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INDUCIBLE CLINDAMYCIN RESISTANCE IN METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS ISOLATES IN TERTIARY CARE HOSPITAL IN SOUTHERN RAJASTHAN.

Microbiology

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ABSTRACT

Background : Increase in the prevelance of β lactum resistance in staphylococcal infection has led to renewed interest in use of macrolide lincosamide-streptogramin B antibiotics for treatment. The routine testing for clindamycin susceptibility fails to detect inducible clindamycin resistance due to erm genes resulting in treatment failure, thus detection by a D test is necessary. **Aim:** Assessing the inducible clindamycin resistance using D test in clinical isolates of Staphylococcus aureu **Methodology:** A total of 100 staphylococcus aureus isolates were tested for routine antibiotic susceptibility by Kirby bauer method and inducible clindamycin resistance using D test. **Result**: Out of 100 samples, inducible resistance to clindamycin was seen in 30% isolates and constitutive resistance in 14% isolates. Out of these, inducible and constitutive resistance is higher in MRSA (39% and 30%) as compared to MSSA (22% and 0%) **Conclusion:** Clindamycin being a reserve drug in staphylococcal skin and soft tissue infections should be tested for inducible resistance to avoid treatment failure.

KEYWORDS

resistance, clindamycin, MRSA

INTRODUCTION:

Antibiotic resistance in Staphylococcus aureus has become a great concern and a big problem among hospitalized patients, persons for long-term in hospital facilities and outpatients. In late 70s, MRSA was being considered a pathogen associated with health care system among patients with associated and recognized risk factors. These strains are commonly seen to present decreased sensitivity to all the b lactum drugs and so are considered resistant.[1]

However, rapid emergence of CA-MRSA (community associated MRSA) in the past many years in patients not possessing any obvious risk factors has caused a difficulty in managing both systemic and focal staphylococcal infections.[1]

In the situation, clindamycin is emerging as the treatment drug for such infections.It is cost effective as compared to the other modalities and can be given by both oral and intravenous route with 90% bioavailability. The penetration in the skin and soft tissue is also better as compared to the other b lactum drugs and may inhibit the toxins of staphylococcus otherwise untouched by other treating antibiotics.2,3 One of the biggest concern regarding the use of clindamycin for MRSA infection is possibly the presence of inducible resistance in clindamycin. The inducible resistance is hardly detected by any of the sensitivity methods such as broth microdilution testing or automated susceptibility testing devices and standard disk diffusion test.[4]

The target site modification, also known as MLSB (macrolide-lincosamide-streptogramin B) resistance, results in resistance to clindamycin, erythromycin and streptogramin B. The mechanism can either be constitutive, in which rRNA methylase is produced always or can be inducible, when methylase is being produced only in presence of an inducing agent. Erythromycin is an effective inducer. Such resistance is seen to be mediated by the erm genes.[5]

The following study focusses on the detection of clindamycin resistance (inducible and constitutive) using 15µg erythromycin and 2µg clindamycin disc and performing D test.

Material and methods:

The study was conducted in Microbiology dept at RNT Medical College Udaipur, in 2019

All the samples including pus, wound swab, blood, urine and body fluids were screened for staphylococcus aureus isolates. 100 samples with staphylococcus aureus isolates were further processed for antibiotic sensitivity testing and D test. Antibiotic sensitivity testing was done by Kirby buaer disc diffusion method using antibiotic discs (6mm) using CLSI guidelines.[6]

MRSA detection was done using Cefoxitin (30 µg) disc as per CLSI guidelines.6 Interpretation : ≤21mm was considered mec A positive (MRSA) while ≥22mm was mec A negative (MSSA).

D test was performed in all the isolates. The inoculum with colony suspension 0.5 Mc Farland was prepared and inoculated on MHA plate. The antibiotic disc of Erythromycin (15 µg) and clindamycin (2µg) are placed on the media plate 12 mm apart. Incubated for 16-18 hrs at ambient temperature (37°c). Flattening of zone of inhibition of clindamycin adjacent to Erythromycin disc shows inducible clindamycin resistance.[6]

Interpretation was done as follows:[7]

ERY-S, CL-S	MLS SENSITIVE (S)
ERY-R,CL-S (D TEST NEG)	MS PHENOTYPE
ERY-R, CL-S(D TEST POS)	MLSB INDUCIBLE (iMLSb)
ERY-R, CL-R	MLSB CONTITUTIVE (cMLSb)

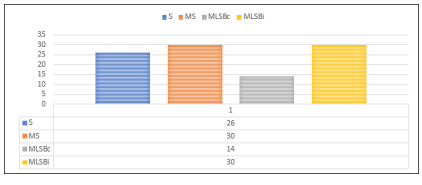
Results:

In present study, maximum isolates of Staphylococcus aureus were seen in pus followed by urine and blood as shown in table 1.

