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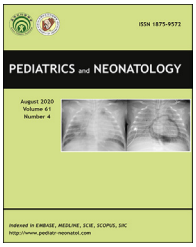

Original Article

Characterization of children younger than 5 Years of age with severe community-acquired alveolar pneumonia (CAAP) requiring Pediatric Intensive Care Unit (PICU) admission

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Key Words
community-acquired alveolar pneumonia;
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Background: The purpose of this study was to determine factors characterizing children admitted to the Pediatric Intensive Care Unit (PICU) with community-acquired alveolar pneumonia (CAAP) to help clinicians assess disease severity upon initial assessment in the emergency department.
Methods: We prospectively collected demographic, clinical, and laboratory data of children <5 years with radiologically confirmed CAAP referred to the Soroka University Medical Center during 2001–2011. Three groups of children were compared: 1) those hospitalized in the PICU (PICU-CAAP); 2) those treated in the emergency department and discharged (ED-CAAP); and 3) those hospitalized in a pediatric ward (Hosp-CAAP).
Results: Of 9722 CAAP episodes, 367 (3.8%) were PICU-CAAP, 5552 (57.1%) Hosp-CAAP and 3803 (39.1%) ED-CAAP. In a univariate analysis, respiratory syncytial virus (RSV) was detected more

Abbreviations: CAAP, Community-acquired alveolar pneumonia; PICU, Pediatric Intensive Care Unit; PICU-CAAP, Children with CAAP hospitalized at the PICU; ED, Emergency Department; ED-CAAP, Children with CAAP treated in the ED and subsequently discharged; Hosp-CAAP, Children with CAAP hospitalized in a general pediatric ward; OR, Odds ratio; CI, Confidence interval; CAP, Community-acquired pneumonia; WHO, World Health Organization; RSV, Respiratory syncytial virus; CRP, C-reactive protein; WBC, White blood counts; ANC, Absolute neutrophils count.

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commonly among PICU-CAAP than in Hosp-CAAP ($P = 0.02$) and ED-CAAP patients ($P < 0.001$). In a multivariate analysis, several factors were associated with PICU hospitalization versus ED-CAAP and Hosp-CAAP: Younger age (ORs: 1.04, [95%CI: 1.02—1.05] and 0.97 [0.96—0.98], respectively); prematurity (ORs: 2.16 [1.28—3.64] and 1.61 [1.15—2.26], respectively), lower O_2 saturation (ORs: 1.32 [1.25—1.41] and 0.94[0.92—0.96]), higher respiratory rate (ORs: 1.06 [1.04—1.07] and 1.00 [1—1.01], respectively).

Conclusion: Children admitted to PICU were younger, had more respiratory syncytial virus (RSV) detection, were premature, had lower O_2 saturation, and had a higher respiratory rate than those admitted to the general ward or those visiting the emergency department and subsequently discharged.

1. Introduction

Community-acquired pneumonia (CAP) is a major cause of morbidity and mortality in children worldwide.[1,2] Etiology of pneumonia differs by age group, and viral infections are considered to be most prevalent among children <5 years old.[2,3] The diagnosis of pneumonia is based on clinical evaluation and laboratory tests, which include chest radiography. Obtaining blood cultures and complete blood count is recommended in cases in which bacterial infection is suspected.[1] However, in most cases, the etiology of bacterial CAP cannot be established with certainty since the lung tissue is not cultured for ethical reasons.[4] Furthermore, it is well established that pneumonia is frequently a result of mixed infections involving combinations of viruses and bacteria.[3,5—9] Due to the lack of diagnostic criteria of CAP in children, the World Health Organization (WHO) has developed standardized radiological definitions for pneumonia defined as alveolar CAP (CAAP), which is often considered a bacterial disease, in many cases caused by *Streptococcus pneumoniae*.[4] This definition has been used in epidemiological and vaccine trials[1] and is used in the current study.

