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Phenotypic and Genotypic Characterization of Methicillin-Resistant Staphylococcus Aureus (MRSA) among Health Care Workers

Anamta Fatama[1], Noor Jahan[2], Neeti Mishra[3]

[1]Author: Research Scholar, Integral University, Lucknow
[2]Co-Authors: Professor & HOD, Integral University, Lucknow,
[3]Professor & HOD, T. S Mishra University, Lucknow

Abstract

Methicillin-resistant Staphylococcus aureus (MRSA) continues to represent one of the most critical challenges in modern healthcare systems due to its ability to cause persistent infections and resist multiple antibiotics. Health care workers (HCWs) are recognized as important reservoirs and vectors for the transmission of MRSA within clinical environments. Accurate phenotypic and genotypic characterization of MRSA in this occupational group is essential to understand its prevalence, clonal distribution, and associated risks. Phenotypic methods, including selective culture media, antimicrobial susceptibility testing (AST), and confirmatory assays such as latex agglutination for PBP2a, provide frontline detection of MRSA. Meanwhile, molecular techniques target mecA/mecC genes, staphylococcal cassette chromosome mec (SCCmec) typing, spa typing, multilocus sequence typing (MLST), and whole genome sequencing (WGS) offer valuable insights into resistance mechanisms, virulence determinants, and epidemiological linkages. This review synthesizes evidence on the characterization of MRSA among HCWs, emphasizing prevalence trends, clonal dynamics, and the role of infection control measures. The discussion highlights significant gaps in global surveillance, particularly in low- and middle-income countries, and stresses the need for integrating genomic tools into routine practice. Overall, phenotypic and genotypic approaches complement each other in addressing MRSA control and guiding decolonization strategies in healthcare environments.

Keywords: Methicillin-Resistant Staphylococcus aureus (MRSA), health care workers, phenotypic characterization, genotypic characterization, SCCmec typing, antimicrobial resistance, infection control.

1. Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) has emerged as a major nosocomial pathogen since its first detection in the early 1960s. Originally confined to hospital-acquired strains (HA-MRSA), the pathogen has since diversified into community-associated MRSA (CA-MRSA) and livestock-associated MRSA (LA-MRSA), broadening its epidemiological footprint.[1] Its capacity for antibiotic resistance is primarily attributed to the acquisition of the mecA gene, which encodes an altered penicillin-binding protein (PBP2a) with reduced affinity for β-lactam antibiotics.[2]

The role of health care workers (HCWs) in MRSA epidemiology is of particular concern. Numerous studies have documented that HCWs, due to their frequent contact with patients and hospital environments, serve as asymptomatic carriers and potential transmitters of MRSA.[3] Carriage rates vary widely depending on geographical regions, healthcare settings, and screening methodologies, with estimates ranging from 1% to over 10% in some institutions.[4] Colonization in the anterior nares, hands, and occasionally the throat or skin, creates an ongoing risk of nosocomial outbreaks.

MRSA infections not only contribute to prolonged hospital stays and increased morbidity but also lead to significant economic burdens due to escalated treatment costs and infection control measures.[5] The accurate characterization of MRSA is therefore indispensable for designing targeted interventions. Phenotypic methods remain central for rapid detection and treatment guidance, whereas genotypic approaches provide deeper insights into clonal dynamics, virulence potential, and mechanisms of resistance.[6]

This review specifically focuses on the phenotypic and genotypic characterization of MRSA among healthcare workers. It seeks to (i) analyze conventional and advanced laboratory techniques for MRSA detection, (ii) evaluate epidemiological patterns among HCWs globally, (iii) review infection control and decolonization measures, and (iv) highlight knowledge gaps and future directions. By integrating laboratory and epidemiological perspectives, this review underscores the importance of comprehensive MRSA surveillance in protecting both patients and frontline healthcare providers.

2. Methods

This review employed a structured search strategy covering studies published between 2000 and 2024. Databases searched included PubMed, Scopus, and Web of Science. Keywords used were “MRSA,” “healthcare workers,” “phenotypic characterization,” “genotypic characterization,” “SCCmec,” and “colonization.” Articles were screened for relevance, and only studies reporting MRSA prevalence or characterization in HCWs were included.

i) Peer-reviewed original studies and reviews on MRSA in healthcare workers.
ii) Studies employing phenotypic and/or genotypic workflows for detection.
iii) Reports published in English.

Phenotypic workflows included selective media, antimicrobial susceptibility testing (AST), and confirmatory assays. Genotypic workflows included PCR detection of mecA/mecC, SCCmec typing, spa typing, Multilocus Sequence Typing (MLST), detection of Panton-Valentine Leukocidin (PVL) genes, and Whole Genome Sequencing (WGS). Extracted data covered prevalence, resistance determinants, clonal lineages, and infection control interventions.

