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Original Research Article

A COMPARATIVE STUDY BETWEEN ERYTHROMYCIN AND AZITHROMYCIN IN DETECTING INDUCIBLE CLINDAMYCIN RESISTANCE AMONG STAPHYLOCOCCUS AUREUS ISOLATES

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ABSTRACT

Background: Staphylococcus aureus is most common pathogen causing infection ranging from skin and soft tissue to nosocomial infections. Clindamycin is preferred antibiotic to treat Staphylococcus aureus infections, due to it's pharmacokinetic properties. Clindamycin resistance can be constitutive or inducible. Inducible clindamycin resistance appears as clindamycin sensitive in vitro. It is important to detect inducible clindamycin resistance in the laboratory. If not detected it will lead to therapeutic failure. It is detected by D test, that is placing erythromycin and clindamycin disc adjacent to each other on a Mueller Hinton Agar Plate. The study was undertaken to assess capability of azithromycin (test method) with erythromycin (reference method) in detecting inducible clindamycin resistance in Staphylococcus aureus. **Materials and Methods:** The study was conducted for 6 months period in a tertiary care hospital at Saharsa. D test for detecting inducible clindamycin resistance was done by placing erythromycin disc (15µg), clindamycin disc (2µg), azithromycin disc (15µg) on the Mueller–Hinton agar plate with lawn culture of Staphylococcus aureus test isolates. **Result:** The test method showed 100% uniformity in detecting inducible clindamycin resistance by erythromycin and azithromycin disk. **Conclusion:** Azithromycin can be used as an alternative agent for erythromycin in detecting inducible clindamycin resistance in Staphylococcus aureus.

INTRODUCTION

Staphylococcus aureus is a widespread pathogen responsible for causing human infections ranging from skin infections to life threatening disease.[1] In the past, methicillin was the antibiotic used for treating infection caused by Staphylococcus aureus strain resistant to penicillin. Due to indiscriminate use of methicillin, there was emergence of Methicillin resistant Staphylococcus aureus (MRSA), which was resistant to all penicillinase resistant penicillins and cephalosporins.[2] Macrolide-lincosamide-streptogramin B (MLSB), a family of antibiotics, is the choice for the treatment of staphylococcal infections.[3] Clindamycin, has a superior pharmacokinetic properties in MLSB family. Owing to this property, it is used to treat methicillin susceptible Staphylococcus aureus (MSSA) and MRSA infections.[4] In patient with β-lactams allergies, clindamycin is an effective alternative agent to treat infections.[5]

Increased resistant to MLSB antibiotics has been reported due to it's random use. Resistant may be due to an efflux mechanism encoded by the methionine sulfoxide reductase A gene or a ribosomal target site modification encoded by the erythromycin ribosomal methylase gene.[6] According to Indian Council of Medical Research (ICMR) annual report on antimicrobial resistance released in 2023, MRSA prevalence was 44.5% and clindamycin resistance was 21% in Staphylococcus aureus strains.[7] In Staphylococcus, clindamycin resistance are either constitutive or inducible. It is due to target site modification mediated by erm genes, which can be constitutive MLSB phenotype or inducible MLSB phenotype. Inducible resistance to clindamycin appear as clindamycin sensitive in vitro. If inducible resistant to clindamycin is not detected it will lead to clinical therapeutic failure8. According to Clinical and Laboratory Standards Institute (CLSI) guidelines, D test is used for detecting inducible clindamycin resistance. It is performed using

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erythromycin and clindamycin disc placed adjacently on Mueller Hinton Agar (MHA) plate.[8,9]

Erythromycin belongs to the first generation macrolides introduced in 1951. It was used to treat many clinical infections but due to lack of stability at low pH, poor penetration into tissues and issues of gastrointestinal tolerability in patients it's use is narrowed. Azithromycin is second-generation macrolides with better pharmacokinetic properties and tolerability in patients.[10] The aim of the study was to assess the capability of azithromycin disc with reference erythromycin disc in detecting inducible clindamycin resistance. The objective of the study was to estimate the prevalence of inducible clindamycin resistance in Staphylococcus aureus isolates.

MATERIALS AND METHODS

This prospective study was conducted in a tertiary care hospital in Saharsa, Bihar over a period of 6 month from August 2025 to January 2026. The study was done after getting approval by the clinical research ethics committee of Lord buddha koshi Medical College and Hospital, Saharsa, via letter no: CREC/2025/01, dated 21/07/2025. Informed consent was not taken as study was done on anonymously stored Staphylococcus aureus isolated from clinical samples. All Staphylococcus aureus isolated from various clinical samples (pus, swab, blood, urine, sterile fluids and respiratory samples) were included in the study. Isolates other than Staphylococcus aureus was excluded from the study. All clinical samples were inoculated on Blood agar, Chocolate Agar, MacConkey agar and incubated overnight at 37°C aerobically.

