

Infection and co-infection patterns of common upper respiratory tract viruses in patients with flu-like symptoms attending a fever clinic of a tertiary care hospital during the COVID-19 pandemic

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Technical review

Reviewer's information			
Date review assigned	14-Oct-23	Date review completed	1-Dec-23
Reviewer name	Rijwan Bhuiyan	Do you have any conflict of interest with the author/s?	No
ORCID	0000-0003-0005-8889	Do you wish to be disclosed to the author?	Yes
Reviewer's comments (13-Dec-23)		Yes/No	Author's response (12-Mar-24)
			[Please write a response if score is less than 6. You must change the manuscript as per your response. Mention line numbers.]
1.	Is the title appropriate?	Yes	-
2.	Is the research question or study objective clearly defined in measurable terms?	No	Revised the objective
3.	Is the abstract accurate, balanced and complete?	No	Revised the abstract
4.	Is the study design appropriate to answer the research question or achieve objective?	Yes	-
5.	Are the Methods described sufficiently to allow others to repeat it?	No	Re-write the Methods section.
6.	Are the operational definitions and ascertainment of key variables given adequately?	No	Revised
7.	Are the outcomes clearly defined?	Yes	-
8.	Are statistics used appropriately and described fully?	No	Revised
9.	Do the Results address the research question or objective clearly?	Yes	-
10.	Are the tables and figures clear and appropriate to address the objective or research question?	Yes	-
11.	Does the Discussion cover the main points of the paper?	No	Revised
12.	Are the strengths and limitations addressed?	Yes	-
13.	Are the conclusions justified by the results?	Yes	-
14.	Are the references up-to-date, and appropriate?	Yes	-
15.	Is the standard of written English acceptable for publication?	Yes	-
Major points			
Abstract			
1.	The objective is not clear. Seems the author stated two objectives. Please revise it in understandable way or separate it into two sentences. For example "To determine the infection and co-infection patterns of common upper respiratory tract viruses in patients with flu like symptoms attending in the fever clinic of a tertiary care hospital during COVID-19 pandemic".		1. Objective is updated according to your example.
2.	Methods seem too small to understand the study procedure. Need a balance between Results and Conclusion.		2. Methods revised as instructed (Page – 2, line 30-32).

Reviewer's information	
3. Conclusion is the repetition of the results. Suggested to state the main message of this study.	3. Conclusion revised as instructed (Page – 2, line 39-40).
4. Highlights points rarely reflect the primary message, strength and selling points of this study.	4. Revised as instructed (Page-2, line 48).
Introduction	
5. Overall, the introduction is not well structured. It seems like gathering information from various sources. Used lots of numbers and figures. Suggested to revise as “Funnel” shape to bring the reader from a wider context to the narrow objective. The author should state why this study is important/ rationale?	5. Revised as instructed. Introduction is rearranged and made “Funnel” (Page-3,4). Rationale and more importance was there before, now rearranged (page-3, line 54-55, 76-80; Page-4, line 85-87).
6. Lines 65 to 68 – Have redundant texts. Advised to make shorter, focusing only on the results and year.	6. revised as instructed. (Page-3, line – 68-70).
7. Lines 73 to 77 – Can reduce the word count by removing “dashboard information statement...” and referring to the references.	7. The lines were removed to make more focused on the objective.
8. The objective stated in abstract and in introduction seems little different. Here author mentioned “to detect the causative viruses and infection rate...” which is confusing.	8. Objective updated as instructed. (Page-2, line 28-30; Page-4, line-89-91).
Methods	
9. Overall, the methods section does not give a clear message to the reader about how this study was done. Suggested to explain such a way that is reproducible for other researchers.	9. Revised as instructed (Page5,6).
10. How 288 patients were randomly selected from the fever clinic from Nov 2021 to Mar 2022 was not clearly mentioned. The total number of patients reported in the outdoor fever clinic during the given time period? How this figure (n=288) has been determined? Sample size calculation?	10. Revised as instructed. Flow chart added for patient selection (Page-5, flowchart 1). Sample size calculation from study added as reference (Page-5, line-114). Financial constraints is mentioned.
11. The statistical part was not well written. Suggested to provide a separate section for statistical analysis, explaining how data were collected, explain the variables used for statistical analysis. etc...	11. Statistical part was mentioned in the study. Data collection criteria was mentioned in flow chart and also starting of methods (Page-5, line 110-112).
12. How were the ethical issues addressed? Was the patient consented? Is there any dropout? Who collected the data? The author can provide a flowchart for patient selection and randomization.	12. Ethical issue addressed (Page-11, Line 268-270). Written consent were taken (Page 12, line-274), No drop out. Author collected the data (Page - 12, line 276).
13. The operational definition of clinical symptoms used in this study for data collection is suggested to explain.	13. As the clinical symptoms were self-explanatory and common to clinicians hence, operational definitions were not explained.
Results	
14. The results section a lack of comprehensiveness to understand the main message.	14. Revised as instructed. (Page – 7-9).
15. Line 164 to 168 – Repetition of Figure 1. The author can state the key findings in one sentence and refer to Figure 1 for details information.	15. Revised as instructed (Page – 7, Line – 167-168).
16. Line 176 to 178 – Only text is enough to explain the status. Figure 2 seems redundant.	16. Revised as instructed. Figure -2 is deleted.

