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Clinical and Laboratory Features of Children with Community Acquired Pneumonia are Associated with Distinct Radiographic Presentations

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*CAP-PRI Community Acquired Pneumonia Paediatric Research Initiative is an international working group of members of ESPID, initiating and coordinating research in the area of childhood pneumonia.

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Abbreviated title: Pediatric CAP in Distinct Radiographic Presentations

What is known

- Community acquired pneumonia in children is diagnosed based on clinical and radiological definitions
- Radiological criteria were standardized by WHO-SICR and have been utilized in vaccine studies

What is New:

- Correlation between the WHO-SICR radiological definitions and clinical and laboratory parameters has not been studied
- Using the WHO-SICR radiological definitions for community acquired alveolar pneumonia (CAAP) and non-CAAP and the study definition for clinical CAP, it was found that the groups are distinct, differing clinically and in laboratory parameters

ABSTRACT

Chest radiographs from children with community acquired pneumonia (CAP) were categorized into three distinct presentations and each presentation was correlated to clinical and laboratory findings. Children <59 months with CAP presenting to pediatric emergency rooms during two years were enrolled prospectively in eight centers across Europe. Clinical and laboratory data were documented and radiographs obtained from patients. Of the 1,107 enrolled patients, radiographs were characterized as 74.9% alveolar CAP, 8.9% non-alveolar CAP and 16.3% clinical CAP. Alveolar CAP patients had significantly higher rates of fever (90.7%), vomiting (27.6%), and abdominal pain (18.6%), while non-alveolar CAP patients presented more with cough (96.9%). A model using independent parameters that characterize alveolar, non-alveolar and clinical CAP demonstrated that alveolar CAP patients were significantly older (OR= 1.02) and had significantly lower oxygen saturation than non-alveolar CAP patients (OR= 0.54). Alveolar CAP patients had significantly higher mean WBC (17,760±8539.68 cells/mm^3) and ANC (11.5±7.5 cells/mm^3) than patients categorized as non-alveolar CAP (WBC: 15,160±5996 cells/mm^3, ANC: 9.2±5.1 cells/mm^3) and clinical CAP (WBC: 13,180±5892, ANC: 7.3±4.7). *Conclusion: Alveolar CAP, non-alveolar CAP and clinical CAP are distinct entities differing not only by chest radiographic appearance but also in clinical and laboratory characteristics. Alveolar CAP has unique characteristics, which suggest association with bacterial etiology.*

List of abbreviations

ANC Absolute neutrophil count

CAP Community Acquired Pneumonia

CAP-RI Community Acquired Pneumonia Pediatric Research Initiative

CRP C-reactive protein

ESR Erythrocyte sedimentation rate

PCV Packed Cell Volume

WHO World Health Organization

WHO-SICR World Health Organization working group - WHO Standardization of Interpretation of Chest Radiographs

WBC White Blood cells

INTRODUCTION

Community-acquired pneumonia (CAP) is the leading cause of childhood morbidity and mortality in industrialized as well as in developing countries, and is responsible for approximately 1.4 million deaths per year which represents 18.3% of all deaths in children <5yrs [11]. CAP has an average annual incidence of 33.8 cases/10,000 in children under the age of 5 [3]. A large number of microorganisms can cause childhood pneumonia both bacterial and viral and sometimes it is caused by multiple pathogens at once as a co-infection [7]. Management of CAP in children involves a number of therapeutic decisions including antibiotic treatment that depends on the infective agent [1]. Treatment for pneumonia is often empirically based on the likelihood that the pneumonia is bacterial in origin, since lung aspirates are too invasive and blood culture unreliable.

The diagnosis of pneumonia is based primarily on an algorithm built on the patient's history, clinical signs and symptoms, laboratory tests and chest radiograph findings. Case definitions for pneumonia can vary by geographic region and even between various hospitals as a result of different institutions using different guidelines [1,6,21]. Laboratory tests measuring the systemic inflammatory response associated with pneumonia are used routinely in clinical practice but their sensitivity and specificity are relatively low [18,19].

