Biomedical Journal of Indonesia
Journal Homepage: https://bji-fk.ejournal.unsri.ac.id

Coagulase-Negative *Staphylococcus* (CoNS) Susceptibility Pattern Towards Antibiotics in Infection Patients at RSUP Dr. Mohammad Hoesin Palembang

Silvia Putri Sudirman[1], Tia Sabrina[2]*, Rizki Andini Nawawi[2], Rima Zanaria[2], Masayu Farah Diba[2]
[1]Undergraduate Program in Medicine, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2]Department of Clinical Microbiology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
CoNS
Antimicrobial resistance
Infection

Corresponding author:
Tia Sabrina

E-mail address:
tiasabrina.ts@fk.unsri.ac.id

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.32539/BJI.v10i2.189

ABSTRACT

Introduction. Coagulase Negative Staphylococcus (CoNS) is a bacterial species commonly causing infection in humans upon entrance into bloodstream. Antibiotics remain the therapeutic modality of choice in eradicating CoNS bacteria. Increasing incidence of antimicrobial resistance has made it difficult to administer the right treatment. In addition, CoNS susceptibility patterns differ between regions and with time. This study aimed to determine the susceptibility pattern of CoNS towards various antibiotics in infection patients at RSUP Dr. Mohammad Hoesin Palembang. **Methods.** This study was a descriptive, observational study using the data from blood cultures of CoNS bacteria undergoing antimicrobial susceptibility test (AST) in the Clinical Microbiology Laboratory, and utilizing demographic and clinical data from the Medical Records Installation from July 1, 2021 to December 31, 2021. **Results.** There were 123 isolates from patient blood cultures which underwent AST. The most frequently identified bacterial species were Staphylococcus hominis ssp hominis, Staphylococcus epidermidis, Staphylococcus haemolyticus, and Staphylococcus saprophyticus. AST results showed that on average, CoNS were susceptible to tigecycline (100%), nitrofurantoin (98.4–100%), linezolid (86.1–100%), and vancomycin (80.6–100%). CoNS were most resistant to benzylpenicillin (100%), oxacillin (85.5–97.2%), and erythromycin (75–97.2%). **Conclusion.** CoNS were resistant towards several available antibiotics in RSUP Dr. Mohammad Hoesin Palembang.

1. Introduction

Infectious diseases are diseases caused by pathogens or their toxic products that arise through transmission from infected humans and animals or contaminated inanimate objects to susceptible hosts. Infectious agents can be viruses, bacteria, parasites (protozoa and worms), and fungi.[1] One agent that often causes infection is bacteria of the genus *Staphylococcus*.[2] *Staphylococcus* can be distinguished based on its ability to produce coagulase enzymes, namely the coagulase-positive *Staphylococcus* (CoPS) and coagulase-negative *Staphylococcus* (CoNS) groups.[3] In contrast to CoPS bacteria which are already known as pathogens, the CoNS group of bacteria is a normal skin flora that is often thought to be less pathogenic or even non-pathogenic, but in some cases it turns out that these bacteria can increase morbidity and mortality rates in patients with certain risks such as very low birth weight and immune system disorders. [4]

The main pharmacological treatment given to patients with bacterial infections is antibiotics. Antibiotics play a role in inhibiting the growth or killing bacteria. The problem of the medical world related to antibiotics to date is the existence of antibiotic resistance that occurs due to irrational, unwise use of antibiotics, lack of government supervision of antibiotic use in the community, and inappropriate antibiotic prescribing patterns.[5] In 2019 *antimicrobial resistance* (AMR) was associated with 4.95 million deaths globally and is estimated to be responsible for 10 million deaths per year by 2050. This figure was dominated by pneumonia which accounted for more than 400,000 deaths.[6]

One of the bacteria that has not received much attention in Indonesia for its resistance to antibiotics is CoNS bacteria.[7] CoNS can be resistant to antibiotics, for example methicillin-resistant coagulase-negative *Staphylococcus* (MR-CNS) with a percentage of 80%.[8] Based on research conducted by Oyong et al in 2016, it was found that CoNS bacteria were resistant to ampicillin and gentamicin.[9] In contrast, the research of Ni Kadek et al. at Denpasar General Hospital in 2019 showed that there was antibiotic resistance to cefepime, meropenem, and ceftriaxone. From the above research, it can be concluded that CoNS is one

group of gram-positive bacteria that experiences resistance to various antibiotics with different sensitivity patterns in each hospital in Indonesia. [5]

Differences in sensitivity patterns function in helping the selection of antibiotics that are appropriate for patients and become material for evaluation every year to reduce morbidity and mortality due to resistance. Based on this, it is important to research CoNS sensitivity patterns in the Palembang area, one of which is at Dr. Mohammad Hoesin Hospital Palembang.

