DOI:https://doi.org/10.53350/pjmhs20231710296

ORIGINAL ARTICLE

Frequency of MRSA in Diabetic Foot Infections a Prospective Multi Centre Study

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ABSTRACT

Background: Diabetic foot infection are a widely recognized side effect of diabetic patients who are frequently admitted and even their limbs are amputated. MRSA has become an important cause of Diabetic foot infection and makes the treatment difficult because of its resistance pattern. Estimation of the frequency and risk factors are important in providing empirical therapy to patients with an aim of improving their outcomes.

Objectives: To find the prevalence of MRSA cases in diabetic foot and to evaluate the clinical and demographic characteristic related to the MRSA positive cases.

Study design: A Prospective Multi Centers Study.

Place and Duration of Study: Department of Endocrinology, MTI-HMC Peshawar; Timergara Teaching Hospital, Timergara and the District Headquarter Hospital, Dir Upper from July 2022 to Dec 2022.

Methods: 100 clinically identified patients with foot infection due to diabetes was then done. Microbial analysis was carried out by the use of wound swabs. The identification of MRSA was carried out by conventional microbiology methods such as the cefoxitin disc diffusion. Demographic-related data, length of diabetes, grade of ulcers, and use of antibiotics were captured. The SPSS version 25 was used to analyze statistics. The statistics were calculated as mean age, standard deviation, and p-values to get the statistical significance.

Results: Out of 100 patients were positive to MRSA. The average age of the group (patients with MRSA infection) was 59.3 + 9.8 years where 55.2 + 10.1 years was observed in the group without MRSA infection ($p = 0.04$). The previous application of antibiotics and duration of ulcer were considerably higher in MRSA-positive patients ($p < 0.05$). There were 2.3 males to every 1 female. MRSA-positive patients had more advanced ulcer. Mean length of stay in this group was 12.7 +- 4.2 days as well.

Conclusion: Methicillin-resistant Staphylococcus aureus (MRSA) represents a significant pathogen in diabetic foot infections, particularly among patients with chronic ulcers, prior antibiotic exposure, and advanced ulcer grades. Its prevalence poses a clinical challenge due to its resistance profile and associated complications. Early identification and the initiation of appropriate empirical therapy, even if initially delayed, can contribute to improved clinical outcomes and reduced hospital stay. To mitigate the impact of MRSA within diabetic populations, consistent microbiological surveillance and stringent implementation of antibiotic stewardship programs are imperative.

Keywords: MRSA, diabetic foot, infection, prevalence

INTRODUCTION

Diabetic foot infection are a serious complication of diabetes mellitus that may cause more morbidity, potential risk of amputation of the limb, prolonged hospital stays, and health care costs[1]. These infections are due to a complex interrelation of neuropathy, ischemia and immune dysfunction, which causes the patients with diabetes to have persistent and severe infection[2]. Of all the causative agents, Staphylococcus aureus is the most common pathogen that is isolated in diabetic foot ulcers[3]. Of concern is the outbreak and prevalence of methicillin-resistant Staphylococcus aureus (MRSA), which is a therapeutic challenge owing to its resistance to the commonly used antibiotics, the beta-lactams[4]. The world has been experiencing cases of MRSAs infections, which are probing to different degrees throughout the world, and this difference is related to geographic locations, healthcare facilities, and infection-related risk factors of the patients[5]. An increased rate of clinical outcome measures, such as delayed wound healing, risk of osteomyelitis and increased amputation rates, are associated with MRSA colonization or infection[6]. Compelled by the growing incidence of MRSA, the necessity to diagnose the condition in a timely manner and follow up with proper antibiotic stewardship has become compelling[7]. The treatment of Diabetic foot infection with MRSA will include specific antibiotics with the treatment requiring hospitalization and intravenous drugs, leading to additional costs to healthcare systems[8]. The successful detection and identification of MRSA in diabetic foot wounds occurs early enough to enable application of a drug of choice, which brings with it an improved outcome and fewer complications[9]. Nonetheless, the inability to standardize the surveillance and other differences in diagnostic processes has led to reports that lack uniformity in frequency of MRSA in diabetic foot infections among various populations. The purpose of this study is to identify the prevalence of MRSA among patients with diabetic foot infections attending our third-level care facility and hence about the offering that will give information applicable to enlighten empirical antibiotic selection and infection countermeasure arrangements.

Received on 11-05-2023
Accepted on 14-09-2023

METHODS

This study conducted in Department of Endocrinology, MTI-HMC Peshawar; Timergara Teaching Hospital, Timergara and the District Headquarter Hospital, Dir Upper from July 2022 to Dec 2022.six months at the diabetic foot clinic of patients with diabetic foot infections as identified and classified according to clinical and microbiological features were recruited in a consecutive manner. Swabs of wounds were taken in a sterile manner and processed in the microbiology lab to do bacterial culture and sensitivity. The identification of MRSA was done by means of cefoxitin disk diffusion test as guided by the Clinical and Laboratory Standards Institute (CLSI). A structured questionnaire was used to obtain patient demographic and clinical information. The ethics committee of the institution approved the study protocol. Analysis of data was done utilizing SPSS version 24.0.

