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SUSCEPTIBILITY PATTERNS OF COAGULASE-NEGATIVE STAPHYLOCOCCUS TO VARIOUS ANTIBIOTICS AT PAKISTAN INSTITUTE OF MEDICAL SCIENCE

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Abstract

The rising prevalence of antibiotic resistance among bacterial pathogens in clinical settings is a critical global health concern. Coagulase-negative Staphylococcus spp. have emerged as significant nosocomial pathogens with a marked ability to resist multiple antimicrobial agents. This study investigates the antibiotic susceptibility patterns of 100 isolates of CoNS collected from clinical specimens at the Pakistan Institute of Medical Sciences. Through a cross-sectional analysis utilizing Kirby-Bauer disk diffusion methods, the sensitivity of isolates towards 12 different antibiotics was assessed. The results indicated a high sensitivity to vancomycin (97%) among CoNS isolates, while resistance was most common against penicillin-G, with 95% of isolates demonstrating resistance. The data underscore the necessity for vigilant antibiotic stewardship and highlight the utility of vancomycin as the first-line treatment for CoNS infections amidst the concerning backdrop of increasing antibiotic resistance. Consequently, this study serves to inform clinical practices and antibiotic policy-making, underscoring the urgency for ongoing surveillance and precise identification of resistance patterns to ensure effective pharmaceutical interventions.

INTRODUCTION

In the last few decades, the incidence of infections caused by Coagulase-negative Staphylococci has risen substantially, drawing attention to these organisms as serious nosocomial pathogens (Asante, J. et al, 2020). Historically considered harmless commensals of the human skin and mucous membranes, CoNS, particularly strains like Staphylococcus epidermidis, have emerged as leading causes of bacteremia and endocarditis, especially in patients with implanted medical devices, intravascular catheters, and compromised immune systems (Mushtaq and Naim, 2015: Koksal *et al.,* 2009). Fourteen species of CoNS have been identified in human isolates (Bannerman *et al.*, 2006).

Coagulase-negative staphylococci are a group of bacteria that belong to the Staphylococcus genus but do not produce the enzyme coagulase (Al-Talib, A, N., Abduljala, H, M. And Hamodat, A, M, Z., 2020). They are commonly found in the environment and on the skin and mucous membranes of humans and animals (Seg, R. et al., 2017). These bacteria are part of the normal flora and typically do not cause disease in healthy individuals (Al-Talib, A, N., Abduljala, H, M. And Hamodat, A, M, Z., 2020). Their pathogenicity has become increasingly concerning due to the development and dissemination of antibiotic resistance. This resistance is a significant complicating factor in the treatment of CoNS-associated infections, often requiring the use of last-resort antibiotics such as vancomycin. However, even the efficacy of such powerful antibiotics is threatened by the global emergence of resistance (Control and Prevention, 2004).

The resistance mechanisms of CoNS include beta-lactamase production, alterations in penicillin-binding proteins, and the formation of biofilms that act as barriers to antibiotic penetration. This resistance poses immense challenges to public health and necessitates a stringent antibiotic stewardship approach (Kloos and Bannerman, 1994: Otto, 2004).

The evolution of antibiotic resistance in coagulase-negative staphylococci is a complex process that involves genetic mutations and horizontal gene transfer. These bacteria can acquire resistance genes through mutations in their own genetic material or through the transfer of resistance genes from other bacteria. These resistance genes can provide the bacteria with mechanisms to inactivate or pump out antibiotics, modify antibiotic targets, or bypass antibiotic pathways (Lim and Webb, 2005)

The present study seeks to address this need by conducting a comprehensive evaluation of resistance across commonly administered antibiotics, thereby contributing essential information to the ongoing discourse on antimicrobial stewardship and resistance mitigation. The study aims to examine the antibiotic susceptibility patterns of CoNS at the Pakistan Institute of Medical Sciences, providing crucial data that could guide empiric antibiotic therapy and reinforce infection control strategies within the hospital and broader region.

