Caspian Journal of Internal Medicine 2025 (Spring); 16(2): 225-232
DOI: 10.22088/cjim.16.2.225

Original Article

Systematic review and meta-analysis of the association between biofilm formation and antibiotic resistance in MRSE Isolated from Iranian patients

Parisa Behshood (PhD) [1]
Elahe Tajbakhsh (PhD) [1*]

1. Department of Biology, Islamic Azad University, Shahrekord Unit, Shahrekord, Iran

*** Correspondence:**
Elahe Tajbakhsh, Department of Biology, Islamic Azad University, Shahrekord unit. Shahrekord, Iran

E-mail:
elahe.tajbakhsh64@yahoo.com
Tel: +98 3152225469

Received: 10 July 2023
Revised: 12 March 2024
Accepted: 11 May 2024
Published: 11 March 2025

Abstract

Background: Biofilms are organized communities of microorganisms encased in a self-produced matrix that adheres to surfaces and can have both beneficial and detrimental effects in various environments. These biofilms have been linked to severe infections in humans. We investigated the association between antibiotic resistance and biofilm formation in methicillin-resistant *Staphylococcus epidermidis* (MRSE) isolates.

Methods: A comprehensive search was conducted through data medical data bases using a combination of mesh terms. The data were analyzed using STATA meta-analysis software, and a random effects model was employed to determine the pooled prevalence with a 95% confidence interval (CI).

Results: Our findings revealed that the prevalence of MRSA was 61.75% (95% CI: 35.6-99.1). The cumulative rate of biofilm formation in MRSE strains was reported to be 83.4% (95% CI: 47.8-99.4). Among the biofilm-related genes, the *SdrG* gene exhibited the highest frequency (98%), followed by the *atlG* gene with a frequency of 84%.

Conclusion: Out of the seven, three documented a positive association. Given the propensity of MRSE strains to form biofilms, it is crucial to implement preventive measures against infections caused by these strains.

Keywords: Methicillin-resistant *Staphylococcus epidermidis*, Biofilm formation.

Citation:
Behshood P, Tajbakhsh E. Systematic review and meta-analysis of the association between biofilm formation and antibiotic resistance in MRSE isolated from Iranian patients. Caspian J Intern Med 2025; 16(2): 225-232.

S*taphylococcus epidermidis* (*S. epidermidis*), a gram-positive and coagulase-negative coccus belonging to the genus Staphylococcus, constitutes a component of the symbiotic flora of human skin (1, 2). This bacterium can instigate hospital-acquired infections among individuals with compromised immune systems. The risk of hospital-acquired infections is heightened in such patients due to the bacterium's propensity to form biofilms on medical devices (3, 4). Biofilm represents the most critical pathogenic factor of bacteria, impeding the infiltration of antibiotics and immune cells (5, 6). The capsule of *S. epidermidis* adheres to pre-existing biofilms through sulfated polysaccharides, facilitating the formation of multi-layered biofilms. Bacterial biofilm enhances antibiotic tolerance and resistance by one hundred to one thousand (7) and, making eradicating biofilm bacteria with antibiotics exceedingly challenging. Antibiotic concentration within the biofilm milieu often fails to reach optimal inhibitory or bactericidal levels (8, 9). Moreover, antibiotic exposure induces stress in bacteria, leading to alterations in their physiological and biochemical functions (10), and promoting the emergence of more resistant and occasionally biofilm-producing bacterial cells in certain species (11, 12). *S. epidermidis* exhibits resistance to numerous antibiotics, including penicillin, amoxicillin, and methicillin (Methicillin-Resistant *S. epidermidis;* MRSE). Consequently, antibiotics prove ineffective against biofilms, necessitating vancomycin in combination with rifampin or aminoglycosides for treatment (13).

