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Original Research Article

Detection and Prevalence of Inducible Clindamycin Resistance in Staphylococcus Species: Insights from a Tertiary Care Centre in Kerala

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Abstract:

Introduction: With the emergence of many multidrug resistant organisms like methicillin resistant Staphylococci, therapeutic options for treating skin and soft tissue infections have become severely limited. Clindamycin is an attractive option for the treatment of such cases especially Community-acquired MRSA (CA-MRSA) because of its excellent tissue penetration and it can be used in penicillin-allergic patients also. But clinical failure can occur due to multiple mechanisms that confer resistance to Macrolide, Lincosamide and Streptogramin B antibiotics. This study was conducted to detect inducible clindamycin resistance in Staphylococci as well as to detect the prevalence of erythromycin induced clindamycin resistance in staphylococcal isolates in the institute.

Materials and Methods: It was a prospective cross-sectional study conducted on the Staphylococcal isolates obtained from routine clinical samples during a period of 1½ years in the Department by systematic sampling method. A total of 300 non-duplicate Staphylococcal isolates from various clinical samples were subjected to antimicrobial susceptibility testing as per the CLSI guidelines. The prevalence of inducible clindamycin resistance in these isolates were tested by using Double disk approximation test (D test), which was supported by automated method (Vitek 2 compact systems) and agar dilution method.

Results: Out of the 300 Staphylococcal isolates included in the study, 90.7% were coagulase positive and 9.3% coagulase negative. It consisted of 34.7% MRSA, 56% MSSA, 5.7% MRCONS and 3.6% MSCONS. Out of the 154 Erythromycin resistant staphylococcal isolates tested, 39 (13%) were found to be D test positive. Inducible clindamycin resistance was exhibited by 18.26% of MRSA, 11.30% of MSSA and 6.66% of MRCONS. Constitutive resistance phenotype, MS phenotype and Susceptible phenotype was exhibited by 27 (9%), 89 (29.7%) and 144 (48%) staphylococcal isolates respectively.

Conclusion: D test is simple and reliable test to detect inducible clindamycin resistance which can be missed if not looked for specifically. Clinical microbiology laboratories should use the double disc approximation test as standard practice with all Erythromycin resistant strains which will help to prevent treatment failure.

Introduction

Staphylococcus is frequently found in the human respiratory tract and on the skin. Although not always pathogenic, it can cause a diverse array of life-threatening infections[1]. Methicilin resistant staphylococcus species were most often found associated with hospitals, but are becoming increasingly prevalent in community-acquired infections as well.

With the emergence of many multidrug resistant organisms, therapeutic options for treating skin and soft tissue infections have become severely limited. Clindamycin is an attractive option, esp for CA-MRSA because of its excellent tissue penetration, good oral absorption and it can be used in penicillin allergic patients also. But clinical failure can occur due to multiple mechanisms that confer resistance to Macrolide, Lincosamide and Streptogramin B antibiotics.

So this study which was carried out for a period of 1 ½ years in Jubilee Mission Medical College and Research Institute, Thrissur, Kerala, aims to detect the prevalence of erythromycin induced clindamycin resistance in staphylococcal isolates in the institute.

Materials and Methods

The study was conducted in the Department of Microbiology, Jubilee Mission Medical College and Research Institute, Thrissur for a period of one and half year (18 months), after getting approval from the Institutional Ethics committee. It was carried out on isolates of *Staphylococcus* obtained from various clinical samples received in the microbiology

laboratory during the study period. The various samples from which the isolates were obtained include pus, blood, urine, CSF, respiratory samples, umbilical vein catheter and central venous catheter. These samples which were collected in appropriate containers by the treating doctors were received and processed in the routine microbiology laboratory. On reaching the laboratory, all the clinical specimens were first inoculated onto blood agar and MacConkey agar plates (Hi Media Mumbai India) and these were incubated at 37^0C for 24-48 hours as per the standard microbiological methods. Colony characteristics were examined and Gram staining of the isolates were done. Isolate that shows Gram positive cocci in groups were further processed and identification done by standard biochemical tests. All Gram positive cocci in clusters that are Catalase positive was identified as Staphylococci and were divided into 2 groups as Coagulase positive Staphylococci (*S. aureus*) and Coagulase negative Staphylococci (CONS) by Slide coagulase and Tube coagulase test.

As per the suggestions from the statistician based on the previous prevalence data from our centre, a minimum of 300 clinically significant Staphylococcal isolates has to be included in the study. In case of CONS, pure growth with plenty of pus cells as well as repeated isolation is warranted. Staphylococcal isolates from environmental samples were not included.

