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Review Article

Role and Impact of Methicillin-resistant *Staphylococcus aureus*: A New Paradigm in Antibiotic Era During COVID- 19 Pandemic

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Abstract

MRSA (methicillin-resistant *Staphylococcus aureus*) is a prevalent cause of infection in hospitals and at community level. It causes bacteraemia, pneumonia, endocarditis, skin and soft tissue infections and bone and joint infections. Although its prevalence has started declining before the pandemic of COVID-19, but extensive use of antibiotics and long-term hospitalization during infection have increases the risk of secondary bacterial infection including MRSA. As a result, occurrences of co-infection and super-infection are on the rise. MRSA is responsible for collateral damage among patients with COVID-19 infection. In this review, recently published comprehensive studies have assessed the MRSA co-infection among hospitalised COVID-19 patients through PubMed, Scopus, Google Scholar, and the WHO COVID-19 databases. According to recent studies, it was found that MRSA co-infections are on the rise among COVID-19 patients which has increased the mortality rate. Improved diagnostic capabilities of laboratories and reducing the necessity of antibiotic that can be helpful in reducing the MRSA co-infection in these patients. Sanitation and preventive measures and strict infection control policies can reduce the burden of MRSA infection.

Keywords: *Staphylococcus aureus;* COVID-19; MRSA

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a bacterium that causes infections in different parts of the body especially in admitted and post-operative patients. It is counted as modern pathogens due to their resistant nature against regularly used antibiotics and become more difficult to treat than other strains of *Staphylococcus aureus* (*S. aureus*). People infected with MRSA, are chance to die up to 64% [1]. MRSA is a subset of frequently causing hospital-acquired pneumonia (HAP) and pneumonia caused by a ventilator. It's also known as nosocomial pneumonia, because it happens 48 hours or more after being admitted to the hospital, showing that it wasn't incubating at the

time of admission [2]. On the basis of their site of infection, MRSA strains are mainly two types; the first one is recognized as a hospital-acquired methicillin-resistant *S. aureus* (HA-MRSA) and the second one as a community-associated methicillin-resistant *S. aureus* (CA-MRSA). HA-MRSA infection mainly found in a patient has any kind of hospitalisation, surgery or medical history [3]. However, CA-MRSA is distinguished by the absence of a prior history of surgery, hospitalisation, or residency in a long-term care facility within the year preceding infection, the absence of a percutaneous device or indwelling catheter and the absence of dialysis within the previous year, hospitalisation 48 hours prior to MRSA culture, or the absence of a previous MRSA infection or colonisation [4]. CA-MRSA is also differ genetically from hospital-associated MRSA (HA-MRSA) due to frequently presence of a cytotoxin Panton-Valentine leukocidin, (PVL) producer *Staphylococcal* cassette chromosome mec (*SCCmec*) gene that it is resistant to fewer non-lactam antibiotics [5].

Moderate and severe patients infected with SARS-CoV-2 virus cause COVID-19 have frequently hospitalised and in extreme cases required intensive care with mechanical ventilation. This can cause co-infections of nosocomial infections (NIs), which acquired during hospitalisation within 48-72 hours. The bacteria *Staphylococcus* spp., *Enterococcus* spp., *Klebsiella pneumoniae, Enterobacter* spp., *Escherichia coli, Acinetobacter* spp., and *Pseudomonas* spp. are the most commonly identified bacterial agents of Nis [6]. They are also transferred frequently through person-to-person contact, devices, and tools. Several studies have pointed to the overuse of antibiotics in COVID-19 patients, as well as the potential of a rise in antimicrobial resistance worldwide. In order to control antibiotic prescriptions, it is critical to understand the prevalence and epidemiology of bacterial infections in these patients [7]. As a result of this scenario, the risk of NIs in general and MRSA in particular, has grown during COVID-19 period.