Despite using radiological findings as a "gold standard" for defining pneumonia, there is considerable variability in diagnosis of radiographic type of CAP due to inconsistent interpretations of chest radiographs among physicians [16]. Thus, the World Health Organization (WHO) working group - "WHO Standardization of Interpretation of Chest Radiographs" (WHO-SICR) developed a standardized radiological diagnosis of CAP attempting to characterize it [2]. These definitions include three entities: 1) alveolar pneumonia: alveolar infiltrate and consolidation, pleural effusion 2) non-alveolar pneumonia: other infiltrates, no consolidation infiltrate, without effusion 3) no infiltrate, consolidations or effusions [2]. Because alveolar pneumonia is considered to more frequently have a bacterial etiology [20], characterizing CAP by radiographic presentation can help predict which types of pneumonia will be reduced by anti-bacterial vaccines such as pneumococcal conjugated vaccines (PCV). These definitions were used to evaluate various PCV in the past. The demonstrated efficacy of the vaccines was between 17.7% and 37.0% [4,10].

Although these radiological definitions of pneumonia are becoming more commonly used, differences in clinical symptoms and laboratory results among the three entities are not well studied.

Because of the established association of alveolar pneumonia with bacterial etiology, we hypothesized in this study that patients with alveolar CAP would exhibit clinical and laboratory features typical of bacterial infections and that the other two presentations (non-alveolar and clinical CAP) would exhibit clinical and laboratory features associated with viral infection. The aim of this study was to compare clinical symptoms and laboratory results between patients with radiographic presentations of alveolar, non-alveolar, and clinical CAP, in order to help physicians to determine appropriate treatment for pediatric pneumonia.

PATIENTS AND METHODS

Setting

This was a prospective observational study, which took place from November 1, 2010 until June 30, 2012. Data was collected as part of the Community Acquired Pneumonia Pediatric Research Initiative (CAP-PRI), a consortium established by different countries across Europe. Participating medical centers are located in eight countries: Greece, Israel, Italy, Lithuania, Portugal, Romania, Spain and UK. In each country one major pediatric hospital or service is included in the consortium, except in Greece where two hospitals participated. Each participating center of CAP-PRI received approval for this study from their local Human Ethics Committee.

Enrollment Criteria

All children attending the emergency departments of the CAP-PRI centers presenting with CAP who were less than 59 months of age, that had a chest radiograph obtained within 24 hours of admission to the hospital were included in the study. All pneumonia episodes were at least one month following the diagnosis of a previous pneumonia episode.

Survey

The following areas were covered by an audit questionnaire collected at enrollment: demographic data (age and gender), medical history including vaccinations, physical findings, and current health status. Information was obtained from medical charts and any missing information was completed by interviewing parents, the pediatricians on duty at the hospital or the primary care physicians for outpatients. Clinical parameters assessed and recorded included: temperature (maximal temperature that was measured during illness), blood O_2 saturation, respiratory rate, if hospitalized and duration of hospitalization, presence of

cough, vomiting, abdominal pain (as reported by parents), rhinorrhea, and vaccination status. The following laboratory tests were documented: white blood cells count (WBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and absolute neutrophil count (ANC). A patient was considered fully vaccinated according to the local vaccination recommendations of each country. All medical centers followed the same protocol that was written by members of the CAP-PRI consortium.

Chest Radiograph x-rays Evaluation

All radiographs were evaluated according to WHO-SICR criteria [2] by a single expert pediatrician who was blinded to the clinical and laboratory data of the patients. Radiographs were from prospectively enrolled children, and were categorized into radiographic categories retrospectively. The WHO-SICR classifications used in the study were as follows:

- ***Alveolar CAP-*** The presence of end-point consolidation (a dense or fluffy opacity that occupies a portion or whole of a lobe or of the entire lung, that may or may not contain air-bronchograms) or pleural effusion that is in the lateral pleural space (and not just in the minor or oblique fissure) and was spatially associated with a pulmonary parenchymal infiltrate (including other infiltrate) OR if the effusion obliterated enough of the hemithorax to obscure an opacity.
- ***Non-alveolar CAP-*** The presence of other (non-end-point) infiltrate as defined above in the absence of a pleural effusion.
- ***Clinical CAP***- absence of end-point consolidation, other infiltrate or pleural effusion

Statistical analysis

Demographic, clinical and laboratory characteristics were described by radiographic type of pneumonia for different age groups: 0-23, 24-59 months and in general. Frequencies and proportions (means and standard deviations) were reported for categorical variables (continuous variables). Chi-square, Fisher, ANOVA, One way-test or Kruskal-Wallis tests were implemented to assess the association between the type of pneumonia and characteristics. When ANOVA (One way-test) was significant, the multiple comparisons Tukey test (Dunnett's Modified Tukey-Kramer) was implemented and if Chi-square was significant a pairwise proportion test was developed.

