

## Study Of Coagulate Negative Staphylococci (Cons) & Their Antibiotic Resistance Profile

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### Abstract:

**Objective:-** Prevalence of CoNS is increasing day by day all over the world including India. They are generally associated with device associated infections and are often resistant to a number of antibiotics. It is a matter of concern for clinicians as such infections are difficult to treat. The aim of this study is to find out implications of CoNS in hospital admitted patients and to determine their resistance profile, so that necessary steps could be taken to prevent spread of such infections and formulate an effective antibiotic policy. **Material and Method :-** Various clinical samples submitted to microbiology lab for culture and sensitivity were processed as per standard laboratory methods for isolation and identification of CoNS. Antibiotic sensitivity profile was determined for these isolates by Kirby-Bauer disc diffusion method as per CLINICAL & LABORATORY STANDARD INSTITUTE (CLSI) guidelines<sup>1</sup>. **Result:-** One hundred (100) isolates of CoNS were obtained during processing of various clinical samples such as blood, sputum, urine, pus and swabs from wound, vagina & throat. Maximum number of CoNS was isolated from blood samples followed by respiratory tract, urine, pus and swabs from wound, vagina and throat. They were subjected to antibiotic sensitivity test by disc diffusion method. Sensitivity test was also done against cefoxitin and Novobiocin. 72% of CoNS were found to be Cefoxitin resistant while 28% were Cefoxitin sensitive. Infection was more common in males than females and preponderance was more in middle age group.

**Keywords:** - CoNS (coagulase negative staphylococci), FBR- BSI (Foreign body related blood stream infections)

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### I. Introduction

CoNS are opportunistic pathogens and represent one of the common organisms among nosocomial infections. They generally colonize skin and mucous membrane of different parts of the body and therefore are continuous source of endogenous infections<sup>2</sup>. They are mainly transmitted by medical and nursing procedures. CoNS are generally associated with use of urinary catheters, I.V. line insertions and transplant devices<sup>3</sup>. Once inserted, foreign bodies tend to become colonized by CoNS resulting in enormous economic & medical burden to the patient. Infections with CoNS are also challenging to the clinicians as they are resistant to multiple commonly used antibiotics. As for other nosocomial pathogens, increasing rate of antibiotic resistance has become more severe problem with CoNS than for S.aureus which further limits therapeutic options.

CoNS have less virulence factors as compared to Staphylococcus aureus therefore have different disease spectrum. S.epidermidis and S. saprophyticus are few common and important members of CoNS. S.saprophyticus is generally associated with urinary tract infections while S.epidermidis is found to be associated with device associated hospital acquired infections. Relevance of CoNS in healthcare system is further increased as number of immunocompromised patients & use of inserted & implanted devices are increasing. Majority of CoNS infections are generally chronic, non-specific, mild & subtle in nature. Bacteraemia or systemic spread of these organisms may lead to infections like endocarditis, meningitis, joint sepsis & local manifestations<sup>4</sup>.

CoNS are very common cause of foreign body related blood stream infections, most of them are catheter related, resulting from insertion of intravascular catheters.

Pathogenicity of CoNS is because of their capacity to colonize & their ability to form biofilm<sup>5</sup>. As far as antimicrobial susceptibility is concerned, Beta-lactam antibiotics have become ineffective. Situation is further deteriorated by appearance of multi drug resistance. Due to continuous loss of susceptibility to commonly available antibiotics like Ciprofloxacin, Erythromycin, Gentamicin, Cephalosporins & Clindamycin, therapeutic

options have become very limited. Further worsening of situation can only be prevented by judicious use of antibiotics.

## II. Material and Methods

Various clinical samples were submitted to bacteriology lab FHMC Etmdpur, Agra for culture & sensitivity. Primary culture was done on blood agar & MacConkey agar. Culture plates were incubated at 37°C for 24 to 48 hours. Catalase test, Oxidase test, gram staining, slide & tube coagulase test were done from suspected colonies. Coagulase negative staphylococcus colonies were further subjected to sensitivity test against various antibiotics including Cefoxitin & Novobiocin. Novobiocin resistant colonies were not included in the study. All the test were done as per standard protocol of the laboratory. Antibiotic susceptibility profile of CoNS isolates were determined by Kirby-Bauer disc diffusion method as per CLSI guidelines. The Antibiotic discs used for these isolates are listed in table 1. Culture media & antibiotic discs were procured from Hi Media labs private limited India. Data regarding age, sex & clinical history was obtained from registration form submitted to microbiology dept. FHMC.

