AKADÉMIAI KIADÓ

Acta Microbiologica et Immunologica Hungarica

69 (2022) 1, 68–76

DOI:
10.1556/030.2021.01580

RESEARCH ARTICLE

Multidrug resistant coagulase-negative *Staphylococcus* spp. isolated from cases of chronic rhinosinusitis in humans. Study from Poland

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Received: August 27, 2021 • Accepted: November 15, 2021
Published online: December 10, 2021

ABSTRACT

For many years, coagulase-negative staphylococci (CoNS) have been considered non-pathogenic bacteria. However, recently, CoNS are becoming more common bacteriological factors isolated from cases of chronic rhinosinusitis in humans. Moreover, most of them represent the multidrug-resistant or/and methicillin-resistant profile, which significantly increases the therapeutic difficulties. The aim of the study was to characterize profile of resistant coagulase-negative staphylococci isolated from cases of chronic rhinosinusitis in patients treated in a Medical Center in Warsaw in 2015–2016.

The study material was derived from patients with diagnosed chronic rhinosinusitis treated at the MML Medical Center in Warsaw. The material was obtained intraoperatively from maxillary, frontal, and ethmoid sinuses.

In total, 1,044 strains were isolated from the studied material. Coagulase-negative staphylococci were predominant, with the largest share of *Staphylococcus epidermidis*. Isolated CoNS were mainly resistant to macrolide, lincosamide, and tetracycline. Among the *S. epidermidis* strains, we also showed 35.6% of MDR and 34.7% of methicillin-resistant strains.

The same values for other non-*epidermidis* species were 31.5% and 18.5%, respectively and the percentage of strains with MAR >0.2 was greater in *S. epidermidis* (32.6%) than *S.* non-*epidermidis* (23.9%). Although the percentage of strains resistant to tigecycline, glycopeptides, rifampicin and oxazolidinones was very small (2.3%, 1.9%, 1.4% and 0.7% respectively), single strains were reported in both groups.

The study has shown a high proportion of MDR and methicillin-resistant CoNS strains, which indicates a large share of drug-resistant microorganisms in the process of persistence of chronic rhinosinusitis; therefore, isolation of this group of microorganisms from clinical cases using aseptic techniques should not be neglected.

KEYWORDS

antibiotic resistance, coagulase-negative staphylococci, chronic rhinosinusitis, *S.epidermidis*

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INTRODUCTION

Chronic rhinosinusitis (CRS) is one of the most common health problems affecting at least 5–12% of the world's population [1]. In general, there are many hypotheses as to the etiology

related to both non-infectious (allergens, toxins) and infectious agents (bacteria, viruses, fungi) and predisposing factors on the host side [2]. It is usually very difficult to identify a pathogen as the cause of CRS, but most cases of this disease are accompanied by bacterial, viral, fungal, or mixed infections [3].

It is estimated that bacterial infections are dominant (60–90% of all cases of CRS) [3]; however, among other groups of pathogens, such as fungi, molds of the genus *Aspergillus* are dominant [4]. Moreover, the presence of viral genetic material in samples collected from ethmoid sinuses in patients with chronic sinusitis symptoms was found, the most common being coronavirus, adenovirus, human rhinovirus, and respiratory syncytial virus [5]. Nevertheless, the most frequently isolated bacterial genus is *Staphylococcus*, mainly *S. aureus, S. epidermidis*, and other coagulase-negative staphylococci (CoNS), including *S. lugdunensis, S. saprophyticus, S. hominis, S. warneri, S. haemolyticus, S. capitis, S. saccharolyticus, S. hyicus, S. auricularis, S. simulans, S. sciuri, S. cohnii, S. xylosus*, and *S. lentus* [6, 7]. Among Gram-negative bacteria, which are less often isolated, *Pseudomonas aeruginosa, Enterobacter aerogenes*, and *Enterobacter cloacae* predominate [8].

