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Original Research Article

Study of Linezolid and Vancomycin Susceptibility in Methicillin Resistant *Staphylococcus aureus* Isolates from Clinical Specimens in a Tertiary Care Hospital

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Abstract

Objectives: (1) To estimate the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections. (2) To study the susceptibility pattern of MRSA to linezolid (LZD) and Vancomycin.

Materials and Methods: A cross-sectional observational study was carried out for a period of one and half years. 370 *S. aureus* isolates from different clinical specimens were studied for their antimicrobial susceptibility pattern to cefoxitin (as a surrogate marker for Methicillin resistance), linezolid and vancomycin as per CLSI guidelines.

Results: Out of 370 isolates of *Staphylococcus aureus*, 165 were MRSA (44.5%). None of the MRSA isolate were resistant to vancomycin and linezolid.

Conclusion: Strict infection control practices should be implemented to prevent the spread of the MRSA in healthcare settings. Also, regular screening of these isolates for development of resistance to Linezolid and Vancomycin is essential to prevent treatment failure.

Keywords: *Staphylococcus aureus, methicillin-resistant Staphylococcus aureus.*

Introduction

Staphylococcus aureus is the most dangerous strain of the staphylococcus genus [1]. It is the agent that is responsible for infections that are obtained in hospitals as well as in the community [2] In 1961, the United Kingdom was the location where the very first isolate of methicillin-resistant *Staphylococcus aureus* (MRSA) was reported. However, at that time period, the frequency of MRSA in Europe and worldwide was minimal, and it

was not actually seen as a serious concern. Although, over the course of the last two decades, it has established a track record of being a considerable risk to the health of patients, in particular who are admitted to the hospital for a lengthy period of time. The general prevalence of MRSA raised from 29% to 59% [3].

In terms of resistance, *S. aureus* developed resistance to beta-lactam antibiotics in the year 1950 by developing an enzyme known as beta-lactamase. Shortly after this, methicillin was made available; but, as was indicated previously, these bacteria eventually evolved resistance to methicillin as well, which occurred a decade after its first use [4]. MRSA has proven to be a very difficult infection to eradicate, particularly in hospital settings around the globe. Since that time, there have only been a limited number of therapeutic choices accessible for the treatment of people suffering with MRSA [5]. Glycopeptides, such as intravenous vancomycin, are one of the few cost-effective therapy options now available for the treatment of MRSA infections in underdeveloped countries [6].

Linezolid (LZD), the first oxazolidinone antibiotic to become commercially accessible, has been shown to be therapeutically effective against multidrug-resistant strains of Gram-positive bacteria. LZD is able to do this by obstructing the development of the 70S initiation complex, which is an essential step in the process of bacterial protein synthesis [7]. In addition, clinical tests have shown that LZD is typically well tolerated for up to 28 days in patients, with little adverse effects on haematological parameters. This information was obtained through clinical studies [8]. Additionally; LZD has shown excellent success in the elimination of infections of the skin and soft tissues [9]. Because the plasma concentrations of intravenous and oral LZD are identical, it is possible to switch between the two delivery methods, which results in a significant reduction in healthcare costs [7] On the other hand, newer drugs like tedizolid, telavancin, and dalbavancin, which have been used for the treatment of MRSA infections, are also more effective. However, because they are so expensive, their use and availability in developing countries is not that common.

The purpose of our study is to estimate the prevalence of the methicillin-resistant *Staphylococcus aureus* (MRSA) and to study their susceptibility pattern to Vancomycin and Linezolid in our hospital.

Materials and Methods

A prospective cross-sectional study was carried out in the Department of Microbiology of a tertiary care hospital over a period of one and half years. 370 isolates of *S. aureus* identified by standard Microbiological methods [10] from various clinical specimens like pus swabs, aspirates, blood, urine, and sputum were included in the study.

MRSA detection by cefoxitin disc diffusion test: Strains of *Staphylococcus aureus* isolated from infected samples were screened for mec-A-mediated methicillin resistance using 30 µg cefoxitin disc (Hi Media) by Modified Kirby-Bauer disc diffusion method and the results were interpreted using CLSI guidelines [11].

Vancomycin resistance detection: Screening of Vancomycin resistance in MRSA isolates was done by Vancomycin screen agar. Spot inoculation (10µ) of 0.5 McFarland suspension of MRSA isolate was done onto MHA agar plates containing 6 µg/ml of vancomycin. The agar plates were then incubated for 24 hours at 35°C in accordance with the criteria provided by CLSI. Resistance was demonstrated when there was >1 colony or light film of growth [11].

Linezolid resistance detection: Linezolid (30 µg) (Hi Media) susceptibility test was performed in all MRSA isolates by the modified Kirby-Bauer disc diffusion method and susceptibility results were interpreted according to CLSI guidelines [11].

