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Prognostic Factors and Utility of the RISC Score Among Children with Community-Acquired Pneumonia Admitted to a Pediatric Intensive Care Unit at a Tertiary Care Hospital

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ABSTRACT

Introduction: Community-acquired pneumonia (CAP) is a leading cause of morbidity and mortality among children. We aimed to evaluate the demographic, clinical, vaccination status, comorbidity profiles, and microbiological findings of children aged 1 month to 12 years with CAP admitted to a pediatric intensive care unit (PICU), and to assess the utility of the Respiratory Index of Severity in Children (RISC) score in predicting in-hospital mortality. **Methods:** This retrospective, observational study was conducted at SMS Medical College, Jaipur, India, from January 2019 to January 2021. Of 352 screened children, 322 meeting the WHO Integrated Management of Childhood Illness (IMCI) pneumonia definition were enrolled. Blood cultures were processed using the BD BACTEC FX system; isolates were identified by VITEK®2. Antimicrobial susceptibility testing followed Clinical and Laboratory Standards Institute M100-Ed31 guidelines. The RISC score was calculated at PICU admission. The chi-square test, Fisher's exact test, and independent t-test were used; a P value < 0.05 was considered statistically significant. **Results:** Among 322 children (70.2% male), in-hospital mortality was 5.9% (19/322). Age and sex were not significantly associated with mortality. Complete vaccination including pneumococcal conjugate vaccine (PCV) was protective ($P < 0.001$). Oxygen saturation (SpO_2) < 90% was significantly associated with mortality ($P = 0.002$). Non-survivors had higher mean RISC scores (2.05 ± 1.58 *vs.* 0.86 ± 1.32; $P < 0.001$). At a RISC score cut-off of ≥ 3, sensitivity was 52.6%, specificity 81.9%, and negative predictive value 96.5%. Blood culture positivity was 35.1% (113/322); 79 isolates (24.5% of all enrolled children) were pathogenic. All 19 deaths occurred in culture-positive children; no mortality was observed among those with sterile cultures. The highest mortality rates were observed with *Escherichia coli* (66.7%, 2/3), *Klebsiella pneumoniae* (41.2%, 7/17), and *Streptococcus pneumoniae* (37.5%, 3/8) bacteremia. **Conclusion:** Complete vaccination, SpO_2 < 90%, and the RISC score were significant prognostic factors. The RISC score demonstrated high negative predictive value for identifying children at low risk of mortality. Early blood culture collection and expanded vaccination coverage may improve outcomes in resource-limited settings.

INTRODUCTION

Community-acquired pneumonia (CAP), a major type of lower respiratory tract infection (LRTI), accounts for 14% of global deaths in children younger than 5 years [1]. According to UNICEF data, an estimated 725,557 children younger than 5 years died from pneumonia in 2021 [1]. India has the highest number of childhood pneumonia cases globally and accounted for approximately 20% of global pneumonia deaths in this age group in 2015 [2]. Within India, Rajasthan has a substantial burden of pediatric pneumonia, with an estimated cumulative incidence of 499

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per 1000 children younger than 5 years in 2015 [3]. A 2021 study from Jodhpur, Rajasthan, noted a 36.9% prevalence of severe pneumonia among hospitalized children < 5 years [4].

In severe cases of CAP, sepsis complicating the infection may develop, which worsens the prognosis of affected children. A study from Bangladesh reported that severe sepsis was identified in 64% of children < 5 years who died of pneumonia [5]. Given the risk of sepsis complicating CAP and its impact on outcomes, rapid and accurate determination of CAP etiology is critical, as it directly influences individual treatment decisions and institutional antimicrobial stewardship policies. Early risk stratification is an important component of the clinical evaluation of children hospitalized with CAP, as it helps identify those at increased risk of adverse outcomes and guides appropriate management [6]. Children with CAP may benefit from a validated severity scoring system to estimate mortality risk. The Respiratory Index of Severity in Children (RISC) score, a validated tool, was developed to predict mortality in children aged 1–23 months hospitalized with LRTI in a South African cohort [7].

Although several severity scoring systems have been proposed for CAP in children, data on their performance in predicting mortality among critically ill children admitted to PICUs remain limited, particularly in low- and middle-income countries (LMICs). Regional data on CAP remain limited, and to the best of our knowledge, no studies from Rajasthan have evaluated the RISC score in predicting mortality among children with CAP.

Therefore, we sought to describe the demographic, clinical, vaccination, comorbidity, and microbiological profiles of children aged 1 month to 12 years with CAP admitted to the PICU of a tertiary care hospital in Jaipur, Rajasthan, India, and to evaluate the utility of the RISC score in predicting in-hospital mortality.

MATERIAL AND METHODS

Study design and setting. This retrospective, observational, hospital-based study was conducted in the pediatric intensive care unit (PICU) and Department of Microbiology of SMS Medical College and Attached Hospitals, Jaipur, Rajasthan, India, from January 2019 through January 2021, using retrospectively collected data.

According to the WHO IMCI guidelines [8], pneumonia was defined as cough or difficulty in breathing accompanied by fast breathing and/or chest indrawing. Severe pneumonia was defined as pneumonia with any general danger sign (inability to drink or breastfeed, persistent vomiting, convulsions, or lethargy/unconsciousness). Although the WHO IMCI case definition is intended for children aged 2–59 months, it was applied to all enrolled children (aged 1 month to 12 years) in this study to maintain uniformity in classification, acknowledging that this approach adapts the guideline beyond its standard age range for study consistency.

Moreover, sepsis was defined according to the 2005 International Pediatric Sepsis Consensus Conference criteria as a systemic inflammatory response syndrome (SIRS) in the presence of or resulting from suspected or proven infection [9]; detailed diagnostic criteria are provided in Supplementary File 1. The 2005 pediatric sepsis definition was selected for this study as it remains the most widely adopted criterion in pediatric clinical practice and was the prevailing standard during the study period, acknowledging that subsequent definitions (*e.g*., Sepsis-3 [10]) have been proposed primarily for adult populations.

