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Full Length Research Paper

Resistance pattern of coagulase positive *Staphylococcus aureus* clinical isolates from Asir region, Kingdom of Saudi Arabia

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The objectives of this study were to determine the prevalence of methicillin resistant coagulase positive *Staphlococcus aureus* (MRSA) infections in two major hospitals in Asir region, Kingdom of Saudi Arabia and to compare it with the community-acquired infections. Two hundreds and ten coagulase positive *S. aureus* recovered from 9831 specimens from various infections at Asir Central Hospital and Abha General Hospital, KSA (Kingdom of Saudi Arabia), were tested against 44 commonly used antibacterial agents. One hundred of the isolates were from hospital-acquired infections, 100 from community-acquired infections and 10 isolates were collected from the hospital environment. All isolates were found resistant to aztreonam, colistin, mecillinam, metronidazole, polymyxin B and nalidixic acid but were sensitive to vancomycin, nitrofurantoin and novobiocin. Various levels of resistant were recorded for the remaining antibiotics. High resistance to antimicrobial agents was detected among hospital acquired infections compared to community acquired infections ($p<0.01$). The resistance rates of *S. aureus* to antimicrobial agents among hospital acquired infections isolates were significantly higher ($p<0.05$) than community acquired infections. This implies that hospital environment is a strong risk factor for the prevalence of MRSA in the hospitalized patients, visitors, and hospital staff with potential risk of spreading to the community.

Key words: *Staphlococcus aureus,* coagulase positive, Kingdom of Saudi Arabia (KSA).

INTRODUCTION

Staphylococcus aureus is one of the most important etiological agents of many hospital-acquired infections as well as community-acquired infections and poses a constant therapeutic problem to clinicians (Klein et al., 2007). In recent years, a strong correlation between isolation of *S. aureus* and occurrence of nosocomial infections became a constant problem to hospitals and clinical centers. Methicillin and its derivatives became the drugs of choice for the treatment of infections caused by *S. aureus*. The appearance of methicillin resistant *S. aureus* (MRSA) was followed by various patterns of resistance to antibiotics (Tacconelli et al., 2008; Goto et al., 2009).

Several surveys have confirmed that the incidence of MRSA varied with region and at increase. MRSA prevalence varied almost 100-fold, from <1% in Northern Europe to >40% in southern and Western Europe. MRSA proportions significantly increased in Belgium, Germany, Ireland, the Netherlands, and the United Kingdom, and decreased in Slovenia (Tiemersma et al., 2004). Antibiograms of ORSA (oxacillin resistant *S. aureus*) from hospitalized patients from 17 institutions in eight countries in Asia, Pacific and South Africa (APAC) have shown that, the proportion of MRSA in the APAC region were higher (ranging from 5.0% in the Philippines to 79.5% in Hong Kong. This proportion was higher than reported in other geographic regions contributing to SENTRY over the same time: Latin America (34.9%), United States (34.2%), Europe (26.3%) and Canada (5.7%) (Diekema et al., 2001).

Prolonged hospitalization and antibiotic therapy especially with β-lactam antibiotics predispose patients to the acquisition of MRSA and oxacillin resistant *S. aureus* (ORSA) (Mattner et al., 2010; Hackbarth and Chambers,

1989). Hospital-acquired MRSA and ORSA are usually associated with increased expression of multiple antibiotic resistance genes, including those coding for aminoglycoside resistance (Deurenberg et al., 2007).

The objectives of this study were to determine the prevalence of coagulase positive MRSA infections in two major hospitals in Asir, K.S.A., and to compare it with community-acquired infections in the region.

MATERIALS AND METHODS

The study was a cross-sectional study, which was undertaken in Asir region, between March and September 2004. Two hundreds and ten (210) coagulase positive *S. aureus* strains were isolated from 9631 clinical specimens and were identified as per standard protocols (Forbes et al., 2002). The isolates were tested for their susceptibility to 44 different kinds of antimicrobial agents using disk diffusion method was used as per the guidelines of the NCCLS (2002). Commercially prepared disks (Mast Diagnostics, DM 160, Mast group MTD, Merseyside, United Kingdom) were used in this study. Concentration of each antibiotic used is shown in Table 1. Antibiotic results were tested against the type of infection using ANOVA test in the SPSS (Statistical Package for the Social Sciences) package (Version 10).