Results

Table 1: Methicillin resistance in *S. aureus* (n=370) isolates from various clinical specimens

Name of the antimicrobial agent	No of resistant isolates
Cefoxitin (As a surrogate marker for Methicillin resistance)	165 (44.5%)

Out of 370 isolates of *S. aureus* from clinical specimens, 165 were found to be resistant to Methicillin. So, the prevalence of MRSA in our study was 44.5%.

Table: 2 Susceptibility pattern of MRSA isolates (N=165) to Linezolid and Vancomycin

Name of the antimicrobial agent	No of susceptible isolates (%)
Linezolid	165 (100%)
Vancomycin	165 (100%)

None of the MRSA isolates was resistant to Vancomycin and Linezolid.

Discussion

In 1959, methicillin became available for use as a treatment for infections brought on by strains of *S. aureus* that were resistant to the antibiotic penicillin. On the other hand, the United Kingdom reported that *S. aureus* isolates had developed resistance to methicillin in the year 1961 [12] Since 1987, the rate of MRSA infection in intensive care units (ICUs) in the United States has grown up to 25-fold, reaching a frequency of 16% [13]. *S. aureus* is most often transmitted from person to person by direct skin contact with an infected person or a contaminated surface.

The term "nosocomial infection" refers to an infection that occurs either within 48 hours of hospital administration or within three days after discharge [14]. The European Prevalence of Infection in Intensive Care Study (EPIC), which included the participation of almost 4500 patients, found that the prevalence rate of nosocomial infections in intensive care units was 20.6%, which is also an alarmingly high number [14]. Over 5000 people lose their lives as a direct consequence of this every year. When compared to a patient who is not infected with a nosocomial infection, a patient who has this kind of illness must remain in the hospital for 2.5 times as long, which results in an extra cost of $3000 [14].

MRSA may be carried in the nose and on the skin by around 1% to 2% of individuals, and some strains of MRSA can be particularly aggressive, leading to staphylococcal infection. According to the findings of a study conducted in Saudi Arabia, surgical wounds are the most prevalent location of infection, followed by the chest and then the central venous catheter [15] An article written in the United States states that pneumonia and septic shock are the illnesses that are most often brought on by MRSA [16]

The prevalence of MRSA varies greatly from one region of the globe to another [17] Studies done in Nigeria, Kenya, and Cameroon reported prevalence rate from 21% to 30% [18] While studies carried out in a variety of European nations found an overall frequency of 20% [19] and Mehta revealed a rate of 33% from wound swabs and pus from patients in India [20]. The prevalence rate was found to be 44.5% in our research, although in Rawalpindi it was 60.40%, which may be regarded a regional high [21] and 41.9% in Lahore, which was found to be almost identical to our study. In

Iran [22] MRSA isolates were examined to see whether or not they were sensitive to LZD, and the results showed that all of the isolates (one hundred percent) were susceptible to it [23] results that were similar were discovered in Kenya [24] When put to the test in large cities in Pakistan like Peshawar and Rawalpindi, LZD came across as an excellent treatment option. This was due to the fact that all isolates were able to be treated by it [25,26]. However, according to the findings of a research that was carried out in the year 2011 in Cleveland, Ohio by Endimiani *et al*., patients who suffered from cystic fibrosis and had a protracted treatment with the antibiotic in question exhibited a resistance rate of 10.4% to LZD that was caused by MRSA [27] On the other hand, a study that was carried out in 2008 in Madrid, Spain by Sánchez Garca *et al*. reported one of the first known clinical outbreaks of LZD-resistant *Staphylococcus aureus* (LRSA). This outbreak involved 12 patients who were admitted to the intensive care unit, all of whom were treated with LZD for a short period of time [28] In our study all isolates of MRSA were susceptible to Linezolid.

With regard to vancomycin susceptibility, heterogenous Vancomycin-intermediate *S. aureus* (hVISA), was first reported in Japan in 1997 and later on Vancomycin-intermediate *S. aureus* (VISA) has been identified globally from various nations like the United States, Japan, Australia, France, Scotland, Brazil, South Korea, Hong Kong, South Africa, Thailand, Israel, and others [29,30].

In Southern India, Menezes *et al* [31] in 2008 stated the emergence of vancomycin- intermediate Staphylococcus species. Of 102 oxacillin-resistant *S. aureus* isolates, one was found to be a VISA strain (MIC 5 µg/ml) [31]. In a study from Western part of India, among 58 clinical isolates of MRSA, the prevalence of hVISA was detected to be 6.9% [32]. In our study all isolates of MRSA were found to be susceptible to Vancomycin.

Conclusion

When compared to studies carried out in Europe and South Asia in the past, our research revealed that the prevalence of MRSA was much higher than that seen in those earlier studies. The high incidence of MRSA, particularly in developing nations, may be attributed to a variety of factors such as poor infection control strategies in hospitals, incorrect antibiotic use and lack of screening.

Therefore, effective infection control policies along with strictly regulated and monitored use of antimicrobials and regular screening for development of resistance is necessary to prevent the further spread of this organism and treatment failure.

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