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RESEARCH ARTICLE

ANTIBIOTIC RESISTANCE PATTERN OF COAGULASE-NEGATIVE STAPHYLOCOCCI ISOLATED FROM CLINICAL SPECIMENS IN SANA'A CITY, YEMEN

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Abstract

Background and aims: Coagulase-negative Staphylococci (*CoNS*) are common skin bacteria that can cause serious infections when they enter the body through invasive procedures or wounds. This study aims to evaluate the antibiotic resistance patterns of *CoNS* isolated from clinical samples in Sana'a city, Yemen, from 2011 to 2021.

Subjects and Methods: Data were collected from 4 laboratories and 3 hospitals using a retrospective cross-sectional design and SPSS software version 25.

Results This study tested 93 antibiotics for 2729 different clinical samples, and identified the *CoNS* species and their resistance patterns. Also, found that *CoNS* were a significant cause of hospital-acquired infections in Sana'a city, with high resistance rates (46.3%). The most common isolated *CoNS* species were *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*, and *Staphylococcus hemolyticus*. *CoNS* showed high resistance to β-lactam antibiotics, such as penicillins (66%) and cephalosporins (55.9%), and macrolides; such as erythromycin (57.1%) and azithromycin (50.8%). The antibiotic resistance trend increased from 2012 to 2015, with the highest peak increase in 2013 (45.2%), and decreased from 2015 to 2020, but increased again in 2021, possibly due to the COVID-19 pandemic and the overuse of antibiotics.

Conclusion: *CoNS* are a significant cause of hospital-acquired infections in Sana'a city, with high resistance rates to commonly used antibiotics. The combination of penicillin and β-lactamase inhibitor showed higher resistance than penicillin alone.

Keywords: antibiotic resistance pattern, clinical samples, *CoNS*, Sana'a city.

INTRODUCTION

The danger of commensal bacteria entering the bloodstream from various sites of infection, such as the skin, has grown as a result of modern medicine, particularly surgery. One of the most frequent types of bacteria to cause bloodstream infections is *CoNS*. Contrarily, the establishment and spread of antibiotic resistance have been attributed to the abuse of antibiotics, a lack of knowledge, a lack of education, and the use of low or inappropriate antibiotic doses by the majority of our community. There are several clinics in our area that treat patients with a single dose. These clinics also employ inefficient antiseptics with low concentration values and do not have infection control plans. Because of this, bacteria develop resistance and change from healthy flora to harmful varieties that can grow biofilms on newly implanted medical equipment[1]. These biofilms increase the bacteria's resistance to drugs and make them more challenging to treat. In addition to being a natural component of human skin and mucous membrane flora, *coagulase negative staphylococci (CoNS)* can also result in opportunistic infections in immuno-suppressed or hospitalized patients[2]. *CoNS* are frequently resistant to several medications, particularly methicillin, which makes managing and preventing *CoNS* infections difficult. Species, source of isolation,

geographic region, and technique of detection all affect the antibiotic resistance patterns of *CoNS*[3].

As a result, it's critical to keep an eye on the frequency and trends of *CoNS* resistance across a range of contexts and groups. The capital and largest city of Yemen, Sana'a, has insufficient information on the antibiotic resistance of *CoNS* isolated from clinical specimens. This project will advance our understanding of *CoNS* resistance in Yemen and give doctors and decision-makers pertinent data to help them better diagnose and treat *CoNS* infections. Additionally, it will aid in locating the weaknesses and difficulties in Sana'a city's *CoNS* surveillance and supervision as *CoNS* infections, can build biofilms on these surfaces and elude the host immune system and antibiotic therapy, they are frequently linked to the use of medical devices such catheters, prosthetic joints, and heart valves[4].