 Publisher: Babol University of Medical Sciences

MRSE can be distinguished from Methicillin-Resistant *Staphylococcus aureus* (MRSA) based on its adverse biochemical reaction to coagulase. Beta-lactams are among the most commonly used antibiotics for treating staphylococcal infections (14). Although a high prevalence of MRSE and β-lactam-resistant populations has been observed, the biofilm-inducing effects of methicillin/β-lactams on MRSE remain unclear. Nonetheless, many sepsis patients receive β-lactam antibiotics alongside vancomycin, potentially stimulating MRSE biofilm growth and compromising vancomycin efficacy in some cases (15, 16). The horizontal transfer of antibiotic resistance determinants among these bacteria has significantly complicated the treatment of such infections. Vancomycin inhibits cell wall peptidoglycan synthesis by blocking transglycosylation and transpeptidation steps in the cell wall synthesis process, which are essential for both plasmid and chromosomal elements. Resistance to vancomycin is mediated by *vanA* and *vanS* genes, which are often carried on plasmids and transposons along with other vancomycin resistance genes, including *vanA*. This transfer of resistance genes frequently occurs between clinical strains of methicillin-resistant staphylococci and vancomycin-resistant enterococci (17, 18). Methicillin resistance and resistance to other β-lactam compounds are commonly encountered in clinical settings due to the association between the *mecA* gene and penicillin-binding proteins (PBP2a or PBP2b) (19).

Today, the resistance of *S.epidermidis* strains to glycopeptide antibiotics and methicillin has increased in clinics. On the one hand, the emergence of isolates that sometimes have multiple drug resistance has made it difficult to treat infections caused by these bacteria (20). On the other hand, the form of antibiotic resistance gene reservoirs drives the spread of resistance in health systems (21). Therefore, knowing the pattern of antibiotic resistance of these pathogenic agents in each geographical area while making it easier to choose the appropriate treatment plays a vital role in preventing the spread of these strains in hospitals (22). In this regard, we investigated the association between antibiotic resistance and biofilm formation in methicillin-resistant *Staphylococcus epidermidis* (MRSE) isolates.

Methods

Search strategy: This study adhered to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). A thorough search was performed across various electronic databases, including PubMed, Web of Science (ISI), MEDLINE, Google Scholar, SID, Magiran, and Scopus. The search terms utilized were as follows: (Biofilms [MeSH Terms] OR biofilm formation [Title/Abstract]) AND (Drug Resistance [MeSH Terms] OR Antimicrobial Drug Resistance [MeSH Terms] OR Antibiotic Resistance [MeSH Terms]) AND (*S. epidermidis* [Title/Abstract] OR *Staphylococcus epidermidis* [MeSH Terms] OR Methicillin-Resistant *Staphylococcus epidermidis* [MeSH Terms] OR Methicillin Resistance [Title/Abstract] OR MRSE [Title/Abstract]) AND (Biofilm-related genes [Title/Abstract]) AND (Prevalence [MeSH Terms]) AND (Iran [MeSH Terms]). The search was conducted between January 1, 2010, and June 30, 2021.

Inclusion criteria: In this review, cross-sectional studies with data reporting on the prevalence of MRSE and biofilm-related genes in *S. epidermidis* isolates from clinical samples in Iran. Studies conducted in Iran that utilized standard microbial identification methods, assessed biofilm formation, and evaluated antibiotic resistance were included in the analysis.

Exclusion criteria: Specific articles were excluded from this review, including review studies, case reports, abstracts, editorials, and studies on soil, water, animals, non-clinical samples, and incomplete analysis were excluded. Additionally, two independent reviewers (P.B. and E.T.) independently assessed the eligibility of the studies.

Outcomes: This study's primary outcomes of interest were the prevalence of MRSE, biofilm-related genes, the frequency and association between multidrug-resistant (MDR) strains and biofilm formation (23). These outcomes were selected based on their relevance to the research question and data availability in the included studies.

Quality evaluation: Quality was assessed via a critical appraisal tool explicitly designed for epidemiological studies. This tool consisted of 10 questions, with a score of 1 assigned to a "yes" response and 0 to a "no" response. The final scores were categorized as weak (0-4), moderate (6-8), or strong (>8). The quality assessment aimed to evaluate the included studies' methodological rigor and potential biases. The quality assessment was performed independently by two reviewers (P.B. and E.T.) (24).

Data extraction: Two reviewers autonomously gathered the pertinent information from each study utilizing pre-designed templates. The gathered information comprised study timeframe, year of publication, sample size, region, prevalence of MRSE and MDR strains, frequency of biofilm formation, biofilm-related genes, and the association between biofilm formation, its type, and

antibiotic resistance. Specifically, the collected data encompassed the author's identity, duration of the study, year of publication, study location, sample size, MRSE prevalence, rate of biofilm formation, diagnostic method employed for MRSE, and source of samples.