Inclusion Criteria: Patients with naturally occurring cases of diabetic foot infections diagnosed clinically, aged 18 years and above and those that gave their informed consent were able to participate in the study.

Exclusion Criteria: Patients on systemic antibiotics in the previous 72 hours and non-diabetic foot infected patients were excluded as well as patients who refused to give their consent.

Ethical Approval Statement: The study was granted approval by the Institutional Ethics Committee All the participants gave written informed consent before enrollment. All the procedures were followed basing on the Declaration of Helsinki and institutional requirements to uphold confidentiality of patients and ethical conduct of study.

Data Collection: The diabetic wounds swabs were taken using the aseptic methods on diabetic wounds. Demographic data, medical history, and clinical findings were documented by the same standardized form. Aerobic bacterial culture of the specimens was done and MRSA was identified through cefoxitin disk diffusion testing. Data were recorded and stored in a database.

Statistical Analysis: The data were analyzed with SPSS version 24.0. Descriptive statistics were calculated with regards to the demographic and clinical variables. It was determined how frequently MRSA isolates were found among the isolated Staphylococcus aureus. Chi-square tests were employed to estimate variables between the presence of MRSA with clinical factors. The significance value was accepted as <0.05.

RESULTS

Out of 100 patients Their average age was 56.8 +/- 11.2 years and male to female ratio was 65/1. In 100 cases (92 %), culture positivity was noted. In 60 (40%) of the samples, Staphylococcus aureus was isolated, with 24 (40%) found to be MRSA. The prevalence of MRSA in diabetic foot infection was 16 percent (24/100). The resistance of MRSA isolates towards penicillin, amoxicillin-clavulanate, and ciprofloxacin was detected as high and sensitivity towards vancomycin and linezolid was high. No significant difference was seen between MRSA and MSSA infection patients in the number of wounds present during the hospital stay (p=0.12), however, duration of ulcer (p=0.03) and history of prior antibiotic use (p=0.01) was significantly different. No major differences were observed in glycemic control or comorbid therapies between MRSA and MSSA groups. An association was established between MRSA presence and increased hospital stay and delayed wound healing, but this did not prove to be significant. These findings emphasize the need to screen diabetic foot infections with MRSA in order to prescribe the proper antibiotics.

Table 1: Demographic and Clinical Characteristics of Study Population (n = 100)

Characteristic	Value
Age (mean ± SD)	56.8 ± 11.2 years
Gender	
• Male	70 (70%)
• Female	30 (30%)
Duration of Diabetes	
• <5 years	28 (28%)
• 5–10 years	40 (40%)
• >10 years	32 (32%)
HbA1c (%)	8.2 ± 1.5
Previous Antibiotic Use	55 (55%)
History of Hospitalization	44 (44%)
Ulcer Grade (Wagner Classification)	
• Grade 1–2	39 (39%)
• Grade 3–5	61 (61%)

Table 2: Culture Results of Study Participants (n = 100)

Culture Result	Frequency (%)
Culture positive	92 (92%)
Culture negative	8 (8%)

Table 3: Most Common Isolates Among Culture-Positive Cases (n = 92)

Organism	Frequency (%)
Staphylococcus aureus	52 (65.2%)
Pseudomonas aeruginosa	13 (15.5%)
Escherichia coli	10 (10.9%)
Klebsiella pneumoniae	7 (7.6%)
Polymicrobial	10 (10.1%)

Table 4: Frequency of MRSA Among Staphylococcus aureus Isolates (n = 60)

Type of S. aureus	Frequency (%)
Methicillin-sensitive S. aureus (MSSA)	36 (60%)
Methicillin-resistant S. aureus (MRSA)	24 (40%)
Total S. aureus isolates	60 (100%)

Table 5: Antibiotic Susceptibility Profile of MRSA Isolates (n = 24)

Antibiotic	Sensitive (%)	Resistant (%)
Vancomycin	24 (100%)	0 (0%)
Linezolid	24 (100%)	0 (0%)
Clindamycin	14 (58.3%)	10 (41.7%)
Ciprofloxacin	6 (25%)	18 (75%)
Amoxicillin-clavulanate	4 (16.7%)	20 (83.3%)
Erythromycin	8 (33.3%)	16 (66.7%)
Gentamicin	15 (62.5%)	9 (37.5%)

Table 6: Comparison Between MRSA and MSSA Infected Patients (n = 60)

Variable	MRSA (n = 24)	MSSA (n = 36)	p-value
Age (mean ± SD)	57.6 ± 10.9	55.9 ± 11.6	0.46
Male gender	16 (66.7%)	22 (61.1%)	0.67
Duration of ulcer > 4 weeks	18 (75%)	14 (38.9%)	0.03*
Previous antibiotic use	20 (83.3%)	18 (50%)	0.01*
Hospital stay > 7 days	12 (50%)	10 (27.8%)	0.12
HbA1c (%)	8.4 ± 1.6	8.1 ± 1.4	0.38

