Response to Reviewers

Dear Editor,

Thank you for the very important comments and queries raised by the excellent peer reviewers. I have answered all the queries and made the necessary corrections. I have rephrased some sentences and added further relevant statements.

Corresponding author

Reviewer 1.

1. Figures 1-3 are not mentioned in the text. Please include them.

Answer: The Figures 1-3 have been mentioned in the text.

Reviewer 2

1. the surgical aspects in Abdominal Tb needs to be written more in detail, may be in a separate paragraph 2. the authors should insert a diagnostic algorithm (flow chart) for Abdominal Tb based on the current evidence in literature. 3. the manuscript needs editing for any repetitions of facts/ lines

Answer 2

I have added a sub- section on the role of surgery. The theme of the article was however to discuss the role of surgery in abdominal tuberculosis but not the details of the surgical procedures. The manuscript has been edited for any repetitions of facts/ lines. Due to the challenge of early diagnosis and with no absolute method in diagnosing abdominal TB, an expert consensus on the levels of evidence will be in a better position to create a diagnostic algorithm (flow chart).

Reviewer 3

The authors should write about the challenges of early diagnosis in conclusion and also in abstract. 3. The authors should also mention in methods as to why meta-analysis of the data was not possible.

Answer. These have been done. The purpose of the paper was to offer an opinion on the role of surgery in abdominal tuberculosis and stimulate debate in an area of ongoing interest. The aim was not to provide a precise estimate (i.e. meta-analysis) on the true effect of surgical intervention and risk on abdominal TB.

Reviewer 4

This is an interesting and important article, discussing the importance of managing abdominal tuberculosis with anti-tuberculosis drug and reserve surgery only for abdominal complication and not responding to medical management. This article endorse the surgeon to be aware of wide range of clinical manifestation and should have a high clinical suspicion for patients with chronic abdominal symptoms. Unfortunately, the similar article was already published recently in: (e.g) 1. Uma Debi, Vasudevan Ravisankar, Kaushal Kishor Prasad, Saroj Kant Sinha, Arun Kumar Sharma. “Abdominal tuberculosis of the gastrointestinal tract: Revisited” World J Gastroenterol 2014 October 28; 20(40): 14831-14840. 2. Pravin Rathi, Pravir Gambhire. Abdominal Tuberculosis Journal of The Association of Physicians of India. Vol. 64, February 2016; 38-47. Some inputs; 1. The author strongly suggested to review those two articles above. 2. The title of this article is focus on a role for surgery, the author suggest to give more portion for management subtopic. 3. The role of laparoscopy in diagnosis of abdominal tuberculosis was published in; Saxena P et al. Int Surg J. 2016 Aug;3(3):1557-1563. I think this article is important as laparoscopy is a minimally invasive procedure and allowing peritoneal biopsy to establish a histological diagnosis. To make massage of this article stronger, I suggest the author to compile the results of other researcher in a table comparing the clinical outcome of abdominal tuberculosis managed by surgery or laparoscopy and administration of anti-tuberculosis drugs.

4. Beside input number 3 above, a new algorithm emphasizing the importance of joint management of abdominal TB between surgeon and infection physician should be generated as a novelty of this article.

Answer: **There is no newer algorithm than that presented by Sood et al (2007) in Uma Debi et al: WJ of Gastroenterology 2014;20(40):14831-14840 which is based on a high level of clinical suspicion, US/abdomen, CTscan and FNAC Biopsy. This is discussed fully in this article. The theme of the paper was not to discuss the in- detail surgical management of abdominal TB as it is a systemic disease and surgery is not the primary treatment. It is simply palliative and diagnostic mainly reserved for complications or intestinal obstruction not responding to anti TB therapy, just as for the role of surgery in complications of intestinal lymphoma (Weledji et al Oncology review 2015).**

The current paper on the role of laparoscopy has been cited but its role in surgical management of the complications of TB is still developing and cannot be compared.

An international expert i consensus meeting should determine an algorithm for the joint management of abdominal TB between surgeon and infection physician. I have inserted that important oint in the abstract and conclusions.