All the confirmed Staphylococcus strains were subjected to routine Antimicrobial susceptibility (AST) using manual and automated methods [Vitek 2 compact systems (bioMerieux Ltd, using GP67 cards)]. The antibiotics used for AST were Penicillin (10U), Cefoxitin (30 µg), Erythromycin (15 µg), Clindamycin (2 µg) and Pristinamycin (15 µg). Quality control tests were carried out with the Standard ATCC strains of Staphylococcus aureus 25923.

Along with routine AST, all the isolates were screened for Methicillin resistance and Macrolide, Lincosamide and Streptogramin B (MLSB) resistance as per the CLSI guidelines. Methicillin resistance was detected using Cefoxitin disc screen test[2]. The MLSB resistance was tested by standard Kirby Bauer disc diffusion method on Mueller Hinton Agar (MHA) using Erythromycin(15 µg), Clindamycin (2 µg) and Pristinamycin (15 µg) discs and by double disc approximation test (D test) and agar dilution test for the detection of inducible clindamycin resistance[3,4]. For D test, a 0.5 McFarland equivalent suspension of test organism was inoculated onto a Mueller-Hinton agar (MHA) as per the CLSI guidelines[5]. Clindamycin (2 µg) and Erythromycin (15 µg) discs were placed 15 mm apart, edge to edge on the MHA. Plates were observed after 18 hours of incubation at 37°C.

Three different phenotypes were appreciated after testing and interpreted as follows [Table:1], [Figure:1]:

1. **MS Phenotype:** Isolates exhibiting resistance to erythromycin (zone size ≤13mm) while being sensitive to clindamycin (zone size ≥21mm) and giving a circular zone of inhibition around clindamycin
2. **Inducible MLS_B Phenotype (MLSBi):** Isolates showing resistance to erythromycin (zone size ≤13mm) while being sensitive to clindamycin (zone size ≥21mm) and giving a D-shaped zone of inhibition around clindamycin with flattening towards erythromycin disc.
3. **Constitutive MLSB Phenotype (MLSBc):** isolates showing resistance to both erythromycin (zone size ≤13mm) and clindamycin (zone size ≤14mm) with circular shape of zone of inhibition if any around clindamycin.
4. **Susceptible phenotype:** isolates which are sensitive to both erythromycin (zone size ≥23mm) and clindamycin (zone size ≥21mm)

Table 1: Interpretation of D test in different phenotypes

Phenotype	Clindamycin interpretation	Erythromycin interpretation	D test interpretation
MLSBi (D+)	R	R	Blunted D shaped clear zone around clindamycin disc proximal to erythromycin disc
MS (D-)	S	R	Clear zone around clindamycin
MLSBc	R	R	Absence of any zone
Susceptible	S	S	Clear zone around the discs

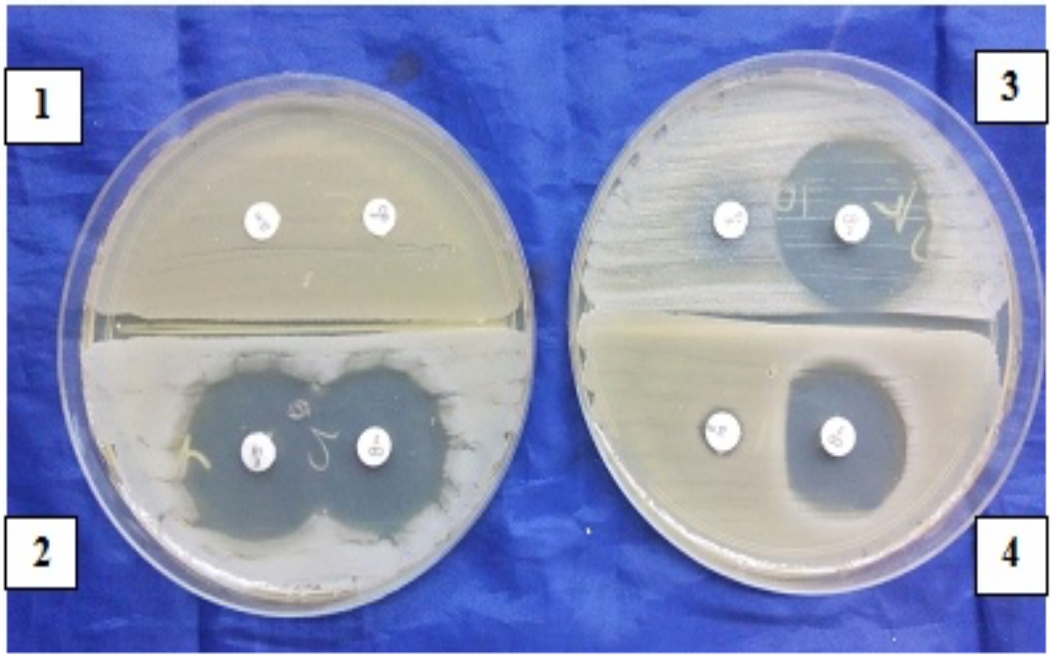


Figure 1: Different phenotypes in MLSB resistance

1. **Constitutive resistance (MLSBc)**
2. **Susceptible phenotype**
3. **MS phenotype**
4. **Inducible Clindamycin resistance [D test +ve] (MLSBi)**

