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Valuable hematological indicators for the diagnosis and severity assessment of Chinese children with community-acquired pneumonia

Prealbumin

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Abstract

Chest X-ray is a "golden standard" for the diagnosis and severity assessment of community-acquired pneumonia (CAP). However, it cannot be used as routine examination of CAP in children. The present study aims to investigate the roles of prealbumin (PA) in CAP in children and further determine the usefulness of PA in diagnosis and severity assessment of CAP in children.

This was a retrospective analysis of 174 cases of hospitalized children with CAP. The following indicators were recorded: vital sign, inflammatory indexes, PA, and respiratory pathogens immunoglobulin M antibody test results. A total of 33 healthy children were selected as the control group. The results of laboratory tests between CAP and control groups were compared. CAP group was further divided into mild CAP and severe CAP groups, and vital signs and laboratory examination results of 2 groups were compared.

The total positive rate of *Mycoplasma pneumoniae* in this study was 27.4%, and there was no significant difference in different seasons ($P=0.356$). Compared with controls, there was no significant difference between procalcitonin and C-reactive protein in CAP group ($P=0.355$, 0.061). The white blood cell count, percentage of neutrophils, neutrophil count, and erythrocyte sedimentation rate in the CAP group were significantly higher than those in control group, and PA was significantly lower than that in the control group (all $P<0.05$). In the traditional cutoff value (<170 mg/L), the sensitivity of PA for the diagnosis of CAP was 0.847, which was significant higher than traditional inflammatory indicators. Moreover, it was found that PA was an independent protective factor for CAP in children based on multivariate analysis (odds ratio: 0.974; 95% confidence interval: 0.956–0.993; $P=0.008$). PA level in severe CAP group was significantly lower than in mild CAP group ($P=0.001$). With a cutoff value of 125 mg/L, the sensitivity and specificity of PA for the severity assessment of CAP were 0.703 and 0.714, respectively.

Combined with traditional inflammatory markers, PA may improve the diagnostic efficacy of CAP in children. PA can be used as a reference marker to complement the chest X-rays for severity assessment of children CAP.

Abbreviations: CAP = community-acquired pneumonia, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, LRI = lower respiratory infections, MP = *Mycoplasma pneumoniae*, PA = prealbumin, PCT = procalcitonin, RR = respiratory rate, WBC = white blood cell count.

Keywords: children, community-acquired pneumonia, diagnosis, prealbumin, severity assessment

1. Introduction

The respiratory infections in children are classified as upper respiratory infections and lower respiratory infections (LRI) based on the site of infection. In LRI, community-acquired pneumonia (CAP) is the major cause of respiratory morbidity and mortality in children, which can be defined as symptoms of pneumonia caused by community acquired infection without predisposing factors in previous healthy children. CAP is one of the most common diseases in children, and also second leading cause of death for children in developing countries. In addition, CAP is one of the most common causes of hospitalization among developed countries. The incidence of CAP is 10 to 40/10,000 for children under 5 years of age and 11 to 16/10,000 for children between the age of 5 and 14 years.[1,2]

Although the clinical manifestations of fever and respiratory symptoms are recommended for the diagnosis of CAP, chest X-ray is still the "golden standard" for the diagnosis and severity assessment. Since it has been suggested that chest X-ray should not be used as routine examination of CAP in children,[3] it is necessary to find new serum markers to replace chest X-ray in order to determine the lung involvement and stratify the children,

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and further decide whether it is necessary to perform radiological examination.

Prealbumin (PA) is a nonspecific host defense effector with a half-life of 1.9 days; thus, the serum level of PA can be rapidly reduced during acute infection, especially which would be more obvious with bacterial infections.[4] Gao et al[5] found that PA level was decreased during the bacterial infection in children, whereas there were no obvious reduction in viral infection and control groups. Thus, as a negative acute phase protein, PA can be used to identify bacterial or viral infections in children with acute infectious disease. However, the role of PA in children with CAP is still unclear, especially its roles in severity assessment of CAP. Therefore, our study aims to investigate the role of PA in the diagnosis and severity assessment of children with CAP in order to guide clinical decision-making.

2. Patients and methods

2.1. Patients

The study was approved by the Ethics Committee of the Soochow University. All patients and their family members signed the informed consent form. Patients' medical records were anonymous. From May 2014 to May 2016, 174 cases of hospitalized children with CAP aged from 3 months to 12.4 years (average age was 4.1 years) were retrospectively analyzed. CAP was defined as the presence of signs and symptoms of pneumonia (fever and respiratory symptoms) and pulmonary condensation on chest radiography in a previously healthy child caused by an infection that was acquired outside the hospital.[6] Children who had received antibiotic treatments for more than 48 hours before admission or had been suffering from an underlying chronic respiratory disease were excluded from the study. A total of 33 healthy children were selected as the control group, aged from 8 months to 9.8 years (average age was 4.7 years). A total of 174 cases of CAP patients were further divided into 4 groups according to the admission time. A total of 47 cases were in spring (March–May), 64 cases were in summer (June–August), 32 cases were in autumn (September–November), and 31 cases were in winter (December–February). According to the scope of X-ray pulmonary infiltration, presence of hypoxemia, and presence of pulmonary or extrapulmonary complications,[7] CAP group was further divided into mild group (133 cases) and severe group (22 cases), 19 cases without performing chest X-ray were not included in the study. The vital signs including body temperature, heart rate, and respiratory rate (RR) were recorded.

