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Research Article

Pediatric Respiratory Severity Score (PRESS) for Respiratory Tract Infections in Children

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Abstract

Background: Respiratory tract infections are common diseases in children. It is crucial therefore to evaluate the severity of the condition during the initial bedside assessment in the emergency department so that further examinations and hospital treatment can be conducted as appropriate. However, there are few such scoring systems for acute respiratory infection in childhood.

Objective: To evaluate a new simple bedside scoring system for the rapid assessment of pediatric respiratory infections in emergency settings.

Methods: We established a respiratory scoring system, namely "Pediatric Respiratory Severity Score (PRESS)", and examined its utility for assessing severity in 202 children who visited our hospital due to respiratory symptoms between January 2010 and November 2011. The PRESS assessed tachypnea, wheezing, retraction (accessory muscle use), SpO_2, and feeding difficulties, with each component given a score of 0 or 1, and total scores were classified as mild (0–1), moderate (2–3), or severe (4–5). In addition, we performed RT-PCR techniques to detect respiratory viruses from nasal swabs and the detected viruses were evaluated in relation to severity.

Results: According to the PRESS scores, the hospitalization rate was significantly higher in the moderate and severe groups than in the mild group. Oxygen therapy was longer in severe cases compared with other cases. There were no significant differences in the viral detection rate between the severity groups.

Conclusion: The PRESS scoring system is useful for the initial assessment of respiratory tract infections in children to identify the need for hospitalization and further examination in emergency settings.

Keywords: Severity score; Child; Respiratory infection; Virus; Triage

Abbreviations

PRESS: Pediatric Respiratory Severity Score; ARI: Acute Respiratory Illness; RSV: Respiratory Syncytial Virus; HRV: Human Rhinovirus; HPIV: Human Parainfluenza Virus; HMPV: Human Metapneumovirus; HEV: Human Enterovirus; HBoV: Human Bocavirus; AdV: Adenovirus

Introduction

Various viruses cause acute respiratory illness in children, including Respiratory Syncytial Virus (RSV), Human Rhinovirus (HRV), Human Parainfluenza Virus (HPIV), and Human Metapneumovirus (HMPV). Various symptoms (e.g., respiratory rate, wheezing, cyanosis, and use of the accessory respiratory muscles) may reflect the severity of respiratory disease and these clinical findings could be important for early diagnosis and treatment. Moreover, it is crucial to treat acute respiratory infection appropriately to avoid the risk of respiratory failure, which is sometimes fatal in children. Severe cases must be triaged and treated immediately; therefore, respiratory condition should be assessed at first contact, in a similar way that the APGAR scoring system is used to assess neonates [1]. In 2006, the American Academy of Pediatrics highlighted the importance of assessing severity for selecting the appropriate outpatient or in-hospital treatment in Diagnosis and Management of Bronchiolitis, a guideline for acute bronchiolitis in infants [2]. Although some studies have evaluated the severity of bronchial asthma and acute respiratory infections in children, few suggest simple methods of bedside assessment [3-10].

To address this issue, we established a scoring system of the severity of respiratory infections in children, which we named the Pediatric Respiratory Severity Score (PRESS), and evaluated its utility for assessing the severity of infection caused by various pathogens and for deciding the necessity of further clinical examinations and the treatment to start. We focused on the severity of the respiratory symptoms because the supportive care required by the patients is not available at home and only available at the hospital. In addition, we examined the relationship between the severity of illness and pathogens profiles.

Materials and Methods

Subjects and samples

This study was carried out at the Department of Pediatrics, National Hospital Organization Yokohama Medical Center, an urban

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Table 1: PRESS Scoring System.

Score Component	Operational definition		Scoring
Respiratory rate	Respiratory rate at rest, on room air*		0 or 1
Wheezing	High-pitch expiratory sound heard by auscultation		0 or 1
Accessory muscle use	Any visible use of accessory muscles		0 or 1
SpO_2	Oxygen saturation <95% on room air		0 or 1
Feeding difficulties	Refusing feedings		0 or 1
	Sum of five components		
PRESS score	0-1: mild 2-3: moderate 4-5: severe		0-5
Criteria of tachypnea*	Month	Respiratory rate	
	<12	60<	1
	12≤, <35	40<	1
	36≤, <156	30<	1
	156≤	20<	1

*Respiratory rate evaluated according to American Heart Association guideline.
PRESS, Pediatric Respiratory Severity Score

emergency hospital in Japan, between January 2010 and November 2011. We enrolled 202 children who visited the outpatient clinic or emergency department because of acute respiratory symptoms. Nasopharyngeal swabs were collected after written informed consent was obtained from the children's parents. The study protocol was approved by the Ethics Committee on Human Research of the National Hospital Organization Yokohama Medical Center.

