The Value of Neutrophil/monocyte Ratio in Early Diagnosis of Children Mycoplasma Pneumoniae Pneumonia

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Abstract

Background: To investigate the value of blood cell analysis in early diagnosis of mycoplasma pneumoniae pneumonia (MP).

Methods: The clinical parameters, including patient characteristics, clinical symptoms, imaging characteristics and laboratory examination data of the patients hospitalized in the Department of Pediatrics, Nanjing Jiangning Hospital from January 2018 to March 2020 due to community-acquired pneumonia were collected for retrospective analysis. The data were analyzed by SPSS 22.0 software for statistical analysis. $P<0.05$ was considered statistically significant.

Results: The levels of white blood cell count (WBC), absolute neutrophil count (NEU), absolute monocyte count (MON), platelet count (PLT), neutrophil/lymphocyte ratio(NLR), mean platelet volume/platelet count (MPV/PLT) and neutrophil/monocyte ratio (NMR) in children with bacterial pneumonia (BP)were significantly higher than those of children withMP and children withviral pneumonia (VP), the NMR level in children withMP was higher than that of children with VP,the NMR levelsin the three groups of children were significantly different ($P<0.05$).Combined with the NMR level, the children's age andpulmonary consolidation information,the AUC areas of MP, BP and VP had high accuracy fordifferential diagnosis of MP.

Conclusion: As a comprehensive indicator of neutrophils and monocytes, NMR may differentiate pneumonia caused by mycoplasma pneumoniae, bacterial and viral infections, which provides new direction for early differential diagnosis of pneumonia.

Background

Mycoplasma pneumoniae is one of the main pathogens causing community-acquired pneumonia (CAP) [1], accounting for 11–15% ofCAPworldwide[2]. Mycoplasma pneumoniae pneumonia (MP) is more common in children. According to the statistics [3], the CAP in children over 5 years old accounts for 40% of the total CAP.CAP is mostly caused by bacteria, viruses, chlamydia and mycoplasma. As an atypical pneumonia, MP is difficult to distinguish from CAP caused by other pathogens in clinical manifestations [4–6]. Pneumonia caused by different pathogens is totally different in the choice of treatment methods such as antibiotics[1, 4], and it is urgent to develop fast and accurate indicatorfor differential diagnosis of MP from other CAPs, which brings about opportunities and challenges to MP diagnosis.

At present, the specific laboratory diagnostic methods commonly used for MP are mainly PCRmethod and serological method [7, 8].PCR method has high cost and technical requirements, takes long time, and may have other problems [9, 10], the serological method has false negative problems due to window period or low antibody content [11–14], and is not suitable to early diagnosis of MP.

As a routine examination item in the clinical laboratory of outpatient and emergency department, blood cell analysis has been widely applied in primary hospitals. The indicators include white blood cell count

(WBC), absolute neutrophil count (NEU),absolute lymphocyte count (LYM), absolute monocyte count (MON), absolute eosinophil count (EO), absolute basophil count(BA) and platelet count (PLT). Neutrophil/lymphocyte ratio(NLR), platelet/lymphocyte ratio (PLR) and monocyte/lymphocyte ratio (MLR) have been proved to be auxiliary diagnostic indicatorsof inflammation and infection [15–19].Moreover, NLR, PLR, MLR and MPV/PLT can predict the nature of infection. In this study, bacterial pneumonia (BP) and viral pneumonia (VP) were used as controls to analyze the clinical characteristics and laboratory parameters of children admitted to the hospital due to MP, and explore clinical significance of blood cell analysis indicators in the differential diagnosis of MP, BP and VP to develop simple, rapid and effective indicators for early differential diagnosis of MP.

Materials And Methods

1. Materials

1.1 General information

A retrospective study was conducted based on clinical parameters, including patient characteristics, clinical symptoms, imaging characteristics and laboratory examination data of the patients hospitalized in the Department of Pediatrics, Nanjing JiangningHospital from January 2018 to March 2020 due to CAP.

1.2 Inclusion criteria

(1) The children were aged from 1 to 12 years old;

(2) All the children had clinical manifestations and pulmonary imaging characteristics of pneumonia, which meet the relevant standards of “ZhuFutangPractice of Pediatrics (8th Edition)” [20];

(3) The children with positive mycoplasma pneumoniae nucleic acid were screened from the children whoreceivedthe multiplex PCRnucleic acid detection of respiratory pathogens and were included asMP group;

(4) The positive cases of bacterial culture were screened from the children whoreceivedthe sputum culture detection and were included asBP group;

(5) The children with one or more positive respiratory viruses (including influenza A, influenza B, respiratory syncytial virus, metapneumovirus, adenovirus and rhinovirus) were screened out from the children whoreceivedthe multiplex PCRnucleic acid detection of respiratory pathogensand were included asVP group.

