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METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)

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ABSTRACT
The aureus bacteria Insufficient methicillin Not able to use methicillin Many infections are caused by Staphylococcus aureus (MRSA), from infections on the skin and soft tissues to infections in the bloodstream that can lead to sepsis, pneumonia, and other serious infections. An important public health issue is MRSA, which makes a lot of people sick and even kills some. What signs do MRSA illnesses show? How common are they? How do they become resistant? This study looks at these questions and more. We're talking about the mecA and mecC genes, which are what makeup MRSA. Additionally, we go over PBP2a and how it stops medicines from doing their job. Not able to use methicillin Hospital infections of Staphylococcus aureus are not the same as diseases that happen in the community. Our conversation centers on the things that help CA-MRSA spread. Like, we look at the past of PCR, diagnostics, and rapid detection tools. Linezolid, daptomycin, phage treatment, and antibiotic peptides are some of the other ways that are talked about to treat Staphylococcus aureus that is not sensitive to methicillin. It's also part of public health to talk about how to stop diseases like MRSA. More studies have been done to try to figure out what causes MRSA and come up with new ways to treat it, like making medicines. As a final point, the fact that MRSA is not killed by antibiotics and has an effect on health care all over the world shows how important it is to keep researching, come up with new ideas, and work together to solve this big public health problem.

KEYWORDS: MRSA, methicillin-resistant *Staphylococcus aureus*, antibiotic resistance, hospital-acquired MRSA, community-acquired MRSA, PBP2a, phage therapy, antimicrobial peptides, vaccine development, infection control, public health.

1. INTRODUCTION

Staphylococcus aureus is a gram-positive bacterium that people carry on their skin, in their noses and in their mouths. Pathogenic means it can turn into an infection-causing agent and lead to a wide range of illnesses, from minor skin problems to serious systemic illnesses like sepsis, endocarditis, and asthma (Nandhini et al., 2022). Toxins and enzymes are some of the virulence factors that help it get into host cells and get past the immune system. Because it can change and is resistant to drugs, S. aureus is important for therapy. Penicillin initially treated Staphylococcus aureus infections. After the discovery of beta-lactamase-resistant methicillin in the 1960s, MRSA emerged (Okwu et al., 2019). The mecA gene generates PBP2a, a beta-lactam antibiotic-inhibiting protein, which contributes to this resistance. MRSA raises healthcare costs, morbidity, and mortality and complicates therapy. MRSA is a leading source of hospital-acquired infections in patients with invasive devices, surgical wounds, or weakened immunity (Brown et al., 2021). Recent decades have seen a rise in CA-MRSA infections in otherwise healthy patients outside of hospitals.

2. Historical Background

Scottish surgeon Alexander Ogston discovered Staphylococcus aureus from abscess pus in the late 19th century. The bacteria was termed "staphylococcus" by its grape-like tiny clusters, from the Greek words staphyle (grape) and kokkos (berry) (Craft et al., 2019). Staphyloxanthin, a carotenoid pigment, gives the species its golden color on agar plates and, therefore aureus. This discovery opened the door to disease-causing bacterium study and advanced our understanding of infection-causing microbes.

2.1 Development of Methicillin Resistance

In antibiotic resistance history, methicillin-resistant Staphylococcus aureus stands out. Despite penicillin's early success in treating S. aureus infections, penicillin-resistant strains appeared in the 1940s. Within a year, UK methicillin-resistant S. aureus reports began (Sharaf

et al., 2021). Resistance came from finding the mecA gene on SCCmec. Due to its low affinity for beta-lactam antibiotics, PBP2a, produced by the mecA gene, avoids them. The rapid spread of MRSA showed its adaptability and antibiotic resistance, allowing it to spread worldwide.

2.2 Key Milestones in the Epidemiology of MRSA

The epidemiology of MRSA has evolved significantly over the decades, marked by several key milestones.

1960s: Emergence of Hospital-Acquired MRSA (HA-MRSA) MRSA was first only found in healthcare settings, where it infected hospitalized patients, especially those who had invasive devices or surgery wounds. HA-MRSA became the main cause of hospital-acquired diseases around the world (Wu et al., 2019).

1990s: Rise of Community-Associated MRSA (CA-MRSA) When CA-MRSA showed up, it changed the way we think about how MRSA spreads. People who were otherwise healthy and had never been in a healthcare setting before got illnesses from these strains. People who got CA-MRSA infections often had infections on their skin and soft tissues. These infections were linked to certain factors that made the bacteria more likely to spread, like the Panton-Valentine leukocidin (PVL) toxin.

