ORIGINAL ARTICLE

Incidence of Coagulase Negative Staphylococci in Neonatal Sepsis

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ABSTRACT

The aim of the study was to identify the incidence and antimicrobial susceptibility of coagulase negative *Staphylococci* in neonatal sepsis. This study was carried out in the Children's Hospital and Institute of Child Health, Lahore, Pakistan during 1st December 2009 to 31st December 2010. A total number of 11541 blood samples from neonates were studied; out of which 388 were positive for coagulase negative *Staphylococci*. Coagulase negative *Staphylococci* showed highest susceptibility to vancomycin (97.7%), linezolid (97.4%), amikacin (85.8%) and teicoplanin (73.5%). The less effective antibiotics were co-amoxiclav (68.2%), ciprofloxacin (57.7%), ampicillin (44.6%), ceftriaxone (41.2%), amoxicillin (33.0%), oxacillin (24.2%) and penicillin (16.0%). It was concluded that the vancomycin and linezolid were the best choice of treatment against highly resistant coagulase negative *Staphylococci* in case of neonatal sepsis.

Key words: Staphylococci, neonatal sepsis, coagulase

INTRODUCTION

Neonatal sepsis is a bacterial infection of the blood characterized by systemic signs and symptoms in the initial month of life[1]. It is the main cause of the neonatal mortality and morbidity throughout the world[2]. It has been recorded that 20% of all neonates develop sepsis in the developing countries[3].

Neonatal sepsis is dangerous and life-threatening clinical disease that requires diagnosis and treatment.[4] Neonatal sepsis is one of the major reasons of admission of neonates in the hospitals.[5] The causative agents of neonatal sepsis change from time to time and from region to region.[6] Organisms that have been implicated in causing late-onset sepsis syndrome include coagulase-negative *Staphylococci* (CoNS)*, Staphylococcus aureus, E. coli, Klebsiella, Pseudomonas, Enterobacter, Candida, Serratia, Acinetobacter* and anaerobes. Coagulase negative *Staphylococci* has become one of the most common causative agent of neonatal sepsis in developing countries[5].

Coagulase negative *Staphylococci* are non-motile, Gram positive cocci, arranged in grape-like clusters. Majority of isolates of coagulase negative *Stapylococci* have the *mecA* gene for beta-lactam antibiotic resistance, which has been implicated for the choice of antibiotics.[8] Antibiotics for the treatment of early onset sepsis are amoxicillin and gentamicin for all neonates. Vancomycin and linezolid are considered as first choice for treatment of infections developed by coagulase negative *Staphylococci* during prolonged hospital stay[7,9] Teicoplanin is another glycoprotein used for coagulase negative *Staphylococcal* infections which helps to achieve adequate serum levels[10] The objective of the study was to evaluate the incidence and antibiogram of Coagulase negative *Staphylococci* isolated from the neonates attending a tertiary care hospital so that the panel of antibiotics being used to treat coagulase negative *Staphylococcal* infections may be revised in neonates.

MATERIAL AND METHODS

This observational study was conducted in the Microbiology Department of The Children's Hospital and Institute of Child Health Lahore, Pakistan, from 1st December 2009 to 31st December 2010. The blood samples received during the study period were collected in the brain heart infusion broth and incubated at 37°C. The blood samples were sub-cultured on Blood and MacConkey agar plates and placed at 37°C for overnight incubation. Following growth, the coagulase negative *Staphylococci* were identified on the basis of colony morphology, Gram's stain, catalase test and coagulase test.

The isolated coagulase negative *Staphylococci* were processed for antimicrobial susceptibility testing to various antibiotics *in vitro* using the Kirby-Bauer disc diffusion method. The antibiotic discs of amikacin (30 µg)*,* ciprofloxacin (5 µg)*,* co-amoxiclav (20/10 µg)*,* vancomycin (30 µg), teicoplanin (30 µg), ampicillin (10 µg), ceftriaxone (30 µg), amoxicillin (20 µg), oxacillin (10 µg), penicillin (10 µg) and linezolid (30 µg) were placed on the Mueller-Hinton agar (Oxoid) plates and incubated at 37°C. After overnight incubation the diameter of each zone of inhibition

was measured in mm. The susceptibility testing results were noted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines.[11]

RESULTS

A total number of 11541 blood samples were collected from neonates during the study period, out of which 1373 showed growth of various organisms. The most frequently isolated organism from neonatal sepsis were coagulase negative *Staphylococci* 388 (28.3%), followed by *Klebsiella* species 322 (23.5%), *Staphylococcus aureus* 178(13.0%), *E. coli* 131(9.5%), *Pseudomonas species* 93 (6.8%), *Acinetobacter species* 54(3.9%), *Enterobacter species* 53(3.9%), *Streptococcus species* 39(2.8%), *Burkolderia cepacia* 41(3.0%) and *Salmonella species* 24 (1.7%). The rest of bacteria were *Serratia species* 15 (1.0%), *Stenotrophomonas maltophilia* 7 (0.5%), *Cryseobacterium indologens* 1 (0.07%), *Flavibacterium oxyzihabitans* 4 (0.3%), *Micrococcus* species 4 (0.3%), *Citrobacter* species 3 (0.22%), *Proteus* species 1 (0.07%) and *Candida* 15 (1.0%) (Fig. 1).

