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Antimicrobial susceptibility profile of Staphylococcus caprae strains isolated from hospitalized patients with bacteremia: The first description of Brazilian strains

Perfil de susceptibilidade a antimicrobianos de cepas de Staphylococcus caprae isolados de pacientes hospitalizados com bacteremia: A primeira descrição de cepas brasileiras

Perfil de susceptibilidad antimicrobiana de cepas de Staphylococcus caprae aisladas de pacientes hospitalizados con bacteriemia: La primera descripción de cepas brasileñas

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Abstract
Staphylococcus caprae is a commensal microorganism in human and animal microbiota. Although infrequent, the literature reports this bacterium as being associated with invasive human infections. However, few studies describe the antimicrobial profiles of *S. caprae* strains, especially in developing countries. This paper aims to report the antimicrobial profiles of *S. caprae* samples isolated from blood cultures in tertiary hospitals in Brazil and investigate the antimicrobial profile worldwide. The sample identification was performed using the MALDI-TOF technique, and the antimicrobial susceptibility profile was evaluated according to the methodology standardized by BrCAST. The global antimicrobial profile was assessed through a brief review. It was observed that fifty percent of the Brazilian samples showed resistance to penicillin and ampicillin, and the fluoroquinolone profile ranged from resistant to susceptible with increased exposure. In the overall antimicrobial profile, β-lactam resistance was the most frequently observed. The results of this study are important and may assist in epidemiological monitoring and appropriate medical management.
Keywords: Bacterial infection; Antimicrobial resistance; Epidemiology; Antibiotic therapy; Hospitalization.

Resumo
Staphylococcus caprae é um microrganismo comensal na microbiota humana e animal. Embora infrequente, a literatura relata que essa bactéria está associada a infecções humanas invasivas. No entanto, poucos estudos descrevem os perfis antimicrobianos das cepas de *S. caprae*, especialmente em países em desenvolvimento. Este artigo tem como objetivo relatar os perfis de suceptibilidade a antimicrobianos das amostras de *S. caprae* isoladas de hemoculturas em hospitais terciários no Brasil e investigar o perfil antimicrobiano mundial. A identificação das amostras foi realizada utilizando a técnica MALDI-TOF, e o perfil de susceptibilidade antimicrobiana foi avaliado de acordo com a metodologia padronizada pelo BrCAST. O perfil antimicrobiano global foi avaliado por meio de uma breve revisão. Observou-se que cinquenta por cento das amostras brasileiras apresentaram resistência à penicilina e à ampicilina, e o perfil das fluoroquinolonas variou de resistente a suscetível com aumento da exposição. No perfil antimicrobiano global, a resistência aos β-lactâmicos foi a mais frequentemente observada. Os resultados deste estudo são importantes e podem auxiliar no monitoramento epidemiológico e no manejo médico apropriada.
Palavras-chave: Infecção bacteriana; Resistência antimicrobiana; Epidemiologia, Antibioticoterapia; Hospitalização.

Resumen

Staphylococcus caprae es un microorganismo comensal en la microbiota humana y animal. Aunque infrecuente, la literatura informa que esta bacteria está asociada con infecciones humanas invasivas. Sin embargo, pocos estudios describen los perfiles antimicrobianos de las cepas de *S. caprae*, especialmente en países en desarrollo. Este trabajo tiene como objetivo informar los perfiles antimicrobianos de muestras de *S. caprae* aisladas de hemocultivos en hospitales terciarios en Brasil e investigar el perfil antimicrobiano a nivel mundial. La identificación de las muestras se realizó utilizando la técnica MALDI-TOF, y el perfil de susceptibilidad antimicrobiana se evaluó según la metodología estandarizada por BrCAST. El perfil antimicrobiano global fue evaluado mediante una breve revisión. Se observó que el cincuenta por ciento de las muestras brasileñas mostró resistencia a la penicilina y a la ampicilina, y el perfil de fluoroquinolonas varió de resistente a susceptible con mayor exposición. En el perfil antimicrobiano general, la resistencia a los β-lactámicos fue la más frecuentemente observada. Los resultados de este estudio son importantes y pueden contribuir al monitoreo epidemiológico y a la gestión médica adecuada.

