International Journal of Advanced Multidisciplinary Research
ISSN: 2393-8870
www.ijarm.com
(A Peer Reviewed, Referred, Indexed and Open Access Journal)
DOI: 10.22192/ijamr Volume 9, Issue 9 -2022

Review Article

DOI: http://dx.doi.org/10.22192/ijamr.2022.09.09.003

A systematic review on Methicillin resistant *Staphylococcus aureus* in patients with surgical wounds

Chidimma Maureen Chukwueze[1], Ogochukwu Vivian Okpala[1] and [*]Emmanuel Ifeanyi Obeagu[2]

1Department of Medical Laboratory Science, Enugu State University of Science and Technology, Enugu State, Nigeria

2Department of Medical Laboratory Science, Kampala International University, Western Campus, Ishaka, Uganda.

E-mail: *emmanuelobeagu@yahoo.com*

[2]https://orcid.org/0000-0002-4538-0161

Keywords

MRSA,
SCCmec,
mecA gene,
antimicrobials

Abstract

MRSA is defined by the presence of staphylococcal cassette chromosome mec (SCCmec); which is a large mobile genetic element that carries the mecA gene which codes for an alternative form of penicillin binding protein (PBP2a). *Staphylococcus aureus* developed resistance to this type of β-lactam antibiotics by acquiring the mecA gene which is carried on the SCCmec element described earlier. Strains which carry this mecA gene are known as methicillin resistant *Staphylococcus aureus* (MRSA), even though they are actually resistant to all β-lactam based antibiotics. Historically, *Staphylococcus aureus* has been known to develop antimicrobial resistance to most antimicrobials rapidly. The bacteria developed resistance to penicillin only a year after the introduction of penicillin into clinical use. It is now estimated that 90%–95% of *Staphylococcus aureus* strains worldwide are resistant to penicillin. The resistance exhibited by MRSA to most antibiotics imply that treatment for suspected or verified severe *Staphylococcus aureus* infections, including common skin and wound infections, must rely on second line drugs.

Introduction

S. aureus infections continue to increase and are increasingly implicated in various stages of infection. Methicillin-resistant Staphylococcus aureus (MRSA) is of particular interest due to its increasing resistance. Most S. aureus infections used to occur in healthcare settings, but are now known to cause serious infections in the community (Knox et al., 2015). The major isolate from postoperative wound infections and other open wounds is Staphylococcus aureus (Bhattacharya, 2016). Awareness of methicillin-resistant Staphylococcus aureus (MRSA), which is often resistant to beta-lactam antibiotics such as penicillins, cephalosporins, and carbapenems, is needed (Bhattacharya, 2016). Staphylococci are the major genus of the family Staphylococci in the order Bacillus. Staphylococcus aureus (S. aureus) is a non-spore-forming, non-motile, facultatively anaerobic, Gram-positive spherical bacterium 0.5–1 μm in diameter. It is positive for both catalase and coagulase and looks like a bunch of grapes under the microscope. When cultured on mannitol salt agar and blood agar, on blood agar he produces round, golden-yellow colonies containing B-hemolysin, fermenting mannitol. H. Make the media yellow (Ryan and Ray, 2014). When S. aureus reproduces asexually by binary fission, the two daughter cells may not completely separate and stick together. This explains why cells are often observed in clusters. This bacterium is the most pathogenic of the staphylococcal species. It takes 20-30 minutes to grow and can grow in high salinity and temperatures of 10-46 °C. A study by Sotto et al. (2010) highlighted the virulence potential of the bacterium and is considered one of the main causes of community-acquired and nosocomial infections, resulting in high morbidity and mortality (Bhateja et al. ., 2010). This organism is part of the normal human microbial flora. It is found on the surface of the skin, intestines, upper respiratory tract, and vagina. It can become pathogenic when temperature and pH conditions are favorable and nutrients are available to support overgrowth (Makgotlho, 2015).

Surgical Wound: An Overview

A surgical wound is a cut or incision in the skin, usually made with a scalpel during surgery (Clyne et al, 2018). Surgical wounds can also be the result of drains placed during surgery.

Surgical wounds vary greatly in size. A surgical wound occurs when a surgeon makes an incision or cut with a surgical instrument called a scalpel. Surgery is required for various medical conditions. The size of the scar depends on the type of procedure and location on the body. All surgical procedures create a surgical wound (Awad, 2012). The chance of wound infection after surgery is 1-3%. Risk factors for developing surgical wounds include other medical problems such as diabetes and a weakened immune system (Clyne et al, 2018).smokers, the elderly and overweight are also at increased risk of infection. Emergency surgery, abdominal surgery, and surgeries lasting more than 2 hours also increase the risk of infection (Breurec et al, 2011). Surgical wounds are often monitored to ensure they are healing properly. According to the Centers for Disease Control and Prevention Trusted Source, the infection may only affect the skin, tissue under the skin, or implants.Signs of surgical wound infection include increased pain and redness around the wound. , delayed healing, presence of pus, foul odors, or wound discharge (CDC, 2016).

A hematoma is a buildup of blood within tissue, causing swelling within the tissue. Hematomas are easily injected by microorganisms. Scratches can be further classified as clean scratches, while dirty scratches have a contamination level of 30% or higher. Class I (clean) atraumatic wounds that do not interrupt the surgical procedure and do not open the focal point of sepsis or internal organs. Class II (cleanly contaminated) wounds are atraumatic and can enter a vicious circle with little interference with the procedure or without significant burial. Class III (contaminated) is trauma from a relatively clean source, large procedural fractures, significant spills from open viscose, or wounds where acute nonsuppurative infection occurs.

