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Prevalence of Methicillin Resistant *Staphylococcus Aureus* (MRSA) in Surgical Site Infections in a Tertiary Care Hospital

***Shagufta Hussain, *Rabia Shams, **Khurshid Ahmad, *Roshan Perveen, *Bushra Riaz**

* Pathology Department, PIMS, Islamabad
** National Institute of Health, Islamabad.

Objective: To determine the prevalence of Methicillin Resistant *Staphylococcus aureus* (MRSA) in post-operative wound infections in surgical wards and surgical ICU and also to define the antimicrobial susceptibility pattern of the strains isolated.

Design: A cross sectional prospective study.

Place and Duration of Study: Departments of Pathology and Surgery, Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan. January 2004 to August 2005.

Patients and Methods: Wound swabs from patients who had undergone surgery and were suspected of having postoperative infection of the wounds were collected and inoculated on blood agar and MacConkey agar plates. After incubation for 24-48 hours, plates were examined for the growth of *S. aureus.* Anti-microbial susceptibility test was performed using oxacillin 1ug disc to detect methicillin resistance. An inhibition zone = or <10mm was taken as indicative of MRSA.

Results: A total of 1310 surgical wound swabs yielded growth of bacterial pathogens out of which 273 (20%) were found to be *S. aureus*. 225 of the affected patients were admitted in surgical wards and 48 in SICU. Analysis of the antimicrobial susceptibility patterns of the isolates revealed that 105 (39%) were strains of Methicillin Resistant *Staphylococcus aureus* (MRSA) as indicated by their resistance to Oxacillin (1ug disc). Significantly higher proportion of the MRSA isolates were from SICU, 31/48 – 65% than from the surgical wards, 74/225 – 35% ($p < 0.05$) indicating the inherent tendency of these strains to become endemic in the critical care units as well as their propensity for nosocomial spread. Susceptibility patterns further revealed that Vancomycin and Teicoplanin were the most effective antimicrobial agents for MRSA infections - 100% of the strains being fully susceptible – followed by Fusidic acid (80% susceptible). The reverse was true as regards the efficacy of Gentamicin and Ciprofloxacin, to which 100% of the isolates were resistant. Other antibiotics yielded variable results.

Conclusions: 273 (20%) out of 1310 post-operative wound infections were caused by *S. aureus*, 105 (39%) were strains of MRSA whose prevalence was found to be significantly higher in surgical ICU than in the surgical wards (65% as compared to 35% respectively –$p < 0.05$). All the isolates were found to be susceptible to Vancomycin. It is concluded that MRSA is a serious nosocomial pathogen in surgical site infections and requires strict intervention for its prevention and control

Key Words: Methicillin Resistance, Nosocomial Pathogen, *S. aureus* , Surgical Site

Introduction

Despite almost universal practice of using potent anti-staphylococcal drugs for peri-operative prophylaxis in patients undergoing clean surgery, *Staphylococcus aureus* remains the most common cause of surgical wound infections[1]. A significant number of these strains are Methicillin- resistant *Staphylococcus*

aureus (MRSA) with the result that over the years, MRSA has established itself as a major nosocomial pathogen world wide[2]. According to a report from National Nosocomial Infection Surveillance (NNIS) unit of Centres for Disease Control (CDC), Methicillin resistance among *S.aureus* in U. S hospitals increased from 2.4% in 1975 to 29% in 1991 with a strong propensity for nosocomial spread, particularly in critical care units. The data from NNIS reveals MRSA accounts for upto 40% of nosocomial *S. aureus* infections in large tertiary care hospitals and 25-30% in smaller hospitals. The prevalence varies considerably from one region to another and among hospitals in the same city[3]. Emergence of MRSA, particularly as a nosocomial pathogen has been attributed to a multifactorial etiology including host factors, infection control practices and antibiotic policies of the hospital[4, 5].

The treatment of infections due to *S. aureus* was revolutionized by the introduction of Penicillin in 1942. However it did not take long for penicillin resistance to emerge and by 1950, 80% of hospital acquired staphylococcal infections were untreatable by Penicillin because of the production of enzyme beta-lactamase by the organisms which destroys penicillin[6, 7]. Almost 100% of hospital strains of *S. aureus* are presently resistant to Penicillin. Soon enough, newer penicillin derivatives including Methicillin, Flucloxacillin and Oxacillin were introduced which were resistant to staphylococcal beta-lactamase. These beta-lactamase-resistant Penicillins remained the drugs of choice for treating staphylococcal infections until the late 20th century, when the organisms developed newer mechanisms for evading the anti bacterial activity of these Penicillins, namely the altered Penicillin Binding Proteins (PBP).

