IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 23, Issue 7 Ser. 3 (July. 2024), PP 01-05
www.iosrjournals.org

The prevalence of inducible (MI SB) and constitutis clindamycin resistance (eMLSB) among the clinical isolates

[1]Deepanshu chaudhary, [2]Purvi Ujlayan
[1]Muzaffarnagr medical College, begrajpur industrial area, Muzaffarnagar
[2]Muzaffarnage medical College, begrajpur industrial area, Muzaffarnagar

Date of Submission: 01-07-2024 Date of Acceptance: 11-07-2024

I. INTRODUCTION

The antibioties Macrolide, Lincosamide, and Streptogramin (MLS) are chemically different, butthey have similar inhibitory effects on bacterial protein synthesis. MLS antibiotics arewidelyused in the treatment of Gram-positive infections. However, due to their widespread use, there hasbeen an increase in the number of MLS antibiotic-resistant staphylococci strains[1]. Clindamycin isan alternative drug for Staphylococcus aureus infections in case of Intolerance to penicillin orresistance to methicillin. Furthermore, clindamycin represents an attractive option for severalreasons.First,clindamycinisavailableinbothintravenousandoralforms.Second,themedicationhasa remarkablepenetrationintoskinandskinstructures.

Finally,methicillin-resistantS.aureus (CA-MRSA), which has recently emerged as a cause ofskinandsoft-tissueinfectionsisfrequentlysusceptibletoseveralantibiotics,includingclindamycin[2].

Finally, clindamycin has been shown to inhibit the production of toxins and virulence factors ingram-positiveorganismsbyinhibitingproteinsynthesis.Clindamycinhasexcellenttissuepenetration (exceptfor the central nervous system),accumulatesin abscesses,and requires norenaladjustments.MacrolideantibioticresistanceinStaphylococcusaureusandcoagulase-negative staphylococci (CNS) can be attributed to an active efflux mechanism encoded by msrA(which confers resistance to macrolides and type B streptogramins only) or to ribosomal targetmodificationaffectingmacrolides,lincosamide,andtypeBstreptogramins(MLSBresistance)[3].erm genes encode enzymes that provide inducible or constitutive resistance to MLSagents by methylating the 23S rRNA, reducing MLS agent binding to the ribosome[4]. The MSphenotype (resistance to erythromycin, inducible resistance to streptogramin B, and susceptibilitytoclindamycin)is conferredbythemsrAgeneviaeffux.

Inducible MLSB resistance strains show in vitroresistance to14- and15-membermacrolides(e.g., erythromycin), but appear susceptible to 16-member macrolides, lincosamides, and type Bstreptogramins;constitutiveMLBresistancestrainsshowinvitroresistancetoallagents.Standard susceptibility test methods, such as broth-based or agar dilution susceptibility tests,cannot detect inducible MLB resistance[5]. This study will be undertaken to find out the prevalenceof inducible (iMLSB) and constitutive clindamycin resistance (MISB) among the clinical isolatesofS.aureus.

AIMAND OBJECTIVE:

Tofindouttheprevalenceofinducible(MISB)andconstitutisclindamycinresistance(eMLSB)amongtheclinicalisolates ofS.aureus.

II. MATERIALANDMETHODS

STUDY DESIGN: The prospective study was conducted in the Department

ofMicrobiology,MMC.Muzaffarnagar,

STUDYPLACE :-MuzaffarnagarMedicalCollegeandhospital

STUDYDURATION:15days

SAMPLESIZE:-Atotalof30 non-duplicateclinicalisolates ofS.aureus werecollected

SAMPLING TECHNIQUE:Simplerandomtechnique

STUDY PROCEDURE: thirty non-duplicate clinical isolates of S. aureus were subjected to D test.Testing of methicillin resistance were done with 30 ug dise of cefoxitin as per Cimical Laboratoryand Standard Institute (CLSI), 2014 guidelines[6]. D-test was performed by placing clindamycinCLI disc 2ug and erythromycin ERY disc 15 approximately 15-26 mm apart measured edge toedge on a Muller Hinton agar plate that has feet inoculated with a Staphylococcus isolate (0.5McFarland standard) and incubated at 35°C in ambient air. Flattening of the zone of inhibitionadjacenttotheerythromycindisc(referred toasaD-zone)inducibleclindamycinresistance.