In some cases, infected surgical wounds may become dry and deep. Fever is also a common symptom. Doctors can diagnose surgical site infections by examining the wound, evaluating symptoms, and taking cultures of fluid drained from the wound. Treatment of surgical wounds may vary depending on where they are on the body. A surgical dressing is typically placed over the wound and may need to be changed periodically (CDC, 2016). The skin around the surgical wound often needs to be washed with soap and salt water. You may also need to rinse the wound with salt water. Fill a syringe with salt water and spray it onto the skin around the wound (Awad, 2012). To treat the infection, your doctor may need to prescribe antibiotics or open and clean the wound. It is usually closed with sutures but may be left open for healing. Surgical wounds can be classified into one of four categories. These categories depend on how contaminated or clean the wound is, the risk of infection, and where the wound is located on the body.

Class I: These are considered clean wounds. They show no signs of infection or inflammation. They often involve the eye, skin, or vascular system.
Class II: These wounds are considered clean-contaminated. Although the wound may not show signs of infection, it is at an increased risk of becoming infected because of its location. For example, surgical wounds in the gastrointestinal tract may be at a high risk of becoming infected.
Class III: A surgical wound in which an outside object has come into contact with the skin has a high risk of infection and is considered a contaminated wound. For example, a gunshot wound may contaminate the skin around where the surgical repair occurs.
Class IV: This class of wound is considered dirty-contaminated. These include wounds that have been exposed to fecal material.

Surgical Site Infections (SSI)

An infection of a surgical site is a frequent complication of surgery and the commonest hospital acquired infection (Awad, 2012).

Microbiology of Surgical Site Infections

SSIs are most often caused by the endogenous flora of the patient and the organism isolated is dependent on the type of surgery performed (Awad, 2012). However, exogenous sources such as the hospital environment has also been implicated (Awad, 2012; Bastola *et al*., 2017). In the hospital setting, these organisms may be acquired by direct contact with hospital staff or other patients and improperly sterilized equipment or materials that are used during the surgical operation (Awad, 2012).

Characteristics of *Staphylococcus aureus*

Staphylococcus aureus is a Gram-positive cocci-shaped bacterium, which are often arranged in clusters like a bunch of grapes (Figure 2.1). They are non- motile (non-flagellated), non-spore forming and non-capsulated (some rare strains are capsulated). They can grow well on nutrient agar to form golden yellow pigment or sometimes white (non- pigmented) colonies. Other phenotypic characteristics used to identify *Staphylococcus aureus* includes their ability to ferment glucose to produce lactic acid, fermentation of mannitol (which differentiates it from *Staphylococcus epidermidis*) and the production of catalase and coagulase.

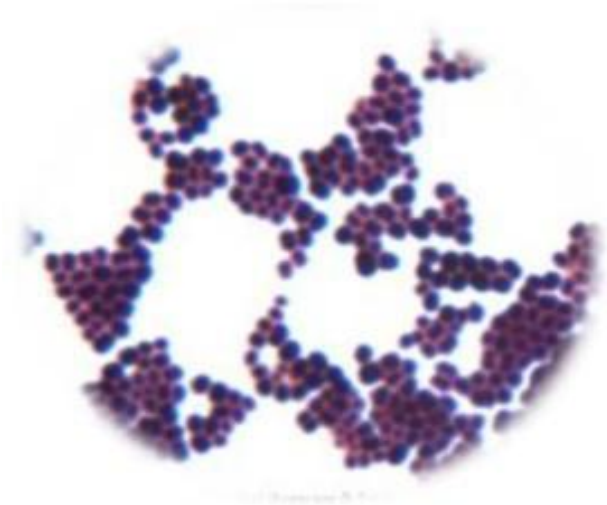

Figure 1: Gram – positive *Staphylococcus aureus* in clusters and short chains(Makgotlho, 2015)

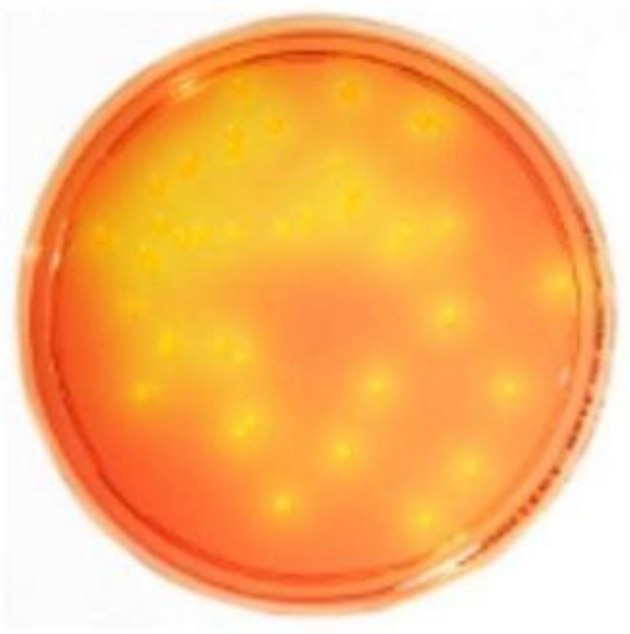

Figure 2: *Staphylococcus aureus* colonies surrounded by yellow zones on mannitol salt agar (Makgotlho, 2015)

Pathogenesis and Virulence of *Staphylococcus aureus* Infections

S. aureus has an extensive arsenal of virulence factors, including both secretory and structural products that play diverse roles in the pathogenesis of infection. It has been observed that one virulence factor has multiple roles in pathogenesis and multiple virulence factors perform similar functions (Gordon and Lowy, 2010).

