



COAGULASE NEGATIVE STAPHYLOCOCCUS SPECIES;

RESISTANCE AND THERAPEUTIC DECISIONS AT THE TURN OF THE NOVEL MILLENNIUM

Eiman Syed¹, Faiza Nawaz Satti², Sumaira Mubasher³, Farhan Rasheed⁴, Muhammad Ilyas⁵, Ambereen Imran Anwar⁶, Waheed uz Zaman⁷

1. Assistant Professor, UIMLT FAHS
The University of Lahore
2. MBBS
Women Medical Officer
Tehsil Head Quarter Hospital Kotli Sattian
3. Women Medical Officer
Tehsil Head Quarter Hospital Talagang
4. M.Phil Microbiology
Assistant Professor Pathology,
Microbiology Section, Pathology Department,
Allama Iqbal Medical College Lahore, Pakistan
5. Student 4th year Bsc Hons
Pathology Department,
Allama Iqbal Medical College (AIMC&JHL) Lahore, Pakistan
6. MBBS, FCPS
Professor of Pathology
Head Dept. of Pathology
Allama Iqbal Medical College,
Lahore, Pakistan
7. Assistant Professor
PhD

Correspondence Address:

Dr. Waheed uz Zaman
Assistant Professor
wuzzaman777@gmail.com

Article received on:

22/01/2018

Accepted for publication:

15/03/2018

Received after proof reading:

04/05/2018

INTRODUCTION

The rise of antimicrobial opposition warrants the need to determine the antimicrobial resistance pattern. Drug resistance coagulase-negative Staphylococcus (CoNS) are the protruding cause of hospital acquired as well as community-acquired infections, manifesting from minor skin infections to life-threatening infections.^{1,2}

Slime production, the most accentuated method in pathogenesis of staphylococcal infections. Slime being much polysaccharide in nature secrete from cell colonize and spread in the hospital environment, besides. It also helps as anti-phagocytic agent.³ Since the 1970s CoNS are Actual potential pathogens of the great concern.⁴ Although there is great advancements in the production of antimicrobial agents, still we are in era of thoughtful difficulties about dealing

ABSTRACT... Objective: Department and sample wise distribution along with drug-resistant pattern and best therapeutic choice of drugs against Coagulase-negative Staphylococcus species (CoNS). **Study Design:** Cross-sectional study. **Setting:** Department of Microbiology AIMC Lahore Pakistan. **Period:** 1st January 2016 to 25th May 2017. **Methodology:** About 4597 samples were collected from various departments and processed for antimicrobial resistant testing. **Results:** Of 4597 samples, culture positive were 40.4% CoNS were 9.0% and 22.3% of total and total culture positive specimens respectively The highest rate isolation rate of CONS was found in ICU 32.4%, Sample-wise 34.1% in blood samples. 0% resistant to Linezolid, Teicoplanin, and Vancomycin, while very high resistant rate against penicillin 77.8%, Cotrimoxazole 60%, Methicillin 59.8%, Co-amoxiclav 54%, Clindamycin 48.7%, Fusidic Acid 46.3%, Doxycycline 45.1%, Erythromycin 44.9%, Amikacin 42%, Ciprofloxacin 41.8% and Gentamycin 23%. **Conclusion:** Linezolid, Vancomycin, and Teicoplanin are the best choice of drugs while emergence of drug-resistant to other basic drugs is alarming

Key words: CoNS Linezolid, Vancomycin, Teicoplanin, Drug Resistance

Article Citation: Syed E, Satti FN, Mubasher S, Rasheed F, Ilyas M, Anwar AI, Waheed uz Zaman. Coagulase negative staphylococcus species; resistance and therapeutic decisions at the turn of the novel millennium. Professional Med J 2018; 25(5):764-769. DOI:10.29309/TPMJ/18.4664

with drug resistant staphylococcus associated infections. Typically, CoNS are reflected as less virulent than staph aureus and present as lethargic rather than acute infections. Despite this, CoNS are associated with a numerous infections i.e causative agents for UTI and catheter-associated infections (CAI).⁵ Furthermore wound infections, breast abscess, osteomyelitis, pneumonia, shunt infections, endocarditis are also associated with CoNS.⁶⁻⁸ In particular, these infections are associated with medical devices; most notably prosthetic valve endocarditis and prosthetic joint infections, because of their propensity to form a protective biofilm.^{9,10}

