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Antimicrobial resistance trends in Methicillin-Resistant *Staphylococcus aureus* (MRSA), India: A *in silico* analysis

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Abstract:

Methicillin-resistant *Staphylococcus aureus* infection is a major cause of hospital- and community-acquired infections in India, necessitating continuous institutional surveillance. This retrospective observational study analysed 5,396 non-duplicate clinical isolates (2015–2025), identifying MRSA using cefoxitin disc diffusion and PBP2a confirmation, with susceptibility testing performed per CLSI guidelines. Annual MRSA prevalence ranged from 37.2% to 62.3% (overall 40.5%), with linezolid maintaining consistently high susceptibility (>90%), while ciprofloxacin showed persistently low efficacy (<40%). Clindamycin, gentamicin and co-trimoxazole demonstrated moderate but fluctuating susceptibility trends over time. MRSA remains a sustained institutional burden, highlighting linezolid as the most reliable agent and underscoring the need for continuous antibiogram surveillance and antimicrobial stewardship to guide therapy and curb resistance.

Keywords: Methicillin-resistant *Staphylococcus aureus* (MRSA), antimicrobial resistance, India, antibiotic susceptibility, hospital-acquired infection, tertiary care surveillance

Background:

Antimicrobial resistance (AMR) represents one of the most critical global public health threats of the twenty-first century. The progressive acquisition of resistance mechanisms by pathogenic bacteria has resulted in diminishing therapeutic options and a substantial increase in morbidity and mortality associated with infectious diseases [1, 2]. Among the principal resistant pathogens, Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most clinically significant causes of both hospital-acquired and community-acquired infections worldwide, responsible for a spectrum of conditions ranging from skin and soft tissue infections to bacteraemia, endocarditis and pneumonia [3, 4]. Resistance to methicillin and all beta-lactam antibiotics in MRSA is primarily mediated by the *mecA* gene, which encodes a modified penicillin-binding protein (PBP2a) with greatly reduced affinity for beta-lactam drugs, rendering the entire class therapeutically ineffective [5]. The frequent co-occurrence of additional resistance determinants for fluoroquinolones, macrolides, aminoglycosides and co-trimoxazole further limits available treatment options and complicates empirical therapy [6]. Over the past two decades, MRSA has spread rapidly through healthcare settings worldwide, increasing dependence on reserve agents such as linezolid and vancomycin [7]. In India, MRSA prevalence in tertiary care hospitals varies widely across institutions and geographic regions, ranging from under 20% to over 80% of *S. aureus* isolates in published series [8, 9]. This variability reflects differences in patient populations, local antibiotic consumption patterns, infection control practices and the circulation of diverse MRSA clones. Indore, in Madhya Pradesh, serves as a major referral centre for central India, yet longitudinal data on MRSA resistance trends from this region remain sparse. Continuous institutional monitoring of antimicrobial susceptibility is fundamental to guiding empirical therapy, updating treatment protocols and designing effective stewardship interventions [10, 11]. Therefore, it is of interest to report the 10-year trends in MRSA prevalence and susceptibility at MGM Medical College and Hospital, Indore, with the aim of informing evidence-based antibiotic stewardship and contributing to regional surveillance data.

Materials and Methods:**Study design and setting:**

This was a retrospective observational study conducted at the Department of Microbiology, MGM Medical College and Hospital, Indore, Madhya Pradesh, India, encompassing the period from January 2015 to December 2025. Laboratory records were reviewed to retrieve data on all *Staphylococcus aureus* isolates processed during this period. Ethical approval was obtained from the Institutional Ethics Committee, MGM Medical College, and Indore. Patient data were anonymised prior to extraction; individual informed consent was waived in accordance with institutional policy for anonymised retrospective audit studies.

Clinical isolates:

A total of 5,396 non-duplicate clinical isolates of *S. aureus* were included. Isolates were obtained from diverse clinical specimens including pus and wound swabs, blood cultures, respiratory specimens (sputum and endotracheal aspirates), urine and other body fluids. Only the first isolate per patient per admission episode was included to avoid duplication. Isolates were derived from inpatient departments including general medicine, surgery, orthopaedics, intensive care units, dermatology and paediatrics.

Identification of *s. aureus* and MRSA:

Staphylococcus aureus was identified by standard microbiological criteria: colony morphology, Gram staining, catalase positivity, coagulase test (tube and slide) and DNase production. Confirmation was performed using the VITEK-2 automated identification system (bioMérieux, France) where indicated. MRSA was identified by cefoxitin (30 µg) disc diffusion; isolates with zone diameters ≤21 mm were classified as MRSA, interpreted per CLSI guidelines and confirmed by PBP2a latex agglutination (Oxoid PBP2' Latex Agglutination Test).

