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Authors

Florin, Todd A
Ramilo, Octavio
Hoyle, John D
et al.

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Radiographic Pneumonia in Febrile Infants 60 Days of Age and Younger

Todd A. Florin, MD, MSCE[1], **Octavio Ramilo, MD**[2], **John D. Hoyle Jr., MD**[3], **David M. Jaffe, MD**[4], **Leah Tzimenatos, MD**[5], **Shireen M. Atabaki, MD, MPH**[6], **Daniel M. Cohen, MD**[7], **John M. VanBuren, PhD**[8], **Prashant Mahajan, MD, MPH, MBA**[9], **Nathan Kuppermann, MD, MPH**[10], **for the Febrile Infant Working Group of the Pediatric Emergency Care Applied Research Network (PECARN)**

[1]Division of Emergency Medicine, Ann and Robert H. Lurie Children's Hospital of Chicago; Department of Pediatrics, Northwestern University Feinberg School of Medicine

[2]Division of Pediatric Infectious Diseases and Center for Vaccines and Immunity, Nationwide Children's Hospital and The Ohio State University

[3]Departments of Emergency Medicine and Pediatrics, Western Michigan University Homer Stryker, M.D. School of Medicine; *Former Affiliation: Department of Emergency Medicine, Helen DeVos Children's Hospital of Spectrum Health*

[4]American Academy of Pediatrics, Elk Grove, IL; Former Affiliation: Department of Pediatrics, St. Louis Children's Hospital, Washington University

[5]Department of Emergency Medicine, University of California, Davis School of Medicine

[6]Division of Emergency Medicine, Department of Pediatrics, Children's National Medical Center, The George Washington School of Medicine and Health Sciences

[7]Section of Emergency Medicine, Department of Pediatrics, Nationwide Children's Hospital and The Ohio State University

[8]Department of Pediatrics, University of Utah

Corresponding Author: Todd A. Florin, MD, MSCE; Ann and Robert H. Lurie Children's Hospital of Chicago; 225 East Chicago Avenue, Box 62; Chicago, IL 60611; (312) 227-6675; taflorin@luriechildrens.org.

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[9]Department of Emergency Medicine, University of Michigan; Former Affiliation: Division of Emergency Medicine, Department of Pediatrics, Children's Hospital of Michigan, Wayne State University

[10]Departments of Emergency Medicine and Pediatrics, University of California, Davis, School of Medicine

Abstract

Objective—Few prospective studies have assessed the occurrence of radiographic pneumonia in young febrile infants. We analyzed factors associated with radiographic pneumonias in febrile infants ≤60 days-old evaluated in pediatric emergency departments (EDs).

Study Design—Planned secondary analysis of a prospective cohort study within 26 EDs in a pediatric research network from 2008–2013. Febrile (≥38°C) infants ≤60-days-old who received chest radiographs (CXR) were included. CXR reports were categorized as "no," "possible," or "definite" pneumonia. We compared demographics, Yale Observation Scale scores [YOS; >10 implying ill appearance], laboratory markers, blood cultures and viral testing among groups.

Results—Of 4,778 infants, 1724 (36.1%) had CXRs performed; 2.7% (n=46) had definite pneumonias, and 3.9% (n=67) possible pneumonias. Patients with definite (13/46, 28.3%) or possible (15/67, 22.7%) pneumonias more frequently had YOS >10 compared to those without pneumonias (210/1611, 13.2%, p=0.002) in univariable and multivariable analyses. Median white blood cell count(WBC), absolute neutrophil count(ANC), and procalcitonin(PCT) were higher in the definite [WBC 11.5 (IQR 9.8,15.5); ANC 5.0 (3.2,7.6); PCT 0.4 (0.2,2.1)] versus no pneumonia [WBC 10.0 (7.6,13.3); ANC 3.4 (2.1,5.4); PCT 0.2 (0.2,0.3)] (WBC p=0.006, ANC p=0.002, PCT p=0.046) groups, but of unclear clinical significance. There were no cases of bacteremia in the definite pneumonia group. Viral infections were more frequent in groups with definite (25/38, 65.8%) and possible (28/55, 50.9%) pneumonias than no pneumonias (534/1185, 45.1%, p=0.02).