Table 1: shows sample distribution of staphylococcus aureus isolates.

Sample	No. of isolates
Pus	50
Urine	20
Blood	20
Sputum	2
Vaginal swab	2
Conjunctival swab	2
Pleural fluid	4

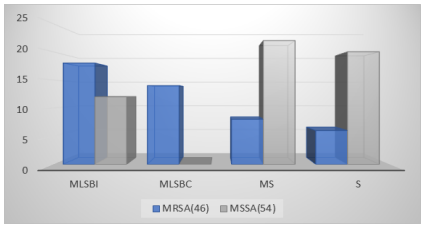
Out of 100 isolates, 30 were of inducible MLSb phenotype, while 14 were constitutive. 30 isolates were MS phenotype, while 26 were sensitive to both Erythromycin and clindamycin.



Graph 1: shows the distribution of four phenotypes of MLSb resistance among staphylococcus aureus isolates.

Out of 100 isolates of staphylococcus aureus, MRSA isolates were 46 while MSSA isolates were 54. Out of 46 MRSA isolates, 18 (39%) were positive for MLSBi phenotype while 14 (30%) were positive for

MLSBc phenotype. Out of 54 MSSA, 12 (22%) were positive for MLSBi phenotype while none of the isolate was positive for MLSBc phenotype. MS phenotype in MRSA was 8 (17%) while in MSSA isolates it was 22 (40%).



Graph 2: shows distribution of four phenotypes of MLSb resostance among MSSA and MRSA.

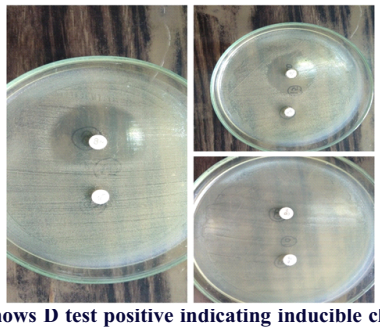


Figure 1: shows D test positive indicating inducible clindamycin resistance (left), MS phenotype (top right) and constitutive resistance (right below).

DISCUSSION:

There are a very few options available for treatment of MSSA and MRSA infections, with clindamycin being one of the good alternatives. However, inducible clindamycin resistance may be present in staphylococcal isolates along with erythromycin resistance. Reporting Staphylococcus aureus as susceptible to clindamycin without checking for inducible resistance may result in institution of inappropriate clindamycin therapy.

In present study, 46% isolates were MRSA while 54% were MSSA. In MRSA isolates 39% were iMLSb, 30 % cMLSb and 17% MS phenotype. This suggests treatment failure may occur in 39% cases of MRSA isolates where erythromycin being resistant, clindamycin is given as treatment therapy if D test is not performed. Similar prevalence of iMLSb was seen in related previous studies. Deotale et al showed 34% iMLSb in MRSA but the prevalence of cMLSb was lower as compared to our study.

As present study states, the iMLSb phenotype was less (22%) in MSSA as compared to MRSA isolates and had no isolates with constitutive phenotype ie. cMLSb and 41% MS phenotype suggesting lower resistance to clindamycin overall.

Table 2: shows comparative analysis of present study with the present study.

Authors name	MRSA			MSSA		
	iMLSb	cMLSb	MS	iMLSb	cMLSb	MS
Present study	39%	30%	17%	22%	0%	41%
Supriyarajvi et al7	21.5%	17%	30%	11%	5%	35%
Deotale et al8	34%	9%	30%	2%	0%	5%
Shetty el al9	27%	52%	17%	11%	22%	14%

CONCLUSION:

Clindamycin is frequently used in treatment of infections because of its proven efficacy, safety and convenience of parenteral and oral administration in patients. But therapeutic failure caused by iMLSb strains is of great concern because these isolates appear as sensitive in routine antibiotic susceptibility testing.

Hence we conclude from the present study that as in present scenario, MRSA is one of the commonest Hospital acquired pathogen, there is a need of performing D test in routine which helps in identifying the isolates resistant to clindamycin and helps the clinicians in judicial use of the drug in skin and soft tissue infections.

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