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OPEN PEER REVIEW

Effects of COVID-19 Pandemic on the Frequency of Complicated Appendicitis in Pediatric Populations

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

2 comments · 24 Jul 2022 – 28 Jul 2022

Referee 1 Reviewer

MAJOR REVISION 24 Jul 2022

METHODOLOGY:
"We enrolled all the patients who underwent appendectomy"..... The case population should include all patients with a definite diagnosis of appendicitis based on pathology, not all patients who underwent surgery for suspected appendicitis. In fact, the preoperative diagnosis is not important; the final diagnosis should be considered.
"Clinically, we diagnosed acute appendicitis in accordance with physical examination, laboratory and imaging studies. We used both Alvarado and Pediatric Appendicitis Score alongside ultrasonography to get the correct diagnosis"..... This is not logical. The authors conducted a retrospective study, so you cannot say that you used these methods. You just selected medical records with a final diagnosis of appendicitis or complicated appendicitis in 2 periods of time.

Result:
"Despite the remarkable decrease in the average leukocyte count"..... In which group?
"no significant correlation was found (p = 0.007)"..... Is p=0.007 not significant?
"Lung CT was the most common screening tool in the patients (54.6%), followed by the combination of CXR and CBC (35.2%). PCR was the only screening test in ten patients (5.1%)"..... This variable is not related to your title. The researchers wanted to investigate the rate of complications of appendicitis in 2 periods of time, not compare COVID-positive and COVID-negative patients. Also, screening is entirely related to your access to tests, such as PCR or rapid tests, so what is the effect of this variable on your final result?
"It is also noteworthy that no significant correlation has been found between the COVID and the development of complicated appendicitis (p=0.978)"..... Please mention how many of your cases were COVID-positive in total, and then report the p-value as a finding. However, the paragraph before this is not necessary.
Discussion :
The first part is not related to the title....
"But it seems that the risk of uncomplicated AA didn't change significantly"..... Based on which study does it seem so? Your study? Why did you use "seems"? Another study? Provide a reference.
References 15,16,17 are not related.
The Discussion needs major revision. The authors should emphasize the differences in the rates of the variables between the 2 groups of cases, explain their opinions about the findings, and compare them with findings from other studies.
Summery:
All changes should be applied to the summary.

Referee 2 Reviewer

MINOR REVISION 28 Jul 2022

Dear author
You cannot say "In our findings the number of diagnosed AA wasn't changed remarkably during the COVID", while the difference is not statistically significant.
Regards

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editor-in-Chief

Thank you for your time reviewing our paper entitled "**Effects of COVID-19 pandemic on the incidence of complicated appendicitis in pediatric population**". I sincerely appreciate your suggestions and modifications. Your pieces of advice were very helpful and gave us a new comprehensive perspective on the way of writing our study.

Now, we have applied the comments and corrected the errors.

Thank you once again for all the support and assistance you put in.

It would be great if you consider following comments in response to your outstanding reviewers:

Reply to the reviewers' comments

Reviewer Number	Comment Number	Original comments of the reviewer	Reply by the author(s)	Changes done on page number and line number
Reviewer #1	1	We enrolled all the patients who underwent appendectomy…….case population should all patient with definite diagnosis of appendicitis based on pathology not all patient	Thank you for valuable comment. I think this is a misunderstanding. We meant that in our institute the diagnosis of appendicitis is made with the aid of Alavardo and Pediatric	Highlighted in yellow On Page 7, Line(s)

		whom under operation and were suspected to appendicitis ,in fact pre-operation diagnosis is not important ,final diagnosis should consider Clinically, we diagnosed acute appendicitis in accordance with physical examination, laboratory and imaging studies. We used both Alvarado and Pediatric Appendicitis Score alongside ultrasonography to get the correct diagnosis.....it is not logical ,authors did retrospective study so you can't say we use this,,,,,,.you just selected medical file with final diagnosis of appendicitis or complicated appendicitis in 2 period of time	Appendicitis Score. This is not a way of case selection. I have written in the methods section that only operated patients were included in the study. Also, at the opening of paragraph I used the term "Clinically" which means we use this tools for initial diagnosis at clinics or emergency rooms. To resolve this misconception I have changed the sentence to "We usually use both Alvarado and Pediatric Appendicitis Score alongside ultrasonography to get the correct diagnosis in our institute". I hope this change will clear your concern in this matter.	84-86
Reviewer #1	2	Result: Despite the remarkable decrease in the average leukocyte count,,,,,in which group? no significant correlation was found (p = 0.007) .....???????p=0.007 is not significant?	Thank you for your careful checks and corrections. It was a mistake in the writing process and interpretation of the tables. I have replaced that sentence completely.	Highlighted in yellow On Page 9, Line(s) 137-138
		Lung CT was the most common screening tool in the patients (54.6%), followed by the combination of CXR and CBC (35.2%). PCR was the only screening test in ten patients (5.1%).....this variable is not related to your title, researcher wanted to search rate of complication of appendicitis in 2 period of time not between covid positive or negative patients ,also screening totally related	Although this paragraph is not totally related to our topic, we preferred to declare these numbers due to the context of our work. This work is somehow related to the pandemic. I think there may be some questions about screening for the readers. However, I have added a statement at the beginning of the aforesaid paragraph. The phrase is also highlighted in yellow.	Highlighted in yellow On Page 10, Line(s) 157-166