Depending on the location of the infection and the underlying medical circumstances of the patients, *CoNS* infections can result in a variety of clinical symptoms, including bacteremia, endocarditis, osteomyelitis, and infections of prosthetic joints[4]. Additionally, *CoNS* infections are a significant factor in the morbidity and mortality of newborns, particularly those who were born prematurely or with low birth weight. This study aimed to determination the pattern of antimicrobial resistance among *CoNS* isolated from clinical specimens in Sana'a City from 2011 to 2021.

MATERIALS AND METHODS

Type of Study: This study was a retrospective study.

Sample size: The study aimed to collect 2729 isolates for the analysis. However, only 451discs considered the most antibiotic available in medical use.

Study period: This study was performed approximately between May 2011 to Sep 2021 on major hospitals and medical laboratories located in Sana'a City.

Sampling technique: The sampling technique was a convenience sampling method, where the isolates were obtained from the records of the microbiology laboratories in the hospitals and laboratories in Sana'a city. Electronic data, the isolates were selected based on the availability of data on their identification and antimicrobial susceptibility testing results. The isolates were also stratified by the source (clinical) and the year of isolation (from 2011 to 2021).

Data collection: The data collection was done by reviewing the laboratory records and extracting the relevant information on the isolates, such as the source, the type, the date, the identification method, and the antimicrobial susceptibility testing results. The data were collected using a data collection sheet that was designed for this purpose. The data were collected from hospitals and medical laboratories located in Sana'a city from science and Technology hospital, Model Hospital 48, Al-Thawra Hospital, National Center for Central Public Health Laboratories (NCPHL), Aulaqi Laboratories, Med Labs Specialized and Modern International Laboratory.

Data analysis: The data analysis was done using SPSS software version 25. The data were entered, cleaned, and coded. Descriptive statistics were used to describe the frequency and percentage of the isolates by their source, type, year, and AMR pattern. Chi-square test was used to compare the AMR rates among different groups of isolates, *p*-value less than 0.05 was considered statistically significant.

RESULTS

Table 1 displays the antibiotic susceptibility patterns of Coagulase-Negative Staphylococci (CONS) isolated in Sana'a City, Yemen, between 2011 and 2021. It details the number (No.) and percentage of isolates classified as sensitive, intermediate or resistant across various antibiotic classes. The bacteria showed the highest susceptibility rates to linezolid (oxazolidinone) with the highest overall sensitivity at 85.6% (540 isolates), Vancomycin (glycopeptide) highly effective at 78.8% sensitivity (1,353 isolates), despite having the largest sample volume, Imipenem (carbapenems), which showed 67.8% sensitivity, and Amoxicillin + Clavulanic acid (β-lactamase inhibitor), which showed 66.1% sensitivity. CONS isolates displayed severe resistance to several common medications, particularly older-generation β-lactams and select cephalosporins. The cefixime (3rd-gen cephalosporin) resistance rate was 84.7%, the cefotaxime clavulanic acid resistance rate was 76.2%, the aztreonam (monobactam) resistance rate was 75.6%, the amoxicillin (amino-penicillin) resistance rate was 74.7%, and the penicillin (natural penicillin) resistance rate was 65.7%. Resistance to methicillin (56.4%) and oxacillin (55.6%) indicates a high prevalence of methicillin-resistant CONS (MR-CONS) strains in the region. Combining amoxicillin with clavulanic acid dramatically dropped resistance from 74.7% (amoxicillin alone) to just 32.8%, highlighting the prominence of β-lactamase-producing strains. The aminoglycoside and fluoroquinolone classes maintained moderate efficacy, with gentamicin, amikacin, levofloxacin, and ciprofloxacin all hovering between 57% and 62% sensitivity. Table 2 illustrates the distribution frequency and percentages of Coagulase-Negative Staphylococci (CONS) isolates collected from clinical specimens in Sana'a city over an 11-year period, from 2011 to 2021. The data tracks a total of 2,729 isolates, showing how the volume fluctuated across the decade. The year 2014 recorded the highest number of CONS isolates with 416 cases, accounting for 15.2% of the total collection. The years 2012, 2013, and 2015 also showed consistently high numbers, each contributing over 11% of the total dataset (ranging between 321 and 356 isolates per year). From 2016 to 2018, the numbers stabilized slightly, hovering between 223 and 244 isolates per year (representing about 8.2% to 8.9% annually). In 2019 and 2020, the frequency experienced a notable decline, dropping to its lowest mature point in 2020 with 133 isolates (4.9%).

