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Antimicrobial susceptibility pattern of Methicillin-resistant Staphylococcus aureus in a tertiary care Hospital

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ABSTRACT

BACKGROUND & OBJECTIVE: Methicillin-resistant Staphylococcus aureus(MRSA) has become a major therapeutic issue worldwide. The current study is designed to evaluate the antimicrobial; susceptibility pattern of MRSA strains.
METHODOLOGY: This study was done in the Microbiology laboratory of Dr. Akbar Niazi Teaching Hospital, Islamabad, after ethical approval. It was a descriptive retrospective cross-sectional study in which 155 culture reports that revealed growth of Staphylococcus aureus were included from May 2021 to December 2021. The known identified strain of MRSA was used for quality control. The susceptibility pattern of MRSA strains was seen against various antibiotics. The data entry was done using SPSS version 25, and data analysis was done using frequency and percentage.
RESULTS: A total of 155(11.07%) isolates of Staphylococcus aureus were obtained from 1400 culture samples. Out of these,90(58.1%) isolates were MRSA. The association was significant between MRSA and the age group of patients (p= 0.053). All the MRSA strains were sensitive to linezolid and vancomycin. The majority of the strains were sensitive to minocycline (71.1%), gentamycin (70%), and clindamycin (68.9). Only 20% of isolates were sensitive to trimethoprim/ sulfamethoxazole, 25.6% to ciprofloxacin, 31.1% to levofloxacin, and 24.4% to erythromycin. MRSA strains were sensitive to nitrofurantoin (in urine only).
CONCLUSION: The frequency of Staphylococcus aureus was 11.07%, and out of these, there was a high frequency of MRSA (58.1%) in our setup. All the MRSA strains were sensitive to linezolid and vancomycin (100%). Seventy-one percent of isolates were sensitive to minocycline, 70% to gentamicin, and 68.9% to clindamycin. Only a few isolates were sensitive to macrolides (24.4%), trimethoprim-sulfamethoxazole (20%), and fluoroquinolones (25.6% to 31.1).
KEYWORDS: Methicillin-resistance, Staphylococcus aureus, Methicillin-resistant Staphylococcus aureus, Sensitivity.

INTRODUCTION

Methicillin-resistant Staphylococcus aureus (MRSA) has become a major therapeutic issue worldwide. The prevalence of MRSA infections has reached epidemic levels worldwide, leading to fewer treatment options [1]. MRSA infections are associated with increased mortality & morbidity, prolonged stay in the hospital, and financial burden [2]. It is one of the most common pathogens in the United States, causing an estimated 80,000 infections and 19,000 deaths annually [3]. Not only in the United States, MRSA infections are also common in other countries, but their prevalence is different from one country to another. The frequency of MRSA is high in Pakistan [4]. The methicillin resistance in Staphylococcus aureus ranges from 42% to 51% in Pakistan. Methicillin-resistant Staphylococcus aureus is resistant to several antibiotics, such as penicillins, cephalosporins, and carbapenems, with only a few treatment options left to treat these strains[5]. With the overall rise in the frequency of MRSA, the use of vancomycin, linezolid, and teicoplanin has also increased [6].

Staphylococcus aureus is present as a colonizer on the skin and nose in 30% of individuals [7]. The major source of transmission of MRSA is hospitals. MRSA is responsible

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for 25-50% of nosocomial infections[8]. Long-term hospitalization, immunosuppression, excessive antibiotic use, indwelling catheterization, invasive medical equipment, drug abuse, and inadequate infection control measures contribute to MRSA transmission [9]. Methicillin-resistant Staphylococcus aureus causes skin & soft tissue infections, arthritis, osteomyelitis, pneumonia, meningitis, brain abscess, endocarditis, urinary tract infection, and septicemia. It also causes toxin-mediated diseases like food poisoning, toxic shock syndrome, and scalded skin syndrome [10].

The emergence of antibiotic resistance on a global scale has threatened the golden era of antibiotic therapy. This leads to the failure of successful empirical therapy. In addition, the number of antimicrobials that are in development is limited. MRSA strains are resistant to all penicillins, cephalosporins, and carbapenems. In addition, these stains are mostly resistant to other groups of antibiotics, such as macrolides, fluoroquinolones, aminoglycosides, and tetracycline loading, to the risk of pan-drug resistance.