2.2. Laboratory methods

In addition, inflammation markers were also recorded, which included white blood cell count (WBC) ($5–12 \times 10^9$/L), percentage of neutrophils (40%–75%), neutrophil count ($2–7 \times 10^9$/L), percentage of monocytes (3%–10%), procalcitonin (PCT), C-reactive protein (CRP), PA, and erythrocyte sedimentation rate (ESR). Routine blood test was performed by Sysmex XN9000 (Hyogo, Japan), PCT was tested by Roche cobas8000 (Indianapolis, IN, USA) system (reference value is 0.021–0.500 ng/mL), CRP and PA were tested by BECKMAN COULTER AU5800 (Brea, CA, USA) (reference value are 0–10.0 and 170–420 mg/L, respectively), and ESR was analyzed by Alifax TEST1 (Padova, Italy) analyzer (reference range: male $\leq$21 mm/h, female $\leq$26 mm/h). Indirect immunofluorescence approach was employed to detect the immunoglobulin M (IgM) antibodies against 9 common respiratory pathogens including *Legionella pneumophila*, *Mycoplasma pneumoniae* (MP), *Coxiella burnetii*, *Chlamydia pneumoniae*, adenovirus, respiratory syncytial virus, influenza type A virus, influenza type B virus, and parainfluenza virus types 1, 2, and 3. The detection was performed by using VIRCELL IFA (Granada, Spain) kit according to the manufacture's instruction. The fluorescence was observed by using fluorescence microscope EUROSTARIII PLUS (Lubeck, Germany).

2.3. Statistical analysis

Statistical analysis was performed using the statistical package for the social scientists (SPSS version 13, Chicago, IL, USA). Skewed distribution data were expressed as 50th percentile with 25th and 75th percentile; quantitative data were expressed as numbers or percentages. Two sets of non-normally distributed data were analyzed by Mann–Whitney *U* test. Proportions were compared with χ^2 test. The diagnostic efficiency of different markers was compared by using receiver operating characteristic (ROC) curve and the area under the ROC curve. Multiple factors analysis was performed using multivariate logistic regression analysis and regression coefficient, and odds ratios were calculated. $P < 0.05$ was considered statistically significant.

3. Results

There was no significant difference in age and the sex ratio between the CAP and the control groups (3.6 [2, 5.6] vs 4.6 [3.5, 5.8] years old, $Z = -1.921$, $P = 0.055$; 104 males, 70 females vs 20 males, and 13 females, $\chi^2 = 0.008$, $P = 0.928$). The results of IgM antibody test in 174 cases of CAP were as follows: 45 cases of MP positive, 119 cases of MP negative, and 10 cases without examination. The total positive rate of MP was 27.4%, and there was no significant difference in positive rate in different seasons (26.7% [12/45] in spring, 20.3% [12/59] in summer, 35.5% [11/31] in autumn, and 34.5% [10/29] in winter, $\chi^2 = 3.238$, $P = 0.356$).

By comparison of inflammation markers between CAP and control groups (Fig. 1), we found that the value of WBC, percentage of neutrophils, neutrophil count, and ESR in CAP group were 10.13 (7.22, 15.34) $\times 10^9$/L, 64.4 (49.9, 76.9)%, 6.12 (3.66, 10.16) $\times 10^9$/L, and 14 (6, 25) mm/h, respectively, whereas the 4 indexes in control group were 6.30 (4.48, 7.66) $\times 10^9$/L, 49.7 (45.1, 56.5)%, 3.22 (2.14, 4.02) $\times 10^9$/L, and 6 (4, 17) mm/h, indicated that the 4 inflammation markers in CAP group were significant higher than values in control group (all $P < 0.05$). The PA of CAP group was significantly lower than that of the control group (134 [111, 162]vs 159 [145, 170] mg/L, $P = 0.003$).

The ROC curve of WBC, percentage of neutrophils, neutrophil count, ESR, and PA for the diagnosis of CAP was shown in Figs. 2 and 3; the parameters obtained from ROC curve were shown in Table 1. Multivariate logistic regression analyses using multiple variables (WBC, percentage of neutrophils, neutrophil count, ESR, and PA) which were statistically significant based on univariate analysis was used to examine the impact of multiple independent indicators on the diagnosis of CAP as a dependent variable. PA was the only significant protective factor (odds ratio: 0.974; 95% confidence interval [CI]: 0.956–0.993; $P = 0.008$) (Table 2).

