

## ORIGINAL RESEARCH

# Increasing Incidence Of Coagulase-Negative *Staphylococcal* Sepsis- An Emerging Challenges

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## ABSTRACT

**Introduction-** Coagulase negative *Staphylococcus* (CoNS), being a part of the commensal flora, have long remained neglected as mere contaminants till their recently reported increased rate of isolation, evidenced their potential as nosocomial pathogens. Treatment is difficult due to confusion in pathogenicity and multi-drug resistance. Aim of the study was to identify the different species of CoNS from blood sample of patients having signs and symptoms of septicemia and to establish their clinical relevance.

**Material and Method:** Blood cultures were processed in BacT/Alert 3-D system (BioMerioux). One hundred fifty three (153) CoNS were isolated from blood culture of different age group patients. A few samples were tested by Microscan autoSCAN4. Biotyping includes coagulase test (both slide and tube), nitrate reduction test, urease test, ONPG test. Disc diffusion tests include polymyxin-B, Bacitracin, novobiocin discs. Tests for biofilm production were carried out by Congo Red Agar (CRA) method and Tube method (TM). Finally antibiotic sensitivity testing was carried out by disc-diffusion method of Kirby-Bauer.

**Result:** 153 CoNS were isolated in period of six months from sepsis patients. Number of *S.epidermidis* (25%) was highest among them followed by *S.haemolyticus* (14%). Most of them (85%) are biofilm producer.

**Conclusion:** This will most accurately promote treatment for those patients with true CoNS infection. It will also avoid unnecessary treatment in those without true infection.

**Keywords:** Coagulase negative *Staphylococci* (CoNS), Blood stream infection (BSI), Biofilm

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## INTRODUCTION

Coagulase-negative *staphylococci* (CoNS) are increasingly implicated as a leading cause of bloodstream infection (BSI).<sup>1</sup> It is accounting for 27% to 32% and 50% of recurrent nosocomial bloodstream infections among adult and paediatric patients, respectively.<sup>2</sup> Coagulase-negative *staphylococci* (CoNS) are divided into more than 44 species and more than twelve subspecies, of which most of them have been associated with humans.<sup>1</sup> Patients at risk include those with prosthetic valves, pacemakers, intravascular catheters or other foreign bodies, neonates and immunocompromised hosts.<sup>3</sup> Among the risk factors the usage of intravascular catheters pose a significant risk to patients for developing a catheter-related infection with a poor prognosis, leading to significant morbidity and mortality.<sup>4</sup> Diagnosis of bacteremia has been made on the basis of one or more positive blood cultures growing a single morphologic type (strain) or species of CoNS as the sole isolate.<sup>5</sup> Culture growing multiple strains or species of CoNS and/or other normal skin flora are regarded as probably contaminant.<sup>6</sup> Biofilm production has important role in pathogenicity and it is also protective from antimicrobials. Thus CoNS develops antibiotic resistance.<sup>7,8</sup>

## MATERIALS AND METHODS

The prospective study was carried out in tertiary care centre KPC Medical college and Hospital, Kolkata. Ethical clearance was obtained from the institute. One hundred fifty three (153) CoNS were isolated from blood culture of different age group patients having signs and symptoms of septicemia in a period of six months (Jan'14 to June'14). Blood cultures were processed in BacT/Alert 3-D system (BioMerioux). Paired blood cultures were processed from the same patient. A few samples were tested by Microscan autoSCAN4. It revealed the same result and confirmed the diagnosis. Clinical correlation was done by taking the proper history of patients. All isolates were oxidase negative as determined by the oxidase reagent, thus excluding micrococci.