Reviewer's information	
17. Line 191 to 194 – Same suggestion as mentioned for line 164 to 168.	17. Figure deleted as it is also present in table -1 (Page-8).
18. Line 191 to 194 – “Among the participants who had respiratory viral infection, 48 (16.7%) were positive for SARS-CoV-2 followed by 42 (14.6%) for Human Rhinovirus, 16 (5.6%) for Adenovirus, 1 (0.3%) for Respiratory Syncytial virus, 1 (0.3%) for Influenza B and 10 (3.5%) were positive for Parainfluenza. However, no sample was found positive for Influenza A.” according to the statement the percentage calculation is not correct. Please check this and explain accordingly.	18. Explained as advised (Page – 8, line 177-183).
19. Table 1 has the repetition of the figure 3. Figure 3 can easily replaced by Table 1 adding the percent of total viruses. The total n shows 288 but the infection found 101 patients which is questionable. Author should clear the denominator. Title of table 1 mentioned “Infection rate...” which is misleading and wrong. Appropriate choice of word is crucial. Here can explain like “Pattern of viruses among infected patients...”	19. Figure -3 is replaced and only table 1 is kept (Page-8), Title changed as advised (Page -8, line - 184).
20. Table 2 can be visualized in a column chart and will be more understandable.	20. Table 2 is deleted as monthly variation has little to tell in this study, according to advise of another reviewer.
21. Line 238 – The term “Co-infection rate” is incorrect. This is simply a prevalence.	21. Revised as instructed (Page – 9, line 199).
22. Discussion: Overall the discussion is the repetition of the results and just matching the findings with other studies. Rarely explained the reasons and the clinical implications of these findings. Suggested to make it small (within 500 words), reduce the repetition of the results and explain in line with the main objectives in separate paragraphs.	22. Revised as instructed (Page-10,11) (word count - 551).
Limitation	
23. Sample size determination was not explained in the Methods section. Need to logicalize why this is small.	23. Revised as instructed (Page-11, Line 255 - 257)
24. How out-door patients’ collection is a limitation when the study was fully done for outdoor patients. The author can explain the possible confounding factors of the outdoor patient collection approach that may affect the study findings.	24. Revised as instructed
25. If the study was done for 18 and above this should not be a limitation, rather can explain focusing on this age group.	25. Revised as instructed.
Minor points	
26. Title seems little confusing. Could be like “Infection and co-infection patterns of common upper respiratory tract viruses in patients with flu like symptoms attending in the fever clinic of a tertiary care hospital during COVID-19 pandemic”.	26. Revised as instructed. (Page – 1, line 4,5).
27. Line 116 to 123 – Can be explained in a single sentence with the reference of maintaining standard procedure of swab collection and storage.	27. Kept as before for better understanding (Page 6 line 135-140).
28. Line 124 to 134 – Can be explained within 2 to 3 small sentences using reference of standard procedure.	28. Total 3 types of kit is used for molecular detection; hence it is kept as it is (Page 6, line 144 - 155).