**Table 1 Zone of interpretative table in accordance with CLSI guidelines<sup>1</sup>**

S.No.	Antibiotic	Symbol	Drug conc. µg	Zone of inhibition		
				Resistant	Intermediate	Sensitive
1	Penicillin	P	10 units	≤28	-	≥29
2	Cefoxitin	CX	30	≤21	-	≥25
3	Ciprofloxacin	CIP	5	15	16-20	21
4	Levofloxacin	LE	5	15	16-18	19
5	Gentamicin	GEN	10	12	13-14	15
6	Erythromycin	E	15	13	14-22	23
7	Clindamycin	CD	2	14	15-20	21
8	Co-trimoxazole	COT	25	≤10	-	≥16
9	Linezolid	LZ	30	12	13-17	18
10	Vancomycin	VA	30	≤14	-	≥15
11	Cefotaxime	CTX	30	22	23-25	26
12	Cefixime	CFM	5	15	16-18	19
13	Cefpodoxime	CPD	10	17	18-20	21

## III. Results

Out of 100 CoNS isolates, maximum number i.e. 37 were obtained from blood samples, followed by 26 from respiratory tract (sputum and bronchial aspirates), 17 from urine, 13 from pus & 7 from wound, vaginal and throat swabs. (table 2)

Age and gender distribution of CoNS isolates has been documented in table 3. Majority of the isolates (64) have been obtained from age group of 25 to 60 years, 23 isolates are from age group of less than 25 years and 13 isolated are from age group of above 60 years. Isolation was more from males as compared to females.

Antimicrobial sensitivity profile of all CoNS isolates were done by disc diffusion method & zone size interpretation was done in accordance with CLSI guidelines as shown in table I. They were also tested for Cefoxitin sensitivity. Results of antimicrobial sensitivity tests are shown in table 5. 72% isolates were Cefoxitin resistant while 28% were Cefoxitin sensitive (table 4). Cefoxitin resistant CoNS have been found to be resistant to most of the tested antibiotics, while Cefoxitin sensitive strains are showing high degree of sensitivity to antibiotics used in the test (table 5)

## IV. Discussion

CoNS represent a regular part of normal flora of skin & mucous membrane of humans. They prefer areas of high humidity such as axilla, gluteal and inguinal areas. They also colonize umbilicus, antecubital area & anterior nares. CoNS isolate exhibit multidrug resistance to antibiotics & antiseptics. Other factors which contribute to the spread of CoNS in hospital are adhesion factors for colonization of foreign bodies, biomaterials and their ability to produce biofilms. Known hygiene related factors such as improper hand hygiene and inadequate disinfection of instruments further contribute to the spread of CoNS infections.

**Clinical Significance-** There has been drastic change in patient population over the years. Number of elderly, chronically ill & immunocompromised patients are increasing. Beside this use, of inserted foreign bodies has also been increased leading to large variety of infections caused by CoNS.

Although less virulent than *S.aureus*, CoNS may cause infections if co-factors such as foreign body insertion, immunosuppression & their ability to biofilm production are present.

CoNS are known to stimulate monocytes to produce cytokines which may be responsible for clinical symptoms<sup>6</sup>.

Every time when CoNS are isolated, question arises whether they represent true infection or only colonization/contamination as it is difficult to validate their role in the implication of infections. This dilemma can be solved only with close cooperation of clinician and microbiologist. Factors suggesting true infections include the isolation of strain in pure culture from infected site & repeated isolation of the same strain over the course of infection.

*S.epidermidis* is the commonest organism causing infection associated with foreign body inserted devices. Most FBR-BSI is catheter related blood stream infections resulting from insertion of intravascular catheters.