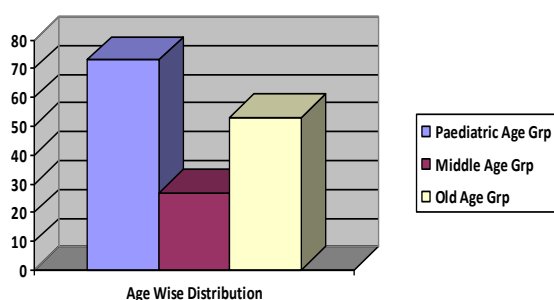
Speciation were done by biotyping. Biotyping includes coagulase test (both slide and tube), Catalase Test, nitrate reduction test (Figure-1), urease test, ONPG (Ortho nitrophenyl  $\beta$  galactoside) test (Figure - 2). Disc diffusion tests include polymyxin-B, Bacitracin, novobiocin discs.<sup>9</sup> Tests for biofilm production were carried out by Congo Red Agar (CRA) method[10] and Tube method (TM).<sup>10</sup> Carrier test was done to evaluate hospital acquired infection. Nasal swab was taken from individual health staff. CoNS formed orange coloured colonies on Mannitol salt agar (MSA).<sup>9</sup> Finally antibiotic sensitivity testing was carried out by disc-diffusion method of Kirby-Bauer.

## RESULT

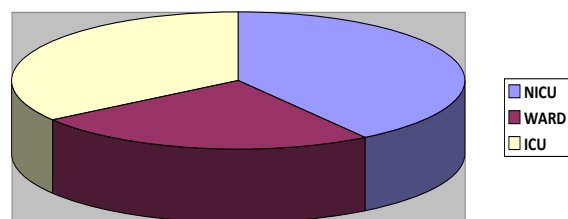
153 CoNS were isolated in period of six months from sepsis patients. Number of *S.epidermidis* (25%) was highest among them followed by *S.haemolyticus* (14%). Most of them (85%) are biofilm producer (Image-3,4). 13 types of species were isolated (table 1). According to descending order, they were – *S.epidermidis*, *S.haemolyticus*, *S.xylosus*, *S.homonis*, *S.cohnii*, *S.simulans*, *S.capitis*, *S.warneri*, *S.lugduncensis*, *S.shleiferi*, *S.sciuri*, *S.carnosus*, *S.saprophyticus*. They caused sepsis more in Pediatric population (Graph-1). It is commonly isolated neonatal intensive care unit (NICU) (Graph-2).

Sl No	Sample	Novobiocin	Ploymyxin-B	Bacitracin	Urcase	NRT	ONPG	Percentage
1	<i>S. epidermidis</i>	S	R	S	P	P	N	25%
2	<i>S. hemolyticus</i>	S	S	R	N	P	N	14%
3	<i>S. hominis</i>	S	S	S	P	N	N	10%
4	<i>S. xylosus</i>	R	S	S	P	N	P	10%
5	<i>S. capitis</i>	S	S	S	N	N	N	8%
6	<i>S.cohnii</i>	R	S	R	N	N	N	8%
7	<i>S.sSimulans</i>	S	S	S	P	P	P	8%
8	<i>S. warneri</i>	S	S	I	P	N	N	6%
9	<i>S. lugduncnsis</i>	S	S	R	N	P	N	4%
10	<i>S. carnosus</i>	S	S	S	N	P	P	2%
11	<i>S. saprophyticus</i>	R	S	S	P	N	P	2%
12	<i>S. schleiferi</i>	S	S	R	N	P	N	2%
13	<i>S. sciuri</i>	R	S	R	N	P	N	2%

**Table-1:** Distribution of different species of CoNS isolated from blood sample



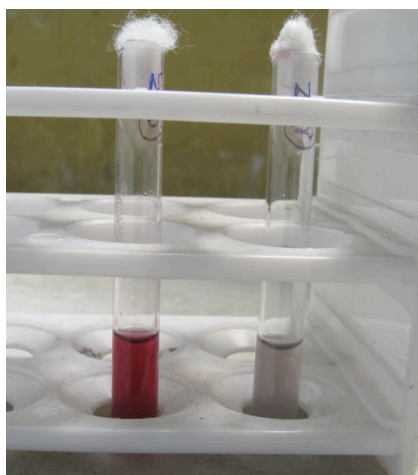
**Graph-1:** Age group wise distribution of CoNS sepsis (total sample 153)