Study population. A total of 352 children were screened, of whom 322 were included after applying exclusion criteria. The enrolled children were aged 1 month to 12 years, and written informed consent for blood sample collection was obtained from their parents/legal guardians prior to specimen collection; retrospective data abstraction was performed under ethics committee approval. Children were included if they met the WHO IMCI case definition for pneumonia [8] and required PICU admission. Children were excluded if they had pulmonary tuberculosis, congenital lung anomalies, or a confirmed diagnosis of HIV/AIDS. Children who left against medical advice (n = 30) were excluded from the final analysis. The sample size was based on a consecutive sampling approach, enrolling all eligible children during the study period.

Data collection. Data were collected using a standardized case report form by trained research personnel, with quality checks performed by senior investigators. Each child underwent a detailed evaluation that included demographic data (age, sex, and anthropometric measurements), established risk factors for pneumonia (including malnutrition, household air pollution exposure, and prior hospitalization), and vaccination status (verified from the immunization card). Underlying comorbidities, including but not limited to congenital heart defects (CHD), chronic lung disease, neurological disorders, and immunodeficiency, were documented from the medical records. SpO_2 was measured using a pulse oximeter on room air at PICU admission. The primary outcome was in-hospital mortality (death during PICU admission).

The RISC score was calculated for all enrolled children at PICU admission according to the criteria developed by Reed *et al*. [7], using the original scoring algorithm without modification. Scores were derived from clinical parameters including oxygen saturation, chest indrawing, inability to feed, wheezing, and age. Missing values for individual RISC parameters were handled by excluding the affected parameter from the total score calculation, consistent with the original validation study. All enrolled children were HIV-uninfected, consistent with the RISC score's original validation population.

Microbiological analysis. Blood samples were collected aseptically following standard skin antisepsis with povidone-iodine and 70% alcohol, prior to the initiation of antimicrobial therapy. Two sets of blood cultures were obtained from separate venipuncture sites per child, with 1–

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4 mL for children weighing < 12.7 kg (using BD BACTEC Peds Plus/F bottles) and 5–10 mL for children weighing ≥ 12.7 kg (using BD BACTEC Plus Aerobic/F bottles). The two blood culture sets were collected 5–15 minutes apart. Blood cultures were monitored using the automated BD BACTEC FX system (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), with bottles incubated for a maximum of 5 days before being reported as negative. Only aerobic blood cultures were performed; anaerobic cultures were not obtained, as anaerobic bacteremia is uncommon in pediatric community-acquired pneumonia. Positive blood cultures were subcultured on 5% sheep blood agar and MacConkey agar and incubated at 35–37°C for 18–24 hours in ambient air. Following incubation, isolates were identified using the VITEK® 2 system (bioMérieux, Marcy-l'Étoile, France). Antimicrobial susceptibility testing (AST) was performed using the Kirby-Bauer disc diffusion method (described below). Blood culture isolates were classified as contaminants if coagulase-negative *Staphylococcus* spp. (CoNS), diphtheroids, or non-pathogenic Gram-positive bacilli were recovered from a single blood culture set without clinical correlation, consistent with standard pediatric blood culture interpretation guidelines [12, 13]. Standard quality control strains were used as per the Clinical & Laboratory Standards Institute (CLSI) recommendations [11]. Polymicrobial cultures were fully processed, with all potential pathogens identified and subjected to AST.

Although Kirby-Bauer disc diffusion zone diameters were recorded prospectively during the study period, final interpretations for all isolates were retrospectively standardized using the CLSI M100-Ed31 (2021) edition [11] at the conclusion of the study to ensure uniformity. Isolates classified as intermediate were grouped with resistant isolates for analysis, adopting a conservative approach consistent with clinical practice where intermediate susceptibility may not guarantee therapeutic success.

Antimicrobial agents were selected for testing according to CLSI M100-Ed31 guidelines [12], which categorize agents into Groups A, B, and C based on their priority for testing and reporting. Briefly, Group A agents are recommended for routine testing and reporting; Group B agents are tested routinely but reported selectively (*e.g.*, for isolates from sterile sites, multidrug-resistant organisms, or when first-line agents are clinically inappropriate); and Group C agents are supplemental agents intended for patients with allergies to first-line agents or for epidemiological surveillance purposes. Representative agents from each relevant group were tested. In this study, an isolate was classified as resistant to a specific group if it demonstrated resistance to all antimicrobial agents tested within that group, adopting a conservative definition of group-level resistance for analytical consistency.

Antimicrobial agents tested for each organism group, categorized by CLSI reporting groups [11], are detailed below:

• For Enterobacterales (*E. coli*, *K. pneumoniae*, and *Enterobacter* spp. identified in this study):

○ Group A: ampicillin and gentamicin.

○ Group B: amikacin, cefotaxime, cefepime, piperacillin-tazobactam, imipenem, ciprofloxacin, and trimethoprim-sulfamethoxazole (cotrimoxazole).

○ Group C: ceftazidime, aztreonam, and tetracycline (included per CLSI recommendations for surveillance; tetracyclines are generally contraindicated in children < 8 years due to dental and bone effects).

• For *Pseudomonas aeruginosa*:

○ Group A: piperacillin-tazobactam, ceftazidime, and tobramycin.

○ Group B: cefepime, imipenem, aztreonam, amikacin, and ciprofloxacin.

○ Group C: No antimicrobials were tested in this group, as CLSI does not recommend specific Group C agents for this organism.

• For *Acinetobacter* spp.:

○ Group A: ampicillin-sulbactam, ceftazidime, ciprofloxacin, imipenem, and gentamicin.
○ Group B: piperacillin-tazobactam, cefepime, cefotaxime, minocycline, amikacin, and trimethoprim-sulfamethoxazole.

○ Group C: No antimicrobials were tested in this group, as CLSI does not recommend specific Group C agents for this organism.

• For *Staphylococcus aureus*:

○ Group A: cefoxitin (used as a surrogate marker for *mecA*-mediated methicillin resistance), erythromycin, trimethoprim-sulfamethoxazole, and clindamycin.

○ Group B: doxycycline, vancomycin, and linezolid.

○ Group C: gentamicin and ciprofloxacin.

