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For whom the bell tolls? Methicillin-resistant *Staphylococcus aureus* infections in India

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ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the common causes of infections in the contemporary era and a major contributor to hospital- and community-acquired infections. The repeated formation of epidemic strains is the main characteristic of epidemiology, despite its genetic diversity. The global and Indian prevalence varied from 13%–74% and 37%, respectively. Most clones independently acquire the staphylococcal cassette chromosome (SCCmec), which comprises genes encoding proteins that cause resistance to most β-lactam antibiotics. SCCmec types I, II, or III are found in most HA-MRSA strains, whereas SCCmec types IV or V are found in CA-MRSA. The major clone present in Indian hospitals is ST772-MRSA-V. These strains produce a vast array of virulence factors, including panton-valentine leucocidin toxins, and when paired with β-lactamase enzymes, most clones show high resistance to different antibiotic classes. Global mortality ranges between 15% and 60% and India witnessed less than 27% mortality. Treatment costs range from $3,220 to $9,388 globally, with an estimated $124 ($45–484) per patient cost in India. The evaluation of novel antibiotics and ancillary services (e.g., source control, and infectious disease consultation) is necessary for effective therapy, which is still difficult to achieve. This review summarizes the epidemiology, transmission, genetic diversity, surveillance, and management of MRSA from an Indian perspective.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA), a Gram-positive bacteria (GPB), is at the forefront of the current worldwide health crisis of antimicrobial resistance (AMR) (Prestinaci *et al*., 2015). The spread of MRSA from hospital to community settings, together with increasing resistance to non-β-lactam antibiotics, has precipitated the crisis (Lohan *et al*., 2021). Methicillin resistance in *S. aureus* was encountered soon after methicillin was approved for clinical use against penicillinase-producing *S. aureus* in 1961. Subsequently, MRSA was encountered in Australia, Europe, the United States (US), and Japan (Udo, 2013). The global prevalence of MRSA is difficult to determine, whereas national surveillance data and publications from all World Health Organization (WHO) regions reported a prevalence ranging from 0% to 100%: African Region (0%–100%), Region of America (21%–90%), Eastern Mediterranean region (10%–53%), European region (0.3%–55%), South-east Asia region (10%–26%), Western Pacific region (4%–70%) (Hassoun *et al*., 2017; Prestinaci *et al*., 2015; Wangai *et al*., 2019). One report from India showed the prevalence ranging between 13% and 74% in different parts of the world (Pradhan *et al*., 2021). MRSA is one of the most common causes of surgical site infections in tertiary care hospitals in North America, accounting for more than 60% of all infections in these units (Chatterjee *et al*., 2018). MRSA is a common emerging pathogen in India, with an overall prevalence rate ranging from 26% to 59% and 13% to 47% in intensive care units (ICUs) (Mehta *et al*., 2020; Taneja and Sharma, 2019). A systematic review and a meta-analysis reported a 37% overall prevalence of MRSA (2015 to 2019) in India. State-by-

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state stratified results of MRSA prevalence varied from 55% in Jammu & Kashmir to 21% in Maharashtra (Fig. 1) (Patil *et al*., 2022).

MRSA is linked to significant morbidity and mortality, in addition to significant economic and societal costs, underlining the importance of accurate surveillance. MRSA infects the skin, soft tissues, bone, and joints, urinary tract in addition to triggering metastatic infections such as septic arthritis, infective endocarditis (IE), osteomyelitis, and device-associated infections associated with prosthetic devices and indwelling catheters (Tong *et al*., 2015). MRSA is a leading cause of bacteremia in developed nations, potentially leading to complications such as sepsis and septic shock (Hassoun *et al*., 2017; Kwiecinski and Horswill, 2020). Due to the more frequent use of different urinary catheters such as indwelling or condom catheters in debilitated patients, the incidence of urinary tract infection (UTI) caused by MRSA is rising globally. A multicentric study from India showed 55% of MRSA were isolated from urine samples (Mendem *et al*., 2016; Mitiku *et al*., 2021). In the pre-antibiotic period, *S. aureus* bacteremia faced more than 80% mortality. Despite the discovery of penicillin G, improving the prognosis substantially in the early 1940s, resistant strains were identified as early as 1942 (Peacock and Paterson, 2015). MRSA is associated with poorer clinical outcomes than methicillin-sensitive *S. aureus* (MSSA) (van Hal *et al*., 2012). WHO reported that MRSA infections are 64% more likely to kill than drug-sensitive infections. A systematic review and meta-analysis showed that the societal cost for one case of community-acquired (CA) MRSA from the Asia-Pacific region was estimated to be $7,070–$20,489 (Wong *et al*., 2018).

Implementing an effective treatment for MRSA infections requires identifying the pathogen. Diagnostic and treatment delays adversely impact clinical outcomes. While standard techniques for microbial identification take 48 to 72 hours, newer rapid diagnostic tests provide results in 3 hours, enabling optimized antimicrobial therapy, and thereby reducing mortality, hospitalization, and healthcare costs (Bauer *et al*., 2010; Palavecino, 2014).

This review outlines epidemiological trends and factors affecting the incidence of MRSA infections, resistance patterns, current diagnostic tools, treatments, prevention strategies, and associated healthcare costs in India.

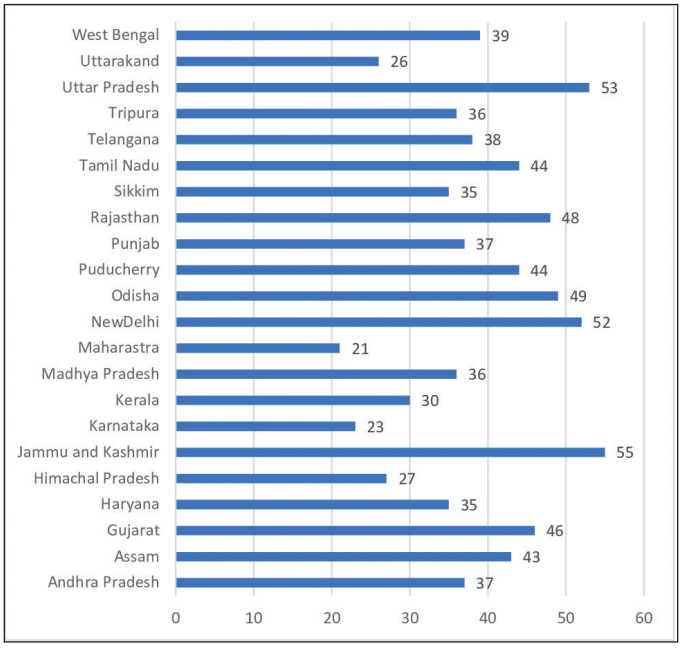

Figure 1. Prevalence of *MRSA* (%) from different states of India between 2015 and 2020.

