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Etiological spectrum of isolated ileo-cecal ulcers in patients with gastrointestinal symptoms

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1st Editorial decision
23-Sept-2022

Ref.: Ms. No. JCTRes-D-22-00126
Etiological spectrum of Isolated Ileo-cecal ulcers in patients with gastrointestinal symptoms
Journal of Clinical and Translational Research

Dear Professor Dixit,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that

the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Oct 23, 2022.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The manuscript focuses on important area. There are some comments and suggestions
1) Introduction- The list of differentials for ICR ulcers is incomplete. The authors should see and cite the two reviews on the topic for the list
a) Ileocecal thickening: Clinical approach to a common problem. JGH Open. 2019 Apr 22;3(6):456-463. doi: 10.1002/jgh3.12186. PMID: 31832544; PMCID: PMC6891021.
b) Ilececum: A Comprehensive Review. Can J Gastroenterol Hepatol. 2019 Feb 3;2019:1451835. doi: 10.1155/2019/1451835. PMID: 30854348; PMCID: PMC6378086.
2. The authors have missed discussing an important study on PET CT entrography which showed that TB and CD were equally frequenct causes of ICR- FDG-PET-CT Enterography Helps Determine Clinical Significance of Suspected Ileocecal Thickening: A Prospective Study. Dig Dis Sci. 2021 May;66(5):1620-1630. doi: 10.1007/s10620-020-06361-9. Epub 2020 Jun 1. PMID: 32488818.
3. The discussion as of now is unfocused. There is no clear message. One clear evidence is the fact that a certain diagnosis may not be achieved at baseline and follow-up clinically and endoscopicalyy is needed. This could be the central message from this work
4. The authors reported the yield of NAAT as compared to liquid culture. What is the previous data on yield of NAAT. The authors should compare their findings with other reports/ systematic review on Xpert in diagnosis of abdominal tuberculosis (especially intestinal tuberculosis)
5. Methods- Clearly state
a) Prospective/retrospective nature of study
b) Ethical clearance
6) Number of eosinophilic colitis is significat- was this EGE or parasitic infestation related

Reviewer #2: I commend the authors on performing this interesting research - attempting to answer the important clinical question regarding the etiology of isolated ulcers in the ileocecal region
comments:
1- It is unclear on what basis did the authors perform their power calculation and arrived at the sample size. I also don't believe it is needed and would remove it.

2- The inferences made from the statistical analyses performed are probably overreaching - there were many multiple analyses performed using many variables even though the analyzed subgroups were small with probable overfitting - the discussion should allude that the statistical findings are hypotheses generating only.
3- Significant English editing is needed throughout the manuscript , specifically the discussion needs to be rewritten

Reviewer #3: The authors aim to determine etiology and clinical outcome of ICR ulcers with gastro-intestinal symptoms. However, in my opinion, the research does not present enough real practical value.
1. How did you define ICR ulcers? It was not mentioned in the article.
2. The tests done in patients with ICR ulcers have not been stipulated to rule out the involvement of other portions of small intestine, such as MRE, enteroscopy... actually, only 40 in 100 patients were examined with Ultrasonography and 32 in 100 were performed by computed tomography in this research.
3. How to determine that the patient's symptoms are caused by ICR ulcers? In fact, most patients with ICR ulcers may have no obvious symptoms.
4. There are some spelling mistakes, such as "gm/dl" in Results. When describing the patient's test results, it is better to provide the normal value.

Authors' response

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Varanasi, October 11, 2022

Re: Revision Ms. No. JCTRes-D-22-00126

Dear Dr Michal Heger,

Thank you for providing us an opportunity to resubmit a revised version of our manuscript entitled '**Etiological spectrum of Isolated Ileo-cecal ulcers in patients with gastrointestinal symptoms'.**

We have addressed all comments of all reviewers. Every modification or rebuttal of the reviewer's comment is detailed per comment in red. We are grateful for the useful comments from the reviewers as a result of which our manuscript has been improved a lot. Any change in manuscript and references has been highlighted in yellow.

Thank you again.

On behalf of the authors, kind regards.

