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ORIGINAL ARTICLE

Staphylococcus epidermidis biofilm formation as a cause of urethritis in males

Staphylococcus epidermidis productor de biofilm como causa de uretritis en el sexo masculino

Staphylococcus epidermidis produtor de biofilme como causa de uretrite em homens

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ABSTRACT

Introduction: *Staphylococcus epidermidis* as an opportunistic pathogen and its ability to form biofilm has become an emergency situation. **Objective:** to identify biofilm-producing *Staphylococcus epidermidis* as a cause of urethritis in males. Study performed throughout 2019 in the Microbiología Lab of the Centro Provincial de Higiene, Epidemiología y Microbiología Lab in Guantánamo**. Method:** an observational, descriptive and cross-sectional study was carried out at the aforementioned lab, envolving a total of 48 male outpatients with a clinical diagnosis of urethritis certified by the family physician, attended in the Microbiology laboratory with their respective urethral discharge culture indication. The variables studied were as follow: coagulase, catalase and oxidase enzyme production test, growth of mannitol salt agar, novobiocin sensitivity, biofilm production and antimicrobial resistance. The sampling results were introduced in a database and processed with the software SPSS version 11.5. **Results:** biofilm-producing *Staphylococcus epidermidis* was identified as the cause of urethritis in the 48 male patients involved in the study. This microorganism showed cero or low resistance to ciprofloxacin, norfloxacin, amikacin, gentamicin, amoxicillin-sulbactam combination, cotrimoxazole and tetracycline. **Conclusions:** *Staphylococcus epidermidis* emerges as a common opportunistic pathogen in male patients with a clinical diagnosis of urethritis, with significant resistance to beta-lactam antibiotics not combined with beta-lactamase inhibitors.

Keywords: urethritis; *Staphylococcus epidermidis*; biofilm; antimicrobial resistance

RESUMEN

Introducción: la emergencia de *Staphylococcus epidermidis* como patógeno oportunista está relacionada a su capacidad de formación de biofilm. **Objetivo:** identificar *Staphylococcus epidermidis* productor de biofilm como causa de uretritis en el sexo masculino, en el laboratorio de Microbiología del Centro Provincial de Higiene, Epidemiología y Microbiología Guantánamo durante el año 2019. **Método:** se realizó una investigación observacional, descriptiva y transversal en el laboratorio antes mencionado, con un universo de estudio conformado por 48 pacientes ambulatorios del sexo masculino con diagnóstico clínico de uretritis realizado por al médico de familia y que acudieron al laboratorio de Microbiología de dicho centro con indicación de exudado uretral con cultivo. Las variables estudiadas fueron: producción de las enzimas coagulasa, catalasa y oxidasa, crecimiento en agar manitol salado, sensibilidad de la novobiocina, producción de biofilm y resistencia a los antimicrobianos. Los resultados de las muestras fueron vaciados en una base de datos y fueron procesados con el programa SPSS versión 11.5. **Resultados:** se identificó *Staphylococcus epidermidis* productor de biofilm como causa de uretritis en los 48 pacientes del sexo masculino estudiados. Este microorganismo mostró resistencia nula o disminuida frente a ciprofloxacina, norfloxacina, amikacina, gentamicina, amoxicilina con sulbactam, cotrimoxazol y tetraciclina. **Conclusiones:** S*taphylococcus epidermidis* emerge como patógeno oportunista frecuente en pacientes del sexo masculino con diagnóstico clínico de uretritis, con significativa resistencia a los antibióticos betalactámicos no combinados con inhibidores de la betalactamasa.