While *S. aureus* has always been considered the primary or concomitant cause of infection due to exotoxin production and biofilm formation [9], other species belonging to this genus, especially coagulase-negative staphylococci, have been perceived primarily as a component of the commensal biota for many years [7]. These microorganisms occur on skin and mucous membranes of humans and animals representing 90% of microorganisms colonizing the surface of the human skin [10]. Unlike coagulase-positive staphylococci, they were regarded as strains contributing only to chronic and subacute infections [7].

However, studies from recent years have shown that CoNS more frequently contribute to the development of different types of infection, especially in immunocompromised individuals or patients with implants and catheters, as well as patients with endocarditis, atopic dermatitis, hard-to-heal wounds, orthopedic infections, or patients suffering from cancers [9, 11–13].

Moreover, *S. epidermidis*, initially considered the cause of endogenous infections, has been confirmed as an example of a species that produces nosocomial genotypes responsible for medical device-related infection, which is facilitated by its ability to form biofilm [14].

Other species of CoNS are isolated with variable frequency from cases of different types of infection. There are single reports about the occurrence of *S. lugdunensis* in cerebral abscesses, meningitis, osteomyelitis, arthritis, and cesarean section complications [15]. Moreover, *S. lugdunensis* strains are often improperly identified as *S. aureus* due to the similar morphology and clumping factor test results, which may underestimate the percentage of infections caused by this species [16].

Campoccia et al. [17] isolated *S. warneri* from patients with orthopedic infections. *S. haemolyticus* is one of the two CoNS species most commonly isolated from blood infections, including sepsis [18]. The ability of *S. hominis* to form a stable biofilm on medical devices and tissues increases the pathogenicity of strains belonging to this species [19].

The biggest problem, however, is the frequent multidrug resistance of coagulase-negative *Staphylococcus* species, especially *S. epidermidis* [14]. Moreover, the very low number of monitoring studies for drug resistance in coagulase-negative staphylococci contributes to the lack of a complete assessment of the risk that specific nosocomial multidrug-resistant clones of these species may cause [9].

Taking into account CoNS as the potential pathogens, it appears that they can not be underestimated in diagnostic (microbiological) procedures. Due to the historical approach to CoNS as a commensal organism, it seems that too often the diagnostic process is terminated at the species identification stage, without further analysis of drug susceptibility or the potential for infection by coagulase-negative species. This may lead to erroneous therapeutic decisions and thus to the generation of antibiotic resistance in the case of antimicrobial treatment without the assessment of drug resistance.

The aim of the study was to characterize antibiotic resistant coagulase-negative staphylococci isolated from cases of chronic rhinosinusitis in patients treated in a Medical Center in Warsaw in 2015–2016.

MATERIALS AND METHODS

The studied material was derived from 650 patients treated at the Medical Center in Warsaw for one year (December 2015–November 2016). Patients with chronic sinusitis were qualified based on the history of the disease and physical examination. Preliminary diagnosis based on clinical symptoms described by Rosenfield et al. [20] was confirmed by endoscopic examination, computer tomography, and histopathology of sinus mucosa. Bacterial strains were isolated from humans who cannot be identified from any material in this manuscript. This study was carried out in accordance with the WMA Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects).

Isolation and identification of staphylococci

The study material was derived from maxillary, frontal, and ethmoid sinuses. Samples of material were collected aseptically in order to minimize contamination and obtain representative bacterial material [21] and delivered to the laboratory within up to an hour. Preliminary isolation and identification were carried out according to a standard laboratory procedure: the material was cultured on Columbia sheep blood agar (5%), MacConkey agar, and Brucella agar (bioMerieux, France) and incubated at 37°C aerobically or anaerobically for 24 h. Morphologically dominant single colonies were typed from each culture for further analysis. Identification was carried out with the use of Matrix-assisted

laser desorption/ionization time-of-flight-mass spectrometry (MALDI-TOF MS), (MALDI Biotyper, BRUKER, 2016) according to procedure described elsewhere [22]. Bruker daltonics library MBT IVD LIBRARY (2019) was used for species identification.