RESULTS

All confirmed 210 coagulase positive *S. aureus* isolates were resistant to aztreonam, colistin, mecillinam, metronidazole, polymyxin B and nalidixic acid. In contrast, all the isolates were sensitive to vancomycin, nitrofurantoin and novobiocin. The tested 210 revealed various levels of susceptibilities against remaining 35 antibiotics. Comparison between resistance rate of the nosocomial infections and community-acquired infections showed in Table 1 and summarized in Figures 1 and 2, respectively.

Two hundred ten *S. aureus* isolates were categorized according to the type of infections, 100 were isolated from hospital-acquired infections, 100 were isolated from community-acquired infections and the remaining 10 were isolated from hospital environment. Comparison between MRSA (methicillin-resistant *S. aureus*), multidrug resistant (MDR, MRSA and non-multidrug resistant (NMDR, MRSA) among nosocomial, community infection isolates and hospital environment isolates is showed in Figure 3. Out of the 100 *S. aureus* isolates which were recovered from nosocomial infections, 54 (54%) were MRSA. Of these 54 MRSA, 46 (85.2%) were MDR MRSA and 8 (14.8%) were NMDR MRSA. Hundred *S. aureus* isolates recovered from community-acquired infections 32 (32%) isolates were MRSA. Of these, 32 were MRSA, 11 (34.4%) were MDR MRSA and 21 (65.6%) were (NMDR) MRSA (Figure 1).

In the present study, the resistance rates among nosocomial isolates to cephalosporins and imipenem were found to be higher than those found in community infections isolates. All MDR MRSA was found to be resistance to imipenem and to all cephalosporins that had been used in the study with the exception of two isolates, which were sensitive to cephalothin, whereas the majority of NMDR MRSA were sensitive to cephalosporins, and all were sensitive to the imipenem (Figure 2).

Comparison of resistance rates among Staphylococcus aureus isolates from nosocomial and community infections to different groups of antibiotics according to their modes of actions is shown in Figure 4.

DISCUSSION

The regular surveillance of hospital-acquired infections of MRSA may be helpful in formulating and monitoring the antibiotic policy. This may also help in preserving antibiotics like vancomycin, only for life-threatening staphylococcal diseases (Pai et al., 2010). Recently, there has been increase in MRSA and ORSA susceptible to gentamicin and variably susceptible to other non beta-lactam antimicrobial agents, namely tetracycline, trimethoprim, erythromycin and ciprofloxacin (Merlino et al., 2002; Mroczkowski et al., 2009).

In the present study, the prevalence of MRSA (ORSA) among nosocomial infections isolates was found significantly higher than those among community acquired infections ($p = 0.002$). The majority of MRSA of nosocomial infection isolates found to be resistant to all β-lactam antibiotics and resistant to more than 15 non-β-lactam antibiotics (Table 1); these isolate had been designated multidrug-resistant methicillin-resistant *S. aureus* (MDR-MRSA). The remaining of MRSA isolates was resistant to the majority of β-lactam antibiotics and resistant to less than 15 non-β-lactam antibiotics. These isolates had been designated non-multidrug-resistant methicillin-resistant *S. aureus* (NMDR-MRSA). The trends noticed in the present study is in accordance with the general trends noticed in other hospital settings (Sakoulas and Moellering, 2008; Tiemersma et al., 2004; Mattner et al., 2010) and in Saudi Arabia (Bukharie, 2010; Al-Mendalawi, 2010; Ghazal et al., 2011). It is noticed that penicillin-resistant *S. aureus* detected in the present study is higher than those reported previously in Saudi Arabia (Bilal and Gedebou, 2000; Akbar et al., 2000).