1.3 Laboratory data

The laboratory data collected in this study included WBC, NEU, LYM, MON, EO, BA, PLT, mean platelet volume (MPV), platelet distribution width (PDW), C-reactive protein (CRP), D-dimer (DD), procalcitonin

(PCT), β2-microglobulin (B2MG),NLR,PLR,MLR,MPV/PLT, and NMR from the patients on the first admission to the hospital.

2. Statistical analysis

The SPSS 22.0 software was used for statistical analysis of the data. Theindependent samplest test or t'testwas used to compare the blood cell indicators of various groups; the ranksum test was used to compare the non-normal distribution groups; the χ^2test or Fisher's exact probability testwas used for the correlation analysis between the blood cell indicatorsand the clinical characteristics; the receiver operating characteristic (ROC) curve was used to evaluate the diagnostic efficiency of each indicator to MP, BP and VP. $P < 0.05$ was considered statistically significant.

Results

1. Clinical characteristics of children hospitalized due to CAP

We collected a total of 48 cases of children hospitalized due to CAPof which 26 cases received bacterial culture detectionand 38 cases receivedmultiplex PCR detectionof respiratory pathogens. According to the infectious pathogens, 48 children with CAP were divided into three groups: 18 cases in MP group (37.5%), 15 cases in BP group (31.25%), and 15 cases inVP group (31.25%).The 8 children with MP were positive forrespiratory pathogenmultiplex PCRdetectionbut negative for thedetection of virus and bacteria; among the 15 children with BP, sputum culture was positive in 14 cases, and blood culture was positive in 1 case; all 15 children withVP receivedthe multiplex PCR detection of respiratory pathogens, and influenza A virus RNA was positive in 2cases, influenza B virus RNA was positivein 8cases, respiratory syncytial virus RNAwas positive in 5cases,adenovirus DNAwas positive in 1 case, rhinovirus RNAwas positive in 1 case, and metapneumovirus RNA was positive in 1 case.

2. Comparison of clinical parameters between children with MP and those with BP

The differences of clinical parameters between the children with MP and those with BP are shown in Table 1. The age of 8-year-old children with MP (interquartile range (IQR)2–12)was older than that of 4-year-old children with BP (IQR2–9), and the difference was statistically significant ($P = 0.018$), of which the age of BP onset was 3–7 years old ($P = 0.009$), and the age of MP onset was 7–12 years old ($P = 0.004$). Based on imaging characteristics, the children with MP were more likely to have pulmonary consolidation ($P = 0.022$).The children with MPincluded12 cases (66.7%) ofpulmonary consolidation, whilethe children with BP included4 cases (26.7%)ofpulmonary consolidation, but there was no significant difference between unilateral and bilateral pulmonary consolidation ($P = 0.35$).

Table 1
Comparison of clinical parameters between children with MP, BP andVP

Parameter	MP(n = 18)	BP(n = 15)	VP(n = 15)	*P* value*	*P*value#
Patient characteristics					
Age (years)				0.018	0.002
Mean ± SD	6.5 ± 3.1	4.3 ± 1.8	3.3 ± 1.5		
Mean	8(2 ~ 12)	4(2 ~ 9)	3(1 ~ 6)		
0 ~ 3 n(%)	3(16.7)	3(20)	6(40)	0.804	0.134
3 ~ 7 n(%)	5(27.7)	11(73.3)	9(60)	0.009	0.062
7 ~ 12 n(%)	10(55.6)	1(6.7)	0	0.004	0.001
Gendern(%)				0.407	0.048
Male	7(38.9)	8(53.3)	11(73.3)		
Female	11(61.1)	7(46.7)	4(26.7)		
Clinical symptoms					
Cough n(%)	18(100)	12(80)	15(100)	0.083	/
Dry cough	14(77.8)	8(53.3)	14(93.9)	0.499	0.215
Expectoration	4(22.2)	4(46.7)	1(6.1)		
Vomitingn(%)	4(22.2)	2(13.3)	0	0.711	0.108
Diarrhean(%)	1(5.6)	1(6.7)	0	0.765	1.000
Duration (days)				/	/
Mean ± SD	12.6 ± 3.0	13.5 ± 5.3	10.7 ± 1.8		
Median	12(7 ~ 15)	13(7 ~ 25)	11(8 ~ 13)		
Body temperature (°C)				/	/
Mean ± SD	39.0 ± 1.1	38.5 ± 1.2	38.9 ± 0.9		
Median	39.0(36.5 ~ 40.3)	39.0(36.5 ~ 40.5)	39.0(36.8 ~ 40.0)		
Imaging changen(%)					