Meta-analysis: All data were analyzed using STATA software, specifically version 14.3. A meta-analysis was performed to obtain pooled prevalence estimates with 95% confidence intervals (CI). A random effects model was used to account for potential heterogeneity between studies. The statistical heterogeneity between groups was assessed using I^2 indexes, and the p-value was set at 0.05. Publication bias was evaluated through funnel plot. Subgroup analyses were conducted based on MRSE, MDR, genes related to biofilm, and types of biofilms to explore potential sources of heterogeneity and provide more detailed insights into the findings.

Results

Study selection: About 185 articles were identified through electronic database searches between January 1, 2010, and June 30, 2021. After a thorough review process, 21 papers were selected for detailed evaluation, eight studies were included. All included studies demonstrated favorable quality scores, ranging from 7 to 8. Importantly, none of the selected studies exhibited biases (25–33) (figure 1).

General effects

Prevalence of MRSE: The prevalence of MRSE strains in clinical samples from Iran varied between 35.6% and 99.1% (figure 2, table 1). Combining the data from these studies, the overall prevalence of MRSE isolates was calculated to be 61.75% (95% CI: 40.8-55.9). Notably, all MRSE isolates were found to carry the *mecA* gene.

Heterogeneity and publication bias: As determined by Cochrane's I2 statistics, Heterogeneity indices indicated significant heterogeneity among the included papers (I2 = 59.80, t = 4.778, P = 0.001). Consequently, a random effects model was selected for the meta-analysis. Furthermore, both visual evaluation of the funnel plot and Egger's linear regression test revealed no evidence of publication bias (figure 3 and 4, P= 0.22).

Association between biofilm formation and antibiotic resistance: The pooled prevalence of biofilm formation in MRSE strains was 83.4% (95% CI: 47.8-99.4) (I2 = 75.2, t = 1.8, P = 0.12; table 2), in which about three studies reported a significant association (table 2).

Abundance of biofilm-related genes: According to the gene analysis, the prevalence of *icaA*, *icaB*, *icaC*, *icaD*, *SdrG*, and *atlG* was found to be 32.6%, 25.4%, 72.3%, 64.8%, 98%, and 84%, respectively. Notably, the *SdrG* gene exhibited the highest frequency of occurrence (98%), followed by the *atlG* gene with a frequency of 84%.

