Author's response to reviews

Title: Low prevalence of 'classical' microscopic colitis but evidence of microscopic inflammation in Asian patients with diarrhoea predominant irritable bowel syndrome

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Author's response to reviews:

Dear esteemed editor and reviewers,

Thank you very much for reviewing our paper. We have tried to answer all the queries and suggestions as outlined below and sincerely hope that you will consider accepting our paper for publication.

Yours sincerely,
Ida Hilmi
Editor

1. Post infectious IBS (PI-IBS) is mentioned in the abstract but not in the paper. Please assure consistency between the abstract and the paper.
   - Were patients with PI-IBS included?
   - If PI-IBS patients were included, what was the prevalence of inflammation in this group?

   PI-IBS was only mentioned as an introduction only as the two most commonly studied IBS groups were PI-IBS and IBS-D. Our patients did not include PI-IBS.

2. What was the prevalence of inflammation in patients with diverticular disease?
   There was no evidence of diverticulitis on colonoscopy in any of the patients. The biopsies were taken away from the diverticulae in the patients who had limited diverticular disease.

3. How were gastro-intestinal infections excluded? Patients with gi-infections might have inflammation in the mucosa and symptoms of IBS-D. Was stool screened for pathogens?

   One set of stool specimens were sent for culture and microscopy

Reviewer 1
1. The title refers to 'classical' microscopic colitis and the authors state that this was >20 IELs/100 epithelial cells "in conjunction with surface epithelial damage". Please give a reference to these criteria for 'classical' microscopic colitis. Reference has been inserted.

2. The patient studied a consecutive series of patients who met the Rome-III criteria for IBS-D but little or nothing is mentioned about selection factors for this population. Had these patients been investigated at primary care level before being referred? How many had undergone colonoscopy before coming to UMMC? If none had had a colonoscopy before, this is vital information that should be included in the manuscript. If a proportion of the patients had undergone colonoscopy with biopsy before it may become necessary to divide them into colonoscopy-naïve and previously endoscoped patients. All patients were referred from primary care and were colonoscopy naïve.

3. In the discussion the authors discuss their findings in relation to those reported by Falodia et al. According to the latter classification 12/74 patients in the present study had microscopic colitis. This is somewhat confusing and I find it difficult to make up my mind whether microscopic colitis was present or not in a significant proportion of Malaysian patients with IBS-D. We agree that sentence is confusing. The Falodia paper suggested that there were many other categories of microscopic colitis so if we were to accept this, then any microscopic inflammation is considered microscopic colitis. However, it is not generally accepted and we have modified that section accordingly.

4. The sentence "Three cases had involvement of the rectum, four cases had involvement of the sigmoid or descending colon but in four cases inflammation was seen only distal to the splenic flexure only" is difficult to understand. First, there is more words only than needed, and secondly, I think it should be "proximal" rather than "distal". Yes, we apologise for that error and the whole section has been modified accordingly.

Reviewer 2

1. There are a few major issues with this article. Firstly the authors say that one of the objectives of the study is to find the prevalence of microscopic colitis in IBS-D patients. This is not possible in a single centre study. We agree that is a limitation of the study.

2. The fact that non specific colitis is present in IBS-D is not new. De Silva et al
Scand J Gastroenterol. 2012;47:619-24, described this and have included cytokine data as well. Strangely this paper is not even referenced although it is methodologically a similar study. Thank you for highlighting this, the study has been included in our discussion accordingly.

3. Diverticulitis is also a cause of inflammation and the authors need to mention that.

There was no clinical and macroscopic evidence of diverticulitis in any of the patients. The biopsies were taken away from the diverticulae in the patients who had limited diverticular disease.