Palabras clave: uretritis; *Staphylococcus epidermidis;* biofilm; resistencia antimicrobiana

RESUMO

Introdução: o surgimento do *Staphylococcus epidermidis* como patógeno oportunista está relacionado à sua capacidade de formação de biofilme. **Objetivo:** identificar *Staphylococcus epidermidis*, produtor de biofilme como causador de uretrite em homens, no laboratório de Microbiologia do Centro Provincial de Higiene, Epidemiología y Microbiología Guantánamo durante o ano de 2019. **Método:** investigação observacional, descritiva e transversal. realizado no referido laboratório, tendo como universo de estudo 48 doentes ambulatórios do sexo masculino com diagnóstico clínico de uretrite feito pelo médico de família e que compareceram ao laboratório de Microbiologia do referido centro com indicação de exsudato uretral com cultura. As variáveis estudadas foram: produção das enzimas coagulase, catalase e oxidase, crescimento em ágar manitol salgado, sensibilidade à novobiocina, produção de biofilme e resistência a antimicrobianos. Os resultados das amostras foram digitados em um banco de dados e processados no programa SPSS versão 11.5. **Resultados:** o *Staphylococcus epidermidis* produtor de biofilme foi identificado como a causa da uretrite nos 48 pacientes masculinos estudados. Este microrganismo não apresentou ou apresentou resistência reduzida contra ciprofloxacino, norfloxacino, amicacina, gentamicina, amoxicilina com sulbactam, cotrimoxazol e tetraciclina. **Conclusões:** *Staphylococcus epidermidis* surge como um patógeno oportunista frequente em pacientes do sexo masculino com diagnóstico clínico de uretrite, com resistência significativa a antibióticos beta-lactâmicos não combinados com inibidores de beta-lactamase.

Palavras-chave: uretrite; *Staphylococcus epidermidis*; biofilme; resistência antimicrobiana

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INTRODUCTION

Urethritis is the inflammation of the urethra, usually of infectious origin and sexually transmitted. In men, it is clinically manifested by urethral discharge and/or dysuria, but may be asymptomatic.

According to the etiological agent, it is classified into gonococcal urethritis produced by *Neisseria gonorrhoeae*, and non-gonococcal urethritis produced mainly by *Chlamydia trachomatis*, *Mycoplasma genitalium, Ureaplasma urealyticum, Haemophilus spp* and *Gardnerella vaginalis*. However, other microorganisms such as staphylococci and Enterobacterias should be taken into account if they are isolated in culture, due to the practice of oral and anal sex and population movement that facilitate the increase of infections.[1]

Staphylococci are one of the main causes of infections in humans, both in the hospital environment and in the community. These microorganisms are responsible for skin and soft tissue infections, bacteremia, endocarditis, urethritis and pneumonia, but they also produce an increasing number of infections related to the use of different types of catheters, joint and vascular prostheses and other medical devices.[2,3]

These microorganisms also have a great capacity to adapt to the environment in which they live; they produce different enzymes and toxins and also have the ability to adhere and develop biofilm on different contact surfaces, which gives them the ability to be invasive and toxigenic.[4,5] They are found as part of the microbiotic of skin and mucous membranes; the main source of infection is endogenous.[6]

The Staphylococcus genus is divided into two groups, based on the presence or absence of the coagulase enzyme, classified as coagulase-positive staphylococci that produce the coagulase enzyme such as *Staphylococcus aureus (S. aureus)* and coagulase-negative staphylococci (CNS) that do not produce this enzyme, among which is *Staphylococcus epidermidis (S. epidermidis)*[2,7]

S. epidermidis normal flora of skin and mucous membranes acts as a probiotic, thus preventing colonization of the body surfaces where it lives by pathogenic bacteria. In the skin, *S. epidermidis* ferments glycerol into butyric acid and acetic acid, which inhibit the colonization of *S. aureus* and other bacteria.[5,7]

In the early 1980s, the pathogenicity of *S. epidermidis* was recognized, and it has become a frequent opportunistic pathogen, able to colonize the niches that a hospital environment offers.

Personal pathological antecedents that facilitate *S. epidermidis* to cause infections include: a compromised or immature immune system, individuals who have undergone surgery, and the presence of permanent medical devices that offer colonization surfaces.[3,7,8]

The growth of *S. epidermidis* infections is due to the production of biofilm (extracellular biopolymer), which protects the bacteria against the host's immune system and serves as a barrier against antibiotic treatments.[7]

Due to the increase of scientific studies in the last three decades, biofilm has acquired great relevance, mainly in the medical area, since 90% of microorganisms have these characteristics, which favors the development of chronic infections.