Antimicrobial susceptibility testing:

Susceptibility was determined by the Kirby-Bauer disc diffusion method on Mueller-Hinton agar, interpreted per current CLSI breakpoints, for: linezolid (30 µg), clindamycin (2 µg), ciprofloxacin (5 µg), gentamicin (10 µg) and co-trimoxazole (1.25/23.75 µg). Inducible clindamycin resistance was assessed by the D-zone test for all erythromycin-resistant, clindamycin-susceptible isolates; D-zone-positive isolates were reported as resistant. Quality control was performed using *S. aureus* ATCC 25923 and ATCC 43300.

Statistical analysis:

Year-wise MRSA prevalence and antibiotic susceptibility rates were compiled in Microsoft Excel. Annual susceptibility was expressed as the percentage of susceptible isolates among all tested in that year. Trends were assessed descriptively by tabulation and graphical representation. No formal inferential testing for trend was performed given the descriptive, surveillance-based nature of the study.

Results:

A total of 5,396 non-duplicate *S. aureus* isolates were analysed across the 10-year study period (2015–2025). Annual isolate volumes ranged from 67 to 724, reflecting variations in clinical workload and case mix. The majority of isolates were recovered from pus and wound swabs, blood cultures and respiratory specimens. Specimens originated from all major inpatient specialties. Annual MRSA prevalence is presented in (Table 1). Prevalence ranged from a minimum of 37.2% in 2024 to a maximum of 62.3% in 2023, exceeding 40% in eight of eleven study years. The overall MRSA rate across the full study period was 40.5% (2,185 of 5,396 isolates). A progressive increase was observed from 2017 to 2021 (41.5% to 59.3%), followed by a notable decline to 38.4% in 2022. A second rise peaked in 2023 before declining and partially recovering in subsequent years. Year-wise susceptibility of MRSA isolates to the five antibiotics is summarised in (Table 2). Linezolid demonstrated the highest and most consistent activity throughout the decade, with susceptibility rates of 100% in 2015 and 2021 and 98.0% in 2025. The lowest recorded value was 86.5% in 2018. Linezolid was the only agent to maintain susceptibility above 85% in every year of the study, confirming its status as the most dependable agent for MRSA infections at this institution [12, 13]. Ciprofloxacin exhibited the poorest overall activity, with susceptibility below 40% in nine of eleven years and a nadir of 10.5% in 2021. An

anomalous value of 63.3% in 2020 likely reflects a change in the clinical source distribution of isolates that year rather than a genuine sustained improvement [14]. Clindamycin showed moderate susceptibility (56%–70%) from 2015 to 2022, followed by a sharp decline to 27.5% in 2023 and recovery to 64.3% in 2024 and 88.5% in 2025. This fluctuation may reflect a transient increase in erm-gene-mediated constitutive MLS_B resistance or changes in D-zone test enforcement. Inducible resistance was assessed by D-zone test throughout the study period [15]. Gentamicin susceptibility ranged from 37.1% (2015) to 74.0% (2016), remaining between 50% and 70% in most years but declining to 44.1% in 2025. The moderate and variable activity of gentamicin supports its use only when susceptibility is confirmed by current antibiogram testing [16]. Co-trimoxazole exhibited the most variable pattern, ranging from 23.8% in 2023 to 68.5% in 2022, without a consistent directional trend. Given this unpredictability, empirical use of co-trimoxazole for MRSA at this institution should be guided exclusively by current susceptibility data [17].

Table 1: Annual MRSA prevalence among clinical *Staphylococcus aureus* isolates, MGM Medical College and Hospital, Indore (2015–2025)

Year	Total <i>S. aureus</i> (n)	MRSA n (%)	MSSA n (%)
2015	205	99 (48.6)	106 (51.4)
2016	330	145 (43.8)	185 (56.2)
2017	284	118 (41.5)	166 (58.5)
2018	412	218 (53.0)	194 (47.0)
2019	310	166 (53.6)	144 (46.4)
2020	448	258 (57.7)	190 (42.3)
2021	550	326 (59.3)	224 (40.7)
2022	456	175 (38.4)	281 (61.6)
2023	438	273 (62.3)	165 (37.7)
2024	459	171 (37.2)	288 (62.8)
2025	504	236 (46.9)	268 (53.1)
Total	5,396	2,185 (40.5)	3,211 (59.5)

MRSA: methicillin-resistant *S. aureus*; MSSA: methicillin-sensitive *S. aureus*

Table 2: Year-wise antimicrobial susceptibility (%) of MRSA isolates, MGM Medical College and Hospital, Indore (2015–2025)

Year	Linezolid	Clindamycin	Ciprofloxacin	Gentamicin	Co-trimoxazole
2015	100	70	34.3	37.1	48.1
2016	99.6	56.4	46.6	74	57.7
2017	98.3	58	20.7	38.9	32.3
2018	86.5	66.5	21.5	51.5	30.3
2019	98	59	22.1	59	31.2
2020	92.2	64.8	63.3	70.8	40.6
2021	100	58	10.5	56.2	59.5
2022	91.5	58.5	26.8	63	68.5
2023	94.7	27.5	12.2	56.1	23.8
2024	96.5	64.3	11.3	57	64.3
2025	98	88.5	38.9	44.1	35.5

All values represent percentage susceptibility. Breakpoints per CLSI guidelines current at year of testing. D-zone test applied for clindamycin throughout.