Determining the severity of pneumonia and which children are most predisposed to severe disease is challenging. Most studies that evaluate risk factors of mortality due to pneumonia are from developing countries with limited resources for prevention and therapeutic measures. Young age, the presence of certain underlying medical conditions, as well as dyspnea, hypoxemia, and lower hemoglobin concentrations, were reported to be associated with mortality. Neither specific pathogens nor laboratory data seem to correlate with mortality.[10—13] A study from Paraguay used an adult severity score (PIRO scale) for pneumonia in children which accurately predicted the probability of mortality in children who presented to the hospital with CAP.[14]

A handful of studies have developed or modified other severity scores such as the Respiratory Index of Severity in Children (RISC)[10] and the modified Wood's clinical asthma score for pneumonia.[15] In addition, several guidelines also include recommendations and severity parameters, some of which are used to predict admission to the Pediatric Intensive Care Unit (PICU).[16,17] In the US, respiratory rate, temperature, altered mental status, heart rate, age, and PaO2/FiO2 ratio were the most important individual predictors of severity.[18] However, there are still no universally accepted severity scores for pneumonia in children, and similar scores have neither been validated nor developed for children in the developed world, where advanced monitoring and therapeutic modalities are available in the Pediatric Intensive Care Unit (PICU) setting.

The purpose of our study was to characterize the demographics as well as clinical and laboratory parameters associated with alveolar CAP admission to the PICU of children <5 years old to identify factors which might be useful in developing a severity score to determine which alveolar CAP patients should be hospitalized in the PICU. The WHO definition for radiologically-confirmed CAAP allows comparisons of clinical and epidemiological characteristics among patients, enabling its use as a study endpoint.[4,12,19] We hypothesized that children admitted to the PICU have distinct characteristics when compared to children admitted to general pediatric wards or those treated in the pediatric Emergency Department (ED).

2. Patients and methods

2.1. Setting

The study was conducted at the Soroka University Medical Center in southern Israel. It is the only hospital in the Negev district of southern Israel for the entire population of a region of 630,700 people, of which 74,400 are children under five years old.[20] Over 95% of the children living in the region are served by the Soroka University Medical Center, enabling population-based studies. The population in the region is composed of two ethnic groups: the Jewish population, generally comparable to a Western population, and the Bedouin population, in transition from semi-nomadism to settlement, generally comparable to a low socioeconomic status population. In 2011, 36,200 children under five years old were Bedouins, and 35,800 were Jewish. Social contacts between these groups are limited, especially between children. Hospitalization rates for respiratory infectious diseases and especially for CAAP are higher among the Bedouin population.[19,21,22]

This study was approved by the institutional and national Ethics Committees and was performed in accordance with the Human Experimentation Guidelines of the Israeli Ministry of Health.

2.2. Study design

This was a prospective cohort study in children younger than five years old with CAAP referred to the Emergency Department at the Soroka University Medical Center in southern Israel from November 2001 through December 2011.

All children <5 years visiting the Soroka University Medical Center ED with radiologically-proven CAAP were included. Children hospitalized in the PICU (PICU-CAAP) were compared with two groups: 1) children treated in the ED and subsequently discharged (ED-CAAP); and 2) children who were hospitalized in the general pediatric wards (Hosp-CAAP). If a patient was in multiple departments throughout their stay at the hospital, they were counted in the study as the most severe status. For example, if a child was in the ward and also the PICU, they were counted in the study as PICU-CAAP. A child was hospitalized in the PICU based on the following criteria: 1) need for immediate mechanical ventilation support; and 2) clinical signs and laboratory tests (i.e., blood gas), demonstrating that the child required strict monitoring.

Children diagnosed as having CAAP ≥48 h from hospital admission were excluded since our aim was to study community-acquired episodes only.

For the purpose of the current study, we defined a case as: 1) The child was younger than five years of age; 2) The child was a resident of the Negev region of southern Israel; 3) A chest radiograph was obtained within 48 h of ED arrival; 4) Alveolar pneumonia was radiologically demonstrated, according to the WHO definitions.[2]

A new episode was defined as radiologically confirmed alveolar pneumonia, which occurred >28 days following a previous pneumonia episode.

2.3. Chest radiograph analysis

Chest radiographs and analyses were performed as described elsewhere.[5] Chest radiographs and blood cultures are protocol for all children admitted to the hospital with respiratory symptoms. All chest radiographs were collected daily and were evaluated separately by two pediatric infectious disease specialists who read all chest radiographs independently. Further analysis was performed by an independent pediatric radiologist who was unaware of the clinical data and pediatricians' analysis, as described previously. The presence of radiologically diagnosed CAAP was confirmed upon agreement of at least one of the study pediatric infectious disease specialists and the study pediatric radiologist. All readers were trained to use the WHO pneumonia criteria.