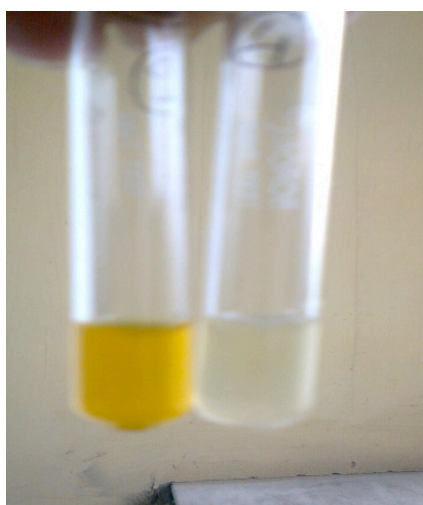
**Graph-2:** Ward wise distribution of CoNS sepsis (total sample 153)

## DISCUSSION

According to the Centres for Disease Control and Prevention, CoNS contribute to over 30% of hospital-wide central-line associated bloodstream infections.<sup>11</sup> There are several mode of entry-skin entry site, the outer surface of the catheter can become colonised with organisms originating from the skin, biofilm inside the catheter, from the hand of hospital staff.<sup>12</sup> Biofilm production is due to Polysaccharide intercellular adhesion (PIA). PIA reacts with Congo red to produce black coloured colonies.<sup>13</sup> Treatment include removal of catheter, change of catheter, antibiotic coated catheter, proper antibiotic.<sup>14</sup> Biosafety practices includes wearing a head cover, a mask, a gown and sterile gloves by the healthcare worker and a body drape for the patient.<sup>15</sup> clinical parameters are used in determining the clinical significance of the isolate.<sup>16</sup> The accurate prediction of likely pathogens and antimicrobial resistance pattern is crucial for successful therapy.<sup>17</sup> In our study, none of the staphylococcal isolates was



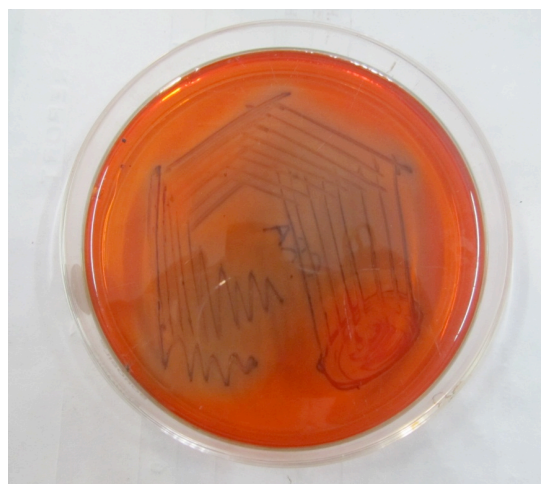
**Figure-1:** Nitrate reduction test (NRT)



**Figure-2:** ONPG test



**Figure-3:** TUBE Method



**Figure-4:** Congo red agar showing black colonies

found to be resistant to glycopeptides, while high penicillin and oxacillin resistance was present in CoNS. The ability of CoNS to form an intravascular catheter-related infection is related to biofilm formation on a catheter. In CoNS, specifically *S. epidermidis*, biofilm formation is encoded by the *ica* ADBC operon. It is advantageous for CoNS to reside in a biofilm. These bacteria are protected from the external environment, allowing microbial communication in the form of horizontal gene transfer and have enhanced virulence due to immune evasion. Biofilm formation is associated with a non-specific mechanism of antimicrobial resistance.<sup>18</sup>

## CONCLUSION

Majority of CoNS cause BSI in paediatric population. Most BSI are IVD associated. Penicillin and oxacillin resistance is high in these isolates. *S. epidermidis* is the commonest isolate (25%). In order to prevent the spread of multidrug-resistant CoNS in the clinical setting vigilant surveillance and infection control policies need to be adapted.

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