Conclusions—Radiographic pneumonias were uncommon, often had viruses detected, and were associated with ill appearance, but few other predictors, in febrile infants ≤60-days-old.

INTRODUCTION

Febrile infants 60 days and younger are at substantial risk of serious bacterial infections (SBI), with an estimated prevalence of 8–13%.[1,2] Although pneumonia is an important diagnostic consideration, there is sparse data on its epidemiology, risk factors and predictors in young febrile infants. Indeed, estimates of the prevalence of pneumonia in this population varies considerably, from less than 0.1% up to 8%.[3–10]

Given the lack of reliability of the clinical examination in young infants, chest radiographs are considered the current diagnostic standard for pneumonia in the developed world.[11,12] The prevalence of radiographic pneumonias in febrile infants without overt respiratory findings is ~1%, based on studies performed nearly three decades ago.[8–10] Lack of data on the current prevalence of radiographic pneumonia, the changing epidemiology of SBI in febrile infants 60 days of age and younger, and the lack of data regarding predictors of

pneumonia in this age group all likely contribute to the substantial variation in performance of chest radiographs.[2,13,14]

The primary objective of this study was to describe factors associated with radiographic pneumonia by conducting a planned secondary analysis of a large cohort of infants ≤60 days-old evaluated for SBI.

MATERIALS AND METHODS

Study Design

We conducted a planned secondary analysis of data from a prospective observational study focused on the evaluation for SBI in febrile young infants in 26 EDs in the Pediatric Emergency Care Applied Research Network (PECARN). Details of the parent study have been described previously.[15] 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

A convenience sample of febrile infants (rectal temperature ≥38°C in the ED, home, or clinic) ≤60 days-old evaluated in any PECARN ED for SBI between December 2008 and May 2013 were included. Eligible infants had to have at least one blood culture obtained as part of the original study aims. Infants with clinical sepsis, a toxic appearance, prematurity, significant comorbidities, 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 analysis. For this analysis, only infants who had chest radiography performed were included. Chest radiographs were performed at the ED providers' discretion.

Study Procedures

For each patient, investigators prospectively recorded demographic information, Yale Observation Scale (YOS) scores, and laboratory results. The YOS is a clinical score that provides a quantitative assessment of risk for SBIs based on simple clinical and observational parameters.[16] It includes 6 items, with each scored on a 1-to-3-to-5 scale, yielding a total YOS score ranging from 6 (perfect score) to 30 (most ill-appearing). A YOS score of 10 or less is considered not ill-appearing.[16] All infants had complete blood counts (CBC) performed, including white blood cell (WBC) count, absolute neutrophil count (ANC), and platelet count. Procalcitonin (PCT) concentrations were recorded when available. All infants had blood and urine cultures performed. Viral testing was performed at the discretion of the treating physician.

Pneumonia Classification

Chest radiograph reports documented by the attending radiologist at the time of clinical care were reviewed at each site. Radiograph reports that were not reported as normal were uploaded into the study database for further review. These chest radiograph reports were independently reviewed by two study investigators (TAF, PM). Disagreements in

classification were adjudicated by a third investigator (NK). Definitions of “definite pneumonia,” “possible pneumonia,” and “no pneumonia” were established by consensus among the investigators *a priori*. Reports classified as “no pneumonia” included definite atelectasis. Classification of “possible pneumonia,” included “pneumonia versus atelectasis.” Lobar infiltrates were considered “definite pneumonia.” If radiographs were classified by the investigators as possible or definite pneumonia, they identified the involved lobes. In addition, investigators noted the presence or absence of pleural effusion in the uploaded radiology reports.

Statistical Analysis

Categorical measures were summarized with counts and percentages, and compared among groups with Chi-square tests. Continuous measures were summarized using medians and interquartile ranges (IQR: 25^{th} percentile, 75^{th} percentile) and compared between groups using the Kruskal-Wallis test due to skewness. Logistic regression was performed to identify laboratory factors associated with pneumonia status (definite pneumonia vs. no pneumonia) controlling for patient demographic variables. In the main modeling analysis we compared the definite pneumonia group with the no pneumonia group. Modeling variables were specified prior to model implementation based on clinical relevance. To account for potential differences in classification of pneumonia, two sensitivity analyses were performed: (1) grouping the infants with definite and possible pneumonia into a single pneumonia category and comparing them to those without radiographic pneumonia and (2) grouping infants with possible pneumonia and no pneumonia into a single no-pneumonia category and comparing those to infants with definite pneumonia.

