

Peer Review File

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Reviewer A

It has been common sense about neutropenia, lymphocytopenia, and thrombocytopenia in influenza A. Therefore, it is not surprising that LMR*PLT is low from blood routine tests of influenza A+ patients. Unfortunately, this result alone is not novel. However, it would be interesting to see how it compares to COVID-19 or other viral infections. Please show a detailed analysis of the A- group and how it differs for each virus. If the authors show the detailed data, this manuscript would be high-quality paper.

Response:

We thank the reviewer for reading our paper carefully and giving your professional correction comments. As you are concerned, a detailed analysis of the non- influenza A patients and the difference from other virus infections would make our article more interesting. However, the composition of A- group were not sufficiently considered in our study design. In our design, we grouped patients into A+ and A- groups by strict criteria and mainly focus on the changes of blood routine parameters.

According to your nice suggestions, we have made corresponding corrections to our manuscript. To delineate the clinical traits of other pathogen infections in A- group, we retrieved the clinical data of 277 children in A- group, and found that 13 of them have perfected the pathogen DNA detections. Moreover, five patients had been confirmed the other pathogen infections, including one mycoplasma infection, three Epstein-Barr virus infection and one human rhinovirus infection. Due to the small sample size tested for other pathogens, we hardly statistically compared the blood routine characteristics of children infected with other pathogens with the children infected with H1N1. However, your suggestions are extremely valuable for us, and we will expand the examinations of other pathogens infections in A- group and provide detailed data in our future studies.

Reviewer B

First of all, this is only a screening test by using blood routine test for influenza A, not a diagnostic test. The authors need to revise the whole paper including the title accordingly. The title also needs to indicate the clinical research design of this study.

Response:

Thank you for your advice. We have revised “diagnostic test” to “screening test” in the whole paper including the title. We are sorry for this ambiguous study design. As you are concerned, we have checked the study design of our article carefully and revised the title of our article as “The blood routine test holds screening values for influenza A in 2023: A retrospective study ” (see Page1, line 1-2).

Second, the abstract needs some revisions. The introduction did not indicate why the addition of blood routine test had potential screening value and what the current knowledge gap was. The methods need to describe the diagnostic method for influenza A, inclusion criteria, test methods for blood routine test, and the calculation of screening accuracy indicators. The results need to describe the sample sizes of the three groups. The screening accuracy parameters are not satisfactory, so the authors need to rephrase the current conclusion.

Response:

Thank you for your advice. We are sorry for this unclear expression of abstract. As you are concerned, we have added more introduction about the potential screening value of blood routine and current knowledge gap (see **Page 3, line 48-56**). Moreover, we have detailed describe the diagnostic method, inclusion criteria, test methods for blood routine test, and the calculation of screening accuracy indicators in the abstract and main text (see **Page 3, line 58-64**). As you are concerned, we have added the sample sizes of the three groups in the abstract and main text (see **Page 4, line 68-69**). To improve the screening accuracy parameters, we apply logistic regression to explore the optimal combinations of different parameters for the screening of influenza A. The results demonstrate this logistic regression model is more accurate than before (see **Page 4, line 76-79**) and we have rephrased the current conclusion according to our results (see **Page 4, line 81-82**).

Third, the introduction of the main text is poor. The authors did not review why the blood routine test could improve the screening accuracy of influenza A, did not review the literature of this research focus, and did not analyze the current knowledge gap. My further major concern for this study is the poor screening accuracy parameters in this study. In fact, this is a failed screening test of blood routine test for influenza A.

Response :

Thank you for your advice. We have reviewed the application of blood routine test in the screening of influenza A and reviewed the current progress in this area (see **Page 5, line 100-101; page 6, line 106-108**). Indeed, the screening accuracy parameters are not very satisfactory in our study, probably because the small sample size, individual difference, disease subtype and other limitations. However, there are still some advantages in our study. This study were a timely study focusing on the screening test of influenza A after covid-19 infection in 2023, which might provide potential clinical value. Furthermore, the grouping strategy of suspected patients in this study is according to the rapid antigen test instead of nucleic acid testing. Although the sensitivity of rapid antigen test is lower than nucleic acid testing, it still has the advantages of high specificity, lower cost and higher speed. To improve the screening accuracy, we have established a logistic regression model, as mentioned **in our Response of Comment 2nd**.

Fourth, in the methodology of the main text, please describe the clinical research design and sample size estimation procedures. In statistics, please consider the combination of these blood test parameters to improve the screening accuracy and provide the threshold values for these accuracy parameters for a good screening test.

Response :

Thank you for your advice. We are sorry for this unclear description about study design and sample size estimation. We have further provided a detailed description of clinical research

design in figure 1 (see **Page 6, line 111**). Besides, we have estimated the minimal samples required in our study by PASS (see **Page 6, line 112; Page 8, line 152-154**). Then, we further expanded the sample size to improve the accuracy and reliability. Moreover, logistic regression was used to further explore the screening value of the combination of different parameters. Interestingly, we found this logistic regression model based on all blood routine parameters significantly improve the screening accuracy for influenza A (see **Page 7, line 146-149; Page 11-13, line 197-224; Page 16, line 279-282; Page 17, line 297-298**).

Finally, please consider to cite some related papers: 1. Han S B, Rhim JW, Kang JH, Lee KY. Clinical features and outcomes of influenza by virus type/subtype/lineage in pediatric patients. *Transl Pediatr* 2021;10(1):54-63. doi: 10.21037/tp-20-196. 2. Jing J, Wang L, Wang G, Dai Z, Ren W, Yi C, Wei J, Xu C. A human infection case with avian-origin H10N3 influenza virus. *Quant Imaging Med Surg* 2021;11(10):4508-4510. doi: 10.21037/qims-21-592. 3. Cite this abstract as: Tsang HTT, Mok CH. AB004. All-cause mortality of seasonal influenza vaccination among the elderly: a systematic review and meta-analysis. *J Public Health Emerg* 2021;5:AB004. 4. He J, Zhang G, Wang Y, Yang H, Dai Q, Guo S, Mai J. The possibility of automatic capillary blood testing in routine blood tests: an evaluation of the automatic mode of the Mindray BC-7500 CRP Auto Hematology Analyzer for capillary blood testing. *Cardiovasc Diagn Ther* 2023;13(3):465-473. doi: 10.21037/cdt-23-84. 5. Sun M, He X, Mao L, Ma T, Deng J, Gao L, Wang P, Chen G. Correlation analyses between age and indices in routine blood laboratory tests suggest potential aging biomarkers. *Ann Blood* 2022;7:36.

Response :

Thank you for your suggestions. We have read these recommended literatures carefully and cited three of them in appropriate position of our article (see **Page 5, line 89; Page 6, line 119; Page 6, line 125**).