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Gene expression analysis of biofilm-associated and vancomycin stress-response genes in clinical *Staphylococcus aureus*

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Abstract

Objective

Regulatory pathways involved in antibiotic resistance and biofilm formation in *Staphylococcus aureus* are complex and involve multiple genetic systems, including the *vraSR* stress-response pathway and the *icaADBC* operon. Understanding the transcriptional response of these genes under vancomycin exposure may provide insight into mechanisms associated with persistence and treatment failure. The study examined how clinical *Staphylococcus aureus* isolates react to vancomycin. The research also focused on antibiotic susceptibility and the activity of genes linked to biofilm growth (*icaA, icaB, icaC, and icaD*) and resistance (*vra*).

Materials and methods

Clinical isolates of *Staphylococcus aureus* were obtained from burn and wound specimens and confirmed by standard microbiological techniques. Vancomycin susceptibility was preliminarily evaluated using the agar well diffusion method. Total RNA was extracted from *S. aureus* cultures.

Quantitative real-time PCR (*qRT*-PCR) was carried out using SYBR Green to perform expression analysis to track changes in the bacteria after exposure to the antibiotic.

Results

Testing showed that isolates responded differently to the drug. Several samples had very small or non-existent inhibition zones. These findings may indicate reduced susceptibility to vancomycin; however, confirmation using MIC-based assays is required. The qRT-PCR results showed that the *icaADBC* operon became more active after treatment. This change was most obvious in isolate number two. The data indicates that exposure to antibiotics might help the bacteria build stronger biofilms. This response is likely to help the bacteria survive and leads to treatment failure. The *vra* gene also showed strong activity across several isolates. This supports its role in managing cell wall stress. The *hpr* gene became more active too. This result suggests the gene might not stay stable enough to work as an internal control in these conditions.

Conclusions

The results show a clear connection between drug resistance and biofilm growth in *S. aureus*. Relying only on vancomycin for MRSA treatment has major drawbacks. Alternative therapeutic strategies targeting biofilm formation and cell wall stress-response pathways may improve treatment outcomes in persistent MRSA infections. These approaches could target the genes that control biofilm production. Another option is to find ways to block the *vraSR* system.

Keywords: biofilm, *Staphylococcus aureus*, vancomycin resistance

Paper type: Research paper.

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Introduction

Staphylococcus aureus was first known for causing pus-filled infections abscesses. It causes numerous infections, both superficial and deep, and infections that may be life threatening. These include skin and soft tissue infections, endocarditis, chronic osteomyelitis, pneumonia, and

bacteremia. Such infections are known to inflict a staggering amount of disease and mortality around the world (Pal et al., 2023). The latter part of the 20th century witnessed the introduction of antibiotics such as penicillin and methicillin which *S. aureus* infections responded to. Unfortunately, *S. aureus* responded to these treatments by developing resistance. The emergence of penicillin-resistant (PRSA) and methicillin-resistant *S. aureus* (MRSA) has become a severe public health concern. Global MRSA infection control remains futile, as the bacteria remains one of the leading causes of healthcare-associated infections, accounting for almost a third of all reported bacterial isolates in Europe and tens of thousands of invasive cases in the United States yearly (Abebe & Birhanu, 2023; Mohammed et al., 2025). Vancomycin, a glycopeptide antibiotic, has been used to treat severe infections and combat MRSA. But the treatment option has become more complicated with the appearance of vancomycin-intermediate *S. aureus* (VISA) with a minimum inhibitory concentration of (MIC) 4 - 8 ug/mL. These variants are troublesome since they are linked to treatment failures. Intermediate resistance emerges due to complicated genetic and physiological changes, such as cell wall thickening and reduced autolysis, which occur because of point mutations. Most importantly, some changes in the expression of Small regulatory RNAs (sRNAs) are conserved during and after the exercise of some antibiotics, meaning they may regulate some pathways of resistance (Wang et al., 2025; Wu et al., 2024). Small regulatory RNAs (sRNAs) are important post-transcriptional regulators in bacteria and have been implicated in the control of stress responses, virulence, and biofilm formation in *Staphylococcus aureus*. Previous studies suggest that sRNA-mediated regulatory networks may influence the expression of biofilm-associated operons such as *icaADBC*. Although the present study did not directly evaluate sRNA expression, the investigated genes may be part of regulatory pathways influenced by stress-responsive non-coding RNAs. In *S. aureus*, sRNAs may inhibit translation by blocking a ribosome binding site, enhance or inhibit translation, and promote mRNA degradation through RNase-mediated mechanisms through RNase interaction, promotion of decay, and transcription termination (Ribeiro et al., 2024). sRNAs are also capable of modulating ribosome translocation as well as intertwine with other so-called non-coding RNAs to regulate large scale networks of genes. Of great promise are sRNAs as novel targets for therapeutic intervention because of their functions in the resistant mechanisms and adaptive changes in the cells (Bronsard et al., 2025; Kazemipour et al., 2025). *Staphylococcus aureus* bacteria are famed for their ability to create biofilms, which are advanced microbial consortia enclosed within a protective matrix. Biofilm formation is a critical virulence factor. It enables bacteria to persist and improve their ability to tolerate antibiotics, especially when the bacteria are anchored to medical devices and tissues over time (Ballah et al., 2022). The *icaADBC* operon governs the synthesis of the biofilm matrix component, polysaccharide intercellular adhesin (PIA). It is involved in the synthesis and

