Staphylococcus warneri: brief literature review

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ABSTRACT

Coagulase-negative *Staphylococcus warneri* is an opportunistic pathogen that is capable of causing several infections, especially in patients with indwelling medical devices. Antimicrobial resistance is a global challenge for the treatment of infections caused by staphylococci. The most important virulence factor of CoNS is the biofilm-producing ability. This brief literature review discusses aspects of the antimicrobial resistance and virulence factors of the *Staphylococcus warneri*. Literature about the *Staphylococcus warneri* listed in PubMed between 2011 and 2021 was reviewed. *Staphylococcus warneri* is a part of the normal flora of the skin, especially the nares, head, legs, and arms. The importance of *S. warneri* as a modern-day pathogen is growing, as it has established itself as a successful nosocomial pathogen. *S. warneri* isolates from these infections are generally resistant to beta-lactam antimicrobial agents. The virulence of *S. warneri* have been suggested to be multifactorial, including adhesins, enzymes, extracellular toxins, capsule, iron uptake systems, virulence regulators and to adhere to produce biofilm, invade and destroy epithelial cells. The pathogenetic mechanisms of infections their mechanisms of bacterial persistence and evasion of the host's immune system have not yet been clearly elucidated. Only with deeper studies, which will allow a more comprehensive understanding of its physiological characteristics, will it be possible to design effective strategies against *S. warneri*.

Keywords: Biofilm, coagulase negative *staphylococcus*, resistance, revie, *staphylococcus warneri*.

RESUMO
O *Staphylococcus warneri* coagulase-negativo é um agente patogénico oportunista capaz de causar várias infecções, especialmente em doentes com dispositivos médicos residentes. A resistência antimicrobiana é um desafio global para o tratamento de infecções causadas por estafilococos. O factor de virulência mais importante da SNS é a capacidade de produção de biofilmes. Esta breve revisão da literatura discute aspectos da resistência antimicrobiana e factores de virulência do *Staphylococcus warneri*. A literatura sobre o *Staphylococcus warneri* listada na PubMed entre 2011 e 2021 foi revista. O *Staphylococcus warneri* é uma parte da flora normal da pele, especialmente as nuaras, cabeça, pernas e braços. A importância de *S. warneri* como um patogénico dos tempos modernos está a crescer, uma vez que se estabeleceu como um patogénico nosocomial bem sucedido. Os isolados de *S. warneri* destas infecções são geralmente resistentes aos agentes antimicrobianos beta-lactâmicos. A virulência de *S. warneri* tem sido sugerida para ser multifactorial, incluindo adesinas, enzimas, toxinas extracelulares, cápsulas, sistemas de absorção de ferro, reguladores de virulência e para aderir para produzir biofilme, invadir e destruir células epiteliais. Os mecanismos patogénicos das infecções, os seus mecanismos de persistência bacteriana e evasão do sistema imunitário do hospedeiro ainda não foram claramente elucidados. Só com estudos mais profundos, que permitirão uma compreensão mais abrangente das suas características fisiológicas, será possível conceber estratégias eficazes contra *S. warneri*.

Palavras-chave: Biofilme, *staphylococcus* negativo coagulase, resistência, revisão, *staphylococcus warneri*.

1 INTRODUCTION

Staphylococci are Gram-positive cocci in clusters that produce catalase. In contrast to the coagulase-positive *Staphylococcus aureus*, coagulase-negative *Staphylococcus* (CoNS) are so named because of their inability to clot plasma because of the lack of production of the secreted enzyme coagulase. CoNS are the most frequent constituent of the normal flora of the skin and mucosa, represent a heterogeneous group, ranging from true nonpathogenic to facultative pathogenic species with low, medium, or even high virulence potential. CoNS was often considered as simple commensal bacteria, but the emergence of nosocomial infections with CoNS has led clinicians and researchers to reconsider the status of these bacteria. Today, these microorganisms are recognized as causative agents of clinically significant infection, including bacteremia and endocarditis [1,2,3,4].

Antimicrobial resistance is a global challenge for the treatment of infections caused by staphylococci and other bacteria, especially hospital-acquired infections. The resistance is usually mediated by a modified penicillin-binding protein 2 (PBP2), with decreased binding affinity to methicillin, and others for beta-lactam antibiotics, which is encoded by the *mec*A gene. The *mec*A gene is carried by a mobile genetic element, the staphylococcal chromosome cassette *mec* (SCC*mec*) which is considered a vehicle for the exchange of resistance factors between CoNS. The estimated prevalence of methicillin resistance is 20% among community

isolates and more than 80% among hospital isolates. Many antibiotic resistance genes are located on mobile genetic elements and thus are supposed to be horizontally transferable between bacterial pathogens A common topic in CoNS is their capacity to easily acquire antibiotic resistance traits, greatly limiting treatment options [4,5].

The most important virulence factor of CoNS is the ability to produce a three-dimensional structured matrix – biofilm, on the surface of indwelling medical devices. The communities of microorganisms within the biofilm stick to each other and/or to surfaces by the production of an extracellular matrix that mostly consists of polysaccharides and proteins and their persistence is implicated in the risk of recurrence infections. Biofilms represent the perfect niche to protect CoNS from both the host immune response and the action of antibiotics. The first biofilm accumulation factor identified was the polysaccharide intercellular adhesin (PIA), which is a poly-N-acetyl-glucosamine. PIA synthesis is carried out by the gene products of the intercellular adhesion (icaADBC) operon [1,3,5,6].