Comparison of general status between mild CAP and severe CAP (Table 3). The IgM antibody test for 155 patients with CAP showed that 38 patients with MP positive, 108 patients with MP negative, and 9 patients who declined to detect. There was no significant difference for MP positive rate between 2 groups (25.6% vs 28.6%, $P = 0.774$).

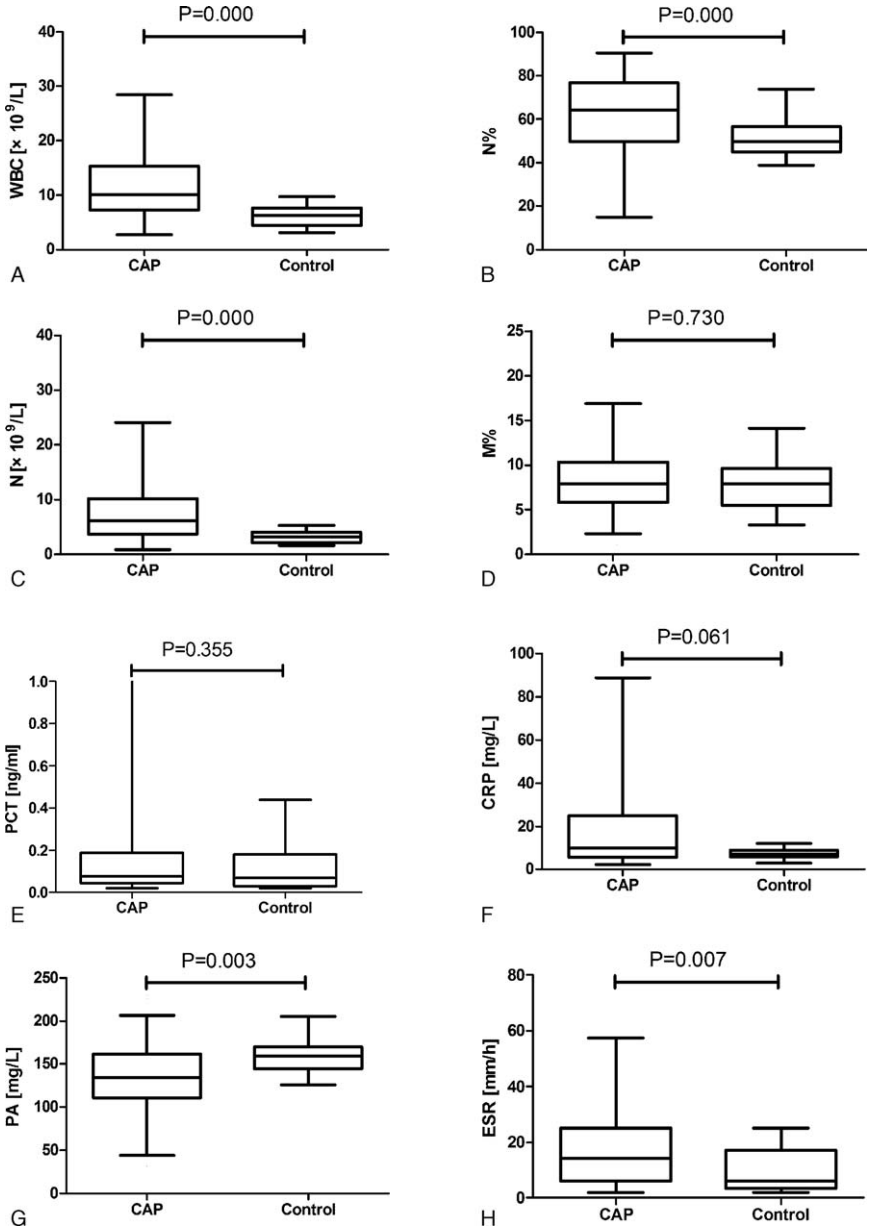

Figure 1. Comparison of inflammation markers between community-acquired pneumonia and control groups. WBC = white blood cell count, N% = percentage of neutrophils, N = neutrophil count, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, M% = percentage of monocytes, PA = prealbumin, PCT = procalcitonin.

By comparison of general status, it was shown that the RR in severe CAP group was significant higher than mild CAP group at the admission ($P < 0.05$). If considering the age, the criteria for tachypnea are as follows: ≥60 bpm (<2 months), ≥50 bpm (2 months–1 year old), ≥40 bpm (1–5 years old), ≥30 bpm (old than age 5 years). There was significant higher rate of tachypnea for severe CAP group (13.6%) than mild CAP group (1.5%) ($\chi^2 = 5.439$, $P = 0.020$). In addition, there were only 2 cases of pleural effusion and 1 case of myocardial damage in the severe CAP group.

