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Is the tail wagging the dog in sepsis?

Rashan Haniffa, FRCA,

Network for Improving Critical Care Systems and Training, Colombo, Sri Lanka & University College London, UK

Abi Beane, and

University of Amsterdam, Amsterdam, Netherlands & Network for Improving Critical Care Systems and Training, Colombo, Sri Lanka

Arjen M Dondorp, PhD

Mahidol Oxford Tropical Medicine Research Unit, Bangkok, Thailand & University of Oxford, Oxford, UK

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Machado and Azevedo highlight both the extensive global inequalities due to sepsis and the very limited data from Low and Middle Income Countries (LMIC)¹. The authors correctly point out that the burden of sepsis - as defined currently and notwithstanding the scarcity of reliable data- is higher in LMICs, not least because nearly 85% of the global population lives outside High Income Countries (HIC). While acknowledging that the consequences of infection to individuals and families are frequently catastrophic, and often higher in LMIC when compared to HIC, this disparity is neither novel nor exclusive to sepsis².

Disease or syndrome definitions, especially when globally applicable, can help in public awareness, timely detection, protocolised management and standardised evaluation (including in the testing of interventions and quality improvement measures). Such definitions can also assist in the transfer of knowledge between diverse settings and enable the evaluation of the effectiveness of any proposed interventions. However, the current conceptual sepsis definition aspires to include the consequences of diseases resulting from organisms as diverse as *Escherichia*, *Mycobacterium*, *Staphylococcus*, *Burkholderia*, Dengue virus, *Leptospira*, *Trypanosoma*, *Plasmodium*, *Candida* and HIV³. The feasibility of the diagnostic criteria and the effectiveness of interventions recommended by the Surviving Sepsis Campaign (SSC) have been questioned, especially for infections common in LMIC settings⁴. Meanwhile, whether clinicians and researchers (and the wider public,) in LMIC settings consider diseases resulting from specific infectious agents, for example malaria, dengue and melioidosis as sepsis - either by diagnostic criteria or by instituting SSC

Corresponding author: rashan@nicslk.com.

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treatment measures is not well known. Consequently, it is also not possible to ascertain to what extent the non-labelling (or recognition) of these diseases as sepsis, the non-implementation of SSC treatment measures, or the inability to rescue from the complications of such treatment (for example, mechanical ventilation) are contributing to the reported high mortality and morbidity; work which is currently being undertaken by our group in LMIC.

Perhaps research should also ascertain whether there are systematic and relatively easily remediable themes for the poor outcomes in resource-limited settings due to acute illness, not only due to infection: the delayed recognition and rescue of the deteriorating patient due to unavailability of vital signs, the lack of repeated clinical examination, non-titration of inexpensive treatment interventions and other barriers to clinical decision-making⁵.

As the burden of infectious diseases in LMIC is greater than in HIC, should not the definition, diagnostic criteria and any treatment recommendations for sepsis, be fundamentally applicable to the major infectious causes of morbidity and mortality in such settings? The infeasibility of the diagnostic criteria is perhaps undermining its very purpose: clinician (and public) awareness, timely recognition and protocolised management. Could the long overdue clamour for diagnostic criteria applicable to sepsis (for the many, not the few!), be an opportunity to better address therein the diversity of the infectious agents and the consequences of their infection?

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