Its biosynthesis is a complex, constant and dynamic process that occurs in four phases: adhesion, aggregation, maturation and disintegration. Each of these phases involves physic-chemical forces and different genetic and molecular mechanisms that regulate the biosynthesis of the extracellular matrix.[9]

Research question: *S. epidermidis* is considered normal skin and mucosal flora. However, it has been frequently isolated in pure culture in urethral exudates of males with a clinical diagnosis of urethritis. Are these isolates biofilm producers and, therefore, the cause of urethritis in males?

The present research aims to identify biofilm-producing *S. epidermidis* as a cause of urethritis in males.

METHOD

An observational, descriptive and cross-sectional research was conducted in the Microbiology laboratory of Centro Provincial de Higiene, Epidemiología y Microbiología in Guantánamo (CPHEM), Guantanamo, during 2019.

The study population consisted of 48 male outpatients (N = 48) with a clinical diagnosis of urethritis made by the family physician and who attended the CPHEM Microbiology laboratory with indication of urethral exudate with culture, which was positive. The study population matched the sample.

The results of the present research were obtained from the processing of the urethral exudate sample, obtained by taking samples from patients who voluntarily presented themselves at the CPHEM laboratory to undergo the urethral exudate indicated by the family physician.

Laboratory procedure

Sampling of urethral exudate in males[10]

1. Before the exudates, the patient must be at least 72 hours without taking any antibiotics, applying no topical medication or sexual activity. The patient should come to the laboratory before the first urination in the morning.

2. The sample was taken with a sterile applicator that was introduced approximately 2 cm into the urethra and gently rotated, discharging it onto a slide for direct examination. A sterile carbonated applicator was used in the same way, discharging the sample onto a chocolate agar and Thayer Martin agar plate.

Incubation and reading

a) Direct examination: it was stained with Gram stain and it was observed if there were images of intra or extracellular gram-negative diplococci. This test is performed to rule out gonococcal urethritis.
b) Culture: chocolate agar and Thayer Martin agar were incubated for 24 to 48 hours at 37 °C in a 5% carbon dioxide atmosphere. The cultural characteristics of the colonies obtained in the culture environment were observed and, consequently, a follow-up was carried out to identify the isolated pathogen.
c) Identification: the colonies obtained in the culture were suggestive of staphylococcus, so Gram staining, coagulase test, catalase, oxidase, sensitivity to novobiocin disc, growth in salted mannitol agar and phenotypic biofilm test were performed.(11)
d) Antimicrobial susceptibility tests: resistance to protocolized antimicrobials was determined by the Bauer-Kirby method.(12)

Data collection and processing techniques

The primary data was obtained directly by the authors from the test results and entered into a database using the Excel program of the Microsoft Office suite, on the Windows 7 platform. The statistical data from the database were processed with the SPSS version 11.5 program and summarized with absolute frequencies and percentage. The results are expressed in two-dimensional tables.

Medical ethics

The four basic ethical principles were complied with at all times: autonomy, beneficence, not-maleficence and justice. The confidentiality and quality of the laboratory procedure was guaranteed at all times. The result was collected directly by the patient.

RESULTS

In the Thayer Martin culture medium designed for the growth of *Neisseria gonorrhoeae* no growth was obtained in 100% of the cultures, but in the chocolate agar a pure culture suggestive of staphylococcus was obtained in the 48 exudates performed, for a 100%.

The tests performed for the identification of this bacterium showed that morphologically they were gram-positive cocci grouped in clusters, did not possess the coagulase enzyme, positive catalase, negative oxidase. In the salty mannitol agar the colonies were red in color because although they resisted the high concentration of salts, it does not use mannitol, sensitive to novobiocin and biofilm producer, so the isolated microorganism was identified as *S. epidermidis* biofilm producer.

Of the 48 urethral exudates performed, direct examination for gonococci was negative for 100%. No intra or extracellular gram-negative diplococci were observed, thus ruling out a possible gonocococcal urethritis.

Resistance to protocolized antimicrobials is shown in Table 1.