To compare the different types of pneumonia, a multinomial mixed Bayesian model with missing values adjusted by age, O2 saturation, hospital (random effect), ANC and vaccine status was developed. Vaccine status and ANC with missing values were imputed in the model taking into account the absence of randomness. Inside the model a logistic regression adjusted by hospital was implemented for imputed vaccine status variable. ANC had no random missing values, the probability of missing values is related to hospitalization and age, and this probability intervened in the imputation process.

RESULTS

A total of 1,107 patients were enrolled. Alveolar CAP was diagnosed in 829 (74.9%), non-alveolar CAP in 98 (8.9%), and clinical CAP in 180 (16.3%) patients (**Figure 1)**.

Children with alveolar CAP were significantly older than those with non-alveolar CAP (**Table 1 and 4)**. Patients with alveolar CAP, had higher rates of fever than those with non-alveolar CAP (90.7% and 87.8% respectively, $p<0.05$) and in addition a higher percentage of patients with alveolar CAP had CRP >70µg/L than non-alveolar CAP (37.8% and 16.6% respectively, $p<0.05$) (**Figure 2).** Vomiting and abdominal pain were also more common in alveolar CAP patients when compared to non-alveolar and clinical CAP patients ($p<0.05$) (**Figure 2**). Rhinorrhea was found at equal rates in alveolar and non-alveolar CAP patients (~64%) but significantly less in clinical CAP patients (41%, $p<0.001$ both) (**Figure 2**). Cough was significantly different amongst all groups and had highest rates in non-alveolar CAP (97%) followed by alveolar CAP (89.5%) and clinical CAP (81.1%) patients (**Figure 1)**. No significant differences in gender, mean temperature, and respiratory rate (when not separated by age) were found between the radiographic groups. Inflammatory markers including WBC, ANC and ESR were highest in the alveolar CAP patient group followed by non-alveolar CAP patient group and lowest in the clinical CAP group (**Table 1**). Mean CRP was highest in the alveolar CAP group, followed by clinical CAP and lowest in non-alveolar CAP (**Table 1)**. Number of days of fever, were also significantly higher for patients with alveolar CAP than non-alveolar and clinical CAP. Vaccination status was not significantly different among groups. **(Tables 2 and 3).**

When divided into two age groups: 0-23 months and 24-59 months different variables were significant in each group. Rate of fever >38.5°C was significant for patients 23-59 months old but not for patients 0-23 months old. Cough was insignificant in the older age group. When respiratory rate was adjusted for age (0-23 months with a cut-off of ≥50 breaths/minute [bpm] and 23-59 months ≥ 40bpm),

respiratory rate was significantly different between radiographic groups. Respiratory rate was significantly higher in those with alveolar CAP than non-alveolar CAP and clinical CAP in the younger group, while in the older group the trend was significantly the opposite and those with alveolar CAP had lower respiratory rate. In the younger age group neither abdominal pain nor hospitalization was significantly different among groups; however in the older group both of these parameters were significantly higher in alveolar CAP patients than clinical CAP patients. CRP >70μg/L was significantly different in patients diagnosed as non-alveolar CAP and clinical CAP in the younger group, and was significantly higher in alveolar CAP patients than non-alveolar and clinical CAP patients in the older group. Mean CRP was only significant in the older group (**Tables 2 and 3**).

In a multi-regression analysis model, patients with alveolar CAP compared to other entities had higher ANC and were older. For each year of age the probability of alveolar pneumonia increases by 2% (OR: 1.02, 95% CI: 1.01-1.04). Fully vaccinated patients were less likely to have alveolar CAP than non-alveolar and clinical CAP. If oxygen saturation was ≤94% the probability of having alveolar CAP was nearly 50% higher when compared to non-alveolar CAP (OR: 0.54, 95% CI: 0.33-0.04). When <92% O_2 saturation was used in the model it was not found to be an independent risk of non-alveolar CAP (**Table 4**).

