Prevalence and Antimicrobial Susceptibility of Bacteria Implicated in Neonatal Sepsis at Pumwani Maternity Hospital

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Neonatal sepsis is one of the most common causes of morbidity and mortality among infants in developing countries. The etiology and antimicrobial sensitivity patterns of bacteria responsible vary in different hospitals. This study identified bacteria in blood cultures of neonates with clinically suspected septicemia and demonstrated their susceptibility patterns. A longitudinal design targeting all neonates at Pumwani maternity hospital with suspected sepsis was used. One hundred and fifty neonates were selected using consecutive sampling. Data was collected using a questionnaire. Out of 150 blood specimens cultured, the cases of confirmed bacterial sepsis were 48(32%). Gram-positive pathogens predominated with *Staphylococcus aureus* and *Streptococcus viridans* accounting for 70%. The only Gram-negative isolates were *E. coli* and *Klebsiella* spp. Gram-positive isolates showed high sensitivity (above 80%) to meropenem, gentamicin, ceftriaxone, ofloxacin, and amikacin. Gram- negative organisms were generally resistant to penicillins and absolutely sensitive to meropenem, ceftazidime and ciprofloxacin.

Keywords: Prevalence, Antimicrobial susceptibility, Neonatal sepsis

INTRODUCTION

Neonatal sepsis is broadly defined as a systemic inflammatory response occurring in the first four weeks of life as a result of a suspected or proven infection [1]. It is a syndrome characterized by systemic signs of infection and accompanied by bacteremia in the first month of life. It is classified as either early or late-onset disease [2]. Early-onset neonatal sepsis (EOS) occurs within the first 72 hours of life, and late-onset neonatal sepsis (LOS) presents beyond 72 hours until the end of the neonatal period.

The syndrome remains a leading cause of mortality and morbidity among infants in developing countries. World Health Organization (WHO) estimates that globally, there are about 5 million neonatal deaths a year [3,4]. Ninety- eight percent of the cases occur in developing countries and accounts for about 26-34% of total deaths each year [5-7]. Prevention of neonatal sepsis and decision making on a rational treatment plan using antibiotic remains a significant clinical problem internationally [8]. The spectrum of organisms responsible for this condition in developing countries differs from those in developed countries [5]. Also, the spectrum of organisms associated with EOS differs from those implicated in LOS sepsis [9]. Antimicrobial drug resistance is a growing threat due to the emergence of microorganisms that are resistant to the currently used medicines [10]. Antimicrobial sensitivity and resistance testing are essential as a guide for rational prescribing. The gold standard for assessing antimicrobial susceptibility is the determination of the minimum inhibitory concentration [11]. Neonatal sepsis is a life-threatening emergency that requires accuracy in the choice of empiric therapy to save lives. Given the above, this study aimed to determine the prevalence of the etiological agents and their susceptibility patterns so that appropriate measures can be taken. This study may help inform timely and accurate empiric decisions in the absence of cultures that may not be feasible in some situations, thereby optimizing therapy.

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MATERIALS AND METHODS

A longitudinal study was carried out at Pumwani Maternity Hospital in Nairobi, where one hundred and fifty neonates with suspected sepsis were selected using consecutive sampling between March and August 2015. The parent or guardian was presented with the consent form, and the purpose, procedures, risks, and benefits of the study were explained. Those who consented were interviewed, and their particulars filled in a data collection form by the investigators or the research assistants. The study was voluntary, and there were no untoward repercussions for those who did not consent. The diagnosis of sepsis was made by the attending pediatrician. After the consent was obtained from the parent/guardian, 1-3ml of blood was obtained from the neonate for culture using aseptic precautions: The skin at the venepuncture site was meticulously prepared using a bactericidal disinfectant that comprised of tincture of iodine, 10% polyvidone-iodine and 70% alcohol. The disinfectant was allowed to dry before blood was drawn by a pediatrician. The specimen obtained was immediately inoculated into BACTEC Peds PlusTM/F culture vials (enriched with Soybean-Casein digest broth with CO2), which are used for aerobic blood cultures. The Culture bottles with the specimen were then incubated at the Pumwani Hospital laboratory at 37 °C until transportation time. Transportation to the Department of Pediatrics laboratory of the University of Nairobi was done by the researcher and the research assistant. This transfer of the samples was conducted in temperature-maintained insulated cool boxes and did not take more than one hour. At the University laboratory, bacteria isolates were identified using standard microbiologic procedures and their susceptibility pattern determined using the Kirby and Bauer Disc Diffusion sensitivity test [12,13]. The testing included the antibiotics that are often used to treat neonatal sepsis at Pumwani Maternity Hospital. These were benzylpenicillin, gentamycin, ampicillin, ceftriaxone, ceftazidime, amikacin, vancomycin, flucloxacillin, meropenem, and amoxicillin-clavulanic acid. Quality was ensured through proper training of research assistants and following laboratory procedures appropriately. Permission to carry out the study was given by the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH-ERC/A/105) and the management of Pumwani Maternity Hospital.

RESULTS

Etiology of neonatal sepsis

The prevalence of bacteria causing neonatal sepsis is summarized in **Table 1.** Out of the 150 blood samples of neonates with suspected sepsis, 48(32%) yielded positive results. Of these, 46 (30.7%) had a single organism, while 2(1.3%) had a combination of two pathogens. The combinations were *Staphylococcus aureus* and *Streptococcus viridans*, as well as *Staphylococcus aureus* and *Streptococcus pyogenes*. *Staphylococcus aureus* was the most common isolate at 30(20%), followed by *Escherichia coli*.