modification of the enzyme poly-N-acetyl glucosamine (PNAG), which plays a vital role in cell adhesion. The genes *icaA* and *icaD* encode the enzymes responsible for PNAG polymerization, while *icaC* and *icaB* are responsible for the export of the polymer and the deacetylation process, respectively. Deacetylation by *IcaB* is important for giving PNAG a positive charge which increases adhesion and makes PNAG more vulnerable to antimicrobial peptides (Peng et al., 2023). Transcriptional repressors and other elements within the genome affect the regulation of the *icaA*DBC operon. The upstream *icaA*DBC region, *icaR*, which is predicted to encode a *TetR* family repressor, would bind to the *icaA* promoter. *TcaR*, a member of the *MarR* family, also represses transcription by binding to the *icaA*DBC promoter (Schwartbeck et al., 2024). Quite remarkably, the 5 bp motif (TATTT) is also found in the intergenic region between *icaR* and *icaA*, which is linked to the mucoid phenotype and the excessive production of PIA. It is proposed that this motif is independent of IcaR which implies that IcaR does not capture everything that is controlling this phenotype. Another newly characterized repressor is Rob, a TetR-like DNA-binding protein of the PIA hyperproduction region. Rob binds to a 25 bp sequence containing the 5 bp motif mentioned earlier. Rob seems to require the ability to bind to the motif for binding, which then causes a cascade that leads to excess biofilm. Rob is part of the glucose-induced biofilm access gene (*gbaAB*) operon and appears to act independently of glucose which adds to the already complex control of biofilms (Shi et al., 2022). In addition to *vra*, the *hpr* gene was investigated as a stress-associated transcriptional marker potentially involved in adaptive responses to antibiotic exposure. Moreover, biochemical tests are incapable of distinguishing different types of microorganisms, such as bacteria, viruses, and parasites (Ahsani et al. 2010; Mohammadabadi et al. 2004; Khabiri et al., 2025). Genomic techniques such as PCR and sequencing are the most modern practical technology in diagnosing infectious diseases and compared with classical techniques, it has been shown to be more rapid, with results obtained in a few hours, and also more reliable (Mohammadabadi et al. 2011; Khabiri et al. 2023; Mohammadabadi et al., 2025). Genomic techniques allow a faster identification directly from clinical samples (Shahdadnejad et al. 2016; Mohammadabadi et al. 2024). Thus, the aim of this study was to evaluate the relationship between vancomycin susceptibility and biofilm-associated gene expression in clinical *Staphylococcus aureus* isolates.

Materials and methods

Bacterial isolate and culture conditions: Clinical isolates of *Staphylococcus aureus* were obtained from burn and wound specimens and confirmed by standard microbiological techniques including Gram staining, catalase, coagulase, and mannitol fermentation tests. Isolates were maintained on tryptic soy agar (TSA) slants and sub-cultured onto fresh media before each

experiment. For all assays, overnight cultures were prepared in tryptic soy broth (TSB) at 37°C Overnight.