Table 1. Resistance of biofilm-producing *Staphylococcus epidermidis* isolated from urethral exudates in males

Antibiotic	Resistance (%) n=48
Penicillin	
Penicillin	52,1
Oxacillin	52,1
Ampicillin	50,0
Cephalosporin	
Cefoxitin	50,0
Cephalexin	41,6
Macrolides	
Azithromycin	31,3
Sulfonamides	
Sulfamethoxa sol trimethropin (co-trimoxazole)	10,4
Tetracyclines	
Tetracyclin	8,3
Carbapenems	
Meropenem	2,1
Beta lactamase inhibitor	
Amoxicillin + sulbactam	2,1
Quinolones	
Ciprofloxacin	-
Norfloxacin	-
Amino glycosides	
Amikacin	-
Gentamicin	-

DISCUSSION

In the present research, infective biofilm-producing *S. epidermidis* was identified as a cause of urethritis in males, microbiologically diagnosed by culture of urethral exudate, where massive growth of this microorganism was obtained.

The emergence of *S. epidermidis* as an opportunistic pathogen is related to its capacity for biofilm formation, which favors its proliferation and resistance to treatment.[8,13,14]

Sanguano A, *et al.*[7] and Pinilla G, *et al.*[15] state that the biofilm is a polymeric matrix that facilitates bacterial survival and is encoded by the operon that involves four genes icaA, icaB, icaC and icaD and contributes to the severity of the infection by decreasing antibiotic absorption and, therefore, the persistence of the pathogen.
Biofilm is defined as communities of microorganisms that grow aggregated and surrounded by an extracellular matrix that they themselves produce. The extracellular matrix consists of proteins, extracellular deoxyribonucleic acid (DNA) and exopolysaccharides (EPS).[9,14]

The EPS matrix favors the exchange of metabolites with the exterior and confers a protective barrier against adverse environments, such as hyperosmolarity, anaerobiosis, antibodies, macrophages and antibiotics. This "protected" growth allows survival in an antagonistic environment.[14]

The extracellular matrix helps microbial cells to evade the host immune response; furthermore, EPS in the extracellular matrix have the ability to induce chronic inflammatory responses.[9]

In the study conducted by Pinilla G, *et al.*[15] it was shown that microbial surface components that recognize extracellular matrix adhesion molecules, known as MSCRAMMs (Microbial Surface Components Recognizing Adhesive Matrix Molecules), considered virulence factors in Staphylococcus, specifically described for *S. aureus*, are also present in clinical isolates of *S. epidermidis*.

This finding is important since *S. epidermidis*, considered a skin commensal or autobiont, is currently an important genetic reservoir and, in turn, due to horizontal gene transfer between these species, has come to be considered a potential pathobiont, within the classification of the human microbiome. *S. epidermidis* and its relationship with biofilm formation is an important factor of bacterial persistence in frequent infections in neonatal and immune compromised patients.

However, although there is much information on MSCRAMMs in Staphylococcus, there is little knowledge on the molecular mechanisms by which these proteins lead to bacterial adhesion.[15]

The treatment and eradication of infections caused by biofilm-producing microorganisms represent a great challenge, since they are much more tolerant to the action of molecules with antimicrobial activity, such as antibiotics and antiseptics.[9]

Antibiotic resistance is currently a global health problem and biofilm-producing *S. epidermidis* has attributes that make it resistant to antimicrobial therapy.

In the current research, high resistance to beta-lactamase antibiotics such as penicillin, ampicillin, oxacillin, cephalexin and cefoxitin was evidenced, with the exception of amoxicillin with sulbactam, with which resistance was insignificant. Diminished resistance was obtained to cotrimoxazole and tetracycline, and none to amikacin, gentamicin, ciprofloxacin and norfloxacin.

Resistance to azithromycin was significant. Cross-resistance of azithromycin with erythromycin has been demonstrated in erythromycin-resistant gram-positive strains and with most methicillin-resistant strains of staphylococci. Azithromycin and erythromycin belong to the macrolide group with the same mechanism of action, since they inhibit protein synthesis, which justifies the cross-resistance between both antibiotics.[16]

The methicillin and oxacillin resistance phenotype is much more frequent among the different species of CNS, with the exception of *Staphylococcus lugdunensis* and *Staphylococcus saprophyticus*, than *in S. aureus*. In the present study, resistance to oxacillin was found to be high.