To induce infection, bacteria use a series of surface proteins called 'microbial surface components that recognize adhesion matrix molecules' (MSCRAMMs). This helps the bacteria adhere to host tissues. MSCRAMM binds to molecules such as fibronectin, collagen and fibrinogen. Different MSCRAMMs can bind to the same host tissue component. This protein appears to play a role in causing bone and joint infections, intravascular infections, and prosthetic device infections (Gordon and Lowy, 2010). Different strains of the bacterium may have different collections of her MSCRAMMs and consequently cause different types of infections (Bastola et al., 2017). Once attached to prosthetic materials or host tissue, S. aureus can grow and persist in a variety of ways. They can form biofilms on the surface of the host or prosthesis and evade host defenses and antimicrobial agents to survive. Biofilm formation in particular makes it very difficult to eradicate prosthetic infections unless the prosthesis is removed. Pathogens are also relatively protected from antibiotics and host defenses, as they can form small colony variants (SCVs) that can "hide" in host cells in vitro without causing significant host cell damage. (CDC, 2016). This may contribute to persistence leading to recurrent infections if they later revert to a more virulent phenotype. In summary, virulence factors are grouped according to their role in virulence. These include;

1. Those involved in attachment; which includes the MSCRAMMS (e.g. fibronectin-binding proteins, collagen, clumping factors, and bone sialoprotein-binding proteins) which are associated with osteomyelitis, endocarditis, prosthetic-device and catheter infections, and septic arthritis.

2. Those involved in persistence which includes accumulation of biofilm which are also associated with relapsing infections, endocarditis, osteomyelitis, septic arthritis, etc.

3. Those involved in destroying the host's defenses; which includes leukocidins (Panton – Valentine leukocidin [PVL]), protein A, capsular polysaccharides, etc. These are associated with necrotizing pneumonia and invasive skin infections (CA-MRSA strains that cause these diseases are often associated with PVL) and abscesses (which are associated with capsular polysaccharides)

4. Those involved in invading or penetrating tissues which also include virulence factors such as hyaluronatelyase, proteases, lipases, nucleases, and metalloproteases which causes tissue destruction and metastatic infections.

5. Those involved in sepsis or toxin-mediated diseases which includes toxic shock syndrome toxin- 1(TSST-1),peptidoglycan, enterotoxins, exfoliative toxins, α-toxin, and lipoteichoic acid which are associated with toxic

shock syndrome, food poisoning, scalded skin syndrome, sepsis and bullous impetigo

6. There are also those which do not have clearly defined role in virulence and these include bacteriocin, coagulase, etc.

(Gordon and Lowy, 2010).

Mechanisms of Infection by *Staphylococcus aureus*

Invasive Mechanisms

Infection begins when the skin or mucosal barrier is breached, allowing bacteria access to nearby tissues or the bloodstream (Cosgrove et al., 2013). Depending on the complex interplay between bacterial virulence factors and host defense mechanisms, infections can be contained or further spread. Although host mucins appear to be an important surface for host colonization in a process involving mucin-carbohydrate-staphylococcal interactions, the method by which bacteria colonize the major reservoir of staphylococci, the nostrils (nasal sinuses). is not fully understood -proteins (Löw, 2014). The risk of contracting Staphylococcus aureus is increased by the presence of foreign bodies. Host immune responses to phagocyte function are severely impaired in the presence of foreign substances. Devices such as infusion catheters are quickly coated with serum components (such as fibrinogen and fibronectin) to which bacteria adhere via an MSCRAMM-mediated mechanism, producing glycocals that further aid colonization (Breurec et al., 2011). Intravenous catheterization has often been identified as a risk factor in the pathogenesis of nosocomial endocarditis (Lowy, 2014).

In nosocomial endocarditis, which is often caused by an intravenous catheter, the catheter causes trauma to the surface of the heart valve, forming a non-bacterial clot on the heart valve and allowing bacteria to later adhere to the heart valve. help. Circulating staphylococci (Figure 2.3) then bind to sites of intravascular injury and platelet-fibrin thrombus (PFT) formation (Clyne et al., 2018). Bacteria can also adhere directly to endothelial cells through adhesin-receptor interactions or through bridging ligands, including serum components such as fibrinogen (Lowy, 2010).