2000s: Global Spread of MRSA As the number of cases in hospital and community settings rose, MRSA turned into a global public health problem (Dadashi et al., 2018). International trade and travel made it easier for MRSA strains to spread between continents, which helped it grow all over the world.

Present Day: Evolution of Multidrug-Resistant MRSA Because MRSA is always changing, new strains have come out that are not affected by many types of drugs. This makes treatment even more limited. This shows how important it is to come up with new ways to fight MRSA, such as new antibiotics, vaccines, and different treatments.

3. Epidemiology of MRSA

3.1 Global Prevalence and Distribution

People all over the world are at risk of getting MRSA because it is so common and medicines don't work on it. Even though the number of attacks is different depending on where they happen, CA-MRSA and HA-MRSA strains are making it worse. Some people say that MRSA is everywhere, but the WHO says that the illness is more common in some places and less common in others. In some countries, 30–50% of hospitals may have HA-MRSA. There is a lot of methicillin-resistant Staphylococcus aureus in the world because people don't clean up after themselves properly and use drugs that don't kill it.

3.2 Factors Influencing MRSA Transmission

A lot of dirty things, like sharing medical tools, can allow MRSA to get into people. Not having good infection control is another way. It's more dangerous to use invasive medical tools and have a weak immune system. MRSA is simple to spread at school, home, and on sports teams (Kadiyala et al., 2018). Sharing razors, towels, and workout equipment can make you sick. Pollution in the air, water, and clothes can help MRSA spread because it can stay on these things for a long time. It gets worse when there is bad drainage, not enough cleaning, and too many people living in public buildings.

4. Mechanisms of Resistance

4.1 Genetic Basis: mecA and mecC Genes

The main way that methicillin doesn't work on Staphylococcus aureus is through the mecA gene. This gene is part of SCCmec, which is a mobile genetic element. As Garoy et al. (2019) say, methicillin and other beta-lactam drugs don't work well against MRSA types because they don't bind well to the changed PBP2a made by the mecA gene. When it comes from an animal, an MRSA type may have both mecA and mecC genes. Most of the time, mecA is present, but mecC makes a PBP2a mutant that is not sensitive to methicillin. Because it has the genes it needs to be tolerant, S. aureus can stay away from beta-lactam drugs.

4.2 Role of PBP2a (Penicillin-Binding Protein)

PBP2a is the main methicillin-resistant protein. It is a changed form of PBP that bugs use to build the walls of their cells. Certain drugs, like methicillin, connect to PBPs and stop germs from building cell walls. This stops the growth of cells. Beta-lactams can't link to PBP2a and stop the building of cell walls, but MRSA can still grow and spread (Hu et al., 2019). Because of how it is built, drugs that stop PBP2a from working might be able to really hurt it.

5. Clinical Manifestations

5.1 Spectrum of MRSA Infections

MRSA can cause a wide range of infections, from mild skin conditions to severe, life-threatening diseases. The clinical spectrum of MRSA infections includes.

1. **Skin and Soft Tissue Infections (SSTIs):** These are the most common MRSA infections. They usually show up as boils, abscesses, cellulitis, or impetigo. These infections usually stay in one place, but they can spread if you don't treat them.
2. **Bloodstream Infections (Bacteremia):** MRSA can lead to bloodstream infections, which often have a high death rate. Most of the time, bacteremia happens after infections in other parts of the body, like the lungs or bones (Parente et al., 2018).
3. **Pneumonia:** Necrotizing pneumonia caused by MRSA is a very bad side effect that can happen, especially to people who are hospitalized or who have long-term lung illnesses. It usually needs harsh treatment and can cause a lot of damage to the lungs.

4. **Endocarditis:** MRSA can infect heart valves, causing endocarditis, which can result in heart failure, stroke, or death if not treated promptly.
5. **Osteomyelitis and Septic Arthritis:** These are bone and joint infections that can be caused by MRSA, leading to long-term disability if untreated.

5.2 Complications Associated with MRSA Infections

Complications from MRSA infections can be severe and include.

- **Sepsis:** A life-threatening response to infection characterized by widespread inflammation, organ failure, and shock (Wangai et al., 2019).
- **Toxic Shock Syndrome:** A rare but severe condition caused by MRSA, often associated with the production of toxic shock syndrome toxin-1 (TSST-1).
- **Necrotizing Fasciitis:** A rapidly progressing infection that destroys tissue, often requiring surgical debridement.