2. Methods

This study was a descriptive observational study using secondary data obtained in November 2022 from the Clinical Microbiology Laboratory and Medical Records Installation of Dr. Mohammad Hoesin Hospital Palembang in the period of 1 July 2021 - 31 December 2021 using consecutive sampling method. The research data were collected in Microsoft Excel and processed using SPSS version 26 for Windows. This study has received ethical approval from the Medical and Health Research Ethics Committee of Medical Faculty of Sriwijaya University (Certificate No. 210-2022).

3. Results

The total number of blood specimens from infectious patients at the Clinical Microbiology Laboratory of Dr. Mohammad Hoesin Hospital Palembang for the period 1 July 2021-31 December 2021 was 123 samples.

Based on age, the age groups of CoNS infection patients with the highest frequency were 0-4 years (26 people, 21.1%), 60-69 years (26 people, 21.1%), and 50-59 years (25 people, 20.3%) (Table 1).

The frequency distribution of patients with CoNS infection based on gender showed that out of 123 samples, 71 people (57.7%) were male and 52 people (42.3%) were female. Most CoNS infection patients were inpatients (Table 2).

The frequency distribution based on the main diagnosis of the patient's disease can be seen in Table 3. Of the 123 patients, most patients (58.5%) were diagnosed with pneumonia, followed by sepsis (8.1%) and hydrocephalus (2.4%). Other diagnoses comprise postoperative infections, such as post-laparotomy and post-craniotomy, cholestasis, cholecystitis, acute pancreatitis, psoriasis, osteosarcoma, osteomyelitis, intracerebral hemorrhage, chordal decompensation, Acquired Prothrombin Complex Deficiency (APCD), Atrial Septal Defect (ASD), low birth weight baby, preterm neonates, t-cell leukemia, and encephalitis.

The distribution of CoNS bacterial species from blood specimens can be seen in Table 4.

Table 1. Age distribution of CoNS infection patients

Age Group	Frequency	%
0-4 Years	26	21.1
5-14 Years	10	8.1
15-29 Years	9	7.3
30-39 Years	3	2.4
40-49 Years	10	8.1
50-59 Years	25	20.3
60-69 Years	26	21.1
≥ 70 Years	14	11.4
Total	**123**	**100**

Table 2. CoNS infection patient care installations

Installation	Frequency	%
Inpatient Installation	104	84.6
Intensive Care Unit	17	13.8
Outpatient Installation	2	1.6
Total	**123**	**100**

Table 3. Main diagnoses of CoNS infection patients

Diagnosis	Frequency	%
Pneumonia	72	58.5
Sepsis	10	8.1
Hydrocephalus	3	2.4
UTI	2	1.6
Endocarditis	3	2.4
Other Diagnoses	33	26.8
Total	123	100

Table 4. Distribution of CoNS species from blood specimens

Species Name	Frequency	%
S. epidermidis	38	29.3
S. haemolyticus	30	24.4
S. hominis ssp hominis	56	45.5
S. saprophyticus	1	0.8
Total	**123**	**100**

Table 5. Sensitivity pattern of *Staphylococcus epidermidis* to antibiotics

Antibiotics	n	R%	I %	S %
Benzylpenicillin	40	100	0	0
Ciprofloxacin	40	52.5	5	42.5
Clindamycin	40	62.5	10	27.5
Erythromycin	40	75	0	25
Gentamicin	40	45	2.5	52.5
Levofloxacin	40	57.5	0	42.5
Linezolid	40	0	0	100
Moxifloxacin	40	42.5	15	42.5
Nitrofurantoin	40	0	0	100
Oxacillin	39	87.1	0	12.9
Quinupristin Dalfopristin	40	0	0	100
Rifampicin	40	50	0	50
Tetracycline	40	20	0	80
Tigecycline	39	0	0	100
Trimethoprim Sulfamethoxazole	40	72.5	0	27.5
Vancomycin	40	10	0	90

