

Commentary: Risk factors for the development of neonatal sepsis in a neonatal intensive care unit of a tertiary care hospital of Nepal

Sulochana Manandhar^{1,2*}, Puja Amatya³, Stephen Baker⁴ and Abhilasha Karkey^{1,2}

¹Oxford University Clinical Research Unit, Patan Academy of Health Sciences, Kathmandu, Nepal

²Centre for Tropical Medicine and Global Health, Medical sciences division, Nuffield Department of Medicine, University of Oxford, Linacre College, Oxford, UK

³Department of Pediatrics, Patan Academy of Health Sciences, Patan Hospital, Kathmandu, Nepal

⁴Cambridge Institute of Therapeutic Immunology & Infectious Disease (CITIID), Department of Medicine, University of Cambridge, Cambridge, UK

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*Correspondence:

Dr. Sulochana Manandhar, Oxford University Clinical Research Unit, Patan Academy of Health Sciences, Kathmandu, Nepal;
Email: smanandhar@oucru.org.

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Neonatal sepsis is a life-threatening complication in NICUs worldwide having great repercussions on the immediate and latter stages of neonatal health. In a prospective cohort study published in *BMC infectious diseases*, the authors have reported a high prevalence of neonatal sepsis¹. Large differences in the burden of neonatal sepsis among the hospitals between high- and low-middle income countries (HICs and LMICs) clearly indicate a huge disparity in the quality of healthcare systems.

Of interest, the authors reported 80% of cultures proven episodes being acquired horizontally from the NICU as these were of late-onset type and absent at the time of NICU admissions. Further, the authors demonstrated how a prolonged use of invasive procedures subsequently increased the odds of sepsis causation among neonates in NICUs. This was an important finding indicating possible oversights in the implementation of hospital infection prevention and control (IPC) measures. Invasive procedures are an integral component of neonatal care in the NICU. This study showed that despite being crucial, such life-sustaining invasive devices often simultaneously serve as portals of systemic infections upon compromise in local IPC practices in the hospital units. Space constraints leading to the unavailability of physically separated isolation rooms and failure to provide secluded intensive care to the culture proven neonates was the most conspicuous gap in the IPC strategy of the hospital during the study period. It probably led to consecutive cross-infection events from infected to uninfected neonates residing in the same unit and sharing the common resources, leading to an outbreak of sepsis.

Reducing the burden of nosocomial infections in hospitals is a fundamental objective of IPC practices which also plays a crucial role in reducing the overall use of antimicrobials and subsequent reduction of AMR. Because of limited resources, the nosocomial infection control is often the least prioritized area in the hospitals of LMICs. Several LMICs often lack formal national guideline for IPC measures. Here, limited IPC practices, poor hospital waste management, poor knowledge of healthcare workers, and inadequate resources of universal precautions are great challenges. One hospital-based survey from Nepal reported that of 17 hospitals surveyed, constituting of five national, nine private, and three semi-government hospitals, 47% lacked any hospital IPC manual, 59% didn't have any functional IPC committee, and 65% of hospitals didn't

have any provision of providing IPC trainings to their staffs². The hospital where this prospective study was conducted was one of the few tertiary hospitals of Nepal with a formal IPC manual and an IPC committee. Nonetheless, available resources in the hospital were limited to enable the manual to be equally operational. The lack of isolation room in high risk departments to seclude the septic patients, limited access to the logistics of universal precaution, high patient to nurse ratio, and insufficient and poor infrastructural designs are still the challenges of the hospital to ensure an optimal functionality of the IPC practices. Departments, such as NICU, where the burden of immune-compromised neonates is high, are specifically at an increased risk of infections. This is especially true during the times of high bed occupancy, understaffing, lack of staff training and audit etc. During the study period as well, infection outbreak events were established in the NICU. A substantial reduction observed in the number of infectious cases after a conscious reinforcement of stringent aseptic measures such as standard hand hygiene practice, deep cleaning of the unit, aseptic protocol for all invasive procedures, timely removal of invasive devices whenever possible, and proper decontamination of equipment before sharing along with seclusion of culture proven cases highlighted the importance of continued IPC intervention practices in the prevention of nosocomial infections.

Horizontal transmission was incriminated as the major mode of infection acquisition in this study. However, an environmental surveillance that was performed fortnightly on frequently touched surfaces could not pinpoint the source of infection in the study. An accurate identification of the source of infection would be an ideal interventional step to break the chain of disease transmission. However, the potential sources to be traced may be diverse and limitless, including any animate or inanimate objects that are frequently used in the NICU. Of these, the high-touch surfaces in the unit, most importantly including the hands of healthcare workers could be the most potential source of infection transmission^{3,4}. Further, among the hospitalized neonates, bacterial colonizers of their gastrointestinal tract are often considered as important reservoirs for subsequent horizontal dissemination⁵⁻⁷. Thus, routine screening of hospitalized neonates for colonization of multi-drug resistant bacterial pathogens might help in tracing the source of infection.

Studies have shown that despite rigorous environmental surveillance, the source of infection could not be identified in most of the infection outbreak events. One review analysis on 75 NICU outbreak studies worldwide reported that the environmental cultures were negative or non-significant in 57% of outbreak incidences³. Due to unlimited possibilities of sampling

spectrum, the attempts to identify the environmental source of infection might be too labour-, time- and cost-intensive, particularly at the peak times of outbreak when microbiology laboratory is likely overloaded. Thus, though being crucial in preventing the spread of infection, the environmental surveillance may be challenging and often not worthy in resource strapped settings like that of LMICs. Instead, an immediate implementation of stringent IPC measures might be more resource efficient strategy to limit the horizontal transmission of infection as observed in this study.

A considerable overlap in clinical manifestations between infectious and non-infectious illnesses in neonates imparts a consideration challenge in clinical management of patients including dilemma in an empirical use of antimicrobials. Additionally, due to an increased risk of rapid deterioration, and high incidence of culture negative results, the broad spectrum antimicrobials are often used extensively and empirically in NICUs, which is likely to play a major role in the emergence and spread of multidrug resistance (MDR)⁸. In the study, the authors have reported a high prevalence of MDR (72%) in the bacterial aetiological agents, with a high phenotypic resistance to third generation cephalosporin (74%), and meropenem (34%). Such high prevalence of AMR portrayed a formidable challenge for the treatment of neonatal sepsis in NICUs, underscoring the need of implementing antimicrobial stewardship so as to ensure an optimal use of antimicrobials. Additionally, advances in the diagnostic markers with increased sensitivity and specificity to timely and accurately identify sepsis would aid in improving a judicious use of antimicrobial in NICUs.

In summary, the study showed the scenario of high burden of hospital-acquired MDR neonatal sepsis in NICU of a low resource setting. The findings of increased odds of sepsis acquisition being associated with an elevated use of several invasive devices of neonatal care highlighted the importance of stringent IPC measures in the prevention of horizontal transmission of infection in high risk units like NICUs.

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