Hospital-Acquired Methicillin-resistant *Staphylococcus aureus* Bacteremia in Prince Muteb Hospital – One Year Retrospective Study

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Abstract

Methicillin-resistant *Staphylococcus aureus* (MRSA) is connected to high rates of morbidity and challenging-to-treat infections. *S. aureus* bacteremia, which has high rates of morbidity, mortality and can lead to severe infections such as infective endocarditis or sepsis, as well as metastatic infections. The majority of *S. aureus* bacteremia cases worldwide are caused by MRSA, which has worse clinical outcomes than methicillin-sensitive *S. aureus*. Infections caused by the nosocomial pathogen Methicillin Resistant S. *aureus* (MRSA) at the hospital as well as in the community are considered a serious global threat. Despite having a wide range of genetic variations, the epidemiology of MRSA is principally characterized by the recurrent appearance of epidemic strains. MRSA continues to be a serious clinical hazard despite recent decreases in occurrence in some areas, and its morbidity and death rates are consistently high. The evaluation of both novel antibiotics and ancillary parts of care, such as infectious disease consultation, echocardiography, and source control, is necessary for successful therapy, which is still difficult to achieve. Leukocyte lysis and tissue necrosis are caused by the virulence factor Panton-Valentine leukocidin (PVL), which is secreted by some strains. Skin and soft tissue infections (SSTIs) are the most common illnesses caused by PVL-associated S. aureus (PVL-SA), although it can also cause invasive infections such as necrotizing pneumonia. Community-associated methicillin-susceptible *S. aureus* (CA-MSSA) and methicillin-resistant S. aureus both carry it (CA-MRSA). MRSA strains are endemic in many parts of Saudi Arabia and it accounts for 23-54% of all clinical isolates. Significantly, 54.2% of Panton-Valentine leukocidin (PVL) genes were found in MRSA strains inside the kingdom. Vancomycin is a drug of choice to treat MRSA infections. The patients admitted to Prince, Mutib, hospital from March 2019 to May 2020 were screened for the prevalence of MRSA. Compact Vitek -2 (biomeriux Leon, France) was used for the identification and antimicrobial sensitivity (AST) test. A total of 64/978 (6.5%) MRSA and 25/978 (2.5%) CoNS were isolated from urine, blood, sputum, nasal swab, throat swab, tracheal swabs, and pleural fluid. Cephamycins were found 100% resistant to vancomycin-resistant MRSA were found in our study.

Key Words Methicillin-resistant *Staphylococcus aureus*; MSSA; Hospital Acquired infection; antibiotic resistance.

Introduction

Staphylococcus aureus, a gram-positive bacterium is a leading cause of infections worldwide (Lakhundi, & Zhang, 2018; kini et al.,2013) In addition, it is a major contributor to osteoarticular, skin and soft tissue, pleuropulmonary, and device-related infections. It is also a primary cause of bacteremia and infective endocarditis (kuller et al., 2016). The molecular epidemiology of methicillin-resistant Staphylococcus aureus has attracted more attention in recent years (MRSA). The MRSA genotype has been analyzed using a variety of methods, which may shed light on a strain's potential for resistance and pathogenicity. Additionally, it sheds light on how they spread and aids in the implementation of effective infection prevention strategies and 30% of individuals are colonized with this bacterium in their nares (Muñoz-Gallego et al., 2020). The three clinically important strains are *S aureus, S saprophyticus,* and *S epidermidis.* The S *aureus* is differentiated from the two other stains by bound coagulase and extracellular coagulase test. In early 1961, the first time Methicillin-resistant *S aureus* (MRSA) was reported due to plasmid-encoded resistance beta-lactamase. Methicillin-resistant *S aureus* (MRSA) is a threat to the modern world due to its high mortality rate (Gu, F et al.,2020). The emergence of community-associated MRSA is around 97% as compared to healthcare-associated MRSA, which in turn suggests that community-associated strains have enhanced virulence and confers its spread worldwide (Gostev et al., 2017; Jevons 1961 and lim et al., 2013). Prevalence of MRSA has increased sharply over the last 15 years and hospital-related MRSA cases have almost doubled due to longer stays at the hospital and costing a financial burden of 15bn USD (Mediavilla et al., 2012; Shallcross et al., 2013). The antibiotic resistance gained by S. *aureus* resulted in a higher incidence of infections over the last 50 years and now the use of penicillin is no longer an effective drug against *S. aureus* (Fu et al., 2020). The meat-producing animals have MRSA and thus help in transmission from food to humans. It was also reported that methicillin-resistant ST398 was of animal origin. In Riyadh, Saudi Arabia the prevalence of MRSA was found around 50% and the number is increasing (Palavecino E. L. 2020; Guo et al., 2020, Bahubali et al., 2018, Deurenberg RH, et al., 2007 and Balkhy HH et al., 2005). This study was conducted in the Aljouf region to explore the MRSA prevalence in patients attending the Prince Muteb Hospital, Sakaka, Aljouf, Saudi Arabia.