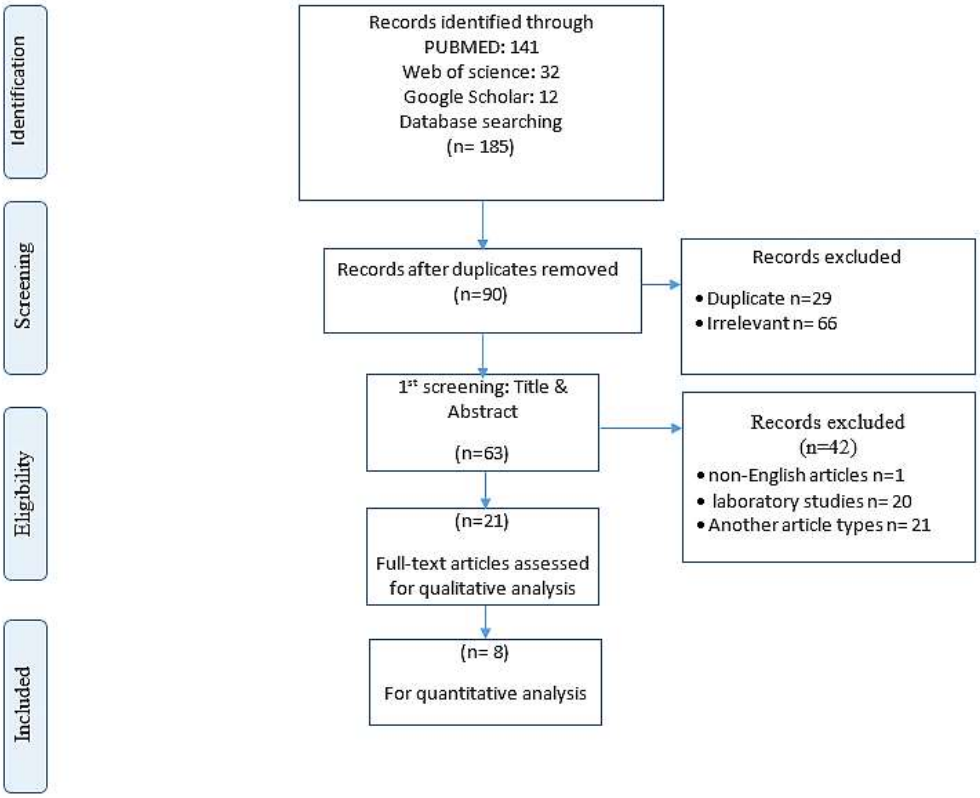

Figure 2. Flow charts for the studies were identified, displayed, and included in the study

Table 1. Studies on Methicillin-Resistant *Staphylococcus epidermidis* isolates

Study	Duration	Publication (year)	Location	Sample size	MRSE (n%)	Biofilm rate	Diagnostic Methods for MRSE	Source of Samples
Mirzaei et al, (2020)	2018-2019	2020		54	54 (100%)	53 (99.1%)	PCR	Blood, Wound, etc
Talebi et al, (2015)	2010-2012	2015	Tehran	90	58 (64%)	-	PCR/BMD	-
Sotoudeh Anvari et al, (2015)	2007-2012	2015		21	8 (35%)	-	DDM	Pericardial
Havaei et al, (2015)	2014	2015		70	61 (87.1)	-	DDM/PCR	Blood, catheters
Borooni et al, (2019)	2016-2017	2019	Isfahan	90	45 (50%)	45 (50%)	DD	Urine
Behshood et al, (2020)	2019	2020		100	60 (60%)	60 (100%)	DD	Urine, Blood, etc
Halaji et al, (2017)	2014-2015	2017		130	70 (53.8%)	-	D.D., PCR	Wound, Blood, etc
Tahmasebi et al, (2018)	2016-2017	2018	Hamedan	55	25 (45.4%)	-	PCR, Etest	Blood, Urine, etc

Table 2. Subgroup Analysis in *S. epidermidis*

Subgroup	Number of Studies	Heterogeneity test	Egger's test		Random model	
		Prevalence (95%cl) (%)	p	I^2	t	p
MRSE	8	61.75% (35.2-87.1)	0.001	59.808	4.778	0.25
Overall effect (Biofilm)	3	83.4% (47.8-99.4)	0.00	75.2	1.8	0.12

