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UNMASKING THE INDUCIBLE CLINDAMYCIN RESISTANCE AMONG STAPHYLOCOCCUS AUREUS: A VITAL DIAGNOSTIC IMPERATIVE FOR EFFECTIVE TREATMENT.

Clinical Microbiology

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ABSTRACT

Introduction- Clindamycin is an important drug in the treatment of various Staphylococcal aureus infection including both MRSA and MSSA strain. The presence of inducible clindamycin resistance can lead to treatment failure with clindamycin.Hence, the accurate detection of ICR is mandatory to guide the clinicians for appropriate treatment modalities and to prevent misuse of antibiotics. **Aim-** To determine inducible and constitutive clindamycin resistance among clinical isolates of S. aureus. **Material and Method-** The present cross sectional retrospective laboratory based study includes non-duplicate 456 S.aureus isolates obtained from various clinical samples. Antimicrobial susceptibility testing was carried out, including detection of inducible clindamycin resistance by vitek-2 identification and antimicrobial susceptibility testing (ID/AST) system by using AST-GP67 card. **Results-** Total of 456 Staphylococcus aureus were isolated, among them 185 were Methicillin sensitive Staphylococcus aureus (MSSA) and 271 were Methicillin resistant Staphylococcus aureus (MRSA).Prevalence of iMLSB, cMLSB and MS phenotype of among all clinical isolates of s.aureus were 34% ,6% and 22% respectively. **Conclusion-** The present study recommends routine testing of inducible clindamycin resistance to guide optimum therapy and to avoid treatment failure.

KEYWORDS

Staphylococcus Aureus, Inducible Clindamycin Resistance(ICR), VITEK-2

INTRODUCTION

Staphylococcus aureus is one of the most common pyogenic bacteria infecting man. The determination of antimicrobial susceptibility of a clinical isolate is often crucial for optimal antimicrobial therapy of infected patients. Emergence of methicillin resistance in Staphylococcus aureus has left us with very few therapeutic alternatives available to treat Staphylococcal infections[1]. The macrolide-lincosamide-streptogramin B (MLSB) family of antibiotics serves as one such alternative, with clindamycin being the preferred agent due its excellent pharmacokinetic properties. Clindamycin is an alternative drug for infections due to Staphylococcus aureus in case of intolerance to penicillin or resistance to methicillin. Furthermore, clindamycin represents an attractive option for several reasons: 1)clindamycin is available in both intravenous and oral formulations.2) the drug has a remarkable distribution into the skin and skin structures. 3) community-acquired methicillin-resistantS. aureus (CA-MRSA), which has rapidly emerged in recent years as a cause of skin and soft-tissue infections, is frequently susceptible to several antibiotics, including clindamycin[2,3].

The development of resistance in Staphylococcus species to Macrolide, lincosamide and streptogramin B has limited the use of these antibiotics. Macrolide resistance may be due to enzymes encoded by a variety of erm genes-MLS B phenotype and may be constitutive (cMLS B phenotype) or inducible (iMLS B phenotype). Another mechanism is active efflux pump encoded by the mrs A gene (MS phenotype). The MS and iMLS B phenotypes are indistinguishable by using standard susceptibility test methods, but can be distinguished by erythromycin-clindamycin disk approximation test (D-test), automated vitek-2 system and demonstration of resistance genes by molecular methods[4].Therefore, the detection of its three resistant phenotypes (MS, iMLSB, cMLSB) is crucial for guiding appropriate antimicrobial therapy.

MATERIALS AND METHOD

This laboratory based retrospective cross-sectional study was undertaken in the Department of Microbiology at Metropolis healthcare private limited, Surat over a time frame of one and half year from AUG 2024- JAN 2026.The study included 456 non-duplicate isolates of S. aureus from various clinical samples of indoor (IPD) and outdoor (OPD) patients received over a period of 1.5 years. Various clinical samples included pus, blood, urine, respiratory specimen, genital specimen, body fluid etc. and distribution of S. aureus strains from origin of recovery is shown in [Table/Fig-1]. Gram staining was done and the culture specimens were inoculated onto Blood agar and MacConkey agar media by standard techniques. The plates were incubated at 37°C under aerobic condition in an incubator for 24 hours and the growth was observed next day.

