

ANSWERING REVIEWERS

September 12, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 4758-Review.doc).

Title: Seasonal variations in the onset of ulcerative colitis in Japan

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

We find the comments of the reviewers to be useful and agree that the suggested changes will substantially improve our manuscript.

Reviewer # 1 Major revise

This is a report about seasonal onset and relapse of ulcerative colitis (UC) in a Japanese cohort. I have some comments to the present manuscript version, which needs to be revised.

Major comments:

1. The authors should specify how their material was collected. Was it a single centre experience (an epidemiological cohort from a well-defined region – or was it collected at a tertiary centre with patients referred from various other hospitals).

(Response) Japanese patients diagnosed with UC in an academic hospital between January 2003 and December 2006 were enrolled. As suggested, we mentioned this issue in Abstract and Materials and Methods.

2. The very strange finding is that UC is considered as having an equal sex distribution, however, in the present material 66% were males (132/198). Please make a comment on this matter.

(Response) As suggested, we mentioned this in Discussions as below.

For UC, a growing number of studies in Asia have shown an equal gender distribution^[12]. There are also several studies demonstrating male predominance^[13]. In our academic hospital-based cross sectional study, there is a preponderance of UC in men. This conflicting data may, at least in part, reflect the small population numbers of the study populations.

3. A flow chart needs to be included for the reader to understand the number of patients in the material (i.e. included or under surveillance). Thus, in Materials & Methods the figures of 198

patients (onset) and 165 (relapse) is mentioned, but in the Results suddenly the number of 265 is stated. This matter also needs further clarification.

(Response) Among 265 Japanese patients with UC observed more than 12 months between 1994 and 2006, 165 patients were relapsed (239 times). We mentioned this issue in Abstract and Materials and Methods and made added a flow chart.

4. The authors should observe, that cigarette smoking DO NOT enhance the onset of UC, which is actually in contradiction to Crohn's disease. Normally patients with UC get an exacerbation when they try to quit smoking. Could it be due to a type-II error, that the conclusion is rather vague (i.e. the material is too small for any valid statistical conclusion)?

(Response)

As suggestions, we discussed this issue and added references in Conclusions as below.

In this study, cigarette smoking does not enhance the onset of UC, which is actually in contradiction to Crohn's disease^[26]. Normally, patients with UC get an exacerbation when they try to quit smoking^[26].

We also mentioned that the material is too small for any valid statistical conclusion in Discussion as below.

The present study is an epidemiological cohort study from an academic hospital in Tokyo and the material is too small for any valid statistical conclusion. Therefore, future studies are needed in Japanese populations using large materials to assess the seasonal variations on the onset and relapse.

Minor comments:

1. Key words should be listed alphabetically.

(Response) As suggested, we corrected it.

2. In Figure Legends, I am in doubt about the word "respectively" in Fig. 1. Further, words are missing in last sentences of Fig. 1 + 2 + 4 (i.e. Fig. 2: population were found both seasonal basis is simply nonsense)!

(Response) As suggested, we corrected it.

3. The references are not listed in accordance with Instructions for Authors of this journal.

(Response) As suggested, we corrected it.

Reviewer #2 Major revise

"Seasonal variations in the onset of ulcerative colitis in Japan" There are many studies published in the previous 40 years providing substantial evidence about the onset of inflammatory bowel disease and the relationship between disease exacerbations and seasonal variations. Therefore a significant contribution to the literature may only be achieved by a better designed study including much more patients. In epidemiological studies, the most important thing to provide significant information is the number of patients included in the cohort. In the present study, the number of patients included is not sufficient to draw conclusions.

(Response) As reviews comments, patient number in this study is small to evaluate conclusions. We mentioned this points in Discussions as below.

The present study is an epidemiological cohort study from an academic hospital in Tokyo and the material is too small for any valid statistical conclusion. Therefore, future studies are needed in Japanese populations using large materials to assess the seasonal variations on the onset and relapse.

Reviewer #3 Accept

The authors have examined seasonal variation in UC incidence in the Japanese population and shown statistically significant differences. This work supports similar observations in western populations. The paper is very well written and the statistical analysis is appropriate. The general presentation, tables and referencing are good. The conclusions drawn are appropriate.

Our manuscript was edited and formatted for *World Journal of Gastroenterology* type by American Journal Experts: <http://www.journalexperts.com>.

We are enclosing the entire revised manuscript and Figures. The underline in the manuscript indicates the changes.

We do appreciate the time and effort that the reviewers have put into helping us with this manuscript and we hope that it is now suitable for publication in *World Journal of Gastroenterology*.

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

Sincerely yours,



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