Antibiotic sensitivity test (well diffusion method) for vancomycin: Antibiotic susceptibility to vancomycin was assessed using the well diffusion method. Mueller-Hinton agar (MHA) plates were inoculated uniformly with standardized bacterial suspensions equivalent to 0.5 McFarland standard. Wells (6 mm diameter) were punched into the agar, and each well was filled with 100 µL of vancomycin solution at the appropriate concentration. Plates were incubated at 37°C for 24 hours, and the zones of inhibition were measured in millimeters. Although, Vancomycin susceptibility was preliminarily evaluated using the agar well diffusion method; however, MIC-based methods are recommended by CLSI for accurate detection of VISA phenotypes. Results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

RNA isolation and purification, cDNA synthesis, and qRT-PCR: Total RNA was extracted from *S. aureus* cultures before and after vancomycin treatment using a commercial bacterial RNA extraction kit according to the manufacturer's instructions. RNA concentration and purity were evaluated using NanoDrop spectrophotometry and agarose gel electrophoresis. Quantitative real-time PCR (*qRT*-PCR) was carried out using SYBR Green chemistry on a thermal cycler equipped for real-time fluorescence detection. Amplification was performed under the following conditions: initial denaturation at 95°C for 8 minutes, followed by 40 cycles of 95°C for 15 seconds and 60°C for 30 seconds. Relative gene expression was calculated using the 2^-ΔΔCt method, with 16S rRNA as the internal reference gene. Gene expression analysis was performed using SYBR Green-based qRT-PCR with the following primers, As illustrate in Table 1.

Statistical analyses: All experiments were performed in triplicate, and data were expressed as mean ± standard deviation (SD). The qRT-PCR data were analyzed using the 2^-ΔΔCt method to determine relative fold changes in gene expression. Statistical analysis was performed using paired Student's t-test on biological triplicates. A p-value <0.05 was considered statistically significant. Data analysis and graphing were performed using GraphPad Prism software.

Results and discussion

Antibiotic susceptibility to vancomycin: The antimicrobial activity of vancomycin against *Staphylococcus aureus* isolates was evaluated using the agar well diffusion method. As shown in Table 2, inhibition zones varied significantly among isolates, ranging from complete resistance (0 mm, isolates 6, 8, and 14) to high susceptibility (33 mm, isolate 1). Several isolates, including

5 and 10, displayed reduced inhibition zones (10 mm and 17 mm, respectively), indicating intermediate resistance profiles.

Table 1. Primers used in the qRT-PCR.

Gene	Forward Primer (5'–3')	Reverse Primer (5'–3')	Amplicon Size	Function
icaA	CGACGTTGGCTACTGGGATAC	AACACATGGCAAGCGGTTCAT	107 bp	Biofilm-associated genes
icaB	TCCTTATGGCTTGATGAATGACGA	TGGAGTTCGGAGTGACTGCTT	101 bp	Biofilm-associated genes
icaC	AGCAAATGGAGACTATTGGAACGT	AAAATGCGTGCAAATACCCAAGAT	100 bp	Biofilm-associated genes
icaD	ATGGTCAAGCCCAGACAGAGG	TCCAAAAGACACACGATATAGCGA	97 bp	Biofilm-associated genes
vra	AAAGTGCCTATGATGATGGAAGGT	GGGGTAGTGCTGTAATTGCGT	156 bp	Vancomycin stress-response gene
hpr	CGCTGGTGAAGAAGGACTATCG	GGCGTTTCTGGTCTGCATAGT	198 bp	Stress-associated target gene
16S rRNA	GACAAAGTGACAGGTGGTGCA	CACCTTCCTCCGGTTTGTCAC	149 bp	Internal reference gene

These results suggest the presence of vancomycin-intermediate *S. aureus* (VISA) or hetero-VISA phenotypes among the tested isolates. This variation in susceptibility reinforces growing global concerns over the declining eff*icac*y of vancomycin, particularly in nosocomial strains of *S. aureus*.

Table 2. Antibiotic susceptibility to vancomycin

Isolate	Inhibition zone (mm)	Isolate	Inhibition zone (mm)
1	33	8	0
2	21	9	27
3	26	10	17
4	25	11	21
5	10	12	26
6	0	13	23
7	21	14	0

The identification of isolates with 0 mm zones indicates complete resistance, which is particularly alarming and highlights the urgent need for monitoring resistance patterns and

optimizing antimicrobial stewardship. These findings may indicate reduced susceptibility to vancomycin; however, confirmation using MIC-based assays is required.

