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Radiographic Pneumonia in Young Febrile Infants Presenting to the Emergency Department: Secondary Analysis of a Prospective Cohort Study

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Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

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This study involves human participants and was approved by an Ethics Committee(s) or Institutional Board(s). The following Institutional Review Boards approved this study: Arizona Health Science Center (1603466288R005), Children's Hospital Boston (IRB-P00022138), Children's Hospital Colorado (16–0390), Children's Hospital of Philadelphia (16–012793), Children's Hospital of Wisconsin/Medical College of Wisconsin (875561), Children's National Hospital (Pro00007492), Cincinnati Children's Hospital Medical Center (2016–1486), Lurie Children's IRB (2016–412), Morgan Stanley Children's Hospital/Columbia University (IRB-AAAQ9321), Nationwide Children's Hospital (1247), Oklahoma University Health Science Center (6710), Primary Children's Medical Center/University of Utah (90496), Texas Children's Hospital (38802), University of California-Davis (877767–13), University of Michigan (93260), University of New Mexico Health Sciences Center (8142), University of Pittsburgh Medical Center (19020322), Washington University School of Medicine/St. Lous Children's Hospital (201603088)

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Abstract

Objective: The lack of evidence-based criteria to guide CXR use in young febrile infants results in variation in its use with resultant suboptimal quality of care. We sought to describe the features associated with radiographic pneumonia in young febrile infants.

Study Design: Secondary analysis of a prospective cohort study in 18 emergency departments in the Pediatric Emergency Care Applied Research Network from 2016–2019. Febrile (≥38°C) infants ≤60 days old who received chest radiographs (CXRs) were included. CXR reports were categorized as "no," "possible," or "definite" pneumonia. We compared demographics, clinical signs, and laboratory tests among infants with and without pneumonias.

Results: Of 2,612 infants, 568 (21.7%) had CXRs performed; 19 (3.3%) had definite and 34 (6%) possible pneumonias. Patients with definite (4/19, 21.1%) or possible (11/34, 32.4%) pneumonias more frequently presented with respiratory distress compared to those without (77/515, 15.0%) pneumonias (adjusted odds ratio, 2.17; 95% confidence interval 1.04,4.51). There were no differences in temperature or heart rate in those infants with and without radiographic

pneumonia. The median serum procalcitonin (PCT) level was higher in the definite (0.7 ng/mL [interquartile range, 0.1,1.5]) versus no pneumonia (0.1 ng/mL [0.1,0.3]) groups, as was the median absolute neutrophil count (ANC) (definite, 5.8 K/mcL [3.9,6.9] vs. no pneumonia, 3.1 K/mcL [1.9,5.3]). No infants with pneumonia had bacteremia. Viral detection was frequent (no pneumonia [309/422, 73.2%], definite pneumonia [11/16, 68.8%], possible pneumonia [25/29, 86.2%]). Respiratory syncytial virus was the predominant pathogen in the pneumonia groups and rhinovirus in infants without pneumonias.

Conclusions: Radiographic pneumonias were uncommon in febrile infants. Viral detection was common. Pneumonia was associated with respiratory distress, but few other factors. Although ANC and PCT levels were elevated in infants with definite pneumonias, further work is necessary to evaluate the role of blood biomarkers in infant pneumonias.

INTRODUCTION

Serious bacterial infections (SBI) occur in 8–13% of febrile infants 60 days and younger in the United States.(1–4) Although the initial diagnostic approach often focuses on urinary tract infections, bacteremia, and bacterial meningitis, pneumonia is also an important diagnostic concern. Prevalence estimates of pneumonia in this population vary considerably, ranging from 0.1% up to 8%.(5–8) These varied estimates reflect the limited data available on the epidemiology, risk factors, and presentation of young febrile infants with pneumonias.

Pneumonia in young infants is challenging to diagnose using clinical evaluation and gestalt alone.(9–11) Chest radiographs (CXRs) are considered the reference standard for the diagnosis of pneumonia, although CXRs have limitations in interpretation as well.(12) Research studies conducted in the pre-pneumococcal vaccine era found that the prevalence of radiographic pneumonias in infants younger than 3 months without respiratory signs or symptoms was about 1%.(6–8) A more recent evaluation using data from 2008–2013 found that although one-third of a cohort of more than 4,500 febrile infants 60 days and younger had a CXR performed, only 3% of those had definite radiographic pneumonias.(5) Infants with radiographic pneumonias had higher Yale Observation Scale (YOS) scores, indicating more ill appearance, and higher rates of hospitalization. That study was limited by a lack of physical examination data; thus, it is unclear if respiratory findings on physical examination were associated with pneumonia. In addition, prior studies of pneumonia in young infants have been limited with regard to available diagnostic testing including molecular viral testing and blood biomarker data.