This resistance is due to the acquisition of the mecA gene, which encodes the penicillin-binding protein and has a low affinity for beta-lactamase. Methicillin resistance involves resistance to all beta-lactamase, including penicillins, combinations of beta-lactamase with beta-lactamase inhibitor, cephalosporins (with the possible exception of cephalosporins ceftobiprole and ceftaroline), not yet introduced in the therapeutic arsenal and whose minimum inhibitory concentration values are less affected), monobactams and carbapenems (with the possible exception of razupenem, also not introduced in the therapeutic stock, and also with a minimum inhibitory concentration less affected).[17]

Methicillin resistance (oxacillin, methicillin, cloxacillin, nafcillin) in staphylococci is due to the acquisition of exogenous DNA encoding the production of a penicillin-binding protein, which is low in affinity for beta-lactamase and is not inhibited by these antimicrobials.[18]

In the present study, resistance to cefoxitin was significant. Ardanuy C, *et al*.[18] propose that cefoxitin is a surrogate marker for the presence of the mecA gene, since it is a more potent inducer of the mecA regulatory system than penicillins and, therefore, enhances the expression of this gene and consequently also improves the detection of methicillin resistance.

The use of the cefoxitin disk is particularly useful and preferable to the oxacillin disk for detecting mecA gene-mediated oxacillin resistance in hetero resistant strains, and should always be used in CNS strains; moreover, it does not present stability problems like oxacillin during storage.

Methicillin resistance of staphylococci is considered a growing problem worldwide. Methicillin-resistant staphylococci are also resistant to beta lactamase antibiotics and other antibiotic groups. Recently, resistance to glycopeptides has been reported.[18]

Garcia A, *et al.*[14] propose that cefoxitin is sufficient to determine the methicillin-resistant phenotype, and was associated with the mecA genotype. Methicillin-resistant strains possessing the mecA gene may present an alternate resistance mechanism.

Portilla ME, *et al.*[19] state that more than 90% of CNS produce beta lactamase and, in turn, more than 70% are resistant to methicillin. Of these, more than half are also resistant to erythromycin, clindamycin, cotrimoxazole, gentamicin and ciprofloxacin. Therefore, these authors consider that treatment is based on the use of vancomycin, linezolid or daptomycin.

Castro Orozco R, *et al.*[6] in their study found methicillin-resistant *S. epidermidis* strains that were resistant to multiple antibiotics such as erythromycin, vancomycin and gentamicin. They also state that *S. epidermidis* is considered a potential reservoir of resistance genes for other bacteria such as *S. aureus*, which increases its potential to colonize and resist antibiotic treatment; therefore, the presence of methicillin-resistant and multidrug-resistant *S. epidermidis* may contribute to the emergence of methicillin-resistant and multidrug-resistant *S. aureus* strains, which would limit the options for treating infections.

The progressive increase of invasive procedures in patients, such as: catheters, invasive therapies, prostheses, among others, as well as the emergence of diseases accompanied by immune suppression and therapies that affect immunity, facilitate the invasion of CNS. In addition, the frequent use of antibiotics, rational or not, acting on pathogenic and non-pathogenic germs, select resistant strains and also create spaces for these new pathogens that colonize hospital environments, medical personnel and patients.[3]

Ortega Peña S, *et al*.[9] in their study found that amikacin has good antibiofilm activity in *S. aureus* and *S. epidermidis*. In the present study, null resistance to amikacin was obtained. The antibiotics with the best antibiofilm activity are rifampicin and fosfomycin; in the case of antimicrobials with reduced activity it is advisable to make combinations with these drugs to improve antibiofilm activity and optimize treatments.