For agar dilution method, MHA incorporated with 3.3% blood was prepared which also contained 1 mg/litre Erythromycin and 0.5 mg/litre Clindamycin. In addition, plates with 1 mg/litre Erythromycin alone, 0.5 mg/litre Clindamycin alone as well as plates without any antibiotics were also prepared. The plates were then inoculated with standardized bacterial suspensions and incubated for 18 hours. Growth was recorded if atleast one colony is grown at the inoculated site. The test was deemed to be positive for inducible clindamycin resistance if there is growth in Erythromycin only and combined plates with no growth in the Clindamycin only plate. It is considered negative if there is growth only in Erythromycin only plate with no growth in Clindamycin alone and combined plates.[4]

All the findings were confirmed by Vitek 2 compact systems (Biomerieux Ltd, using GP67 cards) and agar dilution method. All the instructions of the manufacturers were strictly followed during processing.

Ethics

The study was conducted in accordance with the ethical standards of the Institutional Ethics committee.

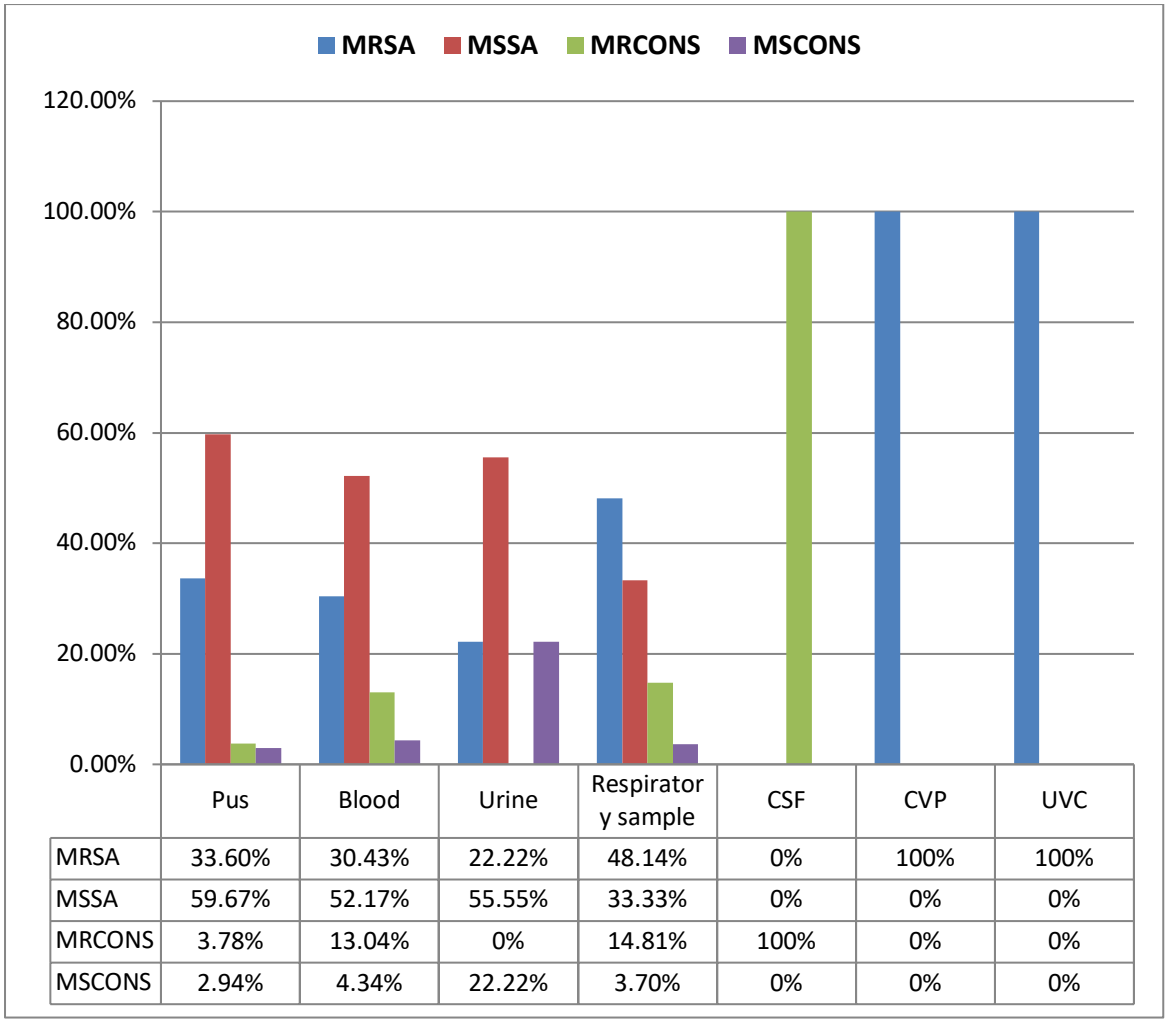
Statistics

Epi info (version 7.1.4.0) Centre for Disease Control and prevention (CDC), Atlanta, Georgia was used for analysis and interpretation of the results. p value was calculated to find out statistical significance. A p value of ≤0.5 is considered as significant association.

Results

The initial one and half year was used for sample collection and processing and the remaining 3 months were taken for data generation. A total of 1868 samples were received in the microbiology laboratory for routine bacterial culture during the study period which includes 386 MRSA, 667 MSSA and 815 CONS. Isolates were included in the study based on their clinical significance. The samples were processed as per the standard microbiological methods.

A total of 300 non-duplicate Staphylococcal isolates were included in the present study. About 79.3% of the staphylococcal isolates were from pus, 9% from respiratory secretions, 7.6% from blood samples, 3% from urine and 0.33% from CSF, CVP and UVC each. Out of the 300 isolates 104 were MRSA (34.7%), 168 MSSA (56%), 17 MRCONS (5.7%) and 11 MSCONS (3.6%) [Figure:2]. Among the 28 CONS isolated, *Staphylococcus haemolyticus* was the commonest species [8 (28.6%)], followed by *S epidermidis* [5 (17.9%)], *S saprophyticus* [3 (10.7%)] and *S lugdunensis* [1 (3.6%)]. Around 11 isolates of CONS could not be speciated in the present study.



