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Original Research Article

Diagnostic Discordance between Cefoxitin Screening by Vitek 2 Compact and Oxacillin Disc Diffusion in Staphylococcus aureus: A Cross-Sectional Study from Central India

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Conflict of interest: Nil

Abstract

Background: Automated antimicrobial susceptibility testing (AST) systems such as Vitek 2 are increasingly used in diagnostic microbiology. Cefoxitin screening via Vitek 2 serves as a surrogate for mecA-mediated methicillin resistance. However, discrepancies with conventional Oxacillin susceptibility testing remain a concern.

Objectives: To assess the diagnostic concordance between Vitek 2 Cefoxitin screening and Oxacillin disc diffusion in Staphylococcus aureus isolates.

Materials and Methods: This cross-sectional study analyzed 604 consecutive S. aureus isolates from diverse clinical samples tested at a tertiary care hospital in Central India (January–December 2024). Cefoxitin screening was performed using the Vitek 2 Compact (AST-GP 628 cards). Oxacillin susceptibility was determined by Kirby–Bauer disc diffusion (1 µg) on Mueller–Hinton agar with 2% NaCl as per CLSI M100 (2024). Diagnostic indices were calculated using Oxacillin results as comparator.

Results: Among 604 isolates, 471 (78.0%) were Cefoxitin-positive and 133 (22.0%) Cefoxitin-negative by Vitek 2.Oxacillin disc diffusion identified 386 (63.9%) resistant and 218 (36.1%) sensitive isolates. Cefoxitin-Vitek 2 screening demonstrated sensitivity 99.5%, specificity 60.1%, positive predictive value 81.5%, negative predictive value 98.5%, and overall accuracy 85.2%. Eighty-seven (18.5%) isolates were Cefoxitin-positive but Oxacillin-sensitive, while two (0.3%) were Cefoxitin-negative yet Oxacillin-resistant.

Conclusion: Vitek 2 Cefoxitin screening is highly sensitive but moderately specific for MRSA detection. Discordant results underline the need for confirmatory mecA/PBP2a testing to prevent overestimation of MRSA prevalence.

Keywords: MRSA, Vitek 2 Compact, Cefoxitin screening, Oxacillin, Staphylococcus aureus, Diagnostic accuracy.

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Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) remains a major global pathogen in both hospital and community settings [1]. Accurate detection of methicillin resistance is critical for patient management and infection-control measures.

Automated systems like Vitek 2 Compact are now widely used for routine antimicrobial susceptibility testing (AST) due to their standardization and efficiency [2]. Cefoxitin is recommended by CLSI as a phenotypic surrogate for mecA detection because it provides clearer endpoint readings and stronger gene induction than Oxacillin [3]. Despite its advantages, discordance between Cefoxitin screening results on automated systems and Oxacillin susceptibility by conventional methods has been reported [4–6].

Factors such as heterogeneous mecA expression, hyper β-lactamase production, or mecC-mediated resistance may contribute to false positivity or

negativity [7–9]. The present study was designed to compare Cefoxitin screening results obtained from the Vitek 2 Compact system with conventional Oxacillin disc diffusion, to determine diagnostic accuracy and assess the clinical implications of discordant isolates.

Materials and Methods

Study design and setting: A cross-sectional observational study was conducted in the Department of Microbiology, Sri Aurobindo Institute of Medical Sciences (SAIMS), Indore, from April 2024 to May 2025.

Sample collection and identification: A total of 604 non-duplicate S. aureus isolates were recovered from pus, blood, urine, body fluids, and respiratory samples. Identification was confirmed by Gram stain, catalase and coagulase tests, and automated identification using Vitek 2 Compact (bioMérieux, France).

Cefoxitin screening by Vitek 2 Compact: Cefoxitin resistance was determined using the AST-GP 628 card, interpreted automatically by Vitek 2 software per CLSI 2024 guidelines [3]. Isolates reported as resistant were considered MRSA by Cefoxitin screening.

Oxacillin disc diffusion: Performed manually using the Kirby–Bauer method with Oxacillin (1 μg) disc on Mueller–Hinton agar supplemented with 2% NaCl, incubated at 35°C for 24 hours. Zone diameter ≤10 mm was resistant, ≥13 mm sensitive. Quality-control strains used: S. aureus ATCC 25923 (susceptible) and S. aureus ATCC 43300 (MRSA).