Vinod Kumar Dixit

Reviewer's comments and reply

Reviewer 1#

Query 1. Introduction- The list of differentials for ICR ulcers is incomplete.

Answer- Relevant literature reviewed and included in the manuscript.

The ileocecal area can be affected by disease process localized to that particular segment of the bowel or can be a part of involvement of other segments of the bowel or any systemic disease. The ICR, being an area of physiological stasis, increased absorptive area, decreased digestive function, and abundant lymphoid tissue and M cells, it is the most common area of the gastrointestinal tract involved by pathological process.

Reference-

Horvath KD, Whelan RL. Intestinal tuberculosis: return of an old disease. Am. J. Gastroenterol. 1998; 93: 692–6.

Moss JD, Knauer CM. Tuberculous enteritis. A report of three patients. Gastroenterology. 1973; 65: 959–66.

The abnormalities of ICR could be detected on imaging or during ileocolonoscopy representing a variety of conditions, including benign or malignant tumors, infections, inflammatory conditions, ischemia, etc. However, these abnormalities on imaging or ileocolonoscopy can be a spurious finding, without any underlying cause. In various studies on bowel wall thickening, a normal ileocolonoscopy has been found in up to one third of cases. Moreover, some patients may have nonspecific ileitis on histopathology and endoscopic abnormalities like nodularity and ulcerations in these patients may be followed without any treatment in absence of symptoms.

Reference –

Iadicola D, De Marco P, Bonventre S et al. Bowel wall thickening: inquire or not inquire? Our guidelines. G. Chir. 2018; 39: 41–4. [PMC free article] [PubMed] [Google Scholar]

Al-Khowaiter SS, Brahmania M, Kim E et al. Clinical and endoscopic significance of bowel-wall thickening reported on abdominal computed tomographies in symptomatic patients with no history of gastrointestinal disease. Can. Assoc. Radiol. J. 2014; 65: 67–70. [PubMed] [Google Scholar]

Kedia S, Kurrey L, Pratap Mouli V et al. Frequency, natural course and clinical significance of symptomatic terminal ileitis. J. Dig. Dis. 2016; 17: 36–43. [PubMed] [Google Scholar]

Etiologies of ICR involvement has been discussed and categorized into common, less common and rare cause in a review and some of these have been described in detail in another review. Common causes included tuberculosis, Crohn's disease, adenocarcinoma, Cecal diverticulitis, appendicitis, Bacterial ileocolitis—Shigella, Salmonella,

Campylobacter, Clostridium difficile, Yersinia, ameboma/iasis and lymphoma. Less common causes were ischemic, Mycobacterium avium complex, systemic vasculitis, histoplasmosis, cytomegalovirus, Other tumors- carcinoid, GIST, metastasis, lipoma and typhlitis. Rare causes were eosinophilic gastroenteritis, endometriosis, lipomatosis of IC valve and IgG4-related disease of ileocecal area.

Reference-

Agarwala R, Singh AK, Shah J, Mandavdhare HS, Sharma V. Ileocecal thickening: Clinical approach to a common problem. JGH Open. 2019 Apr 22;3(6):456-463. doi: 10.1002/jgh3.12186. PMID: 31832544; PMCID: PMC6891021.

Tang SJ, Wu R. Ilececum: A Comprehensive Review. Can J Gastroenterol Hepatol. 2019 Feb 3;2019:1451835. doi: 10.1155/2019/1451835. PMID: 30854348; PMCID: PMC6378086.

Query 2. The authors have missed discussing an important study on PET CT entrography which showed that TB and CD were equally frequenct causes of ICR- FDG-PET-CT Enterography Helps Determine Clinical Significance of Suspected Ileocecal Thickening: A Prospective Study. Dig Dis Sci. 2021 May;66(5):1620-1630. doi: 10.1007/s10620-020-06361-9. Epub 2020 Jun 1. PMID: 32488818.

Answer- Included in the manuscript

To further explore the finding of ileocecal thickening on CT one study demonstrated the role of combined 2-deoxy-2-fluorine-18-fluoro-D-glucose(^{18}F-FDG)-positron emission tomography and computed tomographic enterography (PET-CTE) in discrimination of clinically significant and insignificant diagnosis and concluded that it may help guide the need for colonoscopy in patients suspected to have ICT on CT.

