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A Study on Mupirocin and Clindamycin Resistance in Clinical Isolates of Methicillin Resistant Staphylococcus Aureus from A Tertiary Care Hospital Hassan

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Abstract

Staphylococcus aureus is an important human pathogen causing wide variety of infections. Since the introduction of antibiotics, staphylococcus aureus known to develop resistance to many routinely used antibiotics such as the beta-lactams and macrolides. This study was taken up to study prevalence and phenotypes of MLSB (Macrolide-Lincosamide-Streptogramin B) and mupirocin resistance in MRSA isolates and to determine antibiotic susceptibility pattern of these isolates.

Materials and methods:

All clinical samples from 100 patients over a period of 3 months attending Sri Chamarajendra hospital, Hassan was collected and processed for the aerobic bacterial culture sensitivity. MRSA was identified using Cefoxitin disc following standard operative procedures. Detection of inducible Clindamycin resistance (D test) and Mupirocin resistance was done as per CLSI guidelines.

Results

Out of the 285 S.aureus isolates, 100 (35.08%) were methicillin resistant , 185(54.05%) were methicllin sensitive. Inducible clindamycin resistance was seen in 20% of isolates. Low level mupirocin resistance was seen in 38% isolates and high-level resistance in 34%.

CONCLUSION

Considering the increased rate of MRSA strains, always recommend clinicians to follow antibiogram. Decolonization of MRSA in health care workers should be done and strictly adhere to infection control policies. Clindamycin resistance should be routinely checked based on D test for better treatment response.And also it is recommended that routine testing of MRSA for mupirocin resistance be conducted which assists in the control and spread of mupirocin-resistant MRSA.We also suggest to consider alternative agents to mupirocin to counteract the clinical failure of decolonization regimens .

Keywords: NIL

INTRODUCTION

Staphylococcus aureus is an important human pathogen causing wide variety of infection ranging from localized to systemic disseminated infections. It is one of the most common etiological agents in nosocomial and community-acquired infections worldwide. Since the introduction of antibiotics, staphylococcus aureus known to readily develop resistance to many routinely used antibiotics such as the beta-lactams and macrolides. The rates of MRSA are increasing day by day 1.

Methicillin-resistant Staphylococcus aureus (MRSA) is a problem in hospitals worldwide and is increasingly recovered from nursing homes and the community.

Indiscriminate use of antibiotics, prolonged hospital stay, intravenous drug use, carriage of MRSA in nose, axilla, perineum are important risk factors for MRSA acquisition. The commonly used antibiotic for treatment of MRSA infection is vancomycin or linezolid, while mupirocin (derived from Pseudomonas fluorescens) is an effective topical antibiotic for the elimination of MRSA in carriers. Mupirocin (pseudomonic acid A) specifically binds to bacterial isoleucyl-tRNA synthetase (IRS) and inhibits protein synthesis.The increased use of this antibiotic has been accompanied by outbreaks of MRSA resistant to mupirocin, although the frequency of resistance is still low. Nasal application of mupirocin at clinically effective concentrations may result in the presence of low levels of the antibiotic in the pharynx, which could induce or select for the emergence of mupirocin-resistant MRSA.2

Similarly, the increasing frequency of the infections with MRSA and the changing drug susceptibility patterns have led to a renewed interest in the use of macrolide lincosamide streptogramin-B (MLSB) antibiotics to treat such infections, with clindamycin being the preferred agent due to its excellent pharmacokinetic properties. However, their widespread use has increased the number of the Staphylococcus strains which are resistant to the MLSB antibiotics. The MLSB antibiotics are structurally unrelated but they are related microbiologically because of their similar mode of action. They inhibit the bacterial protein synthesis by binding to the 23S rRNA of the 50S ribosomal subunit.