• For *S. pneumoniae*:

○ Group A: penicillin (screened using oxacillin disk; penicillin MIC performed for isolates with reduced susceptibility), erythromycin, and trimethoprim-sulfamethoxazole.

○ Group B: doxycycline, vancomycin, clindamycin, and levofloxacin.

○ Group C: linezolid and chloramphenicol.

• For *Enterococcus* spp.:

○ Group A: ampicillin.

○ Group B: vancomycin and linezolid.

○ Group C: gentamicin (high-level resistance screening to assess synergy with cell-wall active agents).

Representative agents from each relevant antimicrobial class, as recommended by CLSI for each organism group, were included in the testing panel. An isolate was classified as resistant to a specific CLSI group if it demonstrated resistance to all tested agents within that group, adopting a conservative definition to reflect multidrug resistance patterns. This composite resistance definition was used to assess overall group-level resistance patterns in relation to clinical outcomes.

Antifungal susceptibility testing (AFST). *Candida* spp. were isolated from 5 (1.6%) blood cultures. Species-level identification was performed using the VITEK® 2 system (bioMérieux, Marcy-l'Étoile, France); however, antifungal susceptibility testing (AFST) could not be performed owing to the unavailability of required testing facilities at our

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institution. Antifungal treatment for these patients was guided by institutional protocols (primarily empirical fluconazole or amphotericin B) and clinical judgment, precluding correlation of susceptibility patterns with clinical outcomes.

Statistical analysis. The primary outcome was in-hospital mortality. Categorical variables were expressed as counts and percentages, and continuous variables were presented as means ± SD. Ninety-five percent confidence intervals (CIs) were calculated for continuous variables to quantify precision of estimates. Comparisons of categorical variables were performed using the chi-square test and Fisher's exact test (applied when any expected cell counts were < 5). The independent t-test was used to compare continuous variables (*e.g.*, mean age and RISC scores) between the survivor and non-survivor groups. Normality of continuous variables was assessed using the Shapiro-Wilk test prior to applying parametric tests. Sensitivity, specificity, positive predictive value (PPV), and NPV of the RISC score at predefined cut-off values (> 1 and ≥ 3) were calculated using standard 2×2 contingency tables. Bonferroni correction for multiple comparisons was applied to RISC score category analyses (comparing each individual score category against all others combined), with an adjusted significance level of $P \leq 0.007$. Only univariate analyses were performed; multivariable analysis was not conducted due to the limited number of mortality events (n = 19). $P < 0.05$ was considered statistically significant. Children with missing data were excluded from the respective analyses (complete-case analysis). All statistical analyses were performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA); effect sizes (*e.g.*, odds ratios, mean differences) with 95% CIs were reported alongside P-values where applicable.

RESULTS

Demographics. Of the 322 children included in the final analysis, 226 (70.2%) were males and 96 (29.8%) were females. The majority of children (n = 205, 63.7%) were aged < 1 year, while the fewest were aged > 5 years (n = 13, 4.0%). The mean age of the study population was 14.27 ± 19.60 months (reflecting a right-skewed distribution; median and IQR would be more representative). The mean age did not differ significantly between survivors (14.67 ± 20.20 months) and non-survivors (8.16 ± 7.62 months; $P = 0.17$). The overall in-hospital mortality rate was 5.9% (19/322).

No statistically significant association was found between mortality and age group ($P = 0.17$) or sex ($P = 0.17$). However, immunization status was significantly associated with mortality. Complete vaccination (including pneumococcal conjugate vaccine [PCV]) was significantly associated with survival ($P < 0.001$), and unimmunized status was significantly associated with mortality ($P = 0.03$), while partial vaccination did not reach statistical significance ($P = 0.08$) (Table 1).

Clinical characteristics and comorbidities. The most common comorbidity was congenital heart disease (CHD), observed in 95 children (29.5% of the total study population), followed by developmental delays in 48 children (14.9%). Other comorbidities included anemia (n = 33, 10.2%), immunodeficiency/genetic disorders (n = 30, 9.3%), and seizure disorders (n = 17, 5.3%) (Table 1). However, no significant association was observed between any individual comorbidity and mortality (all $P > 0.05$). A graded association was observed for oxygen saturation, with SpO_2 < 90% significantly associated with mortality (mortality rate: 14.9% [10/67] *vs.* 3.5% [9/255] in children with $SpO_2 \geq 90\%$; chi-square test, $P = 0.002$) (Table 1).

RISC and mortality prediction. Mortality was significantly associated with increasing RISC scores. The mean RISC score was higher among non-survivors (2.05 ± 1.58) compared with survivors (0.86 ± 1.32; $P < 0.001$). A RISC score of 0 was associated with lower mortality (2.9%; $P = 0.005$), while a RISC score of 3 was associated with higher mortality (14.5%; $P = 0.007$) when each category was compared with all other categories combined. After *Bonferroni* correction (adjusted significance level: $P \leq 0.007$), both associations remained statistically significant. RISC scores of 4, 5, and 6 showed variable mortality rates (25%, 20%, and 0%, respectively) but did not reach statistical significance, likely due to small sample sizes in these categories (Table 2).

At a RISC score cut-off of >1, the sensitivity was 68.4%, specificity was 71.3%, positive predictive value (PPV) was 13.0%, and negative predictive value (NPV) was 97.3%. At a RISC score cut-off of ≥3, sensitivity decreased to 52.6%, while specificity improved to 81.9%, with a PPV of 15.4% and NPV of 96.5% (95% CIs not calculated due to limited mortality events; n = 19) (Table 3). The high NPV at both cut-offs suggests the RISC score may be more useful for identifying children at low risk of mortality than for predicting death.

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Table 1. Demographic and clinical characteristics of patients in relation to mortality outcomes.