	Pus	Blood	Urine	Respiratory sample	CSF	CVP	UVC
MRSA	33.60%	30.43%	22.22%	48.14%	0%	100%	100%
MSSA	59.67%	52.17%	55.55%	33.33%	0%	0%	0%
MRCONS	3.78%	13.04%	0%	14.81%	100%	0%	0%
MSCONS	2.94%	4.34%	22.22%	3.70%	0%	0%	0%

Figure 2: Distribution based on Coagulase test

Antibiotic susceptibility of methicillin sensitive strains was compared with that of methicillin resistant staphylococcal isolates. Among *S aureus*, only 16.07% of MSSA were found to be sensitive to penicillin. Among CONS, only 18.18% of MSCONS were found to be sensitive to penicillin. Among 272 *S aureus*, resistance to antibacterial agents like Erythromycin, Clindamycin and Pristinamycin was exhibited by 51.83%, 9.19% and 38.23% of the isolates respectively. In case of CONS, 46.43%, 14.28% and 28.57% exhibited resistance to Erythromycin, Clindamycin and Pristinamycin respectively.

Among MRSA 71.15% isolates were resistant to erythromycin whereas only 17.30% were found to be resistant to clindamycin. Resistance to Pristinamycin in case of MRSA, MSSA, MRCONS and MSCONS were 53.85%, 28.57%, 35.30% and 18.18% respectively. Here also the degree of resistance exhibited by the MRSA was found to be higher than that of MSSA which was proved based on the statistical methods and p value. But comparisons made between the MRCONS and MSCONS didn't yield any statistical significance.

Out of the 154 Erythromycin resistant isolates tested, 39 (13%) were found to be D test positive (inducible clindamycin phenotype). About 144 staphylococcal isolates (48%) were sensitive to both erythromycin and clindamycin and 27 (9%) were resistant to both the antibiotics. Interestingly one MRCONS was found to be sensitive to erythromycin and resistant to clindamycin.

Among MRSA, MS phenotype predominate over susceptible phenotype, inducible MLSB phenotype and constitutive MLSB phenotype (35.57%, 28.84%, 18.26% and 17.3% respectively). The susceptible phenotype predominated over MS phenotype, MLSBi phenotype and MLSBc phenotype (59.52%, 25.59%, 11.3% and 3.57% respectively) among the MSSA isolates. The predominant phenotype among MRCONS and MSCONS were MS phenotype (46.66%) and susceptible phenotype (66.66%) respectively [Table:2].