D-testwasperformedasperClinicalLaboratoryandStandardInstitute(CLST),2014guidelines [6]. Staphylococcus aureus ATCC 25923 strains were used to check the quality control of ERY andCLIdisc.Interpretationof erythromycinandclindamycinzoneswasdoneaccordingtothedescriptiongivenbelowinthetable 1.

Table1. Interpretationoferythromycin, clindamycin zonesins.aureus

	SENSITIVE	INTERMEDIATE	RESISTANT
ERYTHROMYCIN	≥23mm	14-22mm	≤13mm
CLINDAMYCIN	≥21mm	15-20mm	≤14mm

CLSIGuideline2014:performancestandardsforantimicrobialdiscsusspetiblitytestTable2.D-testphenotypecategoriesandtheircharacteristics

Table 2. D-test phenotype categories and their characteristics

D test phenotype	Resistance phenotype	CLI result	ERY result	Double disc test description
D+	Inducible MLS_B	S	R	Blunted, D shaped clear zone around CLI disc proximal to ERY disc
D-	MS	S	R	Clear Zone around CLI disc
R	ConstitutiveMLS_B	R	R	Growth upto CLI and ERY discs
S	No resistance	S	S	Clear zone around discs

STATISTICAL ANALYSIS: The data wascompiled in the form of table's andpercentages.**ETHICAL CLEARANCE:** Ethical clearance was taken from ethical committee ofMuzaffarnagarMedicalCollege,Muzaffarnagar.

III. REVIEWOFLITERATURE -

Staph bacteria are one of the most common causes of skin infections and sometimes producerelatively minor skin infections such as pimples and boils. However, they can cause more seriousillnessessuchassurgicalwoundinfections,bloodstreaminfections,boneinfections,andpneumonia. In the past few decades, a more dangerous form of staph has emerged. This form isknown as methicillin-resistant

Staphylococcus aureus and is usually referred to by the acronymMRSA. What sets MRSA apart is that it is resistant to an entire class of antibiotics called beta-lactams.Thisgroupofantibioticsincludesmethicillin,andthemorecommonlyprescribedpenicillin,amoxicillin,andoxacillinamongothers.

Inducible clindamycin resistance in staphylococci and streptococci can be detected by the **diskdiffusion method** using clindamycin and erythromycin disks or broth microdilution methods. **D-zone** test is performed by disk diffusion, placing a 15-µg erythromycin disk in proximity to a 2-µgclindamycin disk on an agar plate that has been inoculated with a staphylococcal or streptococcalisolate;theplateis thenincubatedovernight.

Astudyconductedby**Prabhuetal**.inIndiaevaluatedtheprevalenceofinducibleandconstitutiveclindamycinresistance among100clinicalisolatesofStaphylococcusaureus.Thestudy foundthat17% of theisolateswereinducibly resistanttoclindamycin,while4%wereconstitutivelyresistant.Thestudyalsofoundthattheresistancetoerythromycinwassignificantlyhigheramongtheinduciblyresistantisolates comparedtotheconstitutivelyresistantisolates.[7]OnesuchstudybyVGuptastudywasaimedtofindoutthepercentageofStaphylococcusaureushavinginducibleclindamycinresistance(iMLSB)inourgeographicareausingD-test.Also,wetriedtoascertaintherelationshipbetweenMethicillin-resistantStaphylococcusaureus(MRSA)andinducibleclindamycinresistance,associationoftheseiMLSBisolateswith communityornosocomialsettingandtreatmentoptionsfortheseiMLSBisolates.Among200Staphylococcusaureusstrains,50(25%)werefoundtobeMRSAand36wereD-testpositive.Also,MRSAisolatesshowedbothhigherinducibleresistanceandconstitutiveresistancetoclindamycinascomparedtoMethicillin-sensitiveStaphylococcusaureus(MSSA).Outof36isolatesofStaphylococcusaureusshowinginducibleclindamycinresistance,24werefromtheoutpatientdepartmentand12wererecoveredfromindoorpatients.AllisolatesofStaphylococcusaureusshowed100%sensitivitytovancomycinandlinezolid.[8]

Overall, these studies suggest that inducible resistance to clindamycin is more common amongclinical isolates of S. aureus than constitutive resistance. Additionally, the prevalence of inducibleresistance is higher among MRSA isolates than MSSA isolates. These findings highlight theimportance of identifying the resistance mechanisms of S. aureus isolates to guide the selection ofappropriateantibioticsforthetreatmentofinfectionscausedbythispathogen.