Table 1: Prevalence of bacteria that cause neonatal sepsis (n=150)

	Categories of neonatal sepsis		
Bacteria	**Early (≤3days) (n)**	**Late (>3-28 days) (n)**	**Total (n, %)**
Staphylococcus aureus	29	1	30 (20)
Escherichia coli	6	0	6 (4)
Streptococcus viridans	5	0	5(3.3)
Streptococcus pneumoniae	3	1	4(2.7)
Klebsiella spp	3	0	3(2)
Coagulase-negative *Staphylococcus*	1	0	1(0.7)
Streptococcus pyogenes	1	0	1(0.7)
TOTAL	**48**	**2**	**50 (33.3)**

Antimicrobial susceptibility patterns of the isolates

The antimicrobial sensitivity characteristics are summarized in **Table 2.** For *Staphylococcus aureus*, the highest sensitivity was observed with meropenem and ceftazidime, followed by ofloxacin and amikacin, gentamicin, and ceftriaxone. *Streptococcus viridans* was 100% sensitive to piperacillin, gentamicin, meropenem, ofloxacin, amoxicillin-clavulanic acid, and amikacin. The highest sensitivity for *Streptococcus pneumoniae* was seen with piperacillin, gentamicin, ceftriaxone, meropenem, and amikacin. There was one isolate of Coagulase-negative *Staphylococcus* (CoNS) that was resistant to ofloxacin and absolutely susceptible to the other drugs. *Streptococcus pyogenes* showed absolute susceptibility to all antimicrobial agents tested. As for *Escherichia coli*, there was absolute sensitivity to ofloxacin and meropenem. The highest resistance for *Escherichia coli* was observed against ampicillin, followed by ceftriaxone. *Klebsiella* spp showed absolute sensitivity to piperacillin, gentamicin, ceftazidime, and meropenem.

DISCUSSION

Staphylococcus aureus was the predominant pathogen isolated [14-16]. In contrast, some studies have shown varied isolates [17, 21]. In Late-onset sepsis (LOS), only *Staphylococcus aureus* and *Streptococcus pneumonia* were isolated and this observation contrasts other studies [5, 21, 24, 25]. The predominance of CoNS in LOS has been reported [18] and the spectrum of isolates was generally similar to those of other developing countries [9, 19, 20]. A difference was observed in the type of bacteria that predominated where Gram-positive bacteria comprised the majority of the isolates, unlike in other studies where the Gram-negative bacteria were the most common [5, 21].

The spectrum of bacteria and their susceptibility patterns vary depending on the prevailing conditions, especially antimicrobial use. *Staphylococcus aureus* showed the highest sensitivity to meropenem, gentamicin, ceftriaxone and amikacin [21,22]. Amikacin showed the highest activity among the aminoglycosides [23]. Some resistance was seen with piperacillin, ampicillin, benzylpenicillin, and amoxicillin-clavulanic acid [24,25]. Studies have found that Methicillin-resistant *Staphylococcus aureus* (MRSA) are resistant to amikacin [24-26]. *Streptococcus viridans, Streptococci pneumoniae, Streptococcus pyogenes,* and Coagulase-negative *Staphylococcus* generally showed an absolute sensitivity to meropenem [26]. *Streptococcus pneumoniae* also showed an absolute sensitivity to piperacillin, gentamicin, ceftriaxone, and amikacin [27]. The highest resistance was seen against flucloxacillin [27, 28]. Only one isolate of CoNS was obtained that showed absolute

Table 2. Antimicrobial sensitivity characteristics of bacteria implicated in neonatal sepsis

Drug	Percentage sensitivity					
	Staphylococcus aureus	***Streptococcus viridans***	***Streptococcus pneumoniae***	***Escherichia coli***	***Klebsiella* spp**	***Streptococcus pyogenes***
Ampicillin	79	100	100	25	0	100
Benzylpenicillin	67	80	100	100	67	100
Piperacillin	60	100	100	67	100	100
Gentamicin	90	100	100	83	100	100
Ceftriaxone	87	80	100	67	100	100
Meropenem	100	100	100	100	100	100
Ceftazidime	100	100	100	100	100	100
Flucloxacillin	87	60	25	60	50	100
Ofloxacin	97	100	75	100	67	100
Ciprofloxacin	91	100	50	100	100	100
Co-amoxiclav	43	100	75	67	100	100
Amikacin	97	100	100	83	67	100

resistance to ofloxacin but susceptible to ampicillin, benzylpenicillin, gentamicin, ceftriaxone, flucloxacillin, ciprofloxacin, and amikacin contrary to other findings [29]. *Escherichia coli* showed high resistance to ampicillin, mild resistance to ceftriaxone, piperacillin, and amoxicillin-clavulanic acid [21, 26]. High sensitivity was observed with meropenem, ofloxacin, gentamicin, and amikacin [21]. *Klebsiella pneumoniae* was isolated in Early-onset sepsis, and it exhibited an absolute sensitivity to piperacillin, gentamicin, ceftriaxone, meropenem, and amoxicillin-clavulanic acid [27]. Marked resistance was observed against ampicillin and moderate ones against benzylpenicillin, flucloxacillin, ofloxacin, and amikacin [22, 26]. Minimal resistance was observed against third-generation cephalosporins and gentamicin [21, 27, 28]. Our results for the sensitivity patterns generally demonstrated that meropenem was the antibiotic of choice in case of treatment failure with the other regimens. The isolates from the blood culture showed low resistance to ciprofloxacin, amikacin, gentamicin, benzylpenicillin, and gentamicin. Some resistance was observed with flucloxacillin among Gram-positive and Gram-negative bacteria.

CONCLUSION

Most cases of neonatal sepsis were due to Gram-positive bacteria. All the isolates were absolutely sensitive to meropenem and ceftazidime. *Staphylococcus aureus* was moderately resistant to penicillins.

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