2.4. Bacteriology

Blood cultures were routinely obtained from febrile children in the ER or upon hospitalization. A blood sample for blood culture is protocol for all children admitted to the hospital with respiratory symptoms. Blood cultures were processed at the Clinical Microbiology Laboratory of the Soroka University Medical Center solely, as previously described.[22,23]

2.5. Virology

Nasopharyngeal wash specimens were obtained upon hospital admission, all year round during working hours but not during weekends and holidays. Only one specimen from each patient was included. Specimens were processed from culture or by polymerase chain reaction (PCR) diagnosis as described elsewhere.[24] Respiratory viruses tested were: RSV, influenza A and B, human meta-pneumovirus, para-influenza 1, 2, and 3 viruses, adenovirus, coronavirus, and enteroviruses. Rhinoviruses were tested only in some of the patients, based on polymerase chain reaction (PCR). The following respiratory viruses were included in the analyses: RSV, influenza A and B, human meta-pneumovirus, and para-influenza 1, 2, and 3 viruses.

2.6. Data collection

Detailed demographic, clinical, and laboratory data were collected from medical files, and any missing details were obtained from questionnaires given to parents. Variables studied included age, gender, ethnic origin, number of siblings, parental age and education, history of wheezing episodes or asthma diagnosis, history of acute otitis media and tympanocentesis, antibiotic treatment in the precedent period, previous hospitalizations, underlying medical conditions, symptoms before ED arrival, symptoms and signs upon arrival to the ED, and presence of pleural effusion in chest radiograph. Laboratory tests included complete blood count, serum electrolytes, urea and creatinine concentrations; C-reactive protein (CRP) concentrations; and viral detections in nasal wash and blood culture results.

2.7. Statistics

Data were recorded using Access Microsoft office software. Statistical analysis was conducted using SPSS 20.0 software.

For comparison between the three groups, contingency table analysis measuring the association among study groups was conducted using Pearson $\chi 2$ tests or Fisher's exact test. To estimate risks such as demographic, clinical, and laboratory features groups, odds ratios (ORs) and 95% confidence interval (CI) were calculated. *P* values and OR were controlled for age, ethnicity, and antibiotic treatment during the last month before enrolment. Logistic regression models were used to evaluate potential risk factors, covariate, and confounders. Variables implicated in the literature and those that were statistically significant at the level of $P < 0.1$ in the univariate analyses were included in the multivariate logistic regression models (age, ethnicity, gender underlying diseases, prematurity, lower body temperature at admission, lower Saturation at admission, and higher respiratory rate at admission). Odds ratios and 95% CIs were calculated to estimate risks of PICU-CAAP cases

Table 1 Demographic characteristics of children <5 years: PICU-CAAP *vs.* Hosp-CAAP or ED-CAAP.

	PICU-CAAP, n = 367[a]	Hosp-CAAP, n = 5,552[a]	*P* value[b]	ED-CAAP, n = 3,803[a]	*P* value[c]
Age (months) (mean ± SD)	10.7 ± 13.6	18.6 ± 15.8	**< 0.001**	25.4 ± 14.8	**< 0.001**
Ethnicity —Bedouin n (%)	295 (80)	3838 (69)	**< 0.001**	1738 (46)	**< 0.001**
Gender — Male n (%)	191 (52)	3023 (54)	0.370	2190 (58)	**0.040**
Maternal age (years) (mean ± SD)	29.0 ± 6.4	29.6 ± 6.0	0.085	30.3 ± 5.8	**0.001**
Breastfeeding (months) (mean ± SD)	6.5 ± 6.4	7.1 ± 6.0	0.390	7.5 ± 5.8	0.150
Number of individuals sleeping in the same room (mean ± SD)	3.6 ± 1.3	3.3 ± 2.1	**0.019**	2.7 ± 1.2	**< 0.001**
Number of siblings (mean ± SD)	3.1 ± 2.4	3.0 ± 2.4	0.630	2.4 ± 2.2	**< 0.001**