Table 6. Sensitivity pattern of *Staphylococcus haemolyticus* to antibiotics

Antibiotics	n	R%	I %	S %
Benzylpenicillin	62	0	0	100
Ciprofloxacin	62	64.5	0	35.5
Clindamycin	62	72.6	3.2	24.2
Erythromycin	62	88.7	4.8	6.5
Gentamicin	62	0	0	100
Levofloxacin	62	63	0	37
Linezolid	62	4.8	0	95.2
Moxifloxacin	62	63	1.6	35.4
Nitrofurantoin	62	0	1.6	98.4
Oxacillin	62	85.5	0	14.5
Quinupristin Dalfopristin	62	1.6	95.2	3.2
Rifampicin	62	12.9	6.5	80.6
Tetracycline	62	32.3	0	67.7
Tigecycline	62	0	0	100
Trimethoprim Sulfamethoxazole	62	46.8	0	53.2
Vancomycin	62	3.2	0	96.8

Staphylococcus epidermidis was most resistant to the antibiotics benzylpenicillin (100%), oxacillin (87.1%), erythromycin (75%), and trimethoprim/sulfamethoxazole (72.5%) and sensitive to linezolid, nitrofurantoin, quinupristin/dalfopristin (100%), vancomycin (90%), and tetracycline (80%) (Table 5).

Staphylococcus haemolyticus was most resistant to the antibiotics benzylpenicillin, erythromycin, clindamycin, and oxacillin with a percentage of (97.2%). It was most sensitive to the antibiotics tigecycline (100%) and nitrofurantoin (100%) (Table 6).

Staphylococcus hominis ssp hominis had the highest sensitivity to benzylpenicillin (100%), gentamicin (100%), tigesicline (100%), nitrofurantoin (98.4%), vancomycin (96.8%), and linezolid (95.2%). Other antibiotics that were still quite sensitive were rifampicin (80.6%), tetracycline (67.7%) and trimethoprim/sulfamethoxazole (53.2%). *Staphylococcus hominis ssp hominis* was most resistant to erythromycin (88.7%), oxacillin (88.5%), clindamycin (72.6%), ciprofloxacin (64.5%), levofloxacin (63%), and moxifloxacin (63%) (Table 7).

Staphylococcus saprophyticus was sensitive to almost all antibiotics, and only resistant to benzylpenicillin (Table 8).

Table 7. Sensitivity pattern of *Staphylococcus hominis ssp hominis* to antibiotics

Antibiotics	n	R%	I%	S%
Benzylpenicillin	36	97.2	0	2.8
Ciprofloxacin	36	88.9	0	11.1
Clindamycin	36	91.7	0	8.3
Erythromycin	36	97.2	0	2.8
Gentamicin	36	63.9	11.1	25
Levofloxacin	36	88.9	0	11.1
Linezolid	36	13.9	0	86.1
Moxifloxacin	36	72.2	16.7	11.1
Nitrofurantoin	36	0	0	100
Oxacillin	36	97.2	0	2.8
Quinupristin	36	11.1	2.8	86.1
Dalfopristin				
Rifampicin	36	44.4	0	55.6
Tetracycline	36	41.7	0	58.3
Tigecyclin	33	0	0	100
Trimethoprim	36	33.3	0	66.7
Sulfamethoxazole				
Vancomycin	36	19.4	0	80.6

Table 8. Sensitivity pattern of *Staphylococcus saprophyticus* to antibiotics

Antibiotics	n	R%	I%	S%
Benzylpenicillin	2	100	0	0
Ciprofloxacin	2	0	0	100
Clindamycin	2	0	0	100
Erythromycin	2	0	0	100
Gentamicin	2	0	0	100
Levofloxacin	2	0	0	100
Linezolid	2	0	0	100
Moxifloxacin	2	0	0	100
Nitrofurantoin	2	0	0	100
Oxacillin	2	50	0	50
Quinupristin	2	0	0	100
Dalfopristin				
Rifampicin	2	0	0	100
Tetracycline	2	0	0	100
Tigecycline	2	0	0	100
Trimethoprim	2	50	0	50
Sulfamethoxazole				
Vancomycin	2	0	0	100

