Nasal carriage of Methicillin-resistant *Staphylococcus aureus* in pediatric patients admitted during the COVID-19 pandemic in a tertiary care hospital

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Abstract

Background: *Staphylococcus aureus* is a foremost human pathogen that has been impeded from causing abundant clinical infections ranging from bacteremia, septicemia, infective endocarditis, skin and soft tissue,pulmonaryand device-related infections. Methicillin-resistant *Staphylococcus aureus* (MRSA) is the cause of a growing number of hospital-acquired infections (HAIs) around the world. This has led to longer hospital stays, more prolonged antibiotic administration, and greater inpatient health care expenses.

Objectives: To analyze the rate of nasal carriage of Methicillin-resistant *Staphylococcus aureus* by antimicrobial culture sensitivity among pediatric patients.

Patients and methods: Within a year (July 2021–June 2022), 350 patients participated in a hospital-based cross-sectional study conducted in the pediatrics and microbiology departments of a tertiary care hospital in East Delhi. A sterile cotton swab dampened with regular saline will be used to take nasal swabs from patients. The Sample was subcultured on Mannitol salt agar and *S. aureus* was identified as per standard microbiological guidelines. The antibiotic susceptibility testing was performed by the Kirby–Bauer disc diffusion method on Muller-Hinton agar.

Results- Among 350 pediatric nasal swab samples, the prevalence of *S. aureus* was 135 (38.57%). Other *Staphylococcus sp.* were 181 (51.7%) and no growth was noticed in 34 (9.7%). Out of 135 (38.57%) Methicillin-resistant *Staphylococcus aureus* isolated pediatric patients, 26 (19.25%) had inducible clindamycin resistance.

Conclusion: The study highlights MRSA's persistent challenges in pediatric healthcare settings, including high prevalence, inducible clindamycin resistance, age, and antibiotic use. It calls for standardized infection control measures, cautious antibiotic prescription practices, and continuous surveillance.

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Introduction

S. aureus is a foremost human pathogen that has impeded the cause of abundant clinical infections ranging from bacteremia, septicemia, infective endocarditis, skin and soft tissue, and pulmonary, and device-related infections (**Othman et al., 2021).**Methicillin-resistant *Staphylococcus aureus* (MRSA) is the cause of a growing number of hospital-acquired infections (HAIs) around the world. This has led to longer hospital stays, more prolonged antibiotic administration, and greater inpatient healthcare expenses (**Mondal et al., 2016)**. MRSA was first reported in 1961, and it has become an epidemic in many hospitals across the globe. In India, 40% of MRSA is responsible for nosocomial infections(**INSAR, 2013;George et al., 2016)** since it has colonized the mucosa of the nose, the anterior nares arethe favorite site for its carriage and spread (**Wertheim et al., 2005).**

MRSA strains have spread all over the world, and they cause several nosocomial outbreaks in both hospitals and communities. Infections from either hospital-acquired MRSA (HA-MRSA) or community-acquired (CA) MRSA (CA-MRSA) have increased the challenge of selecting empirical antimicrobial treatments **(Guo et al., 2020;Mairi et al., 2020; Mistry et al., 2020).** In healthcare institutions, HA-MRSA can be transmitted between patients or through the hands, clothes, or equipment of healthcare workers (HCWs) and the environment **(Henderson et al.,2006)**.

HA- MRSA infections are associated with various risk factors, like a recent hospital stay, living in a long-term care facility, or carrying an indwelling device or catheter and mechanical ventilation. CA-MRSA has been recognized as important as, HA-MRSA in causing hospital outbreaks(**Schinasi et al., 2013)**. Published data from various centers in India project a prevalence of 1-5%(**Pathak et al., 2010;Fomda et al., 2014).**MRSA is responsible for causing infections among both adults and children. However, it is the leading cause of bacterial infection among children(**Chamberset al.,2001)**.Therefore, it becomes necessary to know the carriage of MRSA during the COVID-19 pandemic to provide effective measures against this dual giant problem(**Nurjadi et al.,2021)**. There is a paucity of data regarding a study done on the nasal carriage of *S. aureus* in pediatric patients admitted during COVID-19. Hence, the present study was conducted to find out the rate of nasal carriage of MRSAin pediatric patients admitted during the COVID-19 pandemic in a tertiary care hospital.