The most common infections caused by MRSA include surgical site infections, bacteraemia, lower respiratory tract infections, urinary tract infections and skin infections. The present study attempts to find out the magnitude of the problem as regards the prevalence of MRSA in surgical wound infections in our setup, to define the anti-microbial susceptibility pattern of the isolates and to suggest appropriate intervention measures for their prevention and control.

Patients and Methods

Pus / wound swabs were collected from surgical sites of all those patients which showed clinical evidence of post-operative wound infection.

Specimens were collected using standard collection techniques[8]. Each specimen was inoculated on blood agar and MacConkey agar plates prepared from commercially available dehydrated media (Oxoid, UK). Inoculated plates were incubated aerobically for 24 - 48 hours at 35°C and then examined for growth. Isolates suspected to be *stapylococcoci* were identified by their standard identification features including colonial morphology, Gram stain, catalase production, coagulase test (slide as well as tube) and DNAse production[8].

Anti-microbial susceptibility test was performed according to modified Kirby-Bauer disc diffusion technique on Mueller-Hinton agar (Oxoid, UK) using commercially available anti microbial discs and interpreted according to CLSI (NCCLS) standards[9].

In order to detect resistance to Methicillin for identification of MRSA, Oxacillin 1ug disc (Oxoid, UK) was applied on Mueller-Hinton agar plates which had been inoculated with a standard inoculum of the isolate and incubated at 35°C for full 24 hours. The isolates were considered as Methicillin-resistant if the zone of inhibition was = or < 10 mm[9].

Staphylococcus aureus ATCC 29213 of known susceptibility was included as control strain for comparison.

Results were compiled and analysed using Chi square test of significance.

Results

During the study period, a total of 1310 specimens of pus / wound swabs collected from patient's operation wounds in the post-operative period yielded pathogenic organisms on culture

Table 1: Frequency of Different Organisms Isolated from Pus Specimens (n=1310)

Staphylococcus aureus		Gram Negative Rods	Fungus	Total
MRSA	**MSSA**			
105 (39%)	168 (61%)			
273 (20 %)		1024 (79 %)	13 (1%)	1310

(Table 1). Of these, 273 (20%) isolates were identified as *Staphylococcus aureus*. Susceptibility patterns further revealed that 105 (39%)of these isolates were strains of Methicillin Resistant *Staphylococcus aureus* (MRSA) as shown by their resistance to Oxacillin, while 168 (61%) were strains of Methicillin Susceptible *Staphylococcus aureus* (MSSA).

Table 2: Distribution and Relative Prevalence of MRSA in Surgical Wards and Surgical Intensive Care Unit. (n = 273)

Organisms	SICU (n = 48)	Surgical Ward (n = 225)	Total n = 273)
MSSA	17 (35%)	151 (65%)	168 (61%)
MRSA	31 (65%)	74 (35%)	105(39%)
TOTAL	48 (17%)	225 (83%)	273

Table 3: Anti-microbial Susceptibility of MRSA (n = 105)

Antibiotics	% Susceptibility	% Resistance
Fusidic acid	80%	20%
Doxycycline	40%	60%
Erythromycin	20%	80%
Gentamicin	0%	100%
Co-trimoxazole	12%	88%
Tetracycline	30%	70%
Lincomycin	50%	50%
Enoxacin	50%	50%
Ofloxacin	30%	70%
Ciprofloxacin	0%	100%
Vancomycin	100%	0%
Teicoplanin	100%	0%
Chloramphenicol	70%	30%

A review of comparative prevalence and distribution of MRSA strains between surgical wards and surgical ICU revealed that a much higher percentage of *Staphylococcus aureus* isolates from surgical ICU was MRSA – 31 out of 48 (65%) than those isolated from all the other surgical wards – 74 out of 225 (35%) ($p = < 0.5$). Results are shown in Table 2.

Susceptibility of MRSA strains to various anti-microbial agents is shown in Table 3 Vancomycin and Teicoplanin were found to be the most effective drugs as 100% of MRSA isolates were found to be susceptible to them. Susceptibility to other drugs shows wide variation, with 80% strains susceptible to Fusidic acid, followed by Chloramphenicol (70%) and Lincomycin (50%). On the other hand, 100% of the isolates were resistant to Ciprofloxacin and Gentamicin.