The antibiotic susceptibility was assessed using the spectrophotometric method on the Vitek 2 Compact in accordance with the instructions of the manufacturer of the Biomerieux (VITEK 2-technology device 514740 - 1PL1 04-2013).

The disc diffusion test according to the Clinical and Laboratory Standard Institute [23] was applied when necessary (extension of the antibiograms with additional antimicrobials). Reference strain *S. aureus* ATCC29213 was used as a quality control. Antimicrobial susceptibility testing was determined including assessment of resistance to most reccomended antimicrobials used in staphylococcal infections [24]: methicillin, macrolides, clindamycin (including MLSB phenotype-resistance to macrolides, lincosamides, and streptogramins B), aminoglycosides (gentamicin, amikacin, netilmicin, tobramycin), fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin), β-lactams (cloxacillin), glycopeptides (vancomycin, teicoplanin), oxazylidynones (linezolid), tetracyclin, tigecyclin, sulphametoxazole, and rifampicin.

The multiple antibiotic resistance (MAR) index was calculated using the following formula: MAR = x/y, where x is the number of antimicrobials to which the isolate is resistant and y is the total number of antimicrobials tested. A MAR value greater than 0.2 means that a high risk source of contamination where antibiotics are frequently used.

Statistical analysis was performed using STATISTICA 13.1 (StatSoft, Kraków, Poland). The Mann-Whitney U test was used to show statistically significant differences ($P < 0.05$) for the drug resistance between *S. epidermidis* and other *Staphylococcus* species, between methicillin-resistant and methicillin-susceptible *S. epidermidis* strains, and between methicillin-resistant and methicillin-susceptible *S.* non-*epidermidis* strains.

RESULTS

Bacterial growth was observed in all samples. Since bacterial species were isolated as single or multi-species from the same sample, 1,044 bacterial strains were isolated in total. Most strains were determined as coagulase-negative staphylococci (522 strains) belonging to following species: *S. epidermidis* ($n = 430$), *S. hominis* ($n = 36$), *S. warneri* ($n = 19$), *S. haemolyticus* ($n = 17$), *S. lugdunensis* ($n = 13$), *S. capitis* ($n = 5$), *S. lentus* ($n = 1$), and *S. cohnii* ($n = 1$) (Table 1).

Within the *S. epidermidis* species, we demonstrated multidrug resistance for 35.6% of the strains. Interestingly, this group also included almost all cefoxitin resistant strains (MRSE) (34.7%), except for one isolate, which was additionally resistant only to erythromycin, similarly to strains from the group other than *S. epidermidis*.

Only 13.5% of *S. epidermidis* were susceptible to all tested antimicrobials, and no vancomycin resistance was found in any of the strains belonging to this species.

The MAR index for *S. epidermidis* had a slightly larger range, and 3% of the strains had a value of 0.72, which was not observed in the second group of staphylococci (Table 2). *S. epidermidis* strains with the highest MAR values were mainly resistant to macrolides, clindamycin, all tested aminoglycosides and fluoroquinolones, as well as tetracycline and sulfamethoxazole. Moreover, all of them met the criteria of MRSE. The drug resistance profile of strains with lower MAR values was slightly more varied, with the differences mainly related to drug resistance or susceptibility to aminoglycosides, fluoroquinolones, and sulfamethoxazole, while resistance to erythromycin, clindamycin, and tetracycline was dominant in the case of resistance to only these three antimicrobials (61.3%).

Overall, the multidrug resistance (MDR) in other staphylococci than *S. epidermidis* was 31.5%, with 17 strains (18.5%) resistant to cefoxitin. Nine of them belonged to *S. hominis*, seven were assigned to *S. haemolyticus*, and one was *S. lentus*. Nine methicillin-resistant strains (MRS) also met the criteria for MDR, showing resistance to three to ten antimicrobials tested. Interestingly, as many as six strains were resistant only to cefoxitin, and the other two additionally to erythromycin only.