Materials and Methods

Setting, Design, and data collection

In one of the referral hospitals in Jouf Sakaka, a cross-sectional, single-center study was conducted between March 2019 and May 2020. The study hospital offers a variety of medical and surgical specialties as well as round-the-clock emergency services. The hospital's microbiology department is outfitted with a variety of automated devices for bacterial

identification and antimicrobial testing, including the BD Phoenix system (BD Biosciences, Franklin Lakes, NJ, USA), VITEK-2 Compact system (bioMérieux, Marcy-lÉtoile, France). This unit takes clinical specimens from in-patient and outpatient departments as well as samples that are referred from other hospitals in the area.

All non-duplicate *S. aureus* samples from hospitalized patients, outpatients, and samples that were referred from other hospitals were examined for antibiograms. The compact VITEK-2 system examined these samples for antimicrobial sensitivity and identification.

Isolation and Identification

Samples (blood, wound, nasal swab, throat swab, tracheal wash, pleural fluid, urine, and sputum) were streaked on Blood agar and Mannitol Salt agar and were incubated in aerobic condition at 35 °C. Growth was observed after 24 hrs and isolates were identified based on morphological and biochemical characteristics using standard procedures of the Clinical and Laboratory Standard Institute (CLSI) (Humphries et al., 2021).

Antimicrobial Susceptibility Test

Antimicrobial susceptibility testing were carried out using the automated Vitek-2 Compac system in accordance with CLSI guidelines. The VITEK-2 antibiotic disc panel included the following:- Gentamicin (10µg), Imipenem (10µg), Cephalothin (30µg), Cefoxitin(30µg),Cefotaxim(30µg),Ampicillin(10µg),Amoxicillin-Clavulanate 20+10µg), Penicillin G (10µg), Trimethoprim-Sulfamethoxazole (1.25+23.75µg), Nitrofurantoin (300µg),Ciprofloxacin(5µg),Levofloxacin(5µg),Mupirocin(200µg + 5µg), Erythromycin (15µg), Chloramphenicol (30µg), Tetracycline (10µg), Fusidic acid (10µg), Rifampicin (5µg), Teicoplanin (30µg), and linezolid (30µg), Vancomycin (30µg) Netilmicin (10µg), Oxacillin (1µg), Clindamycin (10µg), Daptomycin (30µg).

Statistical analysis

The study data were analyzed with the aid of SPSS V.17 (SPSS, Inc., Chicago, IL, USA) software. The accuracy of entries was verified twice before entering.

Results

Distribution of Isolates

From March 2019 to May 2020, a total of 978 patients were admitted to Prince Muteb Hospital. The Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Coagulase Negative *Staphylococcus* (CoNS) isolated from various clinical samples were as follows: blood 7.8% and 8.69% (n=230), urine 0.46% and 0% (n=215), sputum 1.9% and 0% (n=210), wound 9.6% & 1.6% (n=250), nasal swab 33.3% and 0% (Figure 1). While CoNS was discovered in more pleural fluid samples than any other substance, it was followed by blood and wound (Table 1). We did not isolate MRSA from pleural fluid, but it predominated in nasal swabs, followed by throat swabs, wounds, and blood.