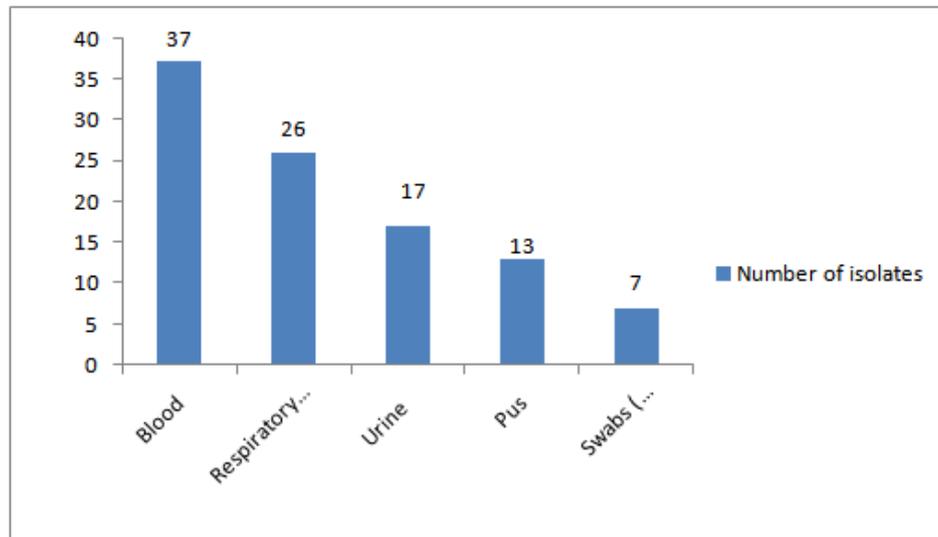
CoNS isolation rate was highest in blood samples (37%) followed by respiratory secretions(26%), urine(17%), pus(13%),and swabs from wound, vagina &throat(7%). In the study of Changdeo S.Aher et al <sup>7</sup>, majority of CoNS were obtained from blood cultures (28 %) followed by urine (21%) , pus (20%),vaginal swab (18%) and miscellaneous (13%). Usha et al<sup>8</sup> reported in their study that majority of CoNS were obtained from blood (52%) followed by pus (32%), urine (12%) throat swab (2%), catheter tip (1%), gastric lavage (1%). Ahmad Farajzadeh Sheikh et al<sup>9</sup> reported that CoNS were obtained from urine (51.5%), blood (25.4%) tracheal tube (9.7 %), body fluid discharge (8.2%) & wounds (5.2%) respectively. Shadhvi Parashar et al<sup>10</sup> reported 45.95% CoNS were isolated from blood cultures, 19.46% from urine, 15.6% from pus, 7.5% from vaginal swab, 11.4% from miscellaneous samples. This difference in the isolation rate of CoNS in various samples is due to difference in sample size and type of specimens included in the study<sup>11</sup>.

In the present study 60% CoNS were isolated from male patients and 40% from females. Our finding correlated with the study of Usha et al who also reported CoNS infection more in males (59%) than in females (41%). Ahmad Farajzadeh Sheikh et al<sup>9</sup> reported that CoNS isolations were 57.5% in males and 42.5% in females. Similarly Surekha Y Asangi et al<sup>12</sup> reported more CoNS isolations in males (65.6%) than females (34.4%) CoNS isolation was more in males in comparison to females, as males seek and reports for medical advice more frequently than females in our community. In our study, prevalence of CoNS isolation was found predominantly in the age group of 25-60 years 64% which is similar to the study Saroj et al <sup>13</sup> who also reported that a majority of CoNS strain were obtained from age group of >40 years. High prevalence in this age group may be attributed to higher incidence of UTI, post operative wound infection and medical and surgical related problems .