Among the 388 isolates of Coagulase negative *Staphylococci* there were 252 (65.0%) males and 136 (35.0%) females (Fig. 2). Coagulase negative *Staphylococci* showed highest susceptibility to vancomycin (97.7%) and linezolid (97.4%) followed by amikacin (85.8%), teicoplanin (73.5%), co-amoxiclav (68.2%), ciprofloxacin (57.7%), ampicillin (44.6%), ceftriaxone (41.2%), amoxicillin (33.0%), oxacillin (24.2%) and penicillin (16.0%) (Table 1).

Fig. 1: Distribution of organisms isolated in neonatal sepsis

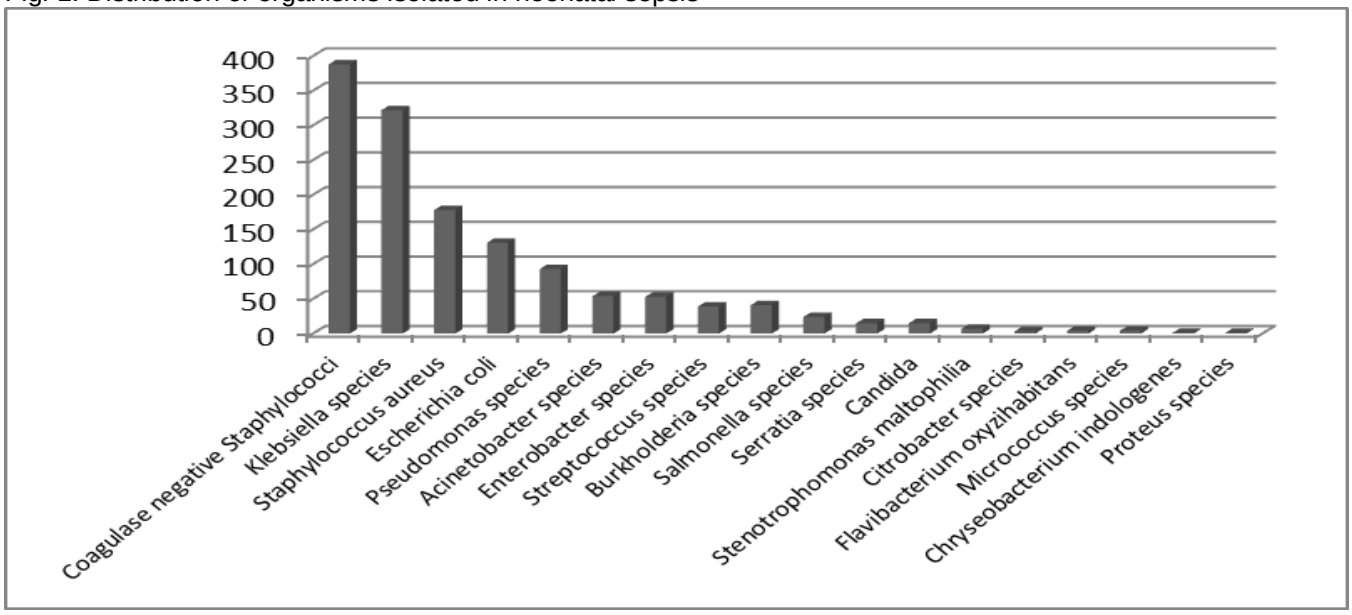

Fig. 2: Gender distribution of Coagulase -ve *Staphylococci*

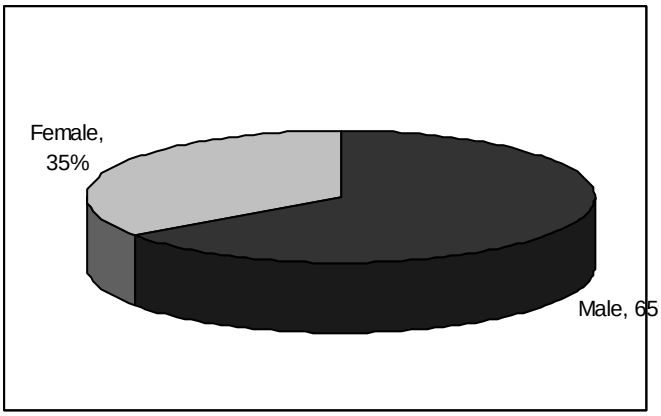

Table 1: Antibiotic susceptibility pattern of Coagulase negative *Staphylococci*

Antibiotic	Susceptibility	Resistance
	No. (%)	No. (%)
Vancomycin	379 (97.7)	9 (2.3)
Linezolid	378 (97.4)	10 (2.6)
Amikacin	333 (85.8)	55 (14.2)
Teicoplanin	285 (73.5)	103 (26.5)
Co-amoxiclav	265 (68.2)	123 (31.8)
Ciprofloxacin	224 (57.7)	164 (42.3)
Ampicillin	173 (44.6)	215 (55.4)
Ceftriaxone	160 (41.2)	228 (58.8)
Amoxicillin	128 (33.0)	260 (67.0)
Oxacillin	94 (24.2)	294 (75.8)
Penicillin	62 (16.0)	326 (84.0)

DISCUSSION

Most of the deliveries (75-90%) in the developing countries occur at homes through traditional birth attendants while in developed countries all the deliveries occur in hospitals with septic preventive measure.[12] Most of the neonates with septicemia have one or more risk factors which include premature rupture of membrane, prematurity, septic delivery and frequent manipulation of the baby.[13] The availability of more potent broad spectrum antibiotic has reduced the incidence of neonatal infection[14].

In the developed countries group B *Streptococcus, E. coli* and *Listeria monocytogens* are most common cause of neonatal sepsis. However in the developing countries these bacteria are replaced by Gram negative *bacilli*, coagulase negative *Staphylococci* and most of these organisms are acquired from the environment[5]. In the present study coagulase negative *Staphylococci* showed the highest incidence in neonatal sepsis. This finding is supported by a research conducted in NICU at Al Nasser and Al Shifa hospital in Gaza. They reported the Gram positive organisms as the major group of isolates in neonatal sepsis. Among this group Coagulase negative *Staphylococci* and *S. aureus* were first and second isolates causing nosocomial blood stream infection in USA. The other organisms isolated from neonatal sepsis were *Klebsiella*, *E. coli* and *Acinetobacter* species[15]. The results of the present study are in accordance with this study in which Coagulase negative *Staphylococci* (28.3%) was the most frequent organism. In another study conducted in Najmiyeh and Baqiyatola hospital in Tehran, the frequency of Coagulase negative *Staphylococci* was 33.7%[16]. A study from Northern India, reported *Klebsiella* (55%) as the most frequently isolated organism[17]. The results of a study from Najmieya Hospital reported 4.9% *Klebsiella*[18].