The lack of evidence-based criteria to guide CXR use in young febrile infants results in variation in its use with resultant suboptimal quality of care. An evidence-based approach to understanding the factors associated with pneumonia would limit unnecessary CXR use for this vulnerable population, while also focusing use on those at risk for pneumonia. The primary objective of this study was to describe the demographic and clinical factors, in addition to blood biomarker and etiologic data, associated with radiographic pneumonia in febrile infants 60 days and younger to fill this important evidence gap.

METHODS

Study Design

This was a planned secondary analysis of data from a prospective observational study of febrile infants ≤60 days old presenting to 18 emergency departments (ED) in the Pediatric Emergency Care Applied Research Network (PECARN) from June 2016 to April 2019. The goal of the parent study was to evaluate different strategies, including host transcriptomic analyses, for the diagnosis of SBI in these infants. Details of the parent study have been described previously.(3, 13, 14) Eligible infants were enrolled upon receiving written informed consent from their parents or guardians. The institutional review boards at all participating sites approved this study.

Study Population

We included a convenience sample (only enrolled when a research coordinator was present) of infants ≤60 days old with fever (rectal temperature ≥38°C) in the ED, at home, or referring clinic in the previous 24 hours and who were evaluated for SBI in a participating site. Eligible infants had at least one blood culture obtained as part of the original study aims. Infants with critical illness, prematurity (<37 weeks' gestation), significant comorbidities, indwelling devices, definitive focal bacterial infections (e.g., cellulitis, but not including otitis media), and those already receiving antibiotics were excluded from the primary study, and therefore this study. For this analysis, only infants who had CXRs performed in the ED were included. CXRs were performed at the ED provider's discretion or according to institutional protocols; CXRs were not mandated by study procedures.

Study Procedures

Demographic characteristics, clinical factors, and laboratory results were prospectively collected for all study participants. Clinical factors included initial vital signs, oxygen saturation, respiratory examination findings, and YOS scores. The YOS provides a quantitative clinical assessment of risk for SBIs based on simple clinical and observational parameters. It includes 6 items (quality of cry, reaction to parental stimulation, state variation, color, hydration, response to social overtures), with each scored on a 1-3-5 scale, yielding a total YOS score ranging from 6 (most well-appearing) to 30 (most ill-appearing). A YOS score of 10 or less is considered not ill-appearing. Increased work of breathing/respiratory distress was defined as the presence of retractions, grunting, nasal flaring, or clinician-defined tachypnea. Clinician-determined tachypnea was defined as the clinician's impression of tachypnea, which may or may not have been determined by a formally counted respiratory rate.

Nearly all (98.4%) infants had complete blood counts (CBC) performed for clinical care, including white blood cell (WBC) count, absolute neutrophil count (ANC), and platelet count. Serum was obtained for procalcitonin (PCT) measurement as part of research procedures. For PCT measurement, we obtained 1 ml of blood which was then centrifuged and stored at −80° C within 6 hours. PCT samples were shipped in batches to a central laboratory for processing and analysis. Research PCT results were not available to the clinicians during clinical care of the infants. If PCT was sent as part of clinical care, these

results were available to the clinician. All infants had blood and urine cultures performed as part of clinical care. Viral testing was performed at the discretion of the treating physician. Results of viral testing performed as part of clinical care were available to the clinicians. In addition, for research purposes, an attempt was made to obtain nasopharyngeal (NP) swabs from all patients for comprehensive multiplex PCR testing for respiratory pathogens using the BioFire® platform. These research swabs were sent to a central laboratory for processing; viral testing results from these research swabs were not available to ED clinicians for decision-making. Participants who did not have a research NP swab performed were included in the analysis of viral infections if they had an NP swab obtained for viruses for clinical use and had testing for adenovirus, influenza, coronavirus (not including SARS-CoV-2), parainfluenza, respiratory syncytial virus (RSV), and rhinovirus/enterovirus, the same viruses as were tested for in the research specimen using Biofire.

