

Dear editor,

We thank the reviewer for their positive comments on the paper. We have modified the manuscript as per reviewer's suggestions and have highlighted the changes in the manuscript. Kindly find the revised manuscript with changes highlighted.

Reviewer 1

The authors of "Differentiating Crohn's disease from intestinal tuberculosis" present the problem of differential diagnosis between Crohn's disease and intestinal tuberculosis. This topic is very important due to the increase in the incidence of tuberculosis, and consequently the increase in the frequency of diagnosing intestinal tuberculosis. Diagnosis of this disease is difficult due to the similarity of clinical symptoms occurring in Crohn's disease and intestinal tuberculosis. The authors of the article present very precisely, in detail the diagnosis of these two diseases, pointing to similarities and differences. In separate sections on individual diagnostic methods: clinical, endoscopic, pathologic, microbiological, radiologic, and serologic parameters, they discuss similar and different features for these diseases. Differential diagnosis is difficult and there is no golden diagnostic standard. The authors point out that in a patient who is unable to explicitly exclude the background of tuberculous enteritis, the optimal solution is the introduction of anti-tubercular therapy. However, anti-cancer therapy is associated with hepatotoxic risk and is the main cause of delay in CD diagnosis and is associated with an increased risk of long-term Crohn's disease complications. Therefore, one should still look for research and create diagrams of differential diagnosis of Crohn's disease and intestinal tuberculosis. In my opinion, the work is very well prepared, discusses a very important clinical problem.

Reply: We thank the reviewer for their positive comment.

Reviewer 2

The article addresses an issue of broad interest, with regard to the assessment of patients with inflammatory intestinal affection: differential diagnosis of Chron's disease vs intestinal tuberculosis. The issue has been a hot topic for several years, yet still leaving room to controversies and missing pieces of the puzzle. In the introduction it is very clearly explained the context that defines the importance of research in this area: the poor sensitivity of tests for diagnosis of ITB and the rise of IBD in TB endemic areas over recent years render the differential diagnosis more difficult. Moreover, the consequences of a possible misdiagnosis can be disastrous, especially in patients with underlying ITB treated with immunosuppressant therapy for suspected IBD. The article is well structured in chapters that cover all the main points of the diagnostic management (clinical examination, biology, radiology, endoscopy and pathology). Each chapter contains a comprehensive enumeration of significant features that might lean towards one direction or another, following a pattern that necessarily includes the sensibility of the examination, its strengths and weaknesses, everything supported by data thoroughly collected from literature. This type of pattern emphasizes the points of most interest and makes the lecture more fluent and easier to read. In order to provide a clear and concise overview, every examination and significant feature is listed in tables with according prevalence in patients with Chron's vs ITB as they appear in several studies. The bibliography is quite impressive; the number of citations reaches 75 for a content of no more than 15 pages. Obviously, the authors made a full literature review before writing the paper, carefully documenting all the details. The citations are up to date, some of them being published in the current year. Considering language accuracy, some adjustments should be done before publishing.

Here are some examples that need to be revised: for example page 4 clinical features: Instead "The clinical features of both disorders include pain abdomen" "The clinical features of both disorders include abdominal pain" Instead of "Both the disorders" "Both disorders" This paragraph: In a recent meta-analysis of 10 studies including 692 patients (316 ITB, 376 CD) caseating necrosis, confluent granulomas, and ulcers lined by epithelioid histiocytes were the most accurate features in differentiating ITB from CD,

with a pooled specificity, sensitivity and area under curve (AUC) of 21%, 100%, 0.99; 38%, 99%, 0.94; and 41%, 95% and 0.90 respectively[35]. Should be changed to: In a recent meta-analysis of 10 studies including 692 patients (316 ITB, 376 CD) caseating necrosis, confluent granulomas, and ulcers lined by epithelioid histiocytes were the most accurate features in differentiating ITB from CD, with a pooled sensitivity , specificity, and area under curve (AUC) of 21%, 100%, 0.99; 38%, 99%, 0.94; and 41%, 95% and 0.90 respectively[35]. . There are some words with no space in between that are easy to find and correct. In conclusion, the article approaches a significant topic of broad interest, providing a brief, yet well documented overview of all the available methods that can be useful in solving the eternal challenge of diagnosing ITB. The experience of the clinic that is located in an area endemic for TB proved to be useful in selecting relevant and practical information. I therefore recommend that the article should be published after revising very few language errors.

Reply: We thank the reviewer for their positive comments, and on pointing out the errors. We are sorry for the language errors and have rectified the same (page 5-line 8 from below; page 6-line 5 from above; page 7-line 9 from below).

Reviewer 3

This is a comprehensive review regarding clues to differential diagnosis between Intestinal tuberculosis and Crohn's disease. though very thorough and covers all aspects from symptoms through endoscopy, lab; radiology, histology etc., unfortunately the summary is disappointing with very few rather rare parameters that are exclusive for either disease. minor remark -the tables can be turned into be somewhat more attractive , or into figures.

Reply: We have modified the summary (page 3-line 3 from line 12 from above) as per the reviewer's suggestions. The tables have also been modified.

Reviewer 4

It is an interesting manuscript,

however the authors did not include data regarding mycobacteria identification in Crohn's disease cases as well as intestinal pseudotuberculosis cases. References from European and other populations are missing. So the author should include and discuss the following papers: J Clin Microbiol. 2005 Oct;43(10):5275-7, World J Gastroenterol. 2006 Nov 28;12(44):7161-4, Int J Infect Dis. 2008 Nov;12(6):607-10,

Reply: We purposefully did not include data regarding mycobacteria identification in Crohn's disease cases as well as intestinal pseudotuberculosis case, as it was not the mandate of the present review. The present review aims to differentiate Crohn's disease and intestinal tuberculosis. Mycobacterium paratuberculosis has been proposed as one of the etiological agents for CD, and does not play any role in differentiating CD and ITB. However, the third reference as suggested by the reviewer, is a case report on varied presentation of TB, and we have included it in our review (page 6-line 4 from above).