Almost one-third of the cefoxitin-susceptible strains (26.6%) also had a multidrug resistance profile, and only in this group we showed isolates susceptible to all antimicrobials tested, including *S. hominis* ($n = 10$), *S. capitis* ($n = 3$), *S. haemolyticus* ($n = 3$), *S. warneri* ($n = 3$), and *S. lugdunensis* ($n = 3$) (Table 1).

The MAR index for all staphylcocci other than *S. epidermidis* ranged from 0.05 to 0.66, and we found 28.2% of strains ($n = 29$) in this group meeting the criteria of MDR (Table 2). We noted different profiles of resistance for each MDR strain, which included insensitivity to three up to 12 antimicrobials tested.

The value of MAR >0.2 was found in a higher percentage of *S. epidermidis* (32.6%) than in strains other than *S. epidermidis* (23.9%).

The analysis of the resistance profile of all tested isolates showed that most strains were resistant to erythromycin (68%), tetracycline (60.9%), and clindamycin (39.2%) (Table 1). Fewer strains were resistant to cloxacillin (32.3%). As many as a quarter of the strains were resistant to cefoxitin; hence, they were classified as MRSE (methicillin-resistant *S. epidermidis*) or MRS (methicillin-resistant *Staphylococcus*). In almost 40% of the strains, we also showed the MLSB phenotype, i.e. insensitivity to macrolides, lincomycin, and streptogramins B. The resistance to individual aminoglycosides was at a comparable level, i.e. from 27.2% to 23.9% to tobramycin, amikacin, and netilmycin; the fewest strains were resistant to gentamycin (only 15.3%). The level of resistance to the tested fluoroquinolones was also comparable, i.e. from 11.3% to 13.3% in the case of ciprofloxacin, levofloxacin, and moxifloxacin. Nearly 10% of strains were reported to be resistant to sulfamethoxazole. Although the

Table 1. Prevalence of resistant coagulase-negative *Staphylococcus* spp. strains isolated from CRS

	Species (n = 522)								
Antimicrobial	*S.epidermidis* (n = 430/%)	*S. hominis* (n = 36)	*S. warneri* (n = 19)	*S. haemolyticus* (n = 17)	*S. lugdunensis* (n = 13)	*S. capitis* (n = 5)	*S. lentus* (n = 1)	*S. cohnii* (n = 1)	Total (n = 522/%)
Cefoxitin	118/27.4	9		7			1		135/25.8
Erythromycin	303/70.5	16	14	12	6	2	1	1	355/68
Clindamycin	211/49.1	12	6	8	5	2		1	245/46.9
MLS_B	179/41.6	8	4	9	3	2			205/39.2
Cloxacillin	120/27.9	7	3	6	1	1	1		139/32.3
Gentamycin	52/12.1	2	2	6	3	1			66/15.3
Amikacin	93/21.6	7	3	8	2	1	1		115/26.7
Netilmicin	94/21.9	2	2	2	2	1			103/23.9
Tobramycin	97/22.6	7	3	6	2	1	1		117/27.2
Ciprofloxacin	48/11.2	1		5	2	1			57/13.3
Levofloxacin	50/11.6	1		2	2	1			56/13
Moxifloxacin	44/10.2			3	1	1			49/11.3
Tetracycline	236/54.9	7	5	8	3	2	1		262/60.9
Teicoplanin	3/0.7			3					6/1.4
Tigecycline	8/1.9			1		1			10/2.3
Linezolid	2/0.4			1					3/0.7
Sulfamethoxazole	33/7.7	4		2			1		40/9.3
Rifampicin	4/0.9			2					6/1.4
Vancomycin		3		3					6/1.4

