# EFFICACY OF CEFTAROLINE AGAINST METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS*: A CROSS-SECTIONAL STUDY

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## ABSTRACT

**Objective:** To evaluate *in vitro* efficacy of Ceftaroline against Methicillin resistant *Staphylococcus aureus* (MRSA) isolated in our setup.

**Material and Methods:** This descriptive cross-sectional study was carried out at Department of Microbiology, Fauji Foundation Hospital, Rawalpindi from November 2018 to April 2019. Clinical samples from respiratory tract, blood, pus, urine and various catheter tips were inoculated on Blood, MacConkey's agar and Incubated at 37°C for 18 to 24h. *Staphylococcus aureus* was identified by standard microbiological procedures. Methicillin resistance of isolated Staphylococci was detected by agar disk diffusion method (Kirby-Bauer) according to CLSI guideline. The Minimum Inhibitory Concentrations (MICs) were determined for ceftaroline and vancomycin by using the Epsilon-test (E-test) method. *S.aureus* ATCC29213 was used as control strain for MIC detection.

**Results:** Total of 55 samples were included according to the inclusion criteria of the study. Frequencies and percentages of sensitive, intermediate and resistant organisms according to MIC of ceftaroline against MRSA isolates were 52(94.5%), 3(5.4%) and 0 respectively. MIC when calculated according to CLSI guidelines, $MIC_{50}$ and $MIC_{90}$ for ceftaroline against MRSA isolates was 0.75 and 1µg/ml respectively.

**Conclusion:** We can safely conclude that *in vitro* ceftaroline is more effective than vancomycin against MRSA.

**Key Words:** Ceftaroline, Methicillin-resistant *Staphylococcus aureus,* Minimum inhibitory concentration.

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## INTRODUCTION

*Staphylococcus aureus* is a major human pathogen that causes serious hospital and community acquired infections. Many types of enzymes and toxins contribute to its pathogenicity [1]. The new threat is MRSA (Methicillin-resistant *S. aureus*) [2]. MRSA is resistant to all beta-lactam drugs. The major element of resistance is *SCCmec,* which contains the *mecA gene.* It encodes PBP-2a which provides resistance against all beta-lactam drugs [3-5]. MRSA can be identified using various antimicrobial susceptibility tests like Disk diffusion method and E-test method recommended by Clinical and Laboratory Standards Institute (CLSI) [6].

Vancomycin is the drug of choice against MRSA but now resistance is developing against it as well especially after the emergence of Vancomycin resistant Enterococci (VRE) and also due to the antibiotic pressure on Vancomycin. Now high level of resistance is reported against Vancomycin and this has made the treatment of MRSA a therapeutic dilemma [7,8].

Ceftaroline, a new beta-lactam drug is effective against MRSA as it can bind PBP-2a along with other PBPs. It is currently the only beta-lactam drug approved by FDA for treatment of infections caused by MRSA and found to be 100% sensitive to Ceftaroline. This drug can be very useful for combating MRSA in future [9-12]. The prevalence of MRSA in India and Pakistan is more than Northern Europe [13]. It is the need of hour to carry out studies to encounter the emerging challenge of successfully treating multi drug-resistant MRSA. The purpose of this research is to determine the susceptibility of Ceftaroline against MRSA isolates.

## MATERIAL AND METHODS

The study was carried out at Microbiology department, Fauji Foundation Hospital (FFH) Rawalpindi, from November 2018 to April 2019. This was a descriptive cross-sectional study. Sampling technique was Consecutive non-probability. All samples yielding growth of MRSA from admitted and outdoor patients of either sex and of represented age of population were included in the study. All duplicate samples during the same episode of illness and all patients already on antibiotics within last 48 hours were excluded. A total of 55 clinical samples isolated from respiratory tract, blood, pus, urine and catheter tips were inoculated on culture media such as Blood and MacConkey's agar. Incubated at temperature of 37°C for 18-24 hrs. *Staphylococcus aureus* was identified by its special features like colony

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morphology, gram staining and positive catalase and coagulase test. Methicillin resistance of *Staphylococci* was confirmed by agar disk diffusion method using a 30 microgram cefoxitin disc in accordance with the guidelines established by CLSI [14]. Minimum inhibitory concentration was determined by E test method. *Staphylococcus aureus* strain ATCC 29213 was used as control for MIC detection.

Data were collected on specifically designed proforma and then analyzed by SPSS version 22.0. Frequencies and percentages were calculated for qualitative variables like gender, frequency and percentage of MRSA isolates against Ceftaroline. In vitro susceptibility of this antibiotic was calculated as frequency and percentage of sensitive and resistant microorganisms according to minimum inhibitory concentration of Ceftaroline against MRSA isolates. Mean and standard deviation was calculated for quantitative variables such as age, Minimum inhibitory concentrations, $MIC_{50}$ and $MIC_{90}$ were calculated. Effect modifiers like samples from different wards, age and gender was controlled by post stratification using chi-square test. P value of <0.05 was taken as significant. All ethical considerations and obligations were duly addressed and the study was conducted after approval of ethical committee of institute.

## RESULTS

Total 55 cases were included in accordance with the inclusion criteria of the study. Mean age (years) in the study was 45.38±16.98 with ranges from 6 to 75 years, as shown in (Table-I). There were 22 (40.0%) male and 33 (60.0%) female patients.