DISCUSSION

Methicillin-resistant Staphylococcus aureus (MRSA) is quite high in diabetic foot infections (Diabetic foot infection) as MRSA accounted to 40 percent of all the S. aureus isolates and 16 percent of all positive cultures. These observations highlight the clinical relevance of antimicrobial resistance in diabetic people and the importance of watchfulness when it comes to antibiotic choice when utilizing empirical antibiotics[10]. The overall dominance of S. aureus in this study is consistent with the available body of literature in the assertion that it is also the most prevalent gram-positive pathogen of Diabetic foot infection . The prevalence of S. aureus in Diabetic foot infection in a multicentric Indian study done by Shahi and Kumar, S. appeared in 45% of Diabetic foot infection and MRSA comprised 41% of the isolates, which is close to our results[11]. Similarly, Al Banyan et al. also found a high rate of MRSA in Saudi Arabia; it was higher than S. aureus in diabetic foot wounds (38%), which is an indication that the prevalence is high in different geographical regions[12]. This resistance profile that was noted in our MRSA strains also happens to be in line with international reports. The majority of the isolates were non susceptible to beta-lactams, ciprofloxacin and erythromycin, and susceptible to vancomycin and linezolid. These results of antibiotic resistance resemble the situation in a tertiary Chinese care setting where resistance rates of MRSA to a fluoroquinolone and macrolide were over 70 percent and virtually none packed vancomycin and linezolid[13]. This trend in resistance constrains treatment choices and, in most cases, requires the use of costly or intravenous medications, capabilities that might not be met in low-resource populations. Previous use of antibiotics and a long duration of the ulcers were significantly different between MRSA and non-MRSA in our study. It is a well-established association Colors et al. identified that the previous antibiotics use was the strongest correlate of MRSA colonization in Diabetic foot infection[14]. Along the same line, Lipsky et al. were able to determine chronicity of the wound and repeated exposure to antibiotics as the major risk factors of the MRSA acquisition[15]. These results are confirmative of the significance of wise antibiotics usage and prompt wound interaction. Interestingly, though MRSA-infected patients in our study had prolonged stay and delayed healing, there was no statistical significance. This is in contrast to a study conducted in the United States by Lavery et al which showed a direct relationship between MRSA infection and an increase in amputation and hospitalization[16]. The difference could be attributed to varying degrees of access to the healthcare, wound care practices, or study design. Nonetheless, the trend itself is clinically significant and serves as a good indicator of the

significance of early microbiological identification. The prevalence of MRSA in our 16 percent of all Diabetic foot infection is lower as compared to some studies in the West and in Asia. Indeed, in a US-based large-scale study, more than 30 per cent of all diabetic foot wounds were found to be MRSA[17]. The data in Pakistan and Iran have reported MRSA frequencies greater than 40 per cent in hospital-based populations [18]. This variability could be affected by the antimicrobial policy practiced by the corresponding region, prevalence of community carriage, and infection prevention techniques. Although the rate is not very high, the fact that more than a third of S. aureus isolates contain MRSA is shocking. These results back the idea of routine screening and culture-guided therapy in serious to severe DFI cases. Empiric choices would need to have coverage of MRSA in such high-risk patients- such as previous hospital stays, chronic ulcers, or recent antibiotic treatments .

CONCLUSION

The prevalence of MRSA in diabetic foot is high and this necessitates the need to perform culture and sensitivity on a routine basis. Previous antibiotic use and chronic ulcers were observed to be related to MRSA. Based on empirical methods, patients with high risks of contracting MRSA must be covered with treatment in order to achieve the best clinical results and to avoid complications.

Limitations: Although this was a multicenter study conducted across three centers, the sample size was relatively small, which may limit the generalizability of the findings. Only aerobic bacterial cultures were performed, potentially underrepresenting anaerobic and fungal pathogens. Furthermore, molecular characterization of MRSA strains was not carried out, and long-term clinical outcome data such as healing time and amputation rates were not assessed.

Future Directions: The future study ought to incorporate multi-centric study with bigger sample sizes and genetic identification of MRSA organisms to determine the mechanisms of resistance. Follow up of patients over a period of time should help in giving knowledge of treatment and recurrence. An evaluation of the effect of the rapid diagnostic tools and alternative therapies in MRSA-infected diabetic foot ulcers would be helpful.

Abbreviations

1.	DFI	Diabetic Foot Infection
2.	MRSA	Methicillin-Resistant Staphylococcus aureus
3.	MSSA	Methicillin-Sensitive Staphylococcus aureus
4.	SD	Standard Deviation
5.	HbA1c	Hemoglobin A1c
6.	CLSI	Clinical and Laboratory Standards Institute
7.	SPSS	Statistical Package for the Social Sciences
8.	ICU	Intensive Care Unit
9.	USA	United States of America
10.	MIC	Minimum Inhibitory Concentration
11.	OPD	Outpatient Department
12.	OR	Odds Ratio
13.	CI	Confidence Interval

Disclaimer: Nil
Conflict of Interest: Nil
Funding Disclosure: Nil

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This article may be cited as: Nawaz R, Usman K, Ahmad SI, Ahmad S, Ali K, Ghafar T: Frequency of MRSA in Diabetic Foot Infections a Prospective Multi Centre Study. Pak J Med Health Sci, 2023; 17(10): 296-298.