Note: * represents MP vs. BP; # represents MP vs. VP

Parameter	MP(n = 18)	BP(n = 15)	VP(n = 15)	*P* value*	*P*value#
Pulmonary consolidation	12(66.7)	4(26.7)	2(13.3)	0.022	0.002
unilateral consolidation	9(75)	2(50)	1(50)	0.350	0.469
bilateral consolidation	3(25)	2(50)	1(50)		
Laboratory examination					
WBC				< 0.0001	0.342
Mean ± SD	8.65 ± 3.42	22.32 ± 9.96	7.59 ± 2.78		
Median	8.12(4.73 ~ 17.29)	20.57(7.59 ~ 38.42)	7.19(2.18 ~ 14.52)		
0–3 years old				0.099	0.228
Mean ± SD	9.44 ± 4.19	14.80 ± 1.08	6.92 ± 1.79		
Median	10.84(4.73 ~ 12.75)	15.37(13.55 ~ 15.48)	6.27(5.22 ~ 9.95)		
3–7 years old				0.008	0.663
Mean ± SD	9.02 ± 4.97	24.79 ± 10.63	8.04 ± 3.31		
Median	7.32(5.07 ~ 17.29)	21.98(7.59 ~ 38.42)	7.25(2.18 ~ 14.52)		
7–12 years old				0.007	/
Mean ± SD	8.23 ± 2.60	17.7			
Median	8.02(4.75 ~ 13.45)	17.7			
NEU				< 0.0001	0.128
Mean ± SD	5.41 ± 2.88	17.11 ± 8.63	3.91 ± 2.52		
Median	4.85(2.06 ~ 13.68)	15.69(5.79 ~ 32.32)	3.81(0.74 ~ 11.21)		
0–3 years old				0.025	0.151
Mean ± SD	4.06 ± 1.79	9.83 ± 2.02	2.59 ± 1.02		

Note: * represents MP vs. BP; # represents MP vs. VP

Parameter	MP(n = 18)	BP(n = 15)	VP(n = 15)	*P* value*	*P*value#
Median	4.60(2.06 ~ 5.51)	8.87(7.92 ~ 11.81)	2.69(1.08 ~ 3.86)		
3–7 years old				0.007	0.618
Mean ± SD	5.81 ± 4.58	19.31 ± 8.99	4.80 ± 2.87		
Median	4.47(2.25 ~ 13.68)	18.44(5.79 ~ 32.32)	4.52(0.74 ~ 11.21)		
7–12 years old				0.002	/
Mean ± SD	5.61 ± 2.21	15.69			
Median	4.97(2.54 ~ 10.05)	15.69			
LYM				0.071	0.508
Mean ± SD	2.50 ± 1.39	3.56 ± 1.88	2.81 ± 1.29		
Median	1.99(1.49 ~ 6.68)	3.24(1.03 ~ 7.56)	2.51(0.90 ~ 5.30)		
0–3 years old				0.695	0.351
Mean ± SD	4.68 ± 2.37	4.02 ± 1.28	3.33 ± 1.68		
Median	5.29(2.06 ~ 6.68)	4.39(2.59 ~ 5.08)	3.07(0.9 ~ 5.3)		
3–7 years old				0.142	0.629
Mean ± SD	2.25 ± 0.44	3.67 ± 1.98	2.46 ± 0.90		
Median	2.21(1.84 ~ 2.96)	3.24(1.34 ~ 7.56)	2.44(1.14 ~ 3.86)		
7–12 years old				0.174	/
Mean ± SD	1.97 ± 0.60	1.03			
Median	1.74(1.49 ~ 3.47)	1.03			
MON				0.002	0.233
Mean ± SD	0.65 ± 0.32	1.49 ± 1.00	0.80 ± 0.35		
Median	0.61(0.32 ~ 1.64)	1.13(0.44 ~ 4.20)	0.79(0.29 ~ 1.73)		