RESULTS

There were 4,778 infants enrolled in the parent study; of those, 1,724 (36.1%) infants had chest radiography performed and were included in this analysis. The median age of infants with chest radiography was 38 days (IQR 25,38) and most (58.6%) were males. Definite pneumonia was present in 2.7% (n=46), and possible pneumonia was present in 3.9% (n=67) infants. Table 1 describes the demographic characteristics of the study population. There was no difference in median age or gender among infants with definite, possible and no pneumonia. Of 874 White children who had radiographs performed, 65 (7.4%) had definite or possible pneumonia. Of 574 Black children who had radiographs performed, 26 (4.5%) had definite or possible pneumonia, while in 191 children of other races who had radiographs performed, 17 (8.9%) had definite or possible pneumonia.

Table 2 describes the clinical characteristics of the study population. A significantly greater proportion of infants with definite or possible pneumonia had a YOS >10, suggesting more frequent “ill-appearance.” In addition, a greater proportion of those with definite or possible pneumonia were admitted to the hospital compared to those without pneumonia. The median WBC count, ANC, and procalcitonin were higher in infants with definite pneumonia compared to those with no pneumonia. Only one patient with definite pneumonia had a pleural effusion noted on chest radiograph (Table 2).

In multivariable logistic regression, only patient race (Other vs. White) and YOS were significantly associated with definite pneumonia. WBC, ANC and platelet counts were not (Table 3). Infants with a YOS >10 had 2.4 times increased odds of having definite pneumonia compared with those with a normal YOS.

Of note, there were no cases of bacteremia in the definite pneumonia group and 2 cases in the possible pneumonia group (one due to Group B Streptococcus, one due to *E. coli* who also had an *E. coli* urinary tract infection, Table 4; online only). Most infants (n=1,278, 74.2%) were tested for viral infection. Among the infants tested for viruses, 65.8% (25/38) with definite pneumonia had viruses detected, a greater proportion than those with possible (28/55, 50.9%) and no (534/1185, 45.1%) pneumonia (p=0.02). There were no significant differences in gender, age, race, temperature, YOS, WBC or ANC, and disposition in infants with definite or possible pneumonia who had viruses detected compared with those who did not, although these analyses are limited by small sample sizes (data not shown). Respiratory syncytial virus (RSV) was the predominant virus in all three groups. In those with definite and possible pneumonia, RSV represented two-thirds of all viruses detected. In those with no pneumonia, there was a larger variety of viruses detected (Table 5).

In the two sensitivity analyses grouping the “possible pneumonia” group with the “definite pneumonia” group and then grouping infants with “possible pneumonia” with the “no pneumonia” group, the results did not significantly differ, except for differences in PCT values (data not shown). Median PCT concentration was significantly greater in the definite/possible pneumonia combined group (median 0.4 ng/dL, IQR 0.2, 1.4) compared with the no pneumonia group (median 0.2 ng/dL, IQR 0.2, 0.3, p=0.03).

DISCUSSION

In this large, multicenter study of febrile infants ≤60 days who presented to the EDs of a multicenter research network, and who had chest radiographs performed, 2.7% had definite radiographic pneumonias. Infants with radiographic pneumonias were more likely to appear clinically ill as assessed by the YOS and had higher rates of hospitalization compared to those without radiographic pneumonias. The median WBC count and ANC were also higher in infants with definite pneumonia compared to those with possible and no pneumonias, although these laboratory markers were not associated with definite pneumonia in multivariable analyses after adjusting for clinical appearance and other factors. In addition, infants with radiographic pneumonias had higher rates of respiratory viruses detected compared with infants without radiographic pneumonias. There were no cases of bacteremia in infants with definite pneumonia.