Differential gene expression of biofilm-associated genes: The expression profiles of the biofilm-associated genes *icaA*, *icaB*, *icaC*, and *icaD* were analyzed in four representative isolates using qRT-PCR. As summarized in Figure 1, all tested genes showed significant upregulation following vancomycin exposure, with isolate 2 demonstrating the highest expression levels across all genes. Specifically: *icaA* was upregulated by 16.22-fold in isolate 2 and by 4.86–8.69-fold in other isolates. The *icaB* showed the most dramatic change in isolate 2 with a 25.63-fold increase. And *icaC* expression ranged from 6.06-fold in isolate 1 to 18.13-fold in isolate 2. Then *icaD* expressions peaked at 12.13-fold in isolate 2. This substantial upregulation of the *icaA*DBC operon suggests that vancomycin exposure induces a biofilm-promoting response in *S. aureus*. Biofilm formation is a well-known defense mechanism that enhances bacterial persistence under hostile conditions, including antibiotic pressure. The elevated expression of these genes may facilitate the production and stabilization of PIA, thereby increase biofilm biomass and promote treatment resistance. These findings are consistent with previous studies reporting that biofilm-associated genes are upregulated in response to stress, potentially contributing to the chronicity and resilience of *S. aureus* infections.

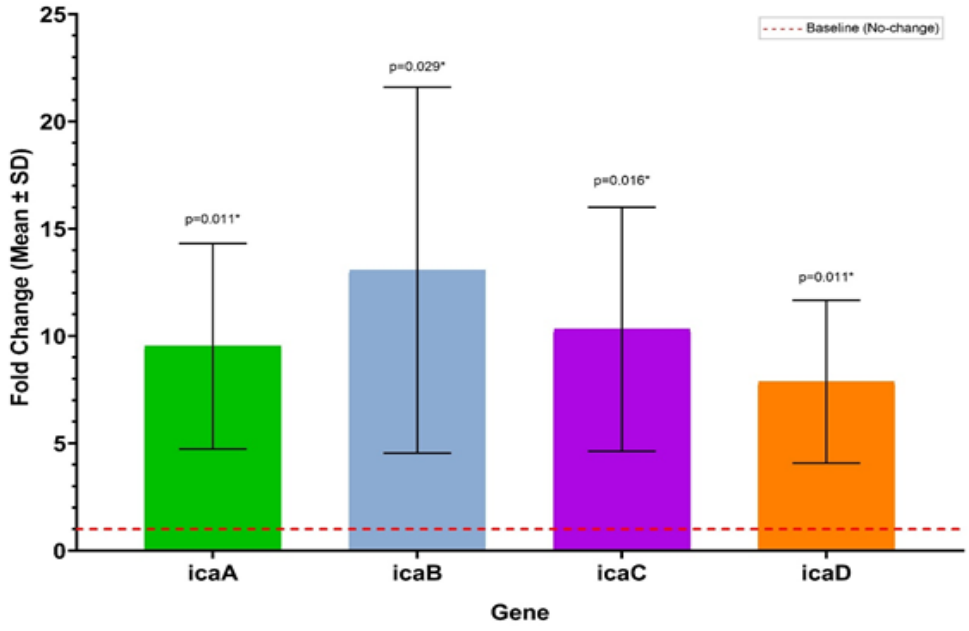

Figure 1. Relative expression levels of biofilm-associated genes (*icaA, icaB, icaC,* and *icaD*) in *S. aureus* isolates following vancomycin exposure. Data represent mean ± SD from three independent experiments. Statistical significance was determined using paired Student's t-test ($p < 0.05$)

Expression of vancomycin response gene *(vra)*: To further understand the molecular response to vancomycin, the expression of the *vra* gene associated with vancomycin-induced cell wall stress was analyzed alongside the housekeeping gene 16S rRNA. As shown in Figure 2, *vra* expression was markedly upregulated in all tested isolates, with fold changes ranging from 2.73 (isolate 1) to a high expression level of 56.49-fold (isolate 7). Similarly, *hpr* expression levels ranged from 2.64 to 68.12, indicating high transcriptional activity in response to antibiotic exposure. The substantial induction of *vra* expression supports its established role in the vancomycin resistance pathway. The *vraSR* two-component regulatory system responds to cell wall damage by activating genes involved in peptidoglycan synthesis and repair. Elevated *vra* expressions in vancomycin-treated isolates may contribute to phenotypic characteristics observed in VISA strains, such as thickened cell walls and reduced autolysis. Expression of the *hpr* gene was also significantly increased following vancomycin exposure, with fold changes ranging from 2.64 to 68.12 across the tested isolates. The observed upregulation suggests that *hpr* may participate in the bacterial stress-response network activated during antibiotic exposure. These findings indicate that vancomycin treatment induces transcriptional changes not only in resistance-associated genes such as *vra*, but also in additional stress-related pathways.

