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Article Review: Staphylococcus Aurous Virulence Factors and it´s Resistance to Antibiotics

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A B S T R A C T

Staphylococcus aureus is naturally colonizing the skin and the naris of healthy people and Staphylococcus aureus exhibits different surface factors of the cell, which play a role in their virulence. This study explained the increasing β-lactamase secrtion by Methicillin Resistant. S. aureus primarily decreases the antibiotic affect, and Methicillin Resistant. S. aureus (MRSA) has increasingly become the most prevalent resistance pathogens in the world. This study stated that Quinolones function antibacterial by inhibiting bacterial topoisomerases, important in the removal of DNA super-coiling and separation of concatenated DNA-strands.

1. INTRODUCTION

Staphylococcus aureus is a Gram-positive bacterium, sometimes found in human and animal skin and nasal passages. S. aureus was shown to be the riskiest of all types of Staphylococci is though, has been implicated in skin infection and food poisoning and many human infections such as pneumonia, infections of the heart valve, bacteremia and urinary tract infection Generally S. aureus did not induce infections by direct contact, but often systemic infections. In health care facilities and in the population, S.aureus is the commonest pathogens and can cause invasive illness (1). Methicillin Resistant S. aureus (MRSA) infection is the most important factors of hospital-acquired infections and severe morbidity, death, period of stay and expense burden are linked with this disease (2). The therapy of bacterial history is distinguished by emergence of resistance of each class، namely penicillin, sulfonamide, tetracycline, glycopeptides and other antimicrobial anti-staphylococcal medications, which complicate therapy. This MRSA isolates were originally primarily limited to the health care community and the individuals who attended to them and were resistant to all antimicrobial ß-lactam. However, new strains discovered in the mid1990s, identified as community associated MRSA.

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(CA) strains. The more popular Methicillin Resistant S. aureus species are prone to several groups of pre- ß-lactam antimicrobials relative to health-associated Methicillin Resistant S. aureus strains are usually treating with drugs in other antimicrobial classes, for example cephalosporins, oxacillins or nafcillins (3). Generally, for the time being, 90 % strains of Staphylococcus aureus are resistant to many penicillin and popular antibiotics such as tetracycline, fluoroquinolones, macrolides, aminoglycosides and chloramphenicol (4). Food-producing animals, mainly cattle and pigs, are important sources of S. aureus to the food chain. Therefore, it is essential to know which virulence factors, structures, Antibiotics and mechanisms this pathogen can exhibit

Pathogenicity of Staphylococcus aureus

Staphylococcus aureus is naturally colonizing the skin and the naris of healthy people; henceforward, it is the leading causative agent of wound infections. Additionally, other sites of the body are exposed to this bacterial species; therefore, a possible infection in this site might occurred. More likely, infections caused by bacterial pathogens take place due to two key mechanisms; invasion and toxin production. Invasion process ensues via several steps, among these, colonization, elaborating adherence factors and evading host defenses ability. While, toxin production by S. aureus can cause detrimental damage to host tissue (5).

Even though a somewhat understated, S. aureus is a highly harmful pathogen either in community-acquired or nosocomial infections. An essential biological characteristic of this species is its capability to colonize healthy tissue, asymptomatically. S. aureus carriers are always the potential victim of being infected, and they are supposed to be a vital source for spreading this bacterium among the population (6). S. aureus is responsible for a vast array of infection; however, three main types of infection could be recognized: (i) topical or superficial lesions such as wound infection, (ii) toxin-mediated infections like food poisoning, and (iii) systemic infections such as life-threatening endocarditis (7). S. aureus colonizes tissues by ~~an~~ aid of a plethora of virulence determinants leading to tissue damage, and dissemination of infection. Almost all strains of S. aureus elaborate variety of extracellular proteins such as exotoxins and enzymes (e.g. collagenase, lipases nucleases, proteases, and hyaluronidase). All these extracellular products may function as tools for converting host tissue into nutrients useful in the growth of bacteria (8).

The Staphylococcal strains produce several cytotoxins such as alpha, beta, gamma and delta hemolysins, and leukocidins. These toxins can lyse host cells, and modulate its immune response such as triggering apoptosis mechanism either caspase-dependent or caspase-independent mechanism. One of the significant virulence factors of S. aureus is the exopolysaccharides. In fact, there are two kinds of exopolysaccharides: polysaccharide intercellular adhesion (PIA) and capsule polysaccharides (9). Regarding the capsule, about 11 capsule serotypes were recognized in S. aureus; nonetheless, serotype 5 and 8 are the most common. Capsular polysaccharides protect S. aureus cell form host immune defenses by virtue of inhibiting phagocytosis. Furthermore, capsule actively participates in bacterial survival inside the polysaccharides intercellular adhesion being a poly-Nacetyl-glucosamine actively contribute to biofilm formation (10).

The Virulence Factors

The co-ordinated presentation of various virulence factors include S.aureus infections, with a few variety of diseases, including the by single staphylococcal exotoxins of the family of S. aureus superantigens. The evident practical redundancy of most toxins and exoenzymes is the secreted virulence factors (11). Virulence factors classified into cell-surface associated and secreted.

Cell Surface Factors

Staphylococcus aureus exhibits different surface factors of the cell, which play a role in their virulence. They involve microbial surface elements identifying, capsular polysaccharide and staphyloxanthin (carotenoid pigment) this involves microbial surface components (12).

1.1. Microbial Surface Component Recognizing Adhesive Matrix Molecules (MSCRAMMs)

Typical members of the MSCRAMM family are:

Staphylococcal protein A(SpA): This is a cell-anchored protein capable of attaching, interacting with opsonicity and phagocytosis, to the fragment crystallizable region of immunoglobulin G (Fc) (13).

Fibronectin-binding proteins FnbpA and FnbpB: They make S. aureus bind to and attack different kinds of cells, including epithelial, endothelial, fibroblast and osteoblast cells. The host cell fibronectin receptor and integrins promote the Invasion.

Collagen-binding protein: It is a cell wall bound protein that is bound to its N terminal domain with a collagen binding site. In vivo it was shown to support the joint colonization of septic arthritis in the early stage and lead to osteomyelitis and chronic endocarditis pathogenicity.

Clumping factor proteins: they mediate fibrinogen clumping and adhesion in the presence of fibronectin.

All MSCRAMMs are shown in figure (1) (14).

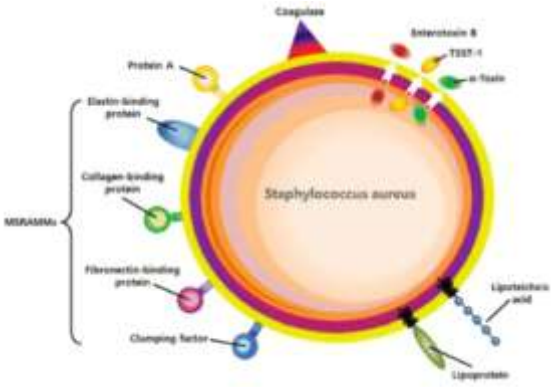


Fig. 1: MSCRAMMs of Staphylococcus aurous (15).

1.2. Capsular Polysaccharides

They function to suppress neutrophil phagocytosis; they increase colonization and survival of bacterial mucous membranes.

1.3. Staphyloxanthin

Some strains of S. aurous generated the bacterial antioxidant, Staphyloxanthin (carotenoid pigment), which is used by the host immune system to destroy pathogens and prevent oxidative stress.

1.3.1. Secreted Factors

One of the main features of bacteria is capacity to produce toxins that play an active role in the disarmament of host

immunity as opposed to defensive and the role of virulence factors attached to the cell- wall described above.

1.3.2.1. Superantigens

Superantigens are a strong category of proteins capable to cause a number of human disorders like toxic shock syndrome (TSS) (16).

1.3.2.2. Various Exoenzymes

About any strain of S. aureus secrete numerous extracellular enzymes that are assumed to disturb host tissues and/or inactivate bacterial growth nutrients and to promote bacterial dissemination. These exoenzymes include coagulase, which clots plasma and covers the bacterial cell possibly to resist phagocytosis. Hyaluronidase (also known as the spreading factor) breaks down and helps in spreading ~~of~~ hyaluronic acid. S. aureus also produces nuclease that breaks down nucleic acid, lipase to digest lipids, proteases such as exfoliating toxinsA and B (ETA and ETB) which inactivate neutrophil activity, staphylokinase (SAK). (17).

1.3.2.3. Cytolytic Toxin (hemolytic toxin)

A significant number of cytolytic toxins are secreted by S. aureus, while structurally complex and with different goals have a common role in cells. These toxins with shape β barrel pore in target cell cytoplasm membranes which cause a cell content leak and cell lysis (18).

The different arsenal of secreted toxins involved in virulence factors is attributed in the extent of S. aureus virulence; these play a leading role. Most S. More. Aureus toxins function by disruption to biological membranes and finally cause cell death. Much of it, S. aureus develops efficient hemolysins and leukotoxins. Neutrophils lymphatically ingested toxins by these cells represent a strictly effective toxin tool against bacterial infections by innate host defense. In comparison to that, S. aureus established various factors which either inhibited the complementary cascades or prevented the host defenses. Quite a lot of more toxins add to this many-sided protocol of S. aureus to escape elimination by the host defense mechanisms (19).

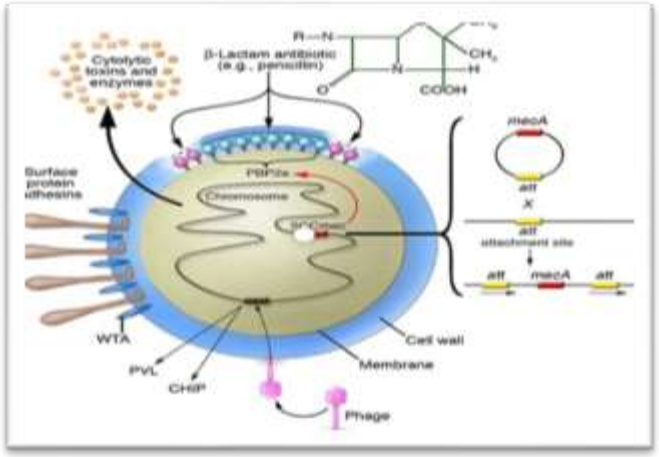
Resistance to Antibiotics

Beta-lactam Resistance

The ß-lactamase enzymes are encoded with chromosomal and transferable, catalyzing hydrolyses of different β lactam antibiotics (including antibiotic items such as carbapenem broadspectrum antibiotics). The antibiotics of β-lactam are effecting in bacteria mainly through 2 mechanisms: firstly, binding to (PBP) which represses mucin synthesizing of cell walls, inhibits bacterial expansion; secondly, by activating the autolytic enzymes of the bacterial walls, by triggering bacterial activity causing autolytic and death. The increasing βlactamase secrtion by Methacilline Resistant S. aureus primarily decreases the antibiotic affect by 2 mechanisms, contributing to Methacilline Resistant (20). Firstly, is the hydrolyses process, which hydrolyzes βlactamase and inactivates βlactam antibiotics; Secondly the pinching process that ensures that a great deal of β-lactamase attaches rapidly and securely to Cellular and Infection Frontiers. *Staphylococcus aureus* endogenous resistance mechanism. (A) Breif initiation of resistance technologies in bacteria (B) S. aureus drug resistance was caused by the mechanism of reduced membrane permeability. (C)The function of efflux in Methacilline Resistant S. aureus resistance (D) The function of enzymes in *S.aureus* resistance to drug. Extracellular antibiotics, which block intracellular antibiotics and thus antibiotics from arriving at the target location eventually contributing to antibiotic resistance in MRSA (21).

1.Resistant to Methicillin

In the 1940s, Fleming identified penicillin and set the way for antibiotic therapy for infection. *S. aureus* caused infectious diseases is well regulated but with penicillin widespread, *S.aureus* resistance to penicillin generates penicillinase that can hydrolyze the β lactam ring and contribute to penicillin resistance. Subsequently, scientists developed modern semisynthetic penicillin (22). Methicillin successfully regulated penicillin-resistant *S.aureus* infections after their introduction to the clinic in 1959 .MRSA Resistance was developed by a gene that coded the 2aor 2′(PBP2aorPBP2′)penicillin-binding protein (mecA) that was inserted into the MSSA chromosomal portion, SCC mec, as shown in figure(2) .MRSA has increasingly become the most



prevalent resistance pathogens in the world ,MRSA is

Fig. 2: The *mec*A gene encodes anovel β-lactam-intensive pencillin binding protein (24).

categorized as MRSA (HA-MRSA) and as MRSA (CAMRSA) obtained by the hospital according to its initial source (23).

2. Resistance to Quinolones

Nalidxic acid, the Quinolone type and second generation ~~of~~ group (eg ciproflxacin and norflxacin) have mainly actives in grams-negative,while S. aureus has demonstrated increased and higher activity against Grams-positive quinolones–(e.g .levofloxacin ,moxefloxacin, gemfloxacin) .Quinolones function antibacterial by inhibiting bacterial topoisomerases, important in the removal of DNAsuper-coiling and separation of conctenated DNA-strands, (topoisomerase IV and DNA-Gyrase) .Quinolone tolerance in *S. aureus* occurs progressively, mainly because of point mutations in the sub-unit of GrlA for the topoisomerase IV and GyrA for the Gyrase. A more mechanism in *S. aureus*, the expression NorA efflux pumps makes *S.aureus* resistant to quinolones. (25). The tolerance to quinolones in *S. aureus* is primarily concerned with tolerance to methicillin, but the tolerance process and coding genes are completely different. This may be attributed to the use of quinolones in hospitals where the incidence of HAMRSA is high and quinolone tolerance is chosen. In the year 2008, tolerance to fluoroquinolones among MRSA isolates in the hospital was 70.3 percent for bacterial skin and skin-structure. Due to such strong resistance in hospital environments to quinolone from MRSA, both third and fourth generation quinolones for MRSA care were not considered. In CA-MRSA, while sensitive to non-betalactam antibiotics like quinolones, the condition in years has changed with the growing occurrence of multi-drug resistant, CAMRSA infections (26).

4. CONCLUSIONS

The study of biological and molecular characteristics of these isolates demonstrated the presence of resistance to several antimicrobial agents and production of different virulence factors related to the pathogenesis of this agent**.**

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عوامل ضراوة المكورات العنقودية الذهبية ومقاومتها للمضادات الحيوية

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الخلاصة:

المكورات العنقودية الذهبية هي مستعمرة طبيعية لجلد الأشخاص الأصحاء والمكورات العنقودية الذهبية تظهر عوامل سطحية مختلفة للخلية، والتي تلعب دورًا في ضراوتها، اوضحت هذه الدراسة زيادة افراز بيتا-لاكتميز واسطة الميثاسيللين المقاوم للمكورات العنقودية الذهبية بشكل أساسي، تأثير المضاد الحيوي والمكورات العنقودية الذهبية المقاومة للميثاسيللين أصبحت بشكل متزايد أكثر مسببات الأمراض المقاومة انتشارًا في العالم. ذكرت هذه الدراسة أن الكينولونات تعمل كمضاد للبكتيريا عن طريق تثبيط التوبويزوميرات البكتيرية، وهو أمر مهم في إزالة اللف الفائق للحمض النووي وفصل خيوط الدنا المتكتلة.