4. Discussion

The most common CoNS species found in this study was *Staphylococcus hominis ssp hominis* with a percentage of 45.5%, in line with research by Priskila et al. in 2019 with the most common CoNS species obtained from blood culture was *Staphylococcus hominis*.[10] Besides being easily multiresistant to antibiotics, it turns out that these bacteria also easily enter the bloodstream. Among other CoNS, *Staphylococcus hominis ssp hominis* is one of the most frequently identified bacteria obtained from the blood of neonates and immunocompromised patients and has been linked as a causative agent of bacteremia, septicemia, and endocarditis. [11]

The sensitivity pattern of each CoNS species to antibiotics showed mixed results. *Staphylococcus epidermidis is* most resistant to benzylpenicillin, oxacillin, erythromycin, and trimethoprim/sulfamethoxazole antibiotics, and sensitive to linezolid, nitrofurantoin, quinupristin/dlfopristin by percentage, vancomycin, and tetracycline. In line with Wirajaya's research in 2015 at the same place, namely at Dr. Mohammad Hoesin Hospital. Mohammad Hoesin, *Staphylococcus epidermidis is* sensitive to vancomycin antibiotics and resistant to benzylpenicillin and erythromycin while based on research in one of the hospitals in Mexico in 2016 *Staphylococcus epidermidis is* resistant to oxacillin, erythromycin, levofloxacin, clindamycin, and trimethoprim/sulfamethoxazole antibiotics and sensitive to vancomycin, tetracycline, and linezolid antibiotics.[12,13] In addition to the ability to produce biofilms and the various mechanisms that make it resistant to antibiotics, *S. epidermidis* produces a number of antibiotics, or antibiotic peptides containing the amino acids lanthionine or methyllanthionine that can suppress the growth of other than CoNS bacteria on the skin surface and mucous membranes.[14]

S. haemolyticus was resistant to benzylpenicillin, erythromycin, clindamycin, oxacillin moxifloxacin, ciprofloxacin, levofloxacin, and gentamicin. whereas

it was sensitive to the antibiotics tigecycline, nitrofurantoin, quinupristin/ dalfopristin, vancomycin, linezolid, trimethoprim/ sulfamethoxazole, tetracycline, and rifampicin. This finding is similar to the *review* report by Eltwisy et al. in 2022 which reported that *Staphylococcus haemolyticus* was resistant to benzylpenicillin, oxacillin and clindamycin. It is also in line with the research of Szczuka et al. in 2018 which reported that *S. haemolyticus* bacteria were resistant to penicillin, erythromycin, gentamicin. [15.16]

Staphylococcus hominis ssp hominis was resistant to erythromycin, clindamycin, oxacillin, ciprofloxacin, levofloxacin, and moxifloxacin. The bacteria are sensitive to benzylpenicillin, gentamicin, vancomycin, tigecycline, nitrofurantoin, linezolid. rifampicin, tetracycline, and trimethoprim/sulfamethoxazole. Mendoza's research in 2013 proved the same results where *Staphylococcus hominis ssp hominis* was resistant to erythromycin, oxacillin, and ciprofloxacin which was thought to be because the biofilm possessed by *S. hominis* can absorb and react with antibiotics thereby reducing the levels of antibiotics available to react with bacterial cells.[11]

Staphylococcus saprophyticus was sensitive to almost all antibiotics such as ciprofloxacin, clindamycin, erythromycin, gentamicin, levofloxacin, linezolid, moxifloxacin, nitrofurantoin, quinupristin/dalfopristin, rifampicin, tetracycline, tigecycline, and vancomycin. *S. saprophyticus was* only resistant to benzylpenicillin. In line with research conducted on female UTI patients in Iran in 2020 that *S. saprophyticus is* still sensitive to antibiotics linezolid, clindamycin, erythromycin, rifampicin, tetracycline, vancomycin, nitrofurantoin, quinupristin / dalfopristin, and trimethoprim / sulfamethoxazole. Research conducted by Garbacz et al. in 2021 proved that *S. saprophyticus is* resistant to the penicillin group but sensitive to erythromycin and tetracycline. [17,18]