Antimicrobial resistance of Methicillin-Resistant Staphylococcus aureus (MRSA) and Coagulase Negative Staphylococcus (CoNS):

MRSA and CoNS are isolated from blood, urine, wounds, tracheal washes, throat swabs, sputum, nasal swabs, and pleural fluid exhibiting high rates of antibiotic resistance. The rate of resistance was discovered to be 100% among beta-lactams, cephamycin, carbapenems, and the fourth generation of cephalosporins. MRSA was found to have a 38% resistance to gentamycin, whereas CoNS had a higher resistance of 50% to 64%. In contrast to the CoNS, where resistance ranged from 50% to 85%, MRSA resistance to Ciprofloxacin ranged from 14% to 46%, with the exception of samples from tracheal wash procedures, where it was 100%. Tetracycline was found to be effective against MRSA with the exception of blood samples, where resistance was found to be 14.3%, and wound samples, where resistance to CoNS was found to be 50%. MRSA and CoNS were successfully treated with Daptomycin, Linezolid, Teicoplanin, and Vancomycin (100% susceptibility) (Figure 2,3).

Discussion

Methicillin-resistant *S. aureus*, a nosocomial pathogen was first observed during the 1960^{s}, and with the evolution of time new strains of MRSA have emerged especially, in the human community, MRSA bacteremia (MRSAB), including infective endocarditis, carries a high mortality rate, with up to 50% of patients failing initial therapy with vancomycin and requiring salvage therapy. Persistent MRSAB can be difficult to successfully eliminate, especially when source control is not possible due to an irremovable focus or the bacteremia still persists despite surgical intervention (Kuller at al., 2016 and Robinson et al., 2012). widespread use of penicillin, sulfamethoxazole-trimethoprim, and tetracycline in the local population, antibiotic susceptibility was comparable to that observed for S. *aureus* infections that occur in different parts of KSA (Asgar et al., 2006; Bukharie., 2010 and Monecke S et al.,2011). Several cell surface and secreted virulence components have a role in *S. aureus* pathogenesis. One such virulence factor is Panton-Valentine leukocidin (PVL), a two-component toxin that causes pores to develop in the complement receptors on the leukocyte cell membrane. These two genes (LukS-PV and LukF-PV) produce a heptavalent leukocidin that is fully encoded by two proteins that are co-transcribed and secreted independently (Al Yousef et al.,2016). This study revealed the prevalence of MRSA and CONs in the Al Jouf region, the study was completed in 14 months. Instead of the prosperous Arab nations in the GCC region, the Levant and North African Arab countries have seen decades of economic and political turmoil, which has had a significant influence on medical resources and healthcare facilities (Abdullahi et al., 2021). Nevertheless, the high MRSA rates observed in KSA cast doubt on this theory (Hassoun et al., 2017 and Self, W.et al., 2016). Our study shows prevalence of 6.5 % (64/978) MRSA in Prince Muteb Hospital, Al Jouf, Saudi Arabia. The MRSA isolated from blood, wound and nasal swab were found 7.8%, 9.6% and, 33% respectively. While CoNS was found as 8.69%, 33.3%, and 1.6% from blood, pleural fluid and, wound respectively. MRSA prevalence in Abu Dhabi, and Kuwait is 27.4% ,

