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Clinico-epidemiology and resistance patterns of community-acquired and hospital-acquired *staphylococcus aureus* sepsis in children

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Abstract

Background: *Staphylococcus aureus* (*S. aureus*) is a virulent bacterium responsible for a spectrum of infections, from superficial dermatological issues to severe, life-threatening sepsis. The emergence of methicillin-resistant *S. aureus* (MRSA) strains, encompassing both hospital-acquired (HA) and community-acquired (CA) variants, presents significant challenges to effective treatment, especially in pediatric sepsis cases. This research endeavored to characterize *S. aureus* sepsis in pediatric patients, differentiate between cases caused by CA *S. aureus* (CA-SA) and HA *S. aureus* (HA-SA), and evaluate patterns of antibiotic resistance.

Methods: This study, conducted between January 2021 and December 2022 at the Postgraduate Department of Pediatrics, Children's Hospital, Srinagar, Kashmir, J&K, investigated patients aged 1 month to 18 years with suspected *S. aureus* sepsis or disseminated disease. Standard methods (BacT Alert and Vitek II Compact) were employed for culturing various samples. Continuous data are presented as mean ± standard deviation (SD), while categorical variables are expressed as proportions.

Results: Out of 56 patients, CA-SA was observed in 66.1% of cases, while HA-SA accounted for the remaining 33.9%. The cohort primarily consisted of males (62.5%) and individuals residing in rural areas (71.43%). Localized musculoskeletal symptoms were a prominent feature, present in 91.9% of patients ($P \leq 0.05$). Pleuropulmonary disease showed an association with HA-SA, whereas necrotizing soft tissue infections were linked to CA-SA. Common clinical manifestations included pneumonia and abscesses. Complications (such as septic shock, respiratory failure, and multi-organ dysfunction) were more frequently encountered in patients with HA-SA. Among 50 culture-confirmed cases, 96% were identified as methicillin-resistant *S. aureus* (MRSA). Survival rates differed between the two groups, with 94.6% for CA-SA patients and 89.5% for HA-SA patients.

Conclusion: The current study reveals a high prevalence of MRSA in pediatric sepsis, emphasizing the critical need for urgent antimicrobial stewardship. The observed distinct clinical profiles of CA-SA and HA-SA further underscore the necessity for tailored management strategies, particularly in resource-limited environments.

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Introduction

Staphylococcus aureus (*S. aureus*) commonly resides as an asymptomatic commensal on human skin and mucosal surfaces. The anterior nares are considered the primary colonization site, although the bacterium can also be isolated from the skin or pharynx. Colonized individuals can facilitate the transmission of these bacteria to others, either through direct contact via their hands or indirectly through airborne droplets originating from the nasal passages. In hospitals, staphylococcal infections are frequently attributed to healthcare workers' hands. Key risk factors for developing such infections involve compromised skin integrity, including but not limited to wounds, dermatological conditions like eczema or epidermolysis bullosa, and burns, ventriculoperitoneal shunts, and indwelling intravascular or intrathecal catheters (1). These infections can manifest across various bodily systems, including the skin, bones, joints, and lungs. Invasive infections often develop following a pre-existing skin and soft tissue infection or a viral respiratory tract infection, particularly influenza. However, they can also manifest spontaneously in healthy children without any identifiable prior infections or risk factors (2). This pathogen is responsible for both community-acquired (CA) and hospital-acquired (HA) infections (3). Notably, staphylococcal infections, especially those attributed to methicillin-resistant *S. aureus* (MRSA), are associated with elevated patient morbidity and mortality rates (4,5). MRSA was initially documented in the United Kingdom in 1961 (6). Historically, MRSA infections, termed HA-MRSA, were predominantly linked to patients in nosocomial environments. However, the last decade has witnessed a substantial epidemiological shift due to the rise of CA-MRSA (7). Notably, *S. aureus* is a leading etiology of sepsis requiring admission to pediatric intensive care units (PICUs), with an estimated incidence ranging from 4 to 26 cases per 100,000 children annually (8,9).