Reference -

Singh AK, Kumar R, Gupta P, et al. FDG-PET-CT Enterography Helps Determine Clinical Significance of Suspected Ileocecal Thickening: A Prospective Study. Dig Dis Sci. 2021;66(5):1620-1630. doi:10.1007/s10620-020-06361-9)

Query 3. The discussion as of now is unfocused. There is no clear message. One clear evidence is the fact that a certain diagnosis may not be achieved at baseline and follow-up clinically and endoscopicalyy is needed. This could be the central message from this work.

Answer- Our study concludes that majority of patients with ICR ulcers have specific etiologies and therefore, require careful evaluation. Imaging in addition to biochemical and histological parameters are helpful in reaching at a specific diagnosis. Repeat colonoscopy and sometimes change of initial therapy are needed in case of non-response to initial treatment making these useful tools for diagnosing specific disease. Findings of isolated lymphoplasmacytic infiltrates in HPE favored nonspecific diagnosis over CD and ITB and presence of granuloma, positive TB PCR, and positive MGIT culture in biopsy sample exclusively favored ITB diagnosis while architectural distortion and goblet cell mucin depletion favored diagnosis of CD over ITB. Non-specific ulcers at ICR can be managed symptomatically; however, close follow up is necessary as sometimes they may harbor underlying specific disease.

Query 4. The authors reported the yield of NAAT as compared to liquid culture. What is the previous data on yield of NAAT. The authors should compare their findings with other reports/ systematic review on Xpert in diagnosis of abdominal tuberculosis (especially intestinal tuberculosis)

Answer-

Intestinal tuberculosis is a form of extrapulmonary tuberculosis which is paucibacillary in nature and thus very low yield of direct microbiological/ pathological evidence (AFB, NAATs, culture and caseating grannulomas).

Reference-

Kumar S, Bopanna S, Kedia S, et al. Evaluation of Xpert MTB/RIF assay performance in the diagnosis of abdominal tuberculosis. Intest Res. 2017;15(2):187-194. doi:10.5217/ir.2017.15.2.187

Du J, Ma YY, Xiang H, Li YM. Confluent granulomas and ulcers lined by epithelioid histiocytes: new ideal method for differentiation of ITB and CD? A meta analysis. PLoS One. 2014;9(10):e103303. Published 2014 Oct 9. doi:10.1371/journal.pone.0103303

In a recent meta analysis, the pooled sensitivity and specificity of Xpert MTB/RIF on intestinal tissue was 23% (95% C.I., 16–32%) and 100% (95% C.I., 52–100%).

Sharma V, Soni H, Kumar-M P, et al. Diagnostic accuracy of the Xpert MTB/RIF assay for abdominal tuberculosis: a systematic review and meta-analysis. Expert Rev Anti Infect Ther. 2021;19(2):253-265. doi:10.1080/14787210.2020.1816169

Query 5. Methods- Clearly state a) Prospective/retrospective nature of study b) Ethical clearance

Answer- Changes done as per suggestion and included in the manuscript.

Present study was a prospective study designed to investigate the etiopathogenesis of isolated ileo-cecal ulcers in all the symptomatic patients who were undergoing ileo-colonoscopic examination and presented with one or more of following symptoms: abdominal pain, unexplained fever, weight loss, overt or occult GI bleed, altered bowel habits, diarrhea, partial bowel obstruction etc. Among these patients with isolated ICR ulcers were included. Patients who refused to give consent (assent in case of minor), patients with prior diagnosis of tuberculosis or inflammatory bowel disease, incomplete colonoscopy and associated colonic lesions other than ICR were excluded from the study. Study was approved by Institutional ethics committee.

Query 6. Number of eosinophilic colitis is significat- was this EGE or parasitic infestation related

Answer-

Eosinophilic predominant infiltrates can also be observed in helminthic infections (e.g. pin worms, hookworms), inflammatory bowel disease, autoimmune disease (e.g. scleroderma, Churg–Strauss syndrome), celiac disease, drug reactions, and in association with the hypereosinophilic syndrome and in present study appropriate tests were not performed individually to exclude possibility these entities, and hence few of our cases could represent these diagnoses if investigated further.