Currently, relatively little attention has been paid to the *Staphylococcus warneri* pathogenicity and antibiotic resistance, even though diseases caused by this microorganism have a significant impact on human health, reported since 1984, like, endocarditis, sepsis, septic arthritis, spondylodiscitis, meningitis, and neonatal infections [7,8].

This brief literature review discusses aspects of the antimicrobial resistance and virulence factors of the *Staphylococcus warneri*.

2 METHODOLOGY

PubMed indexed articles published between 2011 and 2021 were consulted to identify studies relevant to the review. Search terms included: “coagulase negative *Staphylococcus*”, “coagulase negative staphylococci” and “*Staphylococcus warneri”*. The reference lists of all retrieved articles were checked for additional relevant references. Studies published in English was considered in this review.

3 RESULTS

Staphylococcus warneri a member of the CoNS group, are catalase-positive, oxidase negative, facultatively anaerobic, nonmotile and is a part of the normal flora of the skin, especially the nares, head, legs, and arms. Is present in about 50% of healthy adults and represents approximately 1%–7% of all skin staphylococci in healthy adults [8,9,10].

Usually, clinical laboratories do not identify *S. warneri* and report these isolates at group level, referring to them as CoNS. Current biochemical profile identification techniques are rela-

tively slow and not always accurate, although with new technology such as matrix-assisted laser desorption/ionization (MALDI-TOF) laboratory users will increasingly encounter laboratory reports including the exact species name [1,8].

Staphylococcus warneri is a coagulase-negative staphylococcus that is a normal inhabitant of the skin. It is also considered to be an opportunistic etiological agent causing significant infections in human, as severe infections such as bacteremia, endocarditis, vertebral osteomyelitis, ventriculoperitoneal shunt-associated meningitis, discitis, subdural empyema, urinary tract infections, especially in patients with indwelling catheters and artificial medical devices and blood sepsis in neonates. Currently, the importance of *S. warneri* as a modern-day pathogen is growing, as it has established itself as a successful nosocomial pathogen [4,11,12,13].

S. warneri isolates from these infections are generally resistant to beta-lactam antibiotics, with beta-lactamase activity and show susceptibility to other antibiotics with gram-positive activity. The *mec*A gene is responsible for encoding resistance to almost all beta-lactam antibiotics. The indiscriminate use of these antibiotics has led to an increase in the occurrence of multidrug-resistant *Staphylococcus*. It was described for *S. warneri*, genes that can confer resistance to non-beta-lactam antibiotics, such as fluroquinolones and glycopeptides (vancomycin and teicoplanin) [10,14,15].

The adherence of *Staphylococcus* is the first step in colonization and subsequent biofilm formation. Biofilm can be defined as sessile communities of surface-attached cells encased in an extracellular matrix. In biofilm formation, four steps may be distinguished: (a) rapid initial attachment of bacteria to an abiotic or biotic surface mediated by unspecific or specific interactions, respectively; (b) proliferation and expression of intercellular adhesion traits leading the formation of multilayered cell clusters; (c) maturation of the biofilm resulting in a thick, structured matrix composed of various biopolymers; and (d) dissolution of single cells or small agglomerates and dissemination with the blood stream leading to metastatic infection. The main component of staphylococci biofilm is a PIA. In addition to PIA, other polysaccharides, proteins, extracellular teichoic acids, lipids, and extracellular nucleic acids are recognized as biofilm components [6,8,12].

Because of the protective nature of the biofilm matrix, the treatment of bacteria in the biofilm mode of growth is challenging due to the resistance of bacteria to both antibiotics and host defenses is usually failed to eradicate staphylococcal infections. Also, polysaccharides and extracellular DNA are present in the biofilm matrix of *S. warneri*. The cytotoxic activity of *S. warneri* strains allows them to evade the host immune response. Like the other CoNS, the

virulence of *S. warneri* have been suggested to be multifactorial, including adhesins, enzymes (protease, lipase and esterase), extracellular toxins, capsule, iron uptake systems, virulence regulators and to adhere to, produce biofilm, invade and destroy epithelial cells. It should be emphasized that most *S. warneri* strains form biofilm via *ica*-independent mechanisms [8,12].

The first complete genome sequence of *S. warneri* strain isolated from a laboratory is reported in 2013, Canada. However, little attention is given to the genetic basis and biosynthesis of *S. warneri* virulence factors and antibiotics resistance, even though these are emerging issues for this pathogen of considerable clinical significance [8,16].

4 CONCLUSION

In recent years, there has been a brief increase in the amount of data available on *S. warneri*. However, these data are insufficient. "Case reports" are the type of article most found in the literature. The pathogenetic mechanisms of infections ant their mechanisms of bacterial persistence and evasion of the host's immune system have not yet been clearly elucidated. Only with deeper studies, which will allow a more comprehensive understanding of its physiological characteristics, will it be possible to design effective strategies against *S. warneri*.

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