In this large study, we focus on the characteristics specific to radiographic pneumonias in the febrile infants ≤60 days-old, including measures of clinical appearance, laboratory markers and clinical disposition. Three previous studies performed 2 decades ago, each including approximately 200 infants, examined the value of chest radiography in the diagnosis of young febrile infants.[8–10] Those studies found that the overall prevalence of radiographic pneumonias in febrile infants ranged from 6% to 16%. Radiographic pneumonia without respiratory signs or symptoms was detected in approximately 1% of febrile infants.

Although limited by small numbers of infants with documented respiratory findings, Crain et al reported an association between respiratory signs and radiographic pneumonia.[9] However, clinical examination is often unreliable in pneumonia, and more so in the youngest infants.[17] We expand on prior studies by examining laboratory characteristics associated with radiographic pneumonia that are frequently available in the routine evaluation of the febrile infant <60-days old.

The rates of radiographic pneumonia observed in our cohort are on the lower end of the prevalence range previously reported in young febrile infants.[4,6–10] The statistically higher median YOS scores in infants with radiographic pneumonias indicates on average, ill-appearance was more common in those infants. This finding is consistent with prior studies that demonstrate that some patients with pneumonias will have a degree of ill appearance on examination. However, despite the median YOS scores being statistically higher, most (71.7%) infants with definite pneumonias had YOS scores <=10 indicating well-appearance.[8–10] Interestingly, the parent study, of which this is a subanalysis, found that the YOS did not discriminate infants with bacterial infections, as defined by positive blood, cerebrospinal fluid, and/or urine cultures, from those who did not have bacterial infections; radiographic pneumonia was not a part of that analysis.[15] Likewise, a meta-analysis of 7 studies including children up to 36 months of age concluded that the YOS was not useful to confirm or exclude serious infections.[18] Our results are consistent with those findings as most studies consider SBIs to include bacteremia, meningitis and urinary tract infections. Most prior studies of YOS did not examine the utility of YOS in identifying pneumonia specifically.[7,18,19] The multivariable analysis in Table 3 suggests that an elevated YOS score is associated with pneumonia; however, the large proportion of infants with normal YOS scores who also had radiographic pneumonias suggests that the YOS score is not very useful in ruling out radiographic pneumonia when it is less than 10. Almost all infants with pneumonia were hospitalized, versus 80% of those without pneumonia. While causal associations cannot be made, the high hospitalization rate may be related to physicians being reluctant to discharge patients with radiographic findings of pneumonia. Another possibility, however, is that infants with pneumonia appear clnically more ill, as the association of pneumonia with an abnormal YOS in our cohort would suggest.

Our study found that the median WBC count and ANC were highest in the definite pneumonia group. These differences, however, were not significant after adjustment in multivariable analyses. Many studies have examined the association of laboratory tests, such as WBC count, ANC, C-reactive protein (CRP) or PCT, with SBI in infants and young children.[4–6,20,21] Current evidence suggests that procalcitonin has superior performance characteristics when compared to the other more common screening tests for SBI in febrile young infants.[4–6,20] Those studies, however, did not examine the utility of these markers specifically in infants with radiographic pneumonias, as these infants were not included in the invasive bacterial infections (IBI) or SBI analyses. While the median PCT was significantly higher in the definite pneumonia group compared to the no pneumonia group, small numbers precluded us from including PCT in multivariable analyses. Thus, further study is warranted to better understand the possible association of these markers with pneumonia in the young febrile infant.

The important role of viruses in infant pneumonia is emphasized by the finding that two-thirds of infants with definite radiographic pneumonias had positive viral detection. RSV was highly prevalent among infants with radiographic pneumonias who had positive viral studies. This is consistent with previous studies, emphasizing the importance of the role of RSV in infant pneumonia.[22] Although one-third of viruses detected in the infants without radiographic pneumonia were RSV, greater proportions of influenza and rhinovirus were detected in those without pneumonia. In addition, those infants without pneumonia had a greater variety of viruses detected, confirming the important role of viruses in the etiology of fever in the young febrile infant. Some of these results may be related to the variation in how sites across the network performed viral testing, with some sites using rapid antigen testing for RSV and influenza and others relying on multiplex polymerase chain reaction testing where results are known after radiographs are performed. Isolated RSV testing was more frequent than multiplex PCR panels, and therefore the population may have been enriched for RSV. Of those with definite pneumonias who had viral testing performed, 34.2% had no viruses detected. While definitive conclusions cannot be drawn, this group may represent an interesting group for future study to examine the likelihood of bacterial infection. There were no cases of bacteremia in the infants with definite pneumonias; however, with only 46 such infants in this cohort and a very low baseline prevalence of bacteremia in the overall febrile young infant population, it is difficult to draw definitive conclusions regarding prevalence of bacteremia. Given the high prevalence of viral infections with no cases of bacteremia, however, pneumonia in the febrile young infant may provide a target for future antimicrobial stewardship efforts.

