

Format for ANSWERING REVIEWERS

January 6, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript NO: 14981-edited.doc).

Title: Appendicitis in children less than five years old: A challenge for the general practitioner

Authors: Pierluigi Marzuillo, Claudio Germani, Baruch Krauss, Egidio Barbi.

Name of Journal: *World Journal of Clinical Pediatrics*

ESPS Manuscript NO: 14981

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer

(1) We clarified the ambiguity the reviewer found in the title and therefore we modified the manuscript title.

(2) We gave more information about as our manuscript could support the general practitioner and we added a flow chart (figure 2) that could help the general practitioner in the clinical practice.

(3) We clearly spelled out that CT evaluation requires a well justified decision.

(4) We added a sentence about breast feeding and appendicitis in the paragraph "Anatomic and pathophysiologic elements".

(5) We added some sentences regarding the gender situation.

(6) We presented the table 1 data in a differential diagnostic context, as suggested.

(7) We removed the table 2 because, with the modified table 1, the table 2 became redundant

(8) We removed the old figure 1, as suggested.

(9) We added a new author, Baruch Krauss, because he helped us in the revision and in the conceptual improvement of the manuscript. Moreover, BK performed an English revision of the manuscript.

In the next page there are the detailed answers to reviewers.

3 References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Clinical Pediatrics*.

Sincerely yours,

A handwritten signature in blue ink, appearing to read 'Pierluigi Marzuillo'.

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We thank the reviewers for taking the time to read and comment on our manuscript. All the changes have been highlighted in the text.

Reviewer 02731621

Comments: This manuscript, entitled "Appendicitis in the first years of life: a challenge for the general practitioner." is a well designed review. It should be accepted for publishing.

Answer: thank you for your comments

Reviewer 02512137

Comments: I read and review the manuscript entitled " Appendicitis in the first years of life: a challenge for the general practitioner " I agree with authors that the appendicitis in the first years of life continues to be a open problem in general surgery. This paper is very attractive and useful and my opinion is to accept them without changes.

Answer: thank you for your comments

Reviewer 02454257

Comments: With this manuscript the authors present a review on a rare but clinically relevant issue: early childhood appendicitis and its reliable diagnostic. Title: "... in the first years of life..." should be defined by the authors. Within the text the limit is at 5 years, at another stage at 3 years as well as under one year. This requires clarification.

Answer: our topic highlight is focused on acute appendicitis in children less than five years old. In the text, sometimes, the limit changes because we report the data available in literature and not all the studies use as limit the 5 years of age. However all the ages showed in our review are under 5 years of age. As suggested we clarified the ambiguity that the reviewer found and we modified the manuscript title.

Comments: Abstract: The last paragraph of the abstract shows – as well as the title of the manuscript – that a timely diagnosis of early childhood appendicitis is a "challenge". Unfortunately the authors do not provide sufficient data on how their manuscript is supposed to support the general practitioner to meet this challenge.

Answer: as suggested we gave more information about as our manuscript could support the general practitioner (see line 46 of the new version of the manuscript).

Comments: Introduction: The first sentence is misleading: the authors state that appendicitis is the most

common reason for abdominal pain and then: "...with a peak in the 2nd decade...". This age group is not the focus of the manuscript.

Answer: also if the focus of our paper is another age group, we added this information only to let know to the readers at what age there is the peak incidence. However we modified the misleading sentence (see lines 59-61 of the new version of the manuscript).

Comments: Epidemiology: Analysis of cited literature is one of the objectives of a review article. The authors cite the article of Bansal et al from 2012. In this context it should be mentioned that the number of perforated appendices has been assessed from a group of 7(!). It is not possible to draw valid statistical conclusions from this small number of cases; which is not done by Bansal et al, and therefore it remains completely open if the differences in the perforation rate of the different age groups do have statistical relevance.

Answer: we agree with your observation, therefore we modified the text according to your observation (see lines 78-80 of the new version of the manuscript)

Comments: Anatomy and pathophysiology: Approaching the risk factors for childhood appendicitis, the (protective?) effect of breast feeding should at least be discussed.

Answer: we agree with your observation, we added a sentence about breast feeding and appendicitis in the paragraph "Anatomic and pathophysiologic elements" (see lines 105 and 106 of the new version of the manuscript)

Comments: The following sections on history and clinical examination, laboratory and radiological evaluation list older and recent literature. Especially if a decision guidance for a general practitioner is meant to be provided it would be very supportive to present the data in a clinical pathway, flow chart or something similar. The most vigorous deficit of this manuscript is the lack of recommendations for daily routine. These recommendations should be clearly defined; this would require i. e. information on the interval of re-evaluation of children in an unclear situation. The recommendation of repeated ultrasound evaluation should be clearly spelled out. Especially for this there are recent very good articles available showing that repeated ultrasound evaluation in a defined interval increases sensitivity.

Answer: as suggested we added a flow chart that could be supportive to the general practitioner (see lines 46, 214-216 and figure 2 of the new version of the manuscript). We added a sentence about the evidence of increased ultrasound sensitivity with the repeated ultrasound evaluation (see lines 188-189 of the new version of the manuscript)

Comments: CT as diagnostic tools should be assessed in a more critical fashion. It should be clearly spelled out that the CT evaluation of a child less than one year old requires a well justified decision since the radiation dose is high and sequelae may be significant.

Answer: as suggested, we clearly spelled out that CT evaluation requires a well justified decision (see lines 176-178)

Comments: Some sentences are recommended regarding the gender situation. Are there remarkable differences between girls and boys in clinical presentation and time of diagnosis?

Answer: we agree with your observation. We added some sentences regarding the gender situation (see lines 60-61 and 80-81 of the new version of the manuscript).

Comments: Table 1 lacks validity in the presented form. It would be more sensible to present this data in a differential diagnostic context as done in table 2 with the differential diagnostics in gastroenteritis.

Answer: as suggested, we presented the data in a differential diagnostic context (see new table 1).

Moreover, we removed the table 2 because, with the modified table 1 ,the table 2 became redundant.

Comments: Figure 1 has a very limited diagnostic value and should better be presented as text.

Answer: we removed the figure 1. The figure data are shown in the text at lines 90-94.

Comments: In Figure 2 the legend of the x-axis is missing. Obviously it is supposed to be the headline of the figure. It is no good style to start a legend with “%”.

Answer: the figure 2 is now the new figure 1 because as suggested we removed the old figure 1. We added the legend of the x-axis (see new figure 1).

Comments: In the current presentation the scientific value of this manuscript is low. Especially if the target reader is the general practitioner recommendations should be clearly defined.

Answer: We modified the text according to your comments and we added a flow-chart that could be useful to the General Practitioner.