There are different types of mechanism of resistance to Macrolide-Lincosamide-StreptogramiB(MLSB) in Staphylococcal strains. The most common mechanism is by modification of target site, mediated by erm genes which is called constitutive MLSB (cMLSB) where rRNA methylase is always produced or inducible (iMLSB) where methylase is produced in the presence of inducible agent like erythromycin. Another mechanism of resistance is by efflux mechanism mediated through msr A gene which is called MS phenotype. It is reported that treatment of patients harboring iMLSB resistant S. aureus with clindamycin might lead to development of cMLSB resistant strains and subsequently, therapeutic failure. By the standard antibiotic susceptibility test iMLSB phenotype cannot be recognized but need a specific method. D-test detects iMLSB resistance pattern of S. Aureus 1

The overall prevalence rate ranging from 20-40%1. Overall prevalence of MupRL (low-level mupirocin resistant) and MupRH (high-level mupirocin resistant) among staphylococci was found to be 14.7% and 10.5% respectively4.

As the resistance pattern keeps changing from region to region and time to time, antibiotic sensitivity pattern of this region among MRSA isolates also varies. Clindamycin is considered as the reserved drug in MRSA infections and mupirocin, the drug of choice for MRSA colonizers, the resistance pattern of the same also to be focused. As the data regarding prevelance of MRSA, mupirocin resistance and clindamycin resistance was not available in our geographic region and this data is of prime importance in empirical management of patients, this study was taken up to evaluate the scenario in our hospital.

OBJECTIVES

1. To study prevalence of MLSB (Macrolide-Lincosamide-Streptogramin B) and mupirocin resistance in MRSA isolates

2.To determine different phenotypes of MLSB amongst MRSA isolates

3.To determine Antibiotic susceptibility pattern of MRSA isolates showing MLSB and mupirocin resistance

Methods: An observational study was conducted for over a period of 3 months. All clinical samples from patients attending Sri chamarajendra hospital, Hassan was collected and processed by conventional methods for the aerobic bacterial culture sensitivity in department of microbiology7.All the staphylococcal isolates were identified by standard protocol. Antibiotic susceptibility testing done by Kirby bauer disc diffusion method. All the staphylococci isolates were tested for Methicillin resistance by using Cefoxitin disc following standard operative procedures8. All isolates confirmed as MRSA were stored in the laboratory for further studies. The details regarding patient, type of clinical specimen and antibiotic susceptibility pattern were collected from the registers.

- For detection of inducible clindamycin resistance (D test), erythromycin(15µg) and clindamycin (2µg)

Volume 4, Issue 4; July-August 2021; Page No 445-450

discs was placed at a distance of 15 mm edge to edge and three different phenotypes was interpreted as follows:

1. Inducible MLSb (iMLSB) phenotype: Staphylococci showing sensitive (zone size > 21mm) to clindamycin and resistant (zone size < 13 mm) to erythromycin with flattening of zone towards clindamycin disc. (D test positive)

2. Constitutive MLSb (cMSLB) phenotype: Staphylocccal isolates showing resistance (< 13 – 14mm zone size) to both erythromycin and clindamycin discs.

3. MS phenotype: Staphylococcal isolates showed resistance (< 13mm zone size) to erythromycin and sensitive (>21mm zone) to clindamycin disc and negative D test.

- Mupirocin resistance was tested among the MRSA isolates by disk diffusion method using 5µg and 200µg mupirocin disk to determine low-level and high-level resistance.

All isolates with zone diameters less than 14 mm for both 5 µg and 200 µg was considered to be Mupirocin resistant strains.

RESULTS

- Out of the 285 S.aureus isolates, 100 (35.08%) were methicillin resistant and 185(54.05%) were methicllin sensitive. All the isolates were sensitive to Linezolid and Vancomycin and 100% resistance was shown to pencillins.

ANTIBIOTICS	S.aureus (100)	%
P	00	00
E	40	40
CD	94	94
COT	63	62.5
GEN	88	87.5
CIP	50	50
VA	100	100
DOX	57	56.2
LZ	100	100
PTZ	54	53.12
AMX	00	00
AMC	19	18.75
CTR	85	84.3
AK	88	87.5

Figure 1: Antibiotic sensitivity pattern of MRSA isolates.