Pneumonia Classification

CXR reports documented by the attending radiologist at the time of clinical care were reviewed at each site. CXR reports that were not reported as definitively normal were uploaded into the study database for further review by the study investigators, and were classified as “definite pneumonia,” “possible pneumonia,” or “no pneumonia” using definitions established by the investigators *a priori* and consistent with a prior study of pneumonia in young febrile infants.(5) Definite atelectasis was classified as “no pneumonia.” Classification of “possible pneumonia,” included “pneumonia versus atelectasis.” Lobar infiltrates were considered “definite pneumonia.” Presence or absence of pleural effusion was also recorded.

Statistical Analysis

Patient factors, including demographics, clinical characteristics, and laboratory results, were summarized overall and by pneumonia classification (no pneumonia, possible pneumonia, definite pneumonia). Continuous measures were summarized using medians and inter-quartile ranges, and categorical variables using counts and percentages. Fisher’s exact and Kruskal-Wallis tests were used to compare measures across the three pneumonia classification groups (Tables 1 and 2).

Four multivariable logistic regression models were created with adjusted estimates and 95% confidence intervals (CI) for variables deemed most clinically relevant to pneumonia diagnosis. The primary model included all patients with CXR obtained in the study cohort. Secondary models included all patients with comprehensive viral testing but no PCT measurement (N=444), patients without viral testing but with PCT (N=309), and patients with both viral testing and PCT (N=293). Due to the limited number of patients with definite pneumonia and the fact that many clinicians treat patients with CXRs suggestive of pneumonia with antibiotics, adjusted estimates reflect the odds of possible or definite pneumonia vs. no pneumonia. Analyses were performed using SAS 9.4 (SAS Institute; Cary, NC).

RESULTS

There were 2612 infants enrolled in the parent study, of whom 568 (21.7%) had CXRs performed and were included in this analysis. Compared to those who did not receive CXRs, infants who had CXR performed were more likely to be tachypneic, have evidence of increased work of breathing or respiratory distress, admitted to the hospital, and have influenza or RSV detected (Supplemental Table 1). The median age of infants was 38 days (IQR 24, 48) and most (59.2%) were males. Definite pneumonias were present in 3.3% (n=19), and possible pneumonias were present in 6.0% (n=34) of infants. Table 1 describes the demographic characteristics of the study population. There were no differences in median age, sex, race, or ethnicity among infants with definite, possible, and no pneumonia.

Table 2 describes the clinical characteristics of the study population. There were no differences in temperature or heart rate in those infants with and without radiographic pneumonia. Respiratory rate was slightly higher and room air oxygen saturation slightly lower in infants with possible pneumonias, although differences were small, and few infants were hypoxic at presentation. A significantly greater proportion of children with possible (32.4%) or definite (21.1%) pneumonias had increased work of breathing on physical examination compared to those without pneumonia on CXR (15%, p=0.02). There were no statistical differences in YOS; however, a greater proportion of infants with definite pneumonia had a YOS >10, suggesting “ill appearance.” Furthermore, a significantly greater proportion of infants with possible (85.3%) or definite (94.7%) pneumonias were hospitalized compared to those without pneumonia (69.1%).

The median WBC count was slightly higher in infants with possible or definite pneumonias compared with no pneumonias (Table 2). Similarly, the median ANC was higher in infants with possible or definite pneumonias compared with no pneumonias. Of the 324 infants in whom PCT was available, median PCT concentrations were significantly elevated in children with possible and definite pneumonias compared with no pneumonias. A higher proportion of infants with possible or definite pneumonias had influenza or RSV detected (52.9% and 36.8%, respectively) in their nasopharynx compared with those without (21%) pneumonias (Table 2). Additional details of multiplex viral testing performed at the central research laboratory can be found in Supplemental Table 2. Bacteremia was rare in the entire cohort and did not occur in any patients with pneumonias. Only two patients with definite pneumonias had a pleural effusion noted on CXR.

In the multivariable logistic regression analyses, infants with evidence of respiratory distress on physical examination had 2.17 times the odds of having possible or definite pneumonia (95% CI 1.04, 4.51; Table 3). Respiratory rate and YOS were not associated with radiographic pneumonia. In multivariable analyses in the subsets of infants where viral testing or PCT data were available, no factors were associated with possible or definite pneumonia, although these analyses were limited by sample size.

