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Inducible Clindamycin Resistance In Staphylococcus Aureus Isolates From School Children

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A B S T R A C T

Introduction-

Staphylococcus aureus shows increasing resistance to macrolide-lincosamide-streptogramin B (MLSB) antibiotics due to the presence of the erm gene, which mediates either inducible (iMLSB) or constitutive (cMLSB) resistance. Inducible resistance poses diagnostic challenges, as isolates may appear erythromycin-resistant but clindamycin-sensitive in routine tests. Failure to detect iMLSB can result in therapeutic failure. Performing a D-test is essential to identify inducible resistance and ensure appropriate antibiotic selection for effective treatment of Cutaneous and subcutaneous infections.

Objective-

This study was undertaken to determine the presence of MLSB resistance phenotypes in Staphylococcus aureus isolates obtained from school children (carriers), using an in-vitro phenotypic detection method.

Materials and methods-

142 non-duplicate Staphylococcus isolates were tested for antibiotic susceptibility by Kirby-Bauer method, and inducible clindamycin resistance was detected using the D-test on erythromycin-resistant strains per CLSI guidelines.

Result-

Out of 142 isolates, 46 (32.39%) were erythromycin-resistant. Among them, 16 (11.26%) showed inducible and 6 (4.2%) constitutive clindamycin resistance. Twenty-four (16.90%) had the MS phenotype. These findings highlight the importance of D-testing in erythromycin-resistant strains to detect iMLSB resistance and ensure appropriate antibiotic therapy, preventing treatment failure.

Conclusion-

The low prevalence of inducible clindamycin resistance suggests rational antibiotic use; however, continuous surveillance is essential to monitor emerging resistance and prevent outbreaks of resistant Staphylococcus aureus strains.

Keywords: Staphylococcus aureus, D test, Inducible clindamycin resistance, MRSA

Introduction-

Staphylococcus aureus frequently causes community-acquired infections, and its growing resistance to various antibiotics, including methicillin, represents a major public health concern worldwide.[4]

The rise of multi-drug-resistant *Staphylococcus* strains, particularly in the community, has reduced therapeutic options. This problem is worsened by widespread use of macrolide-lincosamide-streptogramin B (MLSB) antibiotics, leading to increased cross-resistance among *Staphylococci*.

Macrolide, lincosamide, and streptogramin B (MLSB) antibiotics are widely employed in the treatment of staphylococcal infections. However, extensive usage has contributed to a notable rise in resistance, particularly to clindamycin, among *Staphylococcus* species.[3]

Clindamycin, belonging to the macrolide-lincosamide-streptogramin B (MLSB) antibiotic group, is frequently prescribed for treating skin and soft tissue infections caused by *Staphylococcus aureus*. Nevertheless, widespread use of MLSB antibiotics has resulted in resistance development, mainly mediated by *erm* genes. These genes encode methyltransferase enzymes that modify the bacterial ribosome, reducing the binding affinity of MLS_B antibiotics and resulting in either inducible ($iMLS_B$) or constitutive ($cMLS_B$) resistance phenotypes.[1]

Detecting inducible clindamycin resistance in routine laboratory testing is challenging because isolates often appear erythromycin-resistant and clindamycin-sensitive in vitro when the antibiotics are not placed close to each other.[4]

MATERIALS AND METHODS-

This study was carried out in the Department of Microbiology at our medical college. Approval was obtained from the Institutional Ethics Committee (Ref: MDC/DOME/386).

142 non-duplicate *Staphylococcus* isolates were tested for antibiotic susceptibility by Kirby-Bauer method, and inducible clindamycin resistance was detected using the D-test on erythromycin-resistant strains per CLSI guidelines.

The study was conducted among children of age group 5-16 years from different schools of Urban Health Centre (UHC)

Staphylococcus aureus was identified phenotypically by growth on MacConkey agar, Gram staining, catalase test, and both slide and tube coagulase tests. Antimicrobial susceptibility testing against penicillin, cefoxitin, erythromycin, and clindamycin was performed using the standard disc diffusion method according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Erythromycin and clindamycin discs were placed 15 mm apart (edge to edge).

Isolates showing resistance to erythromycin (zone diameter $\leq$ 13 mm) but sensitivity to clindamycin (zone diameter $\geq$ 21 mm) were further tested for methicillin resistance using the cefoxitin disc diffusion method with a 30 µg disc.

RESULTS-

Antibiotic susceptibility was evaluated in 142 clinical isolates.

46 (32.39%) demonstrated erythromycin resistanceFurther characterization of these Erythromycin-resistant isolates revealed different patterns of Clindamycin resistance.

16 isolates (11.26%) demonstrated inducible Clindamycin resistance, classified as the inducible macrolide-lincosamide-streptogramin B MLS_B phenotype, as determined by the D-test. Constitutive clindamycin resistance was detected in 6 isolates (4.2%), showing stable resistance to both erythromycin and clindamycin. The remaining 24 isolates (16.90%) displayed the MS phenotype, resistant to erythromycin but sensitive to clindamycin, without D-zone blunting. These results emphasize the need for routine detection of inducible clindamycin resistance in erythromycin-resistant isolates to guide effective treatment decisions.

Identification of resistance phenotypes is crucial for guiding effective treatment strategies and for preventing therapeutic failures due to unrecognized inducible resistance mechanisms.

