

Peer Review File

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Reviewer A

Thank you for the opportunity to review this interesting manuscript.

The results obtained are important and reliable. The objectivity is clear. All procedures in the section Material and Method are well describe. The risk factors associated with community-acquired Clostridioides difficile diarrhea in children was seen.

Some minor revisions or questions

Line 33 reporting the type of study is more appropriate for the methods.

Thanks for your suggestion. We have modified our text as advised (see Page 1, line 33).

Could you analyse type of antibiotics in multivariate logistic regression analysis?

We have carefully considered your opinion. Because the type of antibiotics was not statistically significant in the univariate analysis process, we did not include this factor in the multivariate analysis.

After χ^2 test/t-test, the possible risk factors which statistically significant variables were included in the conditional logistic regression model for stepwise regression analysis (we have modified our text, see Page 7, line 224-228). Thanks.

Reviewer B

1) First of all, the pediatric patients were from only one hospital in Chenzhou, so in the title “in Chenzhou” and elsewhere this term is overstated. The authors should corrected this.

Thanks for your direction. We have carefully discussed your suggestion. Because the Children's Hospital of the First People's Hospital of Chenzhou City is the only comprehensive hospital for children in the Chenzhou region of China, with approximately 90% of pediatric patients seeking medical treatment in the hospital, which can basically represent the characteristics of the Chenzhou region, we have used this title.

2) Second, the abstract is not adequate. The background did not clearly describe the rationale for this study, which should not be “understand this trend”. Risk factor analysis in general is for prevention. The methods need to describe the inclusion of patients, how the controls were selected and matched individually, and measurements of potential risk factors. The current conclusion should be tone down due to the small sample size of patients and no longitudinal cohort design.

We have supplemented the abstract as advised, see Page 6-7, line 197-205; Page 3, line 71-72

3) Third, the introduction of the main text needs to review what has been known on the risk factors of CD in adult patients and the limited number of studies in pediatric patients, analyze the knowledge gaps and limitations of prior studies, and importantly clearly indicate the potential clinical significance of this study. Again, the purpose of case-control studies is not “increasing trend”.

Thank you. We have supplemented the introduction according to your advice, see Page 3-5, line 94-142.

- 4) Fourth, in the methodology of the main text, the authors need to describe the sample size estimation procedures. The small sample size is my major concern. Please specify the source population of controls. Rationale for these selected potential risk factors should be provided. In statistics, please describe the process of selecting factors into the multiple conditional logistic regression and how the final set of factors were selected, as well as the effect size measure for the identified factors. Please ensure $P < 0.05$ is two-sided.

First of all, I strongly agree with your point of view, so we have made a serious supplement. On the one hand, we estimated the sample based on the colonization rate of *Clostridium difficile* in children mentioned in previous studies (see Page 5, line 149-152), and on the other hand, we further explained the sample in the conclusion section and hope for improvement in future studies. I hope to receive your recognition. Thanks.

The statistical methods section has also been supplemented according to your opinion (see Page 7, line 224-228). Thanks

- 5) Finally, please consider to review and cite several related papers: 1. Wang C, Li Z. *Clostridium difficile* infection occurred after radical hysterectomy for cervical cancer—a case report. *Gynecol Pelvic Med* 2021;4:10. 2. Kanika Sehgal, Paul Feuerstadt. The real efficacy of microbiota restoration following standard of care antimicrobial in patients with recurrent *Clostridiodes difficile*. *Transl Gastroenterol Hepatol* 2023 | <https://dx.doi.org/10.21037/>.

Thanks. We have already cited these two papers.