DISCUSSION

The three radiologically-defined categories alveolar, non-alveolar and clinical CAP differ in demographic, clinical and laboratory characteristics. Alveolar CAP was seen in older children, with higher WBC, ANC, ESR, CRP and more vomiting and abdominal pain. Children with non-alveolar CAP had more cough (in younger children), rhinorrhea (in older children) and a slightly lower rate of fever (in younger children) than alveolar and clinical CAP. Clinical CAP presented more similarly to alveolar CAP for clinical parameters and more similarly to non-alveolar CAP in laboratory parameters. From these findings it seems like alveolar CAP has clinical and laboratory characteristics that may indicate bacterial etiology whereas non-alveolar CAP has the clinical and laboratory characteristics that may indicate viral etiology. The characteristics of clinical CAP do not seem to hint toward a specific etiology.

Age is an important parameter that was a significant predictor of risk of alveolar versus non-alveolar CAP. In the present study, alveolar CAP was seen in older patients. It has been shown in previous studies that cases of alveolar pneumonia are usually of more bacterial etiology [2,13,20] that becomes more common with increasing age [7,14]. In the present study we observed a correlation between alveolar CAP

and older age and we can speculate that this is due to the fact that alveolar CAP is more frequently associated with bacterial etiology. In the present study, non-alveolar CAP was more common in younger children. Incidence of viral etiology is higher in those <2 years old [7]. Potentially, in this study, non-alveolar CAP is associated with younger age because it is more often due to viral etiology.

Clinical results from the study show that alveolar CAP is more consistent with bacterial symptoms, while non-alveolar CAP is more consistent with viral symptoms. Abdominal pain was more prevalent in cases of alveolar CAP than in other entities. More abdominal pain was reported in a previous study in patients with pneumococcal pneumonia (one of the most common pathogens for bacterial pneumonia) when compared to patients with RSV pneumonia (the most common etiology of viral pneumonia) [8]. It is thought that abdominal pain in bacterial infection may be caused by mesenteric lymphadenopathies that are present in lobar or segmental pneumonia [12]. In the present study, non-alveolar CAP had more frequent viral signs and symptoms such as rhinorrhea, cough, and high respiratory rate. These clinical presentations are consistent with viral pneumonia [15].

The laboratory results in this study also support the assumption that alveolar CAP cases were more associated with bacterial etiology. Alveolar CAP patients had the highest mean WBC, ANC, ESR and CRP values, while non-alveolar CAP had lower WBC and CRP. Bacterial etiologies of pneumonia characteristically show more inflammatory features (such as higher WBC, ANC, ESR and CRP) when compared to viral etiologies [15]. It was also found in a previous study that RSV pneumonia specifically is associated with low WBC as well as low serum CRP when compared to bacterial pneumonia [8].

Lower O_2 saturation and high respiratory rate were observed in patients 0-23 months old with alveolar CAP, while these findings were not observed in the older age group. Higher respiratory rate and lower oxygen saturation is usually indicative of a viral infection, since these infections tend to be more diffuse and affect both lungs [9,15]. It was shown that pneumonia caused by bacterial-viral co-infection is more common in younger children [7]. We can speculate that in this study, even though alveolar CAP seems to be in most cases due to bacterial etiology, patients aged 0-23 months more commonly have viral-bacterial co-infection and thus exhibit clinical parameters that are consider more as “viral” symptoms compared to older children.

Another observation from this study was that clinical CAP seemed to be most similar to alveolar CAP in clinical symptoms, but more similar to non-alveolar CAP in laboratory parameters. This might be because clinical pneumonia is in fact an early stage of alveolar CAP or non-alveolar CAP, when it is too

early in the progression of the disease to be able to detect infiltration or effusion on a radiograph. Timing of laboratory tests in the progression of pneumonia can greatly influence the diagnostic results as was previously shown [19]. In an animal study by Stark et al. (2006) it was shown that when mice were co-infected with RSV and pneumococcus, it took several days for an immune response to develop [17]. Thus, it is possible that in patients diagnosed with clinical CAP, diagnostic tests were taken too early before an immune response against the pathogen was mounted and thus a pattern in laboratory results could be not be recognized. Future studies addressing the correlation between these radiographic entities and timing of the presentation of the disease might answer this hypothesis.

