ORIGINAL ARTICLE

A Review of Global Epidemiology and Antibiotic Resistance of Staphylococcus Aureus

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ABSTRACT

Background: Staphylococcus aureus is gram-positive cocci, which causes multiple complications such as bone, skin, joint and soft tissue infections. Penicillin was the first antibiotic that showed resistance to S. aureus; however, following penicillin, S. aureus became resistant to Methicillin and became a problem in many parts of the world. Worldwide epidemiology of S. aureus varies by country. In Austria, CA-MRSA accounts for 10% of all MRSA isolates. Many clones of S. aureus were discovered in Asian and as well as in European countries. Many patients in Southeast Asia are infected with various S. aureus variants.

Aim: The aim of this study was to review epidemiology and antibiotic resistance of S. aureus in different countries.

Results: Previous findings revealed that Panton-Valentine leukeocidin (PVL) genes were present in S. aureus strains. Furthermore, most widely accepted antibiotic resistance genes in clinical isolates of S. aureus strains are mecA. S. aureus spread throughout the hospital and into the community as well. They differ from one another in some ways, such as PVL genes and staphylococcal Chromosomal Cassette Mec (SCCmec) subtyping.

Conclusion: It is concluded based on previously published research as well as review articles that different clones are of S. aureus are present in different regions of the world which further shows similar characteristics in some regions while totally different from the clones found in other countries. S. aureus infection can be treated by combining some antibiotics such as Vancomycin with Rifampin and Gentamicin. It can also be avoided by practicing good hand hygiene and avoiding intravenous drugs, which can cause a variety of infections. **Keywords:** Staphylococcus aureus, MRSA, CA-MRSA, HA-MRSA, Resistance

INTRODUCTION

Staphylococcus aureus belongs to cocci group and is Gram-positive bacteria with diameter of 0.5-0.7µm¹. It causes skin and soft tissue infections which may lead to infected ulcers and sepsis. It also causes joint or bone infection in orthopedic surgery through contamination². Nasal carriage, invasive apparatus, the availability of invasive devices, and surgical techniques are all factors that increase the risk of S. aureus infection in resource-rich regions, hospital admission and antibiotic exposure ³. S. aureus is the main pathogen of many infections in Sub-Saharan Africa (SSA) and many survey reports claim that S. aureus is most common bacteria frequently encountered in microbiology laboratory of Nigeria ⁴.

The natural reservoirs for S. aureus are humans. The strain of MRSA which found in hospitals spreads in community ⁵.Epidemiology of MRSA similar to the spread of penicillin-mediated- resistance in S. aureus, the prevalence of MRSA

strains increasing in community, while the origin of both hospitals acquired and community acquired MRSA strains are unknown ⁶. For treating multidrug-resistant S. aureus infections, the options for it are very few. If new strains emerged, options for treating multidrug-resistance S. aureus will become limited with time. Further studies are needed to detect the MRSA infections ^{7, 8}

Asia is not just the world's fastest growing region, but it also has the highest rate of inappropriate medication, such as self-medication with over-the-counter medications; antibacterial drugs are a prominent technique for combating infectious infections ⁹. Hospital-acquired methicillin-resistant S. aureus (HA-MRSA) and Community-Associated Methicillin-Resistant S. aureus (CA-MRSA) are the most common infections in Asia. ^{10, 11}.

In 1944 penicillin was discovered to treat S. aureus. It was 94% effective but later 50% of S. aureus showed resistance till 1950¹². Methicillin was first used to treat S. aureus in 1959 infections which are caused by penicillinresistance S. aureus ¹³. Later on in 1961 in United Kingdom there were cases in which methicillin showed resistance to S. aureus infections. After that MRSA became a problem worldwide in hospitals of European countries, Australia, Japan and United States ¹⁴. MRSA arise when methicillinsusceptible S. aureus (MSSA) obtain insertion of a large DNA fragment of Staphylococcal chromosomal cassette mec (SCCmec) into their genomes, which carries the methicillin resistance determinant gene, mecA ¹⁵. The strain S. aureus which are resistant to penicillin and methicillin are most common in Asian countries ¹⁶. The strains of β-lactam-resistant S. aureus bacteremia is often associated with Health care environments exposed to MRSA can cause a considerable burden of disease ³.The popular S. aureus strains in populations are ßlactamase producers, later became resistant to penicillin and ampicillin¹⁷.