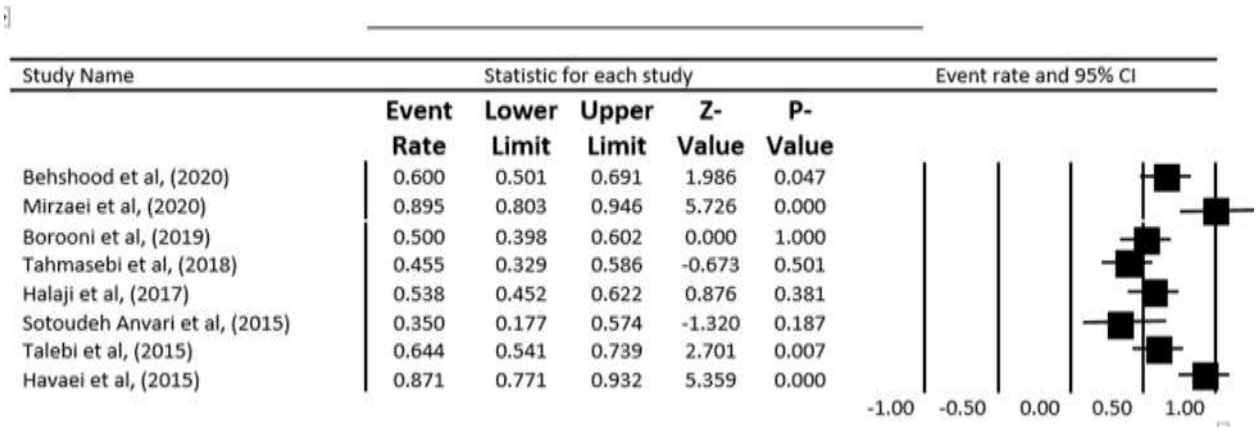

Figure 3. Forest plot of the prevalence of MRSE isolates

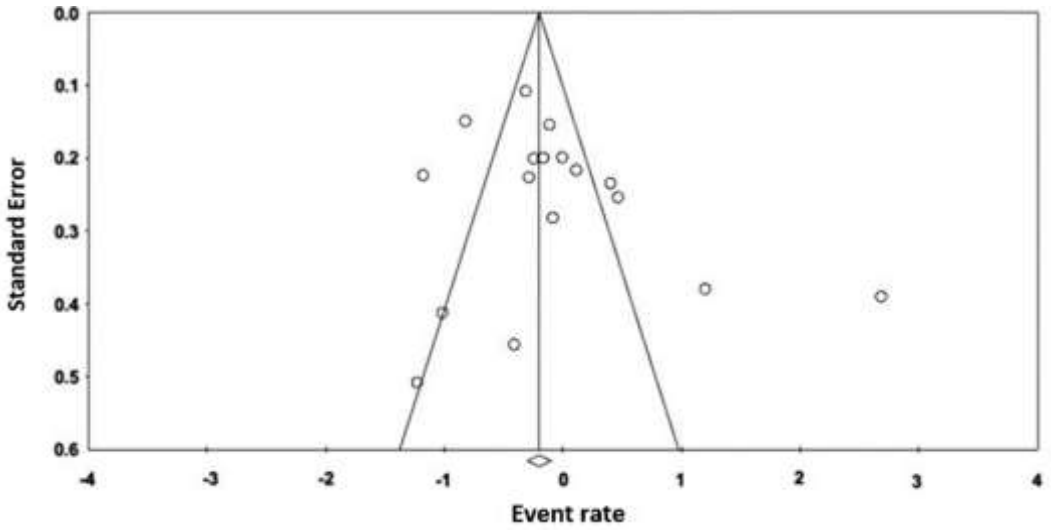

Figure 4. Funnel plot of the MRSE isolates

Discussion

Differences in the prevalence of MRSE (methicillin-resistant *Staphylococcus epidermidis*) among countries and regions can be ascribed to variations in infection control measures, the specific traits of prevalent pathogenic strains, the origin of strain isolation (hospital versus community settings), patterns of antibiotic prescription, and insufficient awareness regarding proper antibiotic utilization (26, 32, 33). Conversely, the proliferation of MRSE in clinical environments can be exacerbated by the absence of preventive health standards, untrained personnel, and suboptimal management practices. Moreover, the rise of MDR-MRSA isolates exacerbates the situation (34).

In our study, the cumulative prevalence of MDR *S. epidermidis* isolates was 46.9%. Remarkably, up to 70% of MDR and MRSE isolates harbored the *icaA-D* gene crucial for biofilm formation. Additionally, our analysis revealed that 83.4% of MRSE isolates exhibited biofilm-producing capabilities, underscoring the significant impact of biofilm formation on treatment duration. Furthermore, one study demonstrated that *S. epidermidis* isolates producing biofilms display high levels of resistance to commonly prescribed antibiotics. Specifically, our review highlighted that approximately 83.4% (95% CI: 47.8-99.4) of MRSE isolates exhibited biofilm-producing phenotypes, indicating the prevalence of MDR strains among MRSE isolates.