By comparison of the laboratory indexes in different CAP group (Fig. 4), we found that PA level was 104 (74, 136) mg/L in severe CAP group, which was significant lower than in mild CAP group (136 [118, 163] mg/L) ($P = 0.001$). The ROC curve of PA for the assessment of CAP severity was shown in Fig. 5, the area under the curve was 0.728, $P = 0.001$, 95% CI was 0.604 to 0.853. The best cutoff value was 125 mg/L, the sensitivity was 0.714, and the specificity was 0.703.

4. Discussion

4.1. MP infection and children CAP

The common pathogens causing CAP include bacteria, viruses, mycoplasma, chlamydia, and so on. In recent years, MP has become most common cause of CAP in children.[8,9] Previous studies have shown that up to 40% of CAP has MP infection, and 18% of them required hospitalization.[10] Recently, Shu et al[11] analyzed 1155 cases of children with CAP in Shanghai, and the detection rate of MP infection was 43.64%, whereas bacterial

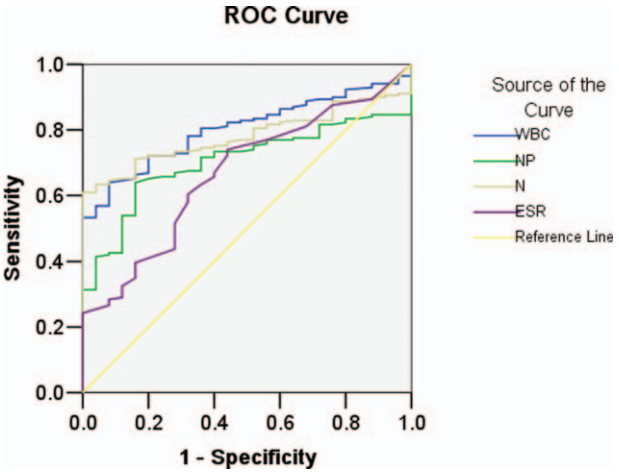

Figure 2. The ROC curve of white blood cell count, percentage of neutrophils, neutrophil count, and ESR for the diagnosis of community-acquired pneumonia. ESR = erythrocyte sedimentation rate, N = neutrophil count, NP = percentage of neutrophils, WBC = white blood cell count.

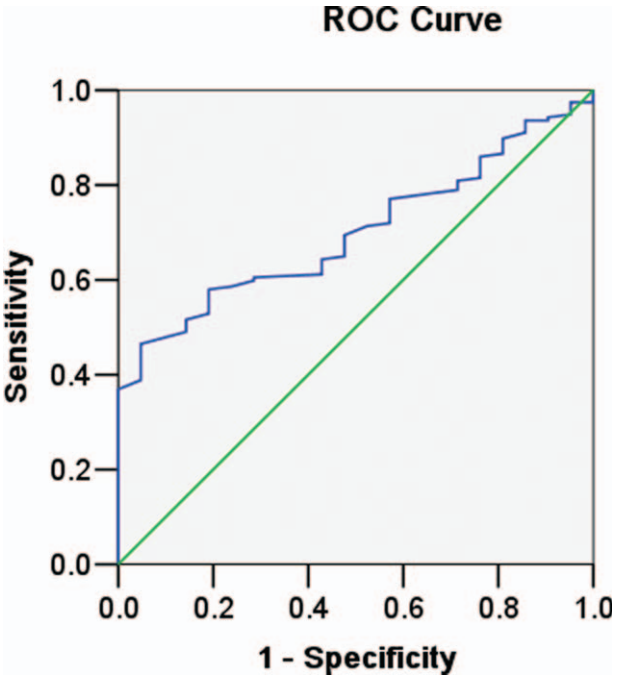

Figure 3. The ROC curve of prealbumin for the diagnosis of community-acquired pneumonia.

infection was only 15.12%, indicating that MP was the most common pathogen of CAP in children in China.

The incidence of MP infection is related to the age and immune status of the patient, and the recurrent infections are rare. Infants and young children under age 3 years often manifest as mild or subclinical infection. The peak age with MP infection is preschool and school-age children, 7% to 30% of patients with CAP between ages 3 and 15 years are caused by MP infection.[12] Shu et al[11] found that children between ages 6 and 14 years have a high detection rate of MP infection (77.4%), and the lowest detection rate was from children under age 1 year (11.2%). In our study, the detection rate of MP was 27.4%, which was lower than 43.64% that reported by Shu, the reason might be attributed to the low average age of children in this study. MP infections can occur throughout the year, and the peak season was different in different regions. The epidemic seasons in north of China is winter but is summer and autumn in the south of China.[12] There was no seasonal difference for positive rate of MP infections in this study, which might be related to the small sample size. In addition, we found there was no significant correlation between the severity of CAP in children and the presence of MP infection; it was possible that bacterial pathogens were the major cause of severe CAP.[13]

