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Manuscript Type: SYSTEMATIC REVIEWS

Title: "Cytomegalovirus pulmonary infection: Case Report and Systematic Review."

Short title: CMV pneumonia: Systematis review

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Author contributions: Both authors contributed to writing and reviewing the final  
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<b><u>Answers</u></b>	<b><u>to</u></b>	<b><u>Reviewers</u></b>
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Reviewer 1

The manuscript is case bases systematic review on CMV in immunocompetent and  
and immunocompromised patients. It is a important topic but many comments need  
to be addressed.

*Thank you so much for taking the time to review our manuscript on CMV infection. Your  
comments and suggestions are greatly appreciated, and we are thankful for the opportunity to*

*improve our work. Again, thank you for your valuable input, and we look forward to submitting an improved manuscript.*

1. why you are correlating COVID-19 with CMV? Your study is based on CMV meta analysis?

*Thank you for your question. While our study is focused on CMV infections in immunocompetent and immunocompromised patients, we made a brief mention of COVID-19 in relation to the case presentation. The reason for this correlation is that both CMV and COVID-19 can present with similar clinical features, including fever, respiratory symptoms, and abnormal liver function tests. Additionally, both infections can affect both immunocompetent and immunosuppressed individuals. Given the current global pandemic, it is important to consider COVID-19 in the differential diagnosis of patients with these symptoms, especially in areas with high prevalence of the disease. However, it is also important to consider other potential causes, such as CMV infection, as early diagnosis and treatment are crucial in improving patient outcomes.*

2. Third para of Introduction "this research aims to demonstrate that CMV lung infection is a rare condition". what is meant by this. your research is not demonstrating this.

*We have suppressed this sentence.*

3. Introduction is not well written and is quite confusing. why this study is important? it should be mentioned in the introduction.

*We have revised the introduction to better address the importance of the study. We have clarified the relevance of the study by highlighting the clinical significance of CMV infection*

*and its potential differential diagnosis with severe COVID-19 in both immunocompetent and immunosuppressed patients.*

4. Please mention the dated in data sources (Material and Methods)

*We apologize for the oversight in not including the date of the search in the data sources section. The search was run on October 22, and we have updated the manuscript to reflect this information.*

5. Please mention about the studies about coinfection of CMV with other bacterial, fungal or parasitic diseases

*Our systematic review aims to analyze the clinical presentation, diagnosis, and treatment of isolated CMV infection in immunocompetent and immunocompromised patients. We have not included studies that specifically focus on the coinfection of CMV with other bacterial, fungal, or parasitic diseases. However, some studies in our review have reported coinfection of CMV with other pathogens. We have included this information in our analysis and discussed the potential implications of these coinfections in patient management.*

6. draw a flow chart showing the main steps of methods and about studies included and excluded

*Figure 2 in our manuscript is a PRISMA flowchart that outlines the main steps of our systematic review process, including the identification, screening, eligibility, and inclusion of studies in our meta-analysis. The flowchart provides a visual representation of the number of studies identified at each stage, the reasons for exclusion of certain studies, and the final number of studies included in our analysis.*

7. Results are insufficient. More results should be added. Results are very brief and is not well written. It is not presenting the exact title and importance of the research.

*We have taken your comments into consideration and have expanded and improved the section to present a more detailed and comprehensive analysis of our findings. We have also ensured that the results are presented in a clear and concise manner that accurately reflects the title and importance of our research.*

8. No graphs are drawn to show the results.

*We have considered the use of graphs, but we believe that in this case, tables are more appropriate for summarizing our findings. We have included Table 1, which provides a clear and concise summary of the data we collected. Additionally, we have added a case report from our clinical practice to better illustrate the disease and its differential diagnosis with COVID-19. We hope that these improvements will make our results section more informative and helpful.*

## Reviewer 2

The paper by Awotar Kanika and Jonathan Soldera propose a kind of meta-analysis regarding cytomegalovirus (CMV) pneumonitis. After a first screening on 445 references in Pubmed (by using cytomegalovirus and pneumonia and respiratory infection, I obtained more than 2000 results!), the authors selected 43 studies reporting 45 case reports of individuals exhibiting this pathology. Then, the paper is limited to a few Tables recapitulating these observations and some general results and to a short discussion paraphrasing the results included in the Table. I am puzzled by the naivety of this analysis that is completely disconnected from the

clinical reality. More than 50 years after the first report of a pneumonia related to CMV, hundreds of patients exhibited this kind of pathology, notably during the first era of AIDS pandemic, with a high number of fatalities. I don't understand how the authors could propose a selection of only 43 studies (less than one per year since 1968) despite the fact that CMV infection is a very common cause of pneumonia and severe respiratory distress in immunocompromised patients. To only give one example of recent paper coming also from the UK, Taherifard et al. reported 12 cases of acute respiratory infection with co-infection by CMV and SARS-CoV-2 in a short review of the literature (Taherifard E, Movahed H, Kiani Salmi S, Taherifard A, Abdollahifard S, Taherifard E. Cytomegalovirus coinfection in patients with severe acute respiratory syndrome coronavirus 2 infection: a systematic review of reported cases. *Infect Dis (Lond)*. 2022;54(8):543-557. doi:10.1080/23744235.2022.2070273). I do not understand the aim of this study. A more interesting angle of view would have been to take into consideration only those CMV pneumonias that occur in immunocompetent individuals. Even if it is very dangerous to withdraw general conclusions from collections of case reports, it would have been more original that the present study that cumulates bias (notably all the recent reports concern atypical situations that merit a case report, often in low-impact journals) and bring no new findings. In addition, there are a lot of spelling mistakes and also a mistake in the reference numbered 29. The PRISMA file is not completed.

*Thank you for your feedback on our paper. We understand your concerns regarding the limited number of studies selected for our meta-analysis, and we have taken your comments into account in our revision. However, we would like to emphasize that our study focuses*

*specifically on isolated CMV infection, and we chose to include studies reporting only on this specific topic.*

*We have expanded the results section and included a case report of severe CMV pneumonitis, which we believe adds value to our paper by illustrating the similarities between CMV infection and COVID-19. We also acknowledge your suggestion to include studies on co-infections of CMV with other respiratory pathogens, and have incorporated this information into the revised manuscript.*

*We appreciate your comments about our writing style and spelling mistakes, and have taken steps to address these issues in our revised version. Additionally, we have reviewed our PRISMA flowchart and corrected any incomplete information.*

*Thank you again for your feedback, and we hope that our revisions have addressed your concerns and improved the overall quality of our manuscript.*