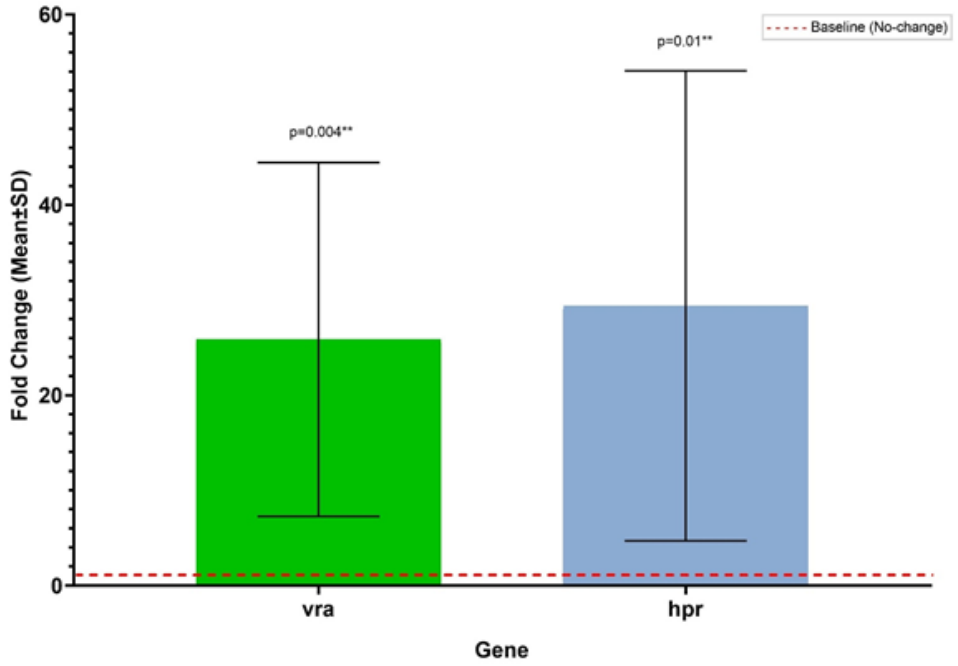

Figure 2. Relative expression levels (mean ± SD) of the stress-response genes *vra* and *hpr* in *S. aureus* isolates following vancomycin exposure

Together, the data from antibiotic sensitivity testing and gene expression profiling provide compelling evidence of adaptive responses in *S. aureus* following vancomycin exposure. Notably,