Study selection

For evaluating the role and impact of MRSA during COVID-19, we have extracted article from National centre for Biotechnology information (NCBI) Pubmed, Medline National Library of Medicine, Microsoft Academic, Scopus, Web of Science and Google scholar as searched term effect of MRSA AND COVID era, prevalence of MRSA pre- COVID and post COVID duration and Impact and future prospects of MRSA after COVID-19. We looked for articles that included patients infected with both COVID-19 and MRSA, provided a timeline and were available in English. We found publications that discussed the impact of the COVID-19 pandemic on antibiotic resistance and have organised research on MRSA. However, fifteen articles were suitable for section of data and table after thorough review. We have evaluated more articles from google scholar for information about its historical prospective, epidemiology, diseases and transmission. Definitions of different diseases caused by MRSA and information about its genomics were taken from review articles and book chapters especially related to MRSA.

Historical prospective and epidemiology of MRSA

S. aureus caused bloodstream infections had a fatality rate of more than 80% before antibiotics were developed [8]. However, the fatality rate of *S. aureus* infections dropped drastically after the discovery of penicillin. Its strains that produce penicillinase were found soon after penicillin was introduced, and these penicillin-resistant germs invaded hospitals and, later, the general public. Between 1953 and 1963, the prevalence of penicillin-resistant *S. aureus* phage type 80 or type 81 increased dramatically [9]. By the late 1970s, penicillin-resistant strains had become more widespread than penicillin-susceptible cases [10]. Further, *S. aureus*-related illnesses and skin and soft tissue infections (SSTI) were treated using methicillin based antibiotics that were effective against penicillinase-producing bacterial infections. Subsequently, *S. aureus* isolates had acquired resistance to methicillin considered as a MRSA, which were first reported in the United Kingdom in 1961, and then MRSA isolates were quickly recovered from other European nations, as well as Japan, Australia, and the United States (US). The proper evolutionary origins of MRSA are poorly known, there is no logical nomenclature, and there is no agreement on the number of significant MRSA clones or the relatedness of clones identified in different nations.

In the late 1990s, epidemic methicillin-resistant *S. aureus* 15 (EMRSA-15) ST22 (CC22) and EMRSA-16 ST36 (CC30) strains emerged as the most common HA-MRSA strain types in the United Kingdom [11]. In continental Europe, the same strain types, ST22 and ST30, predominate among HA-MRSA isolates. ST30 (CC30) has also expanded effectively throughout Asia-Pacific and parts of the Americas [12]. Aside from the widespread distribution of CC30 strains, this clonal complex has been linked to greater rates of invasive infection and death. In India, MRSA has become prevalent and its infection rates jumped dramatically between the 1990s

and the early 2000s. However, the infection rate of hospital- and community-acquired MRSA bloodstream infection has recently decreased, from 74% to 40% between 2005 and 2016, with adjusted rates decreasing by 17.1% each year [13]. Its infections have been also declining in different US and European populations since 2005, particularly in bloodstream and soft tissue infections [14]. MRSA prevalence ranges from 25% in the western part of India to 50% in the southern part [15].

High risk genetic makeup of MRSA

Bacterial genomes are broadly divided into core and accessory components. In case of MRSA, genetic diversity frequently occur within the accessory genome primarily in genomic sequences of mediators of virulence and immune evasion parts and followed to become the responsible for resistance against antibiotics. It consists of mobile genetic elements (MGEs) such as pathogenicity islands, chromosomal cassettes, transposons and plasmids which are acquired by transfer within strains. Genomic studies reveal the role of mutations and antibiotic resistance sequences presented in MRSA [16]. Though, the major sequence type of MRSA evolves from MSSA by acquiring *SCCmec* clones; i.e. strain of MRSA is ST772 mainly causes skin and soft tissue infection. Prior to its arrival in India, it was found in other nations. While Indian genomic surveillance studies ST772-MSSA and -MRSA have been found in Nepal in two recent studies and ST772-MRSA was also found in Pakistan and Bangladesh, but it's unclear if the lineage was endemic there [17].