Limitations

This study has several limitations. First, we were unable to discern the motivation for ordering the chest radiographs. In some institutions, chest radiographs may be part of standard practice, whereas in others radiography may only be ordered in infants with respiratory distress or concern for lower respiratory tract infection.[14] Second, because race (other than White and Black races) was classified with an “other” category, we were unable to ascertain racial details about these infants and therefore cannot draw definitive conclusions. Third, we do not know if the infants had signs and symptoms of respiratory distress as this information was not collected on the case report forms in the parent study. Despite this limitation, it is likely that infants with fever and respiratory distress would have received chest radiographs and therefore would be captured in our analyses. Similarly, detailed physical examination findings were not recorded as part of the parent study; however, prior literature suggests that initial observation, in this case denoted by the YOS, may be the most critical component of the examination of infants with suspected pneumonia and other examination findings, such as auscultatory findings, are relatively unreliable in infants.[11] In addition, viral testing was not performed uniformly in this study, and clinical appearance and other factors such as season of the year may have affected and biased use of viral testing. Studies with uniform and comprehensive viral testing will greatly mitigate this potential source of bias in future analyses. Fourth, in some analyses we were limited by small numbers, precluding definitive conclusions. For example, while PCT was significantly associated with pneumonia when the definite and no pneumonia groups, small sample size limited our ability to include PCT in multivariable analyses. Finally, the radiologists’

interpretations of the chest radiographs were not standardized. We mitigated this limitation in part by including multiple investigators classifying the reports independently. In addition, we performed sensitivity analyses combining the definite and possible pneumonia groups and combining the possible and no pneumonia groups. The results of these different analyses were similar, suggesting that our radiograph report classification system was valid.

CONCLUSIONS

In this large study of the characteristics associated with radiographic pneumonias in febrile infants younger than 60 days, we found that radiographic pneumonias were uncommon, were associated with more ill appearance, but few other predictors, and often had viruses detected when testing was performed. Further research is warranted using larger sample sizes with more detailed clinical findings and laboratory parameters. These should include comprehensive microbiologic assays and inflammatory markers (e.g., PCT and novel biomarkers) to aid clinical decision-making and reliably detect pneumonias in very young febrile infants.

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12. Helen DeVos Children’s Hospital (John D. Hoyle, Jr., MD)

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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