Table 1: Sensitivity, intermediate, and resistance percentage and frequency of *CONS* to different antibiotics.

Antibiotic Name	Antibiotics /classes	Sensitive		Intermediate		Resistant		Total
		No.	%	No.	%	No.	%	
Ceftriaxone	3rd Cephalosporins B-lactam	339	47.7	32	4.5	340	47.8	711
Cefixime		61	13.5	8	1.8	382	84.7	451
Ceftazidime		72	20.9	13	3.8	260	75.4	345
CefotaximeClav		32	22.4	2	1.4	109	76.2	143
Cefotaxime		369	41.6	54	6.1	463	52.3	886
Ceftizoxime		135	44.3	7	2.3	163	53.4	305
Cefoxitin		251	45.5	2	0.4	299	54.2	552
Cefepime	4th Cephalosporins B-lactam	276	41.8	32	4.8	353	53.4	661
Tobramycin	Aminoglycosides	37	45.1	7	8.5	38	46.3	82
Gentamicin		767	62.0	78	6.3	392	31.7	1237
Amikacin		457	58.6	78	10.0	245	31.4	780
Levofloxacin	3rd generation Fluoroquinolones	498	59.6	53	6.3	285	34.1	836
Ciprofloxacin	2nd generation Fluoroquinolones	600	57.1	54	5.1	396	37.7	1050
Meropenem	Carbapenems	274	51.8	40	7.6	215	40.6	529
Imipenem		476	67.8	16	2.3	210	29.9	702
Aztreonam	Monobactams	18	22.0	2	2.4	62	75.6	82
Piperacillin-Tazobactam	B-lactamase-inhibitor	217	50.7	31	7.2	180	42.1	428
Cefuroxime Clavulanic Acid		92	26.6	4	1.2	250	72.3	346
Amoxicillin+ Clavulanic acid		1216	66.1	22	1.2	603	32.8	1841
Azithromycin	Macrolide	268	45.4	22	3.7	300	50.8	590
Piperacillin	Extended-spectrum U reido-penicillin	61	44.9	7	5.1	68	50.0	136
Penicillin	Natural Penicillin	263	29.7	41	4.6	582	65.7	886
Vancomycin	Glycopeptide	1353	78.8	151	8.8	214	12.5	1718
Linezolid	Oxazolidinone	540	85.6	13	2.1	78	12.4	631
ColistinS ulphate	Poly-peptide	38	45.2	1	1.2	45	53.6	84
Amoxicillin	Aminopenicillins	460*	25.0	5	0.3	1376	74.7	1841
Ampicillin		349	29.4	46	3.9	791	66.7	1186
Methicillin	Antistaphylococcal	665	43.5	2	0.1	863	56.4	1530
Oxacillin	peni1cillins	594	44.1	5	0.4	749	55.6	1348
Nitrofurantoin	Other	451	72.0	51	8.1	124	19.8	626
β-lactamase	β-lactam	1376*	74.7	465	25.3	465	25.3	1841

DISCUSSION

The results of this study provide critical insights into the antibiotic susceptibility patterns of Coagulase-Negative Staphylococci (CoNS) in Sana'a City, Yemen, spanning a ten-year period (2011–2021). Historically viewed as harmless commensals, CoNS have emerged as major opportunistic pathogens capable of causing severe healthcare-associated infections. The high levels of resistance observed in this study a troubling therapeutic challenge in the region, driven primarily by the proliferation of multidrug-resistant strains. The high levels of resistance observed in the current study, are similar to that reported before in Yemen in which high resistant rates were occurred for CoNS with the highest rates of resistance occurred against Sulphamethoxazole/ Trimethoprim (85.5%), Ceftazidime (81.07%), Ampicillin (70.4%), Cefuroxime (66.4%), Cefotaxime (32.6%)[5]. Also, high rate of resistance among CoNS isolated from bloodstream infections in the intensive care unit patients of university hospitals in Sana'a city, Yemen (up to 70% for previous antibiotics[6]. Multidrug resistance CoNS was exceptionally high among Gram-positive isolates from wound infections (reaching up to 92.1%)[7].

