Round-1:

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 59830

Title: PREVALENCE AND ASSOCIATED FACTORS OF OBESITY IN INFLAMMATORY BOWEL DISEASE: A CASE-CONTROL STUDY

Reviewer's code:02457753

Position: Peer Reviewer

Academic degree:

Professional title:

Reviewer's Country/Territory: Canada

Author's Country/Territory: Italy

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-09-30 17:18

Reviewer performed review: 2020-10-09 16:09

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Scientific quality	[] Grade A: Excellent[Y] Grade B: Verygood[] Grade C: Good [] Grade D: Fair[] Grade E: Do not publish
Language quality	[] Grade A: Prioritypublishing[Y] Grade B: Minor languagepolishing[] Grade C: A great deal of language polishing[] Grade D: Rejection
Conclusion	[] Accept (High priority)[] Accept(General priority) []Minor revision[Y]Major revision[] Rejection
Re-review	[Y] Yes [] No

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Peer-reviewer statements	Peer-Review:[Y]Anonymous[] Onymous
	Conflicts-of-Interest:[]Yes[Y] No

SPECIFIC COMMENTS TO AUTHORS

The paper by Losurdo G et al. (ID03713791) is a cross sectional evaluation of 807 cases of IBD and 378 patients with functional gastrointestinal disorders followed in a hospital gastroenterology clinic. The purpose is to compare frequency and any clinical differences between Obese among IBD and Control groups. The main findings according to the authors, suggest mostly little differences clinically or frequency among IBD patients and Controls. Some differences relate to age of onset of obesity in IBD and Controls and more abdominal girth increase in IBD over controls. In addition there are some more co-morbidities noted in patients with obesity and IBD.

Comments: The study is of interest. As the authors point out there is a potential relationship between the pandemic of obesity and extension of IBD into previously low incidence regions of the world. Some of the literature reported findings are controversial. Some contrasting papers could be added to focus on controversies. Overall the paper needs some additional details and some discrepancies need to be clarified.

Abstract: there are some facts need to be clarified in the result section; re more frequent co-morbidities in IBD obese,

In the Abstract of revised manuscript, the different prevalence of comorbidities in obese subjects was enclosed.

the figure 1 needs to reflect the statements here as well as in the "results" section (see below).

Figure 1 (now figure 2) has been re-drawn according to the comments of the reviewer.

Methods: It would be relevant to include a time frame for recruitment of study participants.

The recruiting time was the period October 2016–October 2017, as reported in revised paper.

No mention of endoscopic and imaging modalities of IBD diagnoses are given. In how many cases was IBD corroborated by endoscopy or Imagery (eg CT or MR enterography)?

As reported in revised manuscript, the diagnosis was achieved by a combination of endoscopy, histology (in all cases) and, for all CD patients, a transmural evaluation by MR enterography.

Since controls were made up of patients with Functional Gastrointestinal Disorders (eg unclear how many IBS-diarrhea, mixed or constipation patients were included). The use of clinical monitoring of IBD alone may symptomatically overlap with those of the control group. Please comment.

The clinical monitoring, performed by partial Mayo or HBI, was applied only for IBD patients. Subjects with Functional Gastrointestinal Disorders constituted only a control group in which the same indexes were not used nor compared with the IBD group. On the other hand, the above mentioned scores may be applied only to IBD patients (Mayo score for UC and HBI for CD, respectively). Therefore we believe that no overlap may exist between IBD and control groups.

Similarly a statement on how steatosis was diagnosed in the IBD and Control group (ie Abdominal Ultrasound, MRI or/and elastography) I think should be stated. Did all patients and controls undergo tests for steatosis?

Steatosis was diagnosed by abdominal ultrasound, according to known criteria and already described in a previous experience (reference n. 12-13). Controls underwent only anthropometric and clinical history assessment, because all examinations that have been performed for IBD are not indicated nor refunded by Italian Health Service.

Results: The length of time patients with IBD had disease could be stated more

emphatically. For instance the difference between the mean age at the time of study of about 46 and the age of onset of IBD was about 20 years. So are we to conclude that patients had their disease for about 26 years? Was there any difference in age of onset and duration between CD and UC patients?

We agree with the comment of the reviewer. The mean duration of IBD disease was about 20 years, and this is a datum that has been considered in multivariate analysis, despite it was not statistically associated with obesity. On the other hand we did not find any difference of age onset between UC and CD (19.8±6.8 versus 20.4±6.2. p=0.19).

Last paragraph of Results: "Obese IBD patients suffered more frequently….." The results of statistical significance of frequency of co–morbidities in Obese IBD patients is not emphasized in Fig 1 e and f . Significance bars above the graphs should be included like Fig 1g. Also what do the authors think about these frequency differences in "younger Obese IBD " than in obese controls who are older?