PICU-CAAP, children with Community Acquired Alveolar Pneumonia hospitalized at the Pediatric Intensive Care Unit; Hosp-CAAP, children with Community Acquired Alveolar Pneumonia hospitalized in a general pediatric ward; ED-CAAP, children visiting the Emergency Department and being subsequently discharged, SD, standard deviation.
Bold signifies statistical significance was defined as P<0.05.
[a] Total number of patients. There are missing values in some parameters.
[b] *P*-value comparing PICU-CAAP *vs.* Hosp-CAAP.
[c] *P*-value comparing PICU-CAAP *vs.* ED-CAAP.

and children included in the ED-CAAP and Hosp-CAAP groups.

3. Results

Overall, 9722 CAAP episodes were recorded during the study period: 367 (3.8%) episodes required admission to the PICU (PICU-CAAP), 5552 (57.1%) were admitted to the general pediatric wards (Hosp-CAAP), and 3803 (39.1%) were treated in the pediatric ED and discharged home for further ambulatory treatment (ED-CAAP).

Children admitted to the PICU were significantly younger, included a higher proportion of Bedouin children, and lived in more crowded houses compared with the other two groups (Table 1). No differences were found among the groups with regard to gender, history of breastfeeding, and smoking in their household.

Children in the PICU-CAAP group had a significantly higher proportion of underlying medical conditions, such as congenital heart diseases and chronic lung disease, and lower proportions of asthma and wheezing, history of CAP, and use of antibiotics during the month prior to the CAAP episode (Fig. 1).

Compared with hosp-CAAP and ED-CAAP patients, PICU-CAAP patients had significantly lower temperatures, less cough, and they were reported to have less abdominal pain before admission (Table 2). Upon admission, the PICU-CAAP group had significantly lower oxygen saturations and higher respiratory rates (Table 2). No other statistically significant differences were found with regard to signs and symptoms.

With regard to laboratory findings, PICU-CAAP children had lower mean white blood counts (WBC) (14.7 ± 9 *vs.* 16.6 ± 8.6 and 21.1 ± 8.7 cells × 10^3/mm^3) and lower mean absolute neutrophils count (ANC) (8.3 ± 6.8 *vs.* 10.8 ± 7.6

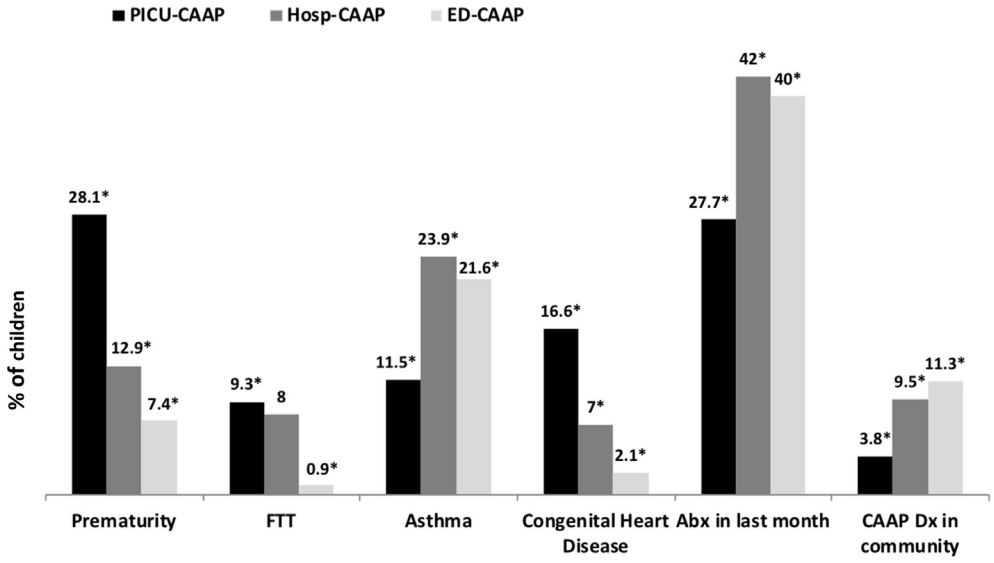

Figure 1 Medical history of children <5 years of age with PICU-CAAP, *vs.* Hosp.-CAAP and ED-CAAP. FTT- Failure to thrive, Abx- antibiotics, Dx- Diagnosis. * *P*-values comparing PICU-CAAP *vs.* Hosp-CAAP or ED-CAAP were statistically significant; $P \leq 0.001$.