Resistance to amoxicillin with sulbactam in this study was negligible. This antibiotic is broad spectrum penicillin associated with sulbactam, which is a potent irreversible beta-lactamase inhibitor. Therefore, sulbactam may restore the bactericidal activity of amoxicillin against resistant bacterial strains by the enzymatic mechanism of beta-lactamase.[16]

From the results of this research, the antibiotics recommended for the treatment of infections caused by biofilm-producing *S. epidermidis* in the patients studied are: amoxicillin with sulbactam, cotrimoxazole and tetracycline, which showed low resistance; and amikacin, gentamicin, ciprofloxacin and norfloxacin, which showed no resistance.

CONCLUSIONS

Biofilm-producing *Staphylococcus epidermidis* emerges as a frequent opportunistic pathogen in male patients with a clinical diagnosis of urethritis, confirmed by urethral exudate. The emergence of strains resistant to beta-lactamase antibiotics not combined with beta-lactamase inhibitors leads to increased costs compared to infections by susceptible strains; therefore, it is important to monitor changes in antimicrobial resistance patterns in order to contribute to the epidemiological study of these infections and to the management of the best antibacterial treatment option for the patient.

REFERENCES

1. Foronda-García-Hidalgo C, Liébana-Martos C, Gutiérrez-SotoB, Expósito-Ruiz M, Navarro-Marí JM, Gutiérrez-Fernández J. Prevalencia en varones de la población general de agentes productores de infecciones no ulcerativas del aparato genital, asistidos en la atención especializada. Rev Esp Quimioter [Internet]. 2020 [cited 12 Jul 2022]; 33(3):225. Available in: https://www.ncbi.nlm.nih.gov/pmc/artiles/PMC6913070
2. Castellano GM, Perozo MA, Leal AJ, Maldonado MC. Frecuencia y resistencia antimicrobiana en Staphylococcus.

Kasmera[Internet]. 2018 [cited 12 Jul 2022]; 46(1):26-39. Available in: https://www.redalyc.org/journal/3730/373061527003/html/

3. Sánchez-Hurtado LM, Velásquez-Pomar J, Mendoza-Contreras D, Caballero-Silva J. Estafilococos coagulasa-negativo causantes de infecciones intrahospitalarias. Rev SocPeruMed Interna [Internet]. 2019 [cited 12 Jul 2022]; 32(4):135-137. DOI: https://doi.org/10.36393/spmi.v32i4.492
4. Llop Hernández A, Valdés-Dapena Vivanco MM, Zuazo Silva JL. Microbiología y Parasitología Médicas. La Habana: ECIMED; 2001.
5. Cruzado-Bravo MLM, Silva NCC, Rodríguez MX, Saldaña E, Contreras-Castillo CJ, Sturion GL. Biopelículas de *Staphylococcus*spp. sobre acero inoxidable utilizando leche y brainheart infusión broth como medios de cultivo. Scientia Agropec [Internet]. 2018 [cited 12 Jul 2022]; 9(4):[aproximadamente 15 p]. DOI: http://dx.doi.org/10.17268/sci.agropecu.2018.04.03
6. Castro-Orozco R, Villafañe-Ferrer L, Rocha-Jiménez J, Alvis-Guzmán N. Resistencia antimicrobiana en *Staphylococcus aureus* y *Staphylococcus epidermidis*: tendencia temporal (2010-2016) y fenotipos de multirresistencia, Cartagena (Colombia). Rev Biosalud [Internet]. 2018 [cited 12 Jul 2022]; 17(2):25-36. DOI: http://dx.doi.org/10.17151/biosa.2018.17.2.2
7. Sanguano A, Yauri MF, Alcocer I. Formación de biofilm en aislados clínicos de *Staphylococcus aureus* y *Staphylococcus epidermidis* de Quito y el Puyo. Rev Ecuator Med Cienc Biol [Internet]. 2021 [cited 12 Jul 2022]; 42(1):37-53. DOI: https://doi.org/10.26807/remcb.v42i1.885
8. Salazar ME, Crispín V. Biopelículas y genes icaA e icaD en estafilococos coagulasa negativos aislados de catéter endovenoso central en Unidad de Cuidados Intensivos de un Hospital Nivel III en Lima, Perú. HorizMed [Internet]. 2018 [cited 12 Jul 2022]; 18(3):19-24. Available in: http://www.scielo.org.pe/pdf/hm/v18n3/a04v18n3.pdf
9. Ortega-Peña S, Hernández-Zamora E. Biopelículas microbianas y su impacto en áreas médicas: fisiopatología, diagnóstico y tratamiento. Bol Méd Hosp Inf Méx [Internet]. 2018 [cited 12 Jul 2022]; 2018(75):79-88. DOI: http://dx.doi.org/%2010.24875/BMHIM.M18000012
10. Toraño Peraza GT, Illnait Zaragozi MT, Hernández Álvarez HM, Rivas Antúnez MA. Obtención, transporte y conservación de muestras clínicas. La Habana: ECIMED; 2020.
11. Ibarguren Quesada S, Juliarena M, Monteavaro C. Identificación de *Staphylococcus* spp. y evaluación de la producción de biofilm. Argentina: Universidad Nacional de Buenos Aires; 2019 [cited 18 Oct 2022]. Available in: https://bit.ly/3KjMC7m
12. Weisntein MP, Lewis JS, Bobenchik AM, Campeau S, Cullen SK, Galas MF, *et al*. Performance estandar for antimicrobial susceptibility testing. 30ed. [Internet]. Pennsylvania: Clinical and Laboratory Standars Institute; 2022 Feb Disponible en: https://clsi.org/media/3481/m100ed30_sample.pdf
13. Lemos M. Staphylococcusepidermidis: qué es, síntomas y tratamiento. www.tuasaude.com. Brazil: Rede D'Or Logo; 2023 Mar [cited 12 Jul 2022]. Available in: https://www.tuasaude.com/es/staphylococcus-epidermidis/
14. García A, Martínez C, Juárez RI, Téllez R, Paredes MA, Herrera MR, Giono S. Resistencia a la meticilina y producción de biopelícula en aislamientos clínicos de