Table 2: Distribution frequency of *CONS* isolates from clinical specimens in Sana'a city according to year of collection.

Years	n (%)
2011	10 [0.3)
2012	356 (13)
2013	321 (11.8)
2014	416 (15.2)
2015	349 (12.8)
2016	223 (8.2)
2017	231 (8.5)
2018	244 (8.9)
2019	198 (7.3)
2020	133 (4.9)
2021	248 (9)
Total	2729 (100)

The rise of methicillin-resistant CoNS (MR-CoNS); A key finding of this study is the high prevalence of methicillin (56.4%) and oxacillin (55.6%) resistance, confirming that over half of the isolated CoNS strains are methicillin-resistant (MR-CoNS). Methicillin resistance in staphylococci is typically mediated by the *mecA* gene, which confers cross-resistance to almost all beta-lactam antibiotics[8-10]. This high burden of MR-CoNS in Sana'a City seriously limits empirical treatment options, as standard penicillins and

cephalosporins cannot be relied upon for severe infections.

Severe beta-lactam and cephalosporin resistance: The isolates demonstrated severe resistance to older-generation beta-lactams and cephalosporins, driven by two primary mechanisms: beta-lactamase production and altered penicillin-binding proteins (PBP2a). The dramatic reduction in resistance when amoxicillin was combined with a beta-lactamase inhibitor (amoxicillin + clavulanic acid, dropping resistance from 74.7% to 32.8%) highlights that enzymatic degradation is a dominant resistance mechanism among these strains. The alarmingly high resistance rates to cefixime (84.7%) and cefotaxime + clavulanic acid (76.2%) is particularly concerning. They indicate that third-generation cephalosporins, which are frequently overprescribed in empirical settings, have lost their clinical utility against CoNS in this region[11].

Efficacy of glycopeptides and oxazolidinones: Fortunately, linezolid (85.6% sensitivity) and vancomycin (78.8% sensitivity) remain highly effective. Vancomycin's robust activity is especially noteworthy given that it maintained a high sensitivity rate despite being tested against the largest sample volume in the study. These findings reinforce linezolid and vancomycin as dependable, first-line fallback options for severe, multi-drug resistant CoNS infections in Yemen. The emergence of bacterial populations with intermediate or complete resistance to these last-resort antibiotics highlights the need for strict, continuous surveillance to block the transmission of fully resistant strains[12]. While numerous publications report total sensitivity to vancomycin, our findings reveal that 21% of the isolated strains exhibit resistance. This aligns with a previous study by Jain N., which documented a 15% resistance rate[13]. Globally, literature indicates that 14% to 17% of coagulase-negative staphylococci (CoNS) isolates display reduced susceptibility to vancomycin[14-19] a trend further supported by the independent findings of Diekema DJ *et al*., and Natoli S. Key drivers accelerating this glycopeptide resistance include the unrestricted use of glycopeptides and beta-lactams, recurrent hospital stays, and concurrent pneumonia infections[20,21]. To mitigate this issue, the Centers for Disease Control and Prevention (CDC) advises limiting vancomycin prescriptions to cases where CoNS is confirmed across multiple blood cultures; it should be avoided if CoNS appears in only a single culture from a series[22,23].