The age distribution of patients with CoNS infection in this study was dominated by the age group 0-4 years and 60-69 years. Based on research by Petrillo et al. in 2021, the average infection due to CoNS occurs at the age of 60-90 years, which is thought to be due not only to old age factors that cause a decrease in the immunity of the immune system but also due to poor hand hygiene factors and exposure to the hospital environment for a long time, allowing the rapid spread of resistant CoNS bacteria.[19] In contrast to research in Ethiopia in 2021 which reported that the average age of patients with CoNS infection was 0-15 years old. This is influenced by an imperfect immune system and medical treatment that does not pay attention to the cleanliness of the equipment. Facts about the theory of the vulnerability of patients with very young or old age to infection can be illustrated from some of the research results above. [20]

The gender of patients with CoNS infection in this study was dominated by men with 71 people (57.7%) rather than women who only numbered 52 people (42.3%). Based on research conducted by Petrillo et al. in 2021, it was found that infectious patients with female gender (51.9%) were more than men (48.1%).

The type of patient care installation that is most occupied in this study is an inpatient installation, followed by an intensive care installation and an outpatient installation. Research by Molina et al. in 2013 proved that there is a statistical relationship between the length of hospital stay and the incidence of bacteremia which can increase patient mortality, especially in patients with critical illnesses treated in intensive care and inpatient care.[20]

The most common diagnosis found in this study was pneumonia. A study conducted by Mittal et al. in 2019 on linezolid-resistant CoNS found that the average pneumonia was caused by *Staphylococcus haemolyticus,* but it is not certain that CoNS is the main cause or only as a secondary bacteria.[21] CoNS bacteria can be said to be the cause of infection in pneumonia if the same germs are found from two different examination materials. Ventilator insertion such as in the case of tracheal intubation can cause bacterial incubation when the patient needs mechanical ventilation for a long time, but if the bacterial specimen taken is not from lung tissue or pleural fluid, it may not be considered as a bacterial cause of infection. In this study, because only blood specimens were used, it has not been determined whether CoNS is the cause or just contamination.[22]

Sepsis is the second most common disease after pneumonia. The presence of CoNS in the blood can lead to acute sepsis or late onset sepsis (>3 days). Immunosuppressed patients and neonates are most susceptible to the onset of sepsis. Besides *Staphylococcus aureus*, *Staphylococcus epidermidis is* the second most common cause of sepsis.[23] The mechanism regarding the nature and role of pro-inflammatory cytokines in sepsis associated with CoNS remains unexplained. Sepsis can increase patient morbidity and mortality especially in neonates.[24]

The patient's *hydrocephalus* may lead to meningitis, which is usually caused by bacterial infection due to *ventriculoperitoneal shunt* (VP shunt) insertion, bloodstream infection due to intravenous catheter insertion, neurosurgery, and so on. The bacteria that cause hydrocephalus include meningitis caused by *S. haemolyticus* and *S. epidermidis. S. haemolyticus*, which is a major pathogen in patients with neurosurgical procedures or head trauma, can cause meningitis in adults.[25]

Endocarditis has the same prevalence as hydrocephalus cases at 2.4%. CoNS accounts for about 5% of endocarditis cases in children and adults involving heart valves. A study conducted by Chu et al. in 2009 found evidence that CoNS in 16% of cases was the cause of infective endocarditis, and 82% of the isolates were identified as *S. epidermidis*.[26]

Other disease diagnoses found in this study were more likely to lead to postoperative infections such as ASD (post cardiotomy), post laparotomy, and post craniotomy. This is related to the number of days before surgery, the duration of surgery, and patients undergoing repeated operations. Meanwhile, diagnoses such as low birth weight (LBW) and preterm neonates are thought to be related to the immune system of neonates or babies who are not perfect and lack of nutrition so that they are easily attacked by infectious diseases.

