Author's response to reviews

Title: The Frequency Of Microscopic And Focal Active Colitis In Patients With Irritable Bowel Syndrome

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We would like to thank very much the reviewers for their contributions. Our responses to the reviewer’s comments are as follows

**Author responses to reviewer’s comments**

Reviewer: Darren Brenner

1. The study is a prospective study, this information has been provided in the first sentence of the material and methods section of the revised manuscript. were recruited into the study.

2. We appreciate for your attention about the diagnosis criteria. At the beginning of the study, Rome II criteria was determined for diagnosis of IBS and IBS subgroups in 2007. We reassessed the patients for IBS and IBS subgroups according to Rome III criteria in concordance with the reviewer’s suggestion. There was no change in patient and control groups as well as IBS subgroups after reassessment.

3. We agree with the reviewer regarding. Our control group naturally consisted of patients who were screened for colorectal cancer above 50 years old. As the reviewer has stated, this may cause a difficulty in comparing our IBS data. Nevertheless, mean age for patients with IBS with MC was 60.57 as demonstrated in Table 4 in revised manuscript and MC was not reported in any patients in the age matched control group.

4. The factors associated with MC such as history of persistent use of medications and tobacco use were investigated and stated in the second paragraph of the material and methods section of the revised manuscript.

5. As the reviewer has stated, FAC can be diagnosed in patients with infections, ischemia, Crohn’s disease, partially treated ulcerative colitis and IBS. However, our study group was compared of patients without any macroscopic colonoscopy findings. As demonstrated in accordance with the reviewer’s request distribution of IBS subgroups with respect to MC and FAC diagnosis have been presented in Table 4.

6. Available tests in our center for celiac assessment are anti endomisium antibody and antigliadin antibody. Upper GI endoscopy was applied to all patients for excluding Celiac disease and other upper GI disorders and biopsies were taken if necessary. The sentence ‘All patients were examined using microscopic evaluation of the stool, a stool occult blood test, digestive stool
analysis, hemogram, erythrocyte sedimentation rate, blood glucose, urea, creatinine, liver tests, thyroid hormones (free T4, TSH), anti-endomisium IgG and antigliadin IgA antibodies, abdominal ultrasonography, upper gastrointestinal endoscopy and colonoscopy.” was changed as ‘All patients were examined using microscopic evaluation of the stool, a stool occult blood test, digestive stool analysis, hemogram, erythrocyte sedimentation rate, blood glucose, urea, creatinine, liver tests, thyroid hormones (free T4, TSH), anti-endomisium IgG and anti-gliadin IgA antibodies with upper gastrointestinal endoscopy (for excluding Celiac disease and other upper GIS disorders), abdominal ultrasonography and colonoscopy.’

7. The female ratio of IBS population was 55% in this study. To show gender distribution of IBS patients in Turkey, we added female ratio of two large series of IBS patients from Turkey as presented reference 2 and 3. ‘The prevalence of IBS in studies from Turkey is 7.4-19.1%.’ sentences were changed as ‘The prevalence of IBS was found 7.4-19.1% with female percentage between 64% and 69%.’.

8. Histological definition for FAC is added to the last sentence of the third paragraph pf the material and methods section as ‘Focal active colitis (FAC) is the term used to describe focal neutrophilic infiltration of colonic crypts. It may consist of one focus in a single biopsy, or multiple foci’, in accordance with reference number 19.

9. In IBS patients, lymphocytic colitis differed between non-constipated(IBS-M and IBS-D) and constipated (IBS-C) subgroups. The sentence ‘However, lymphocytic colitis differed among the IBS subtypes (p <0.01).’ changed to ‘However, lymphocytic colitis differed between non-constipated IBS group (IBS-D and IBS-M) and constipated IBS patients (p <0.01).’.

10. Citation of the second sentence in discussion section was added.

11. In discussion section, the prevalence of MC was higher at the study by Tuncer from our finding and findings from other MC prevalence studies. However, the study of Tuncer et al was consisted of 30 patients diagnosed with IBS solely on symptoms. However, our study group was selected after clinical and endoscopic assessment. The incidence of MC found in our study is consistent with other large series(Reference 27 and 28).

12. The limitations of the study were added as the last paragraph of discussion.
13. In children with focal active colitis, development of Crohn disease is higher percentage than in healthy population. In adult patients, prognosis of FAC is not known. It is important to follow adult patients which their symptoms were consistent with FAC and to apply colonoscopy and biopsy for the development of FAC.

15. Alarm features were determined according to the article of Olden (Reference 25). We aimed to exclude patients which has clinical symptoms and signs suggestive organic disorder.

16. In text, ‘Roma II’ was changed to ‘Rome II’.

17. The sentence starting with ‘MC’ was corrected as ‘Microscopic colitis’.

18. In conclusion, ‘It may be reasonable’ changed to ‘It appears reasonable’.

19. In Table II and III and Figure I, ‘lymphositic’ was corrected as ‘lymphocytic’.

20. As demonstrated in Table 4, the mean age for women with MC was 60.54 years.

21. In the first sentence of background section, ‘disease’ changed to ‘disorder’.

22. We removed the sentence starting with collagenous colitis in the second paragraph of background section.

23. The paragraph in results section starting with ‘The control subjects did not have...’ was removed.

24. In results section, the sentence starting with ‘However, lymphocytic colitis differed...’ was placed before the paragraph starting with ‘Focal active colitis was found...’.
Reviewer: Joel H Rubenstein

1. The ages of MC patients were between 49 and 75. Table about demographic characteristics of patients with MC and with FAC was added to the to the new manuscript as Table 4. In text and Table I, age greater than 50 suggests an organic disorder rather than IBS. However, it is unlikely that IBS isn’t seen greater than age 50. We recruited patients with age between 16 and 84 years.

2. Terminal ileum was intubated in all patients. It is added to the end of material and methods section.

3. As the reviewer has stated, the control group composed of all consecutive patients screened for colorectal cancer and anemia during the study period. Central cases with macroscopic pathology were excluded.

4. There was no patients with collagenous colitis. Only seven patients were found to have lymphocytic colitis. Some authors suggest that lymphocytic colitis is an early phase of collagenous colitis, as mentioned in paper.

5. The classification of Groups I, II and III changed to IBS-C, IBS-D and IBS-M.

6. In the first paragraph of results section, the sentence ‘There was a statistically significant difference in the age distributions of the IBS and control groups (P<0.01).’ show that two groups wasn’t identical for age and gender.

8. Reference numbers for the articles by Kao and Chey in discussion section was added.

9. In discussion section, ‘incidence’ chaned to ‘prevalence’.

10. In discussion section, ‘American’ was added to ‘Collage of Gastroenterology’.

11. In Table II and III and Figure I, ‘lymphositic’ was corrected as ‘lymphocytic’.
12. Figure I and II removed from the paper. Because tables were sufficient to show the data for groups and IBS subgroups.