CoNS associated infections mainly occur in precise groups of patients i.e neutropenic, neonates. Moreover CoNS are associated with indwelling foreign devices infections and

Infections of metastatic sites, i.e central nervous system (CNS), joints heart, bones are especially common, and such infections in these susceptible populations are difficult to treat.^{11,12}

As CoNS are frequently isolated pathogens therefore the knowledge of the prevalence of CoNS and their antibiotic resistant trends becomes essential in the assortment of appropriate empirical treatment. Thus present study was planned to evaluate the distribution and drug-resistant pattern of CoNS in tertiary care hospital.

METHODOLOGY

This cross-sectional study was conducted Microbiology Lab Allama Iqbal Medical College, Lahore, Pakistan from 1st January 2016 to 25 may 2017. About 4597 samples tracheal aspirate urine, sputum, HVS, pus, blood and pleural fluid were enrolled from different departments ICU Surgical Unit, Medical Unit and OPD of Jinnah hospital Lahore. All samples were processed for bacterial culture sensitivity according to standard recommendations identification was carried out by colonial morphology gram stain catalase

test coagulase test.¹³ Each isolate of CoNS was processed for antimicrobial resistant testing.

RESULTS

Out of total 4597 samples, 40.4% were culture positive of which CoNS was 9.0% of the total sample and 22.3% of total culture positive samples.

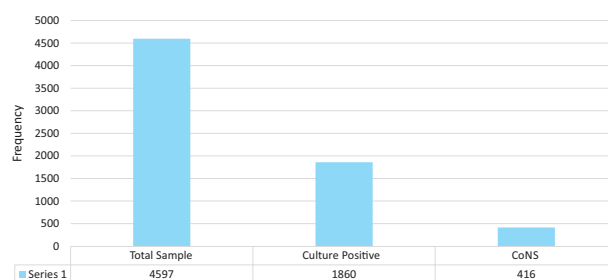


Figure-1. Frequency of CoNS staphylococcus

Table-I. Shows the sample-wise isolation rate of CoNS along with its department wise distribution. The highest rate was found in ICU 32.4% and least rate was found in Medical Unit. Sample-wise maximum isolation rate 34.1% was observed in blood samples.

Groups		Total samples	Total isolates	CoNS
		Frequency + %	Frequency + %	Frequency + %
Departments	ICU	1135 (24.6%)	550 (29.5%)	135 (32.4%)
	Surgical Unit	1470 (31.9%)	750 (40.3%)	110 (26.4%)
	Medical Unit	1017 (22.1%)	316 (16.9%)	96 (23.0%)
	Gynae	975 (21.2%)	244 (13.1%)	75 (18.0%)
Samples	Pus	1235 (26.8%)	922 (49.5%)	137 (32.9%)
	Blood	1065 (23.1%)	441 (23.7%)	142 (34.1%)
	Tracheal Aspirate	749 (16.2%)	181 (9.7%)	12 (2.8%)
	Sputum	330 (7.1%)	78 (4.1%)	0 (0%)
	Pleural fluid	313 (6.8%)	27 (1.4%)	0 (0%)
	Urine	678 (14.7%)	187 (10.0%)	125 (30.0%)
	HVS	227 (4.9%)	24 (1.2%)	0 (0%)
	Total	4597 (100.0%)	1860 (100.0%)	416 (100.0%)