Palabras clave: Infecciones Bacterianas; Farmacorresistencia Microbiana; Epidemiología; Terapia antibiótica; Hospitalización.

1. Introduction

Staphylococcus caprae is a commensal coagulase-negative staphylococci (CoNS) that colonizes human and animal microbiota and was first described as associated with mastitis in goats in the 80s' (Vandenesch et al., 1995; Allignet et al., 2001). However, multiple studies show their ability to promote invasive diseases in humans, such as bacteremia, endocarditis and tissue infection associated with an orthopedic prosthesis, medical devices and patients with comorbidities (Hilliard et al., 2017; Díez de Los Ríos et al., 2023; Domashenko et al., 2023).

The most relevant species in the CoNS group are *Staphylococcus epidermidis* and *Staphylococcus haemolyticus*, which carry a multidrug resistance profile (Nowicka et al., 2023). Unfortunately, other species that comprise the CoNS group are under-researched and still considered contaminants in the microbiological routine, even when their pathogenicity is well-noted. Neglecting these investigations can create a gap in hospital epidemiological surveillance (Pereira-Ribeiro et al., 2022).

Scientific literature shows biofilm formation and antimicrobial resistance as the main virulence factors of *Staphylococcus* spp. (Senobar Tahaei et al, 2021; Silva-Santana et al., 2021; Nowicka et al, 2023). The first-choice empirical treatment antimicrobials correlating with staphylococcal invasive infections are vancomycin and lincosamides, which could be replaced by penicillin and cefalosporins when susceptible (Rodríguez et al., 2021)

Few studies describe antimicrobial resistance profiles related to *S. caprae* strains, considering poorly reported when associated with invasive infections worldwide and in developing countries such as Brazil (Ross et al., 2005; Kato et al., 2010). This study aims to investigate the antimicrobial resistance profiles of *S. caprae* isolates from blood cultures obtained from three hospitals in the Metropolitan area of Rio de Janeiro, Brazil, and compare them with the worldwide profile.

2. Methodology

Clinical strains

The strains were isolated from the blood cultures of patients hospitalized with bacteremia in three hospitals in the metropolitan area of Rio de Janeiro from June 2023 to June 2024. The ethics committee approved this study—CAAE: 67690223000005259.

Identification and antimicrobial susceptibility profile

Preliminary identification was confirmed using Matrix-Aided Laser Desorption/Ionization Time-of-Flight (MALD-TOF-MS), and antimicrobial susceptibility profile verification was performed using BrCAST guidelines (BrCAST, 2025).

Investigation of the antimicrobial susceptibility profile worldwide

The investigation was performed by a short review, selecting case reports on PubMed (US National Library of Medicine), Scielo (Scientific Eletronic Library Online), and Latindex (Regional Online Information System for Scientific Journals from Latin America, the Caribbean, Spain, and Portugal) electronic databases between 1995 to 2025 using the keyword "*Staphylococcus caprae*". It has included articles that could be downloaded in full and published in Spanish, English and French that presented a case report with *S. caprae* as the primary etiological agent and present a complete susceptibility antimicrobial profile, either disk-diffusion test or microdilution method. Duplicate work and studies with *S. caprae* coinfection with other pathogens were excluded. All selected studies

had their abstracts read by two researchers and a third was consulted in case of doubts.

3. Results and Discussion

Bacterial identification and antimicrobial susceptibility profile

During the study period, six samples of *S. caprae* were isolated from the blood cultures of different hospitalized patients in three distinct hospital units and identified by MALDI-TOF MS with scores of up to 2.3. All isolates show susceptibility to tetracycline. Fifty percent of the isolated samples exhibit resistance to ampicillin and penicillin. Other antimicrobials used in this study show different levels of susceptibility. Sample Sc01 presents a resistance profile to different antimicrobials, including methicillin resistance (Table 1).