All the S. aureus were subjected to antimicrobial susceptibility testing including detection of inducible clindamycin resistance and cefoxitin screening test by vitek-2 identification and antimicrobial susceptibility testing (ID/AST) system by using AST-GP67 card, which incorporated to the Advanced Expert System (AES), software which validates and interprets susceptibility test results and detects antibiotic resistance mechanisms. The CLSI susceptibility breakpoints were used. The Vitek 2 AST-GP67 card was used according to the manufacturer's recommenda-tions. Briefly, three to five colonies of an 18 to 24 h-old culture of S. aureus were inoculated in a 0.45% NaCl solution and adjusted to a concentration equivalent to a 0.5 to 0.63 McFarland standard. The solution was then loaded with the card in the Vitek 2 system. The incubation period was determined by the Vitek 2 system. Two wells are used to detect inducible clindamycin resistance in the Vitek 2 card: One with 0.5 mg of clindamycin/liter and another one with a combination of 0.25 and 0.5 mg of clindamycin and erythromycin/liter, respectively. Both the instrument and the Advanced Expert System (AES) results were considered.
Three different phenotypes were isolated after testing and interpreted as follows:
1) iMLSB phenotype: induced clindamycin resistance.
2) cMLSB phenotype: exhibiting resistance to both erythromycin and clindamycin.
3) MS phenotype: demonstrating resistance to erythromycin but susceptibility to clindamycin

RESULT

456 Staphylococcal isolates included in the present study were tested for antimicrobial susceptibility testing including detection of inducible clindamycin resistance and cefoxitin screening test by vitek-2 identification and susceptibility testing (ID/AST) system by using AST-GP67 card.Of the total 456S.aureus isolates, the majority were isolated from pus swabs 367 (80%), then blood sample 21 (5%), blood sample 41(20.5%), respiratory specimen 20 (4%), tissue 14(3%), body fluids 14(3%) and urine 9(2%)(Chart-1).271(59%) of Staphylococcus aureus isolates were foundtobemethicillinresistant (MRSA)and 185(41%) tested sensitive tocefoxitin (MSSA)(Chart-2).

Among 456 S.aureus isolates, MS phenotype, iMLSB and cMLSB phenotypes were seen in 104 (22%), 156 (34%) and 27 (6%) isolates respectively(Table-1).Inducible Clindamycin resistance wassignificantaly higher in MRSA strains (48%)as compared to MSSA strains (15%). ConstitutiveClindamycin resistance in MRSA and MSSA strains were 21% and 26% respectively(Table-2).

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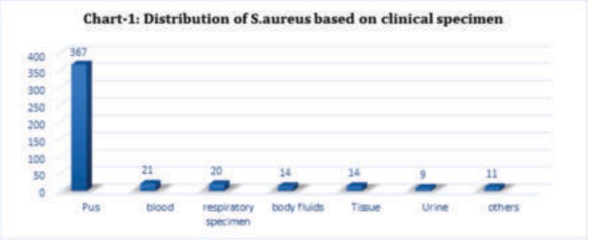
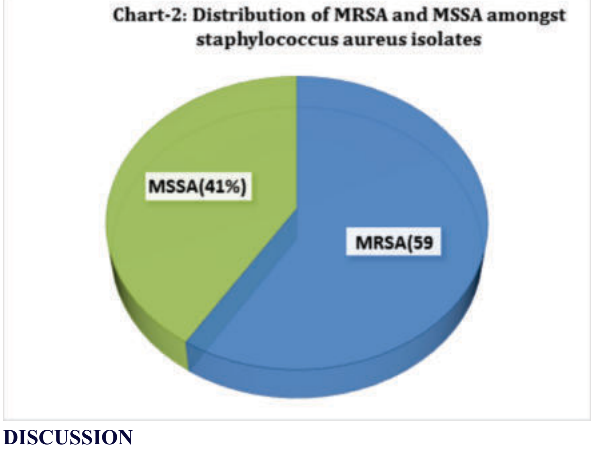