6. Diagnosis

6.1 Laboratory Methods for Identifying MRSA

Accurate diagnosis is necessary to treat and manage MRSA infections. Culture-based approaches are unmatched for MRSA diagnosis. A sample from the infection site (blood, sputum, or wound swab) on selective agar media (mannitol salt or chromogenic) distinguishes MRSA from other Staphylococcus aureus strains (Algammal et al., 2020). To determine antibiotic susceptibility, an isolated organism is sensitivity tested. Because it detects the mecA gene, PCR can identify methicillin-resistant Staphylococcus aureus. PCR is fast (a few hours) sensitive and specific. Multiplexing PCR-based mecA gene and S. aureus detection enables fast and accurate diagnosis. Clinical settings increasingly use immunoassays and lateral flow assays to detect MRSA quickly (Gajdács, 2019). These tools can quickly identify MRSA-specific antigens or molecular markers compared to culture-based methods. Commercial rapid tests can detect MRSA infections in 30 minutes to 2 hours.

6.2 Challenges in MRSA Detection

While diagnostic methods have improved, several challenges remain in the detection of MRSA, including.

- **False negatives:** Especially in cases where the infection burden is low or the sample is inadequately collected.
- **Antibiotic resistance variations:** The emergence of strains with different resistance profiles may require multiple diagnostic tests to ensure accurate identification (Nandhini et al., 2022).
- **Cost and accessibility:** Advanced molecular diagnostic techniques may not be available in all healthcare settings, particularly in low-resource areas.

7. Treatment Options

7.1 Antibiotics Effective Against MRSA

Methicillin, oxacillin, and penicillin are among MRSA's antibiotic resistances. Vancomycin is the first line of treatment for most methicillin-resistant Staphylococcus aureus infections, especially those with bacteremia or pneumonia. It works by inhibiting bacterial cell wall synthesis. The rise of vancomycin-resistant Staphylococcus aureus has complicated treatment regimens (Okwu et al., 2019). With Gram-positive bacteria, it destroys MRSA and other resistant types. Unfortunately, lung surfactant makes pneumonia treatment ineffective. Clindamycin, a popular skin and soft tissue antibiotic, stops CA-MRSA from generating new proteins. TMP-SMX can cure mild to severe MRSA infections, notably skin and soft tissue infections because it works against several MRSA strains.

7.2 Emerging Treatment Approaches

- Phage therapy, which uses bacteriophages to find and kill specific germs that cause disease, is being looked at as a possible way to treat MRSA. This method looks especially good for strains that are immune to more than one drug. New research suggests that phages can be used along with regular antibiotics, which might help solve the problem of resistance (Sharaf et al., 2021).
- It looks like AMPs, like defensins and cathelicidins, could be useful as different medicines to treat MRSA. These peptides can attack a wide range of microbes, including MRSA, by breaking down their membranes. Scientists are still working on making manmade or recombinant AMPs that work better and last longer.
- Nanomaterials, like silver nanoparticles, are being studied to see if they might be able to kill microbes. Silver can stop the spread of MRSA by damaging cell membranes, which suggests that it could be used along with regular antibiotics.

7.3 Issues with Antibiotic Resistance and Treatment Failures

It is hard to treat MRSA illnesses because they are resistant to antibiotics. Because antibiotics are used too much and in the wrong way, new types of bacteria are becoming vancomycin-resistant (Kadiyala et al., 2018). A lot of hospital treatments fail because of serious infections and weak immune systems. Different types of MRSA cells in an illness can't be killed by different drugs. This makes treatment more difficult and needs a mix of drugs.

8. CONCLUSION

Many people get MRSA, which is bad for public health because it can cause dangerous infections and is not easily killed with medicine. This study talks about how methicillin-resistant Staphylococcus aureus gets around, how to find and treat it, and what signs it causes. Even though there are better ways to treat MRSA infections, they are still hard to get rid of, especially types that are

not affected by more than one drug. To make measures work, we need to learn more about how MRSA causes illness, how it builds tolerance, and how to find new treatments. To lower antibiotic resistance, public health efforts must keep working to make healthcare centers and communities better at stopping infections from spreading and to better manage antibiotics. Everyone in the world needs to study MRSA and work together to stop it. New medicines like phage treatment, antimicrobial peptides, and gene editing offer hope, but the most important thing to do is still get vaccinated. Overall, to stop MRSA, we need better ways to find it, new medicines, tracking around the world, and better ways to stop infections. We can help patients get better care and reduce the spread of MRSA around the world if we work together and come up with new ideas.