MATERIALS AND METHODS

A total of one hundred samples were collected from patients hospitalized at PIMS Islamabad from 1st February 2023 to 1st March 2023. Only coagulase negative samples were collected. The appropriate materials were used for susceptibility testing against CoNS in the microbiology laboratory at Pakistan institute of medical sciences (PIMS) hospital. Samples were taken from patients hospitalized in different wards and intensive care units of Pakistan institute of medical sciences, Islamabad. A total 100 identified CoNS were collected. Samples were processed for specie identification by using various standard laboratory procedures. Different samples were taken from different sources like blood, urine, CSF and tracheal secretions. Blood samples were first kept in BacTec machine for the incubation to detect positive samples which were then inoculated on media for culturing. MacConkey agar, Blood agar, CLED agar and Muller Hinton agar were used for routine culture. Several tests like Gram-staining, colony morphology and sugar fermentation tests were performed for specie identification. Several biochemical tests like oxidaze, catalase and coagulase were also performed for the conformation of CoNS organisms.

ANALYTICAL PROFILE INDEX (API)

Analytical profile index (API) was also used for specie identification. Biomerix company kit was used for this purpose. For staphylococci specie, API 20S and API 10S was performed.

SUSCEPTIBILITY TEST

Antimicrobial susceptibility tests were performed by the Kirby-Bauer (Bauer *et al.*, 1966) disk diffusion method as per recommendations of National Committee for Clinical Laboratory Standards (NCCLS) by using Mueller Hinton agar (MHA). A panel of CoNS antimicrobials was as follows: amikacin, azithromycin, co-amoxiclave, cefaxime, sulbactum, ceftrixone, cefuroxine, cefoxatin, chloramphenicol, clindamycin, cotrimoxazole, amoxicillin, imipenem, levofloxacin, vancomycin, oxacillin, penicillin G, piperacillin plus tazobactam, gentamycin, erythromycin and ciprofloxacin.

RESULTS

This study was conducted for antibiotic susceptibility pattern of coagulase negative staphylococci (CoNS). A total of 100 samples were taken, out of which 77 were males and 23 were females. The samples were taken from patients at different wards in the hospital. The male and female ratio is shown in the Fig given below.

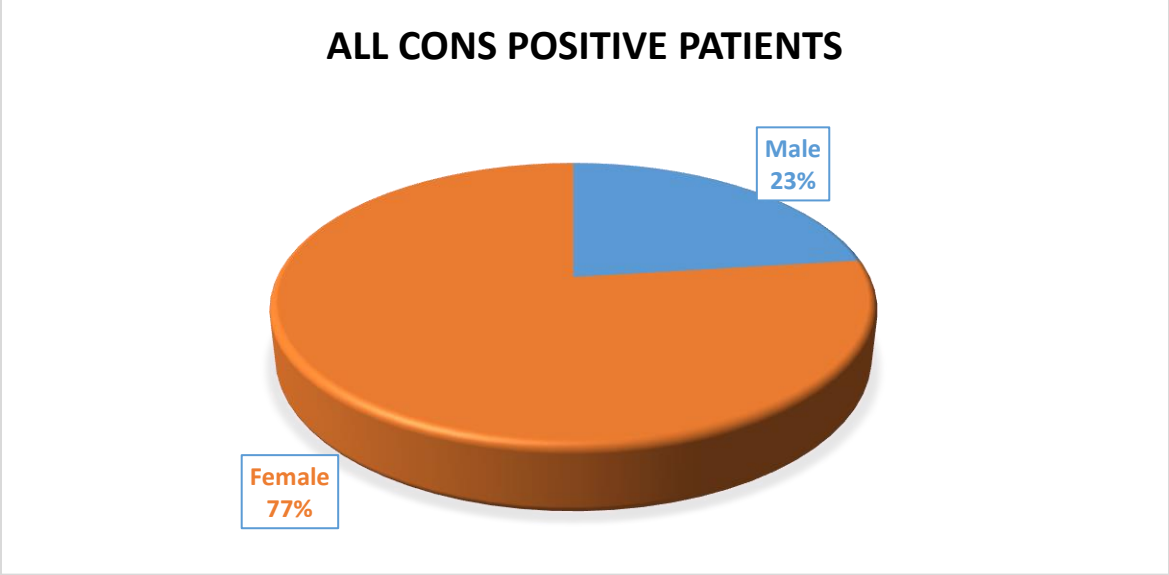

Figure 1: The ratio of males and females patients.

