

**ORIGINAL ARTICLE****INDUCIBLE CLINDAMYCIN RESISTANCE IN CLINICAL ISOLATES OF *STAPHYLOCOCCUS AUREUS* IN A TEACHING HOSPITAL**Vishal Sharma<sup>1</sup>, Anuj Sharma<sup>2</sup><sup>1</sup>Associate Professor Microbiology, GGS Medical college and Hospital, Faridkot, Punjab, India<sup>2</sup>Associate Professor Pathology, Maharishi Markendeshwar Medical College and Hospital, Solan, Himachal Pradesh, India**ABSTRACT:**

Clindamycin is widely used for treatment of skin and soft tissue infections caused by staphylococci. However inducible clindamycin resistance may be missed in routine in vitro susceptibility test for clindamycin. The present study was conducted to determine the prevalence of inducible clindamycin resistance in *Staphylococcus aureus* isolates from various clinical specimens. Isolates were subjected to antimicrobial susceptibility testing for erythromycin, clindamycin and cefoxitin. Inducible clindamycin resistance was tested by D test.

D test was found to be positive in 21.57% of the isolates. Inducible clindamycin resistance was found to be more in methicillin resistant isolates as compared to methicillin sensitive isolates. D test should be used as a routine method for detection of inducible clindamycin resistance, thus avoiding therapeutic failures.

Keywords: Erythromycin , Clindamycin , *Staphylococcus aureus*, D test, Methicillin

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**INTRODUCTION:**

The emergence of methicillin resistance in staphylococci has posed a serious therapeutic challenge as methicillin resistance also predicts resistance to multiple classes of antibiotics besides beta lactams.<sup>1</sup> The macrolide-lincosamide-streptogramin B [MLS<sub>B</sub>] class of antibiotics are commonly used to treat infections caused by staphylococci.<sup>2</sup> Clindamycin is commonly used alternative drug to treat infections caused by staphylococci, both methicillin resistant and methicillin sensitive. It has good tissue penetration, is easily absorbed, does not require dose adjustment in renal impairment, available in oral and parenteral forms and is useful in cases of penicillin allergy.<sup>3,4</sup>

However resistance to these antibiotics in staphylococci, is being reported from different parts of the world. Resistance to macrolides in staphylococci may be due to active efflux (encoded by *msrA*) or ribosomal target modification (usually encoded by *ermA* or *ermC*). MLS<sub>B</sub> resistance can either be constitutive (MLS<sub>Bc</sub>) or inducible (MLS<sub>Bi</sub>). In the MLS<sub>Bc</sub> phenotypes, *erm* genes are expressed consistently and the isolates are resistant to these classes of drugs. MLS<sub>Bi</sub> isolates are resistant to the inducer but remain susceptible to the non inducer antibiotic during antimicrobial susceptibility testing.<sup>1-6</sup> In such cases clindamycin therapy may lead to selection of constitutive *erm* mutants leading to failure of the therapy. Routine in vitro testing of the isolates when erythromycin and clindamycin discs are not placed adjacent to each

other; may fail to detect isolates with inducible resistance to clindamycin resulting in treatment failure.<sup>3,7</sup>

This prospective study was therefore conducted to find the prevalence of inducible clindamycin resistance in *Staphylococcus aureus* isolates in our tertiary care teaching hospital.

**MATERIAL AND METHODS:**

A total of 380 non duplicate clinical isolates of *Staphylococcus aureus* collected between over a two years period (2012-13) were included in the study. The isolates were collected from various clinical specimens ( pus, blood urine, sputum, sterile fluids, etc. ) obtained from inpatients and out patients of our tertiary care institute. All the isolates were identified by the standard procedures. Resistance to methicillin was detected using cefoxitin disc (30 µg) diffusion method. The zone diameters were measured as per the CLSI guidelines.<sup>8,9</sup>

**D test:-<sup>9-11</sup>**

Muller Hinton agar plates were overlaid with the standard inoculum of test strain and erythromycin (15 µg) and Clindamycin (2 µg) discs were placed at a distance of 15 mm apart from each other. The plates were incubated at 35°C for 16-18 hours. The results were interpreted as per CLSI guidelines Blunting of the clear circular area of no growth around the clindamycin disc on the side adjacent to the erythromycin disc is taken as D test positive (MLS<sub>b</sub>i phenotype).