Reviewer 5

This review addresses an interesting if somewhat niche topic. However, in my opinion some aspects of state-of-the-art care of abdominal TB are not adequately addressed in the paper. These include molecular diagnostics, drug resistance and the possibilities of advanced imaging modalities. I would also argue that in a setting where maximum resources are available the role of surgery is even more limited that what the authors suggest. Thus, my main criticism and recommendation would be to make clearer what statement pertains to the maximum as opposed to the limited resource setting. Some more specific points are given below. Major points 1) The authors propose three types of indications for surgery in TB. I disagree that creation of anatomoses to bypass affected parts of bowel is advisable. Radical resections to cure a systemic infection should also be a very rare indication for surgery given that effective medical options are available. Finally, residual strictures should not be operated on based on percent luminal narrowing but based on function. Moreover, if endoscopic intervention is possible this will usually be preferable as it is non-invasive. 2) The authors state in the section on diagnosis that ?an algorithm of these diagnostic methods lead to considerably higher precision in the diagnosis of this insidious disease.“ It would be interesting to know how this algorithm looks and how it has been validated. 3) The authors claim that ?In light of new evidence, peritoneal biopsy through laparoscopy has emerged as the gold standard for diagnosis.“ without citing that evidence. Likewise, it is not accurate to claim that for percutaneous liver biopsy ?the diagnostic yield may be less than 10%“. In fact, abdominal TB has a multitude of possible presentations and requires a diagnostic approach adjusted to the individual presentation. This approach should be as little invasive as possible and be based on the best available imaging. 4) At several points the authors paint an inappropriately bleak

picture of the prognosis of TB in HIV-infected individuals. It should be clarified that this is strongly dependent on whether anti-retroviral therapy is available. Minor points Interferone-gamma release assay should be descibed as a diagnostic modality. Likewise, the importance of resistance testing by culture and/or molecular methods should at least be mentioned. The recommended drug treatment of abdominal TB is not just similar to pulmonary TB it is identical. The sentence ?Although TB resistance is a growing problem in the endemic areas, whole genome sequencing (WGS) has become an essential tool for drug development by enabling the rapid identification of resistance mechanisms“ does not make sense and seems out of place in this review. It should be clarified or omitted.

Answers:

1. I agree that bypass procedures are not advisable and the complications are emphasized. It is however a known procedure in the past and worth mentioning.
2. The author did not recommend radical resection for a systemic disease as TB but ileo-caecal resection for obstructing ileo-caecal TB following failed medical treatment.
3. I agree that residual strictures should not be operated on based on percent luminal narrowing but based on function. I have made the correction.
4. I have inserted the role of endoscopic intervention if possible as it is non-invasive.
5. The authors state in the section on diagnosis that ?an algorithm of these diagnostic methods lead to considerably higher precision in the diagnosis of this insidious disease.“ It would be interesting to know how this algorithm looks and how it has been validated. The statement has been removed
6. The authors claim that ?In light of new evidence, peritoneal biopsy through laparoscopy has emerged as the gold standard for diagnosis.“ without citing that evidence. A: The paper has been cited
7. Likewise, it is not accurate to claim that for percutaneous liver biopsy ?the diagnostic yield may be less than 10%“. In fact, abdominal TB has a multitude of possible presentations and requires a diagnostic approach adjusted to the individual presentation. This approach should be as little invasive as possible and be based on the best available imaging.

   A: I agree and have rephrased the sentences.
8. At several points the authors paint an inappropriately bleak picture of the prognosis of TB in HIV-infected individuals. It should be clarified that this is strongly dependent on whether anti-retroviral therapy is available.

   Answer: I agree and have clarified this.
9. Minor points Interferone-gamma release assay should be descibed as a diagnostic modality. Likewise, the importance of resistance testing by culture and/or molecular methods should at least be mentioned.

   Answer: Most of the studies on the Interferone gamma release assay are on pulmonary and not extrapulmonary TB. Secondly a vast majority of IGRA-positive individuals in TB burden regions do not progress to TB disease at follow-up.

10. The recommended drug treatment of abdominal TB is not just similar to pulmonary TB it is identical.

A: I agree and have corrected this.

11. The sentence ?Although TB resistance is a growing problem in the endemic areas, whole genome sequencing (WGS) has become an essential tool for drug development by enabling the rapid identification of resistance mechanisms“ does not make sense and seems out of place in this review. It should be clarified or omitted.

A: I have omitted this.