Discussion

MRSA strains were first described in England in 1960[10]. Within a short span of time, the organism was able to establish itself as a major nosocomial pathogen with a strong tendency to become endemic particularly in critical care units of large tertiary care hospitals where, once established, these strains became singularly difficult to eradicate. This is amply borne out by the findings of our study, wherein 65% of *S. aureus* isolates from surgical ICU patients were MRSA as compared to only 35% from surgical wards patients. Its prevalence varies considerably from one region to another and even among the hospitals in the same city.

In Denmark prevalence of MRSA peaked at 18% at the end of 1960 and then gradually decreased reaching 2 % in 1999. This was the result of various interventions including increasing awareness of hospital hygiene and an intensive campaign to teach physicians the principles of prudent antimicrobial drug use.[11]

Proximity to an infected or colonised patient increases the rate of acquisition of MRSA; the same is true of MRSA-colonised health care workers. Once strains of MRSA become established as endemic nosocomial pathogens they are difficult to eradicate.

Prevention and control of MRSA infections in hospitals continue to depend upon conventional strategies including stringent surveillance, strict adherence to aseptic practices, judicious antibiotic and disinfectant policies, isolation of infected patients and exclusion of colonized health care staff from the unit but, above all, adherence to a strict regime of hand hygiene practices. Thorough hand washing between attending patients is indisputably the single most important measure for prevention of nosocomial transmission of MRSA in hospitals.

Mechanism of resistance in MRSA has been found to be the production of a unique, low affinity Penicillin Binding Protien, PBP2a. Molecular studies have shown that PBP2a is the product of *mec*A gene which is carried by MRSA strains[9]. Strains possessing this gene (and its product PBP2a) are resistant to all the currently available beta-lactam antibiotics including penicillins, beta-lactam/beta-lactamase inhibitor combinations, cephalosporins and carbapenems (imipenem).

In view of the fact that these infections are often life-threatening, prompt and accurate detection of MRSA strains in a hospital setting is critical. It has been found that routine oxacillin disc diffusion tests fail to detect heterogeneous MRSA population. Recent studies have shown that Cefoxitin 30 microgram disc diffusion test precludes this possibility and the results are comparable to Oxacillin disc diffusion method for routine screening to detect MRSA[9, 12].

The percentage prevalence of our study (39%) compares favourably well with other studies done within the country namely Hafeez 33 %[13] and Bukhari 32 %[14]. While it is comparable to some other countries like Turkey 37.5%[15], the prevalence in some Far Eastern countries like Japan is inexplicably higher - 60%[16].

In our study vancomycin and teicoplenin were the only antibiotics to which the isolates showed 100% susceptibility, which is comparable to other studies[13, 14]. In practice Vancomycin is routinely used as the drug of choice in serious life threatening infections caused by multi-drug resistant MRSA. However recent reports of intermediate resistance to this drug necessities careful monitoring of prevalence of MRSA and its antibiotic susceptibility pattern[17].

Fusidic acid with 80% susceptibility can be considered as a good second alternative which is comparable to the study done by Hafeez[13]. Ciprofloxacin is one of the most widely used antibiotics particularly in Pakistan. Ominously all our isolates were resistant to it as also were those reported earlier by Qureshi et al[18]. No isolate was susceptible to Gentamicin either. Other antimicrobials yielded widely different results. Lincomycin and Enoxabid showed 50% susceptibility and Co-trimoxazole only 12%.

Conclusions

This report highlights the prevalence of MRSA as a major cause of post-operative wound infections in a tertiary care hospital and broadly substantiates other similar findings reported from within the country as well as from abroad. Study also emphasizes the nosocomial nature of MRSA infections with their propensity to become endemic particularly in the surgical ICU, where the prevalence was found to be much higher. Antimicrobial susceptibility patterns of MRSA isolates showed 100% susceptibility to Vancomycin and Teicoplanin. The former therefore continues to be the drug of choice for serious life-threatening infections.

MRSA infections are generally multi-drug resistant and their therapy entails a huge financial drain on hospital resources. Good infection control practices with emphasis on strict hand washing can minimise this burden by reducing their transmission. Identification of MRSA carriers and their treatment along with other measures can reduce it further. Prudent use of antimicrobial agents is one of major steps to reduce growing problem of antibiotic resistance.

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