The current study is designed for the evaluation of the antimicrobial susceptibility pattern of MRSA strains isolated from various clinical samples. The study will provide information about the antimicrobial susceptibility pattern of MRSA strains in a tertiary care hospital in Pakistan.

METHODOLOGY

The study was approved by the Institutional review board (IRB letter No. 53/IMDC/IRB-2021). Written informed consent was taken from all the patients whose samples were used in the study. It was a descriptive retrospective cross-sectional study done in the Microbiology laboratory of Dr. Akbar Niazi Teaching Hospital (ANTH) in Islamabad from May 2021 to December 2021. A total of 155 culture reports that revealed growth of Staphylococcus aureus out of 1400 culture samples were included in the study by nonprobability convenient sampling technique. The patient's age, gender, site of clinical samples, and department were noted on a proforma. The clinical samples included high vaginal swabs (HVS), blood, urine, central venous pressure (CVP) tips, cerebrospinal fluid (CSF), pus/wound swabs, tissue specimens, throat swabs, and sputum.

All the specimens were inoculated on Blood, Chocolate and MacConkey agar except urine. Urine samples were inoculated on Cysteine-lactose-electrolyte deficient medium (CLED). Staphylococcus was identified by colony morphology, gram staining, and catalase test. Coagulase-positive strains were labelled as Staphylococcus aureus, and a cefoxitin disk was used to detect methicillin susceptibility. Antibiotic susceptibility testing (AST) was performed by the modified Kirby-Bauer disk diffusion method. The suspension of the isolates was prepared by inoculating 3-5 isolated colonies from the blood agar plate into normal saline with the help of a sterile wire loop. The turbidity of each suspension was then matched to the 0.5 McFarland turbidity standard and then inoculated on the Muller-Hinton plates using a sterile cotton swab. The antibiotic discs were applied, and the plates were placed in the incubator at 35°C for 24 hours. The zones of inhibition were measured against tested antibiotics in millimetres (mm) and reported according to the Clinical and Laboratory Standards Institute (CLSI) guidelines [11]. The strains which were resistant to cefoxitin were labeled as MRSA, whereas the isolates which were cefoxitin sensitive were methicillin-sensitive (MSSA). The following antibiotics were tested and reported for MRSA strains: linezolid, vancomycin, clindamycin, gentamycin, trimethoprim/ sulfamethoxazole ciprofloxacin, levofloxacin, minocycline, erythromycin, and nitrofurantoin (for urine culture only).

The data entry and analysis were done using the Statistical Package for the Social Sciences (SPSS) version 25. Quantitative variables such as age were expressed as mean and ±SD. Qualitative variables such as gender, the frequency of MRSA, and its antimicrobial susceptibility pattern were expressed using frequency and percentage. A chi-square test was applied to determine the association between MRSA and various variables such as age, gender, department, and clinical samples. The significant p-value was considered as ≤0.05.

RESULTS

A total of 155(11.07%) isolates of Staphylococcus aureus were obtained from 1400 culture samples. Out of these, there were 90(58.1%) MRSA and 65(41.9%) MSSA isolates. The majority of the samples were received from the age group 41-50 years 38(24.5%) followed by the age group <20 29(18.7%) and 21-30 years 29(18.7%). Out of a total of 155 isolates of Staphylococcus aureus, 94(60.6%) were obtained from males, and 61(39.4%) were from females. Among 155 clinical specimens, 120(77.4%) were pus samples, followed by 10(6.5%) blood samples. There were 9(5.8%) CVP tips, 5(3.2%) sputum, 4(2.6%) throat swab, 3(1.9%) urine, 2(1.3%) high vaginal swab (HVS) and 2(1.3%) ear swabs. The majority of the samples were received from the Outdoor department 71(45.8%) followed by the Surgery 38(24.5%) and the Medicine department 30(19.4%). There was no statistically significant association of MRSA with the patient gender (p=0.233), clinical samples (p=0.667), and clinical department (p=0.752). However, the association was significant between MRSA and the age group of patients (p= 0.053). These results are shown in table-I.