Table 1 - Antimicrobial Susceptibility Profiles of *Staphylococcus caprae* Strains Isolated from Blood Cultures in Brazilian Hospitals.

	Beta-lactams			**Fluoroquinolones**	**Aminoglycosides**	**Macrolides / Lincosamides**		**Tetracyclines**	**Oxazolidinones**	**Other agents**			
***S. caprae* strains**	AMP	PEN	CFX	LVX	GEN	ERI	CLI	TET	LNZ	SUT	NIT	RIF	**Local**
Sc01	R	R	R	R	R	R	R	S	S	S	S	R	Hospital 1
Sc02	S	S	S	I	S	S	S	S	S	S	S	S	Hospital 2
Sc03	R	R	S	I	S	S	S	S	S	S	R	I	
Sc04	S	S	S	R	S	S	R	S	S	S	S	S	
Sc05	R	R	S	I	S	S	S	S	S	S	S	S	Hospital 3
Sc06	S	S	S	I	S	S	S	S	S	S	S	S	

The disk diffusion method was performed according to BrCast, 2025. AMP - Ampicillin, PEN - Penicillin, CFX - Cefoxitin, LVX - Levofloxacin, GEN - Gentamicin, ERI - Erythromycin, CLI - Clindamycin, TET - Tetracyclines, LNZ - Linezolid, SUT - Trimethoprim/Sulfamethoxazole, RIF - Rifampicin, NIT - Nitrofurantoin.

Source: Authors.

Global investigation of antimicrobial susceptibility patterns

Using the previously reported methodology criteria, 21 papers were identified. After applying the inclusion and exclusion criteria, 10 papers were selected to compose the review. The data from the selected studies were organized (Table 2). Due to the diversity of techniques and the lack of standardization of antimicrobials in the selected studies, the antimicrobials were grouped into classes.

Table 2 - Distribution of Antimicrobial Susceptibility Profiles of *Staphylococcus caprae* Strains Reported in Scientific Articles from Different Countries.

			Antimicrobial profile																												
			Beta-lactams								Carbapenems		Fluoroquinolones		Aminoglycosides			Glycopeptides		Macrolides / Lincosamides			Tetracyclines		Oxazolidinones	Other agents						
Author, year	**Country**	**Site of infection**	PEN	AMP	AMC	FLX	OXA	CFT	CEF	CFX	MER	IMI	CIP	LVX	GEN	AMK	TOB	VAN	TEI	CLA	ERI	CLI	TET	TIG	LNZ	RIF	SUT	DPT	NIT	FOF	FUA
Sulaiman et al., 2024	USA	Bone biopsy / blood culture	R	-	-	-	S	-	-	-	-	-	-	-	S	-	-	S	-	-	R	R	S	-	-	S	S	-	-	-	-
Fan et al., 2020	China	Bone biopsy	R	-	-	-	S	-	-	-	-	-	S	-	S	-	-	S	-	-	S	S	-	-	S	-	-	-	-	-	-
Rodríguez-Lucas et al., 2019	Spain	Joint fluids	S	-	-	-	S	-	-	S	-	-	S	-	S	-	-	S	-	-	S	S	-	S	S	-	S	S	S	-	-
Hilliard et al., 2017	USA	Blood culture	R	-	-	-	S	-	-	-	S	-	S	S	S	-	-	S	-	-	S	S	S	-	-	-	S	-	-	-	-