There are two mechanisms Staphylococci use for resistance against β -lactam drugs. In the first mechanism, they produce enzyme β -lactamases. This enzyme (β -

lactamases) destroys the β-lactam by hydrolysis ¹⁸. Blactamase produce by activation of a gene named as blaZ gene. The other mechanism include the production of penicillin binding protein 2a (PBP 2a), mec A gene encodes the PBP 2a of S. aureus strain were found among the human pathogens ¹⁹. In the growth and survival of bacteria PBP2 plays an important role 20. In United States in 1980, the first case of community acquired MRSA (CA-MRSA) was reported; hence the MRSA was no longer HA-MRSA but also a CA-MRSA after the first case of community acquired-MRSA. CA-MRSA is not a nosocomial infection, it is community acquired infection. It arises within the community but not in the hospitals or healthcare centers. It mostly affects the skin and soft tissues and found in prisoners, sports players, children and drugs injecting users. In some areas, healthcare-associated MRSA (HA-MRSA) is more common than healthcare-associated methicillin-susceptible S. aureus; MRSA is a major source of healthcare-associated infections 8.

These resistant S. aureus to β -lactam drugs can occur in healthy people who do not have classic MRSA risk factors ²¹. MRSA is developed when MethicillinSensitive S. aureus (MSSA) acquires and inserts a large DNA fragment known as SCCmec into their genomes, which carries the Methicillin Resistance determinant, mecA ⁴.

The mecA gene product, which is a modified form of Penicillin Binding Protein (PBP) known as PBP2a or PBP2' that has a decreased affinity for all-lactam antibiotics ²². Based on the nature of the mec and ccr gene complexes, eleven different SCCmec (20) types have been identified ²³. Within the mec operon, the mecA gene is found on the SCCmec (SCCmec). Several epidemiological investigations of MRSA strains have employed SCCmec typing, which categorises SCCmec elements based on structural differences ²². The majority of MRSA virulence genes, such as extracellular fibrinogen binding protein, are positive for adherence genes ²⁴. SCCmec is divided into nine types: I, II, III, IVa, IVb, V, VI, VII, VIII, and VT; HA-MRSA is found in SCCmec I, II, and III, while CA-MRSA is found in SCCmec IV or V 25. Genetically, CA-MRSA strains differ from HA-MRSA clones. CA-MRSA strains have Panton-Valentine leukeocidin (PVL), SCCmec type IV, and are susceptible to antimicrobials other than -lactams; the latter have SCCmec I, II, or III and frequently have additional antimicrobial resistance genes ²⁶. According to epidemiological research on S. aureus protein A (spa) types, the most prevalent spa types in European countries are t032, t008, and t002, whereas the most common spa types in Asian countries are t037 and t002; the most common spa types in American countries are t008, t002, and t242²⁷.

DISCUSSION

Studies show the prevalence of S. aureus in different regions around the world and show multi drug resistance to different antibiotics. Moreover, HA-MRSA and CA-MRSA has differences in terms of resistance and genes conferencing resistance to different antibiotics. S. aureus harbor different set of genes based on region from where they were isolated and thus some genes confer more resistance as compared to others.

Epidemiology of Staphylococcus aureus

Epidemiology in Europe: Prevalence and differences at molecular level in S. aureus were scrutinized based on previous studies in different European Countries to have a clear picture of MRSA across the globe.

France: According to a report by French Reference Laboratory Staphylococcus risk factors were not recognized till 2002 (²⁸. Moreover prevalence of CA-MRSA is higher than HA- MRSA as reported by Otter and French ²⁹.

Greece: During 2001-2003, PVL positive CA-related MRSA (Community Acquired) accounted for 55% Healthcare-Related MRSA-infected Hospitals these areas³⁰. There is a scarcity of knowledge about MRSA in the Greek community. The PVL-positive European clone (ST80-IV) appears to be the most frequent, although the novel ST377-V clone has just been detected in Greece's south-western region and in Patras. Larissa is a city in central Greece. ³¹

Germany: Reports from German References Laboratory indicates that the prevalence of the S. aureus infections has increased the development of European clones and similar USA300 ST8-IV PVL positive clones, most likely from United States, Analysis of CA-MRSA from Germany revealed a unique Smal-macro-restriction pattern, which is different from popular hospital strains ³². According to several reports of MRSA outbreaks in healthcare facilities caused by the European clone, nosocomial transmission has become common in Germany ²⁹. The proportion of MRSA in invasive S. aureus infections should be used as a marker for monitoring human pathogens, according to a 2017 study by the ECDC (European Centers for Disease Prevention and Control), the EFSA (European Food Safety Agency), and the EMA (European Medicines Agency) ³³.