Table 2. Values of the MAR index in *S. epidermidis* and other species

MAR index	No of *S.epidermidis* isolates (n = 430)	No of isolates other than *S. epidermidis* (n = 92)	Species (n)
0.72	13 (3%)		-
0.66	6 (1.4%)	1 (1.1%)	*S.capitis* (1)
0.61	4 (0.9%)	2 (2.2%)	*S.haemolyticus* (2)
0.55	4 (0.9%)	6 (6.5%)	*S.haemolyticus* (3) *S.lugdunensis* (2) *S.hominis* (1)
0.50	12 (2.8%)		-
0.44	10 (2.3%)	1 (1.1%)	*S.hominis* (1)
0.38	23 (5.3%)	5 (5.4%)	*S.haemolyticus* (3) *S.hominis* (1) *S.lentus* (1)
0.33	14 (3.3%)	2 (2.2%)	*S. warneri* (2)
0.27	27 (6.3%)	2 (2.2%)	*S.hominis* (2)
0.22	27 (6.3%)	3 (3.3%)	*S.hominis* (2) *S. warneri* (1)
0.16	62 (14.4%)	7 (7.6%)	*S.hominis* (5) *S. warneri* (1) *S.capitis* (1)
0.11	87 (20.2%)	19 (20.6%)	*S.hominis* (7) *S. warneri* (6) *S.haemolyticus* (3) *S.lugdunensis* (2) *S.cohnii* (1)
0.05	73 (16.9%)	22 (23.9%)	*S.hominis* (7) *S. warneri* (6) *S.lugdunensis* (6) *S.haemolyticus* (3)

number of strains resistant to glycopeptides, tigecycline, oxazolidinones, and rifampicin was very small, single strains were reported in both groups with the exception of vancomycin-resistant strains representing the species *S. haemolyticus* (n = 3), *S. hominis* (n = 2), and *S. lugdunensis* (n = 1). Except for a single strain of *S. epidermidis* resistant to tigecycline, all other isolates resistant to glycopeptides and/or tigecycline, oxazolidinones, and rifampicin were multidrug resistant and had a MAR index >0.2. Moreover, we observed resistance to linezolid in the methicillin-resistant strains only (n = 3).

A comparative statistical analysis of both *Staphylococcus* groups showed that the *S. epidermidis* strains were characterized by statistically significantly higher resistance to erythromycin, clindamycin, tetracycline, and netilmycin (Fig. 1). Moreover, the MLSB phenotype was statistically significantly more frequent in *S. epidermidis* compared to strains other than *S. epidermidis* (Fig. 1).

By comparing MRSE and MSSE, we showed that MRSE were characterized by statistically significantly higher resistance to cloxacillin, sulfamethoxazole, fluoroquinolones, all tested aminoglycosides, erythromycin, clindamycin, and tetracycline. The presence of statistically significantly higher occurrence of the MLSB phenotype was shown as well (Fig. 2). In turn, the comparative statistical analysis between methicillin-resistant and methicillin-susceptible strains other than *S. epidermidis* did not show any statistically significant differences between the susceptibility profiles in these two groups.

DISCUSSION

The problem of chronic rhinosinusitis is quite common and affects over 16% of the world's population annually and one of the most important infectious causes are coagulase-negative staphylococci [25]. The role of this group of microorganisms is not fully understood, as *S. epidermidis* and other coagulase-negative staphylococci are a natural component of the microbiota of the skin and mucous membranes [21]. Therefore, when considering coagulase-negative staphylococci as the cause of CRS, attention should be paid to whether the material collected for the study is appropriate and not contaminated with residual microbiota. The nasal swab should not constitute a reliable diagnostic material due to the commensal character of coagulase-negative staphylococci and their common occurrence on the skin and mucous membranes, which may lead to misdiagnosis and introduction of inadequate treatment. In the present study, the material for the test was taken intraoperatively, directly from the sinuses, which prevents false-positive results.