Note: * represents MP vs. BP; # represents MP vs. VP

Parameter	MP(n = 18)	BP(n = 15)	VP(n = 15)	*P* value*	*P*value#
0–3 years old				0.057	0.154
Mean ± SD	0.52 ± 0.12	1.06 ± 0.33	0.95 ± 0.44		
Median	0.51(0.40 ~ 0.64)	0.88(0.85 ~ 1.44)	0.87(0.44 ~ 1.73)		
3–7 years old				0.155	0.395
Mean ± SD	0.87 ± 0.51	1.67 ± 1.11	0.69 ± 0.26		
Median	0.66(0.35 ~ 1.64)	1.16(0.44 ~ 4.20)	0.77(0.29 ~ 1.03)		
7–12 years old				0.261	/
Mean ± SD	0.59 ± 0.19	0.82			
Median	0.59(0.32 ~ 0.89)	0.82			
EO				0.305	0.677
Mean ± SD	0.078 ± 0.076	0.133 ± 0.208	0.067 ± 0.075		
Median	0.045(0 ~ 0.3)	0.06(0 ~ 0.8)	0.05(0 ~ 0.24)		
0–3 years old				0.728	0.023
Mean ± SD	0.18 ± 0.13	0.133 ± 0.172	0.032 ± 0.021		
Median	0.20(0.04 ~ 0.3)	0.06(0.01 ~ 0.33)	0.035(0 ~ 0.05)		
3–7 years old				0.548	0.497
Mean ± SD	0.06 ± 0.039	0.125 ± 0.232	0.09 ± 0.090		
Median	0.04(0.03 ~ 0.12)	0.01(1 ~ 0.8)	0.06(0 ~ 0.24)		
7–12 years old				0.012	/
Mean ± SD	0.056 ± 0.046	0.21			
Median	0.04(0 ~ 0.13)	0.21			
BA				0.280	0.999
Mean ± SD	0.02 ± 0.015	0.028 ± 0.030	0.02 ± 0.011		

Note: * represents MP vs. BP; # represents MP vs. VP

Parameter	MP(n = 18)	BP(n = 15)	VP(n = 15)	*P* value*	*P*value#
Median	0.01(0.01 ~ 0.06)	0.02(0 ~ 0.08)	0.02(0 ~ 0.04)		
0–3 years old				0.033	0.171
Mean ± SD	0.01 ± 0	0.057 ± 0.025	0.02 ± 0.011		
Median	0.01(0.01 ~ 0.01)	0.06(0.03 ~ 0.08)	0.02(0.01 ~ 0.03)		
3–7 years old				0.454	0.229
Mean ± SD	0.03 ± 0.019	0.021 ± 0.023	0.020 ± 0.011		
Median	0.03(0.01 ~ 0.06)	0.02(0 ~ 0.07)	0.02(0 ~ 0.04)		
7–12 years old				0.888	/
Mean ± SD	0.018 ± 0.013	0.02			
Median	0.01(0.01 ~ 0.05)	0.02			
PLT				< 0.0001	0.846
Mean ± SD	182.2 ± 45.9	349.9 ± 132.6	185.8 ± 58.8		
Median	178.5(97 ~ 276)	314(195 ~ 596)	188(108 ~ 296)		
MPV				0.226	0.345
Mean ± SD	10.08 ± 1.00	9.55 ± 1.17	9.71 ± 0.91		
Median	9.95(8.3 ~ 11.7)	9.7(7.9 ~ 11.5)	9.6(8 ~ 11)		
PDW				0.336	0.161
Mean ± SD	14.88 ± 2.75	13.97 ± 2.35	13.45 ± 2.78		
Median	16.25(9.3 ~ 17.5)	14.7(9.0 ~ 16.3)	14.4(8.7–17.4)		
CRP				0.081	0.059
Mean ± SD	9.39 ± 8.05	21.87 ± 27.28	3.64 ± 8.50		
Median	7.48(0.5 ~ 29.44)	9.3(0.5 ~ 100.8)	0.5(0.5 ~ 33.68)		
B2MG				0.022	0.081