Volume 4, Issue 4; July-August 2021; Page No 445-450

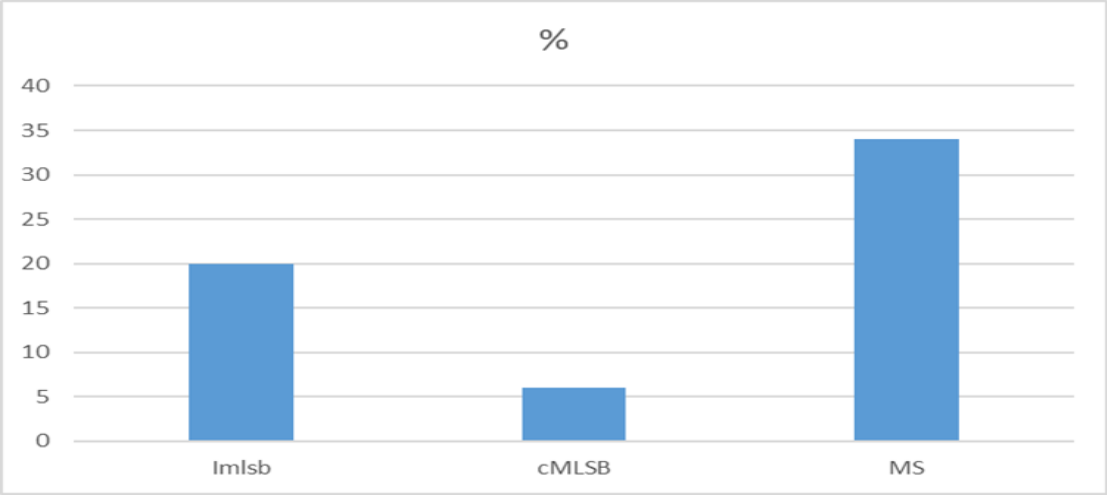

Figure 2: Induible clindamycin resistance was seen in 20% of isolates, constitutive resistance in 06% of isolates and 34% showed MS phenotype.

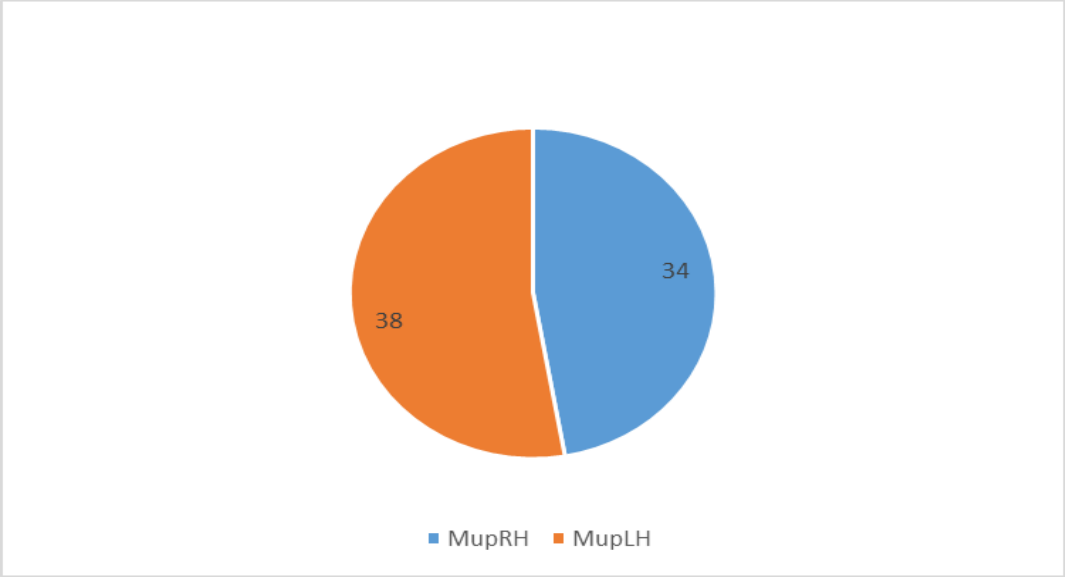

Figure 3: Low level mupirocin resistance was seen in 38% isolates and 34% showed high level resistance to mupirocin.

