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A ten-year review of neonatal bloodstream infections in a tertiary private hospital in Kenya

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Brief Original Article

A ten-year review of neonatal bloodstream infections in a tertiary private hospital in Kenya

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Abstract

Introduction: Neonatal mortality in developing countries is usually due to an infectious cause. The gold standard of investigation in developing countries is a positive blood culture. It is important to know the aetiology of neonatal bloodstream infections so that empiric treatment can be effective.

Methodology: We conducted a retrospective clinical audit over ten years between January 2000 until December 2009, looking at the aetiology of both early and late onset neonatal sepsis. We analysed data from 152 (23%) patient isolates out of 662 suspected cases of neonatal sepsis.

Results: Our study revealed that Gram-positive organisms were the predominant cause of both early and late onset sepsis; the common isolates were *Staphylococcus epidermidis* (34%) and *Staphylococcus aureus* (27%). There were no isolates of group B *Streptococcus. Candida* species was isolated only in patients with late onset sepsis (6.9%). Bacterial isolates were relatively sensitive to the commonly used first- and second-line empiric antibiotics.

Conclusion: Gram-positive organisms remain the major cause of neonatal bloodstream infections in our setup. The findings of this study will guide clinicians in prescribing the right empiric therapy in cases of suspected neonatal sepsis before the definitive culture results are obtained.

Keywords: Neonate; Bloodstream Infections; Early onset sepsis; Late onset sepsis; Aetiology

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Introduction

Correct and timely identification of infectious agents of neonatal sepsis as well as their antibiotic sensitivity patterns are essential as they guide both empiric and definitive treatment. Early onset neonatal sepsis occurs within seven days after delivery while late onset sepsis occurs from the eighth day to the end of the neonatal period, which is considered to be 28 days [1].

In developed countries, bacterial infections in neonates are commonly due to *Escherichia coli*, other *Enterobacteriaceae*, *Listeria monocytogenes*, coagulase negative *Staphylococci* and group B *Streptococcus* [2-4]. Studies have been conducted in developing countries to establish the aetiology of neonatal sepsis. A review of culture-positive cases in India, Africa, the Middle East and West Indies revealed that *Klebsiella* spp. was the most frequently isolated pathogen. *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas* spp. were also commonly isolated [3-5].

Information available in Kenya is principally from studies conducted at public hospitals, where the cause is largely attributed to community acquired bacteremia, because a significant number of neonates are born outside the hospital setting [6,7]. In contrast, at the Aga Khan University Hospital, Nairobi, Kenya, most neonates seen are born in a health-care facility.

This report provides information regarding the common aetiological agents of both early and late neonatal sepsis at our institution.

Methodology

The Aga Khan University Hospital is a 254-bed referral postgraduate teaching hospital located in Nairobi, Kenya. It has a well-equipped neonatal intensive care unit (NICU) and a neonatal high dependency unit (NHDU) with qualified specialists including neonatologists.

This was a retrospective clinical-laboratory study. Laboratory registers were reviewed to identify all positive blood culture isolates in neonates over a

Table 1. Distribution of organisms between early neonatal sepsis and late neonatal sepsis between January 2000 and December 2009

Organism	Early Onset		Late Onset	
	Count	**%**	**Count**	**%**
Staphylococcus aureus	25	26.6	16	27.6
Staphylococcus epidermidis	31	33	21	36.2
Streptococcus pneumoniae	1	1.1	0	0
Streptococcus agalactiae	1	1.1	0	0
Streptococcus spp	11	11.7	1	1.7
Enterococcus spp	10	10.6	2	3.4
Klebsiella spp	7	7.4	7	12.1
Kluyvera spp	0	0	2	3.4
Aeromonas spp	1	1.1	0	0
Pseudomonas aeruginosa	1	1.1	0	0
Escherichia coli	1	1.1	1	1.7
Burkholderia cepaciae	1	1.1	1	1.7
Pasteurella spp	0	0	1	1.7
Candida spp	0	0	4	6.9
Acinetobacter spp	1	1.1	0	0
Aeromonas spp	1	1.1	0	0
Enterobacter spp	0	0	2	3.4
Serratia spp	1	1.1	0	0
Acrobacterium spp	1	1.1	0	0
Total	**94**	**100**	**58**	**100**

ten-year period between January 2000 and December 2009. Subsequently, patient files were reviewed and data from 152 patient isolates was analysed. It is routine practice in our institution to perform a blood culture in all cases of high fever and suspected sepsis. Blood specimens were cultured in BACTEC 9120 and BACTEC 9050 (Becton-Dickinson, New Jersey, USA) automated systems and bacterial identification was performed with standard bacteriological techniques [8]. Antimicrobial susceptibility testing was done by using the modified Kirby-Bauer disc diffusion method according to the Clinical and Laboratory Standards Institute/National Committee on Clinical Laboratory Standards (CLSI/NCCLS) [9].

The laboratory has internal quality management systems in place due to International Organisation for Standardisation (ISO 15189) certification. The microbiology division participates in the UK NEQAS program for bacterial identification and susceptibility tests. Statistical analysis was performed using SPSS software Version 15.0 (SPSS Inc, Chicago, IL, USA).

Results

Out of 665 suspected cases of neonatal sepsis, 152 (23%) neonates had positive blood cultures. A total of 119 (78%) cases had Gram-positive isolates, 29 (19%) had Gram-negative isolates and 4 (3%) had yeast isolates.

Early onset sepsis

Ninety-four neonates presented with early onset sepsis. The predominant organisms *S. aureus*, *S. epidermidis*, *Klebsiella spp*, *Streptococcus spp* and *Enterococcus spp*, are shown in Table 1. The majority of the organisms were isolated within the first 72 hours of life, as shown in Table 2.