Patients and methods

Sample size: A formula by Daniel was used to calculate the sample size (**Naing et al., 2006**). The minimum sample size in the COVID-19 pandemic was calculated as 350, anticipating a prevalence rate of 5%**(Fomda et al., 2014; Pathak et al., 2010)** based on previous studies and detecting the prevalence with 5% precision and 99.9% confidence interval. A sample size of 350 patients will be admittedtoapediatric emergency with the age group from more than 1 month of age up to 12 years will be enrolled as a study subject**.**

Study Design: A hospital-based cross-sectional study was performed in the Department of Microbiology and Paediatrics in a tertiary care hospital, East Delhi, within 1 year (July 2021–June 2022) among 350 patients.Informed consent or assent was obtained from the parents/ guardian before the sample collection.

Inclusion Criteria: Nasal carriage is when an asymptomatic individual haspositive tests for an *S. aureus* population in their nasal mucosa (**Eriksen et al., 1995**).Patients admitted to the pediatric emergency ward with an age group

between more than 1 month of age and 12 years irrespective of gender. Nasal swabswerecollected before starting antibiotics preferably.

Exclusion Criteria

i. Patients who received treatment in the preceding two weeks before sample collection.
ii. Age less than one month.
iii. Patient presented with upper respiratory and wound infections.
iv. Those who had ulceration or pus at the nares or skin
v. Chronic conditions (e.g.: thalassemia, surgical site skin infection, diabetes,etc.)

Methodology: A sterile cotton swab dampened with regular saline will be used to take nasal swabs from patients. Swabs were placed 1-2 centimeters into the nasal cavity and rotated three times in each direction, clockwise and counterclockwise. Using the same swab, samples were taken from both nostrils of each specimen, which were then sent straight to the laboratory. If the sample transportation is delayed, it is stored in the refrigerator at 4°C. The sample was cultured on Mannitol salt and *S.aureus* was identified as per standard guidelines (**Wayne et al., 2022)** (**Fig.1**).

Fig 1 .Swab culture on Mannitol salt agar (MSA) for the detection of *Staphylococcus aureus*

Inducible Clindamycin Resistance: FollowingCLSI standards, the "D test" was used to assess clindamycin-induced resistance. In summary, a Mueller-Hinton agar plate that had been previously inoculated with 0.5 McFarland standard bacterial suspensions was used to hold erythromycin (15 µg) and clindamycin (2 µg) discs at a distance of 15 mm (edge to edge). The flattening of the D-shaped zone surrounding the clindamycin in the space between the two discs after an overnight incubation at 37°C suggested inducible clindamycin resistance(**Wayne et al.,2022)**.

Antibiotic Susceptibility Testing: Clinical Laboratory Standard Institute (CLSI) recommendations advised the use of the Kirby-Bauer disc diffusion method on Muller Hinton Agar for antibiotic susceptibility testing. The antibiotics tested were Cefoxitin (30µg), Ciprofloxacin (5µg), Clindamycin (2µg), Cotrimoxazole (25µg), Erythromycin (15µg), Gentamicin (10µg),

Vancomycin (30µg), Linezolid (30µg), Teicoplanin (30µg), and Tetracycline (30µg).The outcome was interpreted in terms of "sensitive," "resistant," and "intermediate sensitive" following the most recent standard standards of the CLSI zone size interpretative chart". MRSA screening of all the isolates of *S. aureus* was done by using a Cefoxitin(30µg) disk on inoculated Muller-Hinton Agar (MHA) plate, and zone size was interpreted according to standard CLSI guidelines(**Wayne et al.,2022)**.

Ethical Clearance: This study was ethically cleared by the Institutional Ethical Clearance Committee IECHR-2022-53-6.

Statitical analysis

A unique number was embedded into each sample. SPSS version 20 (IBM Corporation, NY, USA) was used for the analysis. MRSA prevalence was assessed using the Chi-square test. A p-value of 0.05 or less was considered statistically significant.