Mazur et al., 2017	Poland	Middle ear fluid	R	-	-	-	-	-	-	-	-	-	-	S	S	-	S	S	S	-	S	S	S	S	S	-	S	-	-	S	S
Kwok et al., 2016	Scotland	Blood culture	R	-	-	S	-	-	-	-	-	-	-	-	S	-	-	S	S	-	-	S	-	-	-	S	-	S	-	-	-
Kato et al., 2010	Japan	Blood culture	R	R	-	-	R	R	R	-	R	R	R	-	-	R	-	S	-	R	R	-	-	-	S	-	-	-	-	-	-
Benedetti et al., 2008	Italy	Cerebral spinal fluid	R	-	R	-	S	-	-	-	-	-	S	-	-	-	-	S	-	-	S	S	-	-	-	S	S	-	-	-	-
Spellerberg et al., 1998	Germany	Blood culture	R	R	-	-	S	-	-	-	-	-	-	-	-	-	-	S	-	-	S	-	-	-	-	-	-	-	-	-	-
Elsner et al., 1998	Germany	Arthrocentesis	S	S	-	S	-	S	-	-	-	-	S	-	S	-	-	S	-	-	S	S	S	-	-	S	S	-	-	R	

S – sensitive; R – resistance; "-" – No tested antibiotic. AMK - Amikacin, AMC - Amoxicillin/clavulanate, AMP - Ampicillin, CLI - Clindamycin, ERI - Erythromycin, GEN - Gentamicin, OXA - Oxacillin, PEN - Penicillin, RIF - Rifampicin, SUT - Trimethoprim/Sulfamethoxazole, TET - Tetracyclines, VAN - Vancomycin, LNZ - Linezolid, CFT - Cefazolin, CEF - Cefepime, MER - Meropenem, IMI - Imipenem, CIP - Ciprofloxacin, CLA - Clarithromycin, LVX - Levofloxacin, CFX - Cefoxitin, DPT - Daptomycin, NIT - Nitrofurantoin, TIG - Tigecycline, FLX - Flucloxacillin, TEI - Teicoplanin, FOF - Fosfomycin, FUA - Fusidic acid, TOB - Tobramycin.

Source: Authors.

Germany and the USA had the most case reports, two in each country (Elsner et al., 1998; Spellerberg et al., 1998; Hilliard et al., 2017; Sulaiman et al., 2024). Different resistance profiles were observed in isolates obtained from the data. The resistance to beta-lactams was most evident (Spellerberg et al., 1998; Benedetti et al., 2008; Kato et al., 2010; Kwok et al, 2016; Hilliard et al., 2017; Rodríguez-Lucas et al, 2019; Fan et al., 2020; Sulaiman et al., 2024). The resistance of Macrolides/Lincosamides (Kato et al., 2010; Sulaiman et al., 2024) and Fosfomicine (Elsner et al., 1998) was observed in some samples, and a sample isolated in Japan presented a resistance of most antibiotic classes like Beta-lactams, Carbapenems, Fluoroquinolones, Aminoglycosides, and Macrolides/Lincosamides (Kato et al., 2010).

4. Discussion

Infections caused by coagulase-negative staphylococci, including nosocomial bacteremia, are a concern in intensive care units, especially related to neonatal units (Ross et al., 2005). CoNS identification down to the species level influences accurate clinical decisions. However, most species belonging to the coagulase-negative staphylococci group are considered contaminants in the laboratory routine, leading to CoNS infections that are often neglected (Pereira-Ribeiro et al., 2022). Even if these bacteria are isolated from invasive infections, there is poor investigation and analysis of these samples at the species level. The MALDI-TOF MS technique is an important ally in routinely identifying microorganisms in clinical microbiology laboratories (Sulaiman et al., 2024). Despite the advantages of the MALDI-TOF technique, one important restriction is the constant updating of databases, limiting the identification of microorganisms, not presenting a significant score to reach the cutoff values recommended by the manufacturer, and often not providing the assurance for the microorganism identification at the species level (Pereira-Ribeiro et al., 2022; Sulaiman et al., 2024).