In India, MRSA is found in all of the main strains present with *SCCmec* gene [18]. In which, *SCCmec* type III and sequence type (ST) 239 strains make up the bulk of HA-MRSA isolates. On the other hand, CA-MRSA was mostly seen in the ST22 (*SCCmec* IV), ST772 (*SCCmec* V), and ST672 (*SCCmec* V) genotypes strains and become increasingly difficult to distinguish from HA-MRSA [19]. It is becoming more invasive and transmissible in present worldwide situation including India. A one more type of MRSA is Livestock-associated MRSA (LA-MRSA) but there is little to known about its genotypes or their potential impact on human infections in India.

Transmission and colonisation of MRSA

S. aureus may be found in the environment and in normal human flora, and it can be detected on the skin and mucous membranes (most often the nasal region) of the healthy peoples. The transmission of infection may vary in all types of MRSA (figure 1). Direct touch is the most common method of transmission. *S. aureus* does not generally cause infection on healthy skin, but if it enters the circulation or internal tissues, it can cause a range of potentially fatal illnesses. In the hospital, contaminated fomites and medical equipment may act as intermediary sources of HA-MRSA infection. Animals can also be potentially serving as a source and/or reservoir for *S. aureus* zoonotic infections, as evidenced by recent reports of human infections caused by MRSA strains connected with pigs [20]. Farmers, slaughterhouse workers, livestock transporters, and veterinarians who come into close touch with MRSA-infected cattle are at a higher risk of contracting LA-MRSA. They may, in turn, spread MRSA to other animals including people [5].

The anterior nares are the most common location of MRSA colonisation; however, *S. aureus* (including MRSA) can also be found in the throat, axilla, rectum, or perineum, and can frequently infect many regions of the body [21]. The presence of *Staphylococcal* enterotoxin P, in particular, has been linked to an increased risk of bacteremia in those who have been colonised by it. Different strain types may be separated, which suggests that colonisation is dynamic. Invasive strains have been shown to switch between distinct bodily areas, and morphologies of methicillin-resistant and susceptible bacteria over the time [15]. As MRSA is a commensal pathogen, there is active interest in whether detection of MRSA colonization followed by an attempt to eliminate carriage can reduce the risk of subsequent infection.

Figure 1: Transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) infection: Schematic representation of major source of all three types MRSA are Community associated (CA-MRSA), hospital acquired (HA-MRSA) and Livestock associated (LA-MRSA) (Source 1. Kluytmans-Vandenbergh MF., *et al*. [3]; 2. Buck, J.M., *et al*. [4]; 3. Lakhundi S., *et al*. [5]).

Infections causes by MRSA

Children, older age and military persons, athletes, those who take intravenous drugs, those with an indigenous background or who live in urban, underserved areas, those who have frequent healthcare contact and those in institutionalised populations, such as prisoners including those with suffering from HIV or cystic fibrosis are more common risk of MRSA infection. It can cause a variety of organ-specific infections, especially the skin and subcutaneous tissues being the most prevalent, followed by invasive infections such as osteomyelitis, meningitis, pneumonia, lung abscess, and empyema. The major characteristics and the role of MRSA in development of these diseases are described here (Figure 2).

Figure 2: Infections caused by MRSA.

Skin and soft tissue infections (SSTIs)

Microbial invasion of the skin and its supporting structures causes skin and soft tissue infections. They are divided into two types: basic (uncomplicated) and complicated (difficult) (necrotizing or nonnecrotizing) form of SSTIs alone or with co-morbities [22]. SSTIs such as cellulitis, necrotizing fasciitis, and diabetic foot ulcers are mainly caused by CA-MRSA. It's also becoming more closely linked to more invasive illness than non-MRSA infections. Multidrug-resistant SSTIs infections are more common, resulting in frequent recurrence, increased hospitalisation, and death [23].

Bone and joint infection

The most prevalent cause of bone and joint infections is *S. aureus* particularly among those individuals who have resistance to oxacillin. By extending a local infection from a wound or as part of a hematogenous infection, MRSA can cause osteomyelitis of the spine and long bones of the upper and lower limbs. MRSA may also induce septic arthritis in both natural and artificial joints [24]. Bone infection, especially in areas with low vascularity, can be difficult to treat, requiring extended courses of antibiotics combined with surgical drainage or debridement. Treatment that is delayed or inefficient results in substantial morbidity, including pain, loss of function, and the need for more surgery and antibiotics [25].

