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OPEN PEER REVIEW

Clinical Characteristics and Outcomes of COVID-19 in Pediatric Cancer Patients: A Retrospective Cohort Study

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1 Original submission

4 comments · 20 Aug 2024 – 14 Sep 2024

Referee 1 Reviewer

MINOR REVISION 20 Aug 2024

Dear Author
Thank you for your submission.
This is a well-written and systematically designed article.
Abstract:
1- What does this sentence mean "Ground-glass opacity on chest imaging was significantly associated with case control (p=0.003)."?
Method:
2- What is score matching? Is it necessary to describe how this matching is implemented?
Discussion:
1- The difference between malignant and nonmalignant COVID19 groups refers to the nature of their malignancy in the case group. Please check this fact.
Conclusion:
1- Please shorten this part.
Best Regards

Referee 2 Reviewer

MINOR REVISION 5 Sep 2024

The article needs native editing.

Referee 3 Reviewer

MAJOR REVISION 13 Sep 2024

Dear Editor,

I have reviewed the manuscript and offer the following recommendations for the authors' consideration:

1. The term "Retrospective case-control study" should be revised to reflect the analysis of prevalent cases. The authors are advised to not state "Retrospective case-control study".
2. P-values must be consistently reported to three decimal places.
3. Odds Ratios should include 95% confidence intervals.
4. The conclusion should be rephrased to ensure it aligns with the study's findings and interpretations. The conclusion has provided a general recommendation.
5. The small sample size is a significant limitation, impacting the assessment of confounders. The authors' claims regarding confounder analysis should be substantiated with relevant data.
6. The analysis should incorporate multiple logistic regression to provide adjusted odds ratios.
7. All odds ratios cited in the text and tables must include 95% confidence intervals.
8. Table 1 needs revision to include percentage data and clearly state the Case and Control groups in the header.
9. The discussion should address the sample size's adequacy in evaluating the exposure-outcome association, to be noted in the limitations section.

10. The methods section should include comprehensive details regarding the matching techniques employed.
Thank you for the opportunity to review this manuscript.

Sincerely,

Associate Editor

MINOR REVISION 14 Sep 2024

Dear AUTHOR
Thank you for your submission.
1- Please review the tables and charts.
2- Matching is an important part. Please clarify the process to confirm the correctness of the results.
3- Please follow the reviewers' recommendations.
Best 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.

To the Editorial Office,

Thank you for inviting us to resubmit a revision of our manuscript, entitled "**Clinical Characteristics and Outcomes of COVID-19 in Pediatric Cancer Patients: A Retrospective Case-Control Study**". All parts of the manuscript have been modified according to the suggestions of the reviewer and the corrections are specified by using track changes mode. We have attached a point-by-point response to each reviewer's comments below and hope our manuscript can now be accepted for publication.

Best regards,
Sh. K.
September 15, 2024

Point-by-point response “Clinical Characteristics and Outcomes of COVID-19 in Pediatric Cancer Patients: A Retrospective Case-Control Study”

Reviewer #1

This is a well written and systematic designed article.

Abstract:

What does this sentence mean "Ground-glass opacity on chest imaging was significantly associated with case control (p=0.003)."?

Response to reviewer

It is corrected in the text and highlighted in yellow. It was a typo.

Method:

What is score matching? Is it needed to describe how this matching is implemented?

Response to reviewer

Propensity score matching is a quasi-experimental method in which the researcher uses statistical techniques to construct an artificial control group by matching each treated unit with a non-treated unit of similar characteristics. We selected 105 patients out of 1208 patients with COVID without malignancy to be able to compare 2 groups of case and control. This technique in statistics is named as: “Propensity score matching”.

Discussion:

The difference between malignant and non-malignant COVID19 groups refers to the nature of their malignancy in the case group. Pls check this fact.

Response to reviewer

As long as the majority of the cases were leukemia in 34.3% and brain tumors in 14.3% and the other malignancies were distributed unequally, a conclusion based on the nature of each malignancy cannot be taken. It is also very unlikely that the specific type of malignancy will impact the clinical, hematological or radiologic findings of the COVID. In addition, it is not discussed in the literature elsewhere.

Conclusion:

Pls brief this part

Response to reviewer

We changed this section to a briefer one.

Reviewer #2

The article needs native editing.

Response to reviewer

It was re-edited.

Reviewer #3

I have reviewed the manuscript and offer the following recommendations for the authors' consideration:

Comment 1: The term "Retrospective case-control study" should be revised to reflect the analysis of prevalent cases. The authors are advised to not state "Retrospective case-control study".