In the present study there were some limitations. One was that each center contributed different amounts of cases from each radiographic characterization, resulting in unequal distribution of cases for each radiographic entity. However, despite this unequal distribution, consistent results were observed across centers (data not presented). An additional limitation was that each country (and thus participating center) has different local guidelines regarding vaccination practices, which might create a potential bias. Although effects of vaccination was beyond the scope of this study, further studies should look only at one specific country to observe local effects of the vaccines (specifically PCV) on a specific entity such as alveolar pneumonia. It was demonstrated that alveolar pneumonia cases declined significantly after the introduction of PCV-13 which also supports the hypothesis that alveolar CAP has a bacterial etiology and may be due to *S. pneumoniae* [5].

The absence of information on etiology is another important issue. Since in most cases of CAP blood culture is negative and only in few places viral etiology is being done routinely, this data is more difficult to acquire. Although in the present study this etiological information was not attainable, it is clear that there are major clinical and laboratory differences between radiological groups. In the future, studies using more sophisticated methods are recommended to try and establish a tighter association between etiology and radiographic findings.

In the present study it was found that alveolar CAP, non-alveolar CAP and clinical CAP are distinct entities differing not only by chest radiographic appearance but also in clinical and laboratory characteristics. A patient with alveolar CAP has unique characteristics, which suggest association with bacterial etiology such as older age, normal O_2 saturation and higher inflammatory responses such as elevated WBC and ANC. These clinical and laboratory parameters in conjunction with the chest radiograph findings can help clinicians to determine their treatment accordingly.

COMPLIANCE WITH ETHICAL STANDARDS:

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Ethical Approval: Trial number 3075 (Soroka Hospital, Israel). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee of the respective countries and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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TABLE 1: Demographic, Clinical and Laboratory Characteristics of Pediatric Patients <5 Years with Radiographically Distinct Presentations of Community Acquired Pneumonia (CAP)

	Alveolar CAP	Non-Alveolar CAP	Clinical CAP	*P*
N	829 (74.9%)	98 (8.9%)	180 (16.3%)	
Age in months mean ±SD	24.7±16.8	20.4±14.8	23.4 ± 15.5	0.038α
Male % (n)	55.9(463)	53.1(52)	52.2(94)	NS
Hospitalization % (n)	84.6(701)	80.6(79)	78.3(141)	0.054β
Mean temperature (°C) ±SD (n)	38.9±1.1(633)	38.8±0.9(81)	38.6 ± 1.0(94)	0.006β
Respiratory rate ±SD (n)	44.6±13.9 (712)	44.3±10.9(91)	44.6±11.9(11	NS
O_2 saturation % (n)	94.8±3.7(823)	94.6±4.1(97)	95.7±3.3(178)	0.0021β, γ
WBC				
N	744	82	138	
Mean (cells/mm^3) ± SD	17760±8540.6	15160±5997	13180±5892	<0.001α, β, γ
% ≥15000 (n)	57.7 (429)	47.6 (39)	30.4 (42)	<0.001β,γ
% ≥20000 (n)	36.2 (269)	22 (18)	10.1 (14)	<0.001α, β, γ
ANC (cells/mm^3) ±SD (n)	11.5±7.5(684)	9.2±5.1(134)	7.3±4.7(80)	<0.001α, β, γ
CRP				
Mean* (μg/L) ±SD (n)	83.9±103.6(254)	43.0±76.6(54)	55.4±69.5(14)	0.008 α
% ≥70 (n)	97 (38.2%)	9 (16.7 %)	4 (28.6%)	0.006 α
Mean ESR (mm/hour) ±SD (n)	46.2±31.0(107)	45.4±34.9(13)	34.3±29.4(3)	NS

α- alveolar vs. non-alveolar CAP
β- alveolar vs. clinical CAP
γ- non-alveolar vs. clinical CAP
NS- not significant
*After log transformation.