DISCUSSION

In this large, multicenter study of febrile infants 60 days and younger who presented to PECARN EDs and had CXRs performed, possible and definite pneumonias were present in 6% and 3.3%, respectively. Signs of respiratory distress occurred substantially more frequently in infants with possible or definite pneumonias. Infants with radiographic pneumonias were hospitalized more frequently compared to those without pneumonia. In addition, ANC and PCT concentrations were significantly higher in infants with definite pneumonias. A higher proportion of infants with pneumonias, however, also had influenza or RSV detected. No infant with radiographic pneumonia had bacteremia.

In a prior PECARN study, we reported on a distinct cohort of 1724 febrile infants 60 days and younger of whom 2.7% had definite pneumonias, while 3.9% had possible pneumonias.(5) The prevalence of pneumonia was somewhat higher in the current study compared with that prior study. In the prior cohort, higher YOS scores were associated with radiographic pneumonia. However, there were many infants with radiographic pneumonias who had normal YOS scores. Several studies, including one performed by PECARN, have found that the YOS score is limited in its ability to confirm or exclude serious bacterial infections in young febrile infants.(15, 16) By evaluating signs and symptoms of respiratory distress, the current study overcomes an important limitation of our prior work, which did not evaluate these signs and symptoms. Although we found no statistically significant differences in YOS in the current study, a significantly greater proportion of children with pneumonias had increased work of breathing on physical examination. This finding persisted in multivariable models, suggesting that clinicians should consider chest radiographs in young febrile infants with increased work of breathing or signs of respiratory distress to evaluate for pneumonia. The prevalence of radiographic pneumonia among those with radiographs obtained in our study was relatively low but it is not known if the 121 infants with work of breathing/respiratory distress who did not have chest radiography performed in our study had pneumonia. Finally, the importance of repeated and accurate respiratory rate measurements is apparent by the discrepancy in number of infants with respiratory rates >60 (as counted by nurse or other clinician and recorded in the medical record) vs. clinician-determined tachypnea (which represented the clinician’s impression of tachypnea).

Many studies have evaluated the role of blood biomarkers, such as WBC count, ANC, C-reactive protein, and PCT, in diagnosing SBI in febrile infants. Of the blood biomarkers examined in our study, ANC and PCT were significantly elevated in infants with definite radiographic pneumonias. This finding corroborates data from both young febrile infants and children with pneumonias.(5, 17, 18) In the parent study for this cohort, PCT was one of three biomarkers, in combination with a normal ANC and a negative urinalysis, found to rule out serious bacterial infections in febrile infants 60 days and younger with a negative predictive value of 99.6 (98.7, 99.9).(3) In the current study, we found a median PCT concentration of 0.7 ng/mL in infants with definite pneumonias, which is greater than the 0.5 ng/mL cut point evaluated in the parent study used to define higher risk of serious bacterial infections in this age group. Interestingly, PCT concentrations in those with possible pneumonias straddled those with no pneumonia and those with definite pneumonia, suggesting lack of a robust inflammatory response in these patients and that at least some in

this equivocal group likely did not have bacterial pneumonia. Although PCT concentrations were elevated in young febrile infants with definite radiographic pneumonias in our cohort, there was no statistical significance when included in a multivariable model with respiratory distress and other findings. This was likely a result of the smaller sample of children who had PCT assays performed, resulting in the need to combine the possible and definite pneumonia groups for multivariable analysis. Given the importance of PCT in predicting SBI in young febrile infants and in children with pneumonia, further work is necessary in larger samples before definitive conclusions can be drawn regarding the role of PCT in evaluating for radiographic pneumonia in febrile young infants.

Similar to our prior study, the current study reinforces the important role of viral pathogens in pneumonias in young febrile infants. We found that among children with complete viral testing, 25 (86.2%) of the 29 infants with possible pneumonias and 11 (68.8%) of the 16 with definite pneumonias had viruses detected in their nasopharynx. In addition, more than half of infants without pneumonia had viruses detected. While RSV was the most prevalent virus in those with pneumonias, rhinovirus was the most commonly detected viral pathogen in infants without pneumonias. Given the substantial numbers of infants in our cohort with positive viral tests and low PCT levels, the role of detected viruses warrants further exploration, as we were not able to fully elucidate if the viral detection was due to colonization, co-infection with a bacterium, or an isolated viral pneumonia.