IV. RESULTS

In our study, 28 (92%) of Staphylococcus aureus isolates were found to be methicillin resistant(MRSA) and 3 (8%) tested sensitive to cefoxitin (MSSA) (Table 3). A total of 11(38%) 5. aureusisolates belonged to iMLSB phenotype. Among 28 MRSA, a total of 11 (39.1%) exhibited iMLS,resistance. 5(17.40%) were of cMLSBphenotype and 3 (8.70%) belonged to MS phenotype.Among 3 isolates of MSSA only 1 (25%) strains exhibited iMLS resistance and rest 2(75%)strainsweresensitivetoclindamycin(Table3).

Table3. Distributionofisolates

Susceptibilitypattern(phenotype)	MRSA(%)	MSSA(%)	Total(%)
ERY-S,CLI-S	9(34%)	2(75%)	11
ERY-R,CLI-R (ConstitutiveMLSB)	5(17%)	0(0%)	5
ERY-R,CLI-S,D-test positive (inducibleMLSB	11(39%)	1(25%)	11
ERY-R,CLI-S,D-Test negative(MS)	3(8%)	0(0%)	3
Total	28	3	30

V. Discussion

Our study revealed an extremely high percentage of MRSA 92(92%). A recent study carried outby the Indian Council of Medical Research (ICMR) in the fifteen selected centres of the countryduring the year 2008- 2009, has reported prevalence of MRSA varying from 21% atApolloHealthCentre(AHC),Hyderabad to84%at RegionalInstituteofMedicalSciences,Imphal[9].

In Korea, the prevalence of MRSA has been estimated to be more than 70% among all clinicalisolatesinearly2010.[10]

PrevalenceofclindamycinresistancefromdifferentcentresinIndiaisgivenintable4.

Author'sname	iMLSB Phenotype %	cMLSB Phenotype %	MS Phenotype %	iMLSB Phenotype %	cMLSB Phenotype %	MS phenotype %

Grapelli etal(2006)[11]	30	38	12	10	15	12
Angel et al(2008)[12]	64	0	12	5	0	25
Ciraj etal(2009)[13]	38	15.3	0	12.9	0	9.7
Vandanaetal(2009)[14]	48.7	.05	37.7	9.5	1.4	56.1
Shrestha etal(2009)[15]	39.7	44.4	11.1	0	2.7	13.7
Deotale etal(2010)[16]	34	9	30	2	0	5
Patetal(2010)[17]	43.6	38.8	18.7	6.93	7.3	10.9
Prabhu etal(2011)[7]	20	16.7	13.3	6.2	6.2	6.2
Mittal et al(2013)[18]	47	9	14	13	7	25

According to reports from different regions of India, the prevalence of inducible clindamycinresistance varies from 20% to 64%. In our centre, it is 38%, similar to reported by Ciraj et al.However,theincidenceofconstitutiveandinducibleMLSresistancevariesbygeographicregionand even from hospital to hospital, with 7 some studies showing higher local incidence of eitherconstitutive orinducible MLS,resistanceinstaphylococcalisolates[19,20,21]

REFERENCES

[1]. Lina G. Quaglia A. Reverdy ME, Leclercq R. Vandenesch F and Etienne J. Distribution ofgenes encoding resistance tomacrolides.lincosamidesandstreptograminsamongstaphylococciAntimicroAgents1999,43:1062-1066.

[2]. Tristan. A. Bes M. Meugnier H. Lina G, Bozdogan B, Courvalin P. Reverdy ME EnrightMC, Vandenesch F. Etienne J.Globaldistribution of Panton Valentine leukocidin-positivemethicillin-resistantStaphylococcusaureus.Emerg InfectDis.2007:13(1):594600.

[3]. Delialioglu N. Aslan G. Ozturk C. Baki V. Sen S and Emekdas G. Inducible ClindamycinResistance in Staphylococci isolated fromClinicalSamples.Jpn J Infect Dis. 2005;58:104-106.