Table-I. Distribution of CoNS Staphylococcus isolates

Age groups	Total samples		Total isolates		CoNS	
	Male	Female	Male	Female	Male	Female
0-20 n=685 (14.9%)	574 19.3%	111 6.8%	135 13.8%	89 10.0%	18 14.2%	22 7.5%
21-40 n=1322 (28.7%)	832 27.9%	490 30.1%	405 41.6%	269 30.3%	11 8.7%	68 23.4%
41-60 n=1383 (30.0%)	735 24.7%	648 39.9%	212 21.7%	331 37.3%	27 21.4%	61 21.0%
61-80 n=941 (20.4%)	679 22.8%	262 16.1%	189 19.4%	116 13.0%	59 46.8%	94 32.4%
81-100 n=266 (5.7%)	153 5.1%	113 6.9%	32 3.2%	82 9.2%	11 8.7%	45 15.5%
Total n=4597 (100.0%)	2973 100.0%	1624 100.0%	973 100.0%	887 100.0%	126 100.0%	290 100.0%

Table-II. Gender and age group based distribution of CoNS

Antibiotic	ICU n=135		Surgical unit n=110		Medical unit n=96		Gynae n=75		Total n=416	
	F	%	f	%	f	%	f	%	F	%
Penicillin	93	69%	86	78%	76	79%	69	92%	324	77.8%
Co-Amoxiclar	101	75%	63	57%	29	30%	32	43%	225	54.0%
Methicillin	100	74%	78	71%	42	44%	29	39%	249	59.8%
Erythromycin	5	4%	73	54%	57	59%	52	70%	187	44.9%
Gentamycin	34	25%	24	18%	19	20%	19	25%	96	23.0%
Ciprofloxacin	62	46%	55	41%	24	25%	33	44%	174	41.8%
Fusidic acid	30	22%	73	66%	76	79%	14	19%	193	46.3%
Cotrimaxazole	81	60%	49	45%	58	61%	61	82%	249	60.0%
Doxycycline	61	45%	43	39%	60	63%	24	32%	188	45.1%
Amikacin	45	33%	47	43%	42	44%	41	55%	175	42.0%
Clindamycin	30	22%	47	43%	69	72%	57	76%	203	48.7%
Linezolid	0	0%	0	0%	0	0%	0	0%	0	0%
Teicoplanin	0	0%	0	0%	0	0%	0	0%	0	0%
Vancomycin	0	0%	0	0%	0	0%	0	0%	0	0%

Table-III. Shows department wise drug resistance pattern of CoNS

Present study reported 0% resistant for Linezolid, Teicoplanin and Vancomycin, while very high resistant rate was observed against penicillin 77.8%, Co-Trimoxazole 60%, Methicillin 59.8%, Coamoxiclav 54%, Clindamycine 48.7%, Fusidic Acid 46.3%, Doxycycline 45.1%, Erythromycin 44.9%, Amikacin 42%, Ciprofloxacin 41.8% and Gentamycin 23%. Figure:2

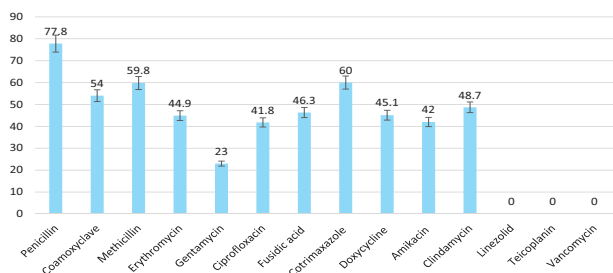


Figure-2. Resistant pattern of CoNS

DISCUSSION

Destructive infection control practices are hindered by multi drug-resistant strains commonly involved in nosocomial infections and expanding infectious disease burden in all over the world. Disparity in isolation rate of CoNS in different areas of the globe is multifactorial, the efficacy of infection control policies and usage of antibiotic differ from hospital to hospital country to country. Prevalence of CoNS in the present study was 9.0% of the total sample and 22.3% of total culture positive samples. Figure:1.

