*Original Article*

# THE CURRENT SUSCEPTIBILITY PATTERNS OF METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* TO CONVENTIONAL ANTI STAPHYLOCOCCUS ANTIMICROBIALS AT RAWALPINDI

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**ABSTRACT**

***Objective:*** To evaluate current susceptibility of MRSA to commonly used anti-staphylococcus antimicrobials at Rawalpindi.

***Design***: An observational study.

***Place and duration of study***: Pathology Laboratories, Army Medical College, Rawalpindi during the period January 2001 to January 2004.

***Material and Methods***: One hundred eighty five consecutive, non-duplicate strains of Methicillin resistant *Staphylococcus aureus* (MRSA) isolated from different clinical samples were identified by standard microbiological methodology between January 2001 and January 2004. They were studied for their susceptibility to co-trimoxazole, erythromycin, tetracycline, gentamicin, chloramphenicol, ciprofloxacin, and vancomycin by disc diffusion technique using modified Kirby-Bauer method.

***Results***: All the MRSA were sensitive to vancomycin. Approximately 38.3% strains revealed resistance to chloramphenicol, 77.2% to co-trimoxazole, 89.7% to erythromycin, 88.6% to tetracycline, 97.8% to gentamicin and 98.9% to ciprofloxacin.

***Conclusion***: Most of the MRSA were multidrug resistant. These strains revealed higher degree of resistance (>75%) to routine anti-staphylococcus antimicrobials in comparison to the previous study of 1985-87. The p-values have been highly significant in case of erythromycin, tetracycline, gentamicin, fluroquinolone and vancomycin. The p-values in case of chloramphenicol has not been significant. Vancomycin is yet a life saving anti-staphylococcus antimicrobial in MRSA infections in Rawalpindi.

**KEY WORDS**: Methicillin resistant *Staphylococcus aureus,* susceptibility patterns, antimicrobials

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## INTRODUCTION

Methicillin resistant *Staphylococcus aureus* (MRSA) is one of the most common cause of nosocomial infections.[1] Methicillin, a semi synthetic penicillinase resistant penicillin was introduced in 1960 for the treatment of penicillinase producing strains of *S. aureus.*[2] Within a year's time resistance to methicillin was detected in the United Kingdom and reported from USA and Italy.[3] MRSA are usually penicillinase producers and frequently multi drug resistant, thus a therapeutic problem in nosocomial and community acquired infections. The expression of methicillin resistance is

often heterogeneous. The percentage of a bacterial population that express the resistance phenotype varies according to the environmental conditions.[4] The first study regarding antimicrobial susceptibility of MRSA was conducted in Rawalpindi more than a decade ago in 1985-87. The introduction of quinolones and other newer anti staphylococcus drugs and rapid developments in therapeutic modalities necessitates the study of the current status of susceptibility patterns of MRSA. This study was planned to evaluate the current susceptibility patterns and to record any change of MRSA response to commonly used anti staphylococcus antimicrobials at Rawalpindi.

## MATERIAL AND METHODS

A total of 185 consecutive non-duplicate clinical isolates of MRSA, isolated from different clinical samples during January 2001 to January 2004 in the Pathology Department of the Army Medical College, Rawalpindi were studied. The isolates were identified on morphological, cultural and biochemical characteristics along with slide / tube coagulase test and D-Nase production test using standard methods as recommended by Duguid.[5] The isolates conferring to be *Staphylococcus aureus* were subjected to the susceptibility test by employing modified Kirby-Bauer disc diffusion method. The isolates were inoculated on Mueller Hinton Agar containing 5% Na Cl and incubated at 35 C for 24 hours. One µg oxacillin disc (Mast Diagnostics Mast Group Ltd., Merseyside, U.K) was used to assess the susceptibility of the isolates to methicillin. The isolates were taken as methicillin resistant if the zone of inhibition was < 10mm.[6] These MRSA were tested for their susceptibility on the day of their isolation to Co-trimoxazole (25µg), Erythromycin (15µg), Tetracycline (30ug), Gentamicin (10µg), Chloramphenicol (30µg), Ciprofloxacin (5µg) and Vancomycin (30µg) by disc diffusion technique on Mueller Hinton agar using the criteria of standard zone sizes of inhibition to define sensitivity or resistance to different antimicrobials. *Staphylococcus aureus* NCTC 6571 of known susceptibility was included as control strain. The data was recorded and finally evaluated at the completion of the study as per recommendations of the NCCLS.[7]

## RESULTS

The distribution of clinical samples and number of MRSA isolated from these samples is presented in Table-I. It shows comparative distribution in different clinical samples. Maximum number of MRSA were isolated from pus. The susceptibility patterns of the isolates is presented in Table-II. All the MRSA were sensitive to vancomycin, 38.3% strains revealed resistance to chloramphenicol, 77.2% to co-trimoxazole, 89.7% to erythromycin, 88.6% to tetracycline, 97.8% to gentamicin, and 98.9% to ciprofloxacin. Most of the MRSA were multi drug resistant. The comparison of the previous study in 1985-87 and the current is

Table–I: Distribution of MRSA (n=185) in different clinical samples (Jan 2001-Jan 2004)

| *Clinical Material* | *MRSA Isolated* |
|---|---|
| Pus/Pus Swab | 154 |
| Miscellaneous | 28 |
| Blood | 2 |
| HVS | 1 |
| Gross Total | 185 |

Table-II: Susceptibility patterns of MRSA (n=185) to the antimicrobials (Jan 2001-Jan 2004)

| *Antimicrobials* | *Sensitive* | *Resistant* |
|---|---|---|
| Chloramphenicol | 114 | 71 |
| Cotrimoxazole | 42 | 143 |
| Erythromycin | 19 | 166 |
| Tetracycline | 21 | 164 |
| Gentamicin | 4 | 181 |
| Ciprofloxacin | 2 | 183 |
| Vancomycin | 185 | 00 |

presented in Table-III. The p-values were highly significant in case of erythromycin ,tetracycline, gentamicin, ciprofloxacin and vancomycin. The p-value in case of chloramphenicol was not significant.