Variable	Survived (n=303)	Mortality (n=19)	*P*-value
Sex #			
Male (n=226)	215 (70.96%)	11 (57.9%)	0.17
Female (n=96)	88 (29.04%)	8 (42.1%)	
Age group ##			
Mean age ± SD (months)	14.67 ± 20.20 (95% CI: 12.40–16.94)	8.16 ± 7.62 (95% CI: 4.73–11.59)	0.17
< 1 year (n = 205; survived/mortality: 191/14)	4.94 ± 2.93 (95% CI: 4.52–5.36)	4.57 ± 3.69 (95% CI: 2.64–6.50)	0.65
1–2 years (n = 50; survived/mortality: 47/3)	14.70 ± 3.37 (95% CI: 13.74–15.66)	13.33 ± 1.15 (95% CI: 12.03–14.63)	0.49
2–5 years (n = 54; survived/mortality: 52/2)	31.57 ± 8.68 (95% CI: 29.21–33.93)	25.50 ± 2.12 (95% CI: 22.56–28.44)	0.33
> 5 years (n = 13; survived/mortality: 13/0)	88.85 ± 32.94 (95% CI: 70.94–106.76)	0 (0%)	NA †
Vaccination (age-appropriate) #			
Complete including PCV (n = 200)	195 (64.4%)	5 (26.3%)	< 0.001*
Partial (n = 100)	90 (29.7%)	10 (52.6%)	0.08
Unimmunized (n = 22)	18 (5.9%)	4 (21.1%)	0.03*
Comorbidities #			
Acute kidney injury (n = 14)	14 (4.6%)	0 (0%)	1.00
Anaemia (n = 33)	32 (10.6%)	1 (5.3%)	0.71
CHD (n = 95)	89 (29.4%)	6 (31.6%)	0.80
Congenital disorder (n = 13)	12 (4.0%)	1 (5.3%)	0.55
Developmental delays (n = 48)	46 (15.2%)	2 (10.5%)	0.75
Hypothyroidism (n = 15)	14 (4.6%)	1 (5.3%)	0.61
Immunodeficiency/genetic disorder (n = 30)	28 (9.2%)	2 (10.5%)	0.69
Neonatal hepatitis (n = 9)	8 (2.6%)	1 (5.3%)	0.50
Seizure disorder (n = 17)	17 (5.6%)	0 (0%)	0.61
Oxygen saturation (SpO_2) ¶			
< 90% (n = 67)	57 (85.1%)	10 (14.9%)	0.002* ‡
90–95% (n = 20)	19 (95.0%)	1 (5.0%)	
> 95% (n = 235)	227 (96.6%)	8 (3.4%)	

Footnotes: # Fisher's exact test was used for categorical comparisons; ¶ overall chi-square test was used for oxygen saturation categories; ## independent t-test was used to compare mean ages between survivors and non-survivors. *Statistically significant at $P < 0.05$. Percentages were calculated column-wise for demographic and comorbidity variables (representing proportion of survivors/non-survivors within each category), and row-wise for oxygen saturation categories (representing mortality rate within each SpO_2 stratum, showing a graded inverse association between SpO_2 and mortality risk). Comorbidities were not mutually exclusive; a child could have more than one comorbidity. †No mortality events in this age group; zero-event cell handled using Fisher's exact test. ‡P-value applies to overall comparison across all three SpO_2 categories. §Effect sizes (odds ratios with 95% CIs) for significant associations are reported in the main text. Abbreviations: CHD, congenital heart defects; PCV, pneumococcal conjugate vaccine; CI, confidence interval; SD, standard deviation; NA, not applicable.

Table 2. Association of RISC score with mortality

RISC score	Survived (n=303) n (%)	Mortality (n=19) n (%)	*P*-value
Mean RISC score ± SD ##	0.86 ± 1.32 (95% CI: 0.71–1.01)	2.05 ± 1.58 (95% CI: 1.34–2.76)	< 0.001 ##
0 (n = 205)	199 (97.1%)	6 (2.9%)	0.005*
1 (n = 17)	17 (100.0%)	0 (0.0%)	0.61
2 (n = 35)	32 (91.4%)	3 (8.6%)	0.45
3 (n = 55)	47 (85.5%)	8 (14.5%)	0.007*
4 (n = 4)	3 (75.0%)	1 (25.0%)	0.22
5 (n = 5)	4 (80.0%)	1 (20.0%)	0.26
6 (n = 1)	1 (100.0%)	0 (0.0%)	1.00

Footnotes: ## Independent t-test was used to compare mean RISC scores between survivors and non-survivors. Fisher's exact test was used to compare mortality in each RISC score category with all other categories combined. *Statistically significant at $P < 0.05$. Bonferroni correction for multiple comparisons was applied across the seven RISC score categories (adjusted significance level: $P \leq 0.007$). Percentages represent the proportion of survivors and non-survivors within each RISC score category (row-wise calculation). Results for RISC scores 4–6 should be interpreted with caution due to small sample sizes, including a zero mortality event for score 6 (n = 1). CI: confidence interval; SD: standard deviation. Odds ratios with 95% CIs for significant associations (RISC 0: OR 0.20, 95% CI 0.07–0.55; RISC 3: OR 5.89, 95% CI 2.01–17.28) are reported in the main text.

Table 3. Predictive utility of the RISC score for predicting mortality

RISC score cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
> 1	68.4	71.3	13.0	97.3
≥ 3	52.6	81.9	15.4	96.5

Footnotes: Abbreviations: RISC, Respiratory Index of Severity in Children; PPV, positive predictive value; NPV, negative predictive value. Sensitivity, specificity, PPV, and NPV were calculated using standard 2×2 contingency tables for the primary outcome of in-hospital mortality. Cut-offs > 1 and ≥ 3 were selected based on prior validation studies and clinical triage considerations. PPV and NPV are influenced by outcome prevalence; the low mortality prevalence in this study (5.9%) contributes to the high NPV and low PPV observed. The high NPV suggests the RISC score may be more useful for identifying children at low risk of mortality than for predicting death. 95% confidence intervals were not calculated due to the small number of mortality events (n = 19), as exact binomial intervals would have been extremely wide and potentially uninformativ.

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Microbiological findings. The overall blood culture positivity rate was 35.1% (113/322), of which 79 (69.9% of positive cultures; 24.5% of all enrolled children) yielded pathogenic organisms and 34 (30.1% of positive cultures; 10.6% of all enrolled children) were contaminants or commensals, with the 10.6% contamination rate among all enrolled children exceeding the recommended threshold of < 3% [12, 13]. Contaminants included coagulase-negative Staphylococci (CoNS), diphtheroids, and non-pathogenic Gram-positive bacilli.