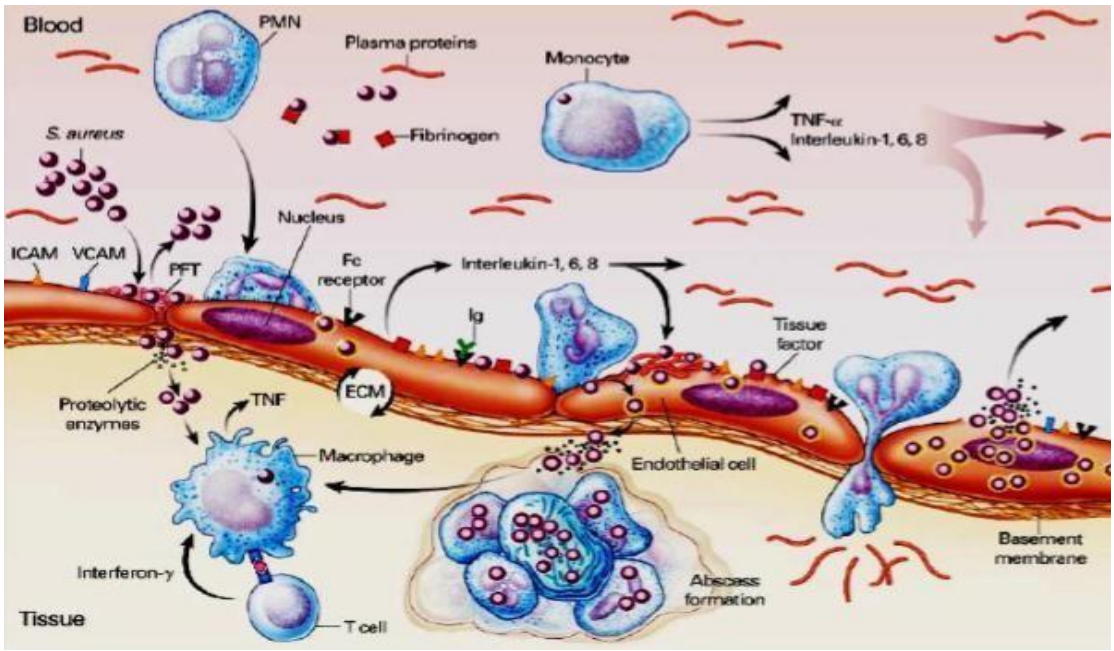

Figure 3: Pathogenesis of *Staphylococcus aureus* by tissue invasion. TNF-Tumour necrosis factor, PFT-Platelet–fibrin thrombi, PMN-Polymorphonuclear leukocyte, ICAM-Intercellular adhesion molecule, VCAM-Vascular cell adhesion molecule, ECM-Extracellular matrix (Lowy, 2010).

Change of the endothelium due to alterations in the micro-environment can signal changes in cell's susceptibility to the infection. *Staphylococcus aureus* produces proteolytic enzymes that facilitate its spread to adjoining tissues and its subsequent release into the bloodstream after their phagocytosis by endothelial cells (Breurec *et al*., 2011). The steps outlined are key to establishing the spread of the infection, and the pathogenesis of endocarditis when cardiac endothelium is involved (Lowy, 2010).

Staphylococcus aureus Toxins

Among their multiple virulence factors, *Staphylococcus aureus* secretes several toxins and other biologically active extracellular enzymes which include α-toxin, exfoliatin, and pyrogenic toxin superantigens (PTSAgs) (Ryan and Ray, 2014).

Pyrogenic Toxin SuperAntigens (PTSAgs)

Superantigens can bind directly to the class II major histocompatibility complex (MHC II) of antigen-presenting cells outside the normal antigen-binding groove and can activate up to one fifth of T cells. Yes (Lowy, 2010). Thus, superantigens can cause excessive proliferation of T cells and release of large amounts of cytokines, leading to symptoms associated with toxic shock. A serious illness characterized by rapid onset of high fever, shock, capillary leakage, and multiple organ dysfunction. PTSAgs also increase susceptibility to the harmful effects of endotoxin (Ryan and Ray, 2014; Lowy, 2010). Once staphylococcal enterotoxins (SE) are formed, they are fairly stable and retain their activity after boiling and exposure to jejunal and gastric enzymes. There are various types such as SE A, B, C, D, E, F, G. In the upper gastrointestinal tract, it acts directly on neuroreceptors to stimulate the vomiting center of the brain. Consuming Staphylococcus aureus food poisoning can cause diarrhea and vomiting. Enterotoxins B and C cause 50% of nonmenstrual cases of toxic shock syndrome (TSS) (Lowy, 2010; Ryan and Ray, 2014). Toxic Shock Syndrome Toxin 1 (TSST-1) is systemically expressed and causes toxic shock syndrome (TSS). TSST-1 is somehow related to enterotoxins but does not induce vomiting (Ryan and Ray, 2014).

Exfoliatin or Epidermolytic Toxins (ETs)

ETs are directly responsible for the symptoms and clinical manifestation of staphylococcal scalded skin syndrome (SSSS) (also called Ritter's disease). This leads to the separation between the living layers and the superficial dead layers within the epidermis (Ryan and Ray, 2014).

The Spectrum of Infections Caused by *Staphylococcus aureus*

This bacterium has been identified as the most common cause of postoperative wound infections. Some strains can also produce toxins that cause a variety of specific symptoms such as TSS and food poisoning (WHO, 2014). Intact skin and mucous membranes are excellent barriers to all types of local tissue invasion, but if either of these are damaged by trauma or surgery, Staphylococcus aureus can enter the underlying tissue, giving rise to its characteristic local It can produce abscess lesions or cause sepsis if it can reach the lymphatic system or bloodstream (Cosgrove et al., 2013). Ingestion of enterotoxins produced by bacteria in contaminated food can lead to food poisoning (Harris et al., 2012). The bacterium has been associated with several diseases, including acute food poisoning, impetigo, folliculitis, staphylococcal scalded skin syndrome (SSSS), cellulitis, and others. as a pathogen. It is also associated with systemic infections such as infective endocarditis, epiglottitis, osteomyelitis, and sinus infections. In England, between 1997 and 1999 he was estimated to have acquired nosocomial infections in more than 4% of patients admitted for surgery to 1 of 96 hospitals. A nosocomial infection is an infection acquired in a healthcare facility where there was no evidence that the infection was present or latent prior to patient admission (Harris et al., 2012). A study by Harris et al. (2012) showed that the hospital environment may also

facilitate the spread of MRSA. They reported that 81% of nosocomial infections are caused by Staphylococcus aureus and 61% of these isolates are methicillin-resistant. Sepsis occurs when bacteria infect blood or other body tissues (Cosgrove et al., 2013).