EPIDEMIOLOGY

Carrier status

MRSA can colonize the normal body flora, particularly in the nose, axillae, anomalous skin (eczema, wounds), urine, rectum, and throat, and act as a reservoir. MRSA can infect, particularly those undergoing prolonged hospitalization in a high-risk unit (critical care, renal unit, etc.) or suffering from underlying diseases, or after antibiotic use. MRSA can colonize the body following trauma, wounds, surgical incisions, and indwelling medical devices (Bradley, 2015). Cutaneous and nasal colonization of MRSA is estimated to be around 7% in US hospitals. Numerous reports suggest that the prevalence of MRSA nasal carriage among healthcare workers (HCWs) was between 5.5% and 34%. (Goes *et al*., 2021). Contact transmission from HCWs to patients is the chief mode of MRSA transmission. Prevalence of MRSA nasal carriers ranges from 1% to 52.3% including children as per multiple reports from India. The highest incidence of MRSA nasal carrier was reported in Brazil, at 74.6% (Chatterjee *et al*., 2009; George *et al*., 2016; Goes *et al*., 2021). A study from India reported the overall prevalence of MRSA carriers among healthcare professionals as 6.5% of whom 28.4%, 21.1%, 9%, and 5.4%, and, 37.5% were physicians, nursing interns, MBBS interns, nurses (5.4%), and others (physiotherapist, housekeeping staff, and helping staff), respectively (Deepashree *et al*., 2021). Another Indian study found that the overall MRSA transmission rate among HCWs who worked with critically ill patients was only 2.5% with female housekeeping staff (13.3%) accounting for the majority of the cases, followed by female nursing staff (2.7%), much lower than the 4.6% identified in a global meta-analysis (Radhakrishna *et al*., 2013). Although the colonized patient (or staff member) does not require treatment, a course of decolonization therapy (e.g., povidone Iodine, chlorhexidine-neomycin nasal cream, mupirocin nasal ointment, and systemic antibiotics) may be administered to eradicate carriage and prevent future infections (Lepelletier *et al*., 2020).

The overall global (reported in 2010) and Indian prevalence between (2015 and 2019) was found to be 13%–74% and 37%, respectively (Patil *et al*., 2022; Pradhan *et al*., 2021).

MRSA is commonly classified as either Hospital (HA) or CA. HA-MRSA generally manifests as a nosocomial infection, often acquired during a surgical or invasive medical procedure when a hospital length of stay (LOS) is more than 48 hours. CA-MRSA is found in people who have not recently been hospitalized or had contact with the healthcare system or those who underwent less than 48 hours of hospitalization

(Sutton and Steiner, 2016). The phenotypic and genotypic differences between CA-MRSA and HA-MRSA are represented in Table 1 (Bukharie, 2010; George *et al*., 2016).

MRSA used to be primarily restricted to hospitals but has dramatically increased its spread among people without risk factors or healthcare exposure. Discovery of novel MRSA strains (CA-MRSA), over the last decade has been linked to the spread. CA-MRSA strains appear to have spread swiftly among the general population around the world, affecting people with and without healthcare exposure (Lohan *et al*., 2021). India currently reports 3.89% to 74% of CA-MRSA isolates (Chatterjee *et al*., 2018; Joshi *et al*., 2013). A systematic review and meta-analysis showed that the global pooled prevalence of CA-MRSA and HA-MRSA ranged from 0% to 23.5% and 0.7% to 10.4%, respectively, with maximum prevalence in India (16.5% to 23.5%) (Wong *et al*., 2018). A study from Finland showed the overall prevalence of CA-MRSA and HA-MRSA as 32% and 68%, respectively (Junnila *et al*., 2020). Figures 2a and b depict the overall prevalence of CA-MRSA and HA-MRSA across different states of India and countries.

Risk factors

The most frequently associated risk factors for MRSA infection are prolonged hospitalization, ICUs, recent hospitalization, admission to nursing homes, co-morbidities, recent antibiotic use, MRSA colonization in HCWs or patient parties, invasive procedures, HIV infection, hemodialysis, open wounds, and discharge with long-term central venous catheters or indwelling urinary catheter (Lee *et al*., 2018).

Table 1. Phenotypic and genotypic differences between CA-MRSA and HA-MRSA.

CA-MRSA	HA-MRSA
Acquired outside health care systems or had less than 48 contact hours of hospitalization	acquired during a surgical or invasive medical procedure while in the hospital for more than 48 hours.
Resistant to all β-lactam antibiotics but susceptible to narrow-spectrum non-β-lactams such as clindamycin, TMP-SMX, and tetracyclines	Generally, multiresistant to almost all antibiotics such as FQ's, aminoglycosides, vancomycin
Strains carry *SCCmec* types IV and V and VI	carry *SCCmec* types I to III
Presence of small *SCCmec* IV allele allowing to thrive and spread readily outside the hospital environment	strains require the hospital milieu for sustained survival
Carry genes for *PVL*, an exotoxin lethal to leukocytes	Absence of such genes
Necrotizing pneumonia and necrotizing fasciitis, appears to be more common	Less common but mostly infect bloodstream and respiratory tracts
Infects healthy, mostly young hosts, without any underlying co-morbidities	Considered as an opportunistic infection

CA-MRSA = Community-acquired methicillin-resistant *S. aureus*; HA-MRSA = Hospital-acquired methicillin-resistant *S. aureus*; TMP-SMX = Trimethoprim-Sulfamethoxazole; SCC = Staphylococcal cassette chromosome; PVL = Panton-Valentine Leucocidin; FQ's = Fluoroquinolones.

Although growing older is not considered a risk factor in and of itself for MRSA infection, elderly people (>65 years) are at substantial risk for hospitalization, implying an indirect link between advancing age and MRSA infection. A major risk factor for MRSA colonization includes living in a high prevalence zone of CA-MRSA or admission to a hospital with a high incidence of HA-MRSA (National Nosocomial Infections Surveillance System, 2004). Numerous studies have shown that risk factors for MRSA infection differ around the globe. An Indian study reported that prolonged hospitalization, surgery, recent hospitalization, presence of a tracheostomy tube, and pressure/venous ulcer were significant independent risk factors for MRSA infection in hospitalized patients (Thimmappa *et al*., 2021). *Staphylococcus aureus* is still the most prevalent bacterium that infects wounds, and surgery increases the risk of infection. Patients with open fractures are more likely to be infected than those with closed fractures or open injuries (Zalavras, 2017).

Molecular characterization of MRSA

Methicillin resistance in clinical isolates entails detecting a methicillin-hydrolyzing-lactamase and mecA-encoded protein-binding protein2a (PBP2a), which reduces the penicillin-binding affinity and increases the rate of release from the bound drug (Stapleton and Taylor, 2002).

