ARCS
African Research Collaboration on Sepsis

DRUM
Drivers of Resistance in Uganda & Malawi

POLICY BRIEF

Improving diagnosis, treatment and outcomes of sepsis patients in low-resource settings

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EXECUTIVE SUMMARY

- In the presence of really severe infections (called "sepsis"), to save lives, doctors need to kill the bugs causing the infection, whilst giving patients supportive therapy such as intravenous fluids.
- Treatment of sepsis needs to target the right bugs. This paper describes what the bugs are in Malawi, that is, the microbiological causes of sepsis.
- The drugs we are currently giving sepsis patients are either over-treating these bugs (risking antibiotic failure as a consequence) or under-treating them (risking patient death).
- We need to be smarter about getting the right treatment into the right patient to target the right bug at the right time – more research is needed to do this, but rapid tests (like urinary lipoarabinomannan [LAM] for TB) will play a role.
- To reduce long-term deaths, sepsis should continue being managed and monitored even after hospital discharge, especially among patients on antiretroviral therapy (ART).

WHAT IS SEPSIS?

Sepsis is defined as the body's overwhelming and toxic response to infection, leading to tissue damage, organ failure and often death.

CONTEXT

Sepsis is a condition where a severe infection triggers the immune system to act in a dysregulated way, attacking the organs, causing organ damage and even death. It can be triggered by any infection, and is a major global health problem, affecting over fifty million people and causing eleven million deaths per year. The World Health Organisation (WHO) has declared sepsis a health priority.[1]

Management of sepsis is getting better and outcomes are improving[2]. However, fatalities are still very high in some developing countries[3]. We lack evidence on what strategies will work best in high-burden, low-resource settings.

Sepsis is initially treated by antibiotics that treat a wide variety of bacterial infections (e.g. ceftriaxone). However, unless antibiotic therapy can become targeted on the basis of diagnostic tests to identify the exact bug causing sepsis, some patients may not get enough of the correct drug. At the same time, all patients that receive antibiotics are at risk of acquiring antibiotic resistant bugs.

A study from Queen Elizabeth Central Hospital (QECH) in Blantyre, Malawi provides evidence on the need to diagnose the precise bug causing sepsis, rationalise antibiotic use, and understand the longer-term outcomes of patients after they leave hospital.

WHAT THE STUDY DID

Between February 2017 and October 2018, the research team recruited 225 adult participants who came to hospital with severe infection (114 men and 111 women). Most participants were aged between 28 to 44 years, and two thirds were HIV-positive. Of these, most (82%) were already on ART, nearly all (94%) of whom were on first line treatment. In total, 37 (16%) participants had previously been treated for TB, and more than one quarter of these (10 people) were still on TB drugs.

The research team collected blood and urine samples to test for the precise bugs causing sepsis, using urinary LAM, antibody and PCR diagnostics. Participants were then contacted at 1, 3 and 6 months after their hospital admission to check-up on them.

[1]Seventieth World Health Assembly update, 26 May 2017. (n.d.). Retrieved March 31, 2021, from https://www.who.int/news/item/26-05-2017-seventieth-world-health-assembly-update-26-may-2017

[2]Rudd, K. E., Johnson, S. C., Agesa, K. M., Shackelford, K. A., Tsoi, D., Kievlan, D. R., ... Naghavi, M. (2020). Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. The Lancet, 395(10219), 200–211. https://doi.org/10.1016/S0140-6736(19)32989-7

[3]Lewis, J. M., Feasey, N. A., & Rylance, J. (2019). Aetiology and outcomes of sepsis in adults in sub-Saharan Africa: a systematic review and meta-analysis. Critical Care, 23(1). https://doi.org/10.1186/S13054-019-2501-Y

WHAT THE STUDY FOUND

Causes of Infection

Laboratory diagnoses identified the most common bugs causing sepsis to be TB (34%) followed by other bacteria (17%), viruses transmitted by mosquitos (13%) and malaria parasites (9%). TB was most commonly diagnosed among HIV-positive patients. The other bacteria, viruses and parasites were more commonly found in HIV-negative patients.

This shows that sepsis in Blantyre is highly varied. TB is very common, and HIV status makes a big difference to the likely cause of the infection. This further shows that not all sepsis cases are susceptible to antibiotics, including the most common one (ceftriaxone). This is a cause for worry as excessive use of antibiotics may result in the development of drug resistance[4].

Treatment

Nearly all participants (92%) were initially treated with antibiotics targeted at bacteria. In hindsight, because the causes were varied, these antibiotics were the correct choice for only 24% of diagnoses. Anti-tuberculosis treatment was given to 28% of patients, while 12% received anti-fungal drugs, and 5% needed anti-malarial therapy. Doctors commonly also prescribed other treatments – for example, 85% of participants received fluids that was administered through the veins.

> "Antibiotics were the correct choice for only 24% of diagnoses"

Outcomes

On average, patients stayed in hospital for five days. Death rates were similar no matter what the exact diagnosis, and were also similar between HIV-positive and HIV-negative patients. Overall, 39 (18%) had unfortunately died by one month, while 24% died by 3 months and 31% at 6 months. This shows that we should be mindful of long-term deaths among sepsis patients, through extra targeted tests during hospital admission. In particular, we need to ensure that HIV-positive patients have a good response to their antiretroviral therapy, as changing failing therapy will reap longer term benefits.

CONCLUSION

In adults admitted to hospital with infection, the "usual" bugs expected by doctors remain important and treatable causes of sepsis. However, healthcare workers and planners should consider a wide range of disease-causing organisms. This should take into consideration HIV status, and fully implement national guidance on the use of point-of-care LAM tests for TB

ACTIONABLE RECOMMENDATIONS

- Put in place guidelines and procedures for best use of antibiotics in all hospitals. These could safely reduce drug usage, slow down AMR[5], and reduce drug costs[6].
- Consider recording longer-term patient outcomes even after hospital discharge. Current health information system data miss a large number of deaths in the community, and secure patient records will be useful in improving sepsis management and outcomes.
- Future research priorities include detection of antiretroviral treatment failure, and addressing other comorbidities for patients presenting with sepsis

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[4]Lewis, J. M., Lester, R., Garner, P., Feasey, N. A., Kariuki, S., & Richard, V. (2020). Gut mucosal colonisation with extended-spectrum beta-lactamase producing Enterobacteriaceae in sub-Saharan Africa: a systematic review and meta-analysis [version 2; peer review: 2 approved] report report. https://doi.org/10.12688/wellcomeopenres.15514.1

[5]AH, H., LS, M., A, S., M, S., S, R., A, K., ... IJ, P. (2016). Understanding the mechanisms and drivers of antimicrobial resistance. Lancet (London, England), 387(10014), 176–187. https://doi.org/10.1016/S0140-6736(15)00473-0