9. REFERENCE

1. Nandhini, P., Kumar, P., Mickymaray, S., Alothaim, A. S., Somasundaram, J., & Rajan, M. (2022). Recent developments in methicillin-resistant Staphylococcus aureus (MRSA) treatment: A review. *Antibiotics*, *11*(5): 606.
2. Okwu, M. U., Olley, M., Akpoka, A. O., & Izevbuwa, O. E. (2019). Methicillin-resistant Staphylococcus aureus (MRSA) and anti-MRSA activities of extracts of some medicinal plants: A brief review. *AIMS microbiology*, *5*(2): 117.
3. Brown, N. M., Goodman, A. L., Horner, C., Jenkins, A., & Brown, E. M. (2021). Treatment of methicillin-resistant Staphylococcus aureus (MRSA): updated guidelines from the UK. *JAC-antimicrobial resistance*, *3*(1), dlaa114.
4. Craft, K. M., Nguyen, J. M., Berg, L. J., & Townsend, S. D. (2019). Methicillin-resistant Staphylococcus aureus (MRSA): antibiotic-resistance and the biofilm phenotype. *MedChemComm*, *10*(8): 1231-1241.
5. Sharaf, M. H., El-Sherbiny, G. M., Moghannem, S. A., Abdelmonem, M., Elsehemy, I. A., Metwaly, A. M., & Kalaba, M. H. (2021). New combination approaches to combat methicillin-resistant Staphylococcus aureus (MRSA). *Scientific reports*, *11*(1): 4240.
6. Wu, S., Huang, J., Zhang, F., Wu, Q., Zhang, J., Pang, R., ... & Wei, X. (2019). Prevalence and characterization of food-related methicillin-resistant Staphylococcus aureus (MRSA) in China. *Frontiers in microbiology*, *10*, 304.
7. Dadashi, M., Nasiri, M. J., Fallah, F., Owlia, P., Hajikhani, B., Emaneini, M., & Mirpour, M. (2018). Methicillin-resistant Staphylococcus aureus (MRSA) in Iran: a systematic review and meta-analysis. *Journal of global antimicrobial resistance*, *12*: 96-103.
8. Barratt, R., Shaban, R., & Moyle, W. (2010). Behind barriers: patients' perceptions of source isolation for methicillin-resistant'Staphylococcus aureus'(MRSA). *Australian Journal of Advanced Nursing, The*, *28*(2): 53-59.
9. Kadiyala, U., Turali-Emre, E. S., Bahng, J. H., Kotov, N. A., & Vanepps, J. S. (2018). Unexpected insights into antibacterial activity of zinc oxide nanoparticles against methicillin resistant Staphylococcus aureus (MRSA). *Nanoscale*, *10*(10): 4927-4939.
10. Garoy, E. Y., Gebreab, Y. B., Achila, O. O., Tekeste, D. G., Kesete, R., Ghirmay, R., ... & Tesfu, T. (2019). Methicillin-Resistant Staphylococcus aureus (MRSA): Prevalence and Antimicrobial Sensitivity Pattern among Patients—A Multicenter Study in Asmara, Eritrea. *Canadian Journal of Infectious Diseases and Medical Microbiology*, *2019*(1): 8321834.
11. Hu, W., Li, C., Dai, J., Cui, H., & Lin, L. (2019). Antibacterial activity and mechanism of Litsea cubeba essential oil against methicillin-resistant Staphylococcus aureus (MRSA). *Industrial Crops and Products*, *130*: 34-41.
12. Parente, D. M., Cunha, C. B., Mylonakis, E., & Timbrook, T. T. (2018). The clinical utility of methicillin-resistant Staphylococcus aureus (MRSA) nasal screening to rule out MRSA pneumonia: a diagnostic meta-analysis with antimicrobial stewardship implications. *Clinical Infectious Diseases*, *67*(1): 1-7.
13. Wangai, F. K., Masika, M. M., Maritim, M. C., & Seaton, R. A. (2019). Methicillin-resistant Staphylococcus aureus (MRSA) in East Africa: red alert or red herring?. *BMC infectious diseases*, *19*: 1-10.
14. Algammal, A. M., Hetta, H. F., Elkelish, A., Alkhalifah, D. H. H., Hozzein, W. N., Batiha, G. E. S., ... & Mabrok, M. A. (2020). Methicillin-Resistant Staphylococcus aureus (MRSA): one health perspective approach to the bacterium epidemiology, virulence factors, antibiotic-resistance, and zoonotic impact. *Infection and drug resistance*, 3255-3265.
15. Gajdács, M. (2019). The continuing threat of methicillin-resistant Staphylococcus aureus. *Antibiotics*, *8*(2): 52.