Discussion:

This 10-year retrospective study documented the MRSA prevalence and antimicrobial susceptibility trends among 5,396 clinical *S. aureus* isolates processed at MGM Medical College and Hospital, Indore. The overall MRSA rate of 40.5% and its annual fluctuation between 37.2% and 62.3% are consistent with data from comparable tertiary care hospitals in India and confirm the substantial institutional burden of MRSA in central India [8, 9].

The temporal increase in MRSA prevalence between 2017 and 2021 likely reflects progressive colonisation pressure in the hospital environment, increasing acuity of admitted patients and possibly antibiotic selection pressure from escalating empirical broad-spectrum antibiotic use during that period. The period from 2019 to 2021 coincides with the COVID-19 pandemic, during which hospital infection control was substantially disrupted, antibiotic consumption increased considerably due to

empirical co-treatment of suspected bacterial co-infections and critically ill immunocompromised patients concentrated in ICUs provided favourable conditions for healthcare-associated MRSA transmission [18, 19]. The decline in 2022 likely reflects the reinforcement of contact precautions and hand hygiene that accompanied pandemic-era infection control initiatives, while the resurgence in 2023 suggests relaxation of those heightened measures. The consistently high linezolid susceptibility maintained over a decade of use at this centre is a clinically important and reassuring finding. The oxazolidinone class inhibits bacterial protein synthesis through a unique ribosomal binding mechanism, explaining the lack of cross-resistance with methicillin or fluoroquinolone resistance determinants [12, 13]. The lowest recorded linezolid susceptibility in this study was 86.5% in 2018, still well above the threshold at which empirical therapy would be unreliable. Emerging linezolid resistance in MRSA mediated by the *cfr* gene has been described globally but remains uncommon in India and no breakpoint failures were observed in a sustained manner in this series. The pervasive ciprofloxacin resistance documented here with susceptibility below 40% in nine of eleven years - is a consistent feature of healthcare-associated MRSA and reflects the co-localisation of fluoroquinolone resistance genes on staphylococcal chromosomal cassettes alongside *mecA*, as well as sustained selective pressure from the widespread use of fluoroquinolones in the region for respiratory, urinary and skin infections [14]. These data unequivocally support the exclusion of fluoroquinolones from empirical therapy for any infection where MRSA is a plausible cause. The marked but transient decline in clindamycin susceptibility in 2023 is among the most clinically significant findings of this study. The rapid recovery in 2024 and 2025 argues against a permanent clonal shift. The most probable explanation is a temporal concentration of isolates carrying constitutive *MLS_B* resistance (*erm* gene) coinciding with a change in the case mix *e.g.*, an increase in burns and trauma admissions from which such strains are more prevalent – compounded by stricter D-zone test reporting introduced in 2022. Irrespective of mechanism, the 2023 data reinforce that clindamycin susceptibility cannot be assumed and must be confirmed on current isolates before prescribing [15]. The variable susceptibility of gentamicin and co-trimoxazole reflects the heterogeneous resistance gene repertoire of circulating MRSA clones and the influence of antibiotic selection pressure on aminoglycoside- and trimethoprim-resistance gene carriage. Neither agent can be recommended empirically for MRSA; both require current susceptibility confirmation. Co-trimoxazole has been evaluated as an accessible oral alternative in resource-limited settings, but its utility at this institution is substantially curtailed by the unpredictability of its susceptibility over time [16, 17]. The principal limitation of this study is its single-centre retrospective design, which limits generalisability. Susceptibility data are pooled across all clinical departments and specimen types; departmental stratification (*e.g.*, ICU versus general ward) was not performed and inter-departmental differences in resistance profiles may exist. Molecular characterisation of MRSA clones and antibiotic consumption data were not

available, precluding mechanistic interpretation of observed trends. Notwithstanding these limitations, the large sample size and uninterrupted 10-year longitudinal scope provide a robust institutional evidence base for antibiotic stewardship decision-making.

Conclusion:

MRSA accounted for 40.5% of clinical *S. aureus* isolates, with substantial annual variation (37.2–62.3%) over the 10-year study period. Linezolid showed sustained high susceptibility (>85%), whereas pervasive ciprofloxacin resistance limits its empirical use for suspected MRSA infections. Routine antibiogram-guided therapy, strengthened antimicrobial stewardship and effective infection-control measures are essential to contain MRSA and preserve therapeutic options.

Declarations:

Ethical approval:

Approved by the Institutional Ethics Committee, MGM Medical College, Indore. Informed consent waived for anonymised retrospective audit data.

Conflict of interest:

The authors declare no conflict of interest.

Funding:

No external funding was received.

Data availability:

The compiled dataset is available from the corresponding author on reasonable request.

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