3. Phenotypic Characterization

Phenotypic approaches form the frontline for MRSA detection in most clinical microbiology laboratories. These methods remain cost-effective, widely available, and indispensable for guiding initial therapeutic decisions. However, they must be interpreted cautiously due to their limitations in distinguishing borderline resistance and atypical strains.

3.1 Culture Media

Selective media play a crucial role in the isolation of MRSA from clinical and screening samples. Mannitol salt agar (MSA) has traditionally been employed for the primary isolation of S. aureus due to its high salt concentration, which inhibits most other bacteria.[7] More recently, chromogenic agar formulations have been developed that allow rapid and more specific detection of MRSA, often producing distinct colored colonies that can be differentiated within 24 hours.[8] These media, while convenient, may show reduced sensitivity for strains with atypical phenotypes.

3.2 Antimicrobial Susceptibility Testing (AST)

AST remains the cornerstone of MRSA identification. The Clinical and Laboratory Standards Institute (CLSI) recommends the cefoxitin disk diffusion test as the gold standard phenotypic marker for mecA-mediated resistance, as cefoxitin is a potent inducer of the mecA regulatory system.[9] Oxacillin disk diffusion and broth microdilution are also utilized but may yield ambiguous results in strains exhibiting heterogeneous resistance. Automated systems such as VITEK 2 and Phoenix allow rapid, high-throughput testing, though discrepancies with manual methods have been reported.[10] Minimum inhibitory concentration (MIC) determination by broth microdilution is considered the most precise phenotypic method. MRSA strains typically exhibit MICs ≥4 μg/mL for oxacillin or cefoxitin.[11]

3.3 Phenotypic Confirmatory Tests

Beyond disk diffusion and MIC methods, rapid confirmatory assays are increasingly deployed. The latex agglutination test for PBP2a, the protein encoded by mecA, provides a highly specific and quick alternative.[12] This test is particularly useful in cases of borderline resistance or discordant results between cefoxitin and oxacillin.

3.4 Quality Control in Phenotypic Testing

Standard quality control (QC) strains ensure reliability and reproducibility. The CLSI recommends S. aureus ATCC 25923 as the methicillin-susceptible control and S. aureus ATCC 43300 as the methicillin-resistant control.[13] Routine QC validation is essential, especially in resource-limited laboratories, where methodological errors can lead to under- or over-reporting of MRSA.

3.5 Limitations of Phenotypic Approaches

Despite their central role, phenotypic methods have limitations. Heteroresistant MRSA populations can yield inconsistent results, particularly with oxacillin.[14] Chromogenic agars, while rapid, may miss atypical strains. Automated systems may overcall or undercall resistance depending on algorithm updates. Hence, phenotypic characterization must often be supplemented with molecular confirmation for accurate epidemiological studies.

3.6 Clinical Significance

In clinical practice, phenotypic methods remain indispensable due to their accessibility and cost-effectiveness. They allow for timely therapeutic decisions and infection control interventions. However, their limitations underline the need for complementary genotypic methods to capture the full diversity of MRSA strains circulating among healthcare workers.[15]

4. Genotypic Characterization

While phenotypic methods remain central in frontline diagnostics, genotypic characterization provides more specific and reproducible insights into MRSA. These approaches help confirm resistance mechanisms, identify virulence factors, and trace the clonal relatedness of strains within and across healthcare facilities.

4.1 mecA and mecC Detection

The hallmark of MRSA resistance is the presence of the mecA gene, encoding penicillin-binding protein 2a (PBP2a). Polymerase chain reaction (PCR)-based detection of mecA remains the gold standard.[16] A variant gene, mecC, first identified in isolates from cattle and humans in 2011, has since been increasingly reported across Europe, though it remains relatively rare compared to mecA.[17] Real-time PCR assays allow for rapid and sensitive detection of both mecA and mecC, making them invaluable for hospital surveillance.

4.2 SCCmec Typing

Methicillin resistance in S. aureus is carried on the staphylococcal cassette chromosome mec (SCCmec), a mobile genetic element that integrates into the bacterial genome. Thirteen SCCmec types (I–XIII) have been described, with types I–III typically associated with hospital-acquired MRSA, while types IV and V are more common in community-associated strains.[18] SCCmec typing provides important epidemiological data to track the spread of clones within healthcare workers and patient populations.

4.3 SPA Typing and MLST

Single-locus spa typing, based on polymorphisms in the Staphylococcus aureus protein A (spa) gene, offers a rapid and cost-effective method for subtyping MRSA isolates.[19] In parallel, multilocus sequence typing (MLST) examines allelic variation in seven housekeeping genes to define clonal complexes (CCs).[20] Both approaches are widely used in epidemiological surveillance to characterize dominant MRSA lineages circulating among HCWs, such as CC22 (EMRSA-15) and CC5.