This prospective study aimed to characterize the demographic, clinical, and microbiological features of invasive *S. aureus* infections in pediatric patients. Secondary objectives included assessing the need for PICU admission and identifying any shifts in antimicrobial resistance patterns.

Methods

This descriptive study was conducted at a tertiary care hospital in Srinagar, J&K, spanning from January 2021 to December 2022. Ethical clearance (Institutional Ethical Committee (IEC) No. F (Minutes-BOPGS) Acad/KU/22) was secured from the institutional ethics committee prior to the study's commencement. Informed consent was obtained in the local language from each patient's guardian before their enrollment.

This study enrolled individuals between one 1 and 18 years of age who fulfilled specific diagnostic criteria. Sepsis caused by *S. aureus* was identified based on the presence of systemic inflammatory response

syndrome (SIRS) concurrently with a culture-confirmed staphylococcal infection. The diagnosis of SIRS adhered to the 2005 International Consensus Criteria on Pediatric Sepsis. The criteria consisted of an abnormal core temperature (>38.5°C or <36.5°C), cardiovascular issues (Mean heart rate >2 standard deviation (SD) above the normal range for age, or bradycardia in infants under 1 year with a mean heart rate below the 10th percentile for their age), respiratory issues (Mean respiratory rate >2 SD above the normal range for age or the requirement for mechanical ventilation), and issues in leukocyte count (Either an elevated or decreased white blood cell count for age or >10% immature neutrophils). Disseminated staphylococcal disease is characterized by pyogenic infection at a minimum of two non-contiguous anatomical sites. This definition requires a clinical suspicion of staphylococcal disease, further supported by either a culture-confirmed *S. aureus* isolation from a sterile site or microscopic identification of gram-positive cocci in clusters within sterile body fluid. Infections were categorized as CA-MRSA if they met the following criteria: Symptom onset occurred prior to admission, cultures were obtained within 48 hours of admission, there was no documented history of *S. aureus* infection (i.e., no prior positive cultures), and no record of admission, surgery, or invasive medical device use within the preceding 12 months. Conversely, infections that did not fulfill these conditions were classified as HA-MRSA (10).

Microbiological cultures of diverse samples were performed using established methodologies. Specifically, blood culture, body fluid, and pus samples were cultured in BacT/Alert blood culture bottles. Bottles indicating a positive result via the BacT/Alert system underwent subculture onto standard bacteriological media. Subsequent microbial growth was then subjected to antimicrobial susceptibility testing utilizing both the automated VITEK 2 Compact system and the manual Kirby-Bauer disc diffusion method. Urine cultures were performed using a semi-quantitative method on Hi-Chrome urinary tract infection (UTI) agar. Antibiotic sensitivity testing was subsequently conducted manually via the Kirby-Bauer disc diffusion method (11). Cefoxitin discs (30 mcg; Himedia Labs India) were utilized to differentiate between MRSA and methicillin-susceptible *S. aureus* (MSSA). Additional antibiotics assessed by disc diffusion included linezolid (10 mcg), gentamicin (10 mcg), amikacin (30 mcg), cotrimoxazole (25 mcg), and clindamycin (2 mcg) (Himedia Labs India). Minimum inhibitory concentrations (MICs) for teicoplanin and vancomycin were determined using the VITEK 2 Compact system.

Statistical analysis

The collected data were systematically organized and initially recorded in a Microsoft Excel spreadsheet. Subsequently, these data were transferred to the SPSS Version 25 (SPSS Inc., Chicago, Illinois, USA) data editor for further analysis. Continuous variables are presented as the mean ± SD, while categorical variables are reported as proportions. For comparisons involving two or more groups with qualitative data, the chi-square test was employed. Statistical significance was established at a $P \leq 0.05$.

