The association between early signs and symptoms and sepsis mortality at a tertiary care hospital in Colombia

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Dear Editor:

I appreciate the article published by Güezguan-Pérez et al. (1), which deals with the interesting issue of sepsis mortality, a study that was conducted in Colombia where, unfortunately, robust statistical data are not available to evaluate the treatment outcomes for this disease. I also congratulate the authors for conducting a prospective study, which produces greater confidence in the reported data. However, below are some considerations that emerged from an analytical reading of the study.

First, it is interesting to note the association between ICU mortality and faster antibiotic administration in patients who were reported to have survived (4 vs. 6 hours). This association, which is counterintuitive in patients with sepsis, could be explained by the fact that clinical outcomes in this disease depend on several factors, like early antibiotic administration (conditioned by the appropriateness of the drug selected, according to the infection being treated). Therefore, an analysis of the timing of antibiotic administration without a corresponding evaluation of its appropriateness in light of the microbiological isolates or compared to institutional guidelines could explain this result. We also lack information on the use of an initial bolus of the antibiotic, combination therapy and route of administration (intermittent boluses vs. extended or continuous infusion) (2, 3).

Second, the article does not mention the use of molecular diagnostic tests (PCR) for rapid identification of the patient´s pathogens. Although their absence could be due to technological or budgetary limitations or merely a lack of testing, it is relevant to note that studies in patients with sepsis and septic shock have shown that these tools significantly increase the rate of pathogen identification, reduce the time elapsed to targeted antimicrobial therapy and are associated with better clinical outcomes (4). This limitation in their use or measurement could explain, in the first place, a delay in appropriate antibiotic therapy in patients with sepsis. On the other hand, their absence introduces confounding factors in the interpretation of data on the use of antibiotic therapy and the outcomes in the article.

Finally, although elevated mortality related to gastrointestinal and respiratory foci is mentioned, the pulmonary focus stands out as one of the most frequent in patients with sepsis and septic shock, accounting for 22.9% of cases. This reinforces the need for more specific diagnostic and treatment strategies for community- and hospital-acquired pneumonias, given their prognostic implications (5).

Dr. Felipe Salas
Residente de 3 año en Medicina de Urgencias, Pontificia Universidad Javeriana,
fesaled90@javerianacali.edu.co

Dr. Alvaro Andrés Montenegro
Esp Epi. Médico Intensivista, Clínica Imbanaco, Docente del Programa de Medicina de Urgencias Universidad Javeriana,
alvaro.montenegro@javeriana.edu.co

Cali (Colombia).

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Response

We would like to thank authors Salas F. and Montenegro A. for their letter, which fosters debate on this study. We are proud to be read and, of course, are open to discussion, which in this case has been very enriching. Below, we will provide an answer to your questions:

Regarding the first point, although early initiation of antibiotics has been identified as a potentially useful strategy for decreasing mortality, especially in patients with septic shock (1), justifying the recommendation to begin antibiotics within the first hour after sepsis diagnosis (2), recent studies have shown that implementing care bundles (which include this strategy) may be insufficient for reducing sepsis-induced mortality (3). This could be partially explained by the high complexity of the mortality outcome, which, as the author of the letter to the editor rightly mentioned, may be affected by both multiple patient factors such as age, severity scale scores and comorbidities (4), as well as treatment-related factors, such as varied treatment effects in populations and their actual effect on individual patients (5).

On the other hand, we recognize that we did not provide information about antibiotic administration, but our goal was not to evaluate causality between mortality and antibiotic therapy. Furthermore, to have done so would have required a thorough analysis of a possible prescription bias with more seriously ill patients receiving antibiotics early, which seems consistent since our results showed higher mortality in older patients with higher SOFA scores and more comorbidity.

On the second point, the goal of this study was to identify which early signs and symptoms might be associated with mortality, to propose pre-hospitalization and emergency room classification and prediction models at the first patient contact that fit our setting, which is something that is being evaluated in our country (6). We recognize that we did not provide information on the use of molecular diagnostic tests and whether adjustments were made according to their results or culture results, which is a crucial issue in the treatment of infections, and we agree that a new adjustment could be made to the logistical model to include microbiological results and even biomarkers (7), which would probably also affect mortality. However, this readjustment should be done in a new prospective study to meet the transparency and methodological rigor of a statistical analysis planned from the beginning of the study.

Regarding the third point, some results that are not minor, like the source of infection and, especially, the respiratory focus (which deserves differentiated strategies because it has proven to have an effect on mortality) (8) were not discussed with sufficient depth because they exceeded the theoretical limits of the study and its objectives. We also point out that our model did not intend to explain all the mortality, because this was an exploratory analysis and more robust statistical analyses are needed for this purpose.

Finally, this letter and its discussion help emphasize that any analysis must be interpreted with caution. For example, it should be noted that this study is very similar to one conducted by another group of Colombian researchers (6); however, the results did not coincide, which does not mean that its conclusions are wrong, but rather that they are specific to the population from which its data were drawn, and their extrapolatability to other populations is limited, as occurs in the vast majority of scientific studies. This could be part of the reason why many study results lose validity after reanalysis (9).

Dres. Jonathan Alexánder Güezguan-Pérez, Andrés Felipe Salazar-Urbano, Laura Daniela Muñoz-Torres

Correspondencia: Dr. Jonathan Alexánder Güezguan-Pérez
alexander.guezguan@gmail.com

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