Table 2: Distribution of Phenotypes in clinical samples

Phenotype	MRSA	MSSA	MRCONS	MSCONS	Total
ER-S, CL-S (susceptible)	30 (28.84%)	100 (59.52%)	6 (40%)	8 (66.66%)	144
ER-R, CL-R (MLSBc)	18 (17.30%)	6 (3.57%)	1 (6.66%)	2 (16.66%)	27
ER-R, CL-S, (D-) (MS phenotype)	37 (35.57%)	43 (25.59%)	7 (46.66%)	2 (16.66%)	89
ER-R, CL-S,(D+) (MLSBi)	19 (18.26%)	19 (11.30%)	1 (6.66%)	-	39
ER-S, CL-R	-	-	1 (6.66%)	-	1
Total	**104**	**168**	**15**	**12**	**300**

Discussion

Multi-drug resistant Staphylococcal isolates especially the Methicillin resistant staphylococci causing life-threatening infections are increasing at an alarming rate. To treat such isolates, physicians are finding a serious drought among the available antibiotics. In this aspect, clindamycin can be considered as a good alternative due to its excellent pharmacokinetic properties. It is a useful drug in the treatment of infections caused by both methicillin sensitive as well as resistant staphylococcal strains[6].

Two primary mechanisms result in resistance to macrolide antibiotics. The first involves a chromosomally encoded efflux pump encoded by msrA gene, which actively expels the drug from the bacterial cell before they can bind to the target site on the ribosome[7]. This confers resistance to macrolides and streptogramin B only and not to lincosamides (MSB phenotype). The second mechanism involves alteration in the target binding site on the ribosome, which is mediated by erm (erythromycin ribosome methylation) genes[7,8] on plasmids or transposons on chromosomes that are self-transferable. This pattern of resistance is commonly referred to as MLSB phenotype.

Phenotypically MLSB resistance may be constitutive, or it may be inducible by sub-inhibitory concentrations of erythromycin or other macrolides that bring about the induction of the methylating enzyme. When an erm gene is present, resistance arises through binding of the macrolide to upstream translational attenuator sequences. This binding leads to alteration of the mRNA secondary structure, exposure of the ribosomal binding site and translation of the erm methylase. For constitutive resistance (MLSBc) to take place, additional changes in the 5' upstream sequences are required which may include deletions, duplications or other mutations. This results in constitutive expression of the methylase gene[8] with obvious resistance to MLSB antibiotics. In inducible type resistance (MLSBi), although the strains are resistant to 14-member (Eg- Erythromycin) and 15-member macrolides (Eg- Azithromycin), they appear to be susceptible invitro to 16-member macrolides (Eg- Spiramycin), lincosamides and group B streptogramins. But when there is exposure to a suitable macrolide inducer (Eg- erythromycin), there may be expression of lincosamide and streptogramin B resistance. However resistance to clindamycin often emerges invivo by selection of mutants that constitutively produce a methylating enzyme, especially in infections with high bacterial density. This will transform MLSBi strains to MLSBc phenotype even in the absence of a macrolide inducer. Here the concern is that this change in expression might be selected in the midst of therapy with a lincosamide leading to failure.[8] Interestingly the streptogramin antibiotics (Quinupristin-dalfopristin), appears to retain its activity against MLSBc strains of staphylococci, although the presence of this phenotype changes the agents activity from bactericidal to bacteriostatic with S aureus [Table:3].

Table 3: Mechanism of MLSB resistance

	Phenotype	Mechanism
ER-S, CL-S	Susceptible	
ER-R, CL-S, (D-)	MS phenotype	Active efflux due to a pump encoded by the msrA gene
ER-R, CL-S, (D+)	MLSBi	Ribosomal methylation mediated by enzymes encoded by one of a variety of erm genes
ER-R, CL-R	MLSBc	Selection of mutation during therapy

Of the 300 isolates included in the present study, 272 (90.7%) were *Staphylococcus aureus* and 28 (9.3%) were coagulase negative staphylococci. When sample wise analysis was performed, it was found that about 79.3% of the staphylococcal isolates were from pus, 9% from respiratory secretions, 7.6%

from blood samples, 3% from urine and 0.33% from CSF, CVP and UVC each. Out of the 272 *S aureus* strains, 81.6% of the clinical samples were from pus, 8.09% from respiratory secretions, 6.9% from blood, 2.6% from urine and 0.7% from UVC and CVP together. This was almost in accordance with the study conducted by Rajaduraipandi K et al[8], exception being the proportion of pus samples (50.7%) which is lower when compared to our study. The proportion of pus samples in our study was similar to the studies conducted by Shanthi M et al[9] (80%) and Mantri SR et al[10] (74.1%).