Results

Among 56 pediatric patients diagnosed with *S. aureus* sepsis or disseminated staphylococcal infection, culture positivity was observed in 50 cases (89.30%). The cohort comprised 37 (66.10%) CA infections and 19 (33.90%) HA infections, resulting in a CA severe sepsis (CA-SS) to HA severe sepsis (HA-SS) ratio of 2:1 (66.1%: 33.9%). Further analysis of the 50 culture-positive *S. aureus* sepsis cases revealed that 48 (96%) were MRSA, while only 2 were MSSA. Linezolid, vancomycin, and teicoplanin demonstrated 100% sensitivity against the isolated strains, followed by gentamicin (70%), amikacin (60%), cotrimoxazole (50%), and clindamycin (30%).

Among the 48 MRSA cases, 32 were identified as CA sepsis, while 16 were HA sepsis. Both MSSA cases presented with CA sepsis. The patient cohort was predominantly male (n = 35, 62.50%) and originated from rural areas (n = 40, 71.43%). Trauma was the most frequently observed predisposing factor (21.42%), with pustules (10.71%), fractures (5.35%), and burns (3.60%) also contributing to the infections.

Upon admission, the prevalent symptoms observed were fever, localized musculoskeletal issues, cough, and altered sensorium. Of these, only localized musculoskeletal symptoms (91.90%) demonstrated a significant association with CA-SA (Table 1). The most frequently noted signs at admission included tachypnea, hypotension, tachycardia, crepitation, and feeble pulses; however, none of these signs showed a statistically significant correlation with either CA-SA or HA-SA (Table 1). Upon admission, common organ system involvements observed in patients with *S. aureus* sepsis included pleuropulmonary disease, necrotizing soft tissue disease, osteoarticular disease, meningitis, and pericardial effusion. A significant association was identified between pleuropulmonary disease and HA-SS, whereas necrotizing soft tissue disease showed a significant association with CA-SS (Table 2). The predominant clinical presentations of the disease were pneumonia, followed by abscess formation (Table 3). Notably, the presence of an abscess was significantly associated with CA-SS.

Patients with HA-SS experienced higher incidences of several complications compared to those with CA-SS, such as septic shock (47.4% vs. 37.8%), respiratory failure (21.05% vs. 5.4%), multi-organ dysfunction (15.8% vs. 5.4%), and pneumothorax (5.3% vs. 2.7%). However, these differences did not reach statistical significance. Additionally, acute respiratory distress syndrome (ARDS) was observed in two CA-SS patients.

No significant association was observed between the presence of abnormal leukocyte count, platelet count, renal function, hepatic function, coagulopathy, or anemia and the occurrence of either CA or HA infections (Table 4). Furthermore, left ventricular (LV) dysfunction was found in comparable proportions across patient groups, specifically in 5.40% of patients with CA-SS and 5.30% of those with HA-SS.

All patients received anti-staphylococcal antibiotics. Additional interventions were nasal prong oxygen for 33 (59%) patients, vasopressor support for 23 (41%) patients, incision drainage for 20 (36%) patients, packed cell transfusion for 19 (34%) patients, heated high-flow nasal cannula for 16 (28%) patients, ventilator support for 6 (11%) patients, intercostal tube drainage for 9 (16%) patients, and pericardiocentesis for 1 (0.02%) patient.

A notable correlation was found between the use of high flow in the HA-SS population (P = 0.025).

The mean ± SD hospital stay was for patients with CA-SS 13.32 ± 4.26 days and 14.78±5.53 days for patients with HA-SS. This difference was not statistically significant. Mortality rates were observed to be higher in the HA-SS group (10.50%) compared to the CA-SS group (5.40%), although this difference also did not reach statistical significance.