Table-III: Comparison of current susceptibility pattern of MRSA with previous study at Rawalpindi

| *Antimicrobials* | *Current Study 2001-2004 % Resistance (n=185)* | *Previous Study 1985-1987 % Resistance (n=66)* | *p-Values* |
|---|---|---|---|
| Chloramphenicol | 38.3 | 30 | p < 0. 30 |
| Erythromycin | 89.7 | 57 | p < 0. 0001 |
| Tetracycline | 88.6 | 26.5 | p < 0. 0001 |
| Gentamicin | 97.8 | 24 | p < 0. 0001 |
| Ciprofloxacin | 98.9 | 0 | p < 0. 0001 |
| Vancomycin | 0 | 22.8 | p < 0. 001 |

## DISCUSSION

ß-lactamase resistant penicillins turned out to be the solution to the problems of ß-lactamase susceptible penicillin resistance in staphylococci in 1960s.[4] However within a year the organism started expressing resistance to methicillin and ß-lactamase resistant penicillins. More than 90% of the staphylococci in our clinical practice have acquired resistance to penicillinase susceptible penicillins[8]. The situation has changed with the passage of time and a significant population of staphylococci have developed resistance to ß-lactamase resistant penicillins like methicillin.

The problem of MRSA has been studied at global level adequately. MRSA are usually multi drug resistant in addition to their resistance to cephalosporins and penicillinase resistant penicillins.[4,9] The susceptibility patterns of MRSA were studied more than a decade ago in1985-87 in Rawalpindi. This necessitates to review the current situation in our settings to formulate guidelines for appropriate antimicrobial treatment for this important nosocomial / community acquired infection.

All the MRSA in the present study were susceptible to vancomycin. Similar results have been reported by Sousa et al from Latin America in 2001,[9] Dahar et al from Karachi in 1994,[10] Cheong et al from Malaysia in 1994,[11] and Dai & Ziang from China in 1992.[12] A recent study published in 2004 from Lahore revealed 96% MRSA susceptible to Vancomycin.[13] The study in 1985-87 at Rawalpindi revealed 22.8% MRSA resistant to vancomycin. This current situation is a blessing for the management of MRSA infection at Rawalpindi.

The MRSA revealed 38.3% strains resistant to chloramphenicol which is 8% higher in comparison to earlier study (30%) in Rawalpindi, but it is less (68%) than the study reported from Karachi.[10]

In case of erythromycin the resistance percentage (89.7%) was significantly higher (57%) than earlier study in Rawalpindi.[8] The current resistance rate at Rawalpindi is also higher than the study (75%) from Karachi.[10]

Ninety seven point eight percent (97.8%) isolates in current study were resistant to gentamicin in contrast to 24% in earlier study at Rawalpindi. It reflects higher degree of resistance than the study of Dahar et al (80%) from Karachi[10] and Zaman & Dibb from Saudi Arabia reporting 83% of MRSA resistant to gentamicin.[14] This gross increase in gentamicin resistance might be due to misuse of gentamicin in our clinical practices.

A longitudinal nation wide study in France in 1992-98 comprising 57,347 *Staphylococcus aureus*[15] have revealed steady decrease in resistance to gentamicin in contrast to our settings.

MRSA presented significantly higher resistance (88.6%) to tetracycline in our study as well as in the study of Zaman & Dibb from Saudi Arabia[13] in comparison to the study of 1985-87 at Rawalpindi revealing 26.5% strains resistant. Seventy seven point two percent MRSA were resistant to co-trimoxazole in current study which is much less than the study of Pulimood et al from India depicting more than 97% resistance.[16] All the MRSA in the study of Tripodi from Italy were reported to be susceptible to co-trimoxazole.[17]

The isolates revealed significantly higher percentage (98.9%) of MRSA resistant to

ciprofloxacin in our current study. Similar results of over 90% resistance has been reported by Pulimood et al. from India[16] contrary to the earlier study at Rawalpindi revealing all the MRSA strains sensitive to fluroquinlone, ofloxacin.

## CONCLUSION

In conclusion MRSA are generally multi drug resistant. There is an over all trend of increased resistance to conventional anti staphylococcus antimicrobials in comparison to 1985-87 at Rawalpindi. MRSA are currently more serious therapeutic problem at Rawalpindi than 1985-87. More than seventy five percent of MRSA are resistant to commonly used anti staphylococcus antimicrobials and more than 95% to gentamicin and ciprofloxacin. This situation may be due to continued injudicious use of antimicrobials including fluroquinolones.

This practice should be stopped forthwith and specific therapy in the light of susceptibility test should be rather mandatory in hospital and community acquired MRSA infections to avoid therapeutic failures. Such studies are recommended at different centers to formualte a policy to control MRSA infections.

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