Among the 28 CONS isolated in our study, 16 (57.14%) isolates were from pus samples, 5 (17.9%) from respiratory secretions, 4 (14.3%) from blood, 2 (7.14%) from urine and 1 (3.6%) from CSF. In the study conducted by Jayanthi RS et al[11], as in our study, pus samples contributed to about 54.54%, but others are different as, blood 24.24%, urine 18.2% and CVP 3%. Meanwhile blood samples predominated over pus samples in the study conducted by Usha MG et al[12] (53% and 32.35% respectively).

Of the 300 staphylococcal isolates, MSSA predominated over MRSA, MRCONS and MSCONS (56%, 34.7%, 5.7% and 3.6% respectively). These results are found to be almost in accordance with Shanthi M et al[9] (55% MSSA), Joshi S et al[13] (58% MSSA) and Angel MR et al[3] (53.81% MSSA). In contrast to this, MRSA was found to predominate over MSSA in the study conducted by Mantri SR et al[10] (39.29% MRSA, 28.07% MSSA).

In the study conducted by Angel MR et al[3] the prevalence of CONS was 21.61%. The prevalence of MRCONS and MSCONS in the studies conducted by Mantri SR et al[10] is 4.21% and 28.42% and that of Jayanthi RS et al[11] is 11.22% and 22.45%.

In the present study MRSA strains showed the highest rate of resistance to erythromycin (71.15%) and pristinamycin (53.85%). This was in accordance with the study conducted by Joshi S et al[13] and Kulkarni S et al.[14] Contrary to the reports by Mantri SR et al[10] who reported 28.57% resistance to erythromycin that is much lower when compared to our study.

Among MSSA, 83.93% exhibited resistance to Penicillin followed by 39.9% to Erythromycin, 35.3% to Pristinamycin and 11.76% to Clindamycin. Resistance.

Among MRCONS, maximum resistance was shown by Penicillin (100%) followed by Erythromycin (58.82%), Pristinamycin (35.30%) and Clindamycin (11.76%). MSCONS also followed similar pattern.

In our study, we found high percentage of erythromycin resistant isolates [154 (51.33%)]. Amongst them 39 (25.32%) isolates tested positive for inducible clindamycin resistance by D test. Out of the 115 erythromycin resistant isolates which were D test negative, 89 showed MS phenotype and 27 exhibited constitutive resistance. These observations suggest the importance of D test. If D test was not performed, around one-fourth of the erythromycin resistant isolates would have been misidentified as clindamycin sensitive resulting in therapeutic failure.

It was also observed that percentages of inducible clindamycin resistance and MS phenotype were higher amongst MRSA (18.26% and 35.57%) as compared to MSSA (11.30% and 25.59% respectively). This was in accordance with a few of the studies reported before – Pal N et al[15] found inducible resistance of 16.4% in MRSA and 6.36% in MSSA; Prabhu K et al[16]showed it to be 20% in MRSA and 6.15% in MSSA, while Gupta V et al[17] reported 20% in MRSA and 17.3% in MSSA. The frequency of inducible clindamycin resistance was found to be higher in the studies conducted by Angel MR et al[3] (64% in MRSA), Mittal V et al[18] (44.8% in MRSA) and Manjunath V et al[19] (57.63% in MRSA and 16.22% in MSSA). On the contrary, Eksi F et al[20] showed higher percentage of inducible resistance in MSSA as compared to MRSA, 6.9% in MRSA and 8.4% in MSSA. In our study constitutive resistance was seen in 17.30% of MRSA and 3.57% of MSSA which is lower when compared to the studies conducted by Sexena S et al[21] (47.4% in MRSA and 33.9% in MSSA), Gupta V et al[17] (46% in MRSA and 10% in MSSA) and Yilmaz G et al[22] (44.20% in MRSA and 14.80% in MSSA).

In our study 13 CONS were found to be erythromycin resistant which consists of 9 MRCONS and 4 MSCONS. Among MRCONS the MS phenotype (46.66%) predominated over inducible (6.66%) and constitutive phenotype (6.66%) whereas in the case of MSCONS, there were equal numbers of MLSBc and MS phenotype (16.66% each). Inducible phenotype was shown by 1 MRCONS (6.66%) whereas none of the MSCONS exhibited this phenotype. This was lower when compared with other studies, ie Yilmaz G et al[22] (25.7% MRCONS, 19.9% MSCONS), Pal N et al[15] (13.75% MRCONS, 3.95% MSCONS), Bansal N et al[23] (25.8% MRCONS, 13.7% MSCONS) and Sexena S et al[21] (30% MRCONS and 23.8% MSCONS).