All the MRSA strains were sensitive to linezolid and vancomycin (100%). The MRSA strains showed varying degrees of sensitivity to other antimicrobials, such as minocycline 64(71.1%), gentamycin 63(70%), and clindamycin 62(68.9%). The strains showed a relatively lower degree of sensitivity to other antimicrobials: trimethoprim/ sulfamethoxazole 18(20%), ciprofloxacin 23(25.6%), levofloxacin 28(31.1%) and erythromycin 22(24.4%). There were only 2(2.22%) MRSA strains isolated from urine samples, they were sensitive to nitrofurantoin. The sensitivity and resistance pattern of different antibiotics are shown in table-II.

Table-I: Distribution of MRSA and MSSA according to Demographic Profile.

Variables	Groups	Staphylococcus Aureus		Total	Chi-square	p-value
		MRSA	MSSA			
Age Groups	<20	14	15	29(18.7%)	10.920	0.053
	21-30	22	7	29(18.7%)		
	31-40	11	8	19(12.3%)		
	41-50	26	12	38(24.5%)		
	51-60	9	10	19(12.3%)		
	>60	8	13	21(13.5%)		
	Total	90	65	155(100%)		
Gender	Male	51	43	94(60.6%)	1.423	0.233
	Female	39	22	61(39.4%)		
	Total	90	65	155(100%)		
Clinical Samples	Pus/Wound swab	72	48	120(77.4%)	4.941	0.667
	Blood culture	6	4	10(6.5%)		
	CVP Tip	4	5	9(5.8%)		
	Sputum	2	3	5(3.2%)		
	Throat swab	3	1	4(2.6%)		
	Urine	2	1	3(1.9%)		
	Ear swab	1	1	2(1.3%)		
	HVS	0	2	2(1.3%)		
	Total	90	65	155(100%)		
Clinical Department	OPD	45	26	71(45.8%)	1.910	0.752
	Surgery	21	17	38(24.5%)		
	Medicine	16	14	30(19.4%)		
	Pediatrics	5	4	9(5.8%)		
	Obstetrics & Gynaecology	3	4	7(4.5%)		
	Total	90	65	155(100%)		

Table-II: Antimicrobial Susceptibility pattern of MRSA.

Sr. No	Antibiotics	Sensitive	Resistant
1	Linezolid	90(100%)	0
2	Vancomycin	90(100%)	0
3	Minocycline	64(71.1%)	26(28.9%)
4	Clindamycin	62(68.9%)	28(31.1%)
5	Gentamycin	63(70%)	27(30%)
6	Trimethoprim/ sulfamethoxazole	18(20%)	72(80%)
7	Ciprofloxacin	23(25.6%)	67(74.4%)
8	Levofloxacin	28(31.1%)	62(68.9%)
9	Erythromycin	22(24.4%)	68(75.6%)
10	Nitrofurantoin (in urine samples only)	2(100%)	0(0%)

DISCUSSION

Methicillin-resistant Staphylococcus aureus causes community-acquired as well as nosocomial infections with significant mortality and morbidity. It is a well-known global threat, and the emergence of MRSA strains with resistance to non-β-lactam drugs has raised the severity of the issue [12]. It has major implications in the treatment and control of MRSA infections, especially when a few numbers of antimicrobials available are considered [13]. This study determined the frequency and antimicrobial susceptibility of MRSA from different clinical samples in a tertiary care hospital in Pakistan.

The present study reports an alarmingly high frequency of MRSA infection. There is a marked geographical variation in the frequency of MRSA infections worldwide [14]. Literature has reported a high prevalence of MRSA in Pakistan, ranging from 42% to 51% [15]. The frequency of MRSA was high in a study conducted in Peshawar and another study done in Islamabad but less than in our study [4,15]. A high prevalence of MRSA has also been reported in other regions. In another cross-sectional study conducted in Eritrea, the prevalence of MRSA was even higher than in our study [12]. Naimi et al. reported almost similar frequency of MRSA in Afghanistan as in our study [16]. In contrast, the prevalence of MRSA was 27.8% in Kenya [17].