The emergence of MDR MRSA causes difficulties in the treatment of infections caused by *S. aureus*. Antibiotic resistant-strain is a problem for the infected patients who are responding poorly to treatment and problem to the hospital, which perform control and prevention programs. The rates of MDR-MRSA originated from nosocomial infections in the present study was found to be significantly higher (85.2% of MRSA) than those in community acquired infection (34.4% of MRSA). Several risk factors for the acquisition of MDR-MRSA among nosocomial infections had been identified: Prolonged hospitalization, severe underlying illness in patients who are exposed to MDR-MRSA in the hospital and

Table 1. Comparative resistant of *S. aureus* isolated from nosocomial infections and community infections.

Antimicrobial agent	Number (%) of resistant isolates from nosocomial infections	Number (%) of resistant isolates from community acquired infections
Inhibition of cell wall synthesis		
Penicillins		
Amoxicillin (10 µg)	82	69
Ampicillin (10 µg)	82	69
A ugmentin (30 µg)	48	28
Carbenicillin (10 µg)	54	30
Mecillinam (33 µg)	100	100
Methicillin (25 µg)	54	33
Oxacillin (01 µg)	54	33
Penicillin G (10 I µ)	91	84
Piperacillin (100 µg)	62	47
Ticarcillin (75 µg)	53	20
Cephalosporins; Cephamycins		
Cefepime (30 µg)	46	16
Cefotaxime (30 µg)	46	16
Ceftriaxone (30 µg)	50	23
Ceftazidime (30 µg)	91	91
Cephalothin (30 µg)	39	04
Cefoxitin (30 µg)	49	17
Cephradine (30 µg)	47	22
Glycopeptides		
Vancomycin (30 µg)	00	00
Imipenem (10 µg)	39	06
Aztreonam (30 µg)	100	100
Bacitracin (10 µnits)	20	15
Inhibition of protein synthesis		
Aminoglycoside		
Amikacin (30 µg)	39	08
Gentamicin (10 µg)	47	11
Neomycin (30 µg)	50	17
Netilmicin (30 µg)	37	08
Tobramycin (10 µg)	45	14
Macrolides		
Erythromycin (15 µg)	15	28
Lincosamides		
Clindamycin (2 µg)	39	10
Tetracycline		
Doxycycline (30 µg)	19	12
Oxytetracycline (30 µg)	29	19
Tetracycline (30 µg)	31	24
Chloramphenicol	3	0
Inhibitors of n µcleic acid synthesis		
Quinolones		
Ciprofloxacin (01 µg)	36	12
Norfloxacin (10 µg)	40	11
Nalidixic acid (30 µg)	100	100
Novobiocin (30 µg)	0	0
Refampins		

Table 1. Contd.

Rifampicin (05 µg)	17	5
Metronidazole (5 µg)	100	100
Increase permeability of the cytoplasm membrane (polypeptide antibiotics)		
Polymyxin B (300 µnit)	100	100
Colistin(Polymyxin E) (10 µg)	100	100
Antimetabolites		
trimethoprim-s ulfamethoxazole (25 µg)	43	9
Other bacteriosidal antibiotics		
F µsidic acid (30 µg)	45	25
Nitrof µrantoin (300 µg)	0	0
Co-trimoxazole (25 µg)	42	12