In our study constitutive resistance was higher among MSCONS (16.66%) when compared to the MRCONS (6.66%). This was found to be in accordance with the study conducted by Sexena S et al[21] (42.8% in MSCONS and 30% in MRCONS). The MS phenotype was found to be predominant among MRCONS (46.66%) than MSCONS (16.66%) [Table:4].

Table 4: Distribution of MLSBc, MLSBi and MS phenotype in various studies

Study conducted by	Organism	MLSBc (%)	MLSBi (%)	MS phenotype (%)
Yilmaz G et al[22] (2007)	MRSA MSSA MRCONS MSCONS	44.20 14.80 38.30 10.20	24.40 4.50 25.70 19.90	- - - -
Angel MR et al[3] (2008)	MRSA MSSA CONS	- - -	64 5 10	12 25 19
Prabhu K et al[16] (2011)	MRSA MSSA	16.66 6.15	20 6.15	13.33 6.15
Pal N et al[15] (2010)	MRSA MSSA MRCONS MSCONS	31.6 7.2 30.6 7.2	16.4 6.36 13.75 3.95	18.6 11.82 15 30.77
Mittal V et al[18] (2013)	MRSA MSSA	8.6 4.5	44.8 8.4	13.3 16.1
Manjunath V et al[19] (2012)	MRSA MSSA	23.73 21.62	57.63 16.22	18.64 62.16
Bansal N et al[23] (2012)	MRCONS MSCONS	51.7 11.8	25.8 13.7	12.4 27.3
Eksi F et al[20] (2011)	MRSA MSSA	39.6 20.4	6.9 8.4	6.9 4.5
Sexena S et al[21] (2014)	MRSA MSSA MRCONS MSCONS	47.4 33.9 30 42.8	28.9 12.6 30 23.8	23.7 53.5 40 33.4
Gupta V et al[17] (2009)	MRSA MSSA	46 10	20 17.3	16 37.3
Shetty J et al[24] (2017)	MRSA MSSA	52.1 22	27.1 11	- -
Prasanth Singh et al[25] (2021)	MRSA MSSA	33.3	23 5	15.2
	MRCONS MSCONS	46.7	27 7	8.9
Our study	MRSA MSSA MRCONS MSCONS	17.30 3.57 6.66 16.66	18.26 11.30 6.66 0	35.57 25.59 46.66 16.66

With the emergence of resistance in Staphylococci, clinicians are only left with limited options. Clindamycin is a good choice since it can given as outpatient therapy and has good oral bioavailability. But the true sensitivity of clindamycin can only be judged after performing D test on the erythromycin resistant isolates. D test is a simple and reliable test for the detection of inducible clindamycin resistance, but can be missed if not looked for specifically and so the clinical microbiology laboratories should use the double-disc approximation test as standard practice with all Erythromycin resistant strains as its early detection will enable the clinician to save time so that therapeutic failures can be avoided.

Limitations

Genotypic studies were not performed due to lack of infrastructure and financial funding.

Conclusions

Even though inducible clindamycin resistance can be detected by many methods, D test remain as the preferred test since it can be performed even in resource limited settings. Hence it should be incorporated as a routine when antimicrobial susceptibility of Staphylococcus species is done.

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References

1. Lowy FD. Antimicrobial resistance: the example of Staphylococcus aureus Science in Medicine. J Clin Invest. 2003;111(9):1265–1273.