The highest rate was found in ICU 32.4% our results are in accordance with previous studies.¹⁴⁻¹⁶ The present study reported 0% resistant to Linezolid, Teicoplanin, and Vancomycin similar

to previous studies.^{15,17,18} Conversely decreased the sensitivity of Vancomycin against CoNS have also been reported in some reports.¹⁹⁻²¹ only 0.1% resistant to linezolid reported in one study.²¹

Alarming very high resistant rate against penicillin 77.8% observed in present study, supported by previous studies reported high rate of penicillin-resistant.^{16-18,22} Similarly we observed methicillin-resistant rate was 59.8% higher than previous studies reported India 41.5-57%²² while lower than other reports Makkah 95%.¹⁶ Similar trend reported from Brazil in 1990 it was 51.6% increased up to 87.5 till 2007.²³ Another report reported very high rate 87% among the neonatal population.²⁴ We reported 44.9% erythromycin resistant while against it is also reported up to 96% from different regions of the world, Makkah 78%.¹⁶ These reports in agreement with SENTRY study reported, USA 81.3% Canada 79% Latin America 70.7% Europe 72% and Western Pacific 66% India 96%.^{16,21,22} Furthermore present study reported 48.7 resistant in case of Clindamycin supported by and also slightly lower than previous studies reported 48% to 93%, Makkah, USA, Canada, Latin America, Europe, Western Pacific and India 60%, 50.9% 46.5% 52.6% 48%, 36% and 93% respectively.^{16,22} Moreover we reported Co-amoxiclav 54%, Fusidic Acid 46.3%, Doxycycline 45.1%, Erythromycin 44.9%, Amikacin 42%, Ciprofloxacin 41.8% and Gentamycin 23%. Figure-2.

Similarly a study conducted in Turkey²⁵ reported, almost 200 CoNS isolates were recovered from blood culture samples of bacteremia patients admitted in intensive care units (ICU) and various other departments of Istanbul University during the period of 1999 to 2006. Staph epidermidis was reported as the most commonly isolated pathogen n=87 followed by Staph haemolyticus n=23 Staphy hominis n=19 Staph lugdunensis n=18 Staph capitis n=15 Staph xylosus n=10 Staph warneri n=8 Staph saprophyticus n=5 Staph lentus n=5 Staphy simulans n=4 Staph chromogens n=3 Staph cohnii n=1 Staph schleiferi n=1 and Staph auricularis n=1. The antimicrobial resistant pattern of CoNS was as followed gentamicin 17%, erythromycin 37%,

clindamycin 18%, trimethoprim-sulfamethoxazole 38%, ciprofloxacin 23%, tetracycline 45%, chloramphenicol 13% and fusidic acid 15%. Vancomycin and Teicoplanin were 100% sensitive against CoNS. Methicillin-resistant was detected 67.5% slightly higher than present study reported 59.8%. Another study from Serbia reported that of 196 CoNS methicillin-resistant isolates 62.2%,⁽²⁶⁾ Another similar additional study from Makkah²⁶ reported of 190 isolates overall drug-resistant was 1.6% to 99.5%. While linezolid and vancomycin were 100% sensitive similar to present study Figure-2 penicillin exhibited very high resistant rate 99.5% ampicillin 99% Oxacillin 93.6% and Augmentin 93%, Synercid 2.2% and Daptomycin 1.6%.

High level of drug resistance could be associated with earlier exposure to antimicrobials drugs to isolates which may have enhanced the development of resistance. There is high-level antibiotic abuse in our societies arising from self-medication which is often associated with inadequate dosage and failure to comply with treatment, and availability of antibiotics to everyone across the counters with or without prescription. It had been observed in developing countries where there are no regulatory policies such as Pakistan that the indiscriminate use of antibiotics without prescriptions have rendered the commonly used antibiotics completely ineffective in the treatment of Staphylococcal infections. This emerging problem encourages us to highlight the resistance profile of staphylococci in tertiary care hospital Pakistan.

CONCLUSION

The emergence of methicillin-resistant along with overall all drug-resistant CoNS isolate is alarming, CoNS should report rather than consider them as a contaminant, it may be the basic reason behind the emergence of drug-resistant because many laboratories in Pakistan did not report CoNS as a pathogen.

