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RESEARCH ARTICLE

A STUDY OF COAGULASE NEGATIVE STAPHYLOCOCCI ASSOCIATED BLOOD STREAM INFECTIONS IN PEDIATRIC PATIENTS IN A TERTIARY CARE HOSPITAL IN KARNATAKA

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ABSTRACT

Background: Coagulase-negative Staphylococcus (CoNS) found in the normal skin ora and mucous membranes have recently got attention as a potential pathogen, speci cally for nosocomial infections. Recent reports suggest coagulase negative Staphylococci as the most common pathogens of blood stream infections.
Aims: To identify and speciate various species of coagulase negative Staphylococci isolated from bloodstream infection and determine their antimicrobial resistance pattern.
Materials and methods: We collected 224 strains of different CoNS species from positive blood cultures obtained from paediatric patients aged less than 6 years during a period of three years-from January 2012 to December 2014.Isolates were identified and antimicrobial susceptibility was performed by MicroScan Walkaway SI system (Siemens).
Results: Among the 224 pediatric patients enrolled, 120 were male and 104 were female babies. Of the 224 clinical isolates, *Staphylococcus hominis* was the most common species found 89(39.7%). The overall drug resistance among the species ranged from 8.5% to 87% to all the drugs tested except to Vancomycin, Linezolid and Streptogramins which were 100% sensitive. The highest drug resistance was exhibited towards Penicillin and Ampicillin (86.6%) and Oxacillin (69.7%). The minimum drug resistance was shown towards Gentamicin (12.3%) and Rifampicin (8.5%). *S.hyicus, S.cohnii, S.xylosus, S.saprophyticus, S.warneri, S.capitis* were 100% sensitive to Gentamicin.
Conclusions: CoNS have emerged as one of the important cause of blood stream infections. High rate of resistance is exhibited against commonly used antibiotics like Penicillins and Cephalosporins. Hence empirical use of antibiotics has to be avoided to prevent development of multidrug resistant strains.

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INTRODUCTION

Coagulase negative Staphylococci (CoNS) are common colonisers of human skin (Roth and James, 1988), anterior nares and ear canals of human (Natoli *et al*., 2009). Previously, these bacteria were mostly regarded as contaminants of clinical specimens from humans. During the last decades CoNS have emerged as important nosocomialpathogens. Risk factors for CoNS infections include breaches in the natural mucocutaneous barrier, prior exposure to antibiotics, immunosuppression, extreme ages and most frequently, the presence of venous catheter or indwelling prosthetic device, among others (Keim *et al*., 2011).

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Clinical studies have indicated *Staphylococcus epidermidis*, *Staphylococcushaemolyticus, Staphylococcus warneri* and *Staphylococcushominis* as the most prevalent CoNS in hospital infections. The emergence of antimicrobial resistant among CoNS isolates is also an important factor in nosocomial infections (Keim *et al*., 2011). Nosocomial blood stream infections are defined as blood stream infections that occur more than 48 hours after admission or in a patient who had been hospitalized within the previous 10 days (Favre *et al*., 2005). CoNS have emerged as a major cause of nosocomial blood stream infection. Nosocomial bacteraemia negatively impacts patient outcome, with an attributable mortality ranging from 14% to 38%; significantly prolongs hospital stay and generates substantial extra costs. The incidence rate of bacteraemia due to CoNS varies according to the type and size of the institution and peaks in intensive care units, where the incidence density is approximately 8 episodes per 1,000 admissions (Favre *et al*., 2005).

But CoNS are regarded predominantly as blood culture contaminants, contamination rates may be institution specific and are related to phlebotomist expertise and efficacies of skin disinfectants, contamination rates of 2% to 3% are recommended as benchmarks (David Souvenir, 1998). For this reason, several clinical and microbiologic guidelines were established to differentiate true bacteraemia from contamination. For instance, growth within 48 hours and multiple blood cultures positive for the same organism (David Souvenir, 1998), or growth in both aerobic and anaerobic bottles and growth within 48 hours are considered suggestive of true bacteraemia, whereas isolation of other skin contaminants, growth of organisms in blood drawn for culture during effective antibiotic therapy and negative additional blood cultures are viewed as more characteristic of contamination (Khatib *et al*., 1995). It has been suggested that the major virulence factor of CoNS is the ability to form biofilm on the surface of indwelling medical devices. In the biofilm, the bacteria seem to be protected against antibiotics and the immune system. They also produce lipases, proteases and other exoenzymes, which are possibly implicated with the bacterial persistence and dissemination in the host tissue. The emergence of antimicrobial resistance among CoNS isolates is also an important factor in nosocomial infections. Furthermore, methicillin-resistant CoNS (MRCoNS) are cross resistant to all other beta-lactam antibiotics (Keim *et al*., 2011). We conducted this study to describe the species distribution and antibiotic susceptibility pattern of CoNS isolated from blood cultures received in our hospital.