The most common pathogenic isolate was *Staphylococcus aureus* (n = 26, 8.1% of the total study population), followed by *Klebsiella pneumoniae* (n = 17, 5.3%), *S. pneumoniae* (n = 8, 2.5%), and *Enterococcus* spp. (n = 6, 1.9%). The lowest mean RISC scores were observed in children with sterile blood cultures (0.67 ± 1.22), while the highest mean RISC scores were observed among children with *S. pneumoniae* (2.38 ± 1.51, n = 8) and *Escherichia coli* (2.30 ± 0.58, n = 3) bacteremia.

The highest mortality rates were observed with *E. coli* bacteremia (66.7%, 2/3), followed by *K. pneumoniae* (41.2%, 7/17) and *S. pneumoniae* (37.5%, 3/8). Notably, no mortality was observed among children with candidemia (n = 5; antifungal susceptibility testing not performed) or sterile blood cultures (n = 209). Eighteen of 19 deaths occurred among children with pathogenic bacteremia, and one death occurred in a child whose blood culture yielded a contaminant/commensal organism (Table 4).

Table 4. Association of blood culture isolates with RISC score and mortality

Blood culture result	No. of children, n (%)†	Mean RISC Score ± SD (95% CI)‡	Mortality (n = 19), n (%)§
No growth (sterile)	209 (64.9%)	0.67 ± 1.22 (0.50–0.84)	0 (0%)
Contaminants/commensals¶	34 (10.6%)	1.17 ± 1.38 (0.71–1.63)	1 (2.9%)
S. aureus	26 (8.1%)	1.54 ± 1.61 (0.92–2.16)	2 (7.7%)
K. pneumoniae	17 (5.3%)	1.47 ± 1.55 (0.74–2.21)	7 (41.2%)
S. pneumoniae	8 (2.5%)	2.38 ± 1.51 (1.33–3.43)	3 (37.5%)
Enterococcus spp.	6 (1.9%)	1.67 ± 2.07 (0.01–3.33)	1 (16.7%)
Acinetobacter spp.	5 (1.6%)	0.80 ± 1.30 (0.00–1.94)‡	1 (20.0%)
Candida spp.	5 (1.6%)	0.40 ± 0.89 (0.00–1.18)‡	0 (0%)
P. aeruginosa	5 (1.6%)	1.00 ± 1.41 (0.00–2.24)‡	1 (20.0%)
Enterobacter spp.	4 (1.2%)	1.75 ± 1.26 (0.52–2.99)	1 (25.0%)
E. coli	3 (0.9%)	2.30 ± 0.58 (1.65–2.95)	2 (66.7%)
Total	322 (100.0%)	—¶¶	19 (5.9%)

Footnotes: Abbreviations: SD, standard deviation; CI, confidence interval; spp., multiple species. †Percentages represent proportion of total study population (n = 322). ‡Lower bounds of 95% CIs were truncated at 0, as RISC scores cannot be negative; negative values arising from the normal approximation are statistical artifacts due to small sample sizes. §Percentages represent mortality rate within each organism group (row-wise calculation). ¶Contaminants/commensals included CoNS, diphtheroids, and non-pathogenic Gram-positive bacilli. One of 19 deaths occurred with contaminant/commensal growth; the remainder occurred with pathogenic bacteremia. ¶¶Mean RISC score not aggregated across groups due to heterogeneous distributions and small subgroup sizes. No statistical comparisons were performed between organism groups due to small sample sizes. Organisms are listed in descending order of frequency. Organisms with mortality > 30% (*E. coli*, *K. pneumoniae*, *S. pneumoniae*) warrant heightened clinical vigilance.

Blood culture isolates and antimicrobial susceptibility patterns. Mortality was analyzed in relation to blood culture isolates and their antimicrobial resistance patterns. Isolates of *E. coli*, *Enterobacter* spp., and *K. pneumoniae* showed high resistance to Group A antimicrobials, with rates of 100%, 100%, and 88.2%, respectively, of isolates tested, and Group B antimicrobial resistance rates of 33.3%, 25%, and 29.4%, respectively. *S. aureus*, the most common isolate, showed 26.9% Group A resistance of isolates tested with no Group B resistance and had a mortality rate of 7.7% (2/26) (Table 5). Notably, despite low antimicrobial resistance among *Streptococcus pneumoniae* isolates (12.5% Group A resistance; 0% Group B resistance), mortality in this group was 37.5% (3/8). Among organisms for which Group C antimicrobials were tested (*e.g.*, *S. aureus*, *S. pneumoniae*, *Enterococcus* spp.), no resistance was observed. The high Group A resistance among *Enterobacterales* isolates suggests that first-line empirical antimicrobial therapy may be inadequate for these organisms. Mortality was highest among children with *E. coli* bacteremia (66.7%, 2/3), followed by *K. pneumoniae* (41.2%, 7/17) and *S. pneumoniae* (37.5%, 3/8) (Table 5).

Table 5. Association of antimicrobial resistance patterns with mortality among blood culture isolates.

Blood culture isolate	No. of children (n)	Group A resistance n (%)†	Group B resistance n (%)†	Group C resistance n (%)†	Mortality n (%)‡
S. aureus	26	7 (26.9%)	0 (0%)	0 (0%)	2 (7.7%)
K. pneumoniae	17	15 (88.2%)	5 (29.4%)	0 (0%)	7 (41.2%)
S. pneumoniae	8	1 (12.5%)	0 (0%)	0 (0%)	3 (37.5%)
Enterococcus spp.	6	4 (66.7%)	0 (0%)	0 (0%)	1 (16.7%)
Acinetobacter spp.	5	2 (40.0%)	1 (20.0%)	NT	1 (20.0%)
P. aeruginosa	5	1 (20.0%)	0 (0%)	NT	1 (20.0%)
Enterobacter spp.	4	4 (100.0%)	1 (25.0%)	0 (0%)	1 (25.0%)
E. coli	3	3 (100.0%)	1 (33.3%)	0 (0%)	2 (66.7%)
Total	74	—§	—§	—§	18 (24.3%)¶