Impetigo is a contagious superficial skin infection spread by direct contact with lesions or by direct contact with nasal carriers of Staphylococcus aureus. It is common in preschool children and some adults. Skin and soft tissues Impetigo, boils, carbuncles, abscesses, cellulitis, fasciitis, myositis suppurativa, surgical and traumatic wound infections Foreign body-related intravascular catheters, urinary catheters Intravascular bacteremia, sepsis , septic thrombophlebitis, infectious carditis Bone and joints Septic osteomyelitis, septic arthritis Respiratory pneumonia, empyema, sinusitis, otitis media Other invasive infections Meningitis, operating room infections Toxin-borne Disease Staphylococcal toxic shock, food poisoning, staphylococcal scalded skin syndrome, bullous impetigo, necrotizing pneumonia, necrotizing osteomyelitis. SSSS is most commonly seen in infants under the age of five. In SSSS, the skin is damaged and sloughed off (Cosgrove et al., 2013).

Folliculitis occurs when hair follicles are damaged by friction with clothing, follicle blockage, or shaving, causing inflammation of one or more hair follicles (CDC, 2016).

Staphylococcal enterotoxins are a major cause of food poisoning, which usually occurs after ingestion of S. aureus-contaminated food through improper handling and subsequent storage at elevated temperatures. Symptoms are immediate (within 2-8 hours) and include nausea and vomiting, and abdominal cramps with or without diarrhea (Bastola et al., 2017). Other diseases caused by Staphylococcus aureus include hordeolum, chalazion, carbuncle, osteomyelitis (Boucher et al., 2010), urinary tract infection (Ajantha et al., 2011), pneumonia (McGrath et al., 2008).), myositis suppurativa (skeletal muscle infection and several other diseases and conditions.

Epidemiology *of Staphylococcus aureus*

Persons colonized with MRSA this way are referred to as carriers. It has been estimated that about 20.0% of individuals almost always carry one type of *Staphylococcus aureus* strain and such people are called persistent carriers). About 60.0% of the population harbors *Staphylococcus aureus* intermittently, and the strains change with varying frequencies; such persons are referred to as intermittent carriers. The organism is both a commensal and a pathogenic bacterium, its main ecological niche on humans are the anterior nares. Other sites which may be colonized include the groin, armpits and gastrointestinal tract. These colonized sites serve as reservoir from where the bacteria can infect its host when host defenses are breached through surgery, shaving, or insertion of an indwelling catheter. Colonization enables the transmission of *Staphylococcus aureus* among individuals in both the hospitals and communities (Gordon and Lowy, 2010). Infection takes place when the bacteria enters a site on the body and multiplies in number in the tissues to cause an immune response and some clinical manifestations of a disease. This is characterized by a rise in the white blood cell count, fever, or purulent drainage from a wound or body cavity (Gordon and Lowy, 2010). Bustamante (2011), gave a worldwide prevalence which ranged between 23.3% - 73%. In 1996, a study showed that Malaysia and South Africa had some of the highest MRSA prevalence. Bustamante (2011), noted how inadequate resources and education has led to the increasing spread of MRSA around the world, and also stated that the factors that have led to the spread of MRSA throughout the world are distinct for different regions of the world. It has become a major cause of systemic infection in the community and hospitals, causing deaths among individuals with no known risk factors and presents a therapeutic challenge for doctors because of the bacteria's complex mechanisms of antibiotic resistance and epidemiology (Kil *et al*., 2010).

Europe has 26% MRSA prevalence with Greece, Italy, Portugal, and Turkey recording some of the highest rates (Bustamante, 2011). Countries such as Taiwan, Singapore, Japan, and Hong Kong in the Asia-pacific region showed very high MRSA prevalence of above 60%. A prevalence of 5%, 27.8%, and 23.8% from the Philippines, China and Australia respectively, were reported based on articles that varied in number of isolates used for the analysis, accuracy of results, and year of data collection (Bustamante, 2011). Bustamante (2011), recounted how the lack of resources and inadequate education has led to the continuous spread of MRSA and the fact that the above observed discrepancy in prevalence were due to the paucity of data from less developed countries. Scarce resources in such countries makes it difficult for adequate funds to be raised for such research.

Epidemiology *of Staphylococcus aureus* – the African Perspective

Breurec *et al*. (2011), cited the poorly documented state of MRSA-related infections in Africa as a leading cause of the spread of MRSA. This assertion was corroborated by Bustamante (2011), through a study which gave a prevalence of 5% - 45% across Africa and also cited inadequate coverage, increase in the use of antibiotic and inaccurate sensitivities as factors that aggravate the challenge of growing MRSA prevalence. Data on MRSA prevalence in Africa is scanty, however, one of the earliest reports in the continent was made in South Africa and studies from the 1980s have been described (Obasuyi, 2013). Falagas *et al*. (2013), sought to assess the prevalence of MRSA in Africa. It was reported that Tunisia recorded an increase in MRSA prevalence from 16.0% to 41.0% between 2002 and 2007, while in Libya a prevalence of 31.0% was recorded in 2007. In South Africa however, the prevalence decreased from 36.0% in 2006 to 24.0% during 2007–2011. In Botswana, the reported prevalence ranged from 23.0% to 44.0% during the period between the years 2000 and 2007. In Algeria, a prevalence of 45.0% was reported during the period spanning the years 2003 and 2005. Within that same period, a prevalence of 52.0% was reported in Egypt. Generally, MRSA prevalence in most African countries was lower than 50% although it appears to have risen since 2000 in many African countries, except for South Africa (Falagas *et al*., 2013).