Our results should be interpreted in the context of several limitations. First, not all patients had viral testing or PCT available, therefore the power of the multivariable analyses was limited. However, median PCT concentrations were higher in infants with definite pneumonias, suggesting a potential association of PCT with radiographic pneumonia that may have been further elucidated with a larger sample. Second, a single radiologist did not interpret all chest radiographs, with interpretations being coded from clinical reports by study investigators. This approach to classification, however, has been shown to be valid previously,(5) and mirrors real-world practice. Third, while we captured vital signs and signs of respiratory distress, we did not capture auscultatory findings. Auscultatory findings in infants can be unreliable,(19) however, and thus it is unclear if collection of these signs would have meaningfully altered our results. Fourth, we did not require that CXRs to be obtained for patients in the parent study. If we had, the denominator would have expanded with most of these infants having normal CXRs, which would decrease the rate of pneumonia. Our approach was pragmatic and mirrors the real-world context where we focused on those infants in whom clinicians chose to get CXRs. However, we did not record the individual clinician's motivation for obtaining the CXR. We also did not know if sites had institutional guidelines in place regarding CXR use in this population, which could introduce variability across sites. Fifth, serial CXRs were not obtained, thus there may be a small subset of children who developed pneumonia after an initially normal CXR. However, the practice of serial CXRs in this population is uncommon and are never obtained in the limited time patients spend in the ED. Given the high negative predictive value of a normal CXR in children (>98%), we expect this phenomenon to be very uncommon and therefore would not substantively alter our results.(20) Regarding the outcome of hospitalization, it may be that CXR findings resulted in the clinician's decision to hospitalize an infant rather than other clinical features. Finally, the number of patients was relatively small with 53

infants with pneumonia, which could limit our statistical conclusions. However, considering the similarities to prior literature on this subject, we believe that our descriptive results are valid.

In summary, in this multicenter study of 568 febrile infants 60 days and younger, we found that radiographic pneumonias were present in 9.3%, with 3.3% being definitive. Signs of respiratory distress, including grunting, nasal flaring, retractions, or tachypnea, were associated with the presence of radiographic pneumonia. This suggests that CXRs should be considered in febrile infants 60 days and younger with respiratory distress. Although the detection of RSV or influenza and elevations in ANC and PCT were associated with radiographic pneumonias in univariable analyses, future work in larger cohorts is necessary to fully understand the role of viral detection and blood biomarkers in aiding clinical decision-making around pneumonias in febrile young infants.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflict of Interest Disclosures:

Dr. Ramilo reports personal fees from Sanofi-Pasteur, Merck, and Pfizer, and grants from Janssen and the Bill & Melinda Gates Foundation. These fees and grants are not related to this study. No other disclosures were reported.

Data Sharing Statement:

No additional data are available.

ABBREVIATIONS:

ANC	absolute neutrophil count
CXR	chest radiograph
CBC	complete blood count
CI	confidence interval
ED	emergency department
IQR	interquartile range
PCT	procalcitonin
PECARN	Pediatric Emergency Care Applied Research Network
RSV	Respiratory Syncytial Virus
SBI	serious bacterial infection
WBC	white blood cell count
YOS	Yale Observation Scale

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What is already known on this topic:

Pneumonia is an important diagnostic consideration in young febrile infants. The lack of evidence-based criteria to guide CXR use in young febrile infants results in variation in its use with resultant suboptimal quality of care.

What this study adds:

Radiographic pneumonias are uncommon in febrile infants, and were associated with signs of respiratory distress, but few other factors. Viral detection, absolute neutrophil count, and procalcitonin were higher in febrile patients with pneumonia compared to those and without pneumonia.

How this study might affect research, practice, or policy:

CXRs should be considered in febrile infants 60 days and younger with respiratory distress. Future work in larger cohorts is necessary to fully understand the role of viral detection and blood biomarkers in aiding clinical decision-making for imaging, disposition, and antibiotic use for pneumonias in febrile young infants.

Table 1.