Note: * represents MP vs. BP; # represents MP vs. VP

Parameter	MP(n = 18)	BP(n = 15)	VP(n = 15)	*P* value*	*P*value#
Mean ± SD	1.79 ± 0.36	1.38 ± 0.55	2.12 ± 0.61		
Median	1.64(1.39 ~ 2.72)	1.23(0.73 ~ 2.63)	2.11(1.17 ~ 3.05)		
DD				0.653	0.331
Mean ± SD	1.28 ± 2.75	0.69 ± 0.95	0.45 ± 0.12		
Median	0.485(0.29 ~ 0.72)	0.41(0.22 ~ 3.35)	0.43(0.3 ~ 0.68)		
PCT				0.137	0.357
Mean ± SD	0.69 ± 0.53	4.52 ± 10.67	0.52 ± 0.33		
Median	0.54(0.02 ~ 1.88)	0.50(0.05 ~ 36.24)	0.54(0.01 ~ 1.08)		
NLR				0.003	0.150
Mean ± SD	2.54 ± 1.63	6.11 ± 4.35	1.75 ± 1.40		
Median	2.07(0.82 ~ 7.13)	4.56(1.75 ~ 15.23)	1.54(0.31 ~ 4.59)		
0–3 years old				0.124	0.673
Mean ± SD	0.90 ± 0.09	2.70 ± 1.61	1.30 ± 1.52		
Median	0.87(0.82 ~ 1.00)	1.80(1.75 ~ 4.56)	0.74(0.31 ~ 4.29)		
3–7 years old				0.082	0.511
Mean ± SD	2.74 ± 2.49	6.21 ± 3.76	2.06 ± 1.32		
Median	1.88(0.97 ~ 7.13)	4.95(2.05 ~ 14.76)	1.73(0.65 ~ 4.59)		
7–12 years old				< 0.0001	/
Mean ± SD	2.94 ± 1.07	15.23			
Median	0.73(0.02 ~ 1.88)	15.23			
MLR				0.064	0.733
Mean ± SD	0.31 ± 0.18	0.47 ± 0.30	0.33 ± 0.22		

Note: * represents MP vs. BP; # represents MP vs. VP

Parameter	MP(n = 18)	BP(n = 15)	VP(n = 15)	*P* value*	*P*value#
Median	0.32(0.08 ~ 0.85)	0.35(0.20 ~ 1.30)	0.25(0.14 ~ 1.06)		
0–3 years old				0.051	0.262
Mean ± SD	0.13 ± 0.06	0.27 ± 0.06	0.38 ± 0.34		
Median	0.12(0.08 ~ 0.19)	0.28±(0.20 ~ 0.33)	0.26(0.16 ~ 1.06)		
3–7 years old				0.594	0.331
Mean ± SD	0.40 ± 0.26	0.49 ± 0.32	0.30 ± 0.12		
Median	0.36(0.15 ~ 0.85)	0.40(0.23 ~ 1.30)	0.25(0.14 ~ 0.47)		
7–12 years old				0.001	/
Mean ± SD	0.31 ± 0.10	0.80			
Median	0.34(0.10 ~ 0.45)	0.80			
PLR				0.061	0.721
Mean ± SD	85.26 ± 32.45	123.73 ± 76.17	80.31 ± 46.09		
Median	80.31(26.65 ~ 128.86)	91.55(29.37 ~ 328.36)	72.22(27.43 ~ 208.89)		
0–3 years old				0.371	0.667
Mean ± SD	35.82 ± 12.97	98.30 ± 32.72	84.01 ± 68.16		
Median	35.82(26.65 ~ 44.99)	83.86(75.29 ~ 135.76)	61.70(27.43 ~ 208.89)		
3–7 years old				0.292	0.949
Mean ± SD	85.77 ± 33.66	119.75 ± 79.12	77.85 ± 28.24		
Median	80.82(32.77 ~ 124.89)	91.55(29.37 ~ 328.36)	72.22(48.77 ~ 129.58)		
7–12 years old				< 0.0001	/
Mean ± SD	94.84 ± 26.38	243.69			
Median	96.22(56.48 ~ 128.86)	243.69			