5.2 % respectively and in Jeddah King Khalid National Guard Hospital MRSA was found between 6.6-8.9 % which is higher to as compared to our results (Udo et al., 2006;Senok et al., 2016 and Abou Shady et al., 2015). Strict implementation of infection control practices and hand wash techniques has resulted in a significant decrease in MRSA incidence in the Riyadh region and Al-Ka'bah al-Musharrafah, the place where Muslims from all over the world congregate each year to perform religious ceremonies, is located in Saudi Arabia. The transmission of different MRSA strains is probably made easier by these congested situations Panton-Valentine leukocidin [PVL+] strains are usually linked to necrotizing pneumonia, skin and soft tissue infections, and leukocyte destruction (Tissot et al., 2014 and Tong et al., 2015). HA-MRSA strains rarely contain PVL, CA-MRSA strains frequently do (Al Yousef et al.,2016; Lina, G et al., 1999). In our study 100% of MRSA were resistant to beta-lactams cephamycins, 14-46% resistant to cotrimoxazole, 38% to tetracycline, 19-61 % to clindamycin and 100% susceptibility to Mupirocin. The CoNS were resistant 25-42% to Mupirocin, 7-50% tetracycline, 50 % to cotrimoxazole,7-25 % to Rifampin. The glycopeptides (Vancomycin and Teicoplanin) remained the drug of choice for MRSA infections. In our study subjects, we did not find any vancomycin-resistant MRSA or CoNS. However, in the UK, Spain, Europe, USA, Hong Kong and Korea vancomycin intermediate resistant strains have been found. Mortality and morbidity of MRSA infections are high worldwide (CDC.,2000).

The study has a number of Limitations, the first and most significant one is just including one institution and basing sampling on isolate availability. This could not be typical of the entire nation. Due to the nature of the study—a retrospective one—it was not able to share the findings with the attending physicians so they might alter patient treatment. Despite the fact that patients were primarily from the local population, occasional admissions within 3 days were all thought to be acquired locally, and illness risk factors were not identified. Due to a paucity of clinical data, the length of hospital stays for many patients was not examined. Due to a lack of data, other clinical outcomes like prognosis and death were not evaluated.

Conclusion

MRSA is spreading globally and community-associated MRSA is found both in hospitals and communities The implementation of hand hygiene and infection control is required to control this dangerous pathogen.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study**.**

Data Availability Statement: The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Conflicts of Interest: The authors declare no conflict of interest.

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Institutional Review Board Statement

Ethical approval The Jouf University's Local Committee on Bio-Ethics approved the research proposal vide 03-04/41 dated: 6th January 2020. Informed consent was taken from the admitted, out-patients, and guardians/relatives of patients admitted in intensive care units in presence of independent witnesses at the time of sample collection.

Table 1: MRSA and CoNS distribution according to site of isolation

Samples	*Staphylococcus aureus* n (%)	CoNS n (%)	Total
Blood	18 (7.8)	20 (8.69)	230
Urine	1 (0.46)	0	215
Sputum	4 (1.9)	0	210
Wound	24 (9.6)	4 (1.6)	250
Nasal	15 (33.33)	0	45
Tracheal wash	1 (5.8)	0	17
Pleural fluid	0	1 (33.33)	03
Throat swab	1 (12.5)	0	08
Total	64 (6.54)	25 (2.5)	978

MRSA = Methicillin-Resistant *Staphylococcus aureus*
CoNS = *Staphylococcus* coagulase Negative

Figure 1: Distribution of Methicillin-Resistant *Staphylococcus aureus* in study samples.