Samples were submitted to laboratory from various wards. Most of the patients with CoNS positive were from emergency ward. The number of patients with CoNS positive specimens and their respective wards is shown in the Table 1.

Table No 1: Distribution of CoNS according to wards

Wards	sample size
Emergency	42
Nephrology	2
Med (ICU)	14
Medical wards	16
General medicines	17
Dermatology	1
Orthopedic	1
Pulmonary	1
Gastro	2
General surgery	2
Oncology	1

The susceptibility of staphylococcal isolates can be observed by the Fig. given below. Isolates were found to be most susceptible towards vancomycin (97%) followed by clindamycin (66%). Organisms were found to be least susceptible towards penicillinG (5%) and co-trimoxazole (33%).

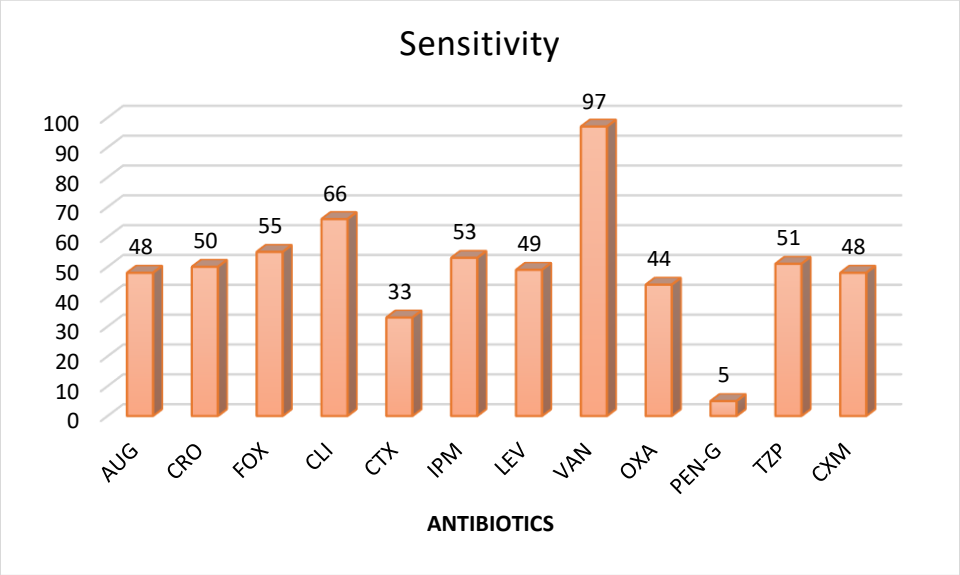

Figure 2: Frequency of staphylococcal isolates towards different antibiotics.

The resistance pattern showed by CoNS against the selected antibiotics is shown in Fig. 3:

The highest resistance rate was observed against penicillin-G (95%) followed by oxacillin (69%). The lowest rate of resistance was observed to be against vancomycin (2%).

Figure 3: Resistance of coagulase negative staphylococci against different antibiotics.