Respiratory tract infections

Pneumonia

MRSA was significantly responsible for high fatality rate of Hospital-acquired pneumonia (HAP) than community-acquired pneumonia (CAP) [26]. Despite its low occurrence, pneumonia caused by MRSA is linked with poor outcomes and frequently warrants empirical antibiotic treatment. Ventilator associated pneumonia refers to the nosocomial pneumonia that develops among patients on ventilators. Ventilator associated pneumonia (VAP) is defined as pneumonia that present more than 48 hours after endotracheal intubation. MRSA strain frequently colonize respiratory secretion in intubated patients therefore one of the most common causes of hospital acquired pneumonia [27].

Central intravenous line infections

The treatment of intravenous line infection due to MRSA first depends on the establishment of a diagnosis. MRSA line infections present with otherwise unexplained fevers and a catheter entry site may or may not appear to be infected. Because intravenous line infections due to S. aureus, either MSSA or MRSA, have the potential to cause endocarditis, antimicrobial therapy is given for 2-4 weeks following central line removal [28].

MRSA is responsible for the majority of global cases of *S. aureus* bacteraemia infections, and in these, MRSA infection showed frequent clinical outcomes as compared to methicillin-sensitive *S. aureus*. Its virulence varies by geographical location as well as healthcare- or community-associated individuals with unique combination of toxin and immune-modulatory gene products [21]. Intravenous drug usage and intravenous catheters are frequent causes of right-sided MRSA endocarditis.

Central Nervous system

Staphylococcal meningitis

Meningitis due to *Staphylococcus aureus* accounts for 1-9% of cases of bacterial meningitis and is associated with mortality

rates of 14-77%. It usually is associated with neurosurgical interventions (e.g., cerebrospinal fluid [CSF] shunts), trauma, or underlying conditions, such Malignancy, Decubitus ulcers, Infected intravascular grafts, Diabetes mellitus, Osteomyelitis and Perirectal abscess. Staphylococcal meningitis may occur as a complication of staphylococcal ABE as the result of meningeal seeding. Staphylococcal brain abscesses may occur following open or closed neuro-surgical trauma [29].

Prevalence of MRSA in pre COVID-19 era

As we seen earlier, MRSA is one of the most common causes of antibiotic-resistant disorders throughout the globe and one of the major health problems of concern. Despite of this different data reports from different regions of world had shown a quite decrease in MRSA active cases. Between 2013 and 2016, the EU/EEA population-weighted mean MRSA proportion fell considerably [30]. A study by Lohan K., *et al*. in the year 2017, out of 25 *Staphylococcus aureus* isolates MRSA were 7 (28%). The prevalence of MRSA increased to 14/44 (31.8%) in 2018 and 60/171 (35.1%) in 2019. It shows a quite increase in MRSA infection in India [31]. In USA, adjusted hospital-onset MRSA bloodstream infection rates decreased 7.3 percent per year in 447 hospitals that supplied data from 2012 to 2017, whereas community-onset MRSA rates did not change significantly [32]. A study in Brazil by Taniela Marli., *et al*. in 2017 found a very low prevalence of MRSA colonization in individuals from the community: 2.3% of the entire population and 5.5% among the persons colonized by *S. aureus* [33]. A study in south Italy by A. Facciolà., *et al*. showed a quite decrease in MRSA infection from 2015 - 2017 in surgical, medical and also in emergency areas of hospital [34]. A prospective observational study in United Arab Emirates by Muna Al Jalaf., *et al*. showed prevalence of MRSA upto 23% and he suggested that MRSA-active antibiotics should be considered for patients [35]. Another study by Ankur., *et al*. demonstrates MRSA infection as major problem in India. His study shows a greater number of MRSA isolates was multidrug resistant as compared with the MSSA isolates [36].