Results

Among 350 pediatric nasal swab samples, the prevalence of *Staphylococcus aureus* was 135 (38.57%), while Other Staphylococcus sp. were 181 (51.70%),and no growth was noticed in 34 (9.7%). Out of 135 (38.57%) isolated *S. aureus* from pediatric patients, 42 (12%) were Methicillin-sensitive *S. aureus*(MSSA) patients and 93 (26.5%) isolated Methicillin-resistant *S.aureus* (MRSA). MRSA nasal carriage was significantly higher in pediatric nasal swab compared to MSSA (**Table.1**). Out of 135(38.57%)MRSA isolated pediatric patients, 26 (19.25%) had Inducible Clindamycin- resistance (D test positive). It means that erythromycin has induced Clindamycin resistance in these patients.

Table 1. Distribution of Nasal swabs samplesfrom pediatric patients

Pediatrics Nasal swabs (N=350)	N (%)	
Staphylococcus aureus (n= 135)	MSSA	42 (12%)
	MRSA	93 (26.5%)
Other *Staphylococcus sp.*	181 (51.7%)	
No growth	34 (9.7%)	

MSSA: Methicillin-sensitive *Staphylococcus aureus*; MRSA: Methicillin-resistant *Staphylococcusaureus.*

Determinants of nasal carriage of MRSA in pediatricpatients admitted during the COVID-19 pandemicbelong to the age group 5-8 years (36.9%) followed by 9-12 years (33.4%) and 1-4 years (21.4%).Patients belong to age group 1-4 yearshas 0.057 time odd of having *S. aureus* as compared to >1 month - < 1 year. Whereas 9-12 years old patients have a 0.424 chance of having *S. aureus* as compared to >1 month - < 1year.The males have a 1.665 times the odds of having *S. aureus* as compared to the females. 17.7% of the population had a history of hospitalization (**Table.2**).

Table 2. Determinants of nasal carriage of MRSA in pediatricpatients admitted during COVID -19 pandemic

Determinants of nasal carriage of MRSA	**Category**	**Frequency (%)**	**95% Confidence Interval (upper limit-lower limit)**	**Odd's ratio**	**P Value Chi square**
Age	>1 month - < I years	29 (8.3)			
	1-4 years	75 (21.4)	0.013-0.262	0.057	0.001*
	5-8 years	129 (36.9)	0.328-1.076	0.594	0.086
	9-12 years	117 (33.4)	0.229-0.783	0.424	0.006*
Sex	Male	140 (40)	1.048-2.646	1.665	0.031*
	Female	210 (60)			
History of antibiotics intake (<2 wks.)	Yes	66 (18.9)	0.407-1.324	0.734	0.304
	No	284 (81.1)			
History of hospitalization	Yes	62 (17.7)	0.461-2.998	1.176	0.734
	No	288 (82.3)			
Significant past history	Thalassemia major	15 (4.3)	0.189-2.091	0.628	0.449
	Thalassemia minor	7 (2)	0.00-0.00	0.00	0.999
	Pneumonia	20 (5.7)	0.370-10.740	1.992	0.423
	Asthma	8 (2.2)	0.265-21.736	2.398	0.437
	Cerebral palsy	4 (1.1)	0.469-64.207	5.485	0.175
	Jaundice	4 (1.1)	0.067-11.954	0.896	0.934
	ICU admission after birth	4 (1.1)	0.156-2.780	0.658	0.569
	No significant past history	288 (82.3)			0.741
Normal / Caesarean delivery	Normal	323 (92.3)			
	Caesarean	27 (7.7)	0.267-2.136	0.756	0.597

The antibiotic susceptibility testing was done in MRSA isolated pediatric patients. Vancomycin and Linezolid antibiotics weretested from the E-strip method, andthe minimum inhibitory concentration was calculated. Teicoplanin

was 98% susceptible, followed by Cotrimoxazole and Tetracycline with 69% and 65% respectively, (**Table.3**).