The susceptibility antimicrobial test is a crucial analysis for clinical treatment guidelines in a nosocomial environment. Empirical treatment for staphylococcal infections differs due to institutional, national, and local policies and hospital protocols; however, it usually includes the use of vancomycin, linezolid, or daptomycin (John, 2020). The antimicrobial treatment could be changed to drugs with better antimicrobial effectiveness and lower toxicity. Soon, continuous monitoring by the hospital infection control team is essential (Hilliard et al., 2017; Rodríguez et al., 2021). Different mechanisms are the role of the emergence of antibiotic resistance in *Staphylococcus* spp., including efflux pumps, production of components that neutralize or decompose antimicrobials, reducing permeability and expression, and mutation of target proteins (Omidi et al, 2021; Kranz et al., 2024). It is not precisely known which virulence mechanisms are applied by *S. caprae* to associate with their antimicrobial resistance profile. Even with this gap in the literature, due to the genetic plasticity of *Staphylococcus* spp., a detailed investigation of these mechanisms would be of clinical interest, especially when phylogenetic studies linked the aim species of the study in the same phylogenetic group as *Staphylococcus epidermidis* (Argemi et al., 2019), which has a well-established and recognized pathogenicity statement in the literature (Nowicka et al., 2023).

Staphylococcus caprae is a species typically colonizing goats' skin and mammary glands and is infrequently associated with human infections (Argemi et al., 2019). However, different papers present these bacteria isolated from invasive infections such as endocarditis, joint infection, meningitis, bone infections, and bacteremia (Elsner et al., 1998; Spellerberg et al., 1998; Benedetti et al., 2008; Kato et al., 2010; Kwok et al, 2016; Hilliard et al., 2017; Mazur et al., 2017; Rodríguez-Lucas et al., 2019; Fan et al., 2020; Díez de Los Ríos et al., 2023; Sulaiman et al., 2024). The samples isolated in this study presented a diversified antimicrobial resistance profile. The antimicrobial resistance profile (Sc01 and Sc04) or sensitivity increasing with exposure (strains Sc02, Sc03, Sc05, and Sc06) to fluoroquinolones. Suggesting a potential spread of resistance to this antimicrobial class, possibly due to the indiscriminate use of this antimicrobial class for treating urinary tract infections. This use is so widespread that resistance mechanisms associated with these antimicrobials are considered common; this fact stimulated new guidelines that should not recommend this antimicrobial class for this infectious condition (Kranz et al., 2024).

The penicillin resistance could be observed in fifty percent of the strains isolated (Sc01, Sc03 and Sc05) and in most of the samples worldwide (Spellerberg et al., 1998; Benedetti et al., 2008; Kato et al., 2010; Kwok et al, 2016; Hilliard et al., 2017; Rodríguez-Lucas et al, 2019; Fan et al., 2020; Sulaiman et al., 2024). Different staphylococci species are penicillinase producers and some are

associated with resistance to methicillin (MRS) (Martins & Cunha, 2007). *S. caprae* methicillin-resistant (MRSc) has been reported in the literature (Ross et al., 2005; Kato et al., 2010). Methicillin resistance is observed in one isolate from the study (strain Sc01). There is no consensus on the available method that can reliably detect penicillinase production in all species of staphylococci. However, methicillin resistance can be possibly related to cefoxitin resistance detection by the Diffusion Disk Method. Evaluating the methicillin resistance of *Staphylococcus* spp. is extremely necessary to help the clinical hospital staff to do better antimicrobial therapy (BrCAST, 2025).

5. Conclusion

Staphylococcal infections caused by CoNS are neglected. The lack of identification of *Staphylococcus* spp. at the species level in clinical laboratories may stem from the limited number of clinical strains in the databases, even when related to conventional phenotypic identification. Identifying *Staphylococcus* at the species level is crucial for choosing an effective antimicrobial treatment, which helps preserve the effectiveness of antibiotics and combat bacterial resistance. Therefore, correct identification helps avoid ineffective therapies and unnecessary antibiotic use.

A poor antimicrobial resistance profile was observed *in S. caprae* strains isolated. The resistance profiles of fluoroquinolone and beta-lactams are present in Brazilian samples. Due to the gap in the literature on the antimicrobial characterization profile of samples for undeveloped countries, the results of this study could help with epidemiological monitoring and guidance for the appropriate clinical management.

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