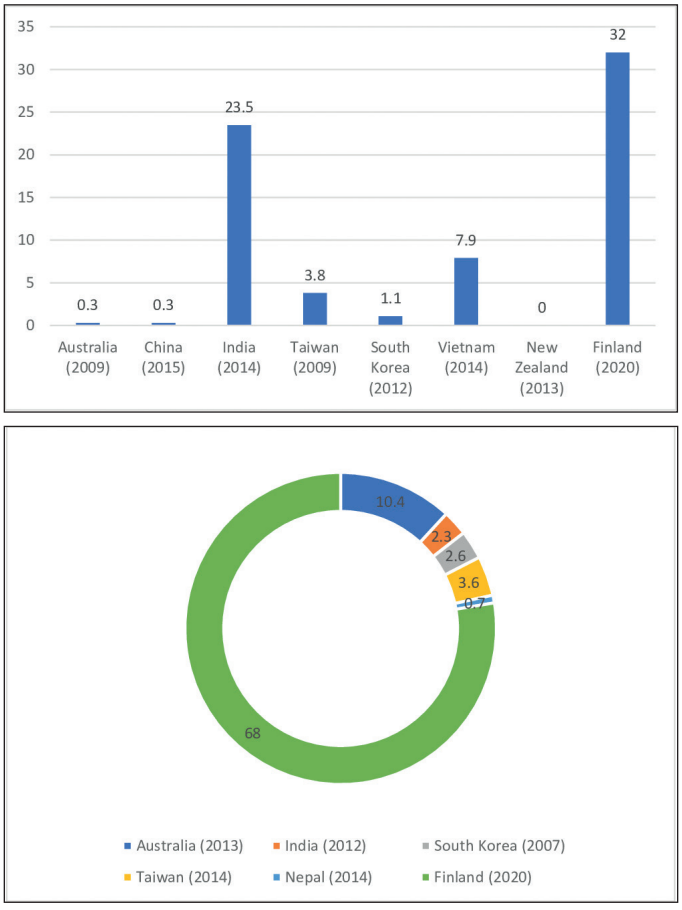

Figure 2. (a) Prevalence of *CA-MRSA* (%) from different studies across the globe. (b) Prevalence of *HA-MRSA* (%) from different studies across the globe.

The acquisition of the mecA gene, which is carried by a mobile genetic element called the staphylococcal cassette chromosome (SCCmec), confers methicillin resistance. According to the International Working Group on the classification of staphylococcal cassette chromosome elements, there are currently **13** recognized SCCmec types (I–XIII), based on the combinations of five mec complexes (A, B, C1, C2, and E) (Urushibara *et al*., 2020). SCCmec types I, II, or III are found in the majority of HA-MRSA strains, whereas SCCmec types IV or V are found in CA-MRSA. Among the mecA-positive strains isolated from Mumbai (2010), 25% were SCCmec III and all were multidrug-resistant (MDR) strains. Others were SCCmec IV and SCCmec V with 34% and 41%, respectively. Seventy-five percent of the strains were susceptible to antimicrobials. The multidrug susceptibility of strains with SCCmec IV and SCCmec V demonstrates the susceptible nature of CA-MRSA. Multiple Asian studies using multilocus sequence typing (MLST) showed clonal expansion of multidrug-susceptible sequence type (ST) 22 (SCCmec IV) and ST 772 (SCCmec V), which may be slowly replacing the multidrug-resistant ST 239 (SCCmec III) in hospitals (D'Souza *et al*., 2010). HA-MRSA has larger SCCmec types than CA-MRSA, which confers resistance to more non-β-lactam antibiotics. Consequently, CA-MRSA is sensitive to a wider variety of antibiotics than HA-MRSA (Loewen *et al*., 2017). In addition, Panton-Valentine Leucocidin (PVL) is a pore-forming toxin encoded by the lukSF-PV genes that encode a potent cytotoxin that is mainly found in CA-MRSA. USA300 is the most common PVL-positive clone in the US. USA300 is an MRSA clone within (MLST) clonal complex 8 that harbors the PVL genes. The prevalence of PVL-positive clones from 2004 to 2008 ranges between 16% and 40% (Brown *et al*., 2012). At present, there are no USA300 clones reported from India. There are very few studies on genotyping MRSA strains from India. The worldwide distribution of PVL among MRSA isolates varies. Kaur *et al*. (2012), Bouchiat *et al*. (2015), and D'souza *et al*. (2010) from India reported the highest prevalence of 85.1%, 68.8%, and 64%, respectively, of PVL-positive clones (Bouchiat *et al*., 2015; D'Souza *et al*., 2010; Kaur *et al*., 2012). Another Indian study found that the PVL gene was present in 70% and 7.8% of CA-MRSA and HA-MRSA, respectively (Preeja *et al*., 2021). The prevalence of PVL-positive clones from different countries is shown in Figure 3 (Afroz *et al*., 2008; Brown *et al*., 2012; Darboe *et al*., 2019; Holmes *et al*., 2005; Lina *et al*., 1999; Moussa and Shibl, 2009).

The major clone of MRSA present in Indian hospitals is ST772-MRSA-V (also called Bengal Bay clone). Originally identified in India, ST772 is noted for its global distribution. Complete genome sequencing showed that ST772 carried several toxin genes such as PVL, staphylococcal enterotoxin (sea) genes, and β-haemolysin (hlb). When compared to prophage-cured strains, virulence studies revealed that ST772 strains induce substantial neutrophil proliferation and cytotoxicity, implying that a novel prophage may contribute to ST772 virulence (Blomfeldt *et al*., 2017; Sunagar *et al*., 2016). Furthermore, there was a complex relationship between the distribution of virulence genes and the source and location of isolation. For instance, a study from India showed that 84% of

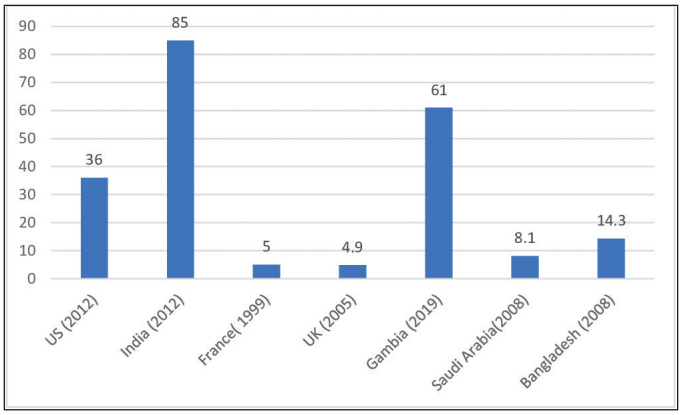

Figure 3. Prevalence (%) of PVL-positive clones from different countries.

MRSA strains isolated from patients with pharyngitis carried the pathogenic gene icaADBC. The same study also found that icaA/icaD-positive MRSA and MSSA were isolated from wound and ocular infections, respectively (Gowrishankar *et al*., 2016). The MRSA ST239 clone, another significant HA infection (HAI)-causing clone discovered in India, exhibits a range of global resistances and susceptibilities to mupirocin, aminoglycosides, and trimethoprim-sulphamethoxazole (TMP-SMX). Despite the large number of genotypes that exist, comparative genomic investigations have revealed that epidemic strains of MRSA seem to be constrained to specific genotypes, some of which are also geographically restricted (Sunagar *et al*., 2016). There is a dearth of information on MRSA ST239 from India, with a significant MRSA prevalence. According to a study conducted in India, ST 239 primarily contained SCCmec V (50%), followed by SCCmec III (32%), SCCmec I (16%), and SCCmec IV (2%) (Abimanyu *et al*., 2012).