We also observed a positive correlation between biofilm formation and antibiotic resistance in three out of eight studies. Several studies in the world reported an association resistance to specific antibiotics and between biofilm formation in *S. epidermidis* isolates, and the results of these studies indicated higher antibiotic resistance among strains capable of biofilm formation (35-37). In the study conducted by Behshood et al. reported abundance of biofilm forming MRSE strains in Isfahan was 37 isolates (61.7%). The prevalence of biofilm-related genes in the isolates was *SesC* (100%), *SesI* (45.9%), *icaA* (29.7%), *icaB* (37.8%), *icaC* (81.08%), *icaD* (70.2%), *arcA* (81.08%), and *opp3AB* (70%). PCR analysis showed that among the 30 isolates of strong and medium biofilm production, 70% (21/30) positive for the *icaADB* gene.Result of antibiotic resistance in this study showed the isolates high resistance to oxacillin (91.8%), tobramycin (64.8%), and, but less resistant to mupirocin (27.02%), and nitrofurantoin (10.8%) (37). Montazri et al. conducted a study where they identified 44 clinical isolates of Methicillin-Resistant Coagulase-Negative Staphylococci (MR-CoNS) using the cefoxitin disc method, confirmed the identification through PCR amplification of the *mecA* gene and tuf gene sequencing for CoNS detection, assessed antimicrobial susceptibility via disc diffusion, and determined SCCmec types using multiplex PCR. Their findings revealed that *S. epidermidis* and *S. hemolyticus* were the most prevalent isolates, representing 45.4% of the total, with the highest resistance against erythromycin and clindamycin of 84.1% and 84.1%, respectively (38).

In another study conducted in the southwestern region of Iran, 65 *S. epidermidis* isolates were obtained from blood cultures of neonates with septicemia, with the majority demonstrating resistance to erythromycin but sensitivity to linezolid and vancomycin. Approximately 53% of the *S. epidermidis* isolates exhibited methicillin resistance, frequently associated with SCCmec type II among MRSE strains, and 65% of the isolates displayed biofilm formation with predominantly polysaccharide matrices. The presence of the *icaA* and *icaD* genes was detected in 40% and 19%

of the isolates, respectively, indicating an increasing prevalence of penicillin-resistant and pathogenic strains in the southwestern region of Iran (39). In conclusion, this review highlights the prevalence of MRSE and multidrug-resistant MRSE isolates in Iranian clinical samples, with a notable correlation observed between genetic related biofilm formation and antibiotic resistance. Consequently, the heightened prevalence of MRSE infections emerges as a pivotal concern for public health in Iran. Consequently, healthcare personnel must undertake stringent measures to mitigate and contain the dissemination of MRSE within clinical environments. Multiple studies reveal a direct correlation between biofilm and antibiotic resistance. Isolates capable of biofilm formation exhibit antibiotic resistance levels ranging from 100 to 1000 times greater than non-biofilm-forming strains, forming more robust biofilms (35-37).

A significant constraint of our study is its restriction to a single country, thereby diminishing the sample size. Moreover, other pathogenic and antibiotic resistance factors of *S. epidermidis* warrant further exploration. Future investigations should encompass global-level assessments of the factors elucidated in the present study alongside other pertinent aspects of S. *epidermidis*, both on a global and regional scale.

The observed decline in MRSE prevalence in Iran may be attributed to enhancements in infection control programs and the interruption of pathogen transmission cycles. Additionally, physicians' substantial reduction in methicillin prescriptions for staphylococcal infections has contributed to this decline. Since MRSE strains possess heightened abilities to form biofilms compared to susceptible strains, preventive measures are imperative to combat the infections they cause.

Acknowledgments

Not applicable.

Funding: Not applicable.

Ethics approval: Not applicable.

Conflict of interests: Authors declare that they have no conflict of interest.

Authors' contribution: P.B. and E.T. wrote the main manuscript text, and P.B. has done analysis. All authors reviewed the manuscript.

