the abstract, "At multivariate analysis, the evolution towards CD was associated to IELs infiltrate >25 (OR=1640.4) and 15-25 (OR=16.95), HLA DQ2/8 (OR=140.85) and DQA1*0501 (OR=15.36), diarrhea (OR=5.56) and weakness (OR=11.57)". What does "HLA DQ2/8 and DQA1*0501"mean? This is the abbreviations, what is the full spelling?

The term HLA means "Human leukocyte antigen", and it defines the locus of genes that encode for proteins on the surface of cells that are responsible for regulation of the immune system in humans. DQ2, DQ8 and DQA1*0501 are different HLA alleles, but they do not represent abbreviations.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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