Table 2 Clinical variables of children <5 years: PICU- CAAP *vs.* Hosp-CAAP or ED-CAAP.

	PICU-CAAP n = 367[a]	Hosp-CAAP n = 5,552[a]	*P* value[b]	ED-CAAP n = 3,803[a]	*P* value[c]
Max temperature °C (mean ± SD)	37.8 ± 1.8	38.8 ± 1.1	< **0.001**	39.4 ± 1.0	< **0.001**
Abdominal pain in prior day n (%)	10 (6)	415 (12)	**0.013**	608 (23)	< **0.001**
O_2 saturation % (mean ± SD)	88.7 ± 7.5	92.2 ± 4.8	< **0.001**	95.9 ± 2.4	< **0.001**
Wheezing n (%)	9 (13)	319 (28.8)	**0.005**	93 (11.1)	0.615
Respiratory rate (mean ± SD)	59.0 ± 19.5	54.6 ± 15.4	< **0.001**	43.0 ± 11.4	< **0.001**
Pleural effusion n (%)	13 (3.5)	95 (2)	**0.011**	23 (0.6)	< **0.001**
Days of hospitalization n (%)	15.1 ± 24.5	3.0 ± 3.7	< **0.001**	NR	
Mortality n (%)	15 (4)	10 (0.2)	< **0.001**	1 (0)	< **0.001**

PICU-CAAP, children with Community Acquired Alveolar Pneumonia hospitalized at the Pediatric Intensive Care Unit; Hosp-CAAP, children with Community Acquired Alveolar Pneumonia hospitalized in a general pediatric ward; ED-CAAP, children visiting the Emergency Department and being subsequently discharged, SD, standard deviation; NR, not relevant.
Bold signifies statistical significance was defined as P<0.05.
[a] Total number of patients. There are missing values in some parameters.
[b] *P*-value comparing PICU-CAAP *vs* Hosp-CAAP.
[c] *P*-value comparing PICU-CAAP *vs* ED-CAAP.

*vs.*14.8 ± 8 cells × 10^3/mm,[3] respectively). Serum urea, sodium, and hemoglobin concentrations were higher in the PICU-CAAP. No clinically significant differences between the groups with regard to levels of CRP, hemoglobin, or thrombocytes were noted (Table 3). All-cause and *S. pneumoniae* bacteremia were more common in the PICU-CAAP children compared to the Hosp-CAAP and the ED-CAAP (Table 3).

Nasopharyngeal washes were obtained in 2764 episodes (28.4% of the study population), with 188 (51.2%) samples in the PICU-CAAP, 2164 (40.8%) in the Hosp-CAAP and 412 (10.8%) in the ED-CAAP. A respiratory virus was detected in 61.2% of the specimens obtained from children in the PICU-CAAP, 59.0% in the Hosp-CAAP, and in only 26.0% in the ED-CAAP. Overall, respiratory viruses were detected significantly more often in nasopharyngeal PICU-CAAP (61.2%) than ED-CAAP (24.3%). Respiratory syncytial virus (RSV) was detected significantly more often in the nasopharyngeal washes of patients in the PICU-CAAP (50.0%) compared with 41.4% in the Hosp-CAAP and only in 8.9% in the ED-CAAP. Regarding other viruses, human metapneumovirus (HMPV) was significantly less prevalent in the PICU-CAAP (1.0% vs. 5.6% in the Hosp-CAAP and 6.7% in the ED-CAAP), whereas parainfluenza was detected in 7.0% of the PICU-CAAP *vs.* 4.3% in the Hosp-CAAP and 1.9% in the ED-CAAP, although the differences were not statistically significant.

In multivariate analysis, the following factors were considered risk factors for PICU hospitalization *vs.* ED-CAAP: younger age, Bedouin ethnicity, prematurity, lower body temperature, lower O_2 saturation and higher respiratory rate (Table 4). The following factors were associated as risk factors for PICU hospitalization vs. hospitalization in the ward: Bedouin ethnicity, and prematurity. Younger age, lower body temperature, and lower oxygen saturation were risk factors for being hospitalized in the ward vs. in the PICU.