DIAGNOSTIC METHODS

Detection of the mecA gene by polymerase chain reaction (PCR) is currently the gold standard test for detecting MRSA. Additionally, Food and drug administration (FDA)-approved assays for molecular identification of the mecA gene and commercially accessible chromogenic agars for MRSA detection are available. Finally, MRSA can be detected via latex agglutination or immunochromatographic membrane testing for PBP2a. Clinical and Laboratory Standards Institute (CLSI) recommends the oxacillin disc diffusion (ODD) test, oxacillin screen agar [mannitol salt agar (MSA)],, and cefoxitin disc diffusion (CDD) test to detect methicillin resistance by phenotypic approaches. CHROMagar (color-based differentiation method), another phenotypic method, uses a chromogenic medium for identifying MRSA. Cefoxitin induces mec-A gene expression more powerfully than other compounds. Because of its extended shelf life, oxacillin is chosen over methicillin (Alipour *et al*., 2014; Kali *et al*., 2014; Lohan *et al*., 2021). Studies have been compared for different parameters like speed, cost of treatment, sensitivity, and specificity with PCR for the mecA gene. A study from India found that the ODD method had a sensitivity and specificity of 93.5% and 83.5%, respectively whereas MSA with the oxacillin

method had a sensitivity and specificity of 87.1% and 89.3% respectively (Pillai *et al*., 2012). A study from Iran, comparing different MRSA detection methods found that the sensitivity and specificity, of the Antimicrobial susceptibility testing (AST) (ODD) method, were lesser than the CDD method and PCR (Table 2) (Pourmand *et al*., 2014). PCR, on the other hand, was found to be faster and less expensive than other procedures. For instance, the sensitivity of "*n*%" indicates among N true positives, only "*n*" will be diagnosed as positives and the remaining "*N-n*" will be misdiagnosed. Misdiagnosing MRSA isolates is unacceptable since the treatment pattern changes. Instead of getting vancomycin, the patient will be recommended another line of treatment for MSSA, compromising the cure rate. That MRSA would have spread to other patients or HCWs by this time is much more disconcerting. Finally, vancomycin will be forced upon the patient, raising the cost of therapy, culminating in the spread of MRSA in both the hospital and the community. Thus costs of a misdiagnosis (missing MRSA) will be significantly greater than the cost of PCR (Pillai *et al*., 2012).

A study from Malaysia developed a unique approach termed monoplex PCR assay for the identification of the non-protein-coding RNA gene (Sau-02) in MRSA, which displayed good sensitivity and specificity (Soo Yean *et al*., 2016).

Susceptibility pattern of MRSA

Methicillin resistance in *S. aureus* is defined as an oxacillin minimum inhibitory concentration (MIC) of ≥4 µg/ml based on antibiotic susceptibilities (Siddiqui and Koirala, 2023). Except for glycopeptide drugs, most MRSA strains are resistant to multiple antibiotics including methicillin, amikacin, tobramycin, gentamicin, ciprofloxacin, norfloxacin, tetracycline, erythromycin, TMP-SMX, and cefoperazone/sulbactam.

Antibiotic sensitivity profiles can be used to categorize MRSA as either healthcare-associated or community-associated. Macrolide–lincosamide–streptogramin B (MLSB) antibiotics such as clindamycin susceptibility, for example, has a 95% sensitivity, 80% specificity, and a likelihood ratio of 4.86 in predicting CA-MRSA. Isolates resistant to three or more non-β-lactam antibiotics are categorized as HA-MRSA (Loewen *et al*., 2017). Resistance to MSLB antibiotics can be either constitutive (cMLSB) or inducible (iMLSB). The cMLSB resistance mechanism is mediated via msrA genes, i.e., efflux of antibiotics in which *S. aureus* strains are resistant to erythromycin but sensitive to clindamycin, both *in vitro* and *in vivo*. The constitutively resistant strains do not develop clindamycin resistance during the therapy. The iMLSB-resistant isolates show resistance against erythromycin but are susceptible to clindamycin. iMLSB resistance develops in the presence of a powerful methylase enzyme inducer like erythromycin. The erm genes encode enzymes that confer inducible or constitutive resistance to MLSB agents by methylating the 23S ribosomal RNA, thereby lowering Macrolide–lincosamide–streptogramin agent binding to the ribosome (Sasirekha *et al*., 2014). Unlike cMLSB resistance, iMLSB resistance cannot be detected by standard susceptibility testing. The inducible clindamycin resistance can be detected by the D-zone test (D-shaped distorted inhibition zone around clindamycin under the *in-vitro* effect of erythromycin) (Fig. 4). iMLSB resistance should be determined for the effective management of *S. aureus*, without which, the administration of clindamycin may result in treatment failure from the emergence of constitutive resistance (Thapa *et al*., 2021). Previous studies (cross-sectional investigations) from India have shown that the prevalence of iMLSB among *S. aureus* ranges between (7% and 94%) (Patel *et al*., 2006).

Vancomycin was first employed as an empirical therapy for nosocomial sepsis in the 1980s, due to the high incidence of MRSA. Vancomycin use in the US increased in the early 1990s because of the growing incidence of coagulase-negative staphylococci (CoNS) infections and clostridium difficile in healthcare institutions (Rubinstein and Keynan, 2014). Consequently, selection pressure mounted, resulting in the establishment of *S. aureus* and other staphylococci strains with increased resistance to vancomycin and other glycopeptides (Szymanek-Majchrzak *et al*., 2018). In 1997, Japan reported the first *S. aureus* strain non-susceptible to vancomycin and teicoplanin, followed by the US in 2002 (Howden *et al*., 2010; Spagnolo *et al*., 2014). Tiwari and Sen (2006) reported the first instance of Vancomycin-resistant *S. aureus*/Vancomycin-resistant *S. aureus* (VRSA/VISA) in India in 2006, despite the absence of the vanA/vanB gene. Therefore, the absence of vanA/vanB genes in these isolates does not rule out the

Table 2. Sensitivity and specificity of different methods used in the detection of *MRSA*.

Author's	Method	Specificity	Sensitivity	Accuracy	PPV	NPV	Time taken	Cost of treatment
Pillai *et al*. (2012)	*PCR*	100	100	100	100	100	18 hours	1,389,650
	ODD/AST	94	84	87	77	96	48 hours	1,401,000
	Oxacillin-MSA	87	89	89	83	92	48 hours	1,122,000
Lohan *et al*. (2021)	CDD	100	100	-	-	-	-	-
	ODD/AST	100	90	-	-	-	-	-
	Oxacillin-MSA	100	96.3	-	-	-	-	-
Pourmand *et al*. (2014)	CDD	100	100	-	100	100	-	-
	ODD	100	80	-	100	83	-	-
	Oxacillin strip	100	92	-	100	92	-	-

All values are expressed in percent. ODD = Oxacillin disc diffusion method; AST = Antimicrobial susceptible testing; MSA = Mannitol salt agar; PPV = Positive predictive value; NPV = Negative predictive value.

