A call for action: time to address neonatal sepsis and antimicrobial resistance in Africa

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Under 5 mortality rates have halved globally since 1990, but neonatal mortality rates remain high and far from the Sustainable Development Goal (SDG) target of under 12 deaths per 1,000 live births by 2030.[1] Sepsis continues to be a leading cause of death in the neonatal period, particularly in sub-Saharan Africa. The profile of bacterial sepsis in the region is dominated by Gram-negative pathogens with substantial antimicrobial resistance (AMR), contributing to the highest AMR-attributable death rates globally.[2] The World Health Organization (WHO)-recommended antibiotic treatment guidelines have not kept pace with the exponential rise of AMR in sub-Saharan Africa, potentially exacerbating neonatal sepsis deaths. As representatives of the African Neonatal Association (https://africanneonatal.org/), we call for urgent action to address the ongoing preventable public health problem of sepsis-related neonatal deaths and encourage innovation across three areas (Table): treatment guidelines-antimicrobial stewardship (AMS), infection diagnosis-surveillance, and infection prevention and control (IPC).

Firstly, the WHO-recommended first-line antibiotic regimen for the treatment of neonatal sepsis has not been updated in decades and was informed largely by neonatal sepsis data from high-income countries. These global recommendations are no longer relevant for use in many African countries where circulating pathogens and their antibiotic susceptibility profiles are discordant.[3] Furthermore, resistance rates to ampicillin plus gentamicin among young infants have risen from 7% to 67% within two decades,[4] reported sepsis mortality rates exceed 50%,[5] and neonatal sepsis beyond the first day of life is overwhelmingly caused by healthcare-associated pathogens, particularly AMR Gram-negative bacilli such as *Klebsiella pneumoniae.*[6] With exceedingly few new antibiotics in development, changes to empiric treatment regimens are long overdue, but hampered by lack of robust data on sepsis epidemiology and pharmacokinetic data to inform neonatal dosing .

In addition to treatment regimen changes, African neonatal units should support and strengthen AMS efforts. AMS is insufficiently taught and monitored, with few staff to support programmes. Options for antibiotic treatment are often limited and subject to stockouts, leading clinicians to use whatever is available. Affordable quality paediatric formulations of antimicrobials, including carbapenems, are needed urgently, in tandem with regular in-service training on AMS.

Secondly, microbiological diagnostic capacity is frequently limited or non-existent in low-resource settings, especially outside of central hospitals, with minimal local data available to inform hospital, regional, and national antimicrobial prescribing recommendations. This is reflected in the sparse data on AMR neonatal bloodstream infections available in the Global Antimicrobial Resistance and Use Surveillance System (GLASS, https://www.who.int/initiatives/glass).

For surveillance, both syndromic and laboratory-based surveillance are key.[7] To consolidate resources and improve workflow, regional reference laboratory networks may be better managed in a centralized hub versus satellite sites. The adoption of a standard set of surveillance methods for African settings that acknowledge the existing resource limitations but still provide useful and actionable data is imperative. This could include point prevalence surveys or proxy markers for infection, such as antimicrobial use, or death after day 7 of life.

Local infection prediction models that use clinical characteristics to estimate the probability of sepsis may improve diagnostic accuracy and rationalize antimicrobial use,[8] and provide clinical decision support for less experienced healthcare providers, especially if models do

not require laboratory tests. Investments in simple, real-time point-of-care sepsis diagnostics for low-resource settings could further transform clinical decision-making, monitoring, and surveillance. These data could be uploaded to a neonatal sepsis network, or GLASS, which itself could be adapted to provide actionable information for clinicians caring for neonates.

Thirdly, current guidelines around IPC reflect a frequently unattainable gold standard, which may lead to their abandonment or piecemeal, non-evidence-based adaptations. IPC initiatives in neonatal and maternity units lack resources for implementation, in particular dedicated IPC staff, materials, and contextually-adapted protocols to manage and prevent healthcare-associated infections. Furthermore, IPC guidelines do not reflect the reality of low-resource settings, where single-use items are routinely reused with sub-optimal reprocessing, and minimal resources to implement rigorous environmental cleaning, hand hygiene, or patient isolation. Other major challenges are the limited capacity to conduct infection surveillance, rapidly detect outbreaks, and evaluate the impact of IPC interventions.

The paradigm shift may be in reframing the root cause of neonatal sepsis in low-resource settings as a problem of inadequate IPC, given that the available data indicate that neonatal sepsis is increasingly a healthcare-associated infection. Prioritizing IPC may therefore be the most expedient approach to reducing neonatal sepsis morbidity and mortality in Africa.[9,10] We need to understand how to reuse single-use items safely, and how to provide literacy-inclusive training to ancillary staff responsible for cleaning high-touch equipment, such as incubators and respiratory equipment.

The neonates we care for are dying of highly resistant organisms and healthcare-associated infections, which are both potentially preventable and treatable. Reframing and updating

neonatal sepsis management guidelines in Africa is a priority issue which must be urgently addressed *now*, if we are to close the gap towards our SDG target. Clinicians on the continent have the requisite knowledge, skills, and understanding of local disease burden to lead efforts to solve these pervasive issues. What we seek is partnership and collaboration across disciplines with institutions and colleagues in the region and globally. This requires investment in resources and funding for translational and implementation research, and the development of protocols that can be continually tested and refined. We appeal for a commitment from governments, multidisciplinary partners, and health ministries to develop context-specific solutions for neonatal sepsis in Africa that acknowledge the realities of our setting. Without it, preventable deaths from neonatal sepsis will continue.

Table. Approaches and stakeholders needed to address neonatal sepsis and AMR in Africa

Thematic areas	Approaches	Stakeholders
Treatment guidelines-antimicrobial stewardship	Develop neonatal and paediatric formulations	Pharmaceutical companies
	Multi-country neonatal pharmacokinetic studies should be conducted to provide dosing and administration guidance for neonates	Institutions, hospitals
	Targeted regimens for specific clinical profiles (e.g. inborn or outborn, routine versus outbreak settings, sepsis on the first day versus after the first day)	Hospitals, Ministry of Health, WHO
	Advocate for equitable access to new antibiotics in African countries	Ministry of Health, WHO
	Replacement of first-line with second-line antimicrobials as empiric treatment in areas with high community AMR rates. e.g. switch first-line regimens to ampicillin plus amikacin	Local guidelines – hospitals Regional guidelines – Ministry of Health, WHO
	Antimicrobial cycling	Researchers to obtain more data on this practice in order to provide guidance on if and how this can be safely implemented
	Rewriting older antimicrobials, e.g. chloramphenicol, an old antimicrobial with a restored favourable susceptibility profile,[4] back into prescribing guidelines with guidance on appropriate monitoring for adverse effects.	Hospitals
	Education and in-service training on antimicrobial stewardship	Hospitals and post-graduate medical training institutions
Infection diagnosis-surveillance	Consideration of a centralized hub versus satellite sites for regional reference laboratory networks.	WHO, Ministry of Health, hospitals, institutions
	Development and adoption of standardized surveillance methods suitable for a low-resource setting	WHO, Ministry of Health
Infection prevention and control	Guidelines for safe processing and reuse of single-use items	WHO
	Promoting strategies for pathogen reduction and decolonization, such as: alcohol-based hand rub for routine hand hygiene, chlorhexidine bathing, skin-to-skin kangaroo care, and exclusive breastfeeding	Hospitals

AMR, antimicrobial resistance; WHO, World Health Organization

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Declaration of interests

PI is a consultant for WHO. We declare no other competing interests.

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