Table 3 Laboratory tests of children < 5 Y: PICU- CAAP *vs.* Hosp-CAAP or ED-CAAP.

	PICU-CAAP n = 367[a]	Hosp-CAAP n = 5,552[a]		ED-CAAP n = 3,803[a]	
			P value[b]		*P* value[c]
CRP (mg/dL) (mean ± SD)	4.7 ± 4.4	16.1 ± 10.1	< **0.001**	11.6 ± 18.0	< **0.001**
WBC (x10^3/mm^3) (mean ± SD)	14.7 ± 9.0	16.6 ± 8.6	< **0.001**	21.1 ± 8.7	< **0.001**
ANC (x10^3/mm^3) (mean ± SD)	8.3 ± 6.8	10.8 ± 7.6	< **0.001**	14.8 ± 8.0	< **0.001**
Hemoglobin concentrations (mg%) (mean ± SD)	11.2 ± 2.1	11 ± 1.4	0.054	10.9 ± 1.2	**0.010**
Serum sodium concentrations (mEq/L) (mean ± SD)	135.7 ± 6.4	135.1 ± 5.3	0.060	134.4 ± 2.5	< **0.001**
Serum creatinine (mg%) (mean ± SD)	0.39 ± 0.53	0.39 ± 3.7	0.982	0.31 ± 0.1	**0.005**
Serum Urea concentration (mg%) (mean ± SD)	30.9 ± 35.6	20.9 ± 10.3	< **0.001**	20.4 ± 7.7	< **0.001**
All cause Bacteremia n (%)	52 (14)	98 (2)	< **0.001**	45 (1)	< **0.001**
Pneumococcus bacteremia n (%)	11 (3)	44 (1)	< **0.001**	32 (1)	< **0.001**

PICU-CAAP, children with Community Acquired Alveolar Pneumonia hospitalized at the Pediatric Intensive Care Unit; Hosp-CAAP, children with Community Acquired Alveolar Pneumonia hospitalized in a general pediatric ward; ED-CAAP, children visiting the Emergency Department and being subsequently discharged, SD, standard deviation.
Bold signifies statistical significance was defined as P<0.05.
[a] Total number of patients. There are missing values in some parameters.
[b] *P*-value comparing PICU-CAAP *vs* Hosp-CAAP.
[c] *P*-value comparing PICU-CAAP *vs* ED-CAPSD-standard deviation.

Table 4 Independent risk factors for PICU-CAAP in children < 5Y (multi-regression analysis): comparison with ED-CAAP and Hosp-CAAP.

Risk Factor	PICU-CAAP *vs.* ED-CAAP OR (95% C.I.)	PICU-CAAP *vs.* Hosp-CAAP OR (95% C.I.)
Younger Age (increment per month)	1.04 (1.02–1.05)	0.97 (0.96–0.98)
Ethnicity- Bedouin	2.67 (1.72–4.16)	1.33 (0.94–1.89)
Prematurity	2.16 (1.28–3.64)	1.61 (1.15–2.26)
Lower body temperature at admission (increment per 1 °C)	2.36 (1.96–2.28)	0.59 (0.53–0.67)
Lower Saturation at admission (increment per 1%)	1.32 (1.25–1.41)	0.94 (0.92–0.96)
Higher respiratory rate at admission (increment per each breath per minute)	1.06 (1.04–1.07)	1.00 (1–1.01)

PICU-CAAP: children with community acquired alveolar pneumonia hospitalized at the Pediatric Intensive Care Unit; ED-CAAP, children with community acquired alveolar pneumonia visiting the emergency department and being subsequently discharged; HOSP-CAAP, children with community acquired alveolar pneumonia hospitalized in a general pediatric ward.

4. Discussion

The objective of the present study was to determine the unique clinical and laboratory characteristics of children <5 years old associated with CAAP admission to the PICU. Demographically, these children were younger and more frequently Bedouin, lived in a crowded environment, and more frequently had specific medical conditions compared to Hosp-CAAP and ED-CAAP patients. Clinically, they presented with signs and symptoms suggestive of viral infection and co-infection with laboratory tests showing a weaker inflammatory response (as expressed by low peripheral WBC, ANC, and lower CRP concentrations).[25] RSV and bacteremia, mainly due to *S. pneumoniae*, were detected more frequently in the PICU group compared to the ED and pediatric ward groups.