TABLE 2: Clinical and Laboratory Characteristics of Pediatric Patients 0-23 Months Old with CAP in Relation to Radiographic Categorizations

	Alveolar CAP	Non-Alveolar CAP	Clinical CAP	*P*
Fever >38.5°C% (n/N)	87.8 (380/433)	78.3 (47/60)	86.8 (79/91)	NS
Rhinorrea% (n/N)	70.0 (303/433)	65.0 (39/60)	44.0 (40/91)	<0.001β, 0.018γ
Cough % (n/N)	90.1 (390/433)	96.7 (58/60)	76.9 (70/91)	<0.001β, 0.002γ
<92 O_2 sat % (n/N)	20.9 (90/431)	16.9 (10/60)	13.2 (12/91)	NS
Respiratory Rate ≥ 50 breaths/min% (n/N)	48.3 (184/381)	33.3 (18/54)	35.6 (21/59)	0.055α, 0.093β
Abdominal Pain% (n/N)	3.5 (15/427)	5.0 (3/60)	2.2 (2/91)	NS
Vomiting% (n/N)	24.9 (108/433)	10.0 (6/60)	15.4 (14/91)	0.016α, 0.068β
Vaccination Complete % (n/N)	67.1 (235/350)	59.2 (29/49)	55.6 (15/27)	NS
Hospitalization% (n/N)	87.8 (380/433)	85 (51/60)	84.6 (77/91)	NS
CRP >70% (n/N)	27.1 (29/107)	11.8 (4/34)	60.0 (3/5)	0.032γ
Respiratory Rate				
mean(breaths/min)±SD	49.8±13.8	46.6±10.7	47.2±11.7	NS
Median (breaths/min)	48	47	44	
min-max	18-94	28-72	24-72	
n	381	54	59	
Days of fever				
mean ± SD	3.6±3.7	2.7±2.2	2.7±1.9	<0.001α,ß
median	2	1	2	
min-max	0-30	0-10	0-9	
n	371	46	76	
WBC				
mean (cells/µl)± SD	17480±8347.4	15750±6372.4	13390±5550.5	<0.001ß
median	16690	14790	12720	
min-max	2000-56100	4790-32700	1820-33020	
n	393	53	78	
ANC				
mean (cells/mm^3)±SD	9.9±6.6	8.6±5.3	6.6±4.1	<0.001ß
median (cells/mm^3)	8.7	8.1	5.9	
min-max	0.47-40	0.877-25.1	0.69-19.69	
n	372	51	74	
CRP				
mean (μg/L)±SD	53±71	37.4±86	108.8±94.2	NS
median(μg/L)	24.7	15.6	12.7	
min-max	0.2-424.9	1.1-499.2	5-212.5	
n	107	34	5	

α- alveolar vs. non-alveolar CAP
β- alveolar vs. clinical CAP
γ- non-alveolar vs. clinical CAP
NS- not significant

TABLE 3: Clinical and Laboratory Characteristics of Pediatric Patients 24-59 Months Old with CAP in Relation to Radiographic Categorizations.