Reviewer's information	
<p>29. Figure 1 can be ordered from ascending to make a clear visualization. In Y-axis only %/ percent is enough. Keep uniform digits after the decimal point or can-do rounding for better understanding.</p> <p>30. Maintain uniform digit after the decimal point throughout the document. Suggested to keep "One" digit after decimal point.</p> <p>31. Odd issue: In author contributions, only three authors contributed to manuscript drafting and final approval of the manuscript. To be an author of others is questionable.</p>	<p>29. One digit after decimal point is kept. More common symptoms are kept first and the less common symptoms are kept at last. (Page 7).</p> <p>30. Revised as instructed.</p> <p>31. Revised as instructed.</p>
Reviewer's Recommendation	Revisions Required

Responsible Editor's comments (13-Dec-23)		Author's response (13-Mar-24)
Name	M Mostafa Zaman	[Please write a response each points. You must change the manuscript as per your response. Mention line numbers.]
ORCID	0000-0002-1736-1342	
1. The objective has to be clearly defined. Does the study aim to determine infections (and co-infections) in patients who attended the Fever Clinic? Or Co-infections with SARS-COV-2 infections? Does it aim to examine sex differences in infections and co-infections. Does it aim to examine the seasonality? These have implications on the subsequent storytelling (and analysis).		1. Objective and aim revised as instructed. Seasonality is omitted. Others also revised as instructed.
2. If identification of seasonality is an issue, the study should have been done for a cycle of 12-months.		2. Seasonality is omitted.
3. What is the practice implication know the infection and co-infection? The objective and Discussion should have made it clear. The Introduction should have focused description to justify the work rather than adding a story of children with SAM in icddr's hospital.		3. Introduction, objective and discussion is revised as instructed.
4. Methods should clearly mention about the number of subjects who attended the Fever Clinic during the study period. Then describe how the randomization was done. This is necessary to learn about the study subject's representativeness to the all patients of the Fever Clinic. I suggest adding a flowchart indicating the number of subjects at all stages. Please use a template from the EQUATOR website.		4. Number of subjects attended the fever clinic were not same every day. Again, subjects came for various reason eg, COVID screening, travelling, elective surgery hence, number of subjects came to fever clinic were not counted rather symptomatic criteria and consent was taken into account. Template was added from MSword. (Page 5, Flowchart 1).
5. Which statistical analysis was done (line 135-136)?		5. Extremely sorry for not finding, which one was you telling about.
6. Figure 2 information could easily be given in text description. Please drop it.		6. Figure 2 dropped and added in text description (Page-8, line 177-178).
7. Why we need Table 1? Does this address any objective of the study? If we drop separate data for sexes, this table will provide the same data given in Fig 2. Therefore, this table can be dropped.		7. Table 1 is kept and figure 3 is dropped as they are giving the same data (Page 8). This table is important to know the pattern of infection of viruses during this period. Though, male and female are almost equally infected but, few journal showed differences, hence it is shown. (Page – 10, Line 236-240).

<p>8. Statistical analysis for Table 2 is not correct. Kruskal-Wallis test is used for quantitative data. Here you present categorical data. It is not clear how all viruses were separately tested statistically. The Methods section should make it clear. Monthly variations given in this table should not be labelled as seasonal variation. The monthly data could be presented in a graph to create a visual impression.</p> <p>9. Seventeen co-infections split in to so many categories does not provide a valid statistical analysis. I suggest reducing number of graphs and tables to maximum three.</p> <p>10. Conclusion: I suggest making the manuscript suitable for a Brief article of 1500 words, 200-word abstract, using three data visuals (tables or graph), and 20 references. However, the revised version will be subject to another round of review.</p>	<p>8. Table 2 is omitted.</p> <p>9. Prevalence of co-infections is shown (page-9, table -2) no statistical analysis given. Graphs and tables reduced to only 3 (page 7-9).</p> <p>10. Manuscript is shortened within 2085 words, 224 words abstract, 1 graph, 2 tables and 23 references.</p>
Editor's Decision	Major Revision

Final decision of the Executive Editor (14-Mar-24)	ACCEPT We shall edit the manuscript soon.
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