REFERENCES

1. Huppler AR, Eickhoff JC, Wald ER. Performance of low-risk criteria in the evaluation of young infants with fever: review of the literature. Pediatrics. 2010;125(2):228–233. [PubMed: 20083517]
2. Aronson PL, Thurm C, Alpern ER, et al. Variation in care of the febrile young infant <90 days in US pediatric emergency departments. Pediatrics. 2014;134(4):667–677. [PubMed: 25266437]
3. Rudinsky SL, Carstairs KL, Reardon JM, Simon LV, Riffenburgh RH, Tanen DA. Serious bacterial infections in febrile infants in the post-pneumococcal conjugate vaccine era. Acad Emerg Med. 2009;16(7):585–590. [PubMed: 19538500]
4. Milcent K, Faesch S, Gras-Le Guen C, et al. Use of Procalcitonin Assays to Predict Serious Bacterial Infection in Young Febrile Infants. JAMA pediatrics. 2016;170(1):62–69. [PubMed: 26595253]
5. Gomez B, Mintegi S, Bressan S, et al. Validation of the "Step-by-Step" Approach in the Management of Young Febrile Infants. Pediatrics. 2016;138(2).
6. Maniaci V, Dauber A, Weiss S, Nylen E, Becker KL, Bachur R. Procalcitonin in young febrile infants for the detection of serious bacterial infections. Pediatrics. 2008;122(4):701–710. [PubMed: 18829791]
7. Baker MD, Avner JR, Bell LM. Failure of infant observation scales in detecting serious illness in febrile, 4- to 8-week-old infants. Pediatrics. 1990;85(6):1040–1043. [PubMed: 2339027]
8. Bramson RT, Meyer TL, Silbiger ML, Blickman JG, Halpern E. The futility of the chest radiograph in the febrile infant without respiratory symptoms. Pediatrics. 1993;92(4):524–526. [PubMed: 8414821]
9. Crain EF, Bulas D, Bijur PE, Goldman HS. Is a chest radiograph necessary in the evaluation of every febrile infant less than 8 weeks of age? Pediatrics. 1991;88(4):821–824. [PubMed: 1896292]
10. Heulitt MJ, Ablow RC, Santos CC, O'Shea TM, Hilfer CL. Febrile infants less than 3 months old: value of chest radiography. Radiology. 1988;167(1):135–137. [PubMed: 3347713]
11. Margolis P, Gadomski A. The rational clinical examination. Does this infant have pneumonia? JAMA. 1998;279(4):308–313. [PubMed: 9450716]
12. Hui C, Neto G, Tsertsvadze A, et al. Diagnosis and management of febrile infants (0–3 months). Evid Rep Technol Assess (Full Rep). 2012(205):1–297.
13. Jain S, Cheng J, Alpern ER, et al. Management of febrile neonates in US pediatric emergency departments. Pediatrics. 2014;133(2):187–195. [PubMed: 24470644]
14. Rogers AJ, Kuppermann N, Anders JF, et al. Variability of Lumbar Puncture and Hospitalization Rates in Febrile Infants ≤ 2 Months in the Emergency Departments of the Pediatric Emergency Care Applied Research Network (PECARN). Paper presented at: Pediatric Academic Societies; May 8, 2017; San Francisco, CA.
15. Mahajan P, Kuppermann N, Mejias A, et al. Association of RNA Biosignatures With Bacterial Infections in Febrile Infants Aged 60 Days or Younger. JAMA. 2016;316(8):846–857. [PubMed: 27552618]
16. McCarthy PL, Sharpe MR, Spiesel SZ, et al. Observation scales to identify serious illness in febrile children. Pediatrics. 1982;70(5):802–809. [PubMed: 7133831]
17. Florin TA, Ambroggio L, Brokamp C, et al. Reliability of Examination Findings in Suspected Community-Acquired Pneumonia. Pediatrics. 2017;140(3).
18. Van den Bruel A, Haj-Hassan T, Thompson M, Buntinx F, Mant D, European Research Network on Recognising Serious Infection i. Diagnostic value of clinical features at presentation to identify serious infection in children in developed countries: a systematic review. Lancet. 2010;375(9717):834–845. [PubMed: 20132979]
19. Galetto-Lacour A, Zamora SA, Gervaix A. Bedside procalcitonin and C-reactive protein tests in children with fever without localizing signs of infection seen in a referral center. Pediatrics. 2003;112(5):1054–1060. [PubMed: 14595045]
20. Gomez B, Bressan S, Mintegi S, et al. Diagnostic value of procalcitonin in well-appearing young febrile infants. Pediatrics. 2012;130(5):815–822. [PubMed: 23109682]

21. Van den Bruel A, Thompson MJ, Haj-Hassan T, et al. Diagnostic value of laboratory tests in identifying serious infections in febrile children: systematic review. Bmj. 2011;342:d3082. [PubMed: 21653621]

22. Jain S, Williams DJ, Arnold SR, et al. Community-acquired pneumonia requiring hospitalization among U.S. children. N Engl J Med. 2015;372(9):835–845. [PubMed: 25714161]

Table 1:

Demographic Characteristics by Pneumonia Status

	Entire Population (N=1724) # (%) Median (IQR)	Definite Pneumonia (N=46) # (%) Median (IQR)	Possible Pneumonia (N=67) # (%) Median (IQR)	No Pneumonia (N=1611) # (%) Median (IQR)	P-value
Gender					0.131[1]
Female	713 (41.4)	25 (54.3)	24 (35.8)	664 (41.2)	
Male	1011 (58.6)	21 (45.7)	43 (64.2)	947 (58.8)	
Age (days)	38 (25, 48)	37.5 (20, 49)	33 (17, 49)	38 (26, 48)	0.321[2]
Race					0.009[1]
White	874 (50.7)	22 (47.8)	43 (64.2)	809 (50.2)	
Black	574 (33.3)	11 (23.9)	15 (22.4)	548 (34.0)	
Other	191 (11.1)	11 (23.9)	6 (9.0)	174 (10.8)	
Unknown[3]	85 (4.9)	2 (4.3)	3 (4.5)	80 (5.0)	
Ethnicity					0.445[1]
Hispanic or Latino	426 (24.7)	13 (28.3)	21 (31.3)	392 (24.3)	
Not Hispanic or Latino	1259 (73.0)	33 (71.7)	46 (68.7)	1180 (73.2)	
Unknown[3]	39 (2.3)	0 (0)	0 (0)	39 (2.4)	

[1] P-values reported are based on the Chi-square test of association for categorical variables.

[2] P-values reported are based on a Kruskal-Wallis test for continuous variables.

[3] Category not included in the statistical test

Table 2.

Clinical Characteristics by Pneumonia Status

	Entire Population (N=1724) # (%) Median (IQR)	Definite Pneumonia (N=46) # (%) Median (IQR)	Possible Pneumonia (N=67) # (%) Median (IQR)	No Pneumonia (N=1611) # (%) Median (IQR)	P-value
Temperature	38.4 (38.2, 38.8)	38.4 (38.2, 38.8)	38.4 (38.2, 38.9)	38.4 (38.2, 38.8)	0.787[2]
YOS Category					0.002[1,4]
<=10	1465 (86.0)	33 (71.7)	51 (77.3)	1381 (86.8)	
>10	238 (14.0)	13 (28.3)	15 (22.7)	210 (13.2)	
White blood cell count	10.1 (7.6, 13.3)	11.5 (9.8, 15.5)	10.2 (7.6, 14.7)	10.0 (7.6, 13.3)	0.022[2,5]
Absolute Neutrophil Count	3.4 (2.1, 5.5)	5 (3.2, 7.6)	3.5 (2.1, 5.2)	3.4 (2.1, 5.4)	0.007[2,6]
Platelet Count	392 (308, 475)	435 (329, 514)	384 (301, 496)	392 (308, 474)	0.296[2]
Procalcitonin	(n=626) 0.2 (0.2, 0.4)	(n=20) 0.4 (0.2, 2.1)	(n=23) 0.3 (0.2, 1)	(n=577) 0.2 (0.2, 0.3)	0.078[2,5]
Viral Status	(n=1278)	(n=38)	(n=55)	(n=1185)	0.019[1,5]
Positive	587 (45.9)	25 (65.8)	28 (50.9)	534 (45.1)	
Negative	691 (54.1)	13 (34.2)	27 (49.1)	651 (54.9)	
Blood Culture Status (Bacteremia)					0.535[1]
Positive	44 (2.6)	0 (0.0)	2 (3.0)	42 (2.6)	
Negative	1670 (97.4)	45 (100.0)	65 (97.0)	1560 (97.4)	
Lobes Involved					----
Unilobar	81 (71.7)	33 (71.7)	48 (71.6)	----	
Multilobar	32 (28.3)	13 (28.3)	19 (28.4)	----	
Pleural Effusion					----
Yes	----	1 (2.2)	----	----	
No	----	45 (97.8)	----	----	
Disposition					0.002[1,4]
Discharged	324 (18.8)	2 (4.3)	5 (7.5)	317 (19.7)	
Admitted	1397 (81.0)	44 (95.7)	62 (92.5)	1291 (80.1)	
Other[3]	3 (0.2)	0 (0)	0 (0)	3 (0.2)	

[1] P-values reported are based on the Chi-square test of association for categorical variables.

[2] P-values reported are based on a Kruskal-Wallis test for continuous variables.

[3] Category not included in the statistical test.

[4] Pairwise comparisons found statistically significant differences between definite vs. no pneumonia (p=0.003), and possible vs. no pneumonia (p=0.027).