A study carried out at Mackay Memorial Hospital reported more sepsis in males (58.9%) than females (41.1%)[19]. This finding correlates with the result of the present study in which frequency of sepsis in males is (65.0%) higher than females (35.0%). Similar results were reported in another research conducted in neonates at Beheshti Hospital, Kashan[20]. A study from Imam Komeini Teaching Hospital, Uremia, reported the ratio of boy and girls was 1.67:1 which is compatible with the results of our study[21].

In the current study vancomycin and leinozoid showed highest antimicrobial susceptibility of 97.7% and 97.4% respectively. Vancomycin and linezolid are the most effective antibiotics in the treatment of highly resistant Gram positive bacteria[7] The over use of these antimicrobial drugs are thought to be responsible for induction of bacterial resistance.[16] A study reported the sensitivity of coagulase negative *Staphylococci* with ampicillin (50%), amikacin (83.3%) and ceftriaxone (50%).[22] In our study ampicillin (44.6%), amikacin (85.8%), ceftiaxone (41.2%) and penicillin (16.0%) gave the similar results. A study from a Tertiary care Hospital of Northern India reported 10.4% antimicrobial susceptibility to penicillin in coagulase negative *Staphylococcal* infection.[25]Another study reported the antimicrobial susceptibility of ampicillin (34.0%), penicillin (47.0%) and ceftiaxone (66.0%).[21] The results of our study are also supported by another study conducted on newborns which showed the antimicrobial susceptibility results for ceftriaxone (41.2%), ampicillin (44.6%), vancomycin (97.7%) and ciprofloxacin (57.8%).[24] In our study amoxicillin showed 33.0% susceptibility which is in accordance with the results of a study conducted in a tertiary care hospital [23].

The development, implementation and evaluation of potentially better practices can reduce the nosocomial infections, especially coagulase negative *Staphylococcal* infections.[26] In conclusion the neonates are at the risk of coagulase negative *Staphylococcal* infections. The neonatal sepsis can be managed by the use of appropriate antibiotics. The vancomycin and linezolid are the best choice of antibiotics in the treatment of highly resistant coagulase negative *Staphylococcal* neonatal sepsis. The high resistant rate is associated with the indiscriminate use of drugs for both prophylactic and therapeutic treatment of hospitalized newborn.

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