4.4 Panton-Valentine Leukocidin (PVL)

PVL, encoded by lukF-PV and lukS-PV genes, is a cytotoxin linked to skin and soft tissue infections and necrotizing pneumonia.[21] While traditionally associated with community strains, PVL-positive MRSA has been increasingly reported in hospital environments, raising concerns about its potential introduction into healthcare settings by colonized HCWs.[22]

4.5 Whole Genome Sequencing (WGS)

Whole genome sequencing provides the highest resolution for characterizing MRSA isolates. WGS can detect resistance genes, virulence determinants, and single nucleotide polymorphisms (SNPs) useful in outbreak investigation.[23] It has been employed to identify transmission chains between HCWs and patients, highlighting its power in infection control.[24] However, high costs and bioinformatics infrastructure requirements remain barriers for routine use in low-resource settings.

Genotypic methods, therefore, complement phenotypic approaches, ensuring robust MRSA surveillance in healthcare environments.

5. Epidemiology in Healthcare Workers

5.1 Prevalence

MRSA colonization among HCWs varies significantly by geographic region. In Europe and North America, prevalence typically ranges between 2–6%, whereas in some Asian and African countries, rates exceeding 10% have been documented.[25] Prevalence is influenced by hospital type, patient load, and infection control practices.

5.2 Risk Factors

Key risk factors include frequent contact with MRSA-positive patients, inadequate hand hygiene compliance, chronic skin conditions, and prolonged antibiotic exposure.[26] Nurses and intensive care unit staff are reported to be at higher risk due to their intensive patient interaction.[27]

5.3 Clonal Lineages

Molecular epidemiology has identified dominant MRSA lineages among HCWs. In Europe, CC22-MRSA-IV (EMRSA-15) remains prevalent, while in Asia, CC239-MRSA-III is a dominant clone.[28] The spread of CA-MRSA clones, such as ST8 (USA300), into healthcare environments has been increasingly observed.[29] These trends highlight the role of HCWs in bridging community and hospital reservoirs.

5.4 Asymptomatic Colonization vs. Infection

Most HCWs remain asymptomatic carriers, harboring MRSA in the anterior nares or on the skin.[30] However, they may still act as vectors, facilitating outbreaks in vulnerable patient populations. Symptomatic infections among HCWs are relatively rare but carry occupational and ethical implications.

5.5 Trends over Time

Longitudinal studies show a general decline in MRSA prevalence among HCWs in high-income countries due to stringent infection control policies.[31] Conversely, data from low- and middle-income countries suggest rising prevalence, likely reflecting inadequate surveillance and control measures.

6. Infection Control and Decolonization

6.1 Standard Precautions

Universal hand hygiene remains the cornerstone of MRSA control. Alcohol-based hand rubs and personal protective equipment (PPE) significantly reduces transmission risk.

6.2 Screening and Surveillance

The role of routine screening of HCWs is debated. Some hospitals restrict screening to outbreak scenarios, while others advocate for proactive surveillance in high-risk departments. Cost-benefit considerations often shape institutional policy.

6.3 Decolonization Protocols

Decolonization regimens commonly include intranasal mupirocin ointment and chlorhexidine body washes.[35] While effective in the short term, resistance to mupirocin and reduced chlorhexidine susceptibility are emerging challenges.

6.4 Institutional Policies and Outcomes

Hospitals implementing comprehensive infection control policies—encompassing hand hygiene audits, targeted HCW decolonization, and patient isolation—have reported significant reductions in MRSA transmission.[32] However, ethical issues arise regarding confidentiality and the stigmatization of colonized HCWs.

7. Knowledge Gaps and Future Work

Despite progress, important gaps remain:

A. Limited epidemiological data from low- and middle-income countries.
B. Underrepresentation of genotypic diversity among HCWs in surveillance programs.
C. Rising concerns about resistance to decolonization agents such as mupirocin.
D. Lack of integration of WGS into routine HCW screening.

Future research should prioritize longitudinal cohort studies, expand global genomic databases, and develop cost-effective rapid diagnostic platforms for use in resource-limited healthcare systems.

8. Limitations

This review has certain limitations. First, most data are derived from published studies, potentially leading to publication bias, as outbreaks are more likely to be reported.[40] Second, heterogeneity in study methodologies, including different phenotypic and genotypic techniques, complicates cross-comparisons. Third, regional gaps persist, particularly in Africa and South Asia, where surveillance data are scarce. Lastly, the review focused primarily on English-language studies, introducing possible language bias.

9. Conclusions

MRSA colonization among healthcare workers continues to pose a significant challenge for hospital infection control. Phenotypic methods remain crucial for frontline detection, while genotypic methods provide deep insights into clonal dynamics and resistance mechanisms. Together, they form a complementary toolkit for surveillance and outbreak management. HCWs act as important reservoirs of MRSA, bridging community and hospital settings. Effective infection control strategies, including targeted decolonization, remain essential, though their long-term sustainability is threatened by emerging resistance. Future integration of genomic surveillance and global collaborative research will be vital in curbing MRSA transmission and safeguarding both patient and occupational health.

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