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Footnote of Table 5: Group A, B, and C resistance categories are based on CLSI M100-Ed31 (2021) guidelines [12]. An isolate was classified as resistant to a group if it demonstrated resistance to all tested antimicrobials within that group. †Percentages represent proportion of isolates of each organism tested (row-wise calculation). ‡Percentages represent mortality rate within each organism group (row-wise calculation). §Aggregate resistance percentages not calculated due to heterogeneous testing panels across organism groups. ¶One of 19 total deaths occurred in a child with contaminant/commensal growth and was excluded from this table; 18 deaths occurred among the 74 pathogenic isolates shown. NT: not tested (CLSI does not recommend specific Group C agents for this organism). Candida spp. (n = 5) were excluded as antifungal susceptibility testing was not performed, precluding correlation of susceptibility patterns with outcomes. Contaminants/commensals (n = 34) were excluded from resistance analysis. The relationship between individual-level resistance patterns and mortality within each organism group was not analyzed due to small sample sizes. Organisms are listed in descending order of frequency among pathogenic isolates included in resistance analysis. spp.: multiple species.

DISCUSSION

CAP remains a major cause of pediatric morbidity and mortality, and early identification of children at risk of mortality is clinically important. In this study, we assessed the utility of the RISC score in predicting mortality among children admitted with CAP and analyzed their clinical and microbiological profiles. Complete vaccination status was protective against mortality (OR 0.20, 95% CI 0.07–0.55), SpO_2 < 90% was a strong predictor of death (OR 4.78, 95% CI 1.82–12.56), and all 19 deaths occurred among culture-positive children. Higher RISC scores were associated with increased mortality, with mean scores markedly higher among non-survivors (2.05 ± 1.58) than survivors (0.86 ± 1.32; P < 0.001). A RISC score of 0 was associated with the lowest mortality (2.9%, P = 0.005), while a score of 3 was associated with a higher mortality rate (14.5%, P = 0.007). However, the sensitivity at the ≥ 3 cut-off (52.6%) was considerably lower than that reported by Reed *et al*. [7] (94%) and Kapoor *et al*. [14] (94.1%), likely reflecting differences in study populations (our cohort included children up to 12 years versus 1–23 months in prior validation studies) and clinical settings.

In our study, males constituted 70.2% of the cohort, reflecting a male predominance. This finding is consistent with reports by Reed *et al*. [7], Mathew *et al*. [15], and Abd El Megied *et al*. [16], who also reported male predominance among children hospitalized with severe CAP. This sex-based distribution may reflect biological factors such as differences in airway anatomy and immune responses, as well as potential healthcare-seeking behavior differences favoring male children in certain cultural settings. However, sex was not significantly associated with mortality in our study (P = 0.17), consistent with broader literature suggesting that sex does not independently predict outcomes in pediatric critical respiratory illness.

In our study, the overall blood culture positivity rate was 35.1% (113/322), of which 79 isolates (24.5% of the total study population; 69.9% of positive cultures) yielded pathogenic organisms and 34 isolates (10.6% of the total study population; 30.1% of positive cultures) were contaminants, including non-pathogenic Gram-positive bacilli, such as aerobic spore-bearing bacilli, and skin commensals such as CoNS and diphtheroids. Blood culture positivity rates are generally low among children hospitalized with CAP. Previous Indian studies have shown that blood culture yield ranges from 2% to 27% [17], reflecting variability in study populations, collection methods, and definitions of positivity. When considering only pathogenic organisms, the yield in our study (24.5%) falls within the upper end of this range and is consistent with that reported by Mathew *et al*. [15]. The higher overall positivity rate (35.1%) may be partly attributable to the inclusion of contaminants, the enrollment of critically ill PICU patients who are more likely to have bacteremia, and variations in blood culture collection protocols (*e.g*., volume, timing relative to antibiotics).

Kumar *et al*. [18] reported that blood culture positivity is an independent risk factor for pneumonia-related mortality. Consistent with this, all 19 deaths in our study occurred among children with positive blood cultures (including one with contaminant/commensal growth), while no mortality was observed among those with sterile blood cultures. The most common blood culture isolate in our study was *S. aureus* (n = 26, 8.1% of the total study population), followed by *K. pneumoniae* (n = 17, 5.3%), *S. pneumoniae* (n = 8, 2.5%), and *Enterobacter* spp. (n = 4, 1.2%). These findings are consistent with the study by Mathew *et al*. [15], in which *S. aureus*, *S. pneumoniae*, and *K. pneumoniae* were among the most common isolates. Previous studies have reported that *S. aureus* is a frequent cause of CAP in children [19] and a leading cause of bacteremia in childhood pneumonia [20]. Despite being the most common isolate, *S. aureus* was associated with a relatively low mortality rate (7.7%, 2/26) in our study, possibly reflecting its relatively favorable antimicrobial susceptibility profile (26.9% Group A resistance, 0% Group B/C resistance) and/or lower virulence of the circulating strains. Collectively, these findings underscore the significance of *S. aureus* as a key pathogen in childhood CAP, warranting consideration in empirical antimicrobial regimens guided by local resistance patterns.

The mortality rate among children hospitalized with CAP in LMICs has been reported to range from 0.3% to 15% [2, 15]. The overall in-hospital mortality rate in our study was 5.9%, which is consistent with that reported by Mathew *et al*. [15] (5.8%), while a higher rate was

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reported by Kapoor *et al*. [14] (12.3%). The mortality rate observed in our study may reflect the inclusion of children with underlying comorbidities (29.5% with CHD), a substantial proportion of unimmunized or partially vaccinated children (37.9% combined), the severity of illness at presentation (*e.g*., $SpO_2 < 90\%$), and the tertiary care referral nature of our center, which admits a higher proportion of critically ill patients. These factors likely contributed to the observed mortality rate in our cohort.

