ABSTRACT

Methicillin-resistant Staphylococcus aureus (MRSA) is a bacterium that causes infection in different parts of the body. It's tougher to treat than most strains of staphylococcus aureus. Because it's resistant to some commonly used antibiotics. Although enough data is available about MRSA prevalence worldwide but here is lack of research and accurate statistics that covers the north regions of Saudi Arabia. The aim of current research is to analyze the MRSA positive cases in Northern region of Saudi Arabia and to identify the diabetic patients with MRSA infection. Isolates of MRSA, recovered from various clinical samples from two different cities Rafha and Quriyat in the north region of Saudi Arabia. Samples were included in this prospective, cross-sectional study from Jan 2013 to June 2017. Agar diffusion method was employed according to the protocols of Clinical Laboratory Standards Institute. Out of total 800 S. aureus strains, the frequency rate of MRSA was 42.5% (n = 340). MRSA infection was found higher among the age group 20-40 years i.e. 33% (n=264), followed by 28% (n=224) in 60-80 years. Frequency of MRSA percentage in male and female was and 53% and 47%, respectively. MRSA was more frequently observed in eye sample 79% (n=632). MRSA showed resistance to antibiotics as cefuroxime (90.16%), streptomycin (59.3%), amikacin (95.8%), azithromycin (63.8%), ampicillin (95.8%), amoxicillin/clavulanic acid (76.4%), Penicillin G (96%), oxacillin (66%), gentamicin (68%), cefoxitine (94%) MRSA infection among diabetic patients showed significant prevalence that was found to be 30% and its alarming to stop the spread at this point.  This study provided sufficient knowledge toward spread of multi drug resistant S. aureus against a number of antibiotics that were used to be sensitive before These results giving us a picture of real threat for spreading a life-threatening infection in the region if not taken serious action particularly the diabetic patients will be on challenge.

Keywords
MRSA, Diabetic, Antibiotic, Staphylococcus aureus.

Introduction
Antibiotic resistance is one of the alarming issues, affecting human health. There are various factors responsible to the emergence of resistance such as, misuse and overuse of antibiotics, patient related factors, inappropriate prescriptions by the physicians, self-medications especially young adults, use of broad-spectrum antibiotics and synergistic combinations, un necessary promotions by pharmaceutical industry, untrained staff in microbiological testing laboratories, lack of awareness with the new guidelines recommended for antimicrobial testing etc [1]. S. aureus is one of the major causes of hospital acquired infections especially patients admitted in ICU (Intensive Care Unit) [2]. It colonizes healthy individuals and causes severe infection in hospitalized patients because of the higher resistance to antimicrobial agents and lack of new drugs development. Staphylococcus aureus infections used to respond to ß-lactam and related group of antibiotics but the emergence of Methicillin-resistant S. aureus (MRSA) has posed a serious therapeutic challenge [3].

Infected and colonized patients in hospitals mediate the dissemination of MRSA strains, and hospital staff is the main source of transmission. This leads to serious endemic and epidemic MRSA infections. The possible predisposing factors that increase
the chance of emergence and spread of MRSA are prolonged and repeated hospitalization, indiscriminate use of antibiotics, lack of awareness, intravenous drug abuse, and presence of indwelling medical devices [4]. Overall, resistance rates keep on increasing and differ according to epidemiology of different geographical locations. Multi drug resistance is getting common phenomenon and resistance of almost all anti-\textit{S. aureus} agents are being reported worldwide.

There is debatable issue of using combination of antimicrobial agents against complicated infections, but usually single antimicrobial agents are recommended for uncomplicated infection [5]. Development of antimicrobial resistance limits the therapeutic options that leads to high mortality and morbidity [6]. The incidence of infectious diseases has escalated so much high that standards of public health in different parts of the world is comparable to pre-antibiotic era [7].

**Material and Methods**

**Sampling**

This cross sectional study was conducted in Microbiology Department, University of Northern Border, from 2013 to 2017. Clinical samples (Wound, Throat, Sputum, Pus, Pleural, fluid, Nose, Nail, Breast, milk, Eyes, Ear, Catheter, Blood, Axilla, urine, vagina, urethra and others) were collected from different hospitals of Rafha and Quriyat.

**Preparation of Agar Media**

Agar plates were prepared using dehydrated media according to the instructions of the manufacturers. After autoclaving, media was allowed to cool down to ~450C, then poured in the Petri plates. These Petri plates can be safely stored in refrigerator with proper precautions for about 2 weeks.

**Antimicrobial Testing**

Antibiotic susceptibility test of \textit{S. aureus} was performed by Kirby Bauer agar diffusion method as per Clinical Laboratory Standard Institute (CLSI) guidelines (CLSI Guideline 2006).

Antibiotic disks used were Etrapenem, Ceforexime, Streptomycin, Amikacin, Moxifloxacin, Azithromycin, Ampicillin, Amoxicillin/Clavulanic Acid, Vancomycin, Trimethoprim, Teicoplanin, Tetracyclin, Rifampin, Pnicillin G, Oxacillin, Nitrofurantoin, Mupirocin, Moxifloxacin, Linezolid, Levofloxacin, Imipenem, Gentamicin, Fusidic Acid, Fosfomycin, Erythromycin, Daptomycin, Clindamycin, Ciprofloxacin, Cefoxitine. Methicillin resistant was determined using cefoxitine and a zone of ≤21 mm considered as positive.