Staphylococcusaureus y *Staphylococcus* coagulasa negativa en México. Biomédica [Internet]. 2019 [cited 12 Jul 2022]; 39(3):513-523 DOI: https://doi.org/10.7705%2Fbiomedica.4131

15. Pinilla G, Bautista A, Cruz C, Chavarro B, Navarrete J, Muñoz L, Gutiérrez J. Determinación de factores de adhesión asociados a la formación de biopelícula en aislamientos clínicos de *Staphylococcus aureus y Staphylococcus epidermidis.* Nova Bogotá [Internet]. 2017 [cited 12 Jul 2022]; 15(27):15. Available in: http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S1794-24702017000100067
16. Ministerio de Salud Pública. Formulario Nacional de Medicamentos [Internet]. La Habana: ECIMED; 2014 [cited 13 Oct 2022]. Available in: https://instituciones.sld.cu/hospmiguelenriquez/files/2018/01/Formulario-nacional-de-medicamentos.pdf
17. RedlabRA. Vigilancia de Staphylococcus aureus resistentes a meticilina [Internet]. RedlabRA; 2021 [citado 13 Oct 2022]. Available in: https://bit.ly/3zDSLoV
18. Ardanuy C, Cercenado E, Morosini MI, Torres C. Detección fenotípica de mecanismos de resistencia en grampositivos. Enf Infec Microbiol Clín [Internet]. 2011 Jun-Jul [cited 13 Oct 2022]; 30(6):325-332. DOI: http://dx.doi.org/10.1016/j.eimc.2011.09.009
19. Portilloa ME, Pozo JL del. Infecciones por estafilococo. Medicine [Internet]. 2018 [cited 12 Jul 2022]; 12(49):2890-4. DOI: http://dx.doi.org/10.1016/j.med.2018.02.002

Conflict of interest:
The authors declare that there were no conflicts of interest in connection with the research.

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Supplementary information (Open Data):
Base de datos *Staphylococcus epidermidis* productor de biofilm como causa de uretritis en el sexo masculino (Biofilm-producing Staphylococcus epidermidis database as a cause of urethritis in males)