[4]. Jenssen WD, Thakker-Varia, Dublin DT and Weinstein MP. Prevalence of macrolide-lincosamide-streptogramin

BresistanceandermgenesclassesamongelinicalstrainsofStaphylococciandStreptococci.AmtimicrobAgentsChemother.1987;31:883-888.

[5].

FiebelkornKR.CrawfordSA,McElmeelML.JogersonJH.PracticaldiskdiffusionmethodfordetectionofinducibleclindamycinresistanceinStaphylococcusaureusandcoagulase-negativestaphylococci.JClinMicrobiol.2003;41:4740-4744.

[6]. ClinicalandLaboratoryStandardsInstitute.PerformanceStandardsforAntimicrobialSusceptibilityTesting:Twenty-FourthInformationalSupplement.CLSIdocument2014;56:883-639.

[7]. Prabhu K, Rao S, Rao V. Inducible clindamycin resistance in Staphylococcus aureusisolatedfromclinicalsamples.J.Lab.Phys.2011;3:25-27.

[8]. GuptaV,DattaP,RaniH, ChanderJ. InducibleclindamycinresistanceinStaphylococcusaureus:AstudyfromNorthIndia.J PostgradMed2009;55:176-9.

[9]. IndianNetworkforSurveillanceofAntimicrobialResistance(INSAR)Group.Methicillinresistant Staphylococcus aureus (MRSA) in India: Prevalence & susceptibility patternIndia.2013;137:363-369.

[10]. ChenCJ, HuangYC. NewEpidemiologyofStaphylooccusaureusInfectioninAsia. ClinMicrobiolInfect.2014;20(7):605-623

[11]. Gadepalli R, Dhawan B, Mohanty S, Kapil A, Das BK, Chaudhry R. InducibleclindamycinresistanceinclinicalisolatesofStaphylococcusaureusInd JMedRes.2006123:571-573.

[12]. AngelMR,BalajiV, PrakashJ,BrahmadathanKN,MathewsMS. PrevalenceofInducibleclindamycin resistance in Gram-positive organisms in a tertiary care centre. Indian J MedMicrobiol.2008;26(3):262-264.

[13]. CirajAM, VinodP,SreejithG,RajaniK. InducibleclindamycinresistanceamongclinicalisolatesofStaphylococcus.IndJ PathMicrobiol.2009;52(1):49-51.

[14]. Vandana KE, Singh J, Chiranjay M, Bairy I. Inducible clindamycin resistance inStaphylococcusaureus:Reasonfortreatmentfailure.JGlobInfectDis.20091:76-77.

[15]. Shrestha B, Pokhrel BM, Mohapatra TM. Phenotypic characterization of nosocomialisolatesofStaphylococcusaureuswithreferencetoMRSA.JInfectDevCtries.2009;3(7):554-560.

[16]. Deotale V, Mendiratta DK, Raut U, Narang P . Inducible clindamycin resistance inStaphylococcusaureus isolatedfromclinicalsamples. IndJMedMicrobiol. 2010;15(28):124-126.

[17]. PalN,SharmaB,SharmaR,VyasL. Detectionofinducibleclindamycinresistanceamongstaphylococcal isolates from different clinical specimens in Western India. J PostgradMed.2010;56:182-185.

[18]. MittalV, KishoreS,andSiddiqueM. Prevalenceofinducibleclindamycinresistanceamongclinicalisolates of Staphylococcus aureus detected by phenotypic method: Apreliminaryreport.J InfectDisImmun.2013;5:10-13

[19]. Robert MC, Sutcliffe J, Courvalin P, Jensen LB, Rood J and Seppala H. Nomenclature formacrolide-lincosamide-streptograminBresistantdeterminants.JAntimicrobAgents.1999;43:2823-2830.

[20]. Jenssen WD, Thakker-Varia, Dublin DT and Weinstein MP. Prevalence of macrolide-lincosamide-streptogramin B resistance and erm genes classes among clinical strains ofStaphylococciandStreptococci.AmtimicrobAgentsChemother.1987;31:883-888.

[21]. DiModugno, V.,M. Guerrini, S. Shah, andJ. Hamilton-Miller. Low-levelresistancetooleandomycinasamarkerofermA instaphylococci.J AntimicrobChemother.2002;49:423–430.