Belgium: The study concluded that in Belgium, the characteristics of Community-Related MRSA are due to the large amount of heterogeneity, while the European Cloning is most frequently stated, In Belgium, there are five PVL-positive CA-MRSA strains belonging to five different genetic lineages, the most common of which are ST80-SCCmec IV clones ^{34, 35}.

Austria: According to the Austrian Reference Laboratory, about 10% of Austrian MRSA isolates are Community-Related MRSA PVL positive ST8-IV (USA300), which is similar to Germany. ³⁶

Spain: Although two Spanish studies show a rising rate of CA-MRSA, the incidence rate of CA-Related MRSA in Spain and Portugal is high (USA300) The most frequent clone is ST8-IV, and PVL-positive isolates from South America, primarily Bolivia and Ecuador, have been linked to immigration. ³⁷.

Italy: Recent studies by an Italian Laboratory showed that 6% strains of S. aureus are USA300 type and probably transported via the passengers coming from USA to Italy ³⁸. On January 1, 2000, the study reviewed the molecular properties of the S. aureus (MRSA)-ST80 clone, concentrating on its proportionate separation from total MRSA strains, PVL production, spa typing, antibiotic resistance, and pathogenicity. Between August 31, 2019, and August 31, 2019, the MRSA-ST80 clone was published ³⁹.

Table 1. Asian Epidemiology of S. aureus

Findings	Reference lab	Reference
The (593) strains of S. aureus were verified for PVL, one In addition, (69) PVL+	Reference Laboratory of France	28
S. aureus isolates have not been defined as CA-MRSA, two patients died		
The prevalence of ST80 clones has risen In 2000, the rate of increase was	Single Hospital of	30
dramatic; no risk factor analysis was given	Greece	
All four patients have not been hospitalized before Admission	Reference Laboratory of	40)
	Germany	
Suggestion of recent portable in three countries 16 PVL+ dissociated patients	Reference Laboratory of Belgium,	34
MRSA was found in 21 percent of 1058 S. aureus isolates, while PVL+ MRSA	Three Hospital of Greece	31
caused 64 percent of the infections in one institution.		
0.6% of PVL was detected in the 1500 isolates tested; seven strains of ACME	Reference Laboratory of Austria	36
positive.		
PVL received 15.5 percent of (1337) MRSA isolates during the research period.	Single Hospital of Spain	37
Isolates MRSA of S. aureus 6% of 188.	Laboratories of Italy	37
Examined, 3.2% (8/248) were recognized as MRSA ST80	Croatia	41

Molecular Epidemiology in Asian Countries

Taiwan: A Prospective study from 2004 to 2005 indicated that the incidence of CA-MRSA infection was 56%, compared to HA-MRSA (41%) between 2001 and 2008. Transmission through droplets among children has been increased from 1.9% 2001 to 10.2% in 2007-08 in Northern Taiwan. ⁴². The ST 239 MRSA isolates are most resistant to Chlorhexadine and other antibacterial agents, MRSA strain with Disinfectant-Resistant qACA/B genes were common in Taiwan (Sheng et al., 2009).

China

Samples collected from five main Paediatrics Hospitals during 2005-2006 were analysed for S. aureus showed that among 1.7% positive samples 0.9% were CA-MRSA. The study of Beijing showed that 1104 SSTI children were hospitalized in 2008-09, 351 31.8% cases were CA-S.

aureus infections, of which 4% were MRSA. The most prevalent clones were ST59-IV-t437, ST910-IVa-t318 and ST1-IVa-t318⁴².

Japan: CA-MRSA was certified in 17-20% of S. aureus Bullous impetigo in a previous study in Japan in the 2000s. It also showed that in a national survey from 2008 to 1990 in 2009 ⁴².