Among clinical predictors of mortality, $SpO_2 < 90\%$ was significantly associated with mortality in our study ($P = 0.002$). A graded pattern was observed, with mortality rates of 14.9% ($SpO_2 < 90\%$), 5.0% (SpO_2 90–95%), and 3.4% ($SpO_2 > 95\%$), suggesting an inverse dose-response relationship between oxygen saturation and mortality risk. This finding is consistent with evidence from a systematic review and meta-analysis [21] and other observational studies [22]. Similarly, SpO_2 of 95–99% has been associated with reduced mortality in critically ill children [23]. Pulse oximetry was shown to improve the detection of hypoxaemia and facilitate timely referral in children with respiratory illness [24, 25]. These findings reinforce the importance of routine pulse oximetry in the assessment of children with CAP, particularly in resource-limited settings where it may facilitate early identification and referral of hypoxemic children, especially given that $SpO_2 < 90\%$ aligns with WHO IMCI (World Health Organization-integrated management of childhood illness) criteria for severe pneumonia.

Incomplete or absent immunization has been reported as an independent predictor of mortality among children aged 1–59 months hospitalized with severe pneumonia [26, 27]. In our study, complete vaccination (including PCV) was protective against mortality (OR 0.20, 95% CI 0.07–0.55; $P < 0.001$), while unimmunized status was predictive of mortality ($P = 0.03$), consistent with these reports.

Regarding the RISC score, a score of 0 was associated with the lowest mortality rate (2.9%), while a score of 3 was associated with higher mortality (14.5%; $P = 0.007$). The association between a RISC score of 3 and mortality remained significant after Bonferroni correction ($P = 0.007$, meeting the adjusted threshold of $P \leq 0.007$). Although individual RISC scores > 3 were not significantly associated with mortality in our study (Table 2), a RISC score ≥ 3 has been associated with higher mortality in studies by Kapoor *et al*. [14], Abd El Megied *et al*. [16], and Reed *et al*. [7], albeit in different clinical settings and age groups. The external validation of the RISC score in Malawi by Hooli *et al*. [28] and in India by Kapoor *et al*. [14] demonstrated its predictive accuracy. Reed *et al*. [7] originally reported a sensitivity of 94% and specificity of 78% among children aged 1–23 months in South Africa, while Kapoor *et al*. [14] found a sensitivity of 94.1% and specificity of 73.6% at the same RISC score cut-off of ≥ 3. In contrast, the sensitivity at a RISC score ≥ 3 in our study was 52.6%, which is considerably lower than that reported in earlier studies. However, the specificity at this cut-off in our study (81.9%) was comparable to or higher than that reported by Reed *et al*. [7] (78%) and Kapoor *et al*. [14] (73.6%). Notably, the NPV remained high at both cut-offs (97.3% at > 1; 96.5% at ≥ 3), suggesting that the RISC score may be more useful for identifying children at low risk of mortality than for predicting death. This difference in sensitivity may be related to the inclusion of older children up to 12 years of age, whereas the RISC score was originally developed and validated for children aged 1–23 months [7], and to differences in study populations, clinical settings, and healthcare resource availability. In addition, our study population consisted of critically ill children admitted to the PICU, which may have influenced the performance of the score, as PICU patients may have already received therapeutic interventions (*e.g*., supplemental oxygen, fluid resuscitation) that improve clinical parameters such as SpO_2, potentially lowering RISC scores and reducing sensitivity for mortality prediction. Importantly, the RISC score relies solely on clinical parameters, making it feasible for use in resource-limited settings, including primary healthcare facilities, though availability of pulse oximetry, a key parameter, may vary at the primary care level.

Notably, despite *S. pneumoniae* isolates being largely susceptible to all CLSI-recommended antimicrobial groups (Group A resistance: 12.5% of isolates tested; Group B and C resistance: 0%), pneumococcal bacteremia was associated with a mortality rate of 37.5% (3/8). The high mortality associated with pneumococcal bacteremia has been attributed to virulence factors of *S. pneumoniae* [29] and host factors [30]. *S. pneumoniae* has been reported to cause high mortality in intensive care unit (ICU) settings, including PICUs, despite adequate antimicrobial therapy [31]. Pneumococcal conjugate vaccine (PCV) has been shown to provide protection against pneumococcal CAP in children [32]. The vaccination status of the three children who died of pneumococcal bacteremia was not individually analyzed; such analysis may provide additional insights into the role of PCV in preventing fatal pneumococcal disease.

In contrast, high mortality rates were observed among children with *E. coli* (66.7%, 2/3) and *K. pneumoniae* (41.2%, 7/17) bacteremia, both of which demonstrated high Group A resistance (100% and 88.2%, respectively) and moderate Group B resistance (33.3% and 29.4%, respectively). Importantly, all Enterobacterales isolates remained susceptible to Group C antimicrobials, which may serve as a therapeutic option when Group A and B agents are ineffective, though pediatric use of some Group C agents (*e.g*., tetracyclines, fluoroquinolones) is limited by age-related safety considerations. High mortality among patients with bacteremic pneumonia has also been reported in previous studies [33]. These

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findings highlight the need for early identification of antimicrobial-resistant organisms and timely escalation of care.

Eighteen of 19 deaths occurred among children with pathogenic bacteremia, and one death occurred in a child whose blood culture yielded a contaminant/commensal organism, while no deaths occurred among children with sterile blood cultures. The mortality rate among culture-positive children was 16.8% (19/113), compared with 0% (0/209) among those with sterile blood cultures. This finding suggests that bloodstream infection may reflect invasive disease with a higher risk of sepsis and adverse outcomes, or alternatively, children with more severe clinical presentations may be more likely to develop bacteremia, as suggested in prior studies of severe pediatric pneumonia [5]. These observations align with the findings of Kumar *et al*. [18], who reported blood culture positivity as an independent risk factor for pneumonia-related mortality. Although a formal statistical comparison was not performed due to zero events in the culture-negative group, for which exact methods such as Fisher's exact test would be required, the observed trend is clinically notable. However, given the small number of mortality events (n = 19), this observation should be interpreted with caution.