MATERIALS AND METHODS

A total of 224 CoNS strains were isolated from blood samples of paediatric patients between the age of one month to six years, who were hospitalized in various departments and in intensive care units of a tertiary care centre in Karnataka, India, during a period of three years from January 2012 to December 2014. The prospective descriptive study was carried out at the Department of Microbiology in the same centre. The isolates were considered clinically significant when isolated in pure culture from two or more blood cultures which coincided with clinical signs and symptoms of bacteremia, leucocytosis and high CRP values. The identification of CoNS species and the sensitivity pattern for each isolate was performed using Microscan Walk Away SI system (Siemens).The Microscan Synergies plus gram-positive identification and susceptibility panel was used. The Microscanmicrotiter plate for gram-positive panel contained separate wells for biochemical agents for identification and separate wells in the same plate for antimicrobial agents with different concentration in double dilutions for sensitivity testing. The test was performed as per manufacturer's instructions (MicroScan Synergies plus Gram Positive Procedure Manual, 2010).

RESULTS

Among the 224 paediatric patients enrolled into the study, 120 were male and 104 were female babies. Of the 224 clinical isolates of CoNS that were identified upto species level in the study, *S. hominis* was the most common species found 89(39.7%), followed by *S.epidermidis* 53(23.6%) and *S.hemolyticus* 24(10.7%) and others. (Table-1)

Table 1. Percentage distribution of CoNS species isolated in the study

CoNS Species	Number (%)
S.hominis	89(39.7)
S.epidermidis	53(23.6)
S.hemolyticus	24(10.7)
S.xylosus	13(5.8)
S.saprophyticus	11(4.9)
S.auricularis	08(3.5)
S.warneri	07(3.1)
S.lugdunensis	05(2.2)
S.capitis	05(2.2)
S.hyicus	02(0.08)
S.scuiri	02(0.08)
S.intermedius	01(0.04)
S.cohnii	02(0.08)
S.simulans	02(0.08)

The overall drug susceptibilty among CoNS species ranged from 13.4% to 100% to all the drugs tested (Figure-1).

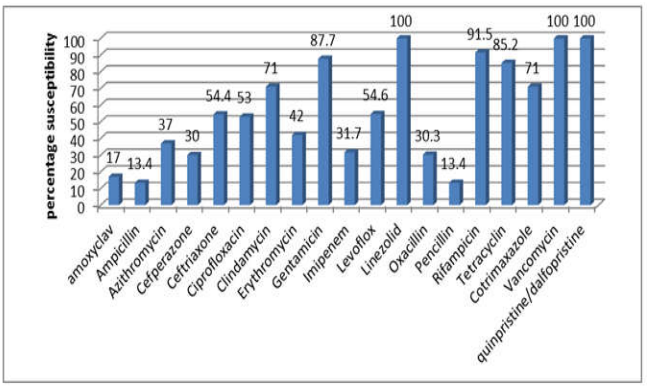

Figure 1. Percentage mean antibiotic susceptibility pattern of CoNS isolates

The highest drug resistance was exhibited toward Penicillin (86.6%) and Ampicillin (86.6%), followed by Oxacillin (69.7%). The highest drug susceptibility was shown towards Linezolid, Vancomycin and Quinipristin/Dalfopristin(100%) followed by Rifampicin (91.5%) and Tetracycline (85.2%). The drug resistance pattern for the first three CoNS species i.e. *S.hominis, S.epidermidis*, *S.haemolyticus* was similar for most of the drugs except for gentamicin where 65% of *S.hominis*, 63% of *S.epidermidis* and33% of *S.haemolyticus* isolates were sensitive. All the three species exhibited high resistance to ampicillin; *S.epidermidis* (88.4%), *S.haemolyticus* (100%) and *S.hominis* (90%). *S.hominis* showed almost equal sensitivity to Ampicillin (10%) and Cephalopsporins (11.2%) and *S.haemolyticu s*and *S.epidermidis* showed sensitivity of 8.3% and 11.6% to each of these drugs respectively. *S.hyicus, S.cohnii, S.xylosus, S.saprophyticus, S. warneri, S. capitis* were 100% sensitive to gentamicin, but differed with clindamycin sensitivity,as they showed 100% susceptibility except *S.warneri* (57.1%), *S.saprophyticus* (91%) and *S.xylosus* (38.4%). Most of the CoNS isolates (69.7%) were resistant to oxacillin. Less frequently isolated CoNS species showed 100% resistance to oxacillin like *S.saprophyticus, S.cohnii*. Whereas *S.epidermidis (*79%), *S.haemolyticus* (83.4%) and *S.hominis* (77.6%) were resistant to oxacillin.