Response to reviewer

Upon careful consideration of your feedback and re-evaluation of our study design, we have revised our terminology throughout the manuscript. We have changed "retrospective case-control study" to "retrospective cohort study" as this more accurately reflects our methodology of comparing two groups of patients (those with and without malignancies) who all had confirmed COVID-19 infection.

Comment 2: P-values must be consistently reported to three decimal places**.**

Response to reviewer

We have carefully reviewed all p-values throughout the manuscript and have updated them to be consistently reported to three decimal places. This change has been applied to all tables and text where p-values are mentioned.

Comments 3: Odds Ratios should include 95% confidence intervals.

Response to reviewer

We appreciate your suggestion and have updated reported “OR” in the manuscript to include its respective 95% confidence intervals.

Comment 4: The conclusion should be rephrased to ensure it aligns with the study's findings and interpretations. The conclusion has provided a general recommendation.

Response to reviewer

It is rephrased.

Comment 5: The small sample size is a significant limitation, impacting the assessment of confounders. The authors' claims regarding confounder analysis should be substantiated with relevant data.

Response to reviewer

We appreciate the reviewer's insightful comment regarding our sample size and confounder analysis. We acknowledge that our study's sample size (210 children, 105 in each group) is relatively small, which indeed limits our ability to conduct comprehensive confounder analyses. To address this limitation, we propose the following changes to our manuscript:

-In the Methods section, we will add a paragraph detailing our approach to confounder analysis, given our sample size constraints. We will explain that we used propensity score matching to control for age and sex, which were the most crucial potential confounders given our study design.

-In the Discussion section, we will expand our limitations paragraph to explicitly state: "The relatively small sample size of our study (210 children) limited our ability to conduct comprehensive confounder analyses. While we controlled for age and sex through propensity score matching, other potential confounders such as specific cancer types, treatment status, and comorbidities could not be fully accounted for in our analyses."

-We will add a sentence in the Conclusion suggesting that "Future studies with larger sample sizes are needed to more robustly assess the impact of potential confounders on COVID-19 outcomes in pediatric cancer patients."

Comment 6: The analysis should incorporate multiple logistic regression to provide adjusted odds ratios

Response to reviewer

In response to your recommendation, we have incorporated multiple logistic regression analysis into our study to adjust for potential confounders. For the imaging findings, we now report the adjusted odds ratios (ORs) along with their corresponding 95% confidence intervals (CIs).

Comment 7: All odds ratios cited in the text and tables must include 95% confidence intervals.

Response to reviewer

Revised.

Comment 8: Table 1 needs revision to include percentage data and clearly state Case and Control groups in the header.

Response to reviewer

Revised.

Comment 9: The discussion should address the sample size's adequacy in evaluating the exposure-outcome association, to be noted in the limitations section.

Response to reviewer

Thank you for your helpful feedback. In response to your comment, we have revised the Discussion and Limitations sections to address the adequacy of the sample size. Specifically, we acknowledge that 1,313 eligible children were considered, and 105 cases with concurrent malignancies were included, matched by age and sex to 105 controls without malignancies. While

this matching strategy improves comparability between groups, we discuss the possibility that the relatively small number of cases may limit the statistical power to detect smaller associations, particularly for subgroup analyses. We have added this point to the revised manuscript in both the Discussion and Limitations sections.

10. The methods section should include comprehensive details regarding the matching techniques employed.

Response to reviewer

Revised.

Associate Editor's Comments:

1- Pls review the tables and charts

2- Matching is an important part, Pls clear the process to confirm the correctness of results

3- Pls follow the reviewers' recommendations

2 Revision 1

3 comments · 3 Oct 2024 – 15 Oct 2024

Referee 3 Reviewer

ACCEPT 3 Oct 2024

The authors have revised the manuscript in light of the comments.

Referee 1 Reviewer

MINOR REVISION 5 Oct 2024

Dear AUTHOR
THANK YOU FOR THE REVISION
The review is complete and comprehensive.
---The most important point is the possibility of differences in hematologic indexes because of the nature of the malignancy, so it is important to know the type of malignancy. Please check this with your statistical adviser.
- The exclusion criteria are from inpatient cases. It is recommended to recheck this point.
Best Regards

Associate Editor

ACCEPT 15 Oct 2024

Dear Author
Thank you for your submission.
Please check the reviewers' recommendations.
If everything is in order, the article is accepted.
Best Wishes