Many authors emphasize the important role of multidrug resistance in the growing problems related to the treatment

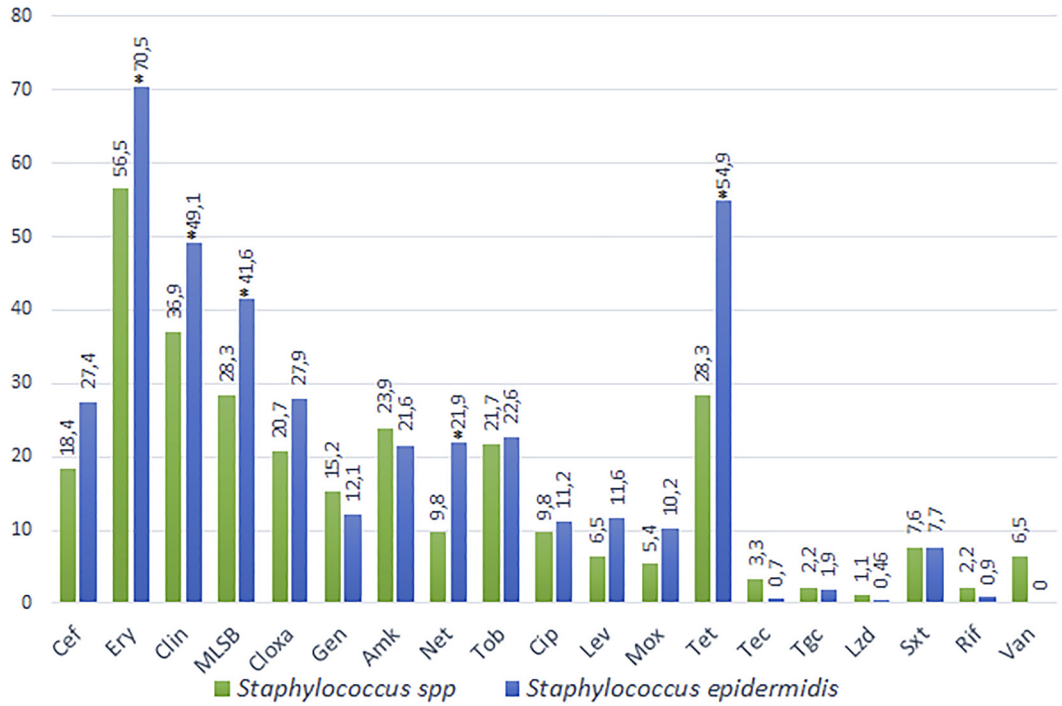

Fig. 1. Percentage of resistant *Staphylococus epidermidis* and *S.* non-*epidermidis* strains
*statistically significant differences Resistance to Cef-Cefoxitin; Ery-Erythromycin; Clin-Clindamycin; MLSB-phenotype resistance to macrolide, lincosamide, streptogramin B; Cloxa- Cloxacillin; Gen-Gentamycin; Amk-Amikacin, Net-Netilmicin; Tob-Tobramycin; Cip-Ciprofloxacin; Lev-Levofloxacin; Mox-Moxifloxacin; Tet-Tetracycline; Tec-Teicoplanin; Tgc-Tigecycline; Lzd-Linezolid; Sxt-Sulfamethoxazole; Rif-Rifampicin; Van-Vancomycin