**RESULTS:**

Resistance to methicillin was detected in 46.84% (178/380) of *S.aureus* isolates. Inducible clindamycin resistance was detected in 21.57% of the total isolates .The results have been tabulated in table 1.

**DISCUSSION:**

With reports of resistance to methicillin in clinical isolates of *Staphylococcus aureus* , the treatment option remain limited. The MLS (macrolide – lincosamide - streptogramin) group of antimicrobials offers an alternative therapeutic option with clindamycin being preferred because of its excellent pharmacokinetic properties.<sup>2,10</sup> There are reports of resistance to this group of antibiotics from different parts of the world.<sup>2,10,12</sup> In the present study resistance to erythromycin was observed in 35.26% (134/380) of the isolates. Different studies have also reported high level of resistance to this drug.<sup>2,11</sup> Inducible clindamycin resistance was noted in 21.5% (82/380) isolates. However many other studies have reported higher percentage and even lower percentage of inducible clindamycin resistance.<sup>2,6,10,11</sup> This may be due to difference in the geographical areas and the pattern of antibiotics being used there . Methicillin resistance was detected in 46.84% of the study isolates. Comparison between inducible clindamycin resistance in MRSA (60/178) and MSSA (22/202) was found to be statistically significant.<sup>11</sup>

Clinical Microbiology laboratories may be unable to detect inducible clindamycin resistance if the two discs (erythromycin and clindamycin) are not used in approximation/ or are used at non adjacent positions.<sup>3,7</sup>

We recommend that D test should be included in the routine antimicrobial susceptibility testing of staphylococci for detection of inducible clindamycin resistance as it is inexpensive, simple to perform and easy to interpret. This would help in deciding the appropriate therapy thus preventing treatment failure

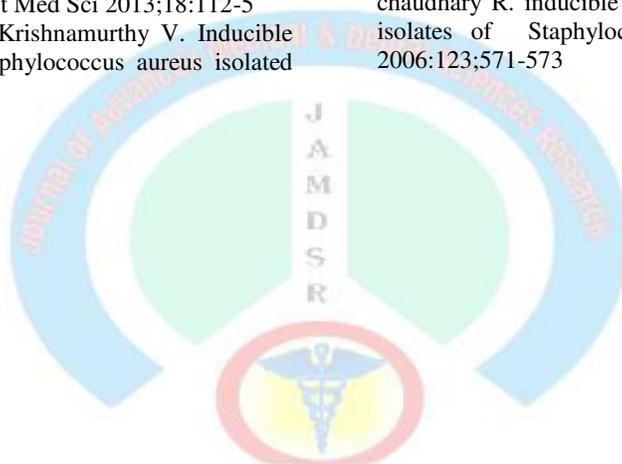
**Table 1:** Isolates of *Staphylococcus aureus* with different resistant patterns

Organism	No. of Isolates	E-resistant, sensitive, D test (MLS <sub>b</sub> i)	C- E-resistant, sensitive, D test positive	C- E-resistant, sensitive, D test negative (MS)	C- E-resistant, resistant (MLS <sub>b</sub> c)	C- E-sensitive, C-sensitive
MRSA	178	60 (33.7%)		12 (6.74%)	20 (11.23%)	86 (48.31%)
MSSA	202	22 (10.89%)		7 (3.46%)	13 (6.43%)	160 (79.20%)
	380	82		19	33	246

MRSA= Methicillin resistant *Staphylococcus aureus*, MSSA=Methicillin sensitive *Staphylococcus aureus*, (MLS<sub>b</sub>c) = Constitutive resistance to clindamycin, (MLS<sub>b</sub>i)= Inducible resistance to clindamycin, MS = MS phenotype, E= Erythromycin, C=Clindamycin

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