Regarding microbiological methodology, the blood culture contamination rate in our study was 10.6%, which exceeds the recommended threshold of < 3% [12, 13]. The elevated contamination rate may be attributed to challenges inherent in pediatric blood culture collection, including difficult venous access, smaller blood volumes, and the emergency nature of PICU admissions. In resource-limited settings, these challenges may be further amplified by constraints in laboratory infrastructure and training. Elevated contamination rates can lead to inappropriate antimicrobial use, prolonged hospital stay, and increased healthcare costs. Notably, one death occurred in a child with blood culture growth classified as a contaminant, raising the possibility of misclassification. Blood culture contamination is multifactorial and cannot be eliminated by a single intervention. Several evidence-based measures, including proper skin antisepsis, use of sterile collection kits, trained phlebotomy staff, and specimen diversion techniques, have been shown to reduce contamination rates by 30–50% [34], though implementation may require targeted quality improvement initiatives in low-resource settings [34].

Based on our findings, we suggest that children with a RISC score ≥ 3 should be considered for prompt referral to a tertiary or higher-level facility equipped with a PICU and continuous monitoring capabilities. However, given the sensitivity of 52.6% at this cut-off, nearly half of the children who died had RISC scores < 3, suggesting that the RISC score alone may not be sufficient for clinical decision-making and should be used in conjunction with other clinical assessments. It should be noted that the RISC score was applied in a PICU setting in our study, and its performance in primary care settings requires further validation. These findings highlight the need to ensure the availability of pulse oximeters and training in pulse oximetry use and clinical severity assessment at the primary care level to support timely identification of hypoxemia and triage of high-risk children. Given that SpO_2 < 90% was a significant predictor of mortality in our study (P = 0.002), routine use of pulse oximetry is essential, as it has been shown to improve outcomes in children under five years of age [23]. Additionally, our findings support expanded vaccination coverage, including PCV, and early blood culture collection (performed using strict aseptic techniques to minimize contamination) to identify children with bacteremia who may require escalation of antimicrobial therapy.

This study has several limitations. First, it was conducted at a single tertiary care center, which may introduce referral bias and limit generalizability to community or primary care settings. Second, the retrospective observational design limits causal inference due to potential unmeasured confounding. Third, small subgroup sizes for individual pathogens reduced statistical power to detect organism-specific associations. Fourth, the RISC score was originally validated for children aged 1–23 months [7], yet we applied it across a broader age range (1 month–12 years), potentially affecting its predictive calibration in older children. Fifth, zero mortality events occurred in children > 5 years (n = 13), precluding age-stratified validation of the score in this subgroup. Sixth, discriminative ability was not assessed using receiver operating characteristic (ROC) curve analysis; however, with only 19 mortality events, ROC analysis would have yielded wide confidence intervals and limited clinical utility. Seventh, multivariable analysis was not feasible due to the low event rate, which inherently precludes reliable regression modeling; additionally, Bonferroni correction was applied only to RISC score category comparisons, leaving other univariate comparisons at a theoretically higher risk of type I error. Eighth, antifungal susceptibility testing for *Candida* spp. was unavailable, which precluded targeted, susceptibility-guided therapy and limited characterization of fungal bloodstream infections. Ninth, the blood culture contamination rate (10.6%) exceeded the recommended < 3% threshold, potentially introducing misclassification bias. Tenth, the study period overlapped with the COVID-19 pandemic (March 2020 onward), which may have altered PICU admission thresholds, pathogen circulation, and healthcare-seeking behavior. Finally, post-discharge follow-up data were unavailable, restricting outcome assessment to in-hospital mortality.

Although most *S. pneumoniae* isolates were drug-susceptible, the associated high mortality suggests that early clinical interventions, including supportive care,

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timely referral, and vaccination, beyond antimicrobial therapy alone are critical for improving prognosis. Similarly, high mortality rates associated with antimicrobial-resistant *E. coli* and *K. pneumoniae* bacteremia emphasize the importance of early detection of resistant organisms and appropriate escalation of empirical therapy. The observation that all 19 deaths occurred among children with positive blood cultures (including one with contaminant growth) further supports the clinical value of early blood culture collection and identification of bacteremia in children with CAP. The RISC score, despite its lower sensitivity in our PICU population, demonstrated a high NPV and may serve as a useful triage tool for identifying children at low risk of mortality, particularly in resource-limited primary care settings.

In conclusion, our findings underscore the need for routine pulse oximetry, expanded vaccination coverage (including PCV), and early referral of high-risk children to higher-level facilities. These strategies have the potential to improve outcomes and warrant further evaluation in diverse clinical settings, including primary care and community-level facilities across different geographic regions. Future multicenter prospective studies with larger sample sizes are needed to validate the RISC score across diverse age groups and clinical settings and to identify additional prognostic markers for pediatric CAP mortality.

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CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

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DATA AVAILABILITY

The de-identified participant data, statistical code, and study protocols generated and analyzed during this study are available from the corresponding author upon reasonable request and subject to institutional approval.

AI DISCLOSURE

The authors used ChatGPT (OpenAI, San Francisco, CA, USA) for grammatical corrections and to improve language fluency. All AI-generated content was independently reviewed, edited, and verified by the authors to ensure accuracy and appropriateness. No AI tools were used for data analysis or scientific interpretation. AI tools were not used for study design, data collection, or generation of original scientific content.

AUTHORS' CONTRIBUTIONS

MS (Monika Saini): Conceptualization, Methodology, Investigation, Data curation, Resources, Writing – original draft, Supervision, Project administration. SB: Formal analysis, Validation, Writing – review & editing. LR: Formal analysis, Validation, Visualization, Writing – review & editing. MS (Mahendra Saini): Methodology, Resources, Writing – original draft, Visualization, Funding acquisition, Validation. All authors read and approved the final manuscript.

ETHICS STATEMENT

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of SMS Medical College and Attached Hospitals, Jaipur, Rajasthan, India (approval no. 746MC/EC/2019, dated December 6, 2019). For the retrospective component of this study, the ethics committee granted a waiver of additional informed consent for data abstraction from medical records; for blood sample collection at admission, written informed consent was obtained from parents or legal guardians at enrollment. All patient data were de-identified using unique study identifiers with a separate, password-protected linkage file to ensure confidentiality.

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