Peer Review File

Article information: https://dx.doi.org/10.21037/jphe-22-77

Reviewer A

Antibiotic resistance is a major public health problem. Procalcitonin is a helpful tool to determine bacterial and non-bacterial infection but its sensitivity and specificity limits its clinical use determining bacterial vs non bacterial infection as PCT level also increase many other inflammatory conditions, Elevated PCT in COVID pneumonia in your study without superadded bacterial infection supports this.

Your study also highlights that symptoms of infection is better marker for superadded bacterial infection compare to PCT level as patients with bacterial infections had symptoms of infection without elevation of PCT.

The important question is what level of PCT is corelate with high risk of bacterial infection or differentiate elevated PCT due to inflammation vs superadded bacterial infection. As you have demonstrated elevated PCT in COVID pneumonia related to inflammation and reflects severity of disease rather than bacterial infection.

Therefore, there is a need to revise guidelines for PCT guided antibiotic therapy for covid pneumonia to decrease antibiotic use, adverse effect of antibiotic including antibiotic resistance.

Reply 1: Guidelines have been developed for antibiotic use based upon PCT levels in the adult lower respiratory tract infections (LRTI):

In our study, using a guideline, 55% of patient could have avoided an exposure to antibiotics Repeat PCT testing could have also been reduced. In the absence of concerning clinical data, repeat PCT may not be warranted, reducing cost without impacting patient safety.

Other key point is only one PCT level is not enough to determine whether elevated PCT due to infection and inflammation, serial PCT is required to determine the acute bacterial infection.

Reply: The literature appears to support use of serial PCTs to de-escalate treatment and provide guidance for exclusionary conditions, such as pregnancy, low creatinine clearance and trauma. We posit that serial testing is only indicated in the higher value groups (>0.24 ng/ml) in this population.

In this study PCT level was included within 72 hours of admission. Use of antibiotic before PCT level may affect PCT level.

Reply: Levels of PCT rise within 2-4 hours of infection onset, peak at 8-24 hours of onset and have a half-life of 24 hours. We agree this represents a weakness in our study. Additionally, patients presented for hospitalization at various times after symptom onset. The onset of symptoms was recorded in our database but is subjective and likely prone to error. However, twenty-seven of the fifty-five patients (49%) a PCT drawn at admission and would thus be concurrent with antibiotic use.

I would suggest if you could provide clear message to your readers as a key point of your study aims, results, interpretations and conclusions about PCT and use of antibiotic in COVID pneumonia and increased risk of bacterial resistance.

The manuscript has been edited as suggested.

Reviewer B

This is an interesting topic and one of public health importance. Using procalcitonin as a tool to determine bacterial and non-bacterial infection in COVID patients provides a unique application and potential future benefits for both clinical and public health practice. The study also highlights the importance of symptom identification and bacterial testing in addition to PCT in COVID patients. Using multiple lines of evaluation is important when correctly diagnosing bacterial infections (and the subsequent use of antibiotics), particularly during a viral pandemic.

It is suggested that throughout the paper there be a stronger and more complete message related to the study's purpose and its specific benefit/s to public health. A much more detailed review of the public health implications of this research would be beneficial. As the title suggests, this paper includes a "Clinical and Public Health Analysis", however, the public health analysis is quite minimal and should be enhanced. It would be beneficial for the paper to provide a more thorough review on the current and projected burden of antibiotic resistance as a public health issue and supported by public health literature and data. Furthermore, highlighting how the study results can help influence public health practice, policy, and research would also add depth to this assessment.

The manuscript has been edited to address these issues.

Similarly, in the closing paragraph in the discussion, I recommend the authors also expand on how the study findings have specific important global and environmental health implications as related to antimicrobial resistant bacterial infections and unnecessary costly resource utilization - as was mentioned in the text. In this case, including a more thorough review supported with scientific literature would be beneficial here.

The manuscript has been edited to address these issues.