Alfadda AA, Storr MA, Shaffer EA. Eosinophilic colitis: epidemiology, clinical features, and current management. Therap Adv Gastroenterol. 2011;4(5):301-309. doi:10.1177/1756283X10392443

Reviewer 2#

Query 1. It is unclear on what basis did the authors perform their power calculation and arrived at the sample size. I also don't believe it is needed and would remove it.

Answer- Corrected in manuscript as per suggestion.

Query 2. The inferences made from the statistical analyses performed are probably overreaching - there were many multiple analyses performed using many variables even though the analyzed subgroups were small with probable overfitting - the discussion should allude that the statistical findings are hypotheses generating only.

Answer- Manuscript corrected as per suggestion

Intergroup analysis was done among three largest groups i. e. non-specific, CD and ITB groups comprising of 45, 20 and 18 patients respectively. Statistical findings of these analyses can be taken for hypothesis generation only as groups are small.

Query 3. Significant English editing is needed throughout the manuscript; specifically the discussion needs to be rewritten

Answer- corrected and highlighted.

Reviwer 3#

Query 1. How did you define ICR ulcers? It was not mentioned in the article.

Answer – Ileo-cecal region (ICR) consists of distal most part of ileum, ileo-cecal valve, cecum and appendiceal orifice. It is very common to find abnormalities including ulcers located at ICR during colonoscopy. An ICR ulcer may be defined as breach and not simple petechie or hyperemic lesion in mucosa at this location at colonoscopic examination.

Query 2. The tests done in patients with ICR ulcers have not been stipulated to rule out the involvement of other portions of small intestine, such as MRE, enteroscopy... actually, only 40 in 100 patients were examined with Ultrasonography and 32 in 100 were performed by computed tomography in this research.

Answer- It is very common to find isolated ICR ulcers during colonoscopy in asymptomatic and symptomatic patients both. Present study was designed to detect isolated ICR ulcers during colonoscopy and to evaluate their etiological origin in patients with symptoms. Utilization of appropriate imaging, enteroscopy and more so fecal markers like fecal calprotectin in all patients could have resulted in specific diagnosis in additional subset of patients. This can be considered as limitation of our study.

Query 3. How to determine that the patient's symptoms are caused by ICR ulcers? In fact, most patients with ICR ulcers may have no obvious symptoms.

Answer- Most ICR ulcers detected in asymptomatic patients are of uncertain significance. One study in 2010 concluded that most isolated terminal ileal ulcers detected incidentally in asymptomatic individuals resolve without any treatment. Even if these lesions persist, it is unusual for them to progress or to cause any symptoms.

Reference-

Chang HS, Lee D, Kim JC, et al. Isolated terminal ileal ulcerations in asymptomatic individuals: natural course and clinical significance. Gastrointest Endosc. 2010;72(6):1226-1232. doi:10.1016/j.gie.2010.08.029

In present study we focused on symptomatic ICR ulcers. Organic diseases discussed in present study could very well be mimicked clinically by functional disorders of bowel especially irritable bowels syndrome (IBS) and other organic diseases not discussed otherwise particularly symptoms like pain abdomen and diarrhea. One way to establish causal association between isolated ICR ulcers and symptoms was to treat the underlying disease followed by resolution of endoscopic lesion and symptoms. In fact overlapping features of many diseases at this location sometimes needed treat first strategy like ATT trial and follow up.

Query 4. There are some spelling mistakes, such as "gm/dl" in Results. When describing the patient's test results, it is better to provide the normal value.

Answer- Corrected and highlighted in yellow in table 1

2nd Editorial decision
13-Oct-2022

Ref.: Ms. No. JCTRes-D-22-00126R1
Etiological spectrum of Isolated Ileo-cecal ulcers in patients with gastrointestinal symptoms
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at http://www.jctres.com/en/author-guidelines/ under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Nov 12, 2022.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

Thank you for taking care of the reviewers' comments.

Before we can proceed to publication of your manuscript, I kindly ask you to address the following:

1) Please provide a CONSORT flow chart as per our author guidelines (see website).