Data Analysis: A 2×2 table was prepared to compare Cefoxitin-Vitek 2 with Oxacillin disc diffusion. Sensitivity, specificity, PPV, NPV, and accuracy were calculated using Oxacillin results as reference.

Results

Out of 604 isolates, 471 (78.0%) were Cefoxitin-positive by Vitek 2 and 133 (22.0%) Cefoxitin-negative. Oxacillin disc diffusion categorized 386 (63.9%) as resistant and 218 (36.1%) as sensitive. As per table 1 and Graph 1 and 2.

Table 1: Comparison of Cefoxitin-Vitek 2 screening and Oxacillin disc diffusion results

	Oxacillin Resistant	Oxacillin Sensitive	Total
Cefoxitin Positive (Vitek 2)	384	87	471
Cefoxitin Negative (Vitek 2)	2	131	133
Total	386	218	604

Calculated indices:

- **Sensitivity:** 99.5 %
- **Specificity:** 60.1 %
- **PPV:** 81.5 %
- **NPV:** 98.5 %
- **Overall Accuracy:** 85.2 %

Discussion

The present study highlights a high sensitivity (99.5%) but moderate specificity (60.1%) of Vitek 2 Cefoxitin screening when compared to Oxacillin disc diffusion. The small number of Cefoxitin-negative but Oxacillin-resistant isolates (1.5%) underscores Cefoxitin's reliability for MRSA detection, whereas the 18.5% Cefoxitin-positive/Oxacillin-sensitive isolates indicate possible overestimation of MRSA.

Similar findings have been reported internationally and within India. Singh et al. (2019) [10] observed a 15% discordance between automated Cefoxitin and manual Oxacillin tests, suggesting the presence of mecA-negative but β-lactamase hyperproducing isolates. Gupta et al. (2017) [11] reported Cefoxitin sensitivity of 98.9% and specificity of 62% in manual testing, closely matching our data.

Automated systems like Vitek 2 provide consistent incubation and reading conditions, yet minor variations in inoculum density or NaCl concentration can influence borderline isolates [12]. The algorithm used by Vitek interprets resistance phenotypically based on growth kinetics rather than actual zone diameters, possibly detecting early heteroresistant subpopulations that remain below detection by disc diffusion [13].

Borderline oxacillin-resistant S. aureus (BORSA) and modified PBP-mediated resistance (MODSA) may appear resistant to Cefoxitin but sensitive to Oxacillin, contributing to diagnostic discordance [7,9]. The emergence of mecC-positive MRSA, which may behave atypically in routine phenotypic tests, also complicates interpretation [14].

False positivity in Cefoxitin-based systems has significant infection control implications. Overdiagnosis of MRSA leads to unnecessary isolation, overuse of glycopeptides, and inflated MRSA surveillance statistics [15]. Conversely, missing genuine MRSA could result in therapeutic failure and outbreaks. Therefore, laboratories should establish reflex confirmatory testing (PBP2a latex or mecA PCR) for all Cefoxitin-positive but Oxacillin-sensitive isolates, as recommended by CLSI and EUCAST [3,16].

In our study, the positive predictive value (81.5%) indicates that nearly one in five VitekCefoxitin-positive isolates might be phenotypically Oxacillin-sensitive. This underscores the importance of continuous internal quality assurance and participation in external proficiency testing.

The negative predictive value (98.5%), however, confirms Cefoxitin's excellent reliability to rule out MRSA. Given resource constraints in developing settings, Cefoxitin-Vitek 2 remains a practical screening tool, provided discordant results are verified.

Conclusion

Automated Cefoxitin screening by Vitek 2 Compact is highly sensitive for MRSA detection but may yield false positives when compared with Oxacillin disc diffusion. Borderline resistance and mecA-independent mechanisms likely contribute to discordant results.

Routine confirmation of Cefoxitin-positive/Oxacillin-sensitive isolates using molecular or PBP2a assays is recommended to ensure diagnostic accuracy and rational antibiotic stewardship.

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