Antibiotics belonging to the aminoglycoside (gentamicin, amikacin) and fluoroquinolone (levofloxacin, ciprofloxacin) classes demonstrated moderate efficacy, with sensitivity rates clustering between 57% and 62%. While these classes cannot be safely relied upon for empirical monotherapy in critical cases, they may still serve as valuable components of combination therapies or as targeted options guided by specific patient culture results. The high baseline resistance rates documented over this decade likely reflect broader public health challenges in Yemen. Factors such as the unregulated over-the-counter availability of antibiotics, lack of standardized stewardship programs, and infrastructure disruptions due to ongoing regional instability have historically accelerated selection pressure for resistant bacteria[6-11].

The 11-year surveillance of Coagulase-Negative *Staphylococci* (CONS) isolates in Sana'a City from 2011 to 2021 reveals significant temporal fluctuations in bacterial frequency. These shifts likely reflect a combination of changing clinical burdens, epidemiological dynamics, and external healthcare disruptions.

The data shows a major surge in CONS isolates between 2012 and 2015, peaking in 2014 with 416 cases (15.2%). This period of elevated frequencies could be attributed to several factors: The first one might be the widespread of nosocomial infections in which CONS are opportunistic pathogens heavily associated with healthcare-associated infections (HAIs), especially through the use of indwelling medical devices like catheters and prosthetics. Increased medical interventions or changes in hospital infection control practices during these years may have driven the surge[12]. The second factor is sociopolitical Disruptions as the escalation of the conflict in Yemen began heavily impacting the infrastructure in late 2014 and 2015. Initial disruptions often cause overcrowding in surviving healthcare facilities, leading to compromised hygiene protocols and accelerated transmission of hospital-acquired pathogens[10,11]. Following a period of relative stability from 2016 to 2018, the dataset notes a sharp decline in isolates, reaching its lowest mature point in 2020 with 133 cases (4.9%). This drop is highly characteristic of the global COVID-19 pandemic era. During 2020, non-COVID healthcare utilization plummeted due to lockdowns, fear of hospital transmission, and the repurposing of clinics; or it might be due to those fewer elective surgeries and reduced routine hospitalizations directly translate to fewer device-associated CONS infections being contracted or cultured. Additionally, the baseline year of 2011 (0.3%) can be disregarded as an epidemiological low point, as it represents a partial tracking period or the inception phase of the study's data collection registry. In 2021, the frequency nearly doubled to 248 isolates (9.0%). The resumption of elective procedures, combined with a potentially strained healthcare infrastructure operating under prolonged resource scarcity in Sana'a, created ideal conditions for the resurgence of opportunistic nosocomial pathogens like CONS[9-11].

Limitations of the study

One of the primary limitations of our study stems from its retrospective design; as it relies on a retrospective cross-sectional approach, the research is based on pre-existing laboratory and hospital records. This often leads to missing data or incomplete patient medical histories, and it precludes the establishment of a direct cause-and-effect relationship over time.

CONCLUSIONS

In summary, CoNS isolated in Sana'a City exhibit high rates of multidrug resistance, particularly against standard beta-lactams, while maintaining high susceptibility to linezolid and vancomycin. These findings emphasize the urgent need for updated local

empirical treatment guidelines, stricter regulations on antibiotic dispensing, and continuous microbiological surveillance to curb the further evolution of resistance.

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AUTHOR'S CONTRIBUTIONS

Al-Huraibi BS: formal analysis, conceptualisation, data organisation, writing original draft. **Al-Shami HZ:** data analysis, manuscript writing. **Al-Shargabi OA:** data analysis, manuscript writing. **Al-Moyed KA:** literature survey. **Al-gunaid EA:** critical review. **Abdu SSA:** literature survey. **Hassan SMA:** critical review, editing. **Al-Shamahy HA:** data analysis. **Al-Haddad AM:** data analysis, editing. Final manuscript was checked and approved by all authors.

DATA AVILIABILITY

The data will be available to anyone upon request from the corresponding author.

CONFLICT OF INTEREST

None to declare.

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