the upregulation of *icaA*DBC genes suggests that vancomycin may inadvertently stimulate biofilm formation, contributing to therapeutic failure and persistent infections. Meanwhile, the sharp increase in *vra* expression underscores its role in vancomycin resistance, particularly in isolates with reduced susceptibility. These observations have important clinical implications. The simultaneous activation of biofilm and resistance genes under vancomycin stress highlights the dual challenge of treating biofilm-related infections in the era of multidrug resistance. Targeting key regulators of biofilm formation, such as IcaR and Rob, or inhibiting the *vra*SR pathway, may provide novel therapeutic opportunities to enhance antibiotic eff*icac*y and mitigate resistance development. The variability in vancomycin susceptibility observed in this study, ranging from complete resistance (0 mm inhibition zones in isolates 6, 8, and 14) to high susceptibility (33 mm in isolate 1), highlights the evolving challenge of treating *S. aureus* infections. Isolates 5 and 10 prominently displayed minimal inhibition zones of 10 mm and 17 mm, respectively, which may suggest that these could be classified as vancomycin-intermediate *S. aureus* (VISA) or hetero-VISA (hVISA). This is consistent with previous studies which noted an increasing trend in the prevalence of VISA and *hVISA* overtime. For instance, (Card et al., 2025: Parsons et al., 2026) noted the phenotypic and genotypic vancomycin resistance in Iranian clinical isolates. More recent studies have linked this resistance to the acquisition of the *vanA* resistance gene from enterococci (Hausberger et al., 2011; Azzam et al., 2023). However, in the absence of *vanA* screening in this study, alternative vancomycin resistance mechanisms such as cell wall thickening and reduced peptidoglycan cross-linking described by (Ashfaq et al., 2022; Basu et al., 2019) cannot be ruled out. Isolates with intermediate resistance, such as 5 and 10, appear to be hetero-VISA, which are known to possess diverged subclone resistance phenotypes that complicate treatment. This strengthens the argument for responding to and modifying the CLSI citatory breakpoints and for the need to implement genomic surveillance to monitor the emerging mechanisms of resistance. In like manner, (Orsholm et al., 2026) observed how prolonged exposure to vancomycin affects thickening of cell walls and metabolic activity of VISA variant superbugs. These trends are especially worrisome in hospital settings, where selective pressure and biofilm formation may accelerate the development of resistant strains. These findings underscore the need for timely molecular and MIC diagnostics to illuminate pathways of resistance and perform susceptibility tests. In this study, all tested isolates demonstrated significant upregulation of the *icaA*DBC operon following vancomycin exposure. Isolate 2 demonstrated the most significant expression, with *icaA* and *icaB* upregulated 16.22 and 25.63 times, respectively. These results agree with the work of (Hausberger et al., 2011), who documented increased biofilm gene expression in *S. aureus* under sub-inhibitory concentrations of antibiotics. Bacteria are presumed to respond to upregulation of biofilm-associated genes

prompted by vancomycin by enhancing their ability to persist to the drug through the production of PIA. According to (Hebert et al., 2003), biofilm resilience coupled with diminished antibiotic susceptibility conferred by elevated PIA synthesis augments bacterial survival. Similarly, (Tamura et al., 2021) linked biofilm formation to antibiotic tolerance, complicating clinical treatment even in the absence of classical resistance. The significant upregulation of *icaA*DBC operon genes (up to 25.63-fold for *icaB*) following vancomycin exposure supports recent evidence that antibiotic stress triggers biofilm formation as a defensive strategy (Qraidi et al., 2025; Chen et al., 2023). The isolate-specific variability in *ica* gene induction with clinical observations where hyper-biofilm-forming strains dominate chronic infections (Tamura et al., 2021). Biofilms enhance bacterial persistence by impairing antibiotic penetration and promoting tolerance (distinct from genetic resistance), which aligns with our data and explains the recurrent failures of vancomycin monotherapy in device-associated infections (Qraidi et al., 2025). Expression analysis of the *vra* gene revealed a marked transcriptional response to vancomycin exposure, with fold changes ranging from 2.73- to 56.49. This observation agrees with (Ashfaq et al., 2022; Basu et al., 2019), who identified the *vra*SR two-component system as a central regulator of the vancomycin stress response. Activation of *vra* leads to upregulation of genes involved in peptidoglycan biosynthesis and cell wall maintenance mechanisms characteristic of VISA phenotypes. Interestingly, the *hpr* gene also demonstrated marked transcriptional upregulation following vancomycin exposure. This finding suggests that *hpr* may be involved in the global stress-response mechanisms activated under antibiotic pressure. The coordinated induction of *hpr* and *vra* may reflect broader adaptive responses associated with bacterial survival and persistence. This observation agrees with the findings of (Martín-Pérez et al., 2023), who reported altered expression of traditional housekeeping genes under stress conditions. Such variability emphasizes the need for careful selection and validation of internal controls in *qRT*-PCR analyses during antibiotic stress studies.

Conclusions: Vancomycin exposure in *S. aureus* not only selects resistant phenotypes but also upregulates biofilm-associated genes, thereby compounding the challenge of treatment. The dual enhancement of resistance (*vra*) and virulence (*icaADBC*) highlights the adaptability of *S. aureus* and emphasizes the need for novel anti-biofilm and anti-resistance therapies. Continuous monitoring of gene expression responses and resistance trends is critical for developing more effective strategies to manage persistent *S. aureus* infections.

Author contributions

R. K. M. and M. K. A.: methodology, M. K. A.: software, A. A. I.: validation, R. K. M., K. D. S. and A. A. I.: formal analysis, M. K. A.: investigation, A. A. I.: resources, R. K. M.: data

curation, A. A. I.: writing—original draft preparation, and M. K. A.: writing review and editing. All authors reviewed and confirmed the paper.