Copyright© 15 Mar, 2018.

REFERENCES

1. Morgenstern M, Erichsen C, Hackl S, Mily J, Militz M, Friederichs J, et al. **Antibiotic resistance of**

- commensal *Staphylococcus aureus* and coagulase-negative staphylococci in an international cohort of surgeons: a prospective point-prevalence study. *PloS one*. 2016;11(2):e0148437.
- Cavanagh JP, Wolden R, Heise P, Esaiassen E, Klingenberg C, Aarag Fredheim EG. **Antimicrobial susceptibility and body site distribution of community isolates of coagulase-negative staphylococci**. *Apmis*. 2016;124(11):973-8.
 - Sheriff R, Sheena A. **Assessment of Biofilm Production in Clinically Significant Isolates of Staphylococcus epidermidis and Comparison of Qualitative and Quantitative Methods of Biofilm Production in a Tertiary Care Hospital**. *INTERNATIONAL JOURNAL OF SCIENTIFIC STUDY*. 2016;4(6):41-6.
 - Obajuluwa A, Onaolapo J, Olayinka B, Adeshina G. **Antibiotics susceptibility pattern of coagulase negative staphylococci isolates from orthopaedic patients**. *International Educational Applied Scientific Research Journal*. 2017;1(3).
 - Becknell B, Mohamed AZ, Li B, Wilhide ME, Ingraham SE. **Urine stasis predisposes to urinary tract infection by an opportunistic uropathogen in the megabladder (Mgb) mouse**. *PloS one*. 2015;10(9):e0139077.
 - Huang Z-G, Zheng X-Z, Guan J, Xiao S-N, Zhuo C. **Direct detection of methicillin-resistant staphylococcus aureus in sputum specimens from patients with hospital-associated pneumonia using a novel multilocus Pcr assay**. *Pathogens*. 2015;4(2):199-209.
 - Mendes RE, Flamm RK, Pfaller M, Castanheira M, Sader HS, editors. **Dalbavancin In Vitro Activity Obtained Against Gram-Positive Clinical Isolates Causing Osteomyelitis in US Hospitals (2011–2015)**. *Open Forum Infectious Diseases*; 2016: Oxford University Press.
 - Begly JP, Sobieraj M, Liporace FA, Dayan A. **Staphylococcus lugdunensis septic arthritis of a native knee: a case report**. *Bulletin of the NYU Hospital for Joint Diseases*. 2016;74(4):314-.
 - Kathpalia S, Vasudev S, Sinha P, Sandhu N, Sharma P, Maurya V, et al. **Methicillin-resistant Coagulase-negative Staphylococci (MR-CoNS) have emerged as an important cause of nosocomial infections especially in patients with prosthetic devices and implants. This study was conducted with an aim to determine the prevalence of methicillin resistance among CoNS isolates at a tertiary care center by both phenotypic and genotypic methods**. This cross sectional study was carried. *Medical Journal Armed Forces India*. 2016;72(1):S135-S7.
 - Carugati M, Petti C, Arnold C, Miro J, Pericàs J, de la Maria CG, et al. **Antistaphylococcal β -Lactams versus Vancomycin for Treatment of Infective Endocarditis Due to Methicillin-Susceptible Coagulase-Negative Staphylococci: a Prospective Cohort Study from the International Collaboration on Endocarditis**. *Antimicrobial agents and chemotherapy*. 2016;60(10):6341-9.
 - Chen C-Y, Tien F-M, Sheng W-H, Huang S-Y, Yao M, Tang J-L, et al. **Clinical and microbiological characteristics of bloodstream infections among patients with haematological malignancies with and without neutropenia at a medical centre in northern Taiwan, 2008–2013**. *International journal of antimicrobial agents*. 2017;49(3):272-81.
 - Bhatia PL, Lilani S, Shirpurkar R, Chande C, Joshi S, Chowdhary A. **Coagulase-negative staphylococci: Emerging pathogen in central nervous system shunt infection**. *Indian Journal of Medical Microbiology*. 2017;35(1):120.
 - Cheesbrough M. **District laboratory practice in tropical countries**: Cambridge university press; 2006.
 - Maria de Lourdes R, Lopes CA, Rugolo LM, Chalita LV. **Clinical significance of coagulase-negative staphylococci isolated from neonates**. 2002.
 - Keim LS, Torres-Filho SR, Silva PV, Teixeira LA. **Prevalence, aetiology and antibiotic resistance profiles of coagulase negative staphylococci isolated in a teaching hospital**. *Brazilian Journal of Microbiology*. 2011;42(1):248-55.
 - Khan M, Faiz A, Ashshi AM. **Clinically significant Coagulase Negative Staphylococci and their antibiotic resistance pattern in a tertiary care hospital**. *J Pak Med Assoc*. 2014;64(10):1171-4.
 - Singh S, Banerjee G, Agarwal S, Kumar M, Singh R. **Simple method for speciation of clinically significant coagulase negative Staphylococci and its antibiotic sensitivity/resistant pat-tern in NICU of tertiary care centre**. *Biomedical research*. 2008;19(2).
 - Amitajain AJ, Banswal S. **Prevalence of methicillin resistant, CoNS in neonatal intensive care units: findings from a tertiary care hospital in India**. *Med Microbiol*. 2004;53:941-4.
 - Garrett DO, Jochimsen E, Murfitt K, Hill B, McAllister S, Nelson P, et al. **The emergence of decreased susceptibility to vancomycin in Staphylococcus epidermidis**. *Infection Control & Hospital Epidemiology*. 1999;20(3):167-70.
 - Nakipoglu Y, Derbentli S, Cagatay AA, Katranci H. **Investigation of Staphylococcus strains with heterogeneous resistance to glycopeptides in a**