Another diagnosis found in this study was osteomyelitis. Although the case is rarely discussed, it turns out that CoNS can cause primary or secondary osteomyelitis in neonates, especially in premature babies. Other diagnoses that are rarely found and are still unclear about the mechanism and direct relationship with CoNS infection through blood are cholestasis, cholecystitis, acute pancreatitis, psoriasis, osteosarcoma, intracerebral hemorrhage, chordal decompensation, Acquired Prothrombin Complex Deficiency (APCD), t-cell leukemia, and encephalitis. These diagnoses have a relationship with immune system disorders that allow secondary infections due to CoNS.[14] Some CoNS species, such as *S. hominis*, *S. epidermidis,* and *S. haemolyticus* that infect through the bloodstream usually occur in cancer and immunocompromised patients.[27]

5. Conclusion

Most of the CoNS bacteria taken from blood specimens at the Clinical Microbiology Laboratory of Dr. Mohammad Hoesin Hospital Palembang for the period July 1, 2021 - December 31, 2021 were *S. hominis ssp hominis* species*.* The results of the antibiotic sensitivity test showed that CoNS on average was most sensitive to the antibiotics tigesiclin (100%) nitrofurantoin (98.4-100%). linezolid (86.1-100%), and vancomycin (80.6-100%). CoNS was most resistant to the antibiotics benzylpenicillin (100%), oxacillin (85.5-97.2%), and erythromycin (75-97.2%).

The demographic characteristics of patients from this study were that the dominating age groups were (0-4) years and (60-69) years (21.1%), the majority of patients were male (57.7%) and most occupied inpatient installations (84.6%). The main diagnosis of patients was dominated by pneumonia (58.5%).

6. References

1. Pott K, Girard V. Common Infectious Diseases. Prim Care. 2021 Mar 1;48(1):45–55p.
2. Sperber WH, Tatini SR. Interpretation of the Tube Coagulase Test for Identification of Staphylococcus aureus. Appl Microbiol. 1975 Apr 29;(4):502.
3. Haddadin Y, Annamaraju P, Regunath Hariharan. Central Line Associated Blood Stream Infections. StrartPearls. National Library of Medicine; 2022.
4. Argemi X, Hansmann Y, Prola K, Prévost G. Coagulase-Negative Staphylococci Pathogenomics. Int J Mol Sci. 2019 Mar 1;20(5).
5. Sukertiasih NK, Fitria M, Dwi Arymbhi S. View of Studi Retrospektif Gambaran Resistensi Bakteri terhadap Antibiotik. Jurnal Kesehatan. 2021;(7):108–109.
6. Huemer M, Mairpady Shambat S, Brugger SD, Zinkernagel AS. Antibiotic Resistance And Persistence—Implications For Human Health And Treatment Perspectives. EMBO Rep. 2020 Dec 3;21(12)
7. University of Oxford. An Estimated 1.2 Million People Died In 2019 From Antibiotic-Resistant Bacterial Infections. University of Oxford. 2019.
8. Shariati A, Dadashi M, Chegini Z, van Belkum A, Mirzaii M, Khoramrooz SS, et al. The Global Prevalence Of Daptomycin, Tigecycline, Quinupristin/Dalfopristin, And Linezolid-Resistant Staphylococcus Aureus And Coagulase-Negative Staphylococci Strains: A Systematic Review And Meta-Analysis. Antimicrob Resist Infect Control. 2020 Apr 22;9(1).3–11
9. Oyong N, Anggraini D, Karina. Pola Resistensi Bakteri Penyebab Sepsis Neonatorum di Instalasi Perawatan Neonatus RSUD Arifin Achmad Riau. Sari Pediatri. Jurnal Kesehatan.2016;17(6):438.
10. Priskila M, Wati D, Suparyatha I, et al. Pola Kepekaan Bakteri Yang Terisolasi Dari Kultur Darah Terhadap Antibiotik Di Unit Perawatan Intensif Anak RSUP Sanglah Denpasar Tahun 2015-2016. 2019 Dec 1 : 576–577.
11. Mendoza-Olazarán S, Morfin-Otero R, Rodríguez-Noriega E, Llaca-Díaz J, Flores-Treviño S, González-González GM, et al. Microbiological And Molecular Characterization Of Staphylococcus Hominis Isolates From Blood. PLoS One. 2013 Apr 9;8(4)1–2.
12. Wirajaya F. Kepekaan Bakteri Dari Kultur LCS Terhadap Antibiotik Di Laboratorium Mikrobiologi Klinik RSUP Dr. Mohammad Hoesin Palembang Periode Januari 2013–Juni 2014. Universitas Sriwijaya.2015.54–55
13. Martínez-Meléndez A, Morfín-Otero R, Villarreal-Treviño L, Camacho-Ortíz A, González-González G, Llaca-Díaz J, et al. Molecular Epidemiology Of Coagulase-Negative Bloodstream Isolates: Detection Of Staphylococcus Epidermidis ST2, ST7 And Linezolid-Resistant ST23. Braz J Infect Disease. 2016 Sep 1;20(5):4:19–28.
14. Toltzis P. Staphylococcus epidermidis and Other Coagulase-Negative Staphylococci. Principles and Practice of Pediatric Infectious Diseases.4th ed. 2018 Jan 1;706-712p.
15. Eltwisy HO, Twisy HO, Hafez MHR, Sayed IM, El-Mokhtar MA. Clinical Infections, Antibiotic Resistance, and Pathogenesis of Staphylococcus haemolyticus. Microorganisms. 2022 Jun 1;10(6);1130.