In our study, the numbers of clinical isolates obtained from males were greater than from females. Similarly, in two other studies, most MRSA strains were isolated from males [16,18]. In contrast, Nabi et al. reported a majority of

the MRSA isolates from females [15]. MRSA infection was greater in the elderly 40-50 years, followed by the age group <20 and 10-30 years. Similar results were found in another study. In Peshawar, MRSA isolates were mostly isolated from the adult age group [4]. The MRSA strains were most common in the age group 41-75 years[16]. However, Garoy et al. reported that MRSA was most commonly isolated from patients <18 years of age [12].

Our study showed that pus was the most common sample from which MRSA were obtained, followed by blood samples. In a study by Garoy et al., pus was the most common specimen from which MRSA was isolated [12]. Another study reported that most MRSA isolates were from pus samples, followed by tracheal aspirate and blood[18]. A study showed that the most common specimen from which MRSA was isolated was pus, followed by urine and blood[15]. However, in Peshawar, the majority of MRSA were isolated from blood samples[4].

Our results showed that all the MRSA strains were sensitive to linezolid and vancomycin. The majority of the isolates were also sensitive to minocycline, gentamycin, and clindamycin. But only a few isolates showed susceptibility to trimethoprim/sulfamethoxazole, ciprofloxacin, levofloxacin, and erythromycin.There were only two strains isolated from urine samples which were sensitive to nitrofurantoin. The results of our study were comparable to another study done in Peshawar.

In that study, all the MRSA strains were sensitive to linezolid and vancomycin. Most of the isolates were also sensitive to clindamycin and minocycline. But unlike our study, the majority of the strains were also susceptible to trimethoprim/sulfamethoxazole [4]. Another study reported that all isolates were sensitive to vancomycin. Almost 90% of strains showed susceptibility to clindamycin which was quite higher than in our study. The majority of the isolates were also sensitive to gentamicin, doxycycline, and tobramycin. The percentage of isolates sensitive to trimethoprim-sulfamethoxazole, ciprofloxacin, and erythromycin was greated in contrast to our study[16].

Another study reported that 100% of MRSA isolates were sensitive to vancomycin. The majority, but not all, of the isolates were sensitive to linezolid. As compared to our study, less MRSA strains were sensitive to clindamycin and gentamycin, but trimethoprim-sulfamethoxazole and levofloxacin sensitivity revealed better results. The results of nitrofurantoin susceptibility were similar to our study[18]. In Kenya, the majority, but not all of the MRSA isolates were sensitive to vancomycin and linezolid. This is worrisome as vancomycin and linezolid are considered the drugs of last resort for treating MRSA infections. The isolates also showed poor sensitivity to tetracycline[17].

In our study, there was no statistically significant association of MRSA with the patient gender, clinical samples, and clinical department. However, the association was significant between MRSA and the age group of patients. According to a study by Garoy et al., there was no significant association of MRSA with the gender of patients. MRSA strains were mostly isolated from patients ≤18 years with a significant association. The association was also statistically significant between MRSA and clinical samples, with the majority of isolates from pus specimens[12].

CONCLUSION

The frequency of Staphylococcus aureus is 11.07%, and out of these, there is a high MRSA frequency (58.1%) in our setup. All the MRSA strains were sensitive to linezolid and vancomycin (100%). Seventy-one percent of isolates were sensitive to minocycline, 70% to gentamicin, and 68.9% to clindamycin. Only a few isolates were sensitive to macrolides (24.4%), trimethoprim-sulfamethoxazole (20%), and fluoroquinolones (25.6% to ciprofloxacin and 31.1% to levofloxacin).

LIMITATIONS:

- The study was conducted in a single institution. A multicenter study should be done, including samples from various hospitals.
- Research on whole-genome sequencing of MRSA isolates should be done to determine the antibiotic resistance genes and comparative analysis of strains in other parts of the world.

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Author's Contribution:

Aqsa Aslam: Substantial contributions to the conception and design of the work.
Wajiha Mahjabeen: Interpretation of data for the work.
Muhammad Zia ul Rehman: Acquisition, and analysis of data for the work.
Sana Qanber Abbasi: Data collecion and analysis.
Nazish Babar: Drafting the work or reviewing it critically for important intellectual content.
Huzaifa Saleem: Acquisition and interpretation of data for the work.

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