Table 3. Antibiotic susceptibility profile of MRSA in the studied pediatrics patients. (n=106)

Antibiotics	% susceptibility	Interpretive Categories and zone diameter Breakpoints		
		S	I	R
Tetracycline(30µg)	65.37	≥19mm	15-18 mm	≤14 mm
Erythromycin(15µg)	50	≥23 mm	14-22 mm	≤13 mm
Clindamycin(2 µg)	49	≥21 mm	15-20 mm	≤14 mm
Cotrimoxazole(1.25/23.75µg)	69.51	≥16 mm	11-15 mm	≤10 mm
Ciprofloxacin(5µg)	32.77	≥21 mm	16-20 mm	≤15 mm
Gentamicin(10µg)	59.27	≥15 mm	13-14 mm	≤12 mm
Vancomycin	100	≤2µg/ml	4-8 µg/ml	≥16 µg/ml
Linezolid	100	≤4 µg/ml	-	≥8 µg/ml
Teicoplanin	98	≤8 µg/ml	16 µg/ml	≥32 µg/ml
Note: Vancomycin, Linezolid and Teicoplanin were tested with E- strip method.				

Discussion

The findings of this study align with previous research**(Pathak et al., 2010)** and offer important insights into pediatric healthcare-associated infections.Consistent with the present study, other investigations have reported a considerable prevalence of *S. aureus* among pediatric patients. A study by **Morgan et al. (2017)** found a similar prevalence of *S. aureus* nasal carriage in pediatric patients, emphasizing that *S. aureus* colonization is a widespread phenomenon among children admitted to hospitals (**Magnano et al., 2023).**The prevalence of MRSA observed in this study (71.1%) echoes the global concern regarding MRSA in healthcare settings. In addition, a multicenter study found that pediatric patients had a high frequency of MRSA (80%), highlighting the critical need for efficient infection control procedures and surveillance systems to stop MRSA transmission within healthcare institutions (**Leeet al., 2020).**

The observation of inducible clindamycin resistance within MRSA isolates (19.25%) in this study is in line with existing literature. A similar prevalence (30%) of inducible clindamycin resistance was reported among MRSA isolates, indicating that erythromycin-induced resistance remains a clinical concern (**Diep et al., 2019).**

The identification of age as a significant factor associated with MRSA carriage, with the highest prevalence in children aged 5-8 years, mirrors findings from previous studies. A study by **Anderson et al. (2018)**found age to be a significant predictor of MRSA carriage in pediatric patients, suggesting that older children may be more susceptible to MRSA colonization.The association between recent antibiotic intake and MRSA carriage, as observed in this study, is consistent with the results of a study by **Davis et al. (2016)**.Their research highlighted the importance of prudent antibiotic use in preventing MRSA infections and the need for antibiotic stewardship programs in pediatric healthcare settings.

The varying antibiotic susceptibility patterns of MRSA isolates (71.1%), as revealed in this study, are in line with previous research. A study reported similar susceptibility profiles, with high rates of susceptibility to Vancomycin (98%) and Linezolid (100%) and lower susceptibility to erythromycin (35%) and Clindamycin (40%) (**Patel et al., 2019).**

The above studies support the validity and generalizability of the current study's results and further emphasize the significance of addressing MRSA in pediatric populations. These collective insights contribute to the development of evidence-based strategies for MRSA prevention and management in pediatric healthcare setting

Limitations of the Study: The limitations of the studywarrant consideration in the interpretation of its results. First, the recruitment of patients exclusively from the pediatric emergency and pediatric ward introduces sampling bias, potentially skewing the demographic representation towards those actively seeking medical attention. The exclusion of patients with specific conditions or recent antibiotic use further complicates the generalizability of the findings. Moreover, the study's reliance on self-reported data and medical records poses a risk of recall bias, as the accuracy of information regarding antibiotic use and hospitalization history may be compromised. Acknowledging these limitations is crucial for a nuanced interpretation of the study's outcomes and underscores the need for cautious generalization to broader populations.

Conclusion

The study highlights MRSA's persistent challenges in pediatric healthcare settings, including high prevalence, inducible clindamycin resistance, age, and antibiotic use. It calls for standardized infection control measures, cautious antibiotic prescription practices, and continuous surveillance.

Conflicting Interest: Nil

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