We collected nasal fluid samples using Advanced Flocked Swabs and Universal Transport Medium (Copan Innovation, Brescia, Italy), and stored the samples at -80 °C until used for viral detection. White blood cell counts (normal range: 7,000-11,000/μL in child) and C-reactive protein (CRP, normal range for children :< 1.2mg/dL) were measured at the first visit. We collected samples for bacterial culture before antibiotic therapy was initiated. We collected clinical data, radiographic evidence, and laboratory data from hospital charts.

PRESS score

We collected data on five components using the PRESS, namely, respiratory rate, wheezing, accessory muscle use, SpO_2, and feeding difficulties (Table 1). Accessory muscle use was defined as visible retraction of one or more of the sternomastoid/suprasternal, intercostal, and subcostal muscles. Wheezing was defined by auscultation performed by experienced pediatricians. SpO_2 was evaluated as above or below 95%. Feeding difficulties were assessed using information provided by the parents. Each component was given 0 or 1 point and the PRESS total score was classified as mild (0–1 points), moderate (2–3 points), or severe (4–5 points). Respiratory rate was evaluated based on the American Heart Association guidelines (Table 1) [11].

Virus detection

Nasopharyngeal swab samples were centrifuged at 3000 × g at 4°C for 15 min for viral DNA/RNA extraction, PCR and RT-PCR, and sequence analysis, and the supernatants were used as described previously [12,13]. RT-PCR was used for RNA virus detection including RSV, HRV, HMPV, HPIV, HEV, and influenza virus, while PCR was used for DNA virus detection such as Adenovirus (AdV)

Table 2: Patient characteristics.

	All patients n=202		Severity	
		mild n=99	moderate n=70	severe n=33
Age (months) †	27.6±31.8	29.8±32.9	23.0±29.7	30.7±32.7
Male/female	123/79	51/48	45/25	6/27
History of wheezing (%)	123 (60.9)	50 (50.5)*	50 (71.4)*	23 (69.7)*
Hospitalization (%)	128 (63.4)	32 (32.3)*	64 (91.4)*	32 (97.0)*
Virus detection (%)	119 (58.9)	53 (53.5)	48 (68.6)	18 (54.5)
White blood cells (/μL) †	11360±5200	12100±6080	10200±4040	12300±5300
CRP (mg/dL) †	2.1±2.6	2.8±3.0	1.59±2.1	1.9±2.6
Duration (days) †				
Fever	2.6±2.7	3.6±2.7*	2.3±2.8*	1.8±1.9*
Hospitalization	7.7±2.7	7.1±3.4	7.8±2.8	8.0±1.5
Oxygen therapy	1.6±2.0	0.2±0.8**	1.5±1.8**	3.7±1.8**
PRESS score (%)				
Respiratory rate	42 (20.8)	0 (0)**	18 (25.7)**	24 (72.7)**
Wheezing	143 (70.8)	45 (45.5)*	65 (92.9)*	33 (100)*
Accessory muscle use	53 (26.2)	0 (0)**	21 (30.0)**	32 (87.0)**
Cyanosis	54 (26.7)	1 (1.0)**	23 (32.9)**	30 (90.9)**
Feeding difficulties	78 (38.6)	6 (6.0)*	47 (67.1)*	25 (75.8)*

†Mean±SD; *p <0.05, mild versus moderate, severe; **p <0.05, mild versus moderate versus severe. Percentages indicate the number of cases in each category/total patients in each severity group.
PRESS, Pediatric Respiratory Severity Score

and Human Bocavirus (HBoV). Viral nucleic acid was extracted using QIAampMinElute Virus Spin Kit (Qiagen, Valencia, CA). The reverse transcription reaction mixture was incubated with random hexamers at 37°C for 15 min, followed by incubation at 85°C for 5 s using the PrimeScript RT reagent Kit (Takara Bio, Shiga, Japan) and amplification by thermal cycling. The PCR procedures for amplification of different viral genomes, including RSV [14], Human Rhinovirus (HRV)/Human Enterovirus (HEV) [15,16], HMPV [17], HPIV type1-4 [18], influenza virus subtypes A–C [19], Adenovirus (AdV) [20], and Human Bocavirus (HBoV) [21] were performed as described previously. Negative control (no virus) and positive controls using the prototype or clinical strains were also examined in each test. Viral RNA/DNA extraction was conducted in a room physically separate from that used for performing PCR to avoid carry-over and cross-contamination. Positive and negative controls were included in all PCR assays. PCR products were determined by electrophoresis on 3% agarose gels. Purification of DNA fragments and nucleotide sequence determination procedures were performed as described previously.