4.2. Inflammation markers and CAP diagnosis in children

Usually, in developed countries CAP diagnosis is mostly clinical and is confirmed by radiographic finding of consolidation. The valuable laboratory tools are also needed in the management of CAP in children, which can offer the useful clinical information on determination of appropriate treatment and courses with antibiotics based on the detected etiology agent, as well as the prognosis of the disease. PCT, a protein containing 116 amino acids, is normally produced by neuroendocrine cells in the thyroid and lungs at a very low rate and is undetectable in serum.[14] Inflammatory and infectious injuries stimulate over-expression of the *CALC1* gene consequently increasing serum PCT. Under these pathologic conditions, synthesis and secretion of PCT become ubiquitous.[15] CRP is an acute phase reaction protein synthesized in the liver and is considered as a good index for early diagnosis of inflammation.[16] The usefulness of PCT and CRP in the management of pediatric CAP has been carefully studied and compared. Overall, the latest data showed that PCT was the best diagnostic marker compared to CRP, especially for the detection of pneumococcal infection.[17,18] However, there was no significant increase of PCT and CRP in our study, which might be attributed to a low rate of bacterial infection. Actually in CAP children infected with virus and mycoplasma, PCT and CRP are not elevated or only mildly elevated.[19,20]

WBC, neutrophil percentage, neutrophil count, and ESR are the traditional indicators for screening the bacterial infections with CAP in children, but recent studies have demonstrated that the above indicators were not specific and sensitive for the diagnosis of bacterial or viral infection.[21] In this study, the above indicators were increased in the patients with CAP, but the sensitivity for diagnosis of CAP was low according to the traditional cutoff value (all $P < 0.5$); thus, the diagnostic value of CAP was limited. The possible reason is that the body's response to infection is poor if the child's immune system is low; thus, the above indicators might be normal.[22]

PA is a carrier protein synthesized in the liver. Because PA can eliminate the toxic metabolites released during the process of infection and is gradually consumed; thus, it is a nonspecific host defense substance. Hrnciarikova et al[23] found that the elevation of serum CRP was correlated with the decrease of PA in old people with infections, suggesting that PA has the similar clinical significance with CRP. Shao et al[24] found that the PA levels were decreased in CAP group that infected with different pathogens, whereas PA reduction was more significant in bacterial infection group. Similar results were found in this study, and the sensitivity for diagnosis of CAP with traditional cutoff value was 0.847, which was significant higher than traditional inflammatory

Table 1

The parameters of different laboratory markers from ROC curve for the diagnosis of CAP.

Markers	AUC	*P*	95% CI	Cutoff	Sensitivity	Specificity
WBC, $\times 10^9$/L	0.803	**0.000**	0.737–0.868	$>12 \times 10^9$/L	0.391	1.000
Percentage of neutrophils	0.704	**0.001**	0.626–0.783	>75%	0.284	1.000
Neutrophil count, $\times 10^9$/L	0.781	**0.000**	0.718–0.844	$>7 \times 10^9$/L	0.432	1.000
PA, mg/L	0.700	**0.003**	0.611–0.789	<170 mg/L	0.847	0.238
ESR, mm/h	0.668	**0.007**	0.567–0.769	>26 mm/h	0.243	1.000

AUC = area under the curve, CI = confidence interval, ESR = erythrocyte sedimentation rate, PA = prealbumin.
Bold means $P < 0.05$.

Table 2

The result from multivariate logistic regression analysis.

Factors	Regression coefficients	*P*	OR	95% CI
WBC, $\times 10^9$/L	0.045	0.865	1.046	0.622–1.759
Percentage of neutrophils	−0.019	0.606	0.981	0.911–1.056
Neutrophil count, $\times 10^9$/L	0.467	0.350	1.595	0.600–4.242
PA, mg/L	−0.026	**0.008**	0.974	0.956–0.993
ESR, mm/h	−0.005	0.873	0.995	0.936–1.057

CI = confidence interval, ESR = erythrocyte sedimentation rate, OR = odds ratio, PA = prealbumin.
Bold means $P < 0.05$.

Table 3

Comparison of general status between mild CAP and severe CAP.