**Result**

Out of total eight hundred clinical isolates of \textit{S. aureus} strains, the frequency rate of MRSA was found to be 42.5% (n = 340). Frequency of MRSA percentage in male and female was and 53% and 47%, respectively. The highest number of sample were obtained from eyes followed by other body parts and secretions. (Figure 1).

MRSA infection was found higher among the age group 20-40 years i.e. 33% (n=264), followed by 28% (n=224) in 60-80 years. (Figure 2).

MRSA showed resistance to the given antibiotics Cefuroxime (90.16%), Streptomycin (59.3%), Amikacin (95.8%), Azithromycin (63.8%), Amoxicillin (95.8%), Amoxicillin/Clavulanic Acid (76.4%), Penicillin G (96%), Oxacillin (66%), Gentamicin (68%), Cefoxitine (94%) (Figure 3).

Antibiotics that showed sensitivity were against MRSA strain from clinical isolates were Etrapenem, (78%) Vancomycin, (99.97%) Trimethoprim, (71%) Teicoplanin, (99.6%) Tetracyclin, (82.6%) Rifampin, (91%), Nitrofurantoin, (99.92%), Mupirocin (92.7%), Linezolid, (67.6%), Levofloxacin (67.8%), Imipenem (93.4%), Fusidic Acid (91.2%), Fosfomycin (97.1%), Erythromycin, (68.6%), Daptomycin, (99.97%), Clindamycin, (63.7%), Ciprofloxacin (64.9%), (Figure 4). Although a number of antibiotics are still effective against MRSA but we cannot ignore the reality that at higher dose they supposed to be pose tremendous side effects given in Table 1.

Figure 1: Patient’s source of clinical sample for MRSA isolation. (N=180), Males Females 126.

Figure 2: Patient age group wise distribution of MRSA.

Figure 3: Shows antibiotics percentage of resistance against methicillin resistance \textit{staphylococcus aureus} shows significant resistance shows moderate to low resistance.

Figure 4: Shows antibiotics efficiency against MRSA.
and linezolid [12] are the most effective antibiotics as compared to our results most effective antibiotic Teicoplanin (99.62%) for treating diabetic patients.

**Conclusion**

In this current study we describe the incidence and distribution of MRSA disease in north area and use these results to estimate the burden of MRSA infection. Our study investigated the use of antibiotic among diabetic MRSA patients and the drug of choice found to be highly effective in skin- and bone-infected lesions in the diabetic foot was Teicoplanin. However, it’s quite alarming that incidence of MRSA is high in the region particularly diabetic MRSA patients. In addition, the maintenance of proper hygiene by hospitalized patients and staff and avoidance to irrational use of broad-spectrum antibiotics and facility of antibiotic stewardship could effectively reduce the rate and spread of multi drug resistant strains.

**Reference**

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**Discussion**

Methicillin resistant *S. aureus* has now emerged as bad bug that has created a serious concern for health care planners as limited option available to treat MRSA [8]. Problems with MRSA are not only confined to developing or poor countries but can be of concern in developed countries including Saudi Arabia. The present study has reported 42% prevalence rate of MRSA strains among *S. aureus*. Similar finding was also reported form another similar study shows MRSA was isolated in 39.5% of the specimens. The prevalence of MRSA was highest among patients who were 56 years old or older (52.2%) [11]. As compare to our study in which the young patients were more susceptible. A study showed that Quinupristin-dalfopristin and linezolid [12] are the most effective antibiotics as compare to our results most effective antibiotic Teicoplanin (99.62%) for treating diabetic patients.

**Figure 4:** Shows antibiotics percentage of sensitivity against methicillin resistance *staphylococcus aureus* shows significant sensitivity shows moderate to low sensitivity.

During the analysis of prevalence of MRSA infection in north region of Saudi Arabia it was found that among total positive cases around 31% of the patients were diabetic. MRSA infection among diabetic patients is an alarming situation because of their low healing progression toward any wound would likely to cause complications as well as spread of the infection.

**Figure 5:** Shows percent of MRSA positive cases among diabetic patients.

<table>
<thead>
<tr>
<th>Sensitive antibiotics (% effective)</th>
<th>Risk factor and possible use</th>
</tr>
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<tbody>
<tr>
<td>Vancomycin (99.97%)</td>
<td>Penetration into target tissues is substantially impaired in diabetic patients and its associated with a risk of nephrotoxicity.</td>
</tr>
<tr>
<td>Nitrofurantoin (99.92%)</td>
<td>Severe nerve damage and neuropathy in feet, legs, arms and hands.</td>
</tr>
<tr>
<td>Teicoplanin (99.62%)</td>
<td>Highly effective in skin- and bone-infected lesions in the diabetic foot.</td>
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<tr>
<td>Fusidic acid (91.24%)</td>
<td>Possess immunosuppressive functions.</td>
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**Table 1:** Risk factors assessment against highly susceptible drugs against MRSA.