2) Eliminate residual spelling/grammar/punctuation errors, particularly the use (or lack of) articles (https://en.wikipedia.org/wiki/Article_(grammar)) should be corrected. Be consistent with all spelling (e.g., always use one decimal point, so 36 should read 36.0). In the phrase "On comparing Colonoscopic character..." -> why the capital C mid-sentence? Please check entire manuscript meticulously.

3) Ensure that all abbreviations are written out in full at first mention.

4) Specify the institutional review board protocol number that was approved in the text.

5) Conclusion (section) should be plural instead of singular.

6) Avoid the use of personal pronouns ("they"). Instead, write out what "they" refers to.

Journal of Clinical and Translational Research
Peer review process file 09.202301.003

Authors' response

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Varanasi, October 17, 2022

Re: Revision Ms. No. JCTRes-D-22-00126R1

Dear Dr Michal Heger,

Thank you for providing us an opportunity to resubmit a revised version of our manuscript entitled '**Etiological spectrum of Isolated Ileo-cecal ulcers in patients with gastrointestinal symptoms'.**

We have addressed all comments of all reviewers. Every modification or rebuttal of the reviewer's comment is detailed per comment. We are grateful for the useful comments from the reviewers as a result of which our manuscript has been improved a lot. Any change in manuscript and references has been highlighted in yellow.

Thank you again.

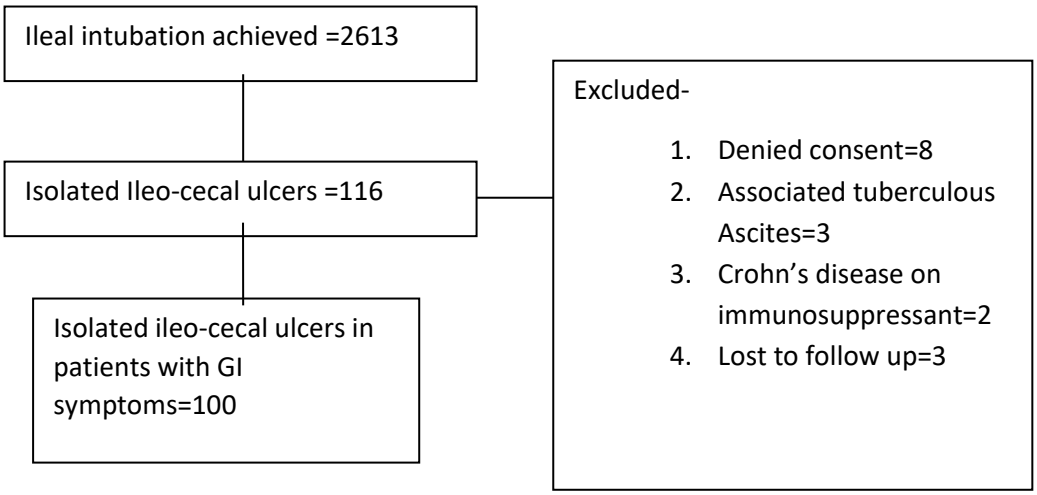
On behalf of the authors, kind regards.

Vinod Kumar Dixit

Reviewer's comments and reply

Query 1. Please provide a CONSORT flow chart as per our author guidelines.

Reply: Patient flow chart added in text as figure 1 (Highlighted in yellow)



Final diagnosis

Non-specific=45	Crohn's disease=20	Tuberculosis=18	Other infective=7	Eosinophilic =6	NSAID= 2	Amoebic =1	Malignant =1

Figure 1. Patient flow chart

2) Eliminate residual spelling/grammar/punctuation errors, particularly the use (or lack of) articles (https://en.wikipedia.org/wiki/Article_(grammar)) should be corrected. Be consistent with all spelling (e.g., always use one decimal point, so 36 should read 36.0). In the phrase "On comparing Colonoscopic character..." -> why the capital C mid-sentence? Please check entire manuscript meticulously.

Reply: Manuscript was checked thoroughly and corrected wherever required.

3) Ensure that all abbreviations are written out in full at first mention.

Reply: Corrected as per suggestion.

4) Specify the institutional review board protocol number that was approved in the text.