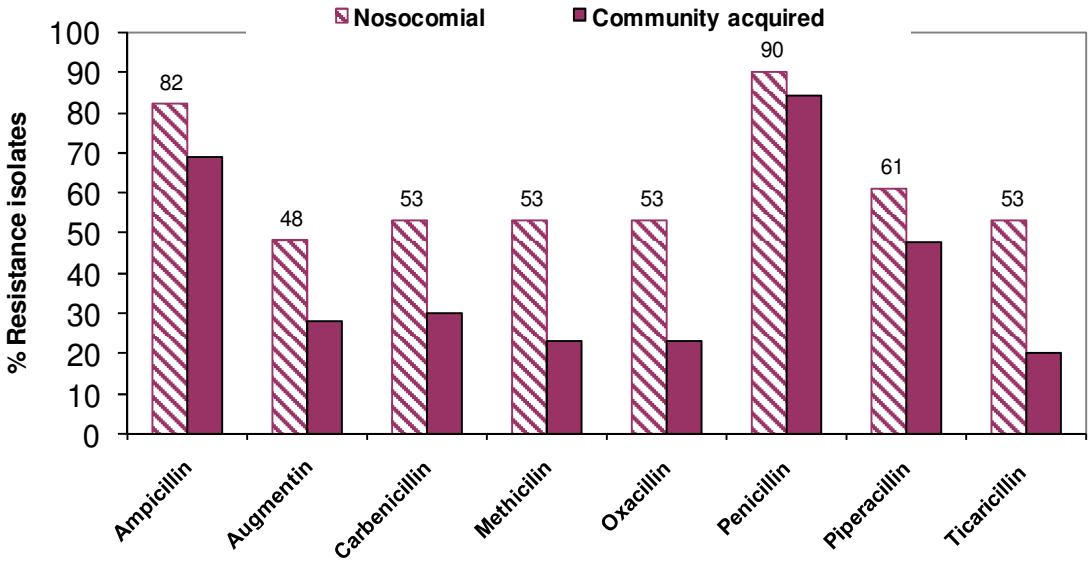

Figure 1. Comparison between resistance rate of nosocomial and community infection of *S. aureus* isolates to penicillins.

prolonged exposure to antibiotics (Dietrich et al., 2004; Lee et al., 2011).

The Society for Healthcare Epidemiology of America (SHEA) has developed guidelines for the prevention of transmission of MRSA and vancomycin-resistant enterococci within health care settings, and chief among the recommendations is an emphasis on adherence to hand hygiene guidelines. Other measures that may prevent the nosocomial transmission of MRSA include improved antibiotic stewardship, staff cohorting, maintenance of appropriate staffing ratios, reductions in length of hospital stays, contact isolation, active microbiologic surveillance, and better staff education (Lee et al., 2011). Currently, the efficacy of many of these individual infection control interventions remains in doubt. Many studies reporting improvement in infection control outcomes (e.g. reduced transmission, decreasing prevalence) involve simultaneous institution of several of these measures, making it impossible to tease out the effects of any of the individual components (Henderson, 2006; Lee et al., 2011).

High prevalence of multiple drug resistance among isolates in the present study clearly indicated the excessive or inappropriate use of antibiotics in community (Maki and Schuna, 1978; Paul et al., 2010). In Saudi Arabia, like in many other developing countries, antibiotics are readily available from the pharmacy desk. Alternatively, pharmacists prescribe medications to patients just based on their external symptoms, causing the intake of wrong antibiotic and/or over or under