Among the exposed group, 46 individuals (32.39%) were carriers of *S. aureus*, with 6 isolates (4.2%) exhibiting inducible clindamycin resistance.

Table 1 -Number of Staphylococcus aureus isolates(n=142)

Nature of isolates	Total Number
MSSA	113(79.8%)
MRSA	29(20.42%)

Discussion

The rise of resistance to macrolide-lincosamide-streptogramin B (MLSB) antibiotics poses a major challenge to effective antimicrobial therapy. In the present study, 33.8% of the isolates demonstrated resistance to Erythromycin. Of these, 11.7% demonstrated inducible clindamycin resistance (iMLSB phenotype), 4.4% showed constitutive resistance (cMLSB phenotype), and 17.4% exhibited the MS phenotype. These findings are consistent with previous studies that report a varying prevalence of MLS_B resistance phenotypes depending on geographic location, bacterial species, and antimicrobial usage patterns.

Inducible clindamycin resistance is of particular concern in clinical practice, as it may remain undetected in standard susceptibility testing without the use of a D-test. When not recognized, iMLSB strains may appear susceptible to Clindamycin in vitro but can lead to therapeutic failure in vivo due to the induction of resistance during treatment. Therefore, the detection of $iMLS_B$ strains is crucial to avoid ineffective therapy, especially in infections caused by Staphylococcus aureus and Streptococcus species, where Clindamycin is commonly used as an alternative to beta-lactams.

The findings of our study align with existing literature regarding MLSB resistance, particularly in Staphylococcus aureus. Similar to our results, Timsina R et al. reported a significant prevalence of inducible clindamycin resistance (iMLSB), emphasizing the importance of routine D-testing in Erythromycin-resistant isolates to avoid therapeutic failure. While our study focused on phenotypic characterization—identifying 11.7% iMLSB, 4.4% cMLSB, and 17.4% MS phenotypes—Timsina R et al. reported an iMLSB prevalence of 23.4% overall and 76.4% among MRSA strains, exceeding many earlier reports.[1] Additionally, they conducted molecular analysis and detected ermA (66.67%), ermB (13.33%), and ermC (73.38%) genes among iMLSB isolates.[1]

In our study conducted in school children, 33.8% of isolates were resistant to erythromycin, with 11.7% showing the iMLSB phenotype, 4.4% cMLSB, and 17.4% MS phenotype. In contrast, the study by Renushri et al., also conducted among healthy carriers, including nursing and pharmacy students, a lower prevalence of inducible clindamycin resistance was observed (11.4%) and did not detect any constitutive (cMLSB) resistance. The higher resistance in our study may be attributed to differences in age groups, geographic region, sample collection sites, or background antibiotic exposure. Our detection of the cMLSB phenotype—absent in their study—suggests the possibility of stable resistance even in a community setting. Both studies emphasize the importance of D-testing for accurate detection of iMLSB resistance, especially in erythromycin-resistant isolates. Despite being conducted in non-hospitalized populations, our findings reveal significant resistance levels, underlining the need for antimicrobial stewardship and surveillance even in community-based, pediatric populations.[2]

Mokta KK et al. reported a slightly higher erythromycin resistance rate (39.14%) and a predominance of the cMLSB phenotype among MRSA isolates (29.62%), followed by iMLSB (28.39%) and MS phenotype (13.58%).[5] The lower prevalence of resistance in our study may be attributed to the community-based setting among school children, in contrast to the hospital-based population in their study, which is more likely to exhibit higher resistance rates due to prior antibiotic exposure and clinical infections.[5]

In contrast, our study showed a greater proportion of the MS phenotype and lower cMLSB rates, reflecting possible regional or geographical variations. Mokta KK et al. also found a significantly higher MRSA prevalence among inpatients, supporting the role of hospital environments in resistance selection—consistent with our emphasis on routine D-testing to prevent therapeutic failures. Despite differences in methodology, both studies highlight the importance of ongoing local surveillance and phenotypic testing to guide effective clindamycin use and curb the spread of inducible resistance.[5] The lower prevalence of resistant strains in our community-based study may be attributed to reduced antibiotic exposure compared to hospitalized patients.[5]

R. P. Adhikari et al., particularly regarding the prevalence and clinical implications of inducible clindamycin resistance in Staphylococcus aureus. Adhikari et al. reported significantly higher rates among MRSA isolates—27.9% iMLSB and 54.4% cMLSB—along with elevated erythromycin and clindamycin resistance. Both studies emphasize the limit2ed effectiveness of clindamycin in erythromycin-resistant MRSA due to the low MS phenotype prevalence and highlight the critical role of routine D-testing to prevent therapeutic failures. Adhikari et al. also associated high resistance with excessive macrolide use, supporting our recommendation for antimicrobial stewardship and regular phenotypic screening.[4]

4. Limitation-

Our study did not include genotypic testing.

5. Conclusion-

The low prevalence of inducible clindamycin resistance in the study population suggests prudent antibiotic use, ongoing antimicrobial surveillance remains essential to prevent potential outbreaks caused by resistant strains.

These differences highlight both community and healthcare-associated risks of clindamycin resistance and reinforce the need for routine D-testing and molecular surveillance,

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