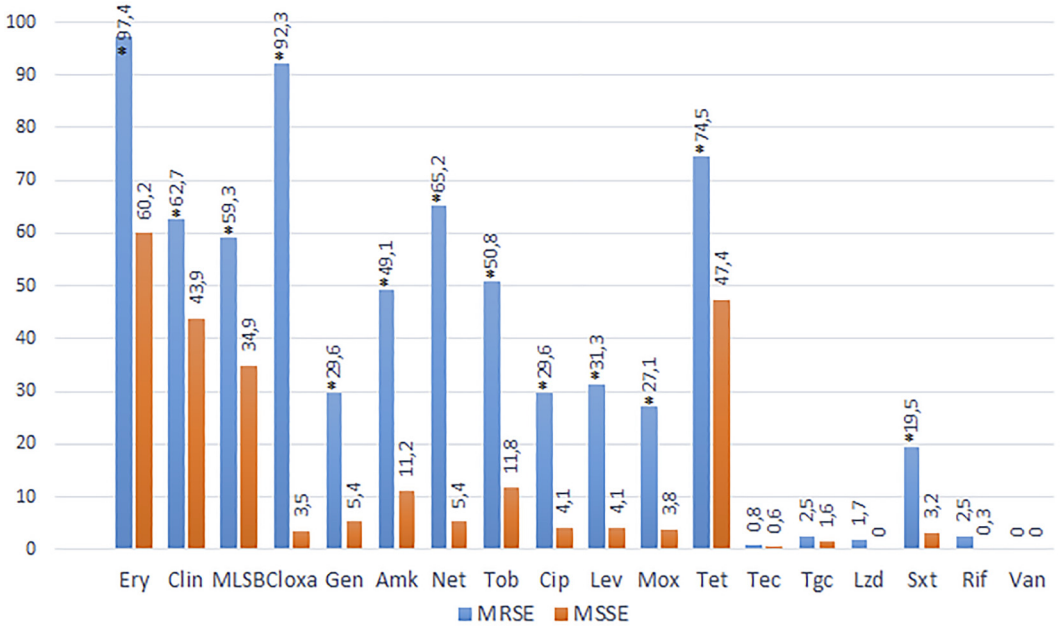

Fig. 2. Percentage of methicillin-resistant and methicillin-susceptible *S. epidermidis*
*statistically significant differences Resistance to Cef-Cefoxitin; Ery-Erythromycin; Clin-Clindamycin; MLSB-phenotype resistance to macrolide, lincosamide, streptogramin B; Cloxa- Cloxacillin; Gen-Gentamycin; Amk-Amikacin, Net-Netilmicin; Tob-Tobramycin; Cip-Ciprofloxacin; Lev-Levofloxacin; Mox-Moxifloxacin; Tet-tetracycline; Tec-Teicoplanin; Tgc-Tigecycline; Lzd-Linezolid; Sxt-Sulfamethoxazole; Rif-Rifampicin; Van-Vancomycin

of infections caused by coagulase-negative *Staphylococcus* species [26–29]. Similarly, our study has shown over 30% of strains resistant to more than three antimicrobials belonging to different groups both within *S. epidermidis* and other CoNS [30]. The multidrug resistance phenomenon was shown in several dozen strains belonging mainly to the species *S. epidermidis*, related to their insensitivity to 13 out of 19 antimicrobials tested (taking into account the MLS_B phenotype as resistance to three antimicrobials). However, the multidrug resistance in the studied group was two times lower than in the study conducted by Asante et al. [31], who showed that over 70% of *Staphylococcus* coagulase-negative strains isolated from different ward types and bloodstream infections met the criteria for multidrug resistance. Such discrepancies may result from the different panels of antibiotics used in a given country or even in a given hospital, the type of infection from which the strain was isolated, the length and type of antimicrobial therapy used, or other environmental factors.

Simultaneously, the MAR index >0.2 for 22.8% and 33.9% of strains other than *S. epidermidis* and *S. epidermidis*, respectively, shown in this study, indicates a high risk of environment contamination where antibiotics are often used, which is very likely in the extended or repeated treatment of CRS [32]. In general, CoNS strains, mainly *S. epidermidis* and *S. haemolyticus*, circulating in the hospital environment show a high level of resistance, even exceeding 70% in the case of resistance to oxacillin and other antibacterial substances, i.e. gentamicin, clindamycin, or fluoroquinolones [33]. Moreover, although CoNS very often colonize the nasal cavity, a statistically higher level of resistance was observed in strains isolated from patients with clinical signs of infection compared to healthy individuals [34].

Interestingly, we did not find a positive correlation between the methicillin resistance and the higher level of resistance to the other antimicrobials in the strains from non-*epidermidis* group tested in the present study. A positive relationship between methicillin resistance and the MLSB phenotype was observed in *S. haemolyticus* strains [35] only, and a similar relationship in relation to aminoglycosides was noted for *S. hominis* strains [29]. In the current study, only half of the methicillin-resistant *S.* non-*epidermidis* strains were multidrug resistant, and even six strains had only methicillin resistance, although methicillin-resistant CoNS species are regarded mainly as the MDR phenotype [35, 36].