Statistical analysis

Data were analyzed using SPSS software (SPSS for Windows, Version 19.0). All data are expressed as mean ± Standard Deviation (SD). We performed Scheffe tests for multiple comparisons between three groups when there were significant differences found in the ANOVA tests. Statistical significance was set at $p < 0.05$.

Results

Of the 202 children enrolled, 123 (60.9%) were boys and 79 (39.1%) were girls, aged 27.6 ± 31.8 months (mean ± SD, 0–13 years old), and 128 in total were admitted to hospital. Patient characteristics are shown in Table 2. According to our respiratory severity scoring system PRESS, 99 (49.0%) participants were classified with mild infection, 70 (34.7%) with moderate, and 33 (16.3%) with severe (Table 2). The history of wheezing rate in moderate/severe cases was higher than in mild cases. The hospitalization rate was 32.3% in mild cases, 91.4% in moderate cases, and 97.0% in severe cases, with significant differences between the hospitalization rates of mild and moderate cases, and between mild and severe cases. There was no significant difference between moderate and severe cases (Table 2). The blood test results were as follows: WBC, 1.21 x 10^3 ± 6.1 x 10^2/μL in mild cases; 1.02 x 10^3 ± 4.0 x10^2/μL in moderate cases; and 1.23 x 10^3 ± 5.3 x10^2/μL in severe cases. CRP was 2.8 ± 3.0 mg/dL in mild cases, 1.59 ± 2.1 mg/dL in moderate cases and1.9 ± 2.6 mg/dL in severe cases. No significant difference among the data was found in the present cases (Table 2). Oxygen therapy was longer in severe cases compared with mild and moderate cases. Duration of fever in severe cases was significantly shorter compared with moderate and severe cases.

Of the 202 patients, 82 were aged 0–11 months, 102 were 12–71 months, and 18 were 72–180 months, and 41.4%, 72.6%, and 83.3%, respectively, had a history of wheezing (Table 3). In patients aged 0–11 months, 36 (43.9%) cases were classified as mild, 34 (41.5%) as moderate and 12 (14.6%) as severe. In the 12–71 months age group, 57 (55.9%) cases were classified as mild, 30(29.4%) as moderate and 17 (16.7%) as severe. In the group aged 72–180 months, 8 (44.4%) cases were classified as mild, 6 (33.3%) as moderate and 4 (22.2%) as severe. There was no significant difference in the percentage of severity cases between each groups ($p<0.05$) (Table 3).

Table 3: Characteristics and PRESS scores of patients.

	All patients	Age (months)		
		0-11	12-71	72-180
	n=202	n=82	n=102	n=18
Age (months)†	27.6±31.8	5.7±3.4	30.5±16.0	111.0±25.4
Male/female	123/79	54/21	59/62	8-Oct
History of wheezing (%)	123 (60.9)	34 (41.4)	74 (72.6)	15 (83.3)
Hospitalization (%)	128 (63.4)	57 (69.5)	60 (58.8)	11 (61.1)
Virus detection (%)	119 (58.9)	53 (64.6)	57 (55.9)	9 (50.0)
White blood cells (/μL)†	11360±5200	10740±4970	12000±5330	11200±5670
CRP (mg/dL)†	2.1±2.6	2.2±2.7	2.1±2.5	0.7±0.6
Duration (days)†				
Fever	2.6±2.7	2.1±2.4*,**	3.4±2.8*,**	2.0±2.9*,**
Hospitalization	7.7±2.7	8.2±3.5	7.2±1.8	7.0±1.4
Oxygen therapy	1.6±2.0	1.2±1.8	2.0±2.0	2.5±2.2
PRESS score†				
Respiratory rate	0.4±0.5	0.2±0.4*	0.6±0.5*	0.5±0.5
Wheezing	0.9±0.4	0.8±0.4	0.9±0.3	1.0±0.0
Accessory muscle use	0.5±0.5	0.4±0.5	0.5±0.5	0.6±0.5
Cyanosis	0.5±0.5	0.4±0.5	0.6±0.5	0.6±0.5
Feeding difficulties	0.6±0.5	0.6±0.5	0.6±0.5	0.7±0.5
Total	1.8±1.5	1.9±1.4	1.7±1.6	2.2±1.6
Severity				
Mild	82(40.6)	36(43.9)	57(55.9)	8(44.4)
Moderate	102(50.5)	34(41.5)	30(29.4)	6(33.3)
Severe	18(8.9)	12(14.6)	17(16.7)	4(22.2)