Late onset sepsis

Fifty-eight neonates had late onset sepsis. The causative organisms are shown in Table 1.

Outcome

Out of the 152 patients with bloodstream infection, 147 were discharged, one was transferred out to another health-care facility, and four died.

Table 2. Distribution of organisms in neonates with early onset sepsis

Organism	Patient Age (days)						
	1	**2**	**3**	**4**	**5**	**6**	**7**
Staphylococcus aureus	10	1	5	4	1	2	2
Staphylococcus epidermidis	9	4	3	1	4	7	3
Streptococcus pneumoniae	0	0	0	1	0	0	0
Streptococcus agalactiae	1	0	0	0	0	0	0
Streptococcus spp	8	2	0	1	0	0	0
Enterococcus spp	4	2	1	2	0	1	0
Klebsiella spp	2	2	0	1	0	1	1
Aeromonas spp	0	0	1	0	0	0	0
Pseudomonas aeruginosa	1	0	0	0	0	0	0
Escherichia coli	1	0	0	0	0	0	0
Burkholderia cepaciae	0	0	0	0	1	0	0
Acinetobacter spp	1	0	0	0	0	0	0
Aeromonas spp	1	0	0	0	0	0	0
Serratia spp	0	0	0	0	0	0	1
Acrobacterium spp	1	0	0	0	0	0	0
Total	**39**	**11**	**10**	**10**	**6**	**11**	**7**

Table 3. Antibiotic susceptibility patterns of bloodstream isolates to first-line antibiotics

Antibiotic	Gram-Positive Isolates	Gram-Negative Isolates
	% Resistance (no. resistant/total isolates tested)	**% Resistance (no. resistant/total isolates tested)**
Ampicillin	46 (55/119)	NT
Gentamicin	16.6% (7/42)	27.6% (8/29)
Cefuroxime	33.7% (29/86)	38.5% (10/26)
Amikacin	11.1% (1/9)	5.9% (1/17)

NT: Not Tested

Antibiotic Susceptibility Patterns

The susceptibility patterns of the isolates to the first- and second-generation empiric antibiotics are shown in Table 3. For the Gram-positive isolates, resistance to ampicillin was high at 46%. There were five methicillin resistant *S. aureus* noted among the 41 *S. aureus* isolates. We only had one *S. pneumoniae* isolate which was sensitive to ampicillin. Ampicillin susceptibility was not tested with the Gram-negative isolates. Resistance to the second-generation cephalosporin cefuroxime was also notable among both the Gram-positive and Gram-negative isolates at 33.7% and 38.5% respectively.

Discussion

Bloodstream infection was confirmed in 23% of suspected cases of neonatal sepsis. In a study done at the national public referral hospital in Kenya, 16.7% of suspected neonatal sepsis had a positive culture [7]. This difference noted in the public hospital may be due to the different time periods in which the studies were conducted as well as the availability of laboratory support which negatively affects their ability to investigate; *i.e.,* the study done at the public referral hospital was done over a different time period and a shorter duration (December 1997 to April 1998).

The predominant aetiological agents in our study were Gram-positive organisms, in both early and late onset sepsis. Coagulase negative *Staphylococci* (CONS) were the most commonly isolated bacteria and this has also been found in other studies, especially as a cause of late onset sepsis [2,10]. However, in our study it was difficult to ascertain whether CONS was a true pathogen or contaminant as the majority of cases had only one blood culture per patient performed. If these isolates were

excluded from our analysis, *S. aureus* becomes the predominant pathogen which is in keeping with other studies published from developing countries [11]. In this study, group B *Streptococcus* was observed only in 1% of the cases whereas in rural Kenya, the isolation rate has been observed up to 9%, especially in cases with early neonatal sepsis [6]. However, other studies from Africa have also shown low isolation rates [10]. No obvious explanation is forthcoming for these differences. It is noteworthy that 46% of the Gram-positive isolates were resistant to ampicillin. There were five methicillin resistant *S. aureus* (MRSA) noted among the 41 *S. aureus* isolates. Unfortunately, there is lack of routine surveillance data on antimicrobial susceptibility patterns in other hospitals in our country for comparison of our results.

In the case of Gram-negative organisms, *K. pneumoniae* was found to be the most predominant pathogen followed by other *Enterobacteriacae*. Despite having the necessary expertise required to isolate *Haemophilus spp*, we were not able to do so in these samples. Generally isolation rates in Africa are low and this has been attributed to the use of Haemophilus B vaccine which was introduced to Kenya in 2001 [6,11,12]. Among Gram-negative isolates, resistance to gentamicin was 27.6%, which is comparable to the observations of a study done at one of the public referral hospitals [7]; however, none of the common isolates in our study exhibited more than 50% resistance to the first- and second-line antibiotics used in empiric treatment of neonatal sepsis (Table 3). Most children with suspected sepsis in our institution are started on empiric treatment with ampicillin and gentamicin as first-line and amikacin and ceftriaxone as second-line antibiotics.

Candida spp. was isolated only in four patients who had late onset sepsis. Two of the patients were born preterm, a known risk factor for candidemia [13]. Prevalence of methicillin resistant *S. aureus* was noted to be low (10.2%) in this neonatal population compared to a similar study looking at bloodstream isolates in all age groups at AKUH-N where it was 21% (76/364) of *S. aureus* isolates [14].

In summary, we can say that Gram-positive organisms remain the major cause of neonatal bloodstream infections in Kenya. The findings of this study will guide clinicians in prescribing the right empiric therapy in cases of suspected neonatal sepsis before the definitive culture results are obtained. Given the limitations encountered in this study, a prospective study will help to resolve the discrepancy concerning CONS as a pathogen or contaminant. This will also facilitate proper characterization of extended spectrum beta lactamase producing Gram-negative organisms, an emerging problem in our institution.

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