

EDITORIAL

SEPSIS FROM THE PERSPECTIVE OF LOW- AND MIDDLE-INCOME COUNTRIES.

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Sepsis and Septic Shock are among the leading causes of death and admission to Intensive Care Units (ICU), with a wide distribution globally. In the current issue of *Andes Pediatr*, the manuscript entitled "Challenges of using the International Pediatric Guidelines 2020 of the Surviving Sepsis Campaign in resource-limited settings: A real-world view beyond academia" (1) by Wooldridge et al. stands out. The article was written by a group of renowned Pediatric Intensivists from about 20 countries, being a bucket of cold water that suddenly connects us with the harsh reality of facing this serious entity in resource-limited scenarios.

Understanding the major public health issue, guidelines, protocols, and best practice recommendations for sepsis, such as the "Surviving Sepsis Campaign," have been developed and periodically updated. Eminent intensive care researchers and clinicians have written these documents, aiming to guide the care of septic patients from all over the world. The authors extrapolate their experience in prestigious academic centers, predominantly in North America and Europe, whose prevalence and burden of sepsis is evidently lower than in Africa, Asia, and Latin America. The development of these guidelines is based on a strong methodological work, the PICO model (*Patient, Intervention, Comparison, Outcome*), which establishes "the best available evidence" at the time of the guideline's elaboration. Unfortunately, most evidence comes from the same researchers' studies, the so-called "academic apartheid". Many items in the guidelines have insufficient evidence, so we must rely on the experts' opinion, an incumbent academic elite. As a result, the recommendations can lead to errors when applied to a context different from where the experts work or where the selected studies were done. Even worst, the statements and suggestions may be simply disconnected from the real world when we try to use them in low- and middle-income countries (LMIC).

One of the best examples is the iconic work precisely published a decade ago by Maitland et al. (2). In that research, large amounts of fluid resuscitation, the standard of care at that time, and one of the central recommendations of the Surviving Sepsis Campaign, increased mortality in African children with severe infections compared to children not resuscitated with fluids. This paradox can have diverse interpretations. The different etiologies of sepsis in LMIC

compared to high-income countries (HIC), the presence of comorbidities, inequity of technological and human resources due to limited access to advanced training, variability in access to tertiary care, late consultation to emergency services due to cultural and educational diversity, to name a few of the potential causes. Beyond the valid interpretations, the objective fact was that vigorous administration of fluids in pediatric sepsis was harmful in a low-resource setting. The study of Maitland et al. also reminds us of the relevance of personalized care of each septic child, when the routine and standardized use of 60 mL/kg of crystalloids (practically one volemia) was the tipping point to consider escalating to other usual life support therapies. That recommendation did not even consider something as basic as the futility of administering a second fluid load in the absence of response to the first fluid challenge in a non-dehydrated child. Currently, the evidence regarding the harmful effects of fluid overload in critically ill children, as well as the advantages of its prevention, are consistent (3,4).

An excellent example of the second situation occurred in previous versions of the Surviving Sepsis Campaign. The recombinant activated Protein C (Xigris®) was incorporated into the protocols after only one positive clinical trial sponsored by the pharmaceutical industry (5). Unsurprisingly, the independent clinical studies that followed did not show the same results. The end of the story was that activated Protein C was voluntarily withdrawn after ten years of commercialization supported by weak or absent research.

When we get into the reality of LMIC, many of these recommendations fall apart. Third-line antibiotics are not always available in tertiary hospitals, having to be purchased dose by dose by families struggling with economic necessities. In addition, the monopoly in the market and the usual profit madness in the pharmaceutical industry is responsible for ridiculously high prices, non-affordable for governments with limited health budget, and even for families with moderate-income families with or without insurance. The lack of appropriate devices, technology, and supplies to perform renal replacement therapies is real. For instance, some health teams must use (the poorly understanding adjective "heroic" for healthcare workers") other devices adapted to perform peritoneal dialysis, such as a chest tube. Or seriously ill and anemic children, transfused without any monitoring, not because of colleagues' lack of knowledge, but because of the scarcity of continuous or discontinuous monitoring tools and the extreme work overload, even more striking in the nursing and non-medical staff.

The inequities in access to Pediatric Intensive Care Medicine are profound, sometimes with deficient transport systems. The mortality of critically ill Latin American children is directly related to the duration of transport to a tertiary care center, with medicalized transport being the exception (6).

Thus, the development of guidelines equivalent to the Surviving Sepsis Campaign adapted to resource-limited settings is crucial. In addition, there are undoubtedly many low-cost preventive measures that are infinitely more useful than Xigris® in reducing the prevalence and mortality of sepsis. Finally, during the last year, a group of clinicians made a joint effort to elaborate regional guidelines focused on grounding the different recommendations to the reality of Latin America. They are also based on secondary outcomes, such as ICU length of stay and days free of mechanical ventilation. It is essential to have ICU beds available in resource-limited settings to provide timely care for the next inevitable critically ill child (7). In conclusion, the universal recommendations for managing sepsis in children should be carefully evaluated, adapting them to the regional and local reality. Its appropriate contextualization may have a more significant impact on the outcomes of this serious entity.

Conflict of interests

The author declares no conflicts of interest

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