[5] Pairwise comparisons found statistically significant differences between definite vs. no pneumonia (WBC p=0.006; Procalcitonin p=0.046; viral status p=0.012).

[6] Pairwise comparisons found statistically significant differences between definite vs. possible pneumonia (p=0.01), and definite vs. no pneumonia (p=0.002).

Table 3.

Multivariable Analyses Examining Factors Associated with Definite Pneumonia[2]

Variable	Odds Ratio[1]	95% CI	P-value
Gender (Female vs. Male)	1.784	0.963, 3.304	0.066
Age (<=28 days vs. 29-60 days)	1.201	0.619, 2.331	0.588
Race (Black vs. White)	0.784	0.367, 1.674	0.529
Race (Other vs. White)	2.559	1.188, 5.513	0.016
Ethnicity (Hispanic or Latino vs. Not)	0.949	0.454, 1.982	0.888
Temperature	1.107	0.584, 2.100	0.755
Yale Observation Score (>10 vs. <=10)	2.360	1.171, 4.754	0.016
White Blood Cell Count	1.056	0.953, 1.171	0.296
Absolute Neutrophil Count	1.010	0.885, 1.154	0.880
Platelet	1.001	0.998, 1.003	0.554

[1]The No Pneumonia group is reference, infants with possible pneumonia excluded from this analysis

[2]Procalcitonin, viral testing and blood culture results were not included due to small numbers

Table 4;

Online Only. Characteristics of 2 Individuals with Possible Pneumonia and Bacteremia

Characteristic	Individual 1	Individual 2
Gender	Female	Female
Race	White	White
Age (days)	28	42
Temperature	38.7	38.9
Yale Observation Score	YOS Score > 10	YOS Score <= 10
Blood Culture Organism	Group B streptococcus (GBS)	E. coli
PCT	--	0.14
WBC	6.9	19.4
Platelets	356	579
ANC	4.209	5.626
Viral Status	Negative	Not Done
Disposition	Admitted to Hospital	Admitted to Hospital
Pleural Effusion	No	No
Lobes involved	Unilobar (RLL)	Unilobar (LLL)
Urinalysis Results	Negative	Positive
Urine Culture Organism		E. coli

Table 5.

Viral Pathogens

Viral Pathogen	Definite Pneumonia (N=38) N (%)	Possible Pneumonia (N=55) N (%)	No Pneumonia (N=1185) N (%)
No viral pathogen detected	13 (34.2)	27 (49.1)	651 (54.9)
Single Virus Detections			
Respiratory Syncytial Virus (RSV)	17 (44.7)	19 (34.5)	183 (15.4)
Rhinovirus	1 (2.6)	2 (3.6)	96 (8.1)
Enterovirus			74 (6.2)
Enterovirus/Rhinovirus			8 (0.7)
Influenza A	1 (2.6)	2 (3.6)	56 (4.7)
Influenza B		1 (1.8)	17 (1.4)
Parainfluenza	1 (2.6)	1 (1.8)	32 (2.7)
Human metapneumovirus (hMPV)	2 (5.3)	1 (1.8)	12 (1.0)
Parechovirus			4 (0.3)
Coronavirus			6 (0.5)
Cytomegalovirus (CMV)/Epstein-Barr Virus (EBV)			2 (0.2)
Rotavirus			11 (0.9)
Norovirus			1 (0.1)
Astrovirus			1 (0.1)
Herpes Simplex Virus	1 (2.6)		4 (0.3)
Multiple Virus Detections			
RSV & Rhinovirus		1 (1.8)	7 (1.3)
Parainfluenza & Rhinovirus	1 (2.6)		3 (0.3)
hMPV & RSV			3 (0.3)
hMPV & Rhinovirus			2 (0.2)
Enterovirus & Influenza A			1 (0.1)
Enterovirus & Parainfluenza & Rhinovirus			1 (0.1)
hMPV & Coronavirus			1 (0.1)
hMPV & Parainfluenza			1 (0.2)
Influenza A & Rhinovirus			1 (0.1)
CMV & Rhinovirus			1 (0.1)
Coronavirus & Parainfluenza			1 (0.1)
Rhinovirus & Rotavirus			1 (0.1)
Other (specific virus not reported)	1 (2.6)	1 (1.8)	3 (0.3)