Resistance to macrolides, tetracycline, and clindamycin as well as the simultaneous presence of the MLSB phenotype is common among CoNS isolates [27, 31, 37], and we obtained similar results in the current study. CoNS strains resistant to aminoglycosides are also frequent in the hospital environment [26, 27, 31]. The highest level of resistance was recorded for tobramycin, which may be related to the frequent use of this group of antibiotics in ophthalmic applications in humans, similar to fluoroquinolones [38].

Resistance to aminoglycosides and fluoroquinolones was comparable for both groups of strains; however, within *S. epidermidis*, we noticed a significantly higher level of resistance to these antimicrobials in the methicillin-resistant strains. Coexistence of resistance to aminoglycosides and methicillin has already been observed in coagulase-negative species [39]. Similarly, much faster development of resistance to fluoroquinolones has been confirmed in methicillin-resistant *Staphylococcus* strains, which is explained by the source of origin (hospital infections) or co-selection with few groups of antimicrobials [40].

Glycopeptides, tigecycline, and oxazolidinones are currently considered the "last resort" drugs in the treatment of multidrug-resistant nosocomial infections [41, 42]. In order to inhibit the phenomenon of the increasing drug resistance as a result of misuse of drugs, in 2017, WHO created a tool called AWaRe [42] aimed at reducing the use of drugs related to the highest risk of resistance, defining the potential for use of drugs in both human and veterinary medicine on a three-point scale. Currently, glycopeptides are in the second category (Watch), while tigecycline and linezolid are in the "Reserve" category and are used only in extreme cases of non-treatable infections. The results of our study confirmed the occurrence of linezolid- or tigecycline-resistant coagulase-negative *Staphylococcus* species in Poland [43]. Tigecycline and linezolid are mainly used to control coagulase-negative and coagulase-positive vancomycin-resistant *Staphylococcus* strains [43]; however, in the case of the strains tested in the present study, vancomycin resistance did not occur in the same strains that were resistant to these two drugs. Although these two antimicrobials have been used for many years, resistance to them has been incidentally reported both in the country and in the world [42, 43]. Nevertheless, it should be assumed that with the increasing use of these drugs, the level of resistance will also increase.

CONCLUSION

Although, coagulase-negative species belonging to *Staphylococcus* genus have until recently been considered only part of the commensal biota in humans and animals, recent reports have repeatedly confirmed their role as etiological factors of a wide range of clinical changes, ranging from local and superficial to blood-stream infections. The problem of coagulase-negative staphylococcal infections seems to result from not only the presence of a diverse panel of virulence factors but also from alarming drug resistance. Thus, this group becomes not only the hard-to-control cause of clinical disorders but also a reservoir for many different resistance mechanisms that can be easily transferred between closely related taxa, including pathogens, via horizontal gene transfer (HGT). Higher resistance may emerge at any time in nosocomial strains or isolates from clinical cases of infection due to the occurrence of various factors. A similar situation has been observed in the case of the increasing plasmid-mediated resistance to colistin or fluoroquinolones in *Enterobacteriaceae* bacteria in recent years, which is most likely caused by an increase in the consumption of these antimicrobials in food-producing animals or by cross-resistance caused by the use of substances from the same group of antimicrobials in animals or humans [44].

Therefore, we must be aware that the controlled and limited use of antimicrobials in the treatment of all types of infections, including those caused by coagulase-negative staphylococci, is the only chance to inhibit progressive multidrug resistance. Simultaneously, screening for drug resistance should be recommended in the case of bacteria previously considered as commensal biota.

Funding sources: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author disclosure statement: Thereby all authors of manuscript (Mateusz Michalik, Aneta Nowakiewicz, Aleksandra Trościańczyk, Cezary Kowalski, Adrianna Podbielska Kubera) declare that there are *no conflict of interest* actual and potential including any financial, personal or other relationships with other people or organizations.

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