†Mean±SD; *: p <0.05, 0-11 months versus 12-71 months; **: p <0.05, 0-11 months versus 72-180 months Percentages indicate the number of cases in each category/total patients in each age group.
PRESS, Pediatric Respiratory Severity Score

Mean severity scores were 1.9±1.4, 1.7±1.6, and 2.2±1.6 in patients aged 0–11, 12–71, and 72–180 months, respectively. There was no significantly different in severity scores between each groups ($p<0.05$) (Table 3).

Virus profiles and severity scores

Viral pathogens were detected in 62.4% of all patients. According to severity grouping, viruses were detected in 53.5% of mild cases, 71.4% of moderate cases, and 69.7% of severe cases. There were no significant differences in the rate of virus detection among the groups. According to age group, the viral detection rate was 64.6% in those aged 0–11 months, 59.8% in those aged 12–71 months, and 66.7% in those aged 71–180 months, with no significant differences found between the groups (Table 4).

Next, HRV (25.6%), RSV (20.7%), and HPIV (4.9%) were detected in the group aged 0–11 months, HRV (25.5%), RSV (18.6%), and PIV (4.9%) in the 12–71 months group, and HRV (33.3%) and RSV (16.7%) in the 72–180 months group (Figures 1, 2 and 3). There was no significant difference in severity scores between each

Table 4: PRESS scores of viruses detected.

		All patients	Severity			Age (months)		
			mild	moderate	severe	0-11	12-71	72-180
		n=202	n=99	n=70	n=33	n=82	n=102	n=18
Virus detection (%)		119 (58.9)	53 (53.5)	48 (68.6)	18 (54.5)	53 (64.6)	57 (55.9)	9 (50.0)
RSV alone	No. of patients	39 (19.3)	17 (17.2)	17 (24.3)	5(15.2)	17 (20.7)	19 (18.6)	3(16.7)
	Score†	1.9±1.3	0.7±0.5**	2.5±0.5**	4.2±0.5**	2.4±1.2	1.5±1.4	1.7±1.2
HRV alone	No. of patients	53 (26.2)	25 (25.2)	19 (27.1)	9 (27.3)	21 (25.6)	26 (25.5)	6 (33.3)
	Score†	1.9±1.6	0.4±0.5**	2.5±0.5**	4.6±0.5**	1.8±1.5	1.8±1.7	2.5±1.9
HMPV alone	No. of patients	1 (0.5)	1 (1.0)	0	0	1 (1.2)	0	0
	Score†	1.0±0.0	1.0±0.0	-	-	1.0±0.0	-	-
HPIV alone	No. of patients	9 (4.5)	3 (3.0)	5 (7.1)	1 (3.0)	4 (4.9)	5 (4.9)	0
	Score†	2.0±1.4	0.3±0.6*	2.6±0.6*	4.0±0.0	1.8±2.1	2.2±0.8	-
HBoV alone	No. of patients	2 (1.0)	0	1 (1.4)	1 (3.0)	1 (1.2)	1 (1.0)	0
	Score†	3.5±0.7	-	3.0±0.0	4.0±0.0	3.0±0.0	4.0±0.0	-
AdV alone	No. of patients	3 (1.5)	3 (3.0)	0	0	1 (1.2)	2 (2.0)	0
	Score†	0.3±0.6	0.3±0.6	-	-	0.0±0.0	0.5±0.7	-
co-detection	No. of patients	12 (5.9)	4 (4.0)	6 (8.6)	2 (11.1)	8 (9.8)	4 (3.9)	0
	Score†	2.1±1.5	0.5±0.6**	2.3±0.5**	4.5±0.7**	2.4±1.3	1.5±1.9	-