CAP groups		Mild CAP	Severe CAP		
Cases		133	22	Z/χ^2	*P*
Gender	Male	78	14	0.195	0.659
	Female	55	8		
MP	Positive	32	6	0.082	0.774
	Negative	93	15		
Age, y		3.8 (2.3, 6.0)	3.1 (1.5, 4.2)	−1.733	0.083
Temperature, °C		38.0 (37.2, 38.6)	38.0 (37.3, 38.4)	−0.162	0.872
HR, bpm		110 (100, 120)	120 (107, 127)	−1.713	0.087
RR, bpm		26 (24, 28)	28 (27, 30)	−3.267	**0.001**

CAP = community-acquired pneumonia, HR = heart rate, RR = respiratory rate, MP = *Mycoplasma pneumoniae*.
Bold means $P < 0.05$.

indicators. Moreover, it was found that PA was an independent protective factor for CAP in children based on multivariate analysis. It was proposed that the combination of PA with the traditional inflammatory indicators may make up the deficiency of their low sensitivity and improve the diagnostic efficacy of CAP.

4.3. Inflammation markers and assessment of CAP severity in children

The children with CAP may have fever (Axillary temperature >38.5°C), coughing, wheezing, rapid breathing, shortness of breath, chest wall inspiratory depression, breath holding, chest pain, headache, abdominal pain, or other symptoms.[6] Smyth et al[25] found that RR was helpful to the severity of pneumonia in children under 1 year of age. The correlation sensitivity of RR > 70/min and hypoxia was 63%, and the specificity was 89%. We also showed that RR was higher in severe CAP group than in mild CAP group. Because rate of tachypnea was still higher in severe CAP than in mild CAP group after considering the age factor; thus, tachypnea was a good sign of CAP severity.

The assessment of pediatric CAP severity defined by the extent of consolidation on chest X-rays and the presence of pleural effusion.[7] Because of this definition, there is no scoring system available for the severity of children CAP. Although X-rays are important for the diagnosis, it should not be used as routine method. Lee et al[26] found that PCT has a higher sensitivity and specificity than CRP in the differential diagnosis of lobar and bronchial pneumonia. Agnello et al[27] reported recently that CRP is better than PCT, neutrophil count, and WBC for the assessment of CAP severity. Our study did not find the advantages of traditional inflammation markers for the differential diagnosis of CAP severity, which may be attributed to the reduction of bacterial infections in CAP and the complexity of pathogens.

Liao et al[28] compared the PA levels from 54 patients with severe acute respiratory syndrome (SARS), 20 patients with pneumonia, and 30 healthy controls and discovered that the decreased levels of PA in SARS group > the pneumonia group > the control group, suggesting that the extent of PA reduction was correlated with the degree of severity of pneumonia. In the present study, the PA in children with severe CAP was