SUMMARY

The antibioties Macrolide, Lincosamide, and Streptogramin (MLS) are chemically different, butthey

have similar inhibitory effects on bacterial protein synthesis. MLS antibiotics arewidelyused in the treatment of Gram-positive infections. However, due to their widespread use, there hasbeen an increase in the number of MLS antibiotic-resistant staphylococci strains. Clindamycin isan alternative drug for Staphylococcus aureus infections in case of Intolerance to penicillin orresistance to methicillin. Furthermore, clindamycin represents an attractive option for severalreasons.First,clindamycinisavailableinbothintravenousandoralforms.Second,themedicationhasa remarkablepenetrationintoskinandskinstructures.

Finally,methicillin-resistantS.aureus(CA-MRSA), whichhasrecentlyemergedasacauseofskinandsoft-tissueinfectionsisfrequentlysusceptibletoseveralantibiotics,includingclindamycin.

Finally, clindamycin has been shown to inhibit the production of toxins and virulence factors ingram-positiveorganismsbyinhibitingproteinsynthesis.Clindamycinhasexcellenttissuepenetration (except for the central nervous system), accumulates in abscesses, and requires norenaladjustments.MacrolideantibioticresistanceinStaphylococcusaureusandcoagulase-negative staphylococci (CNS) can be attributed to an active efflux mechanism encoded by msrA(which confers resistance to macrolides and type B streptogramins only) or to ribosomal targetmodificationaffectingmacrolides,lincosamide,andtypeBstreptogramins(MLSBresistance).erm genes encode enzymes that provide inducible or constitutive resistance to MLSagents by methylating the 23S rRNA, reducing MLS agent binding to the ribosome. The MSphenotype (resistance to erythromycin, inducible resistance to streptogramin B, and susceptibilityto clindamycin) is conferred by the msrA gene via effux. Inducible MLSB resistance strains showinvitroresistanceto14-and15-membermacrolides(e.g.,erythromycin),butappearsusceptibleto 16-member macrolides, lincosamides, and type B streptogramins; constitutive MLB resistancestrainsshowinvitroresistancetoallagents.

Standard susceptibility test methods, such as broth-based or agar dilution susceptibility tests,cannotdetectinducibleMLBresistance.Thisstudywillbeundertakento find out theprevalenceofinducible(iMLSB)andconstitutiveclindamycinresistance(MISB)amongtheclinicalisolatesofS.aureus.

Thirty non-duplicate clinical isolates of S. aureus were subjected to D test. Testing of methicillinresistance were done with 30 ug disc of cefoxitin as per Cinical Laboratory and Standard Institute(CLSI),2014guidelines.D-testwasperformedbyplacingclindamycinCLIdisc2uganderythromycin ERY disc 15 approximately 15-26 mm apart measured edge to edge on a MullerHinton agar plate that has feet inoculated with a Staphylococcus isolate (0.5 McFarland standard)andincubatedat35°Cinambientair.Flatteningofthezoneofinhibitionadjacenttotheerythromycin disc(referredtoasaD-zone)inducible clindamycinresistance.

D-test was performed as per Clinical Laboratory and Standard Institute (CLST), 2014 guidelines.Staphylococcus aureus ATCC 25923 strains were used to check the quality control of ERY andCLIdises.Inourstudy,28(92%)ofStaphylococcusaureusisolateswerefoundtobemethicillinresistant (MRSA) and 3 (8%) tested sensitive to cefoxitin (MSSA). A total of 11(38%) 5. aureusisolates belonged to iMLSB phenotype. Among 28 MRSA, a total of 11 (39.1%) exhibited iMLS,resistance. 5(17.40%) were of cMLSB phenotype and 3 (8.70%) belonged to MS phenotype.Among 3 isolates of MSSA only 1 (25%) strains exhibited iMLS resistance and rest 2(75%)strainsweresensitivetoclindamycin.

D-testshouldbearoutinetestinordertoguidethecliniciananboutthesusceptibilityofS.aureusto clindamycin. Clindamycin is a preferred drug of treatment in skin and soft tissue infections,especially in MRSA and in patients allergic to penicillin. Also, among the paediatrician, this is apreferred antibiotic in children due to the limited choice of the antibiotics. Appropriate use of thisdrug can avoid the therapeutic failure during therapy. Moreover, during this study, we found avery high percentage of MRSA (92%) isolates as compared to other studies in the country.Stringent hospital antibiotic policy and effective infection control measures need to be advocatedimmediately.