2. Mathews AA, Thomas M, Appalaraju B, Jayalakshmi J. Evaluation and comparison of tests to detect methicillin resistant Staphylococcusaureus. Indian J PatholMicrobiol. 2010;53(1):79-82.
3. Angel MR, Balaji V, Prakash JAJ, Brahmadathan KN, Mathews MS. Prevalence of Inducible Clindamycin resistance in gram positive organisms in a tertiary care centre. Indian J Med Microbiol.2008 Jul; 26(3):262-264.
4. Fernandes CJ, Matthew VN, Cai Y, Kong F, Zeng X, Gwendolyn L et al. Agar Dilution Method for Detection of Inducible Clindamycin Resistance in Staphylococcus spp. J Clin Microbiol.2007 Dec;45(12):4018-4020.
5. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fifth informational supplement, Clinical and Laboratory Standards Institute (CLSI).M100- S25; Wayne, PA: CLSI; Jan 2015.
6. Lall M, Sahni AK. Prevalence of inducible Clindamycin resistance in Staphylococcus aureus isolated from clinical samples. Armed Forces Med J India. 2014;70:43-47.
7. Durmaz S, Kiraz A, Ozer TT, PercinD.Macrolide-Lincosamide-Streptogramin B resistance phenotypes in Staphylococcus aureus. Eur J Gen Med. 2014;11(4):217-220.
8. Leclercq R. Mechanisms of resistance to Macrolides and Lincosamides: Nature of the resistance elements and their Clinical implications. Clin Infect Dis. 2002;34(4):482-492.
9. Shanthi M, Sekar U. Antimicrobial susceptibility pattern of Methicillin resistant Staphylococcus aureus at Sri Ramachandra Medical Centre. Sri Ramachandra Journal of Medicine. 2009 June;2(2):1-4.
10. Mantri SR, Karyakarte RA, Ambhore AN, Kombade PS. Prevalence of Methicillin resistant Staphylococcus aureus in tertiary care hospital, Central India. Int J CurrMicrobiolAppl Sci. 2014;3(10):582-586.
11. Jayanthi RS, Jomy J. Phenotypic Characterization of clinically significant Coagulase negative Staphylococci and their susceptibility pattern in a tertiary care hospital. Int J CurrMicrobiol App Sci. 2015;4(4):647-652.
12. Usha MG, Shwetha DC, Vishwanath G. Speciation of Coagulase negative Staphylococcal isolates from clinically significant specimens and their antibiogram. Indian J PatholMicrobiol. 2013 Sep;56(3):258-260.
13. Joshi S, Ray P, Manchanda V, Bajaj J, Chitnis DS, Gautam V, et al. Methicillin resistant Staphylococcus aureus(MRSA) in India: Prevalence and Susceptibility pattern. Indian J Med Res. 2013 Feb;137:363-369.
14. Kulkarni S, Khare A, CharanKaur D. Prevalence of methicillin resistant Staphylococcus aureus- A study in a tertiary care rural hospital. Indian Journal of Basic and Applied Medical Research. 2014 June;3(3):414-421.
15. Pal N, Sharma B, Sharma R, Vyas L. Detection of inducible clindamycin resistance among Staphylococcal isolates from different clinical specimens in Western India. J Postgrad Med. 2010;56(3):182-185.
16. Prabhu K, Rao S, Rao V. Inducible Clindamycin resistance in Staphylococcus aureus isolated from clinical samples. J Lab Physicians. 2011 Jan-Jun;3(1):25-27.
17. Gupta V, Datta P, Rani H, Chander J. Inducible clindamycin resistance in Staphylococcus aureus: A study from North India. J Postgrad Med. 2009;55(3):176-179.
18. Mittal V, Kishore S, Siddique ME. Prevalence of inducible clindamycin resistance among clinical isolates of Staphylococcus aureus detected by phenotypic method: A preliminary report. Journal of Infectious Diseases and Immunity. 2013 Feb;5(1):10-12.
19. Manjunath V, Singh E, Ramya TG, Prakash MR, Sharma A. D-Test – Its role in detection of inducible resistance to Clindamycin in Staphylococcus aureus with special reference to MRSA. Int J Biol Med Res. 2012;3(1):1430-1432.
20. Eksi F, Gayyurhan ED, Bayram A, Karsligil T. Determination of antimicrobial susceptibility patterns and inducible clindamycin resistance in Staphylococcus aureus strains recovered from Southeastern Turkey. J MicrobiolImmunol Infect. 2011;44:57-62.
21. Sexena S, Singh T, Rakshit P, Dutta R, Gupta RK. Prevalence of Inducible Clindamycin resistance in Staphylococcus aureus at a tertiary care hospital: Implications for clinical therapy. Int J CurrMicrobiol app Sci. 2014;3(3):720-725.
22. Yilmaz G, Aydin K, Iskender S, Caylan R, Koksal I. Detection and prevalence of inducible clindamycin resistance in staphylococci. J Med Microbiol. 2007;56:342–345.
23. Bansal N, Chaudhary U, Gupta V. Prevalence of inducible clindamycin resistance in clinical isolates of coagulase negative staphylococci at a tertiary care hospital. Ann Trop Med Public Health. 2012;5(5):427-430.
24. Shetty J, Afroz Z. Prevalence of constitutive and inducible clindamycin resistance among clinical isolates of Staphylococcus aureus in a tertiary care institute in North India. Int J Res Med Sci, 2017;5(7):3120–25.
25. Singh P, Mane P, Singla P, Sangwan J. Prevalence of inducible clindamycin resistance in Staphylococcus: A study from a rural teaching tertiary care hospital in Southern Haryana. Nat.lab.med. 2021;10(2):MO06-MO09.