	Alveolar CAP	Non-Alveolar CAP	Clinical CAP	*P*
Fever >38.5°C % (n/N)	93.9 (372/396)	94.7 (36/38)	88.8 (79/89)	NS
Rhinorrea % (n/N)	58.8 (233/396)	63.2 (24/38)	38.6 (34/89)	<0.001β, <0.019γ
Cough% (n/N)	88.9 (352/396)	97.4 (37/38)	85.4 (76/89)	NS
<92 O_2 sat% (n/N)	12 (47/396)	7.9 (3/38)	10.3 (9/89)	NS
Respiratory Rate ≥ 40 breaths/min % (n/N)	45 (149/331)	62.2 (23/37)	62.7 (32/51)	0.07α, 0.027β
Abdominal Pain% (n/N)	21.5 (85/396)	10.5 (4/38)	12.5 (11/88)	0.075β
Vomiting% (n/N)	30.6 (121/396)	31.6 (12/38)	17 (15/88)	0.016β
Vaccination Complete% (n/N)	64.1 (207/323)	61.8 (21/34)	66.7 (22/33)	NS
Hospitalization% (n/N)	81.1 (321/396)	73.7 (28/38)	71.9 (64/89)	0.06β
CRP >70μg/L% (n/N)	45.6 (67/147)	25 (5/20)	11.1 (1/9)	0.096α, 0.078β
Respiratory Rate				
mean (breaths/min)±SD	38.7±11.47	40.92±10.38	41.59±11.52	NS
median (breaths/min)	36	40	40	
min-max	18-80	24-64	20-68	
n	331	37	51	
Days of fever				
mean ± SD	3.7±3.8	2.5±2.4	2.3±2.2	<0.001α, β
median	3	2	2	
min-max	0-30	0-12	0-10	
n	391	37	83	
WBC				
mean (cells/μl)± SD	18060±8752	14080±5170	12910±6346	<0.001α, β
median	17000	14500	12320	
min-max	2460-51600	5700-25200	3760-38390	
n	351	29	60	
ANC				
mean (cells/mm^3)±SD	13.4±8.1	10.2±4.7	8.2±5.3	<0.001α, β
median (cells/mm^3)	12.1	10.4	6.9	
min-max	1.1-42	2.3-21.5	1.0-25.6	
n	312	29	60	
CRP				
mean (μg/L)±SD	106.4±117.3	52.6±57.7	25.8±25.4	0.004β
median(μg/L)	65	29.7	23.4	
min-max	0.2-771.1	3.6-196.8	1-86.1	
n	147	20	9	

α- alveolar vs. non-alveolar CAP
β- alveolar vs. clinical CAP
γ- non-alveolar vs. clinical CAP
NS- not significant

TABLE 4: A Model Using Independent Parameters that Characterize Alveolar Community Acquired Pneumonia (CAP), Non-Alveolar CAP and Clinical CAP (No Chest X-Ray Defined Pneumonia).

		Alveolar vs. Non-alveolar CAP			Alveolar vs. Clinical CAP			Non-alveolar vs. Clinical CAP		
			CI (95%)			CI (95%)			CI (95%)	
		OR	L	U	OR	L	U	OR	L	U
ANC (cells/mm^3)	>15,000	1.73	0.94	3.66	2.02*	1.10	4.83	2.38	1.18	6.54
Vaccine Status	Fully Vaccinated	0.43	0.21	1.02	0.61	0.27	1.44	0.60	0.25	1.48
Age (years)		1.02*	1.01	1.04	1.00	0.99	1.02	1.00	0.993	1.02
O_2 Saturation	≤94%	0.54*	0.33	0.95	0.77	0.50	1.26	0.79	0.521	1.28

OR- odds ratio
L- lower confidence limit
U- upper confidence limit
*- significant

FIGURE LEGEND

Figure 1: Distribution of radiographic presentations of children < 5 years of age with Community Acquired Pneumonia (CAP).

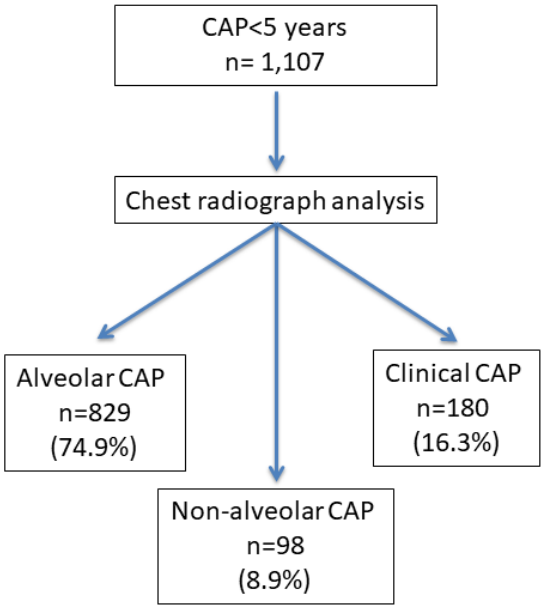

Figure 2: Characteristics of pediatric patients <5 years old with alveolar community acquired pneumonia (CAP), non-alveolar CAP and clinical CAP. Significant differences are denoted by α- alveolar *vs.* non-alveolar CAP, β- alveolar *vs.* clinical CAP, and/or γ- non-alveolar *vs*. clinical CAP and are defined as $P < 0.05$.