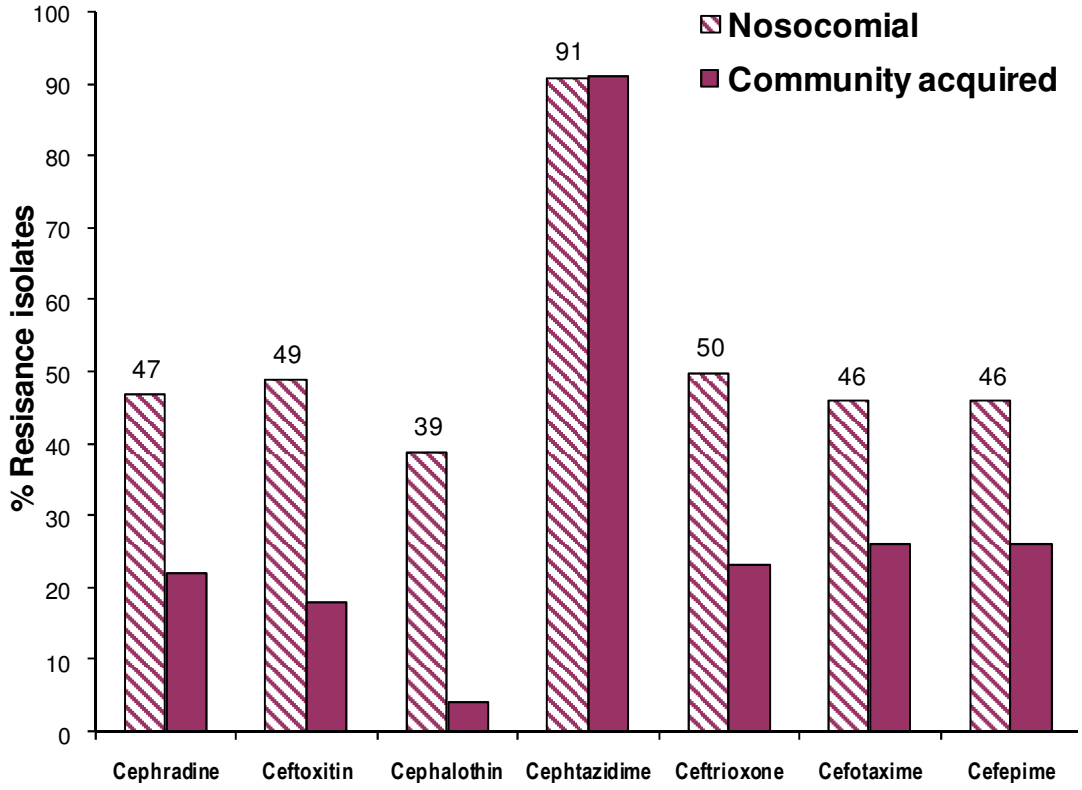

Figure 2. Comparison between resistance rate of nosocomial and community infection of *S. aureus* isolates to cephalosporins.