The widespread use of broad spectrum antibiotics in community and healthcare set up has contributed to drug resistance in Staphylococci. CoNS are gaining more importance due to methicillin resistance which implies resistance to all betalactam antibiotics, cephalosporins and quinilones <sup>14</sup>. An increase in the incidence of nosocomial infections caused by methicillin resistant CoNS has been reported in several studies<sup>11</sup>. Therapeutically CoNS are challenging due to high prevalence of methicillin resistant strains and also increasing number of isolates with less susceptibility to most of the antibiotics. Current therapeutic options for methicillin resistant CoNS are limited to few expensive drug like Vancomycin, Teicoplanin & Daptomycin <sup>15</sup>. Vancomycin should be replaced by beta lactamase resistant penicillins and cephalosporins for methicillin susceptible isolates.Increased use of Vancomycin has led to the emergence of methicillin resistant CoNS isolates with decreased susceptibility to Vancomycin. These MDR strains not only pose a serious therapeutic problem but also serve as a hospital reservoir for the antibiotics resistant strains. The regular antibiotic resistance surveillance of CoNS will be useful for selecting an appropriate antibiotic and to know the changing trends of antibiotic susceptibility pattern, for developing hospital antibiotic policy and for limiting the use of recommended antibiotics like Vancomycin as initial treatment and save it for the treatment of resistant and life-threatening staphylococcal infections. For infections associated with foreign body insertions, removal of the device along with institution of proper antibiotics in right dosage is advisable.

**Table -2 Isolation pattern of CoNS in various clinical specimen**

Clinical specimen	Number of isolates sample wise
Blood	37
Respiratory tract	26
Urine	17
Pus	13
Swabs ( wound , vaginal , throat )	7



Gender and age wise distribution 3

Age groups (years)	Male	Female
<25	12	11
25-60	40	24
>60	8	5

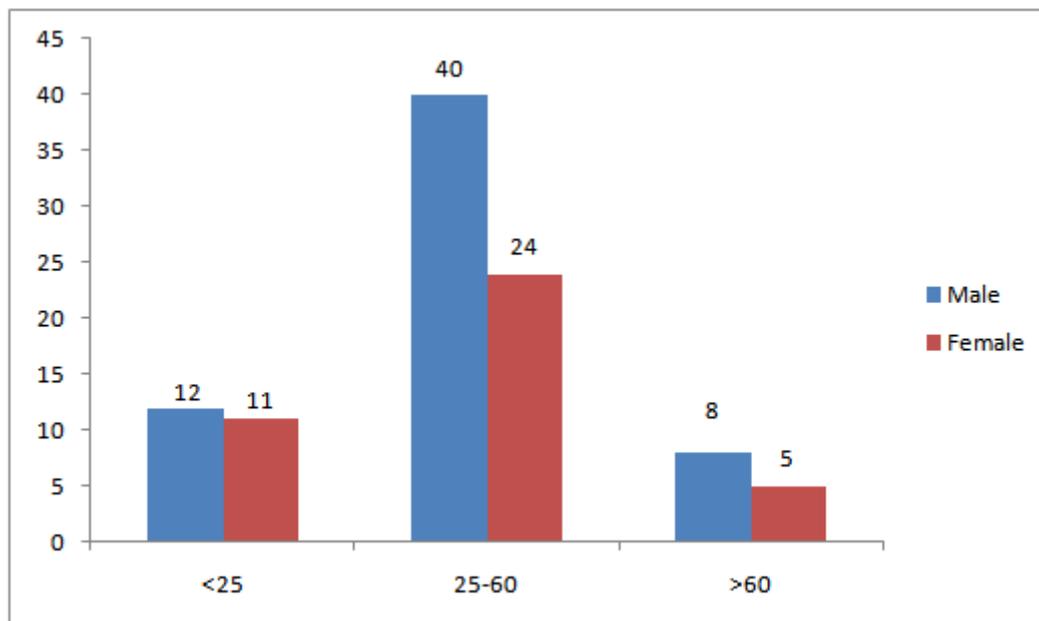


Table -4 Showing methicillin resistance among CoNS isolate

Bacterial isolates	No of strains isolate
Methicillin resistance coagulase negative staphylococcus (MR-CoNS)	72
Methicillin resistance coagulase negative staphylococcus (MS-CoNS)	28