Demographic characteristics by pneumonia status

		Chest X-Ray Result			
	Overall (N = 568)	**No Pneumonia (N = 515)**	**Possible Pneumonia (N = 34)**	**Definite Pneumonia (N = 19)**	**P-value**
Sex					0.66[1]
Male	336 (59.2%)	305 (59.2%)	18 (52.9%)	13 (68.4%)	
Female	232 (40.8%)	210 (40.8%)	16 (47.1%)	6 (31.6%)	
Age (in days)	38.0 [24.0, 48.0]	38.0 [25.0, 48.0]	32.5 [24.0, 48.0]	31.0 [14.0, 55.0]	0.51[2]
Race					0.59[1]
White	391 (68.8%)	357 (69.3%)	22 (64.7%)	12 (63.2%)	
Black	108 (19.0%)	102 (19.8%)	3 (8.8%)	3 (15.8%)	
Other	11 (1.9%)	11 (2.1%)	0 (0.0%)	0 (0.0%)	
Multiple	13 (2.3%)	11 (2.1%)	1 (2.9%)	1 (5.3%)	
Unknown or not reported	45 (7.9%)	34 (6.6%)	8 (23.5%)	3 (15.8%)	
Ethnicity					0.21[1]
Hispanic or Latino	126 (22.2%)	108 (21.0%)	13 (38.2%)	5 (26.3%)	
Not Hispanic or Latino	432 (76.1%)	397 (77.1%)	21 (61.8%)	14 (73.7%)	
Unknown or Not Reported	10 (1.8%)	10 (1.9%)	0 (0.0%)	0 (0.0%)	

[1] P-values reported are based on Fisher's exact text.

[2] P-values reported are based on a Kruskal-Wallis test for continuous variables. Median [Q1, Q3] summary statistics are reported.

[*] Unknown or not reported race category is not included in the statistical test.

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Table 2.

Clinical characteristics by pneumonia status

		Chest X-Ray Result			
	Overall (N = 568)	**No Pneumonia (N = 515)**	**Possible Pneumonia (N = 34)**	**Definite Pneumonia (N = 19)**	**P-value**
Temperature (Celsius)	38.3 [38.1, 38.7]	38.3 [38.1, 38.7]	38.3 [38.1, 38.7]	38.3 [38.1, 38.9]	0.98[1]
Heart Rate (n=562)	168.0 [156.0, 180.0]	168.0 [155.0, 180.0]	167.0 [160.0, 180.0]	164.0 [152.0, 176.0]	0.81[1]
Tachycardia *	44 (7.7%)	40 (7.8%)	2 (5.9%)	2 (10.5%)	0.83[2]
Respiratory Rate (n=560)	44.0 [39.0, 54.0]	44.0 [39.0, 54.0]	48.0 [40.0, 60.0]	40.0 [32.0, 44.0]	0.02[1]
Tachypnea (respiratory rate > 60 breath/min.)	97 (17.1%)	84 (16.3%)	10 (29.4%)	3 (15.8%)	0.15[2]
Room air O_2saturation (%) (n=514)	99.0 [98.0, 100.0]	100.0 [98.0, 100.0]	97.5 [95.0, 99.5]	99.0 [98.0, 100.0]	0.001[1]
Increased work of breathing/respiratory distress	92 (16.2%)	77 (15.0%)	11 (32.4%)	4 (21.1%)	0.02[2]
Retractions	59 (10.4%)	50 (9.7%)	6 (17.6%)	3 (15.8%)	0.17[2]
Nasal flaring	11 (1.9%)	10 (1.9%)	1 (2.9%)	0 (0.0%)	0.66[2]
Grunting	21 (3.7%)	16 (3.1%)	4 (11.8%)	1 (5.3%)	0.04[2]
Tachypnea (clinician impression)	50 (8.8%)	38 (7.4%)	8 (23.5%)	4 (21.1%)	0.002[2]
Multiple categories above	35 (6.2%)	27 (5.2%)	5 (14.7%)	3 (15.8%)	0.02[2]
YOS category *					0.25[2]
6–10	481 (84.7%)	441 (85.6%)	26 (76.5%)	14 (73.7%)	
>10	79 (13.9%)	69 (13.4%)	5 (14.7%)	5 (26.3%)	
White blood cell count (1000/μL) (n=559)	9.9 [7.4, 13.5]	9.8 [7.1, 13.1]	10.5 [8.3, 15.9]	11.6 [9.3, 14.3]	0.05[1]
Hemoglobin (g/dL)	11.8 [10.6, 13.6]	11.8 [10.5, 13.6]	12.9 [11.2, 13.7]	12.2 [10.6, 13.9]	0.24[1]
Absolute neutrophil count (1000/μL)					0.01[1]
n	554	504	33	17	
Median [Q1, Q3]	3.3 [2.0, 5.5]	3.1 [1.9, 5.3]	4.2 [2.2, 8.2]	5.8 [3.9, 6.9]	
Platelet count (1000/μL) (n=555)	371.0 [306.0, 460.0]	370.0 [305.5, 458.0]	434.0 [330.0, 496.0]	397.5 [285.0, 506.0]	0.28[1]
PCT (ng/mL) (n=324)	0.2 [0.1, 0.4]	0.1 [0.1, 0.3]	0.2 [0.2, 0.5]	0.7 [0.1, 1.5]	0.007[1]
Viral Detection (n=467)					<.001[2]
None	122 (21.5%)	113 (21.9%)	4 (11.8%)	5 (26.3%)	