16. Szczuka E, Krzymińska S, Bogucka N, Kaznowski A. Multifactorial Mechanisms Of The Pathogenesis Of Methicillin-Resistant Staphylococcus Hominis Isolated From Bloodstream Infections. Antonie Van Leeuwenhoek. 2018 Jul 1;111(7):1259.
17. Manoharan M, Sistla S, Ray P. Prevalence and Molecular Determinants of Antimicrobial Resistance in Clinical Isolates of Staphylococcus haemolyticus from India. Microb Drug Resist. 2021 Apr 1;27(4):501–508.
18. Hashemzadeh M, Dezfuli AAZ, Nashibi R, Jahangirimehr F, Akbarian ZA. Study Of Biofilm Formation, Structure And Antibiotic Resistance In Staphylococcus Saprophyticus Strains Causing Urinary Tract Infection In Women In Ahvaz, Iran. New Microbes New Infect. 2020 Jan 1:(39)2–3.
19. Petrillo F, Pignataro D, di Lella FM, Reibaldi M, Fallico M, Castellino N, et al. Antimicrobial Susceptibility Patterns and Resistance Trends of Staphylococcus aureus and Coagulase-Negative Staphylococci Strains Isolated from Ocular Infections. Isolated from Ocular Infections Antibiotics. 2021;10:527p.
20. Molina J, Peñuela I, Lepe JA, Gutiérrez-Pizarraya A, Gómez MJ, García-Cabrera E, et al. Mortality and hospital stay related to coagulase-negative Staphylococci bacteremia in non-critical patients. J Infect. 2013 Feb;66(2):155–62.
21. Mittal G, Bhandari V, Gaind R, Rani V, Chopra S, Dawar R, et al. Linezolid Resistant Coagulase Negative Staphylococci (Lrcons) With Novel Mutations Causing Blood Stream Infections (BSI) In India. BMC Infect Disease. 2019 Aug 14;19(1).
22. CDC. Pneumonia (Ventilator-associated [VAP] and non-ventilator associated Pneumonia [PNEU]) Event: Device-associated Module. 2023.6–14.
23. Kavanagh N, Ryan EJ, Widaa A, Sexton G, Fennell J, O'Rourke S, et al. Staphylococcal Osteomyelitis: Disease Progression, Treatment Challenges, and Future Directions. Clin Microbiol Rev. 2018 Apr 1;31(2)8–12.
24. Nguyen TH, Park MD, Otto M. Host Response to Staphylococcus epidermidis Colonization and Infections. Front Cell Infect Microbiol. 2017 Mar 21;(7):90.
25. Azimi T, Mirzadeh M, Sabour S, Nasser A, Fallah F, Pourmand MR. Coagulase-Negative Staphylococci (Cons) Meningitis: A Narrative Review of The Literature From 2000 To 2020. New Microbes New Infect. 2020 Sep 1;(37):100.
26. Chu VH, Miro JM, Hoen B, Cabell CH, Pappas PA, Jones P, et al. Coagulase-Negative Staphylococcal Prosthetic Valve Endocarditis--A Contemporary Update Based on The International Collaboration on Endocarditis: Prospective Cohort Study. Heart. 2009 Apr 95(7):564–569p.
27. Eltwisy HO, Twisy HO, Hafez MHR, Sayed IM, El-Mokhtar MA. Clinical Infections, Antibiotic Resistance, and Pathogenesis of Staphylococcus haemolyticus. Microorganisms. 2022 Jun 1;10(6);1130.