Table-1 :Detection of constitutive and inducible-clindamycin (MLSB)phenotypes.			
Organism	Inducible (iMLSB) resistance n (%)	Constitutive (cMLSB) resistance n (%)	MS Phynotype n(%)
S.aureus	156(34%)	27(6%)	104(22%)

Table-2:Distribution among MRSA and MSSA		
Organism	Inducible (iMLSB) resistance n (%)	Constitutive (cMLSB) resistance n(%)
MRSA	129(48%)	21(8%)
MSSA	27(15%)	6(3%)



DISCUSSION

The increasing frequency of Staphylococcal infections among patients and changing patterns in antimicrobial resistance have led to renewed interest in the use of clindamycin therapy to treat such infections. Clindamycin, a member of the MLSB family, is commonly employed for treating skin and soft tissue infections due to its tolerability, availability in oral form, excellent tissue penetration, good bioavailability, and cost-effectiveness. Macrolide resistance may be constitutive or inducible in the presence of either a macrolide or a lincosamide inducer[(5)].

The VITEK systems from bioMerieux are fully automated instrumentswidely employed in clinical microbiology laboratories globally. These systems play a crucial role in species identification and antimicrobial susceptibility testing for various clinical isolates. VITEK Advanced Expert System (AES) is designed to analyze antimicrobial susceptibility testing (AST) results by utilizing a well-established knowledge base encompassing around 100 species and 20,000 MIC ranges. This allows the system to identify over 2,300 phenotypic antimicrobial resistances[(6)].

The present study evaluated that out of 456 isolates of S.aureus, 80% were isolated from pus samples followed by 5% from blood, 4% from respiratory specimen, 3% from bodyfluids, 3% from urine which was quite similar to the study reported by Sadanandan N[etal(7)]and Tiwari S[etal(8)].

Among 456 isolates of Staphylococcus aureus 271(59%) were MRSA and 185(41%) were MSSA which is comparable with the research under takenby Sadanandan N[etal(7)], Mokta KK[etal(9)] and Dahiya A[etal(10)].

In the current research work Inducible Clindamycin resistance ratewas 34 % and constitutive Clindamycin reistance (cMLSB) rate was 6% which is in accordance with study done by Urmi[etal(11)]and Panwala t.[etal(12)] while 22% isolates showed true Clindamycin susceptibility (MS phenotype)which is similar tothe findings reported by Sadanandan N[et al(7)], Panwala t.[et al(12)] and Lal UAP[et al(12)].These all studies shows that there is a wide variation in incidence of Clindamycin resistance among clinical isolates of Staphylococcus aureus in different geographical areas.The present research assessed that the rate of inducible Clindamycin resistance and constitutive Clindamycin reistance in MRSA was higher than that of MSSA strain of S.aureus isolates which is similar to study done by Panwala t.[et al(12)].The relationship between MRSA and ICR appears to be clinically insignificant even though a highly positive correlation coefficient is in present study observed. This is an alarming sign that Clindamycin therapy failure may occur without prior testing for inducible resistant phenotypes. It should be necessary to prepare local sensitivity data which help in guiding empiric therapy and for preparing antibiotic policy.

CONCLUSION

Treatment of staphylococcal infections has always been a challenge for the treating physician, particularly in the backdrop of changing resistance pattern. Keeping the mode of action, side effects and pharmacokinetics in mind of certain drugs like vancomycin and linezolid, clindamycin should be considered for the treatment of severe and resistant staphylococcal infections. Different studies done across the globe show that prevalence of inducible clindamycin resistance varies from place to place. Therefore, we recommend that whenever clindamycin is intended for treatment of staphylococcal infection the clinical microbiology laboratory should test the isolated organism for iMLSB before clindamycin susceptibility is reported. Present study giving a magnitude of clindamycin resistance among clinical isolates of S. aureus from this region of the country will help clinicians choose an appropriate therapy.

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