Data from developed countries regarding the characteristics of children hospitalized in PICU because of CAAP are scarce. Other than the PIRO scale,[14] no severity scores have been developed and validated in the developed world. Araya et al. showed that the use of the PIRO scale was accurate in predicting mortality in children with CAP. Variables associated with mortality were the presence of apyrexia, tachypnea, leukopenia, pleural effusion, renal injury, acidosis, hypotension, and change in consciousness.[14] Established clinical guidelines,[16,17] recommend hospitalization of children younger than six months old or children with underlying medical conditions. More specifically, indications for PICU hospitalization are impending respiratory failure or children who are hemodynamically compromised, such as those with signs of septicemia. In the present study also, younger age and underlying medical conditions (e.g., congenital heart defects, chronic lung disease, and prematurity) and signs of respiratory distress and tachypnea characterized children with CAAP who were hospitalized in the PICU. This is possibly related to the predisposition of younger children, mainly those who were born prematurely, to acquire a more severe disease. In addition, Bedouin children were more often admitted to the PICU. This is most likely directly related to the lower socioeconomic status typical of this population and not directly associated with ethnicity or genetics.

In the developing world, other factors associated with mortality in pneumonia were age, weight for age, lack of exclusive breastfeeding, lower maternal education, and overcrowding.[11–13] In a meta-analysis designed to evaluate risk factors for death from acute lower respiratory infection in children in low and middle-income countries, a few factors were associated with mortality, such as age <2 months, diagnosis of *Pneumocystis carinii*, chronic underlying diseases, presence of HIV/AIDS, severe malnutrition and socio-economic and environmental factors.[11–13,26] As in those studies, in the present study, younger age and overcrowding were significantly associated with PICU hospitalization, which might indicate the severity of disease, while breastfeeding showed no such association.

Signs of inflammation, such as CRP, WBC, and ANC, were lower in PICU patients compared with the other two groups. These signs of inflammation are more characteristic of viral rather than bacterial phenotype.[8,27,28] Viral detection and bacteremia were also more frequent in PICU patients. The suggestion that the presence of bacterial-viral co-infection results in more severe diseases than that caused by either pathogen alone has already been raised in previous publications.[29,30] Brealey et al. also demonstrated that detection of *S. pneumoniae* was significantly more frequent during RSV infections compared to other respiratory viruses and that co-detection of both pathogens (RSV and *S. pneumoniae*) was associated with higher clinical disease severity scores. Co-infection of viral and bacterial etiologies in community-acquired pneumonia is more common at younger ages (mainly before two years).[3,15] This may explain our findings of viral detection alongside radiographic and bacteriological evidence of bacterial infection.

The present study has several limitations. First, although, nasal pharyngeal aspirate is a procedure that is general protocol in the pediatric department for all children, viral samples were not taken from all patients (especially those who were admitted on weekends or holidays) and usually not from those discharged from the ED. However, since the study included relatively large numbers of CAAP episodes where nasal washes were obtained, the results can still be valid. Second, the study included data mainly from the pre-pneumococcal conjugated vaccine era

and only the first year after the 7-valent pneumococcal conjugate vaccine was included in the national immunization program. Thus, similar studies should be repeated after PCV implementation.[31] Another limitation was that the bacteriological survey was limited to isolates from blood. However, this limitation is not unique to this study and is also inherent as a limitation in other studies. Even though numbers of positive isolates were relatively low (an underestimation), higher bacteremia and pneumococcal events were still found to be higher in PICU-CAAP children when compared to the other groups.

In conclusion, children admitted to PICU were younger, had more respiratory syncytial virus (RSV) detection, were premature, had lower O_2 saturation, and had higher respiratory rate than those admitted to the general ward or those visiting the emergency department and subsequently discharged. Identification of these unique characteristics may help clinicians to determine the severity of disease during an initial assessment of a patient and may be useful in the development of a severity score.

Declaration of Competing Interest

The authors have no conflicts of interest relevant to this article.

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