International Journal of Infectious Diseases 57 (2017) 79–85

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Infectious disease exposures and outbreaks at a South African neonatal unit with review of neonatal outbreak epidemiology in Africa

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ARTICLE INFO

Article history:
Received 30 November 2016
Received in revised form 17 January 2017
Accepted 23 January 2017
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Neonates
Africa
Outbreaks
Nosocomial
Infection prevention

SUMMARY

Background: Hospitalized neonates are vulnerable to infection, with pathogen exposures occurring in utero, intrapartum, and postnatally. African neonatal units are at high risk of outbreaks owing to overcrowding, understaffing, and shared equipment.
Methods: Neonatal outbreaks attended by the paediatric infectious diseases and infection prevention (IP) teams at Tygerberg Children's Hospital, Cape Town (May 1, 2008 to April 30, 2016) are described, pathogens, outbreak size, mortality, source, and outbreak control measures. Neonatal outbreaks reported from Africa (January 1, 1996 to January 1, 2016) were reviewed to contextualize the authors' experience within the published literature from the region.
Results: Thirteen outbreaks affecting 148 babies (11 deaths; 7% mortality) over an 8-year period were documented, with pathogens including rotavirus, influenza virus, measles virus, and multidrug-resistant bacteria (*Serratia marcescens*,*Acinetobacter baumannii*, methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant enterococci). Although the infection source was seldom identified, most outbreaks were associated with breaches in IP practices. Stringent transmission-based precautions, staff/parent education, and changes to clinical practices contained the outbreaks. From the African neonatal literature, 20 outbreaks affecting 524 babies (177 deaths; 34% mortality) were identified; 50% of outbreaks were caused by extended-spectrum β-lactamase-producing *Klebsiella pneumoniae*.
Conclusions: Outbreaks in hospitalized African neonates are frequent but under-reported, with high mortality and a predominance of Gram-negative bacteria. Breaches in IP practice are commonly implicated, with the outbreak source confirmed in less than 50% of cases. Programmes to improve IP practice and address antimicrobial resistance in African neonatal units are urgently required.

Introduction

Hospitalized neonates are a vulnerable population owing to immature immunity and frequent infectious disease exposures through contact with healthcare staff, parents, other patients, equipment, and the hospital environment. Exposure events may lead to microbial colonization or infection with severe morbidity and mortality, as well as nosocomial outbreaks. Outbreaks in neonatal units (NNUs) of high-income countries occur at a rate of 10 per year.[1] The frequency of outbreaks in the NNUs of low- and middle-income countries (LMICs) is unknown, but is likely to be far higher owing to overcrowding, understaffing, and the sharing and reuse of equipment.[2] Despite these risk factors, published outbreak reports from African NNUs are infrequent and hindered by limited microbiology laboratory access and an absence of healthcare-associated infection (HAI) surveillance programmes and infection prevention (IP) resources.[2]

Point prevalence studies in high-income countries report healthcare-associated neonatal bloodstream infection (HA-BSI) as the most frequent infection type affecting hospitalized neonates,[3] although viral respiratory and gastrointestinal infections are also encountered. Given the high rates of HA-BSI reported from some African settings,[4–6] frequent outbreaks of nosocomial bacterial infection could be expected in African NNUs. The limited African neonatal HA-BSI descriptions reflect a predominance of Gram-negative pathogens and substantial antimicrobial

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http://dx.doi.org/10.1016/j.ijid.2017.01.026

resistance.[4–6] A recent systematic review of 30 neonatal outbreaks (2005–2015), identified *Klebsiella pneumoniae* (33%), *Serratia marcescens* (20%), and methicillin-resistant *Staphylococcus aureus* (MRSA) (20%) as the most common pathogens.[7] The mean outbreak duration was 10 months and the outbreak source was identified in 17/30 cases (57%): neonates transferred-in from other facilities ($n = 6$), contaminated ventilator equipment ($n = 5$), healthcare workers ($n = 4$), and colonized mothers ($n = 2$). The lack of resources for outbreak investigation (including laboratory services and molecular testing), hampers efforts to identify outbreak frequency and source in African NNUs.[7]

Reported NNU outbreak mortality rates are high, with the risk of death inversely proportional to the country income level (9–70%).[7] The highest mortality rates are documented among neonates with laboratory-confirmed Gram-negative and fungal BSI pathogens.[4,6,7] A lack of neonatal intensive care units (NICUs) and limited access to appropriate treatment for antimicrobial-resistant infections contribute to increased mortality in LMIC NNU outbreaks.

This article describes the Tygerberg Children's Hospital experience with the detection, investigation, and control of outbreaks in the NNU since 2008, in the context of published outbreak reports from other African NNUs over the last two decades.