**Table-I: Descriptive statistics of Age (years) of patients.**

| | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Age (years) | 55 | 6 | 75 | 45.38 | 16.98 |

Out of 55 patients, sensitive, susceptible dose dependent (SDD) and resistant organisms according to MIC of Ceftaroline against MRSA isolates were 52(94.5%), 3(5.4%) and 0 respectively (Table-II)

**Table-II: Frequency & percentage of sensitive, SDD/ intermediate and resistant of ceftaroline & vancomycin for MRSA.**

| | Ceftaroline | Vancomycin |
|---|---|---|
| Sensitive | 52 (94.5) | 50 (90.9) |
| SDD/intermediate | 3 (5.4) | 3 (5.5) |
| Resistant | 0 (0) | 2 (3.6) |
| **Total** | **55 (100.0)** | **55 (100.0)** |

Effect modifier like age and gender stratification were compared with the frequency & percentage of *in vitro* susceptibility of Ceftaroline for MRSA and found to be insignificant.

Effect modifier like type of wards stratification and compared with the frequency & percentage of *in vitro* susceptibility of Ceftaroline for MRSA. In Surgery and Urology ward, frequency and percentage of in vitro susceptibility of Ceftaroline for MRSA was 11(21.6%) and 18(35.3%) respectively, as shown in (Table-III). When calculated according to CLSI guidelines, $MIC_{50}$ and $MIC_{90}$ for Ceftaroline against MRSA isolates was 0.75 to 1 microgram/ml respectively.

**Table-III: Effect modifier like type of wards with frequency & percentage of *In-vitro* susceptibility of Ceftaroline for MRSA**

| | | In-vitro efficacy of Ceftaroline for MRSA | | Total | p-value |
|---|---|---|---|---|---|
| | | Yes | No | | |
| Type of ward | ENT | 5<br>9.8% | 0<br>0.0% | 5<br>9.1% | 0.739 |
| | Gyane | 5<br>9.8% | 0<br>0.0% | 6<br>10.9% | |
| | Medical ICU | 7<br>13.7% | 1<br>100.0% | 8<br>14.5% | |
| | Neurology | 3<br>5.9% | 0<br>0.0% | 3<br>5.5% | |
| | Oncology | 2<br>3.9% | 0<br>0.0% | 2<br>3.6% | |
| | Surgery | 11<br>21.6% | 0<br>0.0% | 12<br>21.8% | |
| | Urology | 18<br>35.3% | 0<br>0.0% | 19<br>34.5% | |
| Total | | 51 | 1 | 55 | |

## DISCUSSION

*Staphylococcus aureus* is a deadly microorganism which can cause serious types of infections in human beings ranging from less severe skin and soft tissue infections to lethal sepsis. The most problematic issue is regarding antibiotic resistance. The current threat is MRSA (Methicillin-resistant *S. aureus*).

In our study we isolated maximum samples of MRSA from Urology ward which includes pus from surgical site infections, urine, various catheter tips in accordance with a study in Nigeria (71.4% MRSA urine samples) [15], 29% samples from pus in contrast to a study in Rawalpindi (67% MRSA pus samples) [16]. MRSA isolates were also obtained from respiratory tract samples, vaginal swabs and blood samples. Most of the MRSA isolates were obtained from females above 40 years in our study as Fauji Foundation Hospital is a hospital made for

the families of retired army officials. The cases were mostly from urology department followed by surgery and medical wards while most of the MRSA isolates in a study in Lahore were from Intensive care unit (ICU) [17]. Prevalence of MRSA is about 42% on average in Pakistan. Frequency of infection by MRSA in Pakistan is (2%-61%) with the highest frequency in big cities [18].

Vancomycin is the first drug of choice against MRSA but clinical failures, adverse effects and high MIC cause frequent problems in treatment with vancomycin [19]. Now Vancomycin resistant and intermediate strains of MRSA are also reported. The new Antibiotics like Telavancin, Tigecycline and Daptomycin have issues like adverse effects, drug interactions and high prices [20]. Newer antibiotics are required to combat MRSA in future. A new class of Cephalosporin, Ceftaroline has high anti-MRSA activity. This drug acts against PBP-2a thus MRSA is sensitive to it [12]. Ceftaroline has four-fold activity against MRSA than Vancomycin [21]. It is safer and more cost effective than Vancomycin [22,23]. The studies done to test efficacy of Ceftaroline showed demographic variation. Some studies showed 100% sensitivity of MRSA to Ceftaroline. A study from USA hospitals from 2008-2011 showed 97.5% sensitivity. In our study there was 95% sensitivity of MRSA to Ceftaroline. A study done on isolates from Europe and USA showed 98% sensitivity.

Prevention against spread of MRSA is of utmost importance right now. Hand washing is the most effective method in preventing MRSA infection. In hospitals active surveillance of cultures, isolation of the patient harboring the infective organism and infection control protocols must be strictly followed. Misuse of antibiotics must be prohibited.

Limitation of study includes the use of E-Strips for MIC testing of vancomycin and inability to send the isolates to reference laboratory for confirming the resistance of vancomycin.

## CONCLUSION

Ceftaroline is much more effective than Vancomycin in combating MRSA. It is safer and cost effective than Vancomycin and newer Antibiotic drugs for use against MRSA.

## RECOMMENDATIONS

The threat that awaits medical science in future is antibiotic resistance thus pressure on antibiotics must be reduced. New and effective antibiotics like Ceftaroline must be used cautiously. Focus must be paid to counsel health care professionals and communities for prevention of diseases.

## AUTHOR CONTRIBUTION

**Irum Aftab:** Study design, executed the study, proof reading, final approval and supervising the study.
**Umme Farwa:** Executed the study, Drafting, data analysis and revising critically, final approval.
**Fatima Kaleem:** Study design, execution of study, Data analysis, revising critically.
**Hamza Riaz**: Data collection, Data analysis, Draft preparation.
**Mehnaz Khattak:** Discussion, Data statistical analysis, Proof reading.

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