The Staphylococcus aureus isolates were identified based on colony morphology, gram stain, and biochemical tests.[11] D test for detecting inducible clindamycin resistance was also done in accordance with CLSI 2025 guidelines. It was done by placing erythromycin disc (15µg), clindamycin disc (2µg), azithromycin disc (15µg) on the Mueller–Hinton agar plate with lawn culture of Staphylococcus aureus test isolates. The clindamycin disc was placed in between the erythromycin and azithromycin disc. The edge to edge distance of clindamycin disc was 15-26 mm from both the adjacent disc. It was incubated at 37°C for overnight.[9] All antibiotic disc used were of Hi Media (India).

Clindamycin resistance was interpretated as constitutive or inducible resistant. Constitutive-resistant phenotype (cMLSB): resistant to both erythromycin (zone diameter ≤13 mm) and clindamycin (zone diameter ≤14 mm). Inducible resistant phenotype (iMLSB): resistant to erythromycin (zone diameter ≤13 mm) and sensitive or intermediate to clindamycin (zone diameter ≥15 mm) with a characteristic D shaped zone of the clindamycin inhibition zone adjacent to the erythromycin disk.

Clindamycin sensitivity was interpretated as MS phenotype: resistant to erythromycin (zone diameter ≤13 mm) but sensitive to clindamycin (zone diameter ≥21 mm) without D zone. The above mentioned CLSI M100 method for detecting inducible clindamycin resistance using erythromycin disc was also employed for azithromycin disc in the study. The data were entered in Microsoft Excel and SPSS software was used for statistical analysis. Descriptive data were analyzed statistically and expressed as percentage.

RESULTS

A total of 3123 clinical samples were received for culture and sensitivity in microbiology laboratory during study period. Among the clinical samples received, culture positive samples were 1854 (59.4%) and culture negative sample were 1269 (40.6%). Among culture positive samples, Staphylococcus aureus 172 (9.3%) were isolated. These Staphylococcus aureus isolates were included in the study. They were subjected to detect constitutive and inducible clindamycin resistance by standard (erythromycin) and test (azithromycin) method. The test method showed 100% uniformity in detecting constitutive, inducible clindamycin resistance as standard method [Table 1].

Table 1

Staphylococcus aureus phenotypes	Standard method	Test method	Percentage (%)
cMLSB	37	37	100%
iMLSB	49	49	100%
MS phenotype	86	86	100%

Among cMLSB, 32 (18.6%) were MRSA and 5 (2.9%) were MSSA. In iMLSB, 41 (23.8%) were MRSA and 8 (4.7%) were MSSA. Majority 84 (48.8%) were MSSA and 2 (1.2%) were MRSA in MS phenotype [Table 2].

Table 2

Staphylococcus aureus phenotypes	MRSA		MSSA		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
cMLSB	32	18.6%	05	2.9%	37	21.5%
iMLSB	41	23.8%	08	4.7%	49	28.5%
MS phenotype	02	1.2%	84	48.8%	86	50%
Total	75	43.6%	97	56.4%	172	100%

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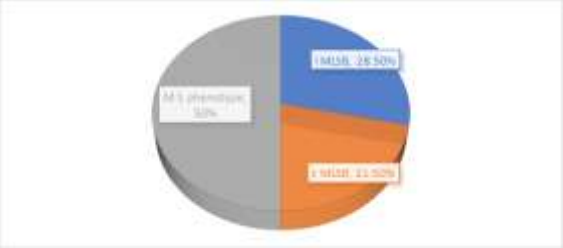

Figure 1: The prevalence of inducible clindamycin resistance among Staphylococcus aureus was 28.5%.

Figure 2: Showing Inducible Clindamycin Resistance

Figure 3: showing constitutive clindamycin resistance.

DISCUSSION

In this study, azithromycin (test method) uniformity was 100% as compared with erythromycin (standard method) in detecting inducible clindamycin resistance. This finding is in accordance with study of Archana et al,[12] Goyal N et al,[13] and Azap et al.[14] They also reported similar finding in their study.

In our study, the prevalence of inducible clindamycin resistance, among Staphylococcus aureus isolates was 28.5%. This finding is in accordance with study of Sadanandan N et al.[15] They reported 26.5% Staphylococcus aureus phenotypes as inducible clindamycin resistance in their study.

In this study, the prevalence of MRSA in inducible clindamycin resistance was 23.8%. which is lower than study of Greesh Ketal.[16] In their study, 37.77% MRSA showed inducible clindamycin resistance. This may be due to difference in geographical region.

Limitation: Due to lack of resources, molecular confirmation of inducible clindamycin resistance gene could not be done. This study findings is based on a single tertiary care hospital so the findings cannot be generalized to other hospital.

CONCLUSION

Azithromycin can be used as an alternative agent for erythromycin in detecting inducible clindamycin resistance in Staphylococcus aureus phenotypes. Very few studies in India has reported an uniform result with use of azithromycin in place of erythromycin in detecting inducible clindamycin resistance phenotypes among Staphylococcus aureus. We also recommend that various multi centric studies in future can further confirm this finding.

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