		to your accessibility to tests, pcr or rapid test ,so what is the effect of this variable on your final result . It is also noteworthy that no significant correlation has been found between the COVID and the development of complicated appendicitis (p=0.978).....pls mention how many of your cases were covid positive,totally, and then as a finding you can announce p value ,but paragraph before this is not necessary.	Besides, I have put the exact number of COVID positives.	
		Discussion : First part is not related to title.... But it seems that the risk of uncomplicated AA didn't change significantly.....it seems from which study? Your study? Why you used "seems". Another study? Put reference Reference 15,16,17 is not related Discussion need major revision , authors should emphasize on different rate of variable in 2 groups of cases and explain their opinion about finding and compare with other researches	Thank you for your valuable comment. The first part of discussion have been moved to the introduction section due to its importance. Also we have completed the discussion section.	Highlighted in yellow On Page 13, Line(s) 214-230
Reviewer #1	3	All changes should apply in summary	The abstract changed based on modifications applied to the whole text.	Highlighted in yellow on Page 2
Reviewer #2	1	the title has to be changed. You can not measure incidence in an open population. It is better to use frequency. Consult with an	Special thanks to you for your good point. I think it was a language misunderstanding. However, I have replaced the word "incidence" with	Highlighted in yellow on Page

		epidemiologist. Effects of COVID-19 pandemic on the incidence of complicated appendicitis in pediatric population;	“frequency” just the way you desired.	1, and Title page
Reviewer #2	2	PCR was the only screening test in ten patients (5.1%). Besides, in only thirteen cases, PCR was taken preoperatively. In that period was not PCR mandatory for surgery	Dear reviewer, I have added some statements at the beginning of that paragraph to clear this concern. We are aware that preoperative screening was not mandatory for surgery. And the results of screenings (either PCR or lung CT) did not affect the inclusion or exclusion.	Highlighted in yellow On Page 10, Line(s) 157-158
Reviewer #2	3	you did not inform about MISC signs and symptoms which can cause appendicitis in covid period	I have inserted a paragraph discussing this matter.	Highlighted in yellow On Page 12, Line(s) 198-203
Reviewer #2	4	please complete your discussion.	The discussion modified and completed.	Highlighted in yellow On Page 13, Line(s) 214-230
Reviewer #3	1	You cannot say “In our findings the number of diagnosed AA wasn’t changed remarkably during the COVID”, while the difference is not statistically significant.	This sentence have been changed to “In our study, despite the increased number of cases after the pandemic, we didn’t find any significant difference in the number of cases (p = 0.232).”	Highlighted in yellow On Page 13, Line(s) 171-175
Associate Editor's	1	Add monthly trend of definite AA, complicated AA (gangrenous, ...), and pseudoappendicitis, using joint-point	Dear editor, Unfortunately, our dataset doesn’t include the exact date of admission.	

Comments		regression analysis (strongly recommended).	Thus, we cannot do this suggestion. Nevertheless, our dataset can be sent to the editor for confidential purposes.	
Associate Editor's Comments	2	What is the significant p-value in your study?? "Also, patients with positive tests for COVID had statistically higher hospitalization duration."???? No information is provided in the results section!!! What and where are the statistical results?	Thank you for the comment. All the results are represented in tables (1-3). Also, the result section includes a lot of p-values. If you mean the results section of abstract, I have added the required p-value at the end of that section.	Highlighted in yellow on Page 2, Line 20.
Associate Editor's Comments	3	Abstract: "Methods: In a retrospective observational cohort study, we enrolled all the patients ..." add eligible patient's age.	This modification has been done.	Highlighted in yellow on Page 2, Line(s) 11-12.
Associate Editor's Comments	4	remove phlegmon, add "SARS-CoV-2"	The required modification was done in the keywords.	Highlighted in yellow on Page 3, Line 29.
Associate Editor's Comments	5	In the "Material and methods", Study design section: First, this is not an "observational retrospective cohort study," your study is an example of a "cross-sectional analytical study", correct study type in the whole text.	Thank you for your reminding. I have changed all the “cohort” terms to “cross-sectional analytical study”	Highlighted in yellow on Page 2, Line 10 and Page 6, Lines 65-68
Associate Editor's Comme	6	Second, replace "perioperative circumstances" with better words. "circumstances" is not informative.	Thank you for your reminding and suggestions. I have changed the suggested comment. I removed the “Perioperative circumstances”, and	Highlighted in yellow on Page