Availability of data and materials: The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Sah S, Bordoloi P, Vijaya D, et al. Simple and economical method for identification and speciation of Staphylococcus epidermidis and other coagulase negative Staphylococci and its validation by molecular methods. J Microbiol Methods 2018; 149: 106–19.
2. Lee SM, Keum HL, Sul WJ. Bacterial crosstalk via antimicrobial peptides on the human skin: Therapeutics from a sustainable perspective. J Microbiol 2023; 61: 1–11.
3. Brown MM, Horswill AR. Staphylococcus epidermidis—Skin friend or foe? PLoS Pathog 2020; 16: e1009026.
4. Severn MM, Horswill AR. Staphylococcus epidermidis and its dual lifestyle in skin health and infection. Nat Rev Microbio. 2023; 21: 97–111.
5. Li P, Yin R, Cheng J, Lin J. Bacterial biofilm formation on biomaterials and approaches to its treatment and prevention. Int J Mol Sci 2023; 24: 11680.
6. Adhikari RP. Staphylococcal infections: Host and pathogenic factors. Microorganisms 2021; 9: 1080.
7. Mirzaei R, Alikhani MY, Arciola CR, et al. Prevention, inhibition, and degradation effects of melittin alone and in combination with vancomycin and rifampin against strong biofilm producer strains of methicillin-resistant *Staphylococcus epidermidis*. Biomed Pharmacother 2022; 147: 112670.
8. Hemati S, Sadeghifard N, Ghafurian S, Maleki F, Mahdavi Z, Hassanvand A, et al. The association of biofilm formation and sub-minimal inhibitory concentrations of antimicrobial agents. J Bas Res Med Sci 2016; 3: 26-30
9. Ciofu O, Rojo-Molinero E, Macià MD, Oliver A. Antibiotic treatment of biofilm infections. APMIS 2017; 125: 304–19.
10. Yousefpour Z, Davarzani F, Owlia P. Evaluating of the effects of sub-MIC concentrations of gentamicin on biofilm formation in clinical isolates of Pseudomonas aeruginosa. Iran J Pathol 2021; 16: 403.
11. Jin Y, Guo Y, Zhan Q, et al. Subinhibitory concentrations of mupirocin stimulate Staphylococcus aureus biofilm formation by upregulating cidA. Antimicrob Agents Chemother 2020; 64: 10–1128.
12. Nagasawa R, Sato T, Nomura N, Nakamura T, Senpuku H. Potential risk of spreading resistance genes within extracellular-DNA-dependent biofilms of Streptococcus mutans in response to cell envelope stress induced by sub-MICs of bacitracin. Appl Environ Microbiol 2020; 86: e00770-20.