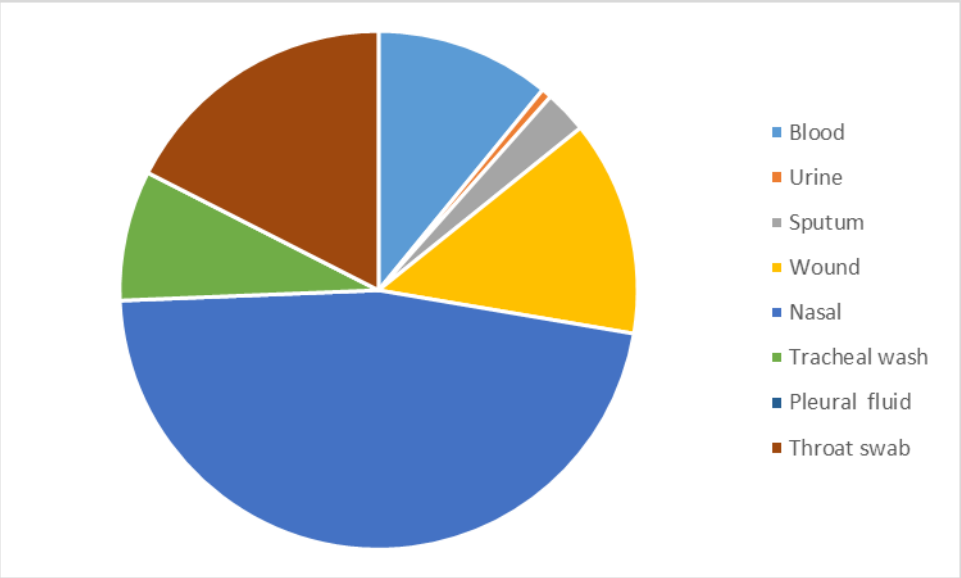


Figure 2: Antibiotic resistance pattern of Methicillin-Resistant *Staphylococcus aureus*