Another different research has been done in 2019 in different regions of the world. A study in USA by Weiner-Lastinger LM., *et al*. showed that 1689 cases of MRSA infection in total 3176 AMR cases (53.2%) [37]. A retrospective study in India by Saini V and Jain C., *et al*. 108 cases of MRSA in total 844 cases of bacterial infection (12.8%) [38] (Table 1). A comparative study of MRSA infection during pre-COVID and COVID-19 era by Polly M., *et al*. in Brazil shows that before covid there is a decline in cases of MRSA infection incident density [39]. Another comparative study in Italy by Pasquini Z., *et al*. showed the impact of COVID-19 on MRSA infection [40].

S. No.	Author's Name of original work	Country/ Location	Duration of the study	Source of sample	Pre- COVID-19 infection	Reference No.
1.	Lohan K., *et al*.	India	January 2017 to December 2019	Pus, blood and body fluids	81/240 (33.75%)	[31]
2.	Kourtis AP., *et al*.	USA	2005-2017	-	17 % (declined rate of HA MRSA) 6.9% (declined rate of CA MRSA)	[32]
3.	Bes TM	Brazil	2018	Pus, blood and body fluids	7/300(2.3%)	[33]
4.	Facciolà., *et al*.	Italy	2017	-	35%	[34]
5.	Muna Al Jalaf., *et a*l.	United Arab Emirates	2011-12	Blood culture	18/78 (23%)	[35]
6.	Kumar A., *et al*.	India	2015	-	29%	[36]

7.	Weiner-Lastinger LM	USA	2019-2020	-	1689/3176 (53.2%)	[37]
8.	Saini V and Jain C., *et al*.	India	1 March 2019 - 31 Dec 2020	Blood and urine isolates	108/844 (12.8%)	[38]
9.	Polly M., *et al*.	Brazil	Jan 2017 -Dec 2020	Blood and Urine culture	0.24 Incident density	[39]
10.	Pasquini Z., *et a*l.	Italy	1 Jan - 30 June 2020	Blood stream	23/1000 (.23%)	[40]

Table 1: Prevalence of MRSA before pandemic of COVID-19.

Proportion of CA MRSA and HA MRSA in Pre COVID era

The proportion of MRSA among HA *S. aureus* infections was low in India (22.6%) and The Philippines (38.1%) but was high in Sri Lanka (86.5%), South Korea (77.6%) and Vietnam (74.1%). The proportion of MRSA among CA S. aureus infections differed according to different sites: Sri Lanka, 38.8%; Taiwan, 34.8%; The Philippines, 30.1%; Vietnam, 30.1%; South Korea, 15.6%; Hong Kong, 8.5%; India, 4.3%; and Thailand, 2.5% (Figure 3) [41].

Figure 3: The proportion of CA MRSA and HA MRSA Pre COVID--19 era in India (Source: Lai C-C., *et al.* [51]).

Prevalence of MRSA in COVID-19 era

Antibiotic resistance is now being monitored and reported by a record number of studies worldwide, marking a huge step forward in the worldwide fight against drug resistance as per reported by WHO. However, the information they provide reveals that an alarming number of bacterial infections are growing increasingly resistant to conventional therapies [1]. Bacterial infections in patients caused by *S. aureus*, which are resistant to extended-spectrum antibiotics commonly used to treat life-threatening bacterial infections, are a concern, especially in ICU patients. Therefore, MRSA infection is endemic to the hospital environment. As a result of the COVID-19 pandemic, many immune-compromised people were hospitalised and many COVID-19 patients were diagnosed with secondary illnesses, making them more susceptible to MRSA infection. In comparison to patients who are just infected with COVID19, co-infection with COVID-19 and *S. aureus* leads to a greater risk of patient death during hospitalisation.