DISCUSSION

Coagulase negative Staphylococi are increasingly being incriminated as a significant pathogen associated with

healthcare infections. Reports from National nosocomial infections surveillance system in early 1990's have reported CoNS as fifth most commonly reported pathogen (Abdulhadi Hassan, 2009). CoNS is the most common blood culture isolate and is a significant pathogen, therefore there is a need for identification of CoNS up to species level as has been emphasised by many investigators (Ahmad Khan *et al*., 2014; Singh and Banerjee, 2008; Sundaram *et al*., 2009). The species identification is important in monitoring the reservoir and distribution of CoNS involved in healthcare-associated infections and will help to understand the pathogenic potential of individual CoNS species.

In our study, *Staphylococcus hominis* was the most common isolate found 89 (39.7%), followed by *S.epidermidis,* 53 (23%) and *S.haemolyticus*, 24 (10.7%). Most of the studies have shown *Staphylococcus epidermidis* causes 60 to 93% of CoNSbloodstream infections, several other CoNS species are reported to cause blood stream infections in infants. Recently, *Staphylococcus hominis* has emerged as an important pathogen in neonatal blood stream infection. Our study has recorded about 39.7% of the isolates as *S.hominis* which is in agreement with studies conducted by Chaves *et al*. (2005) and Klooz *et al* (1998).Similar results were recorded by other studies conducted in India,in which the order of appearance of the three species was different, with there was variation in their percentages i.e., *S.epidermidis*, 234 (40%), *S. haemolyticus*, 84 (14%) and*S.hominis*,65 (11%) (Jain *et al*., 2004).

Studies conducted in Saudi Arabia, showed the three species being predominantly isolated as in our study but *S.epidermidis* (75.8%) being the highest, followed by *S.hemolyticus* and *S.hominis* (11%) (Ahmad Khan *et al*., 2014). In our study, CoNS species showed maximum resistance towards penicillins and ampicillin(86.6%),this is in agreement with other studies where CoNS exhibited 99.5% resistance to penicillins and 99% towards ampicillin (Ahmad Khan *et al*., 2014). Another study in India showed 94% resistance to penicillin and 98% to ampicillin (Jain *et al*., 2004).

CoNS are gaining more importance due to methicillin resistance. Methicillin-resistant coagulase negative Staphylococci (MRCoNS) have become predominant organism in hospitalised patients. Studies carried out by SENTRY Antimicrobial Surveillance Program, have reported about 70-75% of CoNS are resistant to methicillin (Ahmad Khan *et al*., 2014). Our study has recorded that about 69.7% of the CoNS isolates are resistant to methicillin. Some studies from India and Turkey showed a similar rate of methicillin resistance among CoNS,66% in India (14) and 67.5% in Turkey (15). Several other studies have recorded high incidence of about 93.6% as well (Ahmad Khan *et al*., 2014).

The acquisition of methicillin resistance in Staphylococci results from the recombinase-mediated insertion of Staphylococcal cassette chromosome mec (SCC*mec*), the mobile genetic element carrying mecA, at the 3′ end of a chromosomal open reading framewhich directs the synthesis of low affinity penicillin binding protein, PBP-2a, and it may easily spread to all methicillin-resistant CoNS, probably through transposons (Koksal *et al*., 2009). In the present study 79% of *S.epidermidis,* 83.4% of *S.haemolyticus* and 77% of *S.hominis* were resistant to Oxacillin. These results are in agreement with the studies conducted in Brazil where 73.2% isolates of *S.epidermidis* and 85.7% isolates of *S.haemolyticus* were resistant to oxacillin, but only 28.6% of *S.hominis* were resistant to oxacillin (Pereira VC*et al*., 2013). Other studies have demonstrated high oxacillin resistance in *S.epidermidis*and *S.haemolyticus* (95%) (Jain *et al*., 2014). Our study has recorded about 58% resistance to erythromycin. Other studies conducted by Khan *et al*. (2014) and Koksal *et al.* (2009) have shown a very high resistance to erythromycin about 78% and 80% respectively.

Resistance to fluoroquinolones like ciprofloxacin has been recorded upto 47% of isolates. This is study conducted by Mohan and Jindal *et al.* (2002) which recorded 51% resistance towards ciprofloxacin. With CoNS isolates being resistant to many commonly used antibiotics, the glycopeptide vancomycin has been considered to be the antibiotic of choice. Our study recorded high sensitivity to vancomycin (100%), this is in agreement with other studies which show uniform susceptibility of CoNS to vancomycin (Jain *et al*., 2014; Mohan *et al*., 2002).Other studies with decreasing susceptibility to vancomycin have been published (Miguel FajardoOlivares *et al*., 2011). Our study has recorded 100% susceptibility of CoNS isolates to newer drugs like Linezolid and Quinpristine/Dalfopristine which is in concordance with studies from India have shown 100% sensitivity to Linezolid (Mohan *et al*., 2002).

Conclusion

CoNS have emerged as one of the important causes of blood stream infections. High rate of resistance is exhibited against commonly used antibiotics like penicillins and cephalosporins. The increasing rate of methicillin resistance and inappropriate use of antibiotics has led to development of multidrug resistant strains. Hence use of antibiotic on rotation is advisable for long term treatment.

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