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Data availability statement

The data contributing to the findings of this study are available from the investigating researcher upon request.

Ethical considerations

The authors avoided data fabrication, falsification, plagiarism, and misconduct.

Conflict of interest

The authors declare no conflict of interest regarding the publication of this paper.

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تحلیل بیان ژنی ژن‌های مرتبط با بیوفیلم و پاسخ به تنش وانکومایسین در *Staphylococcus aureus* بالینی

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چکیده

هدف: مسیرهای تنظیمی دخیل در مقاومت آنتی‌بیوتیکی و تشکیل بیوفیلم در *Staphylococcus aureus* پیچیده بوده و چندین سیستم ژنتیکی از جمله مسیر پاسخ به تنش *vra*SR و اپرون *icaA*DBC را در بر می‌گیرند. درک پاسخ رونویسی این ژن‌ها در مواجهه با وانکومایسین می‌تواند بینشی درباره مکانیسم‌های مرتبط با پایداری عفونت و شکست درمان ارائه دهد. این مطالعه واکنش ایزوله‌های بالینی *Staphylococcus aureus*به وانکومایسین را بررسی کرد. همچنین حساسیت آنتی‌بیوتیکی و فعالیت ژن‌های مرتبط با تشکیل بیوفیلم (*icaA, icaB, icaC, and icaD*) و مقاومت (*vra*) مورد ارزیابی قرار گرفت.

مواد و روش‌ها: ایزوله‌های بالینی *Staphylococcus aureus* از نمونه‌های سوختگی و زخم جمع‌آوری و با روش‌های استاندارد میکروبیولوژی تأیید شدند. حساسیت به وانکومایسین ابتدا با روش انتشار در چاهک آگار ارزیابی شد .RNA تام از کشت‌های *S.*

aureus استخراج گردید. سپس واکنش qRT-PCR با استفاده از رنگ SYBR Green برای تحلیل بیان ژنی و بررسی تغییرات باکتری پس از مواجهه با آنتی‌بیوتیک انجام شد.

نتایج: آزمون‌ها نشان دادند که ایزوله‌ها پاسخ‌های متفاوتی به دارو داشتند. برخی نمونه‌ها دارای هاله مهاری بسیار کوچک یا فاقد هاله بودند. این یافته‌ها ممکن است نشان‌دهنده کاهش حساسیت به وانکومایسین باشند، هرچند تأیید آن با آزمون‌های مبتنی بر MIC ضروری است. نتایج qRT-PCR نشان داد که اپرون *icaA*DBC پس از درمان فعال‌تر شده است و این تغییر به‌ویژه در ایزوله شماره ۲ واضح‌تر بود. داده‌ها نشان می‌دهند که مواجهه با آنتی‌بیوتیک ممکن است به باکتری‌ها در تشکیل بیوفیلم قوی‌تر کمک کند. این پاسخ احتمالاً موجب بقای بیشتر باکتری و شکست درمان می‌شود. ژن *vra* نیز در چندین ایزوله فعالیت بالایی نشان داد که نقش آن را در مدیریت تنش دیواره سلولی تأیید می‌کند. علاوه بر این، ژن *hpr* نیز افزایش بیان داشت که نشان می‌دهد ممکن است در این شرایط پایداری کافی برای استفاده به‌عنوان کنترل داخلی نداشته باشد.

نتیجه‌گیری: نتایج این مطالعه ارتباط آشکاری میان مقاومت دارویی و رشد بیوفیلم در *S. aureus* نشان داد. اتکای صرف به وانکومایسین برای درمان MRSA دارای محدودیت‌های قابل توجهی است. راهبردهای درمانی جایگزین که تشکیل بیوفیلم و مسیرهای پاسخ به تنش دیواره سلولی را هدف قرار دهند، می‌توانند نتایج درمانی را در عفونت‌های پایدار MRSA بهبود بخشند. این راهبردها ممکن است ژن‌های کنترل‌کننده تولید بیوفیلم یا سیستم *vra*SR را هدف قرار دهند.

کلمات کلیدی: استافیلوکوکوس اورئوس، بیوفیلم، مقاومت به وانکومایسین

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