We are sorry for the inconvenience. We have added all p values in figure 1 (now figure 2). Regarding the fact that obese IBD were younger, our thoughts were reflected in the discussion as follows "obese IBD subjects are younger than control counterpart, and this could be explained by the fact that, during the long term history of the disease, some factors such as steroid assumption could have favored weight gain. However, only at univariate analysis, steroid use was a predictor of obesity in IBD".

Perhaps a similar figure plot for steatosis in Figure 1;

We added figure 2h reporting steatosis differences between the two groups (p=0.49).

Obese IBD and Obese Controls could be included to emphasize the differences in co-morbidities between Obese IBD and Obese control. There is another discrepancy between statements made in the results. In the First paragraph, sentence starting with "Another features…… less frequently a large abdominal circumference.. ". Also noted in Figure 1g. The figure shows >80 % Circumference in obese IBD vs 40% obese controls

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p<0.001. Then in the Discussion first paragraph and explanation is given why there is less large abdominal circumference in IBD. This is confusing and the true result should be verified and corrected.

We are sorry for the misunderstanding. The incongruity found by the reviewer may be linked to the fact that the comparison in figures 1g (now figure 2g) refers to obese IBD versus obese controls, and not all IBD patients versus all controls (this analysis is reported in table 2). We have checked and confirmed the results. Additionally, we added in the cited paragraph this sentence "Unfortunately, we did not take other anthropometric measurements, therefore we were unable to confirm this hypothesis."

Was there any available information on the number of relapses patients with and without obesity suffered in the previous few years before inclusion into the study? Also was there any differences in relapse rates between CD and UC patients ? (this topic was touched upon as a limitation in the paragraph starting with "Furthermore….."). However, perhaps some more details could be given: like was there any differences in relapse rates between Obese IBD and non Obese IBD prior to the time of study inclusion (if data available).

Unfortunately, the number of relapses occurred during the clinical history of patients was not collected from medical records. We acknowledge that this may be a limitation and we emphasized this concept in the dedicated Discussion paragraph.

In Table 2 Abdominal girth frequency between IBD and controls is not shown to be significant. Yet in the Figure 1g there is a significant difference in frequency of abdominal girth between obese IBD and obese controls.

Table 2 reports the comparison between all IBD and all controls, while in figure 1g (now figure 2g) the comparison is between obese IBD and obese controls. Therefore there is no discrepancy, the results are simply different because the comparisons are different.

Please explain further the meaning of no significant difference between IBD and controls

in Table 2, this is somewhat confusing.

In table 2 we showed that IBD and controls were homogeneous for age, sex, BMI, obesity, diabetes and abdominal circumference, while more smokers and more subjects with hypertension were observed among controls.

The word " assumption" in all relevant places should be replaced by "consumption"

We performed the requested change.

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SPECIFIC COMMENTS TO AUTHORS

The manuscript by Losurdo etc sought to investigate the prevalence of obesity in IBD patients and associate possible factors with IBD condition. They analyzed the data collected from 807 IBD patients and age and sex-matched 378 controls. They concluded that obese IBD patients seem to have features similar to general obese population, and there is no disease-specific factor (disease activity, extension or therapy) that may foster obesity in IBD.

Critics:-It would be very helpful if the authors could include a flowchart illustrating the process of selection of patients and controls.-

In the revised manuscript, we enclosed a figure reporting the process of patients selection (Figure 1).

On page 4, METHODS, "Patients", 1st paragraph, "who refused to participate to the study" – should be "participate in".-

Thank you for your suggestion. We performed the requested change.

On page 6, DISCUSSION, "A Scottish study based on a population of 489 IBD patients showed that the 18% of patients had the features of obesity …; obese patients with CD were the 18%, while obese patients with UC were the 17.5%" – please remove "the" before the percentage (such as the 18%, the 17.5%).-

Thank you for your suggestion. We performed the requested change.

On page 6, DISCUSSION, "some factors such as steroid assumption could have favored weight gain" – should be "steroid consumption".

Thank you for your suggestion. We performed the requested change.

Round-2:

The revised paper clarifies questions raised previously. Please change `assumption in the middle of results in the abstract on pg 2 and on pg 6, 2nd paragraph on the page, 4th

line from the bottom of the paragraph.

Sir Editor, In the second version of the revised manuscript, I have replaced as suggested by one of the reviewers "assume" with "consume". Alla changes have been performed in blue font. You will find in attachment the final version of the manuscript.

Best regards

dr. G. Losurdo