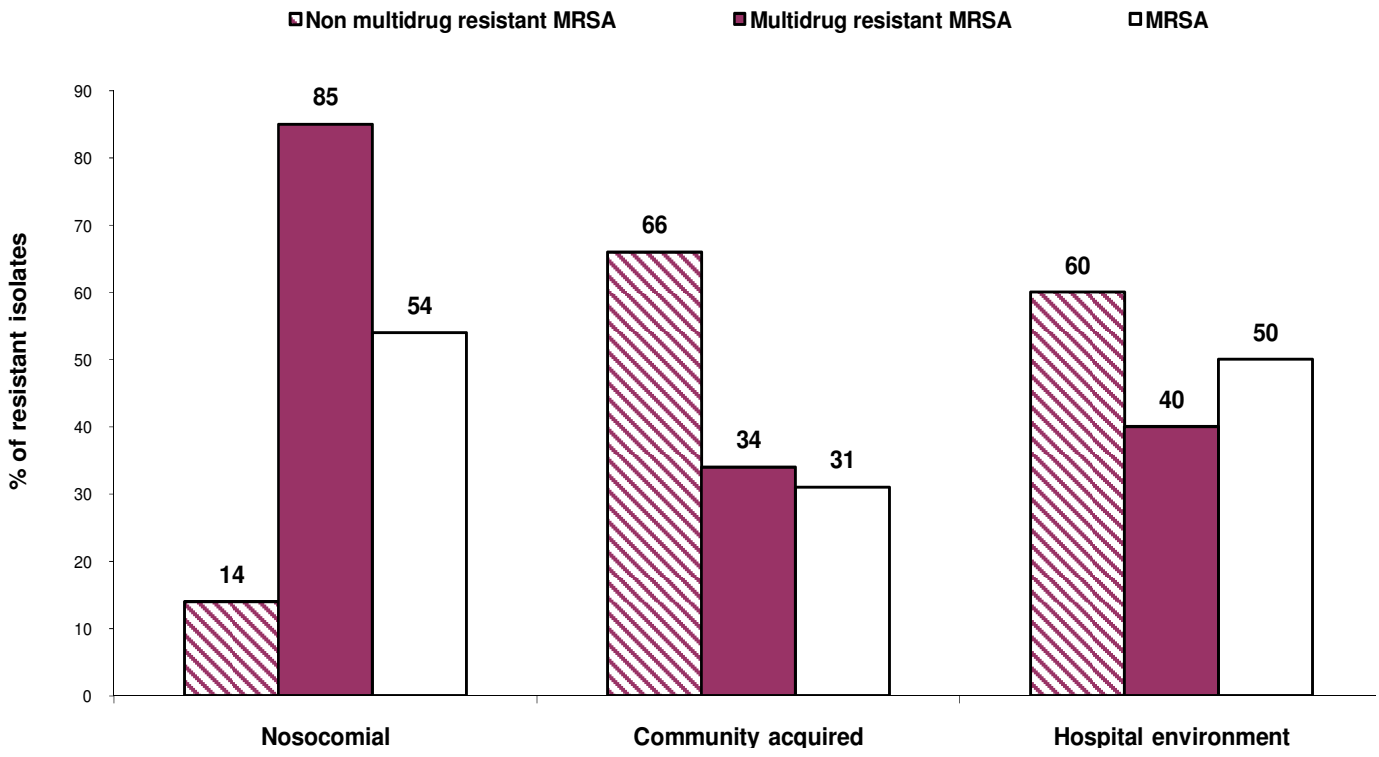

Figure 3. Comparison between MRSA, multidrug resistant MRSA and non-multidrug resistant MRSA among nosocomial, community infection of *S. aureus* isolates and hospital environment isolates.

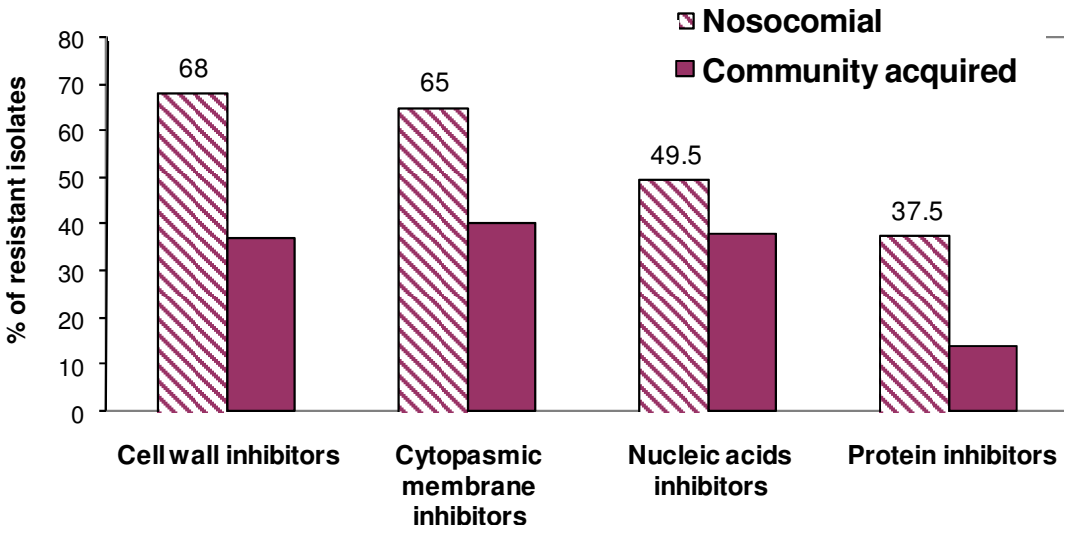

Figure 4. Comparison of resistance rates among *S. aureus* isolates from nosocomial and community infections to different groups of antibiotics according to their modes of actions .

dosage. Moreover, in majority of cases, patients do not complete the prescribed course of antibiotics. This causes patients to be at the hospital harboring resistant strains. These strains may cause endogenous or exogenous infections in other patients.

In conclusion, the resistance rates of *S. aureus* to antimicrobial agents among hospital acquired infections isolates were found significantly higher ($p<0.05$) than community acquired infections. Hospital environment is a risk factor for the prevalence of MRSA in the hospitalized patients, visitors, and hospital staff and may spread a major risk to the community. Efforts are therefore needed to reduce the spread of MRSA by strict application of infection control guidelines (Lee et al., 2011).

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