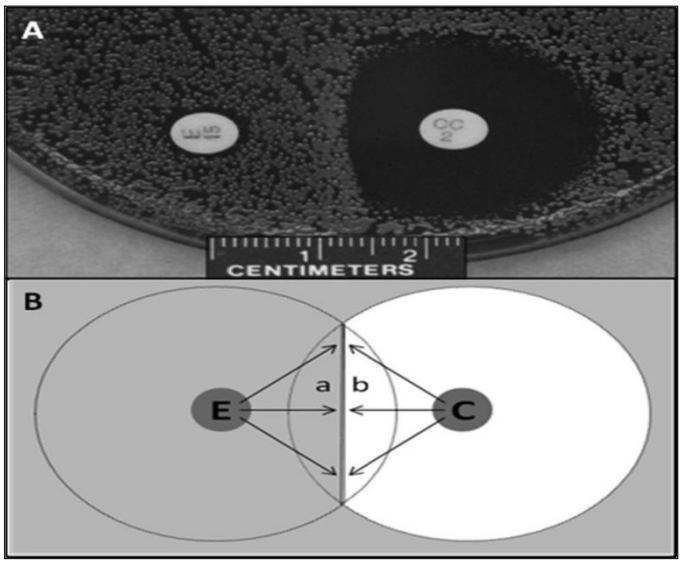

Figure 4. A positive *D*-test. A positive *D*-shaped inhibitory zone is visible around clindamycin in Figure A. The left and right discs are for erythromycin and clindamycin, respectively. The projected O-shaped clindamycin zone of growth inhibition in all negative *D*-test is blunted on the side that faces the erythromycin disc, resulting in a *D*-shaped zone.

Figure B is a stylized representation of the *D*-test. Erythromycin molecules diffuse into the area of the clindamycin zone denoted "a" prior to clindamycin molecules, triggering the methylase, granting resistance, and permitting microbiological growth despite the arrival of clindamycin concentrations that would otherwise be inhibitory. Before erythromycin molecules can get there to cause resistance, quantities of clindamycin that impede growth get to the area marked "b." Gray areas represent microbial growth on the agar surface. White areas denote growth inhibition; E stands for the erythromycin disc; C stands for the clindamycin disc. The image is adapted from the study by Charles *et al*. (2009).

possibility of vancomycin resistance. Vancomycin resistance in GPB was thought to be rare until recently, but vancomycin resistance in *S. aureus*, CoNS, and *Enterococcus* spp., has been reported across the globe. Before 2010, and between 2010 and 2019, the global distribution of VRSA was reported to be 1.2% and 2%, respectively (Fig. 4) (Shariati *et al*., 2020).

Table 3 provides the susceptibility data from various parts of India resistance patterns of CA-MRSA and HA-MRSA have been combined because most studies do not report them separately. Various Indian investigations found that MRSA is responsive to last-resort antibiotics like linezolid and teicoplanin. Vancomycin and doxycycline are still effective in treating MRSA infections in Indian clinical settings.

SUPERINFECTION WITH MRSA IN COVID-19 INDIVIDUALS

Hospitalized patients with COVID-19 frequently develop acute pneumonia and other life-threatening conditions. There is considerable variation in methodologies and outcomes between research, which may contribute to the elusiveness of the precise burden of MRSA pulmonary infection in individuals with COVID-19. Frequent use of vancomycin (one of the last resorts) as an empirical therapy, has raised concerns over the efficacy of vancomycin against MRSA for the past decade (Punjabi *et al*., 2020). In relation to research revealing the prevalence of MRSA lung infection along with other complications A study from the US reported patients with COVID-19 superinfected with MRSA (45%) who had pneumonia also developed additional serious illnesses such as bacteremia in 19% of cases, and 30-day mortality of 67%. The most commonly used empiric therapy was the vancomycin-cefepime combination (Cusumano *et al*., 2020). The WHO "Watch list of antibiotics" for 2019 includes agents like vancomycin as critical stewardship priorities (Punjabi *et al*.,

Table 3. Resistance pattern of *MRSA* from different Indian studies.

Author's	Place	*T*	*L*	Ri	Tet	CL	Dox	Van	Cef	Cip	TS	Net	Ami	Gen	Cli	Ery	Oxa/ Cefox	*p*
D'souza *et al*. (2010)	Maharastra	-	-	55	92	30	-	-	-	98	-	95	89	98	95	98	-	-
Joshi *et al*. (2013)	Multicentric	-	0	-	-	-	-	0	-	64	30	-	-	31	21	48	-	-
Kali *et al*. (2014)	Pondicherry	-	-	-	-	-	-	-	-	81	85	-	-	66	-	-	-	-
Chadha *et al*. (2014)	Kerala	-	-	7	86	-	-	0	-	69	76	18	24	93	68	94	-	-
Kaur *et al*. (2015)	Maharastra	0	3	28	-	-	-	0	0	100	25	-	-	100	97	100	100	-
Abbas *et al*. (2015)	Rajasthan	16	-	-	-	-	-	-	-	55	32	-	-	46	47	63	-	-
Neetu and Murugan (2016)	Tamil Nadu	-	0	0	100	76	-	0	-	100	100	-	-	100	76	-	100	79
Bhattacharya *et al*. (2016)	West Bengal	-	0	-	-	-	28	1	-	24	72	36	-	82	43	-	100	-
Gosh and Banerjee (2016)	West Bengal	-	0	-	-	-	-	0	-	91	55	-	-	-	55	82	100	-
Pal *et al*. (2019)	Uttarkand	0	0	0	-	-	-	0	82	44	27	-	15	47	36	50	100	91
Kaur *et al*. (2020)	Punjab	0	0	13	-	-	19	0	-	63	-	-	33	43	43	-	-	-
Preeja *et al*. (2021)	Karnataka	-	0	11	12	4	6	0	44	86	28	2.5	0	41	41	67	100	100
Lohan *et al*. (2021)	Haryana	12	7	-	-	-	-	12	-	59	53	-	-	47	66	77	-	100

T = Teicoplanin, L = Linezolid, Ri = Rifampin, Tet = Teracycline, CL = Chloramphenicol, Dox = Doxycycline, Van = Vancomycin, Cef = Ceftaroline, Cip = Ciprofloxacin, TS = Co-trimoxazole, Net = Netilmicin, Ami = Amikacin, Gen = Gentamicin, Cli = Clindamycin, Ery = Erythromycin, Oxa/Cefo = Oxacillin/Cefoxitin, P = Peniicllin, - = antibiotics not tested in the study.

2020). There is a severe lack of information on bacterial secondary infections in India, and only a very small number of studies—out of hundreds—report secondary infections, and even those do not provide specific information on the pathogens that caused the infections, or their drug susceptibility profiles. The fact that almost all of the studies are from various Asian countries, such as China, may restrict the generalizability of the conclusions. There are no studies that provide data on MRSA superinfection and its management. India needs such prospective studies, which should contain epidemiological, clinical, and microbiological data on superinfections. These data can be utilized to create successful antimicrobial stewardship policies, which can be extremely important for administering the right amount of antibiotics.

MORTALITY

Clinically, MDR HA-MRSA infections are linked to high mortality and morbidity, limiting the choice of appropriate antibiotics (Moosavian *et al*., 2017). Table 4 shows the global case fatality rate due to MRSA infection-induced complications. HA-MRSA bacteremia increased ICU and LOS, antibiotic prescription length, and attributable mortality in multiple investigations (Chatterjee *et al*., 2018). This could be because MRSA caused more invasive infections, with multiple co-morbidities and complications, delaying the proper antibiotic therapy, all of which retard recovery. The global mortality due to MRSA ranges from 15% to 60% (Siddiqui and Koirala, 2023). An Indian study showed a 27% case fatality rate due to MRSA bacteremia, with the presence of the PVL gene in most of the strains (Table 4) (Eshwara *et al*., 2013). An Iranian study showed that SCCmec type III was responsible for MRSA's lower sensitivity to various antibiotics (Moosavian *et al*., 2017). An Indian study found SCCmec type II behind higher LOS, poor antibiotic susceptibility, and death (Chatterjee *et al*., 2018).