†Mean±SD; *p<0.05, mild versus moderate; **p<0.05, mild versus moderate versus severe; ***p<0.05, HEV versus severe. Percentages indicate the number of cases in each category/total patients in each severity or age group.
PRESS: Pediatric Respiratory Severity Score; RSV: Respiratory Syncytial Virus; HRV: Human Rhinovirus; HPIV: Human Parainfluenza Virus; HMPV: Human Metapneumovirus; HEV: Human Enterovirus; HBoV: Human Bocavirus; AdV: Adenovirus

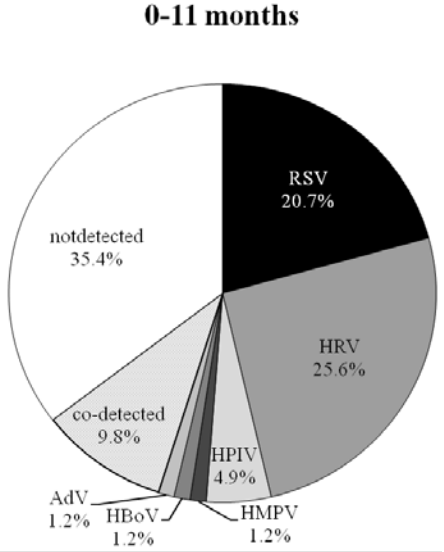

Figure 1: Viruses detected in patients aged 0-11 months.

groups, with the exception of Human Enterovirus (HEV) (Table 4). Bacterial respiratory infections were diagnosed when laboratory reports showed white blood cell counts >10,000 /μL and C-reactive protein levels >5.0 mg/dL. According to our criteria, only 13 (6.4%) patients were diagnosed with bacterial infection. We performed nasopharyngeal cultures for 121 patients and detected *Moraxella catarrhalis* in 12 (9.9%) cases, *Streptococcus pneumoniae* in 16 (13.2%), and *Haemophilus influenza* in 7 (5.8%); a combination was detected in 61 cases (50.4%).

Discussion

Severity score and clinical course

Respiratory tract infections in childhood can readily lead to respiratory distress and sometimes to severe dyspnea, which requires further examinations and hospitalization. An objective bedside assessment of the respiratory symptoms would enable such examinations and treatment to be commenced quickly, to avoid the condition worsening. In emergency settings particularly, medical staff must quickly assess a patient's respiratory condition and general health to decide management. The World Health Organization has suggested that infected children exhibiting drowsiness, feeding difficulties, vomiting, convulsion, and dyspnea should be hospitalized quickly [22]. To avoid inappropriate antibiotic use, Ishiwada et.al reported a scoring system that differentiates between pediatric bacterial pneumonia and atypical pneumonia [23]. In the present study, we evaluated the effectiveness of a simple scoring system based on respiratory symptoms for assessing the need for further examinations and hospitalization.

Guidelines for the Management of Respiratory Infectious Diseases in Children in Japan 2011 proposed the following criteria for hospitalization in community-acquired pneumonia cases: moderate or severe cases determined according to the guidelines, under 1 year old, difficulty in taking oral medications, poor response to oral antibiotics, underlying disease, dehydration, and the patient's doctor opting for hospitalization [24]. The guidelines define the criteria for severity assessment of pediatric community-acquired pneumonia as auscultation, respiratory rate, condition of respiratory assistance muscles, cyanosis, and radiographic data. Recent studies have described previous scoring systems for pediatric respiratory infections

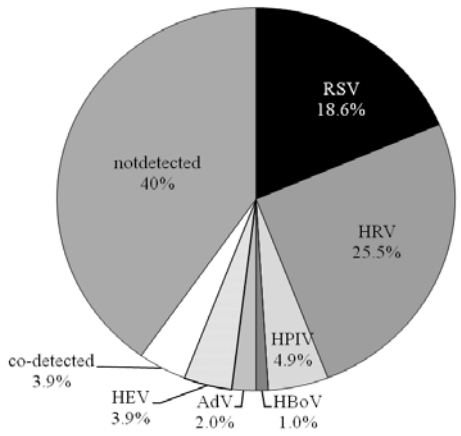

Figure 2: Viruses detected in patients aged 12-71 months.

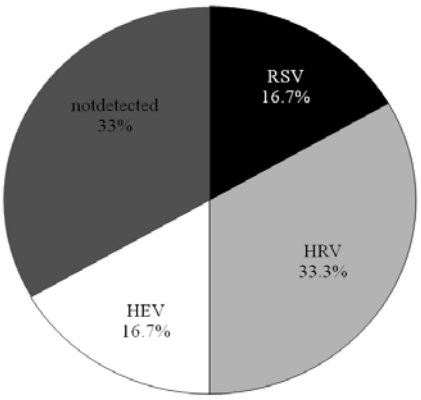

Figure 3: Viruses detected in patients aged 72-180 months.