We have included seven major studies based on retrospective case series during pandemic era of COVID-19 (Table 2). An Indian study Saini V., *et al*. observed that 63/494 (12.6%) samples of SARS-Co-V-2 positive patients were also infected with MRSA as reported as pre-COVID-19 era due to decrease in susceptibility to commonly prescribed drugs [38]. A large study conducted in a gulf country found that MRSA was also co-infected the COVID-19 patients as seventh commonest microorganism identified from all positive culture obtained during hospitalization [42]. Another research in the US found a 34% rise in MRSA infections during COVID-19, greater than cases in 2019**,** which might be attributed to poor management methods and central line insertion [37]. A study by CD Punjabi., *et al*. shows that increase in prevalence of MRSA in hospitalized patients was depend on duration of hospitalization [43]. A USA based another study also analyzed the onset of bloodstream infection among on hospital admission (<48 hrs) and noscomial (>48 hrs.) patients with COVID-19, MRSA was also the predominant pathogen as co-infection [44]. A recent Brazilian study, the incidence density (ID) of all Multi Drug Resistant (MDR) infections increased 23% during COVID-19 especially by MRSA increased up to 94% cases among healthcare-associated infections [39]. Another study by Pasquini Z., *et al*. MRSA incidence increased 20.4-fold higher including 5.1% frequent cases in COVID-19 era [40]. A study by Raychaudhuri D., *et al*. shows that COVID infected

children with MRSA co-infection required much more mechanical breathing and other supportive therapies and spent significantly longer in the PICU than children without co-infection [45]. Another USA based study by Wolfe., *et al*. shows that patients who have tested positive for SARS-CoV-2 are more likely to test positive for other respiratory bacteria and viruses [46]. A study in Spain by Garcia., *et al*. shows that in hospitalised COVID-19 patients, bacterial, fungal, and viral co-infections and superinfections are uncommon; but, when they do occur, they can produce serious illnesses with poor results [47]. Overall, all studies showed increase rate of secondary infection of MRSA become the major concern of random exercise of antibiotics and hospitalization in pandemic era of COVID-19.

S. No.	Author's Name of original work	Country/ Location	Duration of the study	Source of sample	During COVID-19 infection	Reference No.
1	Saini V and Jain C., *et a*l.	India	1 March 2019 - 31 Dec 2020	Blood and urine isolates	63/494 (12.6%)	[38]
2.	Senok A and Alfa-resi M	United Arab Emirates	1 Feb- 31 July 2020	Blood, endotracheal aspirate, urine etc.	50/392 (12.7%)	[42]
3.	Weiner-Lastinger LM	USA	2019-2020	-	6926/9914 (69.9%)	[37]
4.	Punjabi C.D., *et al*.	New Yark, USA	13 March - 17 May 2020	Respiratory Culture at 28th day of admis-sion	27/472 (5.7%)	[43]
5	Bhargava A., *et al*.	USA	March - June 2020	Blood Culture	11/39 (28.2%)	[44]
6	Polly, M., *et a*l.	Brazil	Jan 2017 - Dec 2020	Blood and Urine culture	0.46 Incident density	[39]
7	Pasquini Z., *et a*l.	Italy	1 Jan - 30 June 2020	Blood stream	24/1000 (0.24%)	[40]
8	Raychaudhuri D., *et a*l.	India	June - December 2020	Blood, respiratory culture and CSF	6/22 (27.27%)	[45]
9	Wolfe., *et al*.	USA	March 24th to April 27th, 2020	-	55.8%	[46]
10	Garcia., *et al*.	Spain	28 February to 22 April 2020	Blood culture and respiratory culture	11/74 (14.86)	[47]

Table 2: Prevalence of MRSA during pandemic of COVID-19.

The increased incidence of MRSA as secondary infection in COVID-19 patients can be attributed to mainly four factors (not mutually exclusive). First, immune system dysregulation, owing to two mechanisms: a 'cytokine storm' generated by the virus, and a significant decrease in IFN- production, resulting in a drop in Th1 polarisation of $CD4^{+}$ T cells and cytotoxic activity [48]. Second, prolonged hospitalisation times are associated with a greater probability of ICU admission, increasing the risk of nosocomial infections. Third factor is widespread use of immunosuppressive medicines such as corticosteroids, anti-IL6 drugs, etc. [49]. Fourth factor, dysbiosis in the gut microbiota causes gut-lung axis dysfunction. Other factor may include