13. Eladli MG, Alharbi NS, Khaled JM, et al. Antibiotic-resistant Staphylococcus epidermidis isolated from patients and healthy students comparing with antibiotic-resistant bacteria isolated from pasteurized milk. Saudi J Biol Sci 2019; 26: 1285–90.
14. Mirzaei R, Yousefimashouf R, Arabestani MR, Sedighi I, Alikhani MY. The issue beyond resistance: Methicillin-resistant Staphylococcus epidermidis biofilm formation is induced by subinhibitory concentrations of cloxacillin, cefazolin, and clindamycin. PLoS One 2022; 17: e0277287.
15. Tang B, Gong T, Cui Y, et al. Characteristics of oral methicillin-resistant Staphylococcus epidermidis isolated from dental plaque. Int J Oral Sci 2020; 12: 15.
16. Kollef MH. Limitations of Vancomycin in the management of resistant Staphylococcal infections. Clin Infect Dis 2007; 45: S191–5.
17. Peterson E, Kaur P. Antibiotic resistance mechanisms in bacteria: Relationships between resistance determinants of antibiotic producers, environmental bacteria, and clinical pathogens. Front Microbiol 2018; 9: 2928.
18. Gill SR, Fouts DE, Archer GL, et al. Insights on evolution of virulence and resistance from the complete genome analysis of an early methicillin-resistant Staphylococcus aureus strain and a biofilm-producing methicillin-resistant Staphylococcus epidermidis strain. J Bacteriol 2005; 187: 2426–38.
19. Morosini MI, Díez-Aguilar M, Cantón R. Mechanisms of action and antimicrobial activity of ceftobiprole. Rev Esp Quimioter Publ Of la Soc Esp Quimioter 2019; 32 Suppl 3: 3–10.
20. Eltwisy HO, Twisy HO, Hafez MH, Sayed IM, El-Mokhtar MA. Clinical infections, antibiotic resistance, and pathogenesis of *Staphylococcus haemolyticus*. Microorganisms 2022; 10: 1130.
21. Pain M, Hjerde E, Klingenberg C, Cavanagh JP. Comparative genomic analysis of Staphylococcus haemolyticus reveals key to hospital adaptation and pathogenicity. Front Microbiol 2019; 10: 2096.
22. Eltwisy HO, Abdel-Fattah M, Elsisi AM, et al. Pathogenesis of Staphylococcus haemolyticus on primary human skin fibroblast cells. Virulence 2020; 11: 1142–57.
23. Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. Int J Heal policy Manag 2014; 3: 123.
24. DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. Contemp Clin Trials 2015; 45: 139-45.
25. Mirzaei B, Faridifar P, Shahmoradi M, et al. Genotypic and phenotypic analysis of biofilm formation Staphylococcus epidermidis isolates from clinical specimens. BMC Res Notes 2020; 13: 1–6.
26. Talebi M, Shafiee M, Sadeghi J, et al. Genotypic diversity of methicillin-resistant coagulase-negative staphylococci isolated from inpatients and outpatients. Microb Drug Resist 2016; 22: 147–54.
27. Anvari MS, Kianinejad R, Boroumand MA, Arzhan S, Jalali A. Bacterial pericarditis and antimicrobial resistance at the Tehran Heart Center, Iran. J Infect Dev Ctries 2015; 9: 780–4.
28. Havaei SA, Namvar AE, Moghim S, Lari AR. Evaluation of various staphylococcal cassette chromosome mec (SCCmec) types in Staphylococcus epidermidis invasive strains from hospitalised patients in Iran. Le Infez Med 2015; 23: 18–22.
29. Borooni S, Nourbakhsh V, Nourbakhsh F, Tajbakhsh E, Yazdanpanah A. Biofilm formation and its genes expressions in Staphylococcus epidermidis isolated from urinary tract infections of children in Isfahan. Int Arch Heal Sci 2019; 6: 41–5.
30. Behshood P, Tajbakhsh E, Momtaz H. Recognition of (Sesc) for easy identification of Staphylococcus epidermidis and molecular and phenotypic study of B-Lactam resistance in Staphylococcus epidermidis isolates in Isfahan. Reports Biochem Mol Biol 2020; 9: 309.
31. Halaji M, Karimi A, Shoaei P, et al. Distribution of SCCmec elements and presence of Panton-Valentine Leukocidin in Methicillin-Resistant Staphylococcus epidermidis isolated from clinical samples in a University Hospital of Isfahan City, Iran. J Clin Diagn Res 2017; 11: DC27.
32. Tahmasebi H, Dehbashi S, Arabestani MR. Determination of antimicrobial resistance pattern in methicillin-resistant Staphylococcus saprophyticus and Staphylococcus epidermidis and detection of resistance Genes to clindamycin and Erythromycin. Iran J Med Microbiol 2018; 12: 169–78.
33. Sahal G, Bilkay IS. Multi drug resistance in strong biofilm forming clinical isolates of Staphylococcus epidermidis. Brazilian J Microbiol 2014; 45: 539–44.
34. De Backer S, Sabirova J, De Pauw I, et al. Enzymes catalyzing the TCA-and urea cycle influence the matrix composition of biofilms formed by methicillin-resistant Staphylococcus aureus USA300. Microorganisms 2018; 6: 113.
35. Razavi S, Dadashi M, Pormohammad A, et al. Methicillin-Resistant Staphylococcus epidermidis in

Iran: A Systematic Review and Meta-Analysis. Arch Clin Infect Dis 2018; 13: e58410.

36. Trang VT, Takeuchi H, Kudo H, et al. In vitro antimicrobial activity of aminoreductone against the pathogenic bacteria methicillin-resistant Staphylococcus aureus (MRSA). J Agric Food Chem 2011; 59: 8953–60.
37. Behshood P, Tajbakhsh E. Random Amplified Polymorphic DNA (RAPD)-PCR analysis of genotypic and phenotypic characteristics of MethicillinResistant Staphylococcus epidermidis (MRSE) strains involved in biofilm formation. Trop J Pharm Res, January 2024; 23: 99-107.
38. Abbasi Montazeri E, Seyed-Mohammadi S, Asarehzadegan Dezfuli A, et al. Investigation of SCC mec types I–IV in clinical isolates of methicillin-resistant coagulase-negative staphylococci in Ahvaz, Southwest Iran. Biosci Rep 2020; 40: BSR20200847.
39. Farajzadeh Sheikh A, Asareh Zadegan Dezfuli A, Navidifar T, Fard SS, Dehdashtian M. Association between biofilm formation, structure and antibiotic resistance in Staphylococcus epidermidis isolated from neonatal septicemia in southwest Iran. Infect Drug Resist 2019; 12: 1771–82.