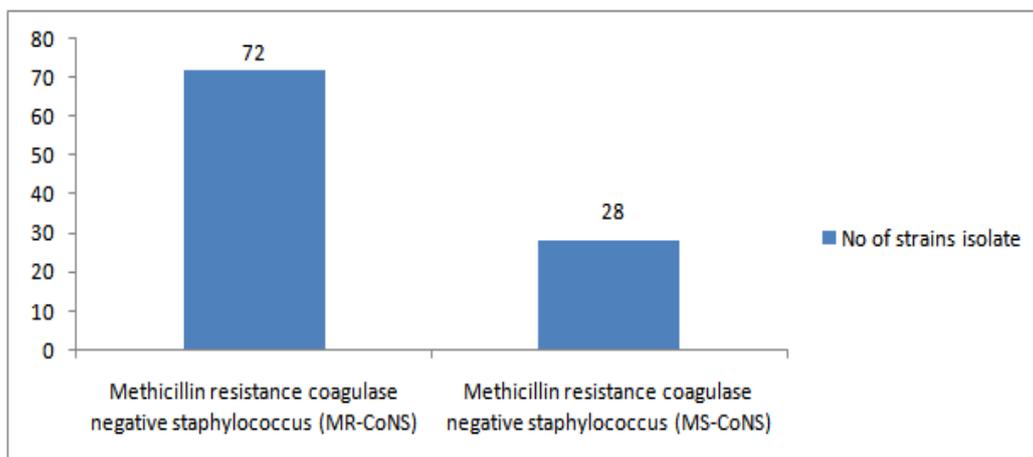
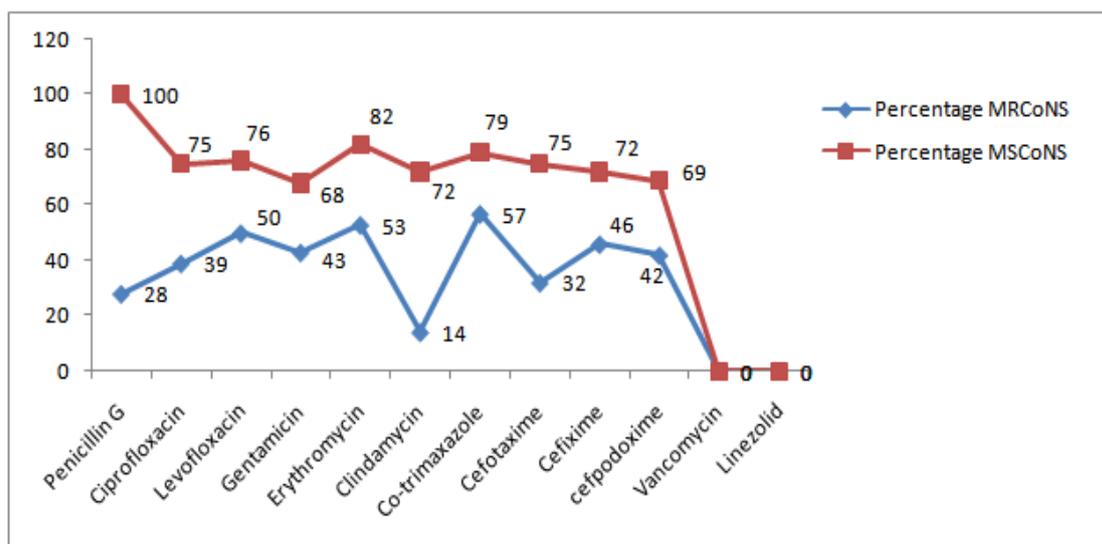


Table -5 Antibiotic resistance pattern of MRCoNS and MSCoNS

Anitibiotics	MRCoNS(N=72)	Percentage	MSCoNS(28)	Percentage
Penicillin G	72	100	8	28
Ciprofloxacin	52	75	11	39
Levofloxacin	55	76	14	50
Gentamicin	49	68	12	43
Erythromycin	59	82	15	53
Clindamycin	51	72	10	14
Co-trimoxazole	57	79	16	57
Cefotaxime	54	75	9	32
Cefixime	52	72	13	46
cefpodoxime	50	69	12	42
Vancomycin	0	0	0	0
Linezolid	0	0	0	0



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