Turkish university hospital. BMC infectious diseases. 2005;5(1):31.

21. Diekema D, Pfaller M, Schmitz F, Smayevsky J, Bell J, Jones R, et al. **Survey of infections due to Staphylococcus species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe, and the Western Pacific region for the SENTRY Antimicrobial Surveillance Program, 1997–1999.** Clinical Infectious Diseases. 2001;32(Supplement_2):S114-S32.

22. Deepa S, Kumari A, Venkatesha D. **Increasing trends of methicillin resistant coagulase negative Staphylococcus in neonatal septicaemia-A study in a tertiary care hospital, Mysore, South India.** Online J Health Allied Scs. 2010;9(4):11.

23. Pereira VC, Cunha MdLRd. **Coagulase-negative staphylococci strains resistant to oxacillin isolated from neonatal blood cultures.** Memórias do Instituto Oswaldo Cruz. 2013;108(7):939-42.

24. Hira V, Sluijter M, Estevão S, Horst-Kreft D, Ott A, de Groot R, et al. **Clinical and molecular epidemiologic characteristics of coagulase-negative staphylococcal bloodstream infections in intensive care neonates.** The Pediatric infectious disease journal. 2007;26(7):607-12.

25. Koksai F, Yasar H, Samasti M. **Antibiotic resistance patterns of coagulase-negative staphylococcus strains isolated from blood cultures of septicemic patients in Turkey.** Microbiological research. 2009;164(4):404-10.

26. Považan A, Vukelić A, Kurucin T, Hadnađev M, Milošević V, Gusman V. **Non-susceptibility trends among methicillin-resistant coagulase-negative staphylococci isolated from blood cultures.** Archives of Biological Sciences. 2014;66(1):79-86.

“

*Challenges are what make life interesting.
Overcoming them is what makes life meaningful.*

– Unknown – ”

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Eiman Syed	Manuscript Writing	
2	Faiza Nawaz Satti	Results interpretation	
3	Sumaira Mubasher	Statistical Analysis	
4	Farhan Rasheed	Manuscript Writing	
5	Muhammad Ilyas	Lab Work	
6	Ambereen Imran Anwar	Final Editing	
7	Waheed uz Zaman	Proof Read	