DISCUSSION

The emergence of drug resistance among Staphylococci is an increasing problem. Methicillin resistant S. aureus (MRSA) is a notorious nosocomial pathogen and its rate has dramatically increased in the recent years.[11] In our study also an increased rate of MRSA is observed i.e. 35.08%. This is in comparasion with study done by chada et al where they had 36.18% (131/362) isolates which were MRSA. Similarly, Madhumathi et al isolated 54.06% of MRSA in their study. Almost all these isolates were 100% sensitive to Vancomycin and linezolid in the studies.

We had focussed on Clindamycin and mupirocin resistance among these isolates in our study. Clindamycin, has long been an option for treating Staphylococcal skin, soft tissue and bone infections because of its proven efficacy, low cost, the availability of its oral and parenteral forms, tolerability, excellent tissue penetration, its good accumulation in abscesses and because no renal dosing adjustments are required. But staphylococcus is showing increased rate of resistance to the same as observed in the study. Of the 100 MRSA isolates, A total of 60 (60%) isolates which were resistant to Erythromycin, iMLSB phenotype was seen in 20

Volume 4, Issue 4; July-August 2021; Page No 445-450

isolates (20%), cMLSB in 06 isolates (06%) and 34 isolates (34%) showed MS phenotype.This is comparable with study conducted by Umamaheswari SS et al., In which Analysis of clindamycin resistance in 52 (26%) MRSA isolates showed 42.30% of inducible clindamycin resistance, 30.76 % of constitutive clindamycin resistance and 26.92% were sensitive to both erythromycin and clindamycin. Similar results were obtained in study done by Shivanna et al where out of 100 staphylococcal isolates, 26 showed constitutive Clindamycin resistance (cMLSB) and 7 isolates were inducible Clindamycin resistant (iMLSB).[4]

But in a study done in north india inducible Clindamycin resistance was much lower compared to our study 45 (12.1%). This may be because of decreased exposure to antimicrobials as the study was done in a rural population .[11]

Kavitha Prabhu et al., looked for the Inducible Clindamycin Resistance in Staphylococcus and found to be higher in MRSA as compared to MSSA (20%, 16% and 6%, 6%, respectively)

Mupirocin is a topical antibiotic agent that interferes with bacterial protein synthesis, which can be used for eradication of staphylococcal nasal colonization and control of MRSA transmission in Health Care Facilities.[9]

In our study, out of the 100 MRSA isolates, 34(34%) isolates showed High level resistance (HLR) to mupirocin and 38(38%) isolates were sensitive to mupirocin. HLR found to be 50% in iMLSB, 100% in cMLSB and 16.6% in MS phenotypes which is high compared to other studies .Study done by Chaturvedi et al found 15 mupirocin resistant isolates , 8 (53.3%) isolates were high-level resistant (MuH) and 7 (46.7%) isolates were low-level resistant (MuL).[5] High-level Mupirocin resistance (Mup RH) was detected in 13 isolates and low-level Mupirocin resistance (Mup RL) was seen in 4 isolates in a study done by shivanna et al.[4] Similarly Oomen et al found Twelve (7%) of the total 167 isolates to be resistant to both 5 and 200 µg mupirocin discs. [2]

This high rate of resistance may be due to multiple factors, one is since it is plasmid coded, chances of cross transmission may occur. Second is over the counter availability of the drug.

One more reason which we can comment on is , mupA gene which encodes mupirocin resistance is transferred from commensal flora of skin to MRSA during mupirocin therapy. So these factors contribute to mupirocin resistance. Therefore, the sensitivity to mupirocin should be confirmed before it can be used as a decontaminating agent and should be factored into local infection control policies.

CONCLUSION

Considering the increased rate of MRSA strains, always recommend clinicialns to follow antibiogram. Decolonization of MRSA in health care workers to be done and strictly adhere to infection control policies. Clindamycin being an effective drug, its resistance should be routinely checked based on D test for better treatment response. And also, it is recommended that routine testing of MRSA for mupirocin resistance be conducted which facilitates the early detection of resistance and assists in the control and spread of mupirocin-resistant MRSA.

Alternative agents to mupirocin should be considered to counteract the clinical failure of decolonization regimens and to prevent the selection of multiple resistant strains.

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Volume 4, Issue 4; July-August 2021; Page No 445-450

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Volume 4, Issue 4; July-August 2021; Page No 445-450