Table 1. Distribution of studied population as per symptoms and signs at admission

Symptoms	Total (N)	Community-Acquired N (%)		Hospital-Acquired N (%)	P-Value
Fever	52	36	97.30	16 (84.20)	0.71795
Localized musculoskeletal symptoms	38	34	91.90	4 (21.10)	0.00001
Cough	16	10	27.00	6 (31.60)	0.960148
Altered sensorium	12	7	18.90	5 (26.30)	0.523013
Breathlessness	9	6	16.20	3 (15.80)	0.967161
Signs					
Tachypnea	30	18	48.60	12 (63.20)	0.30264
Hypotension	23	17	45.90	5 (26.30)	0.154414
Tachycardia	21	15	40.50	6 (31.60)	0.511912
Crepitation	21	15	40.50	6 (31.60)	0.511912
Feeble pulses	20	13	35.10	7 (36.80)	0.899557

Table 2. Distribution of studied population as per organ involvement at admission

Disease spectrum	Total (N)	Community-Acquired N (%)		Hospital-Acquired N (%)	P-Value
Pleuropulmonary disease	41	24	64.90	17 (89.50)	0.048964
Necrotizing soft tissue disease	38	30	81.10	8 (42.10)	0.003107
Osteoarticular disease	11	9	24.30	2 (10.50)	0.218506
Meningitis	6	2	5.40	4 (21.10)	0.07306
Pericardial effusion	1	1	2.70	0	1

Table 3. Distribution of studied population as per disease spectrum

Disease spectrum	Total (N)	Community-Acquired (N) (%)	Hospital-Acquired N (%)	P-Value
Pneumonia	35	21 (56.80)	14 (73.70)	0.2154
Abscess	30	26 (70.30)	4 (21.10)	0.000471
Pleural effusion	9	5 (13.50)	4 (21.10)	0.467034
Empyema	7	4 (10.80)	3 (15.80)	0.59377
Septic arthritis	7	5 (13.50)	2 (10.50)	0.748947
Osteomyelitis	4	4 (10.80)	0	0.29
Cellulitis	8	4 (10.80)	4 (21.10)	0.299731
Meningitis	6	2 (5.40)	4 (21.10)	0.07306
Pericardial effusion	1	1 (2.70)	0	1

Table 4. Distribution of studied population as per laboratory investigations

Laboratory investigations	Total (N)	Community-Acquired N (%)	Hospital-Acquired N (%)	P-Value
Leukocytosis	35	23 (62.20)	12 (63.20)	0.941907
Leukopenia	5	2 (5.40)	3 (15.80)	0.196969
Thrombocytopenia	5	5 (13.50)	0	0.147
Anemia	23	15 (40.50)	8 (42.10)	0.910276
Abnormal liver function tests	10	6 (16.20)	4 (21.10)	0.654571
Abnormal kidney function tests	8	5 (13.50)	3 (15.80)	0.817745
Coagulopathy	6	2 (5.40)	4 (21.10)	0.07306

Discussion

This study investigated the demographic, clinical, and microbial characteristics of *S. aureus* sepsis in infants and children admitted to the Postgraduate Department of Pediatrics, GB Panth Children Hospital, Srinagar, Kashmir. Of the 56 pediatric patients admitted with *S. aureus* sepsis, a male predominance was observed, consistent with findings from other Indian studies (12,13). Furthermore, the majority of the enrolled children (71.43%) resided in rural areas. This demographic trend may be attributed to a higher prevalence of undernutrition in rural households, which is known to elevate susceptibility to childhood infections (14).

Trauma, skin infections, and fractures have been identified as primary predisposing factors for sepsis. Specifically, a history of trauma frequently correlates with *S. aureus* sepsis, likely due to the inoculation of bacteria into skin and soft tissues, leading to bacteremia and subsequent complications. It is important to consider that this relationship may be temporal. Consistent with these findings, Baranwal et al. (15) reported pustules (26%), blunt trauma (15%), and injections (8%) as prevalent predisposing conditions in their study.

In our study, we observed that the predominant form of *S. aureus* sepsis among patients was CA-SA sepsis, accounting for 66.10% of cases. The ratio of CA-SS to HA-SS can serve as an indicator of two key factors: the standard of aseptic care maintained within healthcare facilities and the prevalence of *S. aureus* within the broader community.