COST OF MRSA INFECTION

The economic implications of MRSA infections have been studied extensively. Lee *et al*. (2015) reported the overall cost of SSTIs caused by MRSA in the US at $13.8 billion in 2012, with per capita cost of $22 706. Frequent hospitalizations and expensive second-line antibiotics increase treatment costs substantially. A study from the US showed that intravenous (IV) antibiotic administration is associated with 42% of SSTIs hospital admissions in the US, suggesting that shifting healthcare delivery away from the inpatient setting, as well as the use of longer half-life antibiotics (e.g., oritavancin, dalbavancin) could help to reduce costs (Wiseman *et al*., 2015).

Table 4. Global mortality rate due to *MRSA* infections.

MRSA complications	Global mortality (%)
HA-pneumonia	30%–40%
CA-pneumonia	56%–63%
Bacteremia	15%–60%
IE	30%–37%

HAP = Hospital-acquired pneumonia; CAP = Community-acquired pneumonia; IE = Infective endocarditis.

Similarly, LOS in SSTI also influences healthcare costs. A study from the US showed that surgical wound infections resulted in increased LOS (5.81 days) and the highest overall expenses ($9388). Co-morbidities such as diabetes, renal insufficiency, and immunological compromise, increase SSTI costs by prolonging LOS (Kaye *et al*., 2019, 2015).

Furthermore, MRSA infections have been linked to poorer patient outcomes and higher healthcare expenses than MSSA infections. A study from China found that MRSA colonization or infection involves higher total hospital costs ($3,220 to $9,606), as well as extra LOS of 6–14 days (Zhen *et al*., 2020). There is a dearth of data on the cost of MRSA infections in India. A study (2011) from India found that the median overall cost of anti-MRSA therapy was roughly $124 ($45–$484), excluding the expense of treating coexisting diseases. The usage of additional antibiotics to treat MRSA infection from the date of infection diagnosis to the date of discharge or death, it was found that the median cost of therapy per day was roughly $17. Based on World Bank data from 2005, Chen *et al*. (2010) stated that the median cost of anti-MRSA therapy alone (including drug preparation and administration) was more expensive than the quarterly incomes of more than 40% of the 1.2 billion inhabitants living in India (Chen and Ravallion, 2008; Christopher *et al*., 2011).

India needs more data on rising MRSA infections to help hospitals and regulatory bodies plan resource allocation, frame regulations, and guide insurance companies to create budgetary plans.

AVAILABLE TREATMENT FOR MRSA INFECTIONS

Since 2005, the FDA has granted fast-track approval to several novel antibiotics for MRSA, especially for SSTIs. These medications consist of omadacycline, ceftaroline, delafloxacin, dalbavancin, tedizolid, oritavancin, and telavancin. However, these medications are only taken into account as alternatives or are completely absent from the current Infectious Diseases Society of America (IDSA) guidelines for MRSA infection and SSTIs (Hindy *et al*., 2022). Currently, vancomycin or daptomycin is the approved empirical therapy for MRSA infections (Siddiqui and Koirala, 2023). Telavancin, ceftaroline, and linezolid are utilized as second-line therapy (Choo and Chambers, 2016).

Vancomycin and teicoplanin (slower bactericidal activity than vancomycin) are the gold standards for treating drug-resistant GPBs. However, concerns about declining susceptibility and sluggish bactericidal effects may be partly associated with clinical failures in IE and bacteremia. Vancomycin's limitations have prompted the development of other antibiotics (Choo and Chambers, 2016). Limitations include the antibiotic's low penetration into infected tissues in the lungs, heart, and meninges, which has been linked to poor treatment outcomes in serious infections such as pneumonia, IE, and meningitis. Second, numerous *S. aureus* strains produce biofilms, restricting vancomycin's antimicrobial action. Third, enterococci and staphylococci strains have started developing vancomycin resistance. An increase in the MICs of vancomycin against MRSA was linked to worse outcomes. The CLSI lowered vancomycin's breakpoint from 4 to 2 g/ml for susceptible strains, from 8–16 to 4–8 g/ml for intermediately

susceptible strains, and from 32 to 16 g/ml for resistant strains (Dunbar *et al*., 2008).

Vancomycin is effective when coupled with a wide range of β-lactam antibiotics, possibly because of the "see-saw" effect, in which lower vancomycin susceptibility suppresses mecA transcription, thereby increasing β-lactam susceptibility (Barber *et al*., 2014). A retrospective study and a randomized clinical trial showed an increased rate of clearance of bacteremia in patients on a combination of vancomycin and β-lactam than vancomycin alone (Dilworth *et al*., 2014). However, there is little evidence in favor of vancomycin coupled with other antistaphylococcal drugs. In another retrospective study, in which vancomycin was continued in 12 patients, with an aminoglycoside added in 6, rifampin in 4, and both aminoglycoside and rifampin added in 2, only two cases were cleared of bacteremia after 72 hours (Jang *et al*., 2009).

The synergistic combination of daptomycin and β-lactam is significantly better than daptomycin alone in lowering the risk of clinical failure in MRSA bloodstream infection (Jorgensen *et al*., 2020). Table 5 provides the IDSA treatment guidelines for managing different types of MRSA infections in adults and children.

Reports of growing resistance to vancomycin, linezolid, and dalfopristin have raised doubts about their effectiveness. Clindamycin, a reserved option, was chosen by clinicians to treat MRSA isolates because of the drug's superior pharmacokinetics. However, repeated use of MRSA is developing clindamycin resistance with time (Thapa *et al*., 2021).

Clindamycin as monotherapy or in combination with other antibiotics has not presented sufficient evidence, despite being advised as a second-line agent for MRSA pneumonia. *Staphylococcus aureus* susceptibilities to clindamycin have dropped below 40% over the past few years in the US, therefore, it is crucial to make sure the isolate is susceptible. D-testing can rule out any inducible resistance. As for the tetracyclines, support for minocycline was based on data from limited retrospective studies (Liu *et al*., 2011; Park, 2019).

Although clindamycin, doxycycline, minocycline, and TMP-SMX have good bioavailability and lung penetration (ideal characteristics), there is a paucity of evidence to employ them in MRSA pneumonia. Therefore, physicians should consider each case carefully and base their choice to use these medications on the findings of susceptibility tests. To establish the effectiveness of these medications, more clinical study is necessary (Hong *et al*., 2019).

Telavancin, a lipoglycopeptide, is used in the management of serious clinical infections caused by GPBs (MRSA, VISA), such as complicated skin and skin structure infections (cSSSI) and pneumonia. Phase II (FAST trial) and phase III trials suggest that telavancin can treat cSSSI rapidly in a concentration-dependent manner, with bactericidal properties and excellent efficacy. Comparing IV telavancin 10 mg/kg od to standard therapy (IV nafcillin 2 g qid or IV vancomycin 1 gm bd), it was found that the telavancin-treated group had a higher clinical success rate with 96% versus 94%, and 88% and 87%, in Phase II and Phase III trials, respectively (Polyzos *et al*., 2012). Another trial revealed that telavancin-treated patients experienced adverse events (AEs) more frequently than vancomycin (90% *vs.* 72%), with a 7% drug discontinuation rate in both treatment groups. Additionally, the telavancin group had a higher prevalence of clinically significant elevations (1.5 mg/dl or at least 50% greater than baseline) in blood creatinine (20% *vs.* 7%) (Stryjewski *et al*., 2014).