South Korea: Two clones dominate HA-MRSA isolates in South Korea, with the emergence of ST239 and ST5 CA-MRSA initially reported in Kyungnam Province in 2004-05². **South East Asia:** The study presented the emergency department among the six regional hospitals covering half of the Hong Kong population, of which 298 suffers from supportive SSTI, 13 out of 125 S. aureus strains (10%), and 12 out of 241 Abscesses (5%) are related to PVL positive S. aureus ⁴².

Table 2. Asian	Epidemiology	of S. aureus
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Findings	Reference lab	Reference
Rate of S. aureus infection was 56% (102 out of 183 children	Taiwan	
MRSA 38 (0.9%) is CA-MRSA. Children in Beijing 1104 SSTI	China	
351 (31.8%) cases in which 14 (4%) cases were MRSA	Japan	(⁴²
ST89-II-t375 (Ten isolates), ST72-IVa-t324 or t664 were the three clones found in 23 CA-MRSA isolates (11 isolates).	South Korea	
13 out of 125 strains of S. aureus (10%) and 12 of 241 Abscesses (5%) are due to PVL positive S. aureus.	South East Asia	
Showed 49% prevalence from the total reported cases.	Pakistan	43

Worldwide Epidemiology in other Countries

South America: The USA300 isolate typically carries genes encoding Panton-Valentine Leukocidin PVL and arginine catabolism elements, but rarely carries Staphylococcal enterotoxin genes. As a result, the USA300 isolate has shown to be more resistant to antibiotics such as Levofloxacin, Erythromycin, Mupirocin, and Tetracycline, and has spread to Europe, Australia, and South America ⁴⁴. The CDC (Center for Disease Control and Prevention) has proven in recent research that MRSA Nasal Carriage is exceedingly low in healthy people in the United States. According to previous findings, men to men sex (MSM) has a shockingly high transmission rate (6-8 percent) of MRSA among homeless, immunocompromised HIV positive individuals. If CA-MRSA clones are introduced into hospitals along with PVL toxin, it may result in a significant

increase in drug-resistant S. aureus infections, making successful chemotherapy more difficult⁴⁵

Australia: Multi-drug resistant MRSA (m-MRSA) was found in Victoria, Australia, which is a Hospital-Acquired infection. In Western Australia, people discovered a Non-Multi-Drug Resistant MRSA (nmMRSA) in the community. This is named WA-MRSA (Western Australia-MRSA). These strains of nmMRSA have not spread in hospitals. This CA-MRSA is also spread in other countries around the world, including Canada, the United States, France, Denmark and Finland ⁴⁶.The rising prevalence of CA-MRSA in Central Australia is 32 % compare with 20 % previous in the same decade. From 2003 to 2005, the ARMed project collected isolates of more than 5000 susceptibility test results of S. aureus from blood cultures. It is included 62 hospitals of Algeria, Cyprus, Egypt, and Jordan, turkey, Malta, Morocco and Tunisia. The countries included Jordan, Egypt, and Cyprus has reported the highest proportion of MRSA, and invasive isolates were more than 50% of Methicillin-Resistance. It is concluded that in Mediterranean region most of the countries are under the surge of MRSA infection (Coombs et al., 2004). For MRSA a descriptive study was done. In this study 147 S. aureus isolates were collected foe screening of MRSA in Nigeria. In the results forty-five (45) of 88.2% isolated of MRSA were associated with infection and 6 of 11.8% isolates of MRSA were strains of colonization. All screened MRSA isolates were resistance to more than two antibiotics three MRSA isolates were sensitive to Vancomycin. By the correct use of antibiotics, hand washing, the spread of MRSA can be controlled specially in health care centers ⁴⁷.

Resistant antibiotics

Penicillin: The spread of antibiotic resistance in S. aureus can be imagine as a series of waves as the first wave was started in mid 1940s which causes penicillin resistant strains of S. aureus ^{48, 49}. Penicillin was discovered in 1944 to treat S. aureus infections. At that time penicillin was about 94% susceptible to Staphylococcus but later in 1950 penicillin shows resistance by half of the isolates of S. aureus ⁵⁰. Some of the strains of S. aureus produces β-lactamase that hydrolysis the critical β-lactam bond or ring which is essential and destroyed the Drug's Antibacterial Activity ⁴⁸. In S. aureus infections some genes also shows resistance to Penicillin in which the BlaZ gene is a distinctive serine β -lactamase enzyme which showed resistant to Penicillin ⁵¹.