In the studied cohort, fever was the predominant symptom, observed in 92.85% of individuals, with musculoskeletal symptoms being the next most frequent. This observation aligns with findings from prior research, specifically those reported by Bathla A, et al. (12) and Mathew et al. (16).

In our study, pneumonia was observed in 73.70% of HA-SS cases and 56.80% of CA-SS cases. Hospitalized individuals are susceptible to rapid oropharyngeal colonization by nosocomial flora, which can subsequently culminate in lower respiratory tract infections caused by these organisms (17).

In staphylococcal illnesses, the organ systems most frequently affected include necrotizing soft tissue, pleuropulmonary, pericardial effusion, osteoarticular, and meningitis, as reported by Baranwal et al. (15). Our study specifically revealed a significant correlation between pleuropulmonary disease and HA-SS, while necrotizing soft tissue disease was significantly associated with CA-SS.

Untreated *S. aureus* sepsis can lead to complications such as septic shock, respiratory failure, multi-organ dysfunction, and pyopneumothorax (18). Our clinical observations align with these findings, as we have also encountered patients exhibiting similar complications.

Abnormalities in leucocyte count, platelet count, renal function, hepatic function, coagulation, or erythrocyte levels were not found to be significant predictors of either CA or HA infections.

A notable proportion of patients, specifically 31 (55%), required ICU admission for critical interventions, including vasopressor administration, heated high-flow nasal cannula oxygen therapy, and mechanical ventilatory support. A statistically significant correlation was observed between the utilization of high-flow therapy and the cohort of patients with HA-SS. This association is likely attributable to the elevated prevalence of severe pulmonary disease within this particular subgroup. In our clinical setting, high-flow therapy is routinely employed as a primary therapeutic modality for pediatric patients presenting with acute respiratory distress accompanied by hypoxia within the PICU.

In the present investigation, *S. aureus* sepsis was identified in cultures from 50 patients. Of these, MRSA accounted for 48 isolates, while MSSA comprised the remaining 2. Further categorization of the MRSA isolates revealed that 32 originated from CA infections, with the remaining 16 being HA. Both MSSA isolates were also determined to be CA. These findings contrast with a prior study conducted at the same institution in 2019 by Qadri, I et al. (19), which reported a lower prevalence of methicillin resistance, with only 35% of specimens identified as such. In an Iranian investigation, a substantial prevalence of methicillin resistance (48%) was observed among *S. aureus* isolates,

with all strains confirmed to carry the *mecA* gene (20). This finding aligns with global trends, as evidenced by a multicenter study conducted by Camacho-Cruz, J. et al., which reported a 38% incidence of methicillin-resistant isolates (21). These converging data suggest a shift in the community resistance patterns, likely attributable to the widespread misuse of antibiotics.

This study has several limitations. We were unable to obtain MIC values for all antibiotics, and we did not perform molecular characterization, including the detection of Panton-Valentine leukocidin (PVL) and *mecA* genes. Furthermore, the proportionate carriage of *S. aureus* was not determined. Finally, due to the cross-sectional design of the study, we could not establish causality for identified risk factors.

Conclusion

Our research indicates that CA-SA sepsis continues to be more prevalent than HA-SA cases. A significant observation, both within our specific setting and globally, is the marked shift in the antimicrobial sensitivity patterns of *S. aureus*, characterized by a concerning increase in methicillin-resistant strains. This evolving trend necessitates immediate focus to inform the development of effective treatment strategies and robust infection control measures.

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Ethical statement

The present study was approved by the Institutional Ethics Committee (IEC No. F (Minutes-BOPGS) Acad/KU/22).

Conflicts of interest

No conflicts of interest.

Author contributions

Mohd Suhail and Umer Qureshi: Conceiving and designing the experiments, Analyzing the data, and Preparing the figures; Rayees Khanday: Writing the main manuscript; Sahar Siddiqui: Collecting samples and Performing the experiments. All authors reviewed and completed the manuscript, played a role in the article, and approved the submitted version.

Data availability statement

The data are available.

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