Methods

Study setting

Tygerberg Children's Hospital in Cape Town, South Africa is a 124-bed neonatal referral centre located within a 1384-bed tertiary government hospital. The NNU provides medical and surgical care for sick and/or low birth weight (LBW, <2500 g) neonates, with prematurity, perinatal asphyxia, and neonatal sepsis being the predominant reasons for admission. The NNU consists of an eight-bed NICU (combined surgical and medical), a four-bed high-care, two high-care wards, one low-care ward, and a kangaroo mother care unit. Bed occupancy rates in the NNU range from 83% to 138%, with a high demand for NICU beds. The hospital performs around 8000 neonatal deliveries annually, with a LBW rate of 39%. Mothers with complicated pregnancies are referred in from the surrounding socioeconomically deprived communities.[8]

In the Western Cape Province, antenatal HIV prevalence increased between 2009 and 2013, from 16.1% to 16.9% (vs. 29.5% nationally).[9] Combination antiretroviral therapy (cART) has been available since 2004, with universal cART in pregnancy (irrespective of CD4 count) introduced from 2013. Between 2009 and 2011, a national prevention of mother-to-child HIV infection transmission (PMTCT) programme achieved a reduction in the Western Cape Province perinatal HIV transmission rate from 3.6% to 1.4%.[8,10]

Study period and method

Data on NNU outbreaks investigated by the infection prevention service and/or the paediatric infectious diseases team between May 1, 2008 and April 30, 2016 were collected prospectively. An outbreak was defined as any infectious disease (ID) cluster affecting two or more babies with the same pathogen within 7 days (isolated from sterile sites, with the same antibiogram for bacterial pathogens), or isolation of a single unusual or important pathogen, e.g., measles, *Pseudomonas spp.*[11] For each outbreak, the pathogen, NNU ward/s affected, number of cases and case fatality rate, the presumed or known source, and the IP measures instituted for outbreak control were documented.

Investigation for suspected neonatal sepsis

Sick neonates with any clinical, radiological, and/or laboratory features suggesting infection undergo at least one blood culture with/without accompanying cerebrospinal fluid and urine culture specimens, at the discretion of the attending clinicians. Symptoms and signs that trigger investigation for sepsis include lethargy, apnoea, need for increased respiratory support, poor feeding, temperature instability, abdominal distension, and raised white cell count or C-reactive protein, among others. Given the high prevalence of extended-spectrum β-lactamase (ESBL)-producing *Enterobacteriaceae* at the study institution, the empirical treatment of hospital-acquired infection usually includes meropenem. Vancomycin is added if MRSA is considered a likely pathogen, e.g., with suspected central line or soft tissue infection. Fluconazole prophylaxis is not routinely used. Investigation for potential viral pathogens is undertaken based on clinical presentation, e.g., gastroenteritis (rotavirus and adenovirus) and respiratory tract infection (respiratory syncytial virus (RSV), adenovirus, human rhinovirus, parainfluenza virus 1/2/3, influenza virus A/B, and human metapneumovirus) using rapid assays, ELISA, or PCR panel testing.

Outbreak surveillance, investigation, and management

The hospital has an on-site unit for infection prevention and control (UIPC) that conducts laboratory surveillance for selected bacterial 'alert' pathogens: *K. pneumoniae*, MRSA, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, *S. marcescens*, and *Acinetobacter baumannii*). Clinician reports of infection clusters are also an important trigger for outbreak investigation. Four IP nurse practitioners are employed (ratio 1:350 patients), with one dedicated to the neonatal, paediatric, and maternity service. Most infection clusters and outbreak alerts are initially investigated by line-listing of affected patients and a review of IP practices on the NNU. The detection of additional related cases results in an outbreak being officially declared with the assembly of an outbreak team, institution of IP measures based on the suspected source and route of transmission, and further epidemiological investigations where necessary. Institutional changes that may have influenced NNU infection rates and outbreak frequency include the installation of automated alcohol hand-rub dispensers (in 2013) and the introduction of a central line-associated BSI (CLABSI) programme in the NICU (in 2012). Other than increasing admission volumes and ongoing staff shortages, there were no significant changes in patient profile or physician practices during the study period.

Literature search terms

PubMed, Scopus, and the online outbreak database http://www.outbreak-database.com were searched using the terms "neonate", "Africa", "nosocomial", "healthcare-associated infection", and "outbreaks" for English-language papers published from January 1, 1996 to January 1, 2016. Each publication or outbreak database record was reviewed to extract the following information (when available): year of outbreak, country, neonatal setting, pathogen, number of clinical cases, deaths reported, presumed source or factors implicated in the evolution of the outbreak, and IP measures implemented for outbreak control.

Results

Over the 8 years, Tygerberg Children's Hospital NNU experienced 13 outbreaks affecting 148 babies with 11 deaths (7% mortality) (Table 1). Multidrug-resistant bacteria were the most frequent pathogens, followed by outbreaks of viral diseases