ventilation or central venous catheter installation, which are the most common patient treatments [50]. During pandemic period of COVID-19*, S. aureus* depicted reduced susceptibility to all classes of drugs and the widespread use of antibiotics for respiratory illness in ICUs is also increases the bacterial resistance. The use of commonly used antibiotics such as clindamycin, erythromycin, and fluoroquinolones has reduced dramatically since the COVID-19 era, which is responsible for high susceptibility of MRSA infection [38]. Although these first-line therapies for decompensating patients with severe COVID-19 infection may increase the risk of *S. aureus* bacterial co-infection and, as a result, mortality, but they are often unavoidable over the course of the patient's therapy.

Proportion of CA MRSA and HA MRSA during COVID -19 in India

During Pandemic several studies claimed that one of the strains of *S. aureus* was identified as MRSA. This organism plays an important role in the severe complication of infections in ICU environments. Although these infections are more common in nosocomial settings, community-acquired secondary infections are also increasing. A high index of suspicion for drug-resistant organisms is needed based on the community prevalence of these isolates. Post-Influenza MRSA pneumonia is a well-defined entity, but post-COVID-19 MRSA pneumonia has not been well described in the literature [51].

Post-influenza pneumonia with positive MRSA cultures was shown to occur in nearly 6% of the patients enrolled in a recent review. Different studies have also shown that lower respiratory tract infections caused by MRSA can be associated with a significant level of mortality in the patients admitted to ICUs.

Figure 4: Proportion of CA and HA MRSA during COVID -19 in India (Source: 1. McCraw C., *et al*.; 2. Saini V., *et al*. [48]).

Impact and future prospects of MRSA after COVID-19

MRSA is likely to cohabit with humans indefinitely. It is still a high-priority MDR organism that requires continued research and development of new medicines as well as novel prevention strategies. Universal screening is not practicable because of the wide range of etiological agents and the low yield of culture techniques, but early detection is critical for early intervention and improved management of MRSA infection. There is a growing public awareness of communicable diseases, the need of infection prevention, particularly hand cleanliness, and antibiotics' incapacity to cure viral infections. This provides a chance to educate healthcare professionals and the general public on the growing problem of antimicrobial resistance. Although some progress has been made, there is still a long way to go to keep up with the new resistance. There is a need of holistic, ecological strategy to prevent future biological health dangers to humanity.

Improved diagnostic capabilities of microbiology laboratories are also required to reduce the need for empiric antibiotic treatment by lowering COVID-19 testing turnaround time as well as specimen processing for secondary bacterial infection like MRSA identification [52]. If urgent specific diagnostic and antibiotic stewardship strategies are not developed, irrational antibiotic use for COVID-19 patients in this pandemic may have a long-term impact on the prevalence of antimicrobial resistance.

Conclusion

Co-infection has a vital role in determining the prognosis of COVID-19 infection. The rise in antibiotic resistance seen during the pandemic compared to the year before COVID-19 was consistent with previous observations. Assessing the exact impact of COVID-19 on AMR is difficult at this time but it does offer a crucial opportunity to raise awareness about the effects of infectious illnesses on human health. The use of strict infection control policies in hospitals is critical in minimising nosocomial infection, and the appearance of COVID-19 serves as a stark reminder of the ongoing and urgent need for new antimicrobial research and development in the future. Along with this, the possibility of outbreaks from these infections should be recognised by infection control teams. Antimicrobial usage in hospitalised COVID-19 patients should be reduced, and correct PPE use should be ensured. The association between antibiotic prescribing trends during COVID-19 and increases in MDR incidence need

wisely prescription and investigation. Many information gaps and significant problems need to be addressed, necessitating continued attention from researchers, policymakers, and funders, as well as those in charge of MRSA treatment and control. Along with this, there is urgent need of widespread co-infection screening should be done. Universal screening is not possible due to the wide range of etiological agents and the low yield of culture techniques. But early diagnosis and preventive measures, on the other hand, is critical for early intervention and improved management of co infection in COVID-19 patients.

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Conflict of Interest

Authors have no conflict of interests.

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