Linezolid has been found effective against cSSSIs, including diabetic foot infections (DFIs) without accompanying osteomyelitis, caused by MRSA and MSSA, simple SSSIs caused by MSSA, Community-acquired pneumonia (CAP), and bacteremia caused by MSSA have all been observed to respond favorably to linezolid (Hashemian *et al*., 2018).

According to the most recently published recommendations for treating MRSA pneumonia, linezolid is a first-line antibiotic. Linezolid has also been demonstrated in multiple tests to be more effective than vancomycin in treating various diseases. In treating situations like SSSIs and nosocomial pneumonia, linezolid may still be preferable to vancomycin, but this is still up for discussion. Recent research has confirmed the clinical effectiveness of linezolid in cSSSIs, including DFIs without osteomyelitis (Liu *et al*., 2011; Rodvold and McConeghy, 2014; Wunderink *et al*., 2012).

Linezolid and vancomycin are equally effective in treating HAP, according to a systematic review and meta-analysis. Additionally, the findings revealed that linezolid, comparator vancomycin, and teicoplanin did not differ statistically from one another in the study of infection eradication. The incidence of AE, such as gastrointestinal problems and thrombocytopenia, was higher with linezolid than with glycopeptides (Hashemian *et al*., 2018).

In another study, the effectiveness of linezolid against vancomycin for treating burns, abscesses, cellulitis, infected ulcers, or deeper soft tissues was examined. When treating MRSA-infected SSTIs, found linezolid therapy was superior to vancomycin and the drug-related AE was similar in both the linezolid and vancomycin groups (Fu *et al*., 2013; Yue *et al*., 2014).

Studies have shown that linezolid administration is more cost-effective than vancomycin in the treatment of MRSA infection due to early hospital discharge In general, compared to vancomycin, linezolid may lower patient mortality (Hashemian *et al*., 2018; Reveles *et al*., 2015).

In addition to appropriate antibiotic therapy, consultation for infectious diseases lowers the death rate due to MRSA bacteremia (Lahey *et al*., 2009). This improved result is probably at least partially attributable to the adoption of a number of quality practices advised by consultants, such as follow-up blood cultures, and echocardiography, to ensure clearance and a thorough search for additional infection foci requiring surgical management. American Heart Association recommends surgery for IE because *MRSA* is associated with valve dysfunction, potentially leading to heart failure, anatomic complications (e.g. heart blocks, valve perforations, and perivalvular extension), or with a high risk of embolization (Punjabi *et al*., 2020).

Prevention of MRSA infection in hospital settings

Centers for disease control and prevention recommends contact precautions in acute care settings for

Table 5. Antibiotic treatment guidelines for different types of *MRSA* infections in adults and children based on IDSA treatment guidelines.

Type of MRSA infections	Conditions	Available treatment
CA-Skin and soft tissue infections • Skin and soft tissue infection	Simple abscesses Infection with β-hemolytic streptococci	• I&D. No antibiotics needed
	For out-patients Severe or extensive abscesses (multiple sites) abscesses in areas difficult to drain (e.g., face, hand, genitalia)/lack of response to I&D Pending culture results Presence of other co-morbidities/immunosuppression/septic phlebitis/cellulitis (purulent/non-purulent)	• PO clindamycin (600 mg tid) or PO TMP-SMX (160/800 mg od)/Tetracycline (100 mg bd) + PO Amoxicillin (500 mg tid) or Linezolid (600 mg bd) for 5–10 days
	For hospitalized patients complicated skin and soft-tissue infections (i.e., deeper soft-tissue infections, surgical or traumatic wound infection, major abscesses, cellulitis, or infected ulcers and burns)	For 7–14 days • IV Vancomycin 15–20 mg/kg bd (normal RF) • PO/IV Linezolid 600 mg bd • IV Daptomycin 4 mg/kg od • Telavancin 10 mg/kg od • PO/IV Clindamycin 600 mg tid
	For non-purulent cellulitis	• Addition of β-lactam antibiotic (e.g., IV cefazolin 250–500 mg tid) • Routine cultures recommended for the clinical response
	For children skin infections (e.g., impetigo) or secondarily infected lesions (e.g., eczema, ulcers, lacerations)	• Mupirocin 2% cream,
	without bacteremia or intravascular infection	• IV Clindamycin 10–13 mg/kg tid or qid (n.m.t. 40 mg/kg/day) can be switched over to oral if the strains are susceptible
	12 years old	• PO/IV Linezolid (600 mg bd)
	<12 years	• PO/IV Linezolid 10 mg/kg tid
Bacteraemia and IE, Native valve		
• Uncomplicated bacteremia	positive blood culture results + no IE, no implanted prostheses, defervescence within 72 hours of initiating effective therapy; and no evidence of metastatic sites of infection	• LD of IV Vancomycin 25–30 mg/kg, then MD 15–20 mg/kg bd (with normal RF) or IV Daptomycin 6 mg/kg od for 2 weeks
• Complicated bacteremia	positive blood culture results with the presence of IE, implanted prostheses, follow-up blood cultures performed on 2 to 4 days after the initial set that do not grow MRSA; no defervescence within 72 hours of initiating effective therapy; and evidence of metastatic sites of infection	• LD of IV Vancomycin 25–30 mg/kg, then MD 15–20 mg/kg bd (with normal RF) or IV daptomycin 8–10 mg/kg od for 4–6 weeks
• IE		• IV Vancomycin/Daptomycin 6 mg/kg or Daptomycin 8–10 mg/kg od for 6 weeks

Continued

Type of MRSA infections	Conditions	Available treatment
• IE + prosthetic valve	Before Valve replacement surgery considered	• PO/IV Vancomycin and rifampin (300 mg tid for 6 weeks) + IV gentamicin (1 mg per kg tid for 2 weeks)
	For children Bacteraemia and IE, endovascular infection, and metastatic infection	• IV vancomycin 15 mg/kg qid for 2–6 weeks • IV daptomycin 6–10 mg/kg od can be considered as an alternative
• Pneumonia	pending sputum and/or blood culture results, for hospitalized patients with severe CAP (a requirement for admission to the intensive care unit, necrotizing or cavitary infiltrates, or empyema)	• IV Vancomycin 1g tid or IV Linezolid/Clindamycin 600 mg tid • PO Doxycycline 100 mg bd
	For children	• IV Vancomycin 15 mg/kg qid or Clindamycin 10–13 mg/kg qid (upto 40 mg/kg/day), if the resistance rate is >10%, then linezolid is an alternative option
Bone and joint infections • Osteomyelitis	Presence of extensive soft tissue abscesses	• Main stay treatment: surgical debridement with drainage of associated soft-tissue abscesses. • If necessary, antibiotics could be administered for 8 weeks • IV Vancomycin 1 g bd • IV daptomycin 6 mg/kg od or PO/IV TMP-SMX (4 mg/kg bd)+ Rifampin (600 mg od)/linezolid or clindamycin (600 mg tid)
	Drainage or debridement of the joint space should be performed.	• Please follow the therapy of osteomyelitis atleast for 3–4 weeks
• Septic arthritis	For children with acute hematogenous MRSA osteomyelitis and septic arthritis without bacteremia or intra-vascular infection	• IV Vancomycin 15 mg/kg qid • Clindamycin 10–13 mg/kg qid (upto 40 mg/kg/day), if the resistance rate is >10%, then linezolid or daptomycin is an alternative option • 3–4 weeks for septic arthritis and and 4–6 weeks for osteomyelitis
Central nervous system infections • Meningitis	Shunt removal is recommended (if central nervous system shunt infection is present) and not be replaced unless CSF cultures are repeatedly negative	• LD IV Vancomycin 25–30 mg/kg and MD 15–20 mg/kg tid (normal RF) +Rifampin 600 mg/day or IV linezolid 600 mg tid or IV TMP-SMX 5 mg/kg tid for 2 weeks
• Brain abscess, subdural empyema, and Spinal epidural abscess	Presence of brain abscess, subdural empyema, or spinal epidural abscess.	• I&D • Please follow the meningitis therapy for 4–6 weeks
	For children	• IV Vancomycin 15 mg/kg qid