Reply: This study was approved by Institutional ethics committee [Approval No.

Dean/EC/2737].

Highlighted in yellow.

5) Conclusion (section) should be plural instead of singular.

Reply: Corrected

6) Avoid the use of personal pronouns ("they"). Instead, write out what "they" refers to.

Reply: Corrected

3rd Editorial decision
18-Oct-2022

Ref.: Ms. No. JCTRes-D-22-00126R2
Etiological spectrum of Isolated Ileo-cecal ulcers in patients with gastrointestinal symptoms
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at http://www.jctres.com/en/author-guidelines/ under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Nov 17, 2022.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

Please take my request to improve the language seriously and revert to the options I have proposed in my previous decision letter.

Attached to this decision letter you will find your manuscript that I started modifying (abstract and keywords). However, when I got to the introduction the amount of errors, which also involve syntax errors, became too overwhelming.

The sentence "The ICR, being an area of physiological stasis, increased absorptive area, decreased digestive function and abundant lymphoid tissue and M cells is the most common area of the gastrointestinal tract involved by pathological processes [2, 3]" is simply not correct English.

Please trust that I will keep your paper from being published unless you make an actual effort to improve the text according to academic standards.

I kindly ask you to continue in the draft I appended.

Thank you and good luck,

Michal Heger
Editor

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

Authors' response

Vinod Kumar Dixit
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Varanasi, October 30, 2022

Re: Revision Ms. No. JCTRes-D-22-00126R2

Dear Dr Michal Heger,

Thank you for providing us an opportunity to resubmit a revised version of our manuscript entitled '**Etiological spectrum of isolated ileo-cecal ulcers in patients with gastrointestinal symptoms'.**

We have addressed the issue of grammatical errors in the manuscript as suggested by reviewer (s). However, if there is any deficiency left, we would like to rectify it further. We are grateful for the useful comments from the reviewers as a result of which our manuscript has been improved a lot.

Thank you again.

On behalf of the authors, kind regards.

Vinod Kumar Dixit

4th Editorial decision
30-Oct-2022

Ref.: Ms. No. JCTRes-D-22-00126R3
Etiological spectrum of Isolated Ileo-cecal ulcers in patients with gastrointestinal symptoms
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at http://www.jctres.com/en/author-guidelines/ under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Nov 29, 2022.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

Thank you for the attempt to improve the language.

However, the work that was done did not yield the desired results.

3 examples in Introduction:

1) "It is common to find abnormalities including ulcers located at ICR during colonoscopy" should read ->
It is common to find abnormalities such as ulcers located in the ICR during colonoscopy

2) "An ICR ulcer may be defined as a breach and not simple petechiae or hyperemic lesion in mucosa at this location" ->
"breach" constitutes a syntax error and the text should read "and not as simple..."

3) "One study concluded that more than 50% of isolated ulcers end up in specific diagnoses" ->
the phrase "end up in specific diagnoses" is incorrect and should be replaced by phrasing to the effect of more than 50% of isolated ulcers are misclassified or misdiagnosed.

Please do a better job with the language polishing.

Thank you,

Michal Heger
Editor

Authors' response

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Varanasi, November 2, 2022

Re: Revision Ms. No. JCTRes-D-22-00126R3

Dear Dr Michal Heger,

Thank you for providing us an opportunity to resubmit a revised version of our manuscript entitled '**Etiological spectrum of isolated ileo-cecal ulcers in patients with gastrointestinal symptoms'.**

We have addressed the issue of grammatical errors in the manuscript as suggested by reviewer (s). Correction of language has also been done and major changes in the manuscript are highlighted in yellow. However, if there is any deficiency left, we would like to rectify it further. We are grateful for the useful comments from the reviewers as a result of which our manuscript has been improved a lot.

Thank you again.

On behalf of the authors, kind regards.

Vinod Kumar Dixit

5th Editorial decision
04-Nov-2022

Ref.: Ms. No. JCTRes-D-22-00126R4
Etiological spectrum of Isolated Ileo-cecal ulcers in patients with gastrointestinal symptoms
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.
Please notify our assistant editor/production editor when you receive the proofs if your article should belong a speical issue specifying the issue's title.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: