Short Communication

Precipitated probe on aetiology of MRSA skin infections: a global concern

Abstract

MRSA (Methicillin-Resistant *Staphylococcus aureus*) infection is the type of communicable skin disease caused by staph bacteria, named *Staphylococcus aureus* which become antibiotic resistant while treating patients. Staph bacteria are found to present ubiquitously in the skin and mucous membranes especially in nasal area in human. However, these pathogenic staph bacteria cause lethal skin diseases due to getting antibiotic resistant when enter in blood streams/ internal tissues. Previous studies based on antibiotic susceptibilities, it was confirmed that methicillin resistance in *Staphylococcus aureus* lead to cause of nosocomial infections with notable morbidity and mortality of admitted patients. Hence, MRSA infections can be of two distinct types: community-associated (CA-MRSA) infection and hospital-associated (HA-MRSA) infections differing with respect of aetiology, epidemiology and antibiotic susceptibility-oriented treatment. Patient treatment has been become a medical challenge due to its emergence of multi-drug-resistant strains termed, MRSA (Methicillin-Resistant *Staphylococcus aureus*). It mostly develops due to either intake of inappropriate antibiotic consumption or antibiotic overconsumption without any physician supervision or any accidental medical negligence. So, this brief and precipitated review can come up with cure and preventing MRSA skin infections in human by knowing emerging negative impacts of drug-resistant *staphylococcus aureus* bacteria that develop intricated drug efflux mechanism due to random consumption of antibiotics.

Keywords: *Staphylococcus aureus*, MRSA skin infection, staph bacteria, methicillin resistant pathogen.

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Introduction

MRSA (Methicillin-resistant *Staphylococcus aureus*) skin human infection is caused by ubiquitous pathogen; a staph bacterium also associated with a wide spectrum of mild cutaneous infections including severe systemic diseases. MRSA is found to be global health crisis and unpredictable so far. Its capacity for genetic adaptation and the serial emergence of successful epidemic strains makes it a major threat to human health. MRSA infection was reported a major health concern within healthcare premises during hospitalization of patients with other clinical comorbidities. Hence, patient treatment became challenges due to emergence of multidrug resistant staph strains.[1–3] In bygone decade, MRSA skin infections are found to at increased risk of outbreak in creche, athletic teams, old age homes and slum areas.[4–6] Penicillin is first choice of treatment clinically offered to patients suffering from fatal and lethal pathogenesis since 1940s when discovered followed with the synthesis of its first semi-synthetic anti-staphylococcal penicillin in 1960. Methicillin-resistant *S. aureus* (MRSA) was then observed within a year of their first clinical use of synthetic anti-staphylococcal penicillin.[8] MRSA staph strain is found to carry *mec* gene on staph bacterial chromosome as long Staphylococcal chromosomal cassette *mec* (SCC*mec*) region imparting multiple antibiotic resistance on the SCC*mec* type.[7,8] The gene *mecA* is reported for encoding penicillin-binding protein 2a (PBP2a) that helps in crosslinking of peptidoglycans in cell wall of bacteria due to having low affinity for β-lactams resulted antibiotic resistance.[9] Bacterial genomes core is studied to confirm for carrying about 75% of 2.8 Mb genome of *Staphylococcus aureus*.[10] High end genetic diversity of MRSA staph stain is observed where reconciler of immune evasion, virulence, immune evasion and antibiotic resistance are exists as accessory component of about 25% of the total *Staphylococcus aureus* genome. As result therefore, loss of virulence determinants have major role in MRSA bacterial adaptability, virulence and survival possess 20–65 kb SCC*mec* element inserted within the *orfX*; RNA methyltransferase gene.[11] Over 90% of known staph bacterium genome, MRSA strain is found to possess SCC*mec* containing mecA gene complex that imparted methicillin resistance including set of site-specific recombinase genes (named, ccrA and ccrB along with four predominant clonal like CC5, CC8, CC398 & CC30) defined by multilocus sequence typing.[12] This studied transducing phage genome pattern is described for horizontal acquisition of SCC*mec* on MRSA staph strains carrying 45 kb of bacterial host DNA that have vital role for contributing antibiotic resistant of *Staphylococcus aureus* strains.[13] Henceforth, we must to design future efforts to understand biological perspectives of MRSA staph skin infections via exploring dermatological validations on proposed animal models for evaluating epigenetics, transcription, proteomics, genomics, and metabolomics. So, this precipitated brief review can be helpful for exploring progressive insights of clinically well-characterized patients diagnosed with MRSA staph skin infections. Hence, it is needed to propose high-quality clinical trials to develop potent vaccines and treatments to prevent MRSA skin infections in most susceptible patients.

Previous experimentation activities explored for studying antibiotic resistance genes in MRSA staph bacterial genome

MRSA staph strains is confirmed to carry a *mec* gene on bacterial chromosomal and *Staphylococcus aureus* strains start to synthesize PBP-2A that led to resistant against cephalosporin, methicillin, nafcillin and oxacillin.[2,4] Previous observations of studied community-associated infections termed as CA-MRSA, staph strains were found to

sustain eventually in one decade and soaring global healthcare concern in Canada.[14,15] A vital clinical statistics of 15-year study was done in Taiwan where community-associated MRSA; CA-MRSA strains was found to replace hospital-associated MRSA; HA-MRSA in neonatal models samples.[16] Prevalence of community-associated MRSA infections; CA-MRSA were found to main cause of soft skin tissues infections in various proposed dermatological studies in China, USA, Australia and North Africa.[17–20] Those reported community-associated MRSA; CA-MRSA strains were found to exhibit Sccmec IV and V as tiny Staphylococcal Chromosomal Cassettes (SCC) carries methicillin resistance gene mecA.[21] Though, hospital-associated MRSA; HA-MRSA strains were found to carry long SCCmec types (I, II, and III) that have potential to carry antibiotic resistance genes like fusC, ermA, and tetK.[21–23] Apart this, Panton-Valentine Leukocidin (PVL) as its bi-component termed as LukS-PV and LukF-PV (present in respiratory routes) are found to have cytotoxicity as pore-forming cytotoxin when patients diagnosed with MRSA skin infections with chronic clinical sequelae (patient record carrying previous OPD and Indoor history during hospitalization).[14,24] Panton-Valentine Leukocidin (PVL) is reported a potent marker of community-associated MRSA infections: CA-MRSA is found to have remarkable epidemiological association with Hospital-associated MRSA isolates as HA-MRSA isolates to postulate emergence of CA-MRSA in studied niche. Panton-Valentine Leukocidin (PVL) *Pvl*-positive strains were further studied for leukocyte lysis and tissue necrosis in PVL-associated *S. aureus* (PVL-SA) infected patients which make it untreatable skin and soft-tissue infections (SSTIs) including invasive infections like necrotizing pneumonia in MRSA infected patients.[1,25]

Clinical update of MRSA-skin infections vaccine

Although, no licensed prophylactic vaccine and immunotherapeutic procedure were not confirmed yet against MRSA staph strain. Apart this, NDV-3 vaccine has been subjected for evaluation in surgical site infections that confirmed to cause by MRSA staph strain in HA-MRSA patients. Proposal of other clinical available MRSA vaccines are still under evaluation and validation because of less profound understandings of MRSA skin infectious strain at cellular and molecular level. Thus, the current studies are addressed these important clinical goals using multiple techniques in a well-established model of infection that mimics key features of human disease.[26] Presently, human intravenous polyclonal immunoglobulin (IVIG) therapy was proposed for the treatment of MRSA/MSSA severe sepsis as successful therapy regime. Effective commercial IVIG preparation was synthesized via studying its cytopathic effect of recombinant Panton-Valentine leukocidin (PVL). Successful regime was under clinical validation in which immunization carried by using purified PVL components that confirmed to confer notable protection against PVL-induced dermonecrosis and necrotized pneumonia caused by MRSA staph strain.[27,28] A virulent, *pvl*-positive, community-associated MRSA; CA-MRSA isolates was confirmed for emerged cause of endemic globally as distinct *Staphylococcus aureus* genetic lineages having multiple resistance to non-β-lactams in selected CA-MRSA isolates.[29–31]

Conclusion and future perspectives

MRSA staph bacterial strain is reported a more formidable and fast mutating pathogen that causing fatal effects in immunocompromised patients in provided healthcare settings: hospital-associated MRSA (HA-MRSA) as well as in immunocompetent individuals in the community-associated MRSA (CA-MRSA). Community-associated MRSA (CA-MRSA) strains emergence is still under clinical investigation in various hospitals and healthcare centres worldwide if compared with hospital-associated MRSA (HA-MRSA) strains. Resistance profiles of MRSA isolates was studied where resistance of staphylococcal pathogens to non-beta-lactam antibiotics confirmed against norfloxacin, trimethoprim, ciprofloxacin, erythromycin and trimethoprim-sulfamethoxazole.[31–33] Isolates of MRSA *Staphylococcus aureus* was found to express resistance against various antimicrobial groups e.g. folate, quinolones and macrolides pathway antagonists. Comparatively, these MRSA staph strains profiles are studied in Kuwait and Saudi Arabia in which MRSA-MDR staph strains confirmed to exhibit SCCmec type III followed by SCCmec V that belong to the MRSA clones ST22-IV (Barnim/UK-EMRSA-15) and ST772-V (Bengal Bay Clone).[34–38] Hence, various clinical researchers, clinicians, molecular biologists and microbiologist are needed to take strict measures to come up with synergistically followed by national/ international infection control boards and antibiotic stewardship committees. So that, we can be able to implement various clinical preventive health measures to stop colonization of MRSA staph strains in healthcare premised and to attenuate the transmission of Panton-Valentine leucocidin (PVL) producing CA-MRSA *Staphylococcus aureus* strains. Dermatologists, researchers and clinicians are also have need to carry out progressively futuristic attempts to develop MRSA staph skin infections vaccine to combat its fatal effects in susceptible patients.

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Conflicts of interest

The author declares that there are no conflicts of interest.

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