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## ANSWERING REVIEWERS



April 20, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9756-review.doc).

**Title: Similar Clinical Characteristics of Familial and Sporadic Inflammatory Bowel Disease**

**Author:** Sook Hee Chung, Soo Jung Park, Hye Sun Lee, Jae Hee Cheon, Sung Pil Hong, Tae Il Kim, and Won Ho Kim

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 9756

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 #1.

1) comment 1. modify a bit the conclusions since you did observe some differences

Answer: We modified the conclusions at page 2, line 18 and page 8, line 10 and mark it with yellow bar like this: "In conclusion, a family history of IBD does not seem to be an important predictive factor affecting clinical characteristics or disease course even if there is a more frequent use of anti-TNF antibodies in familial CD patients compared to sporadic CD patients."

2) comment 2. In the title you might want to add may be "in Korea"?

Answer: We added the “ in Korea” in title and marked it with yellow bar.

3) comment 3. You should address the different follow-up time in the 2 groups

Answer: We address the different follow-up time in the 2 groups at page 6, line 5 and mark it with yellow bar like this:”Median (min-max) follow-up duration in familial and sporadic CD patients was 84 (24-312) and 36 (8-240) months, respectively ( $P=0.008$ ). Median (min-max) follow-up duration in familial and sporadic UC patients was 96 (12-240) and 60 (12-85) months, respectively ( $P = 0.170$ )”.

4) comment 4. discuss more the prevalence of IBD in FDR in Korea as opposed to western countries

Answer: We stated the prevalence of IBD in FDR in Korea as opposed to western countries at introduction part, page 3 line 17 and mark it with yellow bar like this :”In the first-degree relatives of patients with IBD of Korean and western countries, the rates of familial IBD was reported to be 1.88 % (Korea) and 5-18 % (western countries)<sup>[1-8]</sup>”

5) comment 5. English needs to be improved

Answer: We revised our manuscript through English editing services by a native American.

Reviewer #2.

1) comment: Abstract - be clear that cases are those that have a family history.

Be clear if this is first-degree relatives.

Answer: We inserted this sentence in Abstract part at page 2 line 5 and method part at page 4 line 7

and mark it with yellow bar like this: “Seventeen patients (2.5%) with CD and 27 patients (2.4%) with UC were identified as having a familial history of IBD including the first and second degree relatives.”

2) comment: intro - some more detail on past studies of IBD outcomes and family history

Answer: We stated more about past studies of IBD outcomes and family history in introduction part at page 3 line 16 and mark it with yellow bar like this.

A family history of IBD was shown to increase the risk of developing IBD 10- to 15-fold in unaffected first-degree relatives and three-fold among close relatives of IBD patients<sup>[9-11]</sup>. In first degree relatives of patients with IBD of Korea and western countries, the rates of familial IBD was reported as 1.88 % (Korea) and 5-18 % (western countries)<sup>[1-8]</sup>. Even if genetic factors are associated with familial IBD,<sup>[12]</sup> a family history of IBD does not mean that all patients IBD share a specific gene, as family members of IBD patients could be exposed to similar environmental factors<sup>[13]</sup>. Some studies showed that there were no differences in clinical characteristics between familial and sporadic IBD<sup>[14,15]</sup>. Even if other studies demonstrated differences between familial and sporadic IBD, there have not been consistent results<sup>[16-18]</sup>. Despite several studies of familial IBD, there is still insufficient knowledge regarding the differing characteristics between familial and sporadic IBD.

3) comment 3.: Methods: - need to be very clear who controls are = is this first degree relative or any relative? if FH documented for all patients?

-Answer: In the introduction part at page 2, line 7 and method part at page 4, line 9 we clarified the “control case” and mark it with yellow bar like this: “For each control case, three times the number of age-, sex-, and diagnosis year-matched CD and UC patients without family history of IBD patients were randomly selected in this case control study.”

4) comment 4: as this is retrospective, you need to be very clear how the mayo index and cdai were calculated. If these are collected in all patients prospectively, it should be stated. Otherwise, retrospective CDAI and mayo has not been studied.

Answer: Despite the nature of retrospective study, there were data about CDAI and partial Mayo score of every IBD patient in our clinic using well-organized electronic medical database from every visit of clinic since 2005. Therefore we had a data about activity index (CDAI and Mayo score) of IBD patients at every visit. In addition, we had IBD cohort system in our hospital and specialized nurse for IBD patients. They works for measuring disease activity of IBD and taking history of IBD patients at every visit of patients.

We inserted this sentence at page 4 line 20 to to be clear how the mayo index and cdai were calculated and mark it with yellow line like this:” Mayo index and CDAI at diagnosis were calculated at the time of initial diagnosis at the hospital.”

5) Comment 5: Better definition for relapse would be needed for change in medical therapy.

Answer: We added the definition for relapse in the method at page 5, line 14 and mark it like this.:

Additionally, change of therapies because of clinical aggravation was included in criteria of relapse of IBD<sup>[19]</sup>.

6) Comment 6: Why mention of Behçet's?

Answer: Our hospital is the biggest center for treating patients with Behçet's disease and frequently published the data about Behçet's disease compared with IBD<sup>[20-26]</sup>. In fact, intestinal Behçet's disease should be differentiated with Crohn's disease because of similar lesions of the colon. Even if Behçet's disease and Crohn's disease are different, the therapy of them is similar in the meaning of controlling inflammation of the colon. Therefore, intestinal Behçet's disease was a kind of inflammatory disease of the colon in a broad sense. That is the reason why we mention the Behçet's disease in this study. In our study, we confirm the presence of Behçet's disease in the family of IBD patients.

7) Comment 7: Results section should be shortened if all the details are in the tables.

Answer:

Answer: We shortened the result by deleting the sentence that explains the details in table 2.

We also mention the most important summary in the result part.



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Sincerely yours,

Park

Soo Jung Park, MD, PhD, Professor of Department of Internal Medicine and Institute of Gastroenterology, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea

Tel.: +82-2-2228-1963

Fax: +82-2-365-2125

E-mail: [sjpark@yuhs.ac](mailto:sjpark@yuhs.ac)

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