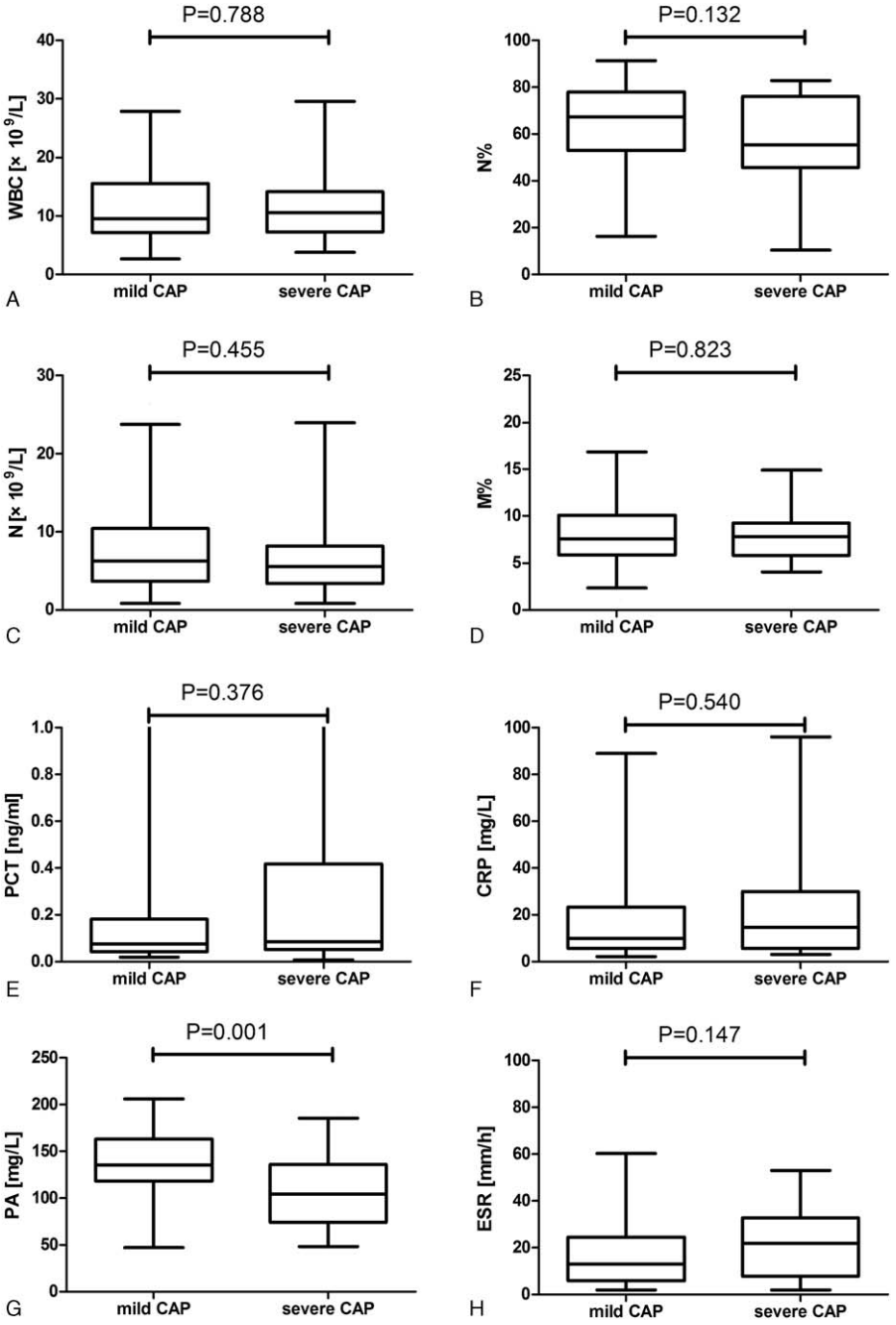

Figure 4. Comparison of inflammation markers between mild community-acquired pneumonia (CAP) and severe CAP groups. CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, M% = percentage of monocytes, N% = percentage of neutrophils, N = neutrophil count, PA = prealbumin, PCT = procalcitonin, WBC = white blood cell count.

significantly lower than in children with mild CAP, which was consistent with the findings of the aforementioned adult study. ROC analysis showed that PA had a high sensitivity and specificity in assessing the severity of CAP when the cutoff value was 125 mg/L, which was lower than the traditional cutoff value (<170 mg/L), indicating that PA can be used as an indicator for severity assessment of pediatric CAP.

In conclusion, PA was highly sensitive to the diagnosis of CAP in children. Combined with traditional inflammatory markers such as WBC, percentage of neutrophils, neutrophil count, and ESR, PA may improve the diagnostic efficacy of CAP. In addition, PA was an independent protective factor for CAP in children. The reduction of PA was correlated with the severity of CAP, which can be used as a reference index to assess the severity of CAP except for X-ray, so as to guide clinical decision-making. Of course, there were some limitations in our study, such as the small sample size, low severe CAP ratio, and the mild degree of inflammation, which need to be further improved.

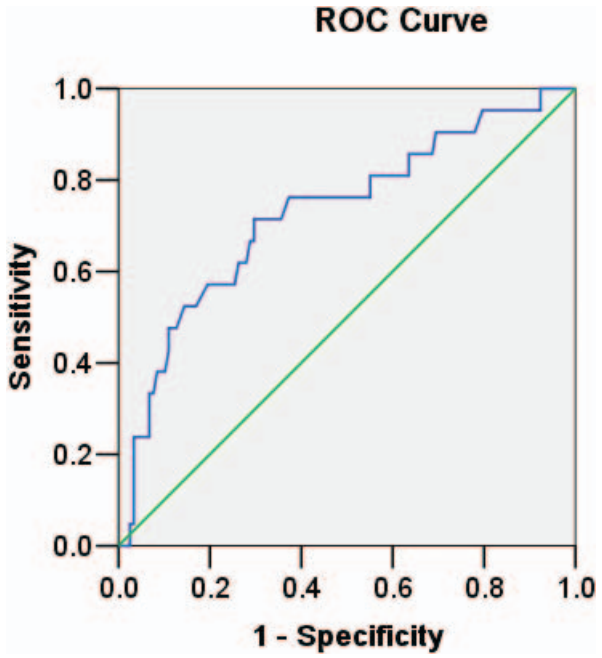

Figure 5. The ROC curve of prealbumin for severity assessment of community-acquired pneumonia.

References

[1] Clark JE, Hammal D, Hampton F, et al. Epidemiology of community-acquired pneumonia in children seen in hospital. Epidemiol Infect 2007;135:262–9.

[2] Cardinale F, Cappiello AR, Mastrototaro MF, et al. Community-acquired pneumonia in children. Early Hum Dev 2013;89:S49–52.

[3] Harris M, Clark J, Coote N, et al. British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. Thorax 2011;66(suppl 2):ii1–23.

[4] Myron Johnson A, Merlini G, Sheldon J, et al. Clinical indications for plasma protein assays: transthyretin (prealbumin) in inflammation and malnutrition. Clin Chem Lab Med 2007;45:419–26.

[5] Gao HL, Zhang CG, Zhu LL, et al. Clinical significance of determinations of serum procalcitonin, prealbumin and C-reactive protein in children with infection diseases. J Appl Clin Pediatr 2009;24:889–904.

[6] Subspecialty Group of Respiratory Diseases T, Society of Pediatrics C M AGuidelines for management of community acquired pneumonia in children (the revised edition of 2013) (I). Zhonghua er ke za zhi 2013;51:745–52.

[7] Subspecialty Group of Respiratory Diseases T, Society of Pediatrics C M AGuidelines for management of community acquired pneumonia in children (the revised edition of 2013) (II). Zhonghua er ke za zhi 2013;51:856–62.

[8] Michelow IC, Olsen K, Lozano J, et al. Epidemiology and clinical characteristics of community-acquired pneumonia in hospitalized children. Pediatrics 2004;113:701–7.

[9] Defilippi A, Silvestri M, Tacchella A, et al. Epidemiology and clinical features of *Mycoplasma pneumoniae* infection in children. Respir Med 2008;102:1762–8.

[10] Waites KB. New concepts of *Mycoplasma pneumoniae* infections in children. Pediatr Pulmonol 2003;36:267–78.

[11] Shu LH, Xu JJ, Wang S, et al. Distribution of pathogenic microorganisms and its relationship with clinical features in children with community-acquired pneumonia. Chin J Contemp Pediatr 2015;17:1056–61.

[12] Yin Y, Lu Q, Yan X. Epidemiology of *Mycoplasma pneumoniae* infections. Zhonghua Er Ke Za Zhi 2016;54:91–3.

[13] Howie SR, Morris GA, Tokarz R, et al. Etiology of severe childhood pneumonia in the Gambia, West Africa, determined by conventional and molecular microbiological analyses of lung and pleural aspirate samples. Clin Infect Dis 2014;59:682–5.

[14] Snider RH, Nylen ES, Becker KL. Procalcitonin and its component peptides in systemic inflammation: immunochemical characterization. J Investig Med 1997;45:552–60.

[15] Muller B, White JC, Nylen ES, et al. Ubiquitous expression of the calcitonin-i gene in multiple tissues in response to sepsis. J Clin Endocrinol Metab 2001;86:396–404.

[16] Sierra R, Rello J, Bailén MA, et al. C-reactive protein used as an early indicator of infection in patients with systemic inflammatory response syndrome. Intensive Care Med 2004;30:2038–45.

[17] Yo CH, Hsieh PS, Lee SH, et al. Comparison of the test characteristics of procalcitonin to C-reactive protein and leukocytosis for the detection of serious bacterial infections in children presenting with fever without source: a systematic review and meta-analysis. Ann Emerg Med 2012; 60:591–600.

[18] Pereira JM, Teixeira-Pinto A, Basilio C, et al. Can we predict pneumococcal bacteremia in patients with severe community-acquired pneumonia? J Crit Care 2013;28:970–4.

[19] Zheng XL, Xue LH. The changes in hs-CRP and PCT levels and cellular immunity indicators in peripheral blood and their clinic significance in children pneumonia. J Clin Pediatr 2013;31:22–5.

[20] Gilbert DN. Procalcitonin as a biomarker in respiratory tract infection. Clin Infect Dis 2011;52(suppl 4):S346–50.

[21] Lee H. Procalcitonin as a biomarker of infectious diseases. Korean J Intern Med 2013;28:285–91.

[22] Rey C, Los Arcos M, Concha A, et al. Procalcitonin and C-reactive protein as markers of systemic inflammatory response syndrome severity in critically ill children. Intensive Care Med 2007;33: 477–84.

[23] Hrnciarikova D, Juraskova B, Hyspler R, et al. A changed view of serum prealbumin in the elderly: prealbumin values influenced by concomitant inflammation. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2007;151:273–6.

[24] Shao ZL, Sun BL, Zhao JM. Clinical value of serum adenosine deaminase and prealbumin in identification of pathogens isolated from children with pneumonia. Chin J Nosocomiol 2016;26:2361–3.

[25] Smyth A, Carty H, Hart CA. Clinical predictors of hypoxaemia in children with pneumonia. Ann Trop Paediatr 1998;18:31–40.

[26] Lee JY, Hwang SJ, Shim JW, et al. Clinical significance of serum procalcitonin in patients with community-acquired lobar pneumonia. Korean J Lab Med 2010;30:406–13.

[27] Agnello L, Bellia C, Di Gangi M, et al. Utility of serum procalcitonin and C-reactive protein in severity assessment of community-acquired pneumonia in children. Clin Biochem 2016;49:47–50.

[28] Liao WJ, Li YM, Chen T, et al. Determination of serum acute phase reaction protein in patients with severe acute respiratory syndrome. Chin J Preventive Mes 2004;38:92–3.