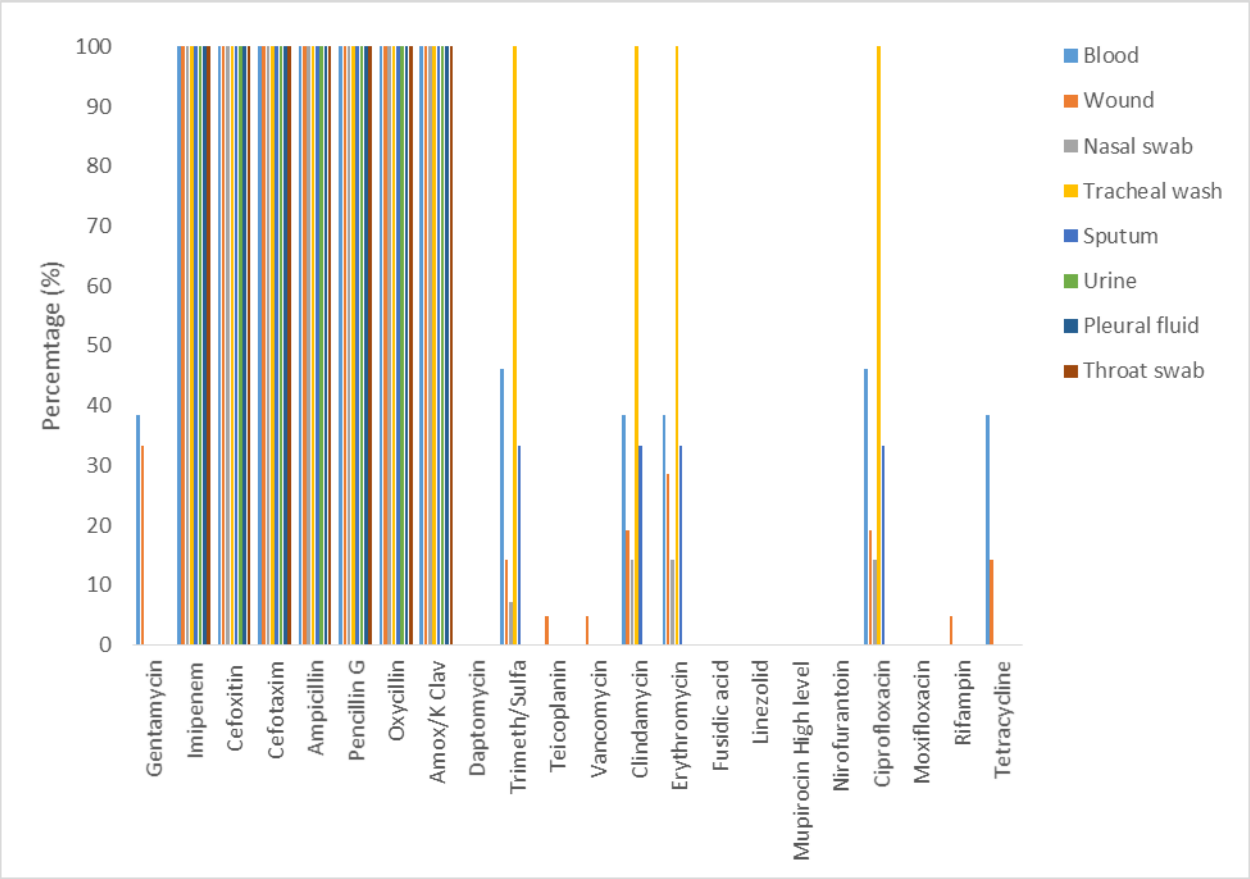
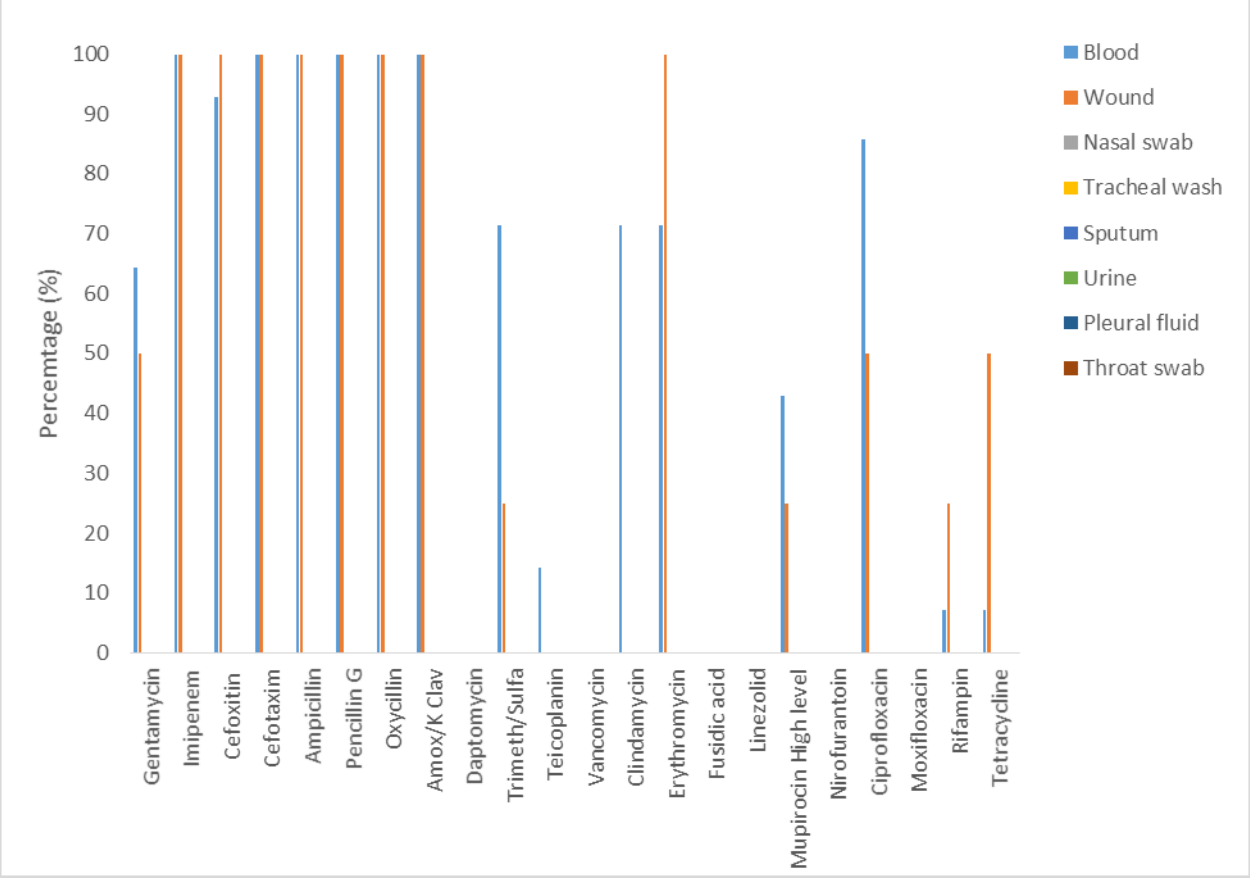


Figure 3: Antibiotic resistance pattern of *Staphylococcus* coagulase Negative



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