Continued

Type of MRSA infections	Conditions	Available treatment
Decolonization	Nasal Full body	• Mupirocin bd for 5–10 days • chlorhexidine for 5–14 days, or dilute bleach baths (1 teaspoon bleach/1 gallon water) given for 15 minutes twice per week for 3 months
UTI		
Uncomplicated		• Ciprofloxacin (immediate-release, 250 mg bd for 3 days; extended-release, 500 mg od for 3 days) or doxycycline (200 mg od) or TMP-SMX (160/800 mg for 3–10 days).
Complicated		• IV Vancomycin (15 mg/kg qid) or Teicoplanin (400 mg on first day then 200 mg), If contraindicated, consider daptomycin (6 mg/kg od for 2–6 weeks). • For catheter-associated UTI : remove the catheter with or without single dose of gentamycin.

I&D = Incision and drainage; IE = Infective endocarditis; PO = per oral; IV = Intravenous; od = once daily; bd = twice daily; tid = thrice daily; qid = four times a day; LD = loading dose; MD = Maintenance dose; TMP-SMX = Trimethoprim-Sulphamethoxazole; CSF = Cerebrospinal fluid; UTI = Urinary tract infection.

inpatients known to be colonized or infected with MRSA or any other MDR organisms. In the US, between 2005 and 2014, the estimated incidence of invasive MRSA infections from normally sterile sources (pleural fluid, blood, etc.) decreased by 40%, while the estimated incidence of invasive HA-MRSA infections decreased by 65%. Both contact precautions and hand hygiene likely played a role in such declines (CDC, 2020).

Although debated, there is minimal concrete evidence for an environmental role in *S. aureus* transmission, except in burns units. Dust, environmental surfaces, and medical devices (e.g. curtains, switches or buttons such as in ventilators, feeding and infusion pumps, phones, computer keyboards, touch panel screens, door handles, light switches, bed tables, bed rails, mattresses, and even pens act as reservoirs for MRSA and other GPBs in general, which easily transfer to hands upon touch (Price *et al*., 2017). Experts agree that preventing MRSA transmission by hand is the most important aspect of MRSA control. Hand hygiene should be ensured before and after each physical contact with a patient or their immediate environment, including before aseptic procedures, handling or manipulating invasive devices, injections through venous catheters, emptying drains or catheters, entering and exiting critical care units, isolation rooms, and open rooms where MRSA cases are cohorted (Mathur, 2011).

All HCWs and administrative personnel with clinical involvement must comprehend the significance of hand hygiene, and follow the national recommendations of "NATIONAL GUIDELINES FOR INFECTION PREVENTION AND CONTROL IN HEALTHCARE FACILITIES" India (NCDC, 2020). The use of protective clothing such as long-sleeved apron, gowns, and gloves are an important component of the control of healthcare-associated infection. Emerging evidence suggests that nurses' uniforms readily get contaminated in high-risk environments like critical care units. Before leaving the patient's environment, the protective apron/gown is removed (WHO, 2014).

Prevention of MRSA infection in the community settings

For patients with skin and soft-tissue infections, clinicians should provide recommendations on personal hygiene and wound care. Clean, dry bandages should be used to cover draining wounds. Hand cleaning with soap and water or an alcohol-based hand gel is recommended on a regular basis, especially after encountering diseased skin or an item that has come in. Recurrent infections despite appropriate personal hygiene and wound care can be remedied by decolonization. Nasal decolonization with mupirocin and topical body decolonization with a skin antiseptic solution (e.g., chlorhexidine) are all options for decolonization. Oral antibiotic medication should only be used to treat active infections; it is not indicated for decolonization. Asymptomatic household contacts may also benefit from decolonization initiatives (Creech *et al*., 2015).

Population surveillance program for CA-MRSA and HA-MRSA in India

Indian Council of Medical Research (ICMR) and the National Centre for Disease Control have established a nationwide network of laboratories to monitor AMR. Infection control systems are in place at many private hospitals and autonomous institutes. Network laboratories conduct surveillance on AMR trends in different geographical regions of India. Surveillance also includes documenting the emergence of methicillin resistance among community isolates of *S. aureus* to inform empirical therapy; describing the occurrence and impact of severe *S. aureus* disease in a community, regardless of resistance pattern; and facilitating timely identification of potential outbreaks. HAI surveillance is available in NABH-accredited hospitals. The All India Institute of Medical Sciences and the ICMR have collaborated to build an HAI surveillance network with 35 public and private sector centers. ICMR has developed web-based tools such as ICMR's Antimicrobial Resistance Surveillance system, ICMR's Data import app, and ICMR's Antimicrobial Resistance Surveillance system using integrative technologies to track HAIs and CAIs. The one-stop AMR data repository has collected over 0.4 million patient records thus far. The entire system is currently being used to collect human susceptibility

testing data; but, utilizing the 'One Health' paradigm, it can be extended for AMR surveillance (Kaur *et al*., 2022; NCDC, 2020; Walia *et al*., 2019).

CONCLUSION

MRSA has become a pervasive infectious agent. MRSA, which is becoming more virulent than ever, continues to aggravate morbidity and mortality. MRSA can also become resistant to new therapeutic agents, with the exception of vancomycin, which has been regarded as effective for the past 40 years. The current circumstance emphasizes the importance of ongoing MRSA and antibiogram surveillance in tertiary care settings as well as outlying hospitals. Regular MRSA surveillance of HCWs, strong hand hygiene compliance, and the framing of antibiotic policies with efficient infection control procedures are the most effective ways to avoid MRSA infection. Studies on COVID-19 superinfections and the cost of MRSA infection should be undertaken to assist hospitals in allocating healthcare resources and making appropriate medical decisions, as well as patients and insurance companies in budgeting. We need to get the information out loud and clear: we're running out of antibiotics against *S. aureus*, and unless we stop abusing antibiotics, we'll be left with no way to fight this dreadful pathogen. All HCWs must practice good hand hygiene. If put into practice, these control measures might help prevent the spread of this dreaded bacterium both in hospitals and among the general population.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

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The authors declare no conflict of interest.

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