Note: * represents MP vs. BP; # represents MP vs. VP

Parameter	MP(n = 18)	BP(n = 15)	VP(n = 15)	*P* value*	*P*value#
MPV/PLT				0.0002	0.824
Mean ± SD	0.060 ± 0.022	0.032 ± 0.014	0.058 ± 0.022		
Median	0.053(0.034 ~ 0.118)	0.028(0.013 ~ 0.057)	0.055(0.031 ~ 0.099)		
NMR				0.003	0.020
Mean ± SD	8.54 ± 3.07	12.75 ± 4.31	5.56 ± 3.90		
Median	8.18(4.62 ~ 15.28)	13.16(6.16 ~ 19.24)	4.32(1.59 ~ 14.56)		
0–3 years old				0.520	0.020
Mean ± SD	7.71 ± 2.86	9.68 ± 3.91	3.17 ± 1.78		
Median	7.19(5.15 ~ 10.80)	9.00(6.16 ~ 13.89)	2.86(1.59 ~ 5.75)		
3–7 years old				0.003	0.701
Mean ± SD	6.38 ± 1.56	13.01 ± 4.00	7.16 ± 4.18		
Median	6.43(4.68 ~ 8.34)	13.16(7.37 ~ 19.24)	6.77(2.55 ~ 14.56)		
7–12 years old				0.021	/
Mean ± SD	9.87 ± 3.18	19.13			
Median	9.70(4.62 ~ 15.28)	19.13			
Note: * represents MP vs. BP; # represents MP vs. VP					

Laboratory examination showed thatthe children with BP had significantly increasedindicators than the children with MP.WBC was higher inthe children with BPthan in the children with MP (22.32×10^9/L vs. 8.65×10^9/L,$P < 0.0001$).Compared to 0–3-year-old group,the 3–7-year-old group (24.79×10^9/L vs. 9.02×10^9/L, $P = 0.008$) and the 7–12-year-old group (17.7×10^9/L vs. 8.23×10^9/L, $P = 0.007$) both hadsignificant difference. NEU was higher inthe children with BPthan in the children with MP(17.11×10^9/L vs. 5.41×10^9/L, $P < 0.0001$), and was significantly different in 0–3-year-old group(9.83×10^9/L vs. 4.06×10^9/L, $P = 0.025$), 3–7-year-old group (19.31×10^9/L vs. 5.81×10^9/L, $P = 0.007$), 7–12-year-old group (15.69×10^9/L vs. 5.61×10^9/L, $P = 0.002$).MON was higher inthe children with BPthan in the children with MP(1.49×10^9/L vs. 0.65×10^9/L, $P = 0.002$), buteach age group had no significant difference;PLT was higher inthe children with BPthan in the children with MP(349.9×10^9/L vs. 182.2×10^9/L, $P < 0.0001$); NLR was higher inthe children with BPthan in the children with MP(6.11 vs. 2.54, $P =$

0.003),andthere wassignificant difference in the7–12-year-old group (15.23 vs. 2.94, $P < 0.0001$), while the 0–3-year-old group and the 3–7-year-old grouphad no significant difference;NMR was higher inthe children with BPthan in the children with MP(12.75 vs. 8.54, $P = 0.003$), and there was significant differenceinthe 3–7-year-old group(13.01 vs. 6.38, $P = 0.003$) and the 7–12-year-old group (19.13 vs. 9.87, $P = 0.021$), while the 0–3-year-old group hadno significant difference.The indicators of B2MG (1.38 μg/L vs. 1.79 μg/L, $P = 0.022$) and MPV/PLT (0.032 vs. 0.06, $P = 0.0002$) were lower in the children with BP than in those with MP.

The children with BP and those with MP hadno significant differences in gender, dry cough or expectoration, vomiting, diarrhea, duration of disease and body temperature change;and had no significant differences inLYM, EO, BA, MPV, PDW, CRP, DD, PCT, MLR and PLR.

3. Comparison of clinical parameters between children with MP and VP

The difference of clinical parameters between the children with MP and VP was shown in Table 1. The age of 8-year-old children with MP (IQR2–12)is older than that of 3-year-old children with VP (IQR 1–6), and the difference was statistically significant ($P = 0.002$), of which the age of VP onset was 3–7 years old ($P = 0.062$), and the age of MP onset was 7–12 years old ($P = 0.001$). It is noteworthy that the incidence of VP in the 0–3-year-old group was 40%, higher than that in the MP group (16.7%) and BP group (20%) ($P = 0.134$). The incidence of males in the children with VP was higher than that in the children with MP ($P = 0.048$).From the imaging characteristics, the children with MP were more likely to have pulmonary consolidation ($P = 0.002$).Thechildren with MP included12 cases (66.7%) ofpulmonary consolidation, whilethe children with VP included 2cases (13.3%)ofpulmonary consolidation, but there was no significant difference between unilateral and bilateral pulmonary consolidation ($P = 0.469$).