nts			added a more clear term (significant changes in the course of the disease)	6, Line(s) 67-68.
	7	The following statement starts with unclear words: "For screening of the cases during the pandemic, ...", what did you intend to screen?	For having a safer operating room for the personnel, scrub nurses, technologists, and doctors, all the patients who require surgery, should have some kind of COVID screening. For being more clear, I have inserted a statement at the beginning of aforesaid paragraph.	Highlighted in yellow on Page 7, Line(s) 94-95.
Associate Editor's Comments	8	Third, in the "Inclusion and exclusion criteria" section, did you exclude possible MISC with acute abdomen? Also, define this statement clearly: "Also, only the cases who underwent surgery were included the study.", Open surgery? laparoscopic surgery?	These modifications have been made in the inclusion and exclusion section.	Highlighted in yellow on Page 7, Line(s) 107-108.
Associate Editor's Comments	9	Forth, replace "(Kurtosis and skewness)" with a proper test used for testing normality such as Shapiro–Wilk test or Kolmogorov–Smirnov test.	Special thanks to you for your good comments. We replaced the words kurtosis and skewness with “Kolmogorov–Smirnov”, and highlighted in the text.	Highlighted in yellow on Page 8, Line 121

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2 Revision 1

1 comment · 17 Sep 2022

Associate Editor

MINOR REVISION 17 Sep 2022

Editorial comments
Dear authors
The manuscript's overall presentation improved after amendments. Although your replies to the concerns of the reviewers are satisfactory, the authors should consider the following shortcomings:
Use a similar style for "COVID-19" throughout the manuscript. Remove other unfamiliar styles such as "COVID".
Regarding my comment in the previous round, "Add monthly trend of definite AA, complicated AA (gangrenous, ...), and pseudoappendicitis, using joint-point regression analysis (strongly recommended).", your response is not acceptable. You can simply use joint-point regression analysis with the raw frequency of definite AA and complicated AA.
Lines 216-217: the following statement needs to be clearer. "There was a significant increase in complicated AA (21%) [before/after COVID-19 pandemic??] while the rate of uncomplicated AA was diminished notably [before/after COVID-19 pandemic??]"
Lines 218: the following statement needs to be clearer. "increase in complicated AA in this period [during COVID-19 pandemic??]"
Lines 225-227: Rewrite the statement. My suggestion: "We found a statistically non-significant increase (1.9%) in the frequency of perforated appendicitis during the COVID-19 pandemic in our study."

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Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editor-in-Chief

Thank you for your time reviewing our paper entitled "**Effects of COVID-19 pandemic on the incidence of complicated appendicitis in pediatric population**". I sincerely appreciate your suggestions and modifications. Your pieces of advice were very helpful and gave us a new comprehensive perspective on the way of writing our study.

Now, we have applied the comments and corrected the errors.

Thank you once again for all the support and assistance you put in.

It would be great if you consider following comments in response to your outstanding reviewers:

Reply to the reviewers' comments

Reviewer Number	Comment Number	Original comments of the reviewer	Reply by the author(s)	Changes done on page number and line number
Associate Editor 1	1	Use a similar style for "COVID-19" in the whole manuscript. Remove other non-familiar styles such as "COVID".	I have changed all the "COVID" words to a similar style "COVID-19"	All changed words are marked

				with a green highlight throughout the text.
Associate Editor 1	2	Regarding my comment in the previous round: "Add monthly trend of definite AA, complicated AA (gangrenous, ...), and pseudoappendicitis, using joint-point regression analysis (strongly recommended).", your response is not acceptable. You can simply use joint-point regression analysis with the raw frequency of definite AA, and complicated AA.	Thank you for reminding this shortcoming. I have performed the analysis using NIH cancer's join point regression software. The final plot graph with respective monthly trend has been added as Figure2.tiff. Also, this figure is mentioned within the text.	Highlighted in green On Page 10, Line(s) 155-156
Associate Editor 1	3	Lines 216-217: the following statement needs to be more clear. "There was a significant increase in complicated AA (21%) [before/after COVID-19 pandemic??] while the rate of uncomplicated AA was diminished notably [before/after COVID-19 pandemic??]"	Thanks for your point. I have added some statements after those phrases to be more clear.	Highlighted in green On Page 14, Line(s) 217-218
Associate Editor 1	4	Lines 218: the following statement needs to be more clear. "increase in complicated AA in this period [during COVID-19 pandemic??]"	I have added the adverb "during the pandemic"	Highlighted in green On Page 14, Line(s) 219
Associate Editor 1	5	Lines 225-227: Rewrite the statement. My suggestion: "We found a statistically non-significant increase (1.9%) in the frequency of perforated	Thank you so much for taking the time to modify the sentence. I have replaced the existing sentence with your suggested phrase completely.	Highlighted in green On Page

		appendicitis during the COVID-19 pandemic in our study."		14, Line(s) 227-229

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3 Revision 2

1 comment · 9 Oct 2022

Associate Editor

ACCEPT 9 Oct 2022

I read the revised manuscript.
I have no further comments to add. I thank the authors for their very detailed replies to my comments.