Methicillin: Methicillin was introduced in 1959 to treat infections which are caused by Penicillin- Resistance S. aureus. In 1961, later on there were cases in which Methicillin shows resistance to S. aureus in United Kingdom called MRSA (Methicillin-Resistance S. aureus). MRSA were become a problem in worldwide hospitals of European countries Australia, Japan and United ⁵¹. Different cases of MRSA were arising in different countries in which a case of 5-year-old girl with surgical scalp wound also reported. The patient was treated with Vancomycin, Clindamycin which are susceptible to S. aureus (MRSA). After sometime, it again shows same the infection with MRSA. Again surgery was performed and a patient was treated with Vancomycin and Rifampin which shows progress in strains that spread and affect cell wall biosynthesis and homeostasis during Prolonged treatment by acquiring multiple mutations in chromosomal genes.

The most noticeable and conspicuous situation is that the spread of MRSA strains result in the resistance of many commonly used antibiotics ⁵². After the Penicillin, Methicillin was the second wave of resistance of antibiotics towards S. aureus. In S. aureus infections some specific gene mecA (methicillin resistance) is responsible for Methicillin; this gene also encodes the low-affinity Penicillin-Binding Protein PbP2a (also known as PbP2'). Methicillin Resistant is broad in the spectrum of its activity ⁴⁸. In west Bengal 11% to 56% of S. aureus infections are Methicillin Resistant ⁵³. After mecA gene, MecC gene a distinct PBP2a was discovered recently with only 63% remaining identity to MecA gene. In Europe the gene MecC occurs predominantly in a single lineage of MRSA ⁵⁴.

Vancomycin: In 1950's, a Glycopeptides antibiotic was introduced which namely Vancomycin. It is used to treat the infection caused by S. aureus. Vancomycin has the good activity at that time against S. aureus but due to spread of

MRSA the extreme use of Vancomycin results in the resistance of Vancomycin towards S. aureus. In Japan in 1997, the first case was reported of clinical strain (Mu50) of VRSA ⁵⁵. Vancomycin was discovered more than 50 years ago. It remains an acceptable treatment option for MRSA infection. The discovery of two distinct VRSA strains from one patient in the recent incidences of Vancomycin Resistance indicates that MRSA is continuously spreading like a superbug ⁵⁶

Other Antibiotics Resistance (Clindamycin, Oxacillin and Erythromycin): A study was conducted in which Oxacillin shows 100% resistance towards S. aureus infections. Oxacillin also shows resistant to S. aureus infections in a survey of APAC (Asia Pacific) region in different hospitals on patients about 45.9%. In hospitalized patients Oxacillin-Resistance S. aureus (ORSA) is the main and important cause of infections 57. In Recent study, the 100% Erythromycin Resistance was found and noted 52. In a recent research ermA, ermC (Erythromycin Resistance) were studied 58, 59. A D-test (Double Disk Diffusion Test) was performed for determination of inducible Clindamvcin Resistance on all ErythromycinResistant S. aureus isolates. Therefore, only from 2009 to 2014 trends of Clindamycin resistance were analyzed. MRSA was found to be less resistant to Gentamycin, Cloxacillin and Clindamycin ⁶⁰. Many binding sites of the antibiotic overlap and in the drug's mechanisms of inhibition there are some similarities in it.

Some antibiotics used to treat Staphylococcal infections in man and animals which includes; Linezolid, Florfenicol, Clindamycin, Pleuromutilins, Streptogramins and Macrolides 61. Linezolid shows resistant towards cfr (Chloramphenicol-Florfenicol Resistance) gene which carrying plasmids and mediates resistance. Inducible resistance to Streptogramin B, Macrolide and Lincosamide (Clindamycin) in S. aureus is allocate and encoding an enzyme by erm (Erythromycin Ribosome Methylase) gene which Methylate Adenine Remnants of 23s rRNA (Ribosomal Ribonucleic Acid). In Clindamycin resistance cfr gene also mediates resistance 62. In recent studies some Staphylococcus isolates were tested by disk diffusion method for Inducible Clindamycin Resistance (iMLSB) and Mupirocin resistance 52. In a recent report CA-MRSA isolates were resistant to Amoxicillin/Clavulanic acid, Cefazolin, Erythromycin, Oxacillin, and Penicillin 63.