Methicillin-Resistant *Staphylococcus aureus* (MRSA)

MRSA is defined by the presence of staphylococcal cassette chromosome mec (SCCmec); which is a large mobile genetic element that carries the mecA gene which codes for an alternative form of penicillin binding protein (PBP2a). PBP2a has a low binding affinity to β-lactams. Since MRSA was first identified in clinical specimen in the early 1960s, the strains have spread throughout the world. By the mid - 1980s MRSA emerged as the most important hospital acquired pathogens worldwide (Pinho *et al*., 2011).

Function of β-lactam Antibiotics and Resistant Mechanisms of MRSA

B-lactams are bactericidal agents which act against the susceptible bacterialcell wall. They target the transpeptidation step of the peptidoglycan synthesis. B-lactams acts to inactivate the transpeptidase domain of PBPs in the cell wall by binding and inactivating the transpeptidase. B- Lactam are structural analogues of the natural substrate of PBPs, D-alanyl-D-alanine of the peptidoglycan stem peptide. Penicillin binding proteins (PBPs) are involved in the assembly of the bacterial cell-wall peptidoglycan. B-lactam antibiotics include penicillin, cephalosporin, and penicillinase-insensitive β-lactams like oxacillin and methicillin (Bastola *et al*., 2017). The reaction between a β-lactam antibiotic and PBP starts with a non-covalent association between these two molecules. The intermediate may either dissociate or undergo an irreversible reaction of acylation, and then the PBP covalently binds the antibiotic at its active site to cut the cyclic amide bond in the β-lactam ring.

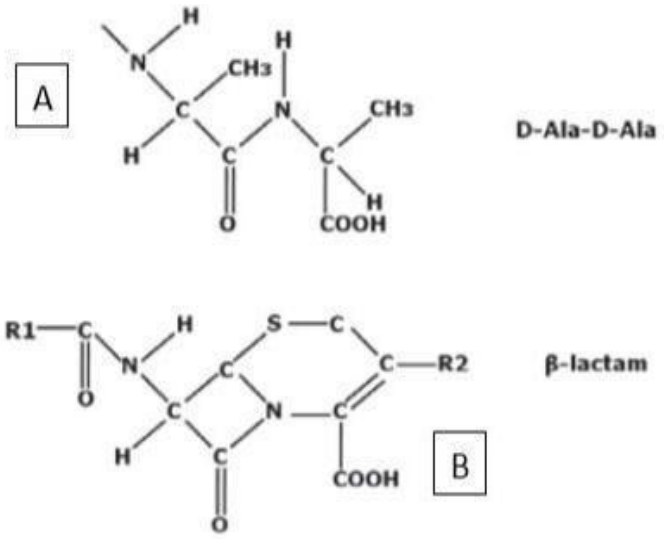

Figure 4: A is the structure of D-Alanyl-D-Alanine and B is the structure of β-lactam antibiotic: They both have similar structures that allow them to be bound by PBPs. R1 and R2 indicate groups that differ among various β-lactam antibiotics (Plata *et al*., 2015).

Mechanism of Resistance to Semi-synthetic β-lactams (e.g. Methicillin,Nafcillin and Oxacillin)

Staphylococcus aureus developed resistance to this type of β-lactam antibiotics by acquiring the mecA gene which is carried on the SCCmec element described earlier. Strains which carry this mecA gene are known as methicillin resistant *Staphylococcus aureus* (MRSA), even though they are actually resistant to all β-lactam based antibiotics. B-lactam resistance in MRSA is achieved by the addition of the newly acquired PBP2a to the complement of the four native staphylococcal PBPs (Pinho *et al*., 2011). PBP2a is encoded by the mecA gene and it has low affinity for β-lactam antibiotics which enables these strains of *Staphylococcus aureus* to grow in antibiotic concentrations that hitherto, inactivates all native PBPs. PBP2a is a member of a group of PBPs with high molecular mass (78 kDa), comprising of a transpeptidase domain and a non-penicillin binding domain whose function is unknown. PBP2a does not appear to be an active enzyme, compared to other indigenous PBPs which synthesize very well cross-linked peptidoglycan. Even when transpeptidase activity of all the indigenous PBPs is inhibited by the presence of methicillin, PBP2a was found to rely on transglycosylase, which is the β-lactam-insensitive domain of the indigenous PBP2, thereby conferring resistance to the bacterium. Another model of methicillin resistance suggested by Pinho *et al*. (2011), assumes that the PBP2a takes over the cell wall's biosynthetic functions of normal PBPs in the presence of β-lactam antibiotics; this rapidly acylate (and inactivate) the four indigenous PBPs at concentrations far below the minimum required to inhibit the growth of most MRSA strains.

Other Antimicrobials MRSA is Resistant to

Historically, *Staphylococcus aureus* has been known to develop antimicrobial resistance to most antimicrobials rapidly. The bacteria developed resistance to penicillin only a year after the introduction of penicillin into clinical use. It is now estimated that 90%–95% of *Staphylococcus aureus* strains worldwide are resistant to penicillin. Linezolid-resistant MRSA strain was also described only a year after the introduction of linezolid into clinical use in the year 2000. MRSA developed resistance to daptomycin within 2 years after it was introduced in 2003. Vancomycin which has proven quite effective against MRSA after some decades of its introduction also seems to be losing out to the MRSA threat. It took about 40 years for the first resistance strain to this antimicrobial to be identified in Japan in 1996. Resistance to fluoroquinolone drugs which include ciprofloxacin, ofloxacin and norfloxacin also emerged in US hospital in 1988 after the introduction of ciprofloxacin and a 38% resistance in *Staphylococcus aureus* was later evaluated in 2000 (Makgotlho, 2015).