		Chest X-Ray Result			
	Overall (N = 568)	**No Pneumonia (N = 515)**	**Possible Pneumonia (N = 34)**	**Definite Pneumonia (N = 19)**	**P-value**
Influenza/RSV	133 (23.4%)	108 (21.0%)	18 (52.9%)	7 (36.8%)	
Other	212 (37.3%)	201 (39.0%)	7 (20.6%)	4 (21.1%)	
Blood Culture					1.000[2]
Unable to classify	4 (0.7%)	4 (0.8%)	0 (0.0%)	0 (0.0%)	
Positive	8 (1.4%)	8 (1.6%)	0 (0.0%)	0 (0.0%)	
Negative	556 (97.9%)	503 (97.7%)	34 (100.0%)	19 (100.0%)	
Pleural effusion	2 (0.4%)	0 (0.0%)	0 (0.0%)	2 (10.5%)	0.001[2]
Disposition Status					0.02[2]
Discharged	164 (28.9%)	158 (30.7%)	5 (14.7%)	1 (5.3%)	
Admitted	403 (71.0%)	356 (69.1%)	29 (85.3%)	18 (94.7%)	
Transferred	1 (0.2%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	

[1] P-values reported are based on a Kruskal-Wallis test. Median [Q1, Q3] summary statistics are reported.

[2] P-values reported are based on Fisher's exact test.

[*] There were 6 patients with unknown tachycardia status. There were 8 patients with unknown tachypnea (respiratory rate > 60 breath/min) due to missing respiratory rate. No patients with possible or definite pneumonias were missing heart rate or respiratory rate variables. YOS was not entered for 8 patients.

Table 3.

Multivariable Analyses Examining Factors Associated with Definite or Possible Pneumonia[1]

	Odds Ratio (95% CI)[2]	P-value
Clinical Model without Viral or PCT Results (N=539)		
ANC (per 1000/μL increase)	1.09 (1.00, 1.17)	0.049
Respiratory Distress/ Increased WOB	2.17 (1.04, 4.51)	0.046
Respiratory Rate (per breath/min. increase)	1.00 (0.97, 1.02)	0.74
YOS Score (>10 vs. 6–10 reference)	1.31 (0.59, 2.92)	0.52
Clinical Model with Viral Results but no PCT (N=444)		
ANC (per 1000/μL increase)	1.09 (1.00, 1.19)	0.052
Respiratory Distress/ Increased WOB	1.93 (0.89, 4.18)	0.11
Respiratory Rate (per breath/min. increase)	1.01 (0.98, 1.03)	0.59
YOS Score (>10 vs. 6–10 reference)	1.55 (0.65, 3.70)	0.34
Positive Viral Finding	1.40 (0.65, 3.70)	0.34
Clinical Model without Viral Results but with PCT (N=309)		
ANC (per 1000/μL increase)	1.04 (0.92, 1.17)	0.53
Respiratory Distress/ Increased WOB	1.97 (0.75, 5.20)	0.19
Respiratory Rate (per breath/min. increase)	0.99 (0.95, 1.02)	0.52
YOS Score (>10 vs. 6–10 reference)	1.19 (0.39, 3.62)	0.77
PCT (per ng/mL increase)	1.03 (0.98, 1.08)	0.29
Clinical Model with Viral and PCT Results (N=293)		
ANC (per 1000/μL increase)	1.04 (0.92, 1.18)	0.51
Respiratory Distress/ Increased WOB	1.99 (0.74, 5.34)	0.19
Respiratory Rate (per breath/min. increase)	0.99 (0.96, 1.03)	0.71
YOS Score (>10 vs. 6–10 reference)	1.27 (0.40, 3.99)	0.69
Positive Viral Finding	0.92 (0.36, 2.36)	0.86
PCT (per ng/mL increase)	1.03 (0.98, 1.08)	0.29

[1]The variables in this table represent all of the variables included in each model.

[2]The No Pneumonia group is reference.

ANC = absolute neutrophil count, PCT = procalcitonin, YOS = Yale Observation Score