S.No	Resistant Antibiotics	Year of Showing Resistant	References
1.	Penicillin	1940 1950	6 12
2.	Methicillin	1961	14
3.	Vancomycin	1997	55

Sensitive and Susceptible Antibiotics: In a recent research Vancomycin were susceptible towards all S. aureus isolates ⁶⁴. Some studies reported 100% susceptibility to Vancomycin in S. aureus infections. In Africa the susceptibility of MRSA isolates to Vancomycin is between 82% and 100% ⁶⁵. For Gentamycin higher sensitivity pattern was observed about (93.9%) as compared to Vancomycin (76.8%). Several authors working in SSA (Sub-Saharan Africa) also reported High

susceptibility to Gentamycin. However, higher frequency of Gentamycin and Erythromycin resistance reported by other authors ⁶⁵.

In a study Clindamycin shows sensitivity towards CA-MRSA which was conducted from 20022003 on 10 patients who are in contact with prisoners. All CA-MRSA infections treated and responded well to Clindamycin, Mupirocin. Clindamycin, Rifampin,

Trimethoprim/Sulfamethoxazole, and Vancomycin all were sensitive in the positive MRSA cultures in which sensitivity patterns was similar (Dominguez, 2004). In China, a study was also conducted in which CA-MRSA and HA-MRSA were susceptible to both Vancomycin and Linezolid ⁶⁶

Linezolid shows low resistance towards both S. aureus (18.41%) and MRSA (21.22%) in a recent study. (Kulkarni et al., 2014) Rifampin has more effective when used in combination with Vancomycin, and has high characteristics including its potent Bactericidal Activity and ability to penetrate cells which are potentially effective against S. aureus. In a recent survey in response, 72% shows that Vancomycin could be used but with combination of second antibiotics, specially Gentamycin and Rifampin ⁶⁷. The percent rate of Gentamycin showing 22.8% susceptibility towards MRSA isolates in recent study ⁶⁸.

Table 4. Sensitive Antibiotics towards S. aureus

S.No	Sensitive Antibiotics	References
1.	Vancomycin	64, 65
2.	Clindamycin	63
3.	Topical Mupirocin	63
4.	Gentamycin	65
5.	Vancomycin	63, 65

CONCLUSION AND RECOMMENDATIONS

We concluded this study from many investigations on S. aureus infectionsin which HAMRSA and CA-MRSA are different at some points like PVL genes, and SCCmec subtypes. CA-MRSA is high as compared to HA-MRSA in different countries like Germany, Belgium, Australia, Spain Portugal and South America due to poor hygiene of health workers and other individual like Athletes, Prisoners and Non-Hospitalized patients; they are the main cause of transmitting S. aureus infection. The resistant and susceptibility of S. aureus towards different antibiotics may be changes sometime. MRSA is mostly Multidrug Resistant including; Methicillin, Vancomycin, Penicillin, Clindamycin, Erythromycin, and Oxacillin etc. If antibiotics combines with second antibiotics it shows positive results in the treatment of S. aureus infections and it can be treated easily e.g. Vancomycin with combination of Gentamycin and Rifampin and Clindamycin and Topical Mupirocin in the different states of the USA. We observed that resistance genes in clinical S. aureus strains are mecA, ermA, ermB, and ermC, mupA, msrA and msrB, tet, ant (4)-la, aac (6)- le/aph (2). It is also concluded that HA- MRSA clones have SCCmec types (mainly I, II and III). SCCmec types are identified in various MRSA clones including SCCmec, which together with SCCmec Type V represents one of the two Chromosomal Cassettes identified in all CA-MRSA. According to the epidemiological studies of S. aureus we

get the information that different types of clones like ST80, ST8, ST30, ST5, ST22, ST59 V, ST72 and many more were reported in different regions around the world in different periods which may Associated to Hospital or Community, similarly we observed the different infections in different groups of people with their percent (%) prevalence, so we get the enlightening knowledge about their spreading rate that the strains of S. aureus are present in different regions around the world. S. aureus is an issue in both the Community and the Hospital Associated, with increased prevalence of Methicillin-Resistant strains worsens the situation. S. aureus and declining efficacy of Vancomycin and Methicillin. Research studies on various antibiotics such as Vancomycin, Gentamycin, and Rifampin should be conducted in various countries for treating MRSA infections. Despite the recent availability of multiple new antibiotics for S. aureus, new policies for treatment and prevention are required for this extremely prevalent source of human illness.

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