Detection of MRSA Colonization

MRSA identification is based on phenotypic and genotypic investigations. The methods used include culture methods and molecular testing (PCR). Phenotypic investigations include Gram staining, catalase, coagulase, DNAse, and

morphological characteristics on mannitol salt agar. After identifying *Staphylococcus aureus* by Gram staining (Gram-positive cocci), catalase (positive), fermentation tests (oxidase positive) and tube coagulase (positive) or DNAse (positive), the sample is grown on mannitol salt agar for 24 hours at 37ºC. *Staphylococcus aureus* colonies appear yellow and are then subjected to Cefoxitin sensitivity test by the Kirby Bauer disk diffusion method. Other commercially available methods include latex agglutination test kits (Brown *et al*., 2010).The various molecular techniques for rapid identification and characterization of MRSA strains are based on the identification of the mecA gene which is unique to MRSA (Makgotlho, 2015).

Public Health Implications and Economic Impact of MRSA Infections

The resistance exhibited by MRSA to most antibiotics imply that treatment for suspected or verified severe *Staphylococcus aureus* infections, including common skin and wound infections, must rely on second line drugs. Thus standard prophylaxis with first-line drugs for orthopedic and other surgical procedures will not have much effect in many settings. Second-line drugs for *Staphylococcus aureus* are more expensive and also have severe side-effects for which monitoring urine treatment is required which further increases costs. Through systematic reviews of scientific literature, it was established that patients with infections caused by bacteria resistant to a specific antibacterial drug generally have an increased risk of worse clinical outcomes and death, and they may consume more healthcare resources, than patients infected with the same bacteria not demonstrating that resistance pattern. However, data available are insufficient to estimate the wider societal impact and economic implications when effective treatment for an infection is completely lost as a result of resistance to all available drugs (World Health Organization, 2014). Based on this premise, they embarked on a study to evaluate the cost of an incident of noncompliance with hand hygiene by a hospital worker during patient care. It was finally deduced that in a 200-bed capacity hospital, an amount of $1,779,283 was incurred in annual MRSA infection–related expenses attributable to hand hygiene noncompliance. They further stated that a 1.0% increase complying with hand hygiene compliance can result in yearly saving of $39,650 to a 200-bed hospital. An overview of findings to address whether there is an excess cost due to infections caused by *S. aureus* resistant to methicillin revealed that there is an excess cost in hospitalization, antibacterial therapy, medical care and an excess cost in additional cost variable which include costs specifically related to the MRSA infection , daily hospital or patient costs; costs before or after infection; costs for specific allied health care; costs broken down into very specific categories; costs related to inpatient or outpatient treatment; costs reported by a specific time period (vs. entire stay), or adjusted or modelled cost variables were produced in the study (WHO, 2014).

Conclusion

The resistance exhibited by MRSA to most antibiotics imply that treatment for suspected or verified severe *Staphylococcus aureus* infections, including common skin and wound infections, must rely on second line drugs.

References

Ajantha, G. S., Kulkarni, R. D., Upadhya, A. K., Kalabhavi, A. S., Patil, S. S., Shetty P. C., Shubhada R. M. & Jain P. A. (2011). Urinary Tract Infection in a Tertiary Care Hospital with Special Reference to Methicillin Resistant *S. aureus* (MRSA). *Indian Journal of Medical Microbiology,23*(1), 52-55.

Awad, S. S. (2012). Adherence to Surgical Care Improvement Project Measures and Post-Operative Surgical Site Infections. *Surgical Infections, 13*(4), 234-237.

Bastola, R., Parajuli, P., Neupane, A. &Paudel, A. (2017). Surgical Site infections, Distribution Studies of Sample, Outcome and Antimicrobial Susceptibility Testing.

Journal of Medical Microbiology & Diagnosis, 06(01), 2161-703.

Benson, H. J. (2011). Microbiological Applications-laboratory Manual in General Microbiology, Eighth Edition, and McGraw hill companies. *Journal of Antimicrobial Chemotherapy*, *56*(6), 10-18.

Bhateja, P., Mathur, T., Pandya, M., Fatma, T. & Rattan A. (2015). Detection of Vancomycin Resistant *Staphylococcus aureus*. A Comparative Study of three Different Phenotypic Screening Methods. *Indian Journal of Medical Microbiology*, *23*(1), 52-55.

Breurec, S., Fall, C., Pouillot, R., Boisier, P., Brisse, S., Diene-Sarr, F. & Laurent, F. (2011). Epidemiology of Methicillin-susceptible *Staphylococcus aureus* lineages in five major African towns, High Prevalence of Panton-Valentine Leukocidin Genes. *Clinical Microbiology and Infection, 17*(4), 633-639.

Btattacharya, S. (2016). Surgical site infection by Methicillin Resistant *Staphylococcus aureus* in nursing homes. Antimicrobial Resistance and Infection Control.

Bustamante, N.D. (2011). Methicillin-resistant *Staphylococcus aureus* (MRSA): A Global Threat, MD Thesis, UT Southwestern Medical School.

Centers for Disease Control and Prevention (2016). Antibiotic resistance threats in the United States, 2013. Centers for Disease Control and Prevention, US Department of Health and Human Services.