[3-10] and clarified that respiratory rate, wheezing, retraction, and SpO_2 are all useful criteria for the assessment of respiratory status. In children, feeding difficulties are a very important sign of illness, so we adopted these former and latter components for our PRESS scoring system. We did not adopt heart rate and blood pressure because these parameters are difficult to evaluate in a crying child.

In our study, respiratory rate, retraction scores and Oxygen demand were significantly different between mild, moderate and severe cases, and wheezing and feeding difficulty scores differed significantly between mild and moderate/severe cases. Accordingly, these components are useful for assessing respiratory status. CRP 12100±6080 in mild,

There were no significant differences between the groups for criteria such as WBC and CRP ($p>0.05$), and duration of fever in severe cases was significantly shorter compared with moderate and severe cases. It suggested that clinical respiratory symptoms and feeding difficulties are the more useful assessment criteria.

In this study, the hospitalization rate in moderate/severe cases was significantly higher than in mild cases ($p<0.001$). In addition, the duration of oxygen therapy was significantly longer in severe cases compared with mild and moderate cases ($p<0.001$). The PRESS score can help predict the duration of in-hospital treatment and the clinical course.

Severity score and viral infection

Previous reports have clarified that respiratory viruses can cause not only acute respiratory infections but also infant wheezy illnesses, bronchial asthma, and exacerbation of asthma [25-27]. Friedlander et al. reported that viral infections are the main cause of exacerbations in 80% of child asthma patients and in 50% of adult asthma patients, and HRV contributed strongly to these cases at all ages [28]. Johnston et al. reported that respiratory viral infections contribute to asthma exacerbations in 80–85% of school-aged children with bronchial asthma and viruses such as HRV, enterovirus, corona virus, influenza virus, parainfluenza virus, and RSV were detected in these children [29]. Hamano et al. reported bacterial infection, including *M. pneumonia* and *Chlamydia pneumonia*, at a rate of 49.6%, viral pneumonia at 43.1%, and mixed infection (bacteria and virus) at 25.8% in 2008 after a comprehensive analysis of pediatric community-acquired pneumonia cases, using real-time PCR techniques [30,31]. The main cause of acute respiratory infections in children may be viral infection. Thus, we also compared the severity with the detected viruses. In the present study, there were no significant differences between each group for detection rate of viruses. HRV, RSV, and HPIV were detected in almost all patients, and both HRV and RSV were continuous. We detected viral pathogens in 60% of cases; therefore, it is clear that viral infections are very common and are major causative agents in pediatric respiratory infections, as reported previously [32]. There were no significant differences of severity scores between each virus, with the exception of (HEV). In a recent report, HEV infections are very common and are associated with more severe diseases compared with other common viruses such as RSV [33]. There is a possibility that HEV was included in our examination. HRV was the main causative pathogen for exacerbations of asthma in our school-aged children. To validate this, however, larger studies may be needed because the number of patients in the present cohort was relatively small.

The mechanism of respiratory distress caused by these viruses has not been clarified. The WHO Pneumonia Fact Sheet, 2013, reported that it is difficult to determine the causative agents in cases of bacterial and viral infections [34]. Ishiwada et al. suggested criteria to help discriminate between bacterial and community-acquired pneumonia and defined community-acquired pneumonia as follows: age >6 years, no prediagnosed diseases, no prescribed beta-lactam antibiotics in the last week, good general health, no wet cough, no crackles on auscultation, infiltration area on chest radiograph, <10,000/μL of white blood cells, and <4.0 mg/dL of C-reactive protein [23]. We defined bacterial infection as WBC >10,000/μL and C-reactive protein >5.0 mg/dL. According to these criteria, 13 of our patients (6.4%) were diagnosed with bacterial infection. On the other hand, major bacterial pathogens such as *Moraxella catarrhalis*, *S. pneumoniae*, and *H. influenza* were detected in nasopharyngeal cultures from 59.9% of patients.

Conclusion

The PRESS, with its simple components of respiratory rate, wheezing, retraction, SpO_2, and feeding difficulties, may be useful and applicable to triage and assessment of respiratory status by medical staff at the initial bedside examinations. It would likely be useful in prehospital settings.

Patient Consent

Nasopharyngeal swabs were collected after written informed consent was obtained from the parents of subjects.

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