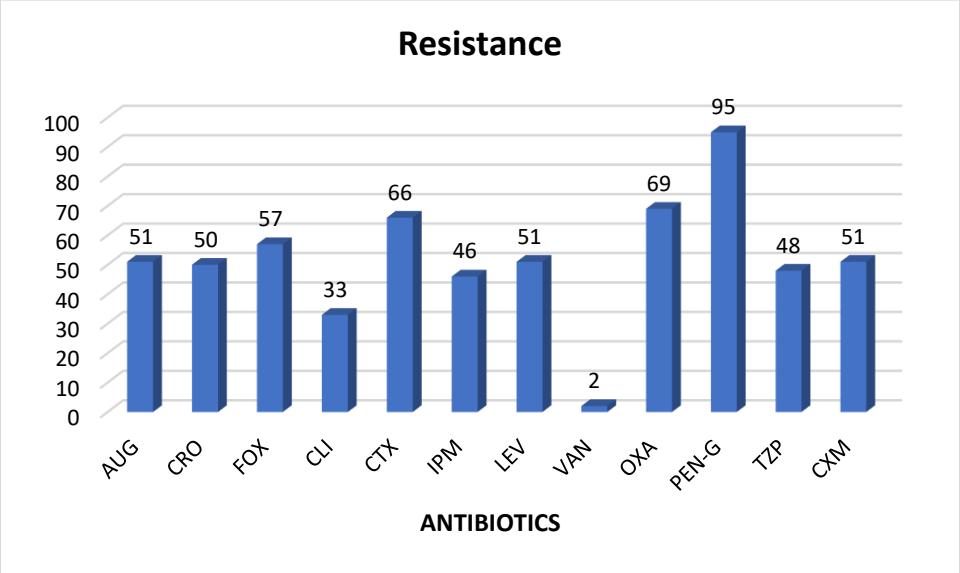

Table No 2. Susceptibility towards antibiotics shown by coagulase negative staphylococci

S No.	Antibiotics	Sensitivity percentage	Resistance percentage
1	AUG	48%	51%
2	CRO	50%	50%
3	FOX	55%	57%

4	CLI	66%	33%
5	CTX	33%	66%
6	IPM	53%	46%
7	LEV	49%	51%
8	VAN	97%	2%
9	OXA	44%	69%
10	PEN-G	5%	95%
11	TZP	51%	48%
12	CXM	48%	51%

DISSCUSSION

Coagulase negative staphylococcus is the prominent cause of nosocomial septicemia and bacteremia having high mortality and morbidity rate, especially in immunedeficient and malignant patients (Mayhall, 2012).Since these bacteria have a great ability of to adapt antibiotic resistance, this pathogen has become a foremost medical community concern and great attempts are sit to improve antimicrobial agents against it (Livermore, 2000).

In the present study, 100 CoNS isolates were isolated from patients admitted in different wards of Pakistan Institute of Medical Sciences (PIMS) Islamabad Pakistan. The isolates were from various sources like, blood, cerebrospinal fluid, urine, and tracheal secretions. Different antibiotics were tested against CoNS. The results of present study showed that vancomycin is highly active towards coagulase negative staphylococci, with the sensitivity rate of 97%. Similar results were found from the work performed at Department of Microbiology, Sri Ramchandra University Chenai in which 97.5% of CoNS were sensitive towards vancomycin(Begum *et al.*, 2011). Nearly similar results were found from the research conducted by PE Akpaka *et al* at Microbiology Department, University of West Indies who demonstrate that all CoNS isolates were 100 % susceptible to vancomycin(Akpaka *et al.*, 2006). Until now the only drug of choice for CoNS infection was vancomycin to which no resistance of CoNS was studied because 100% of CoNS isolates were sensitive to vancomycin(Koksal *et al.*, 2009). In the present study, it was found that CoNS are also developing resistance to vancomycin which is a worrying issue for medical concern. So the proper identification of organism, before prescribing an antibiotic is necessary, because the miss use and over dosage of antibiotics compel the bacteria to create resistance against various antibiotics.

The results of present study also revealed that highest resistance was shown towards penicillin-G (95%) followed by oxacillin (69%). Same results were found in a recent work that CoNS were highly resistant (>70%) to penicillin G(Ma *et al.*, 2011). The results of this work indicated that the CoNS have developed excessive resistance against penicillin-G from in a very short duration of 2011 to 2016. The resistance to oxacillin was 74.5% in the results of research conducted on CoNS susceptibility (Del'Alamo *et al.*, 1999). Oxacillin is also least effective against CoNS because of higher resistance development by these bacteria, which were only 31% active towards CoNS in the present thesis.

CONCLUSSION

Results of the present study clearly demonstrated that CoNS have developed resistance to most of the used antibiotics like penicillin-G, oxacillin, co-trimoxazole and cefoxitin. Highest resistance is observed against penicillin-G (95%). Cotrimoxazole is found to be the second least active antibiotic. Vancomycin is observed to be highly active against coagulase negative *Staphylococcus* bacteria with a susceptibility rate of 97%. Thus, this study shows that vancomycin is the drug of choice to treat the infections caused by coagulase negative staphylococci. It is also concluded that the use of some antibiotics like penicillin-G is pointless as CoNS have developed high resistance against these. This work clarifies that penicillin G is not effective against CoNS which should be avoided in the

treatment of CoNS infections. Therefore, vancomycin should be used when needed and miss use and over dose should be controlled to avoid the rise of vancomycin resistant CoNS.

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