Chambers, H. F. & DeLeo, F. R. (2013). Resistance of *Staphylococcus aureus* in the Antibiotic era. *National Revised Microbiology, 7*(9), 650-667.

Clyne, M., De Azavedo, J., Carlson, E. &Arbuthnott, J. (2018). Production of Gamma-hemolysin and Lack of Production of Alpha-hemolysin by *Staphylococcus aureus* Strains associated with Toxic Shock Syndrome. *Journal of Clinical Microbiology, 26*(3), 535-539.

Cosgrove, S. E., Sakoulas, G., Perencevich, E. N., Schwaber, M. J., Karchmer, A. W. &Carmeli,

Y. (2013). Comparison of Mortality Associated with Methicillin Resistant and Methicillin Susceptible *Staphylococcus aureus* Bacteremia, A Meta analysis. *Clinical Infectious Diseases*, *36*(1), 53-59.

Falagas, M. E., Karageorgopoulos, D. E., Leptidis, J. &Korbila, I. P. (2013). MRSA in Africa, Filling the Global Map of Antimicrobial Resistance. *Lancet Infectious Disease*, *8*(10), 427- 34.

Gordon, R. J. & Lowy, F. D. (2014). Pathogenesis of Methicillin-resistant *Staphylococcus aureus*

infection. *Clinical Infectious Diseases*, *46*(36), 350–359.

Harris, L. G., Foster, S. J. Richards, R. G. (2012). An Introduction to *Staphylococcus aureus*, and Techniques for Identifying and Quantifying *Staphylococcus aureus* Adhesions in Relation to Adhesion to Biomaterials. *European Cells and Materials*, *7*(4), 39-60.

Kil, E. H., Heymann, W. R. & Weinberg J. M. (2017). Methicillin-Resistant *Staphylococcus aureus*, An Update for the Dermatologist, Part 1 Epidemiology, Continuing Medical Education. *Journal of Hospital Infection,81*(90), 247-254.

Knox, J., Uhlemann, A. and Long F. D. (2015). *Staphylococcus aureus* Infection and Transmission within Household and the Community. *Trends in Microbiology*, *23*(7), 437-444.

Lowy, F. D. (2010). *Staphylococcus aureus* Infections, *The New England Journal of Medicine,339*(8), 520-532.

Makgotlho, P. E. (2015). Molecular Characterisation of Methicillin-resistant *Staphylococcus aureus* strains, University of Pretoria, Faculty of Health, and Department of Medical Microbiology. *Journal of Microbial Drug Resistance,20*(1), 57.

McGrath, B., Rutledge, F. &Broadfield, E. (2016). Necrotising Pneumonia, *Staphylococcus aureus* and Panton-

Valentine leukocidin. Intensive Care Society *Journal of Global Antimicrobial Resistance*, *1*(4), 189-193.

Monnet, D. L., Mackenzie, F. M., Lopez-lozano, J. M., Beyaert, A., Camacho, M., Wilson R., Stuart, D. & Gould, I.M. (2014). Antimicrobial Drug use and Methicillin-resistant *Staphylococcus aureus*. *Journal of Infectious Disease10*(8), 1432-1441.

Moses, A., Uchenna, U. & Nworie O. (2013). Epidemiology of Vancomycin Resistant *Staphylococcus aureus* among Clinical Isolates in a Tertiary Hospital in Abakaliki, Nigeria. *American Journal of Epidemiology and Infectious Disease*, *1*(3), 24-26.

Obasuyi, O. (2013). Molecular Identification of Methicillin-resistant *Staphylococcus aureus* in Benin City Nigeria. *African Journal of Clinical Expert Microbiology,14*(1), 1-4.

Pinho, M. G., Lencastre, H. & Tomasz, A. (2011). An Acquired and a Native Penicillin-binding Protein Cooperate in Building the Cell Wall of Drug Resistant Staphylococci. *British Journal of Healthcare Management*, *17*(2), 64-71.

Ryan, K.J., & Ray,C.G. (2014). "Sherris Medical Microbiology," 4th Editon, McGraw-Hill, New York.

Sotto, A., Lina, G., Richard, J. L. Combescure, C., Bourg, G., Vidal, L.(2008). Virulence potential of *Staphylococcus aureus* strains isolated from diabetic foot ulcers. Diabetes care 31, 2318- 2324.

WHO, (2012). World Health Organization, Hand hygiene in Outpatient and Home-based Care and Long-term care facilities, Guide to the Application of the WHO Multimodal Hand Hygiene Improvement Strategy and the "my five moments for Hand Hygiene Approach, WHO Document Production Services, Geneva, Switzerland. *Journal of Clinical Infectious Diseases*, *54*(6), 826-831.

WHO, (2014). World Health Organization, Antimicrobial Resistance Global Report on Surveillance, WHO Press, Geneva, Switzerland. *Journal of Clinical Infectious Diseases,54*(6), 826-831.

Access this Article in Online

Website: www.ijarm.com

Subject: Microbiology

Quick Response Code

DOI:10.22192/ijamr.2022.09.09.003

How to cite this article:
Chidimma Maureen Chukwueze, Ogochukwu Vivian Okpala and Emmanuel Ifeanyi Obeagu. (2022). A systematic review on Methicillin resistant *Staphylococcus aureus* in patients with surgical wounds. Int. J. Adv. Multidiscip. Res. 9(9): 25-36.
DOI: http://dx.doi.org/10.22192/ijamr.2022.09.09.003