Laboratory examination showed that the blood cell analysis data of the MP group were similar to those ofthe VP group, except that the NMR ratio in the MP group was significantly increased (8.54 vs. 5.56, $P = 0.020$).After being further grouped by age, there was significant difference in the 0–3-year-old group(7.71 vs. 3.17, $P = 0.020$), but not in the 3–7-year-old group.The CRP value7.48 (IQR 0.5–29.44) of the children with MP was significantly higher than 0.5 (IQR0.5–33.68) that of the children with VP ($P = 0.0586$).

The children with VP and MP hadno significant differences in gender, dry cough or expectoration, vomiting, diarrhea, duration of disease and body temperature change.Laboratory examination data showed that the children with VP and MP hadno significant differences in WBC, NEU,LYM, MON, EO, BA, PLT, MPV, PDW, DD, B2MG,PCT, NLR, MLR,PLR andMPV/PLT.

4. NMR levels were significantly different in children with MP, BP and VP

The children with MP and BPhad significant difference in the levels of WBC, NEU, MON, PLT, NLRand NMR ($P < 0.05$), with higher levels in the children with BP. The children with MP and BPhad significantly

difference in the levels of B2MG and MPV/PLT($P < 0.05$), with higher levels in the children with MP.The children with BP and VPhad significant difference in the levels of WBC, NEU, MON, PLT, CRP, NLRand NMR ($P < 0.05$), with higher levels in the children with BP. The children with BP and VP had significant difference in the levels of B2MG and MPV/PLT($P < 0.05$), with higher levels in the children with VP.The children with MP and VPhad significant difference in the NMR level($P < 0.05$),with higher levelin the children with MP.In summary, the average levels of NMR in the children with MP, BP and VPwere 8.54, 12.75 and 5.56, respectively, and showed significant difference between the children withMP and BP, between the children withMP and VP, and between the children withBP and VP ($P < 0.05$)(Fig. 1).

5. NMR may be used as an indicatorfor differential diagnosis of MP, BP and VP

Next we analyzedWBC, NEU, LYM, MON, PLT, CRP, B2MG, NLR, MLR, PLR, MPV/PLT and NMR indicatorsforthedifferential diagnosis of MP, BP and VP. Only the area under the curve (AUC) areas of NMR diagnosis of MP, BP and VPwas greater than 0.70, with good accuracy and diagnostic value. When MPwas compared with BP, the AUC of NMR was 0.77; when MP was compared with VP, the AUC was 0.78; when BP was compared with VP, the AUC was 0.90.The cutoff value of diagnosis of MP and BP was 8.4577, and that of diagnosis of MP and VP was 4.5041 (Fig. 2).

6. Effectivediagnosis of MP, BP and VP by combining NMR, children age, and pulmonary consolidation

By combining NMR level, childrenage, and pulmonary consolidation information,the AUC area of MP, BP and VP was allgreater than 0.90, and hadgood accuracy and diagnostic value(Fig. 3).

Discussion

MP is an atypical bacterial infectionpneumonia, and its clinical symptoms are difficult to distinguish from bacterial and viral pneumonia. Due to the lack of cell walls, mycoplasma pneumoniae is naturally resistant to β-lactam antibiotics, which is totally different from the useof antibiotics for treating bacterial pneumonia.Pediatricians commonly treat pneumonia with the combined use of cephalosporin and macrolide antibiotics, which has led to a rise in the proportion of mycoplasma pneumoniae resistant to macrolide antibiotics in recent years[21, 22].Therefore, early diagnosis of the pathogen type of pneumonia and timely adoption of targeted therapeutic plan can not only effectively improve drug resistance of pathogens, but also reduce the treatment costs of patients, and reduce the incidence of side effects caused by combination of drugs.

The diagnosis methods for MP mainly include serological detection of antibody, PCR detection of pathogen nucleic acid, but these methods take some time and are of little help to early diagnosis. As a routine examination item, blood cell analysis has become the most commonly used examination indicator in the auxiliary diagnosis of diseases. The indicators and related ratios in the blood cell analysis are closely related to inflammatory infection and even tumor prognosis.

We found that the levels of WBC, NEU, MON, PLT, NLR, MPV/PLT and NMR in the children with BP were significantly higher than those in the children with MP and VP, the NMR level in the children with MP was significantlyhigher than that in the children with VP. The NMR levels in the three groups of children were different. Because the virulence of bacterial infection is higher, thevirulence of mycoplasma and viral infectionsis lower, and inflammatory response in human body depends on the virulence of the pathogen, bacterial infection leads to higher production ofinflammatory factors in human body than mycoplasma and virus [23].Among the indicators of blood cell analysis,NEU and MONare recognized inflammatory factorsclosely related to the nature of infection and the prognosis of the disease. In the patients with bacterial infection, the level of neutrophils is generally elevated[24];in the patients with viral infection, the level of monocytes is generallyelevated[25], in the patients with mycoplasma pneumoniae infection, the level of neutrophils is generally elevated, but the increase is lower than that of the patients with bacterial infection [26]. Therefore, the level of NEU/MON ratio is significantly different in the children with MP, BP and VP.

It is well known that the level of neutrophils is increased significantly during bacterial infection, and NMR can differentiate BP from non-BP depending on the absolute value of NEU. Our results showed that the changes of blood cells in the children with MP and BP were similar. NMR can differentially diagnose MP and VP, not only depending on the difference of the change of NEU but also depending on MON. Monocyte is the largest blood cell in the blood, andbelieved as the precursor of macrophage. Monocytes phagocytize and remove injured and aging cells and their fragments, but the specificity is not strong. Monocytes also participate in the immune response. After phagocytosis of antigens, they transfer the carried antigenic determinants to lymphocytes and induce specific immune response of the lymphocytes. Monocytes are also the main cell defense system against pathogenic bacteria and parasites in cells, and have the ability to recognize and kill tumor cells.NLR has been proved to be an auxiliary diagnostic indicator of inflammation and infection, but we found no significant differenceinlymphocytesbetweenchildren with MP and BP in the early stage of infection.Lymphocytesare the cells with specific immune function in the body, are the main component of cellular immunity, and have strong specificity. Among them, T lymphocytes mainly participate in cellular immune response, while B lymphocytes participate in humoral immune response. As the pathogen of MP, mycoplasma pneumoniaehas no cell walls. Therefore, the antibioticsaiming at the inhibition of bacterial cell wall synthesis are ineffective against mycoplasma pneumonia.At present, macrolide antibiotics are generally recognized as the first choice drug in the treatment of MP. The mechanism of action is to inhibit the synthesis of bacterial proteins, but they have strong side effects, and“medication and stop ofmedication”may be one of the reasons for repeated infections. In summary, because mycoplasma pneumoniaehas nocell walls andantibiotic treatment is time-limited, it is easy to be colonized andcauses repeated infections when the body’s immunity is low. As the most phagocytic cells in blood cells, monocytesplay a role in the early stage of pathogens invading the body, while lymphocytes cannot play a clearing role until they undergo antigen presentation and other processes, which may be the keyreason for the differential diagnosis of MP, BP and VP byNMR.

According to the standard that the area under theROC curve is greater than 0.70,NMR can effectively differentiate MP, BP and VP. In addition, NMR combined with pulmonary consolidation and children age (high incidence at 3–7 years old) have a high accuracy in the diagnosis of MP, and the AUC is greater than 0.9.

In conclusion, as a comprehensive indicator of neutrophils and monocytes, NMR maydifferentiatepneumonia caused by mycoplasma pneumoniae, bacterial and viral infections, which providesnew direction for the differential diagnosis of pneumonia.

Abbreviations

MPP: mycoplasma pneumoniae pneumonia;BP: bacterial pneumonia;VP: viral pneumonia;WBC: white blood cell count;NEU: absolute neutrophil count;MON: absolute monocyte count;PLT: platelet count; NLR: neutrophil/lymphocyte ratio;MPV/PLT: mean platelet volume/platelet count; NMR: neutrophil/monocyte ratio; CAP: community-acquired pneumonia.

Declarations

Ethics approval and consent to participate

This research was approved by the Ethical Committee of the affiliated Jiangning hospital of Nanjing Medical University

Consent for publication

Informed consent was obtained from all individual participants included in the study.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no conflict of interest.

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Authors' Contributions

Yan Li and Shasha Yao designed the experiments. Yan Li analyzed the corresponding results. Shasha Yao performed all experiments and analyzed the results with Yao Xie and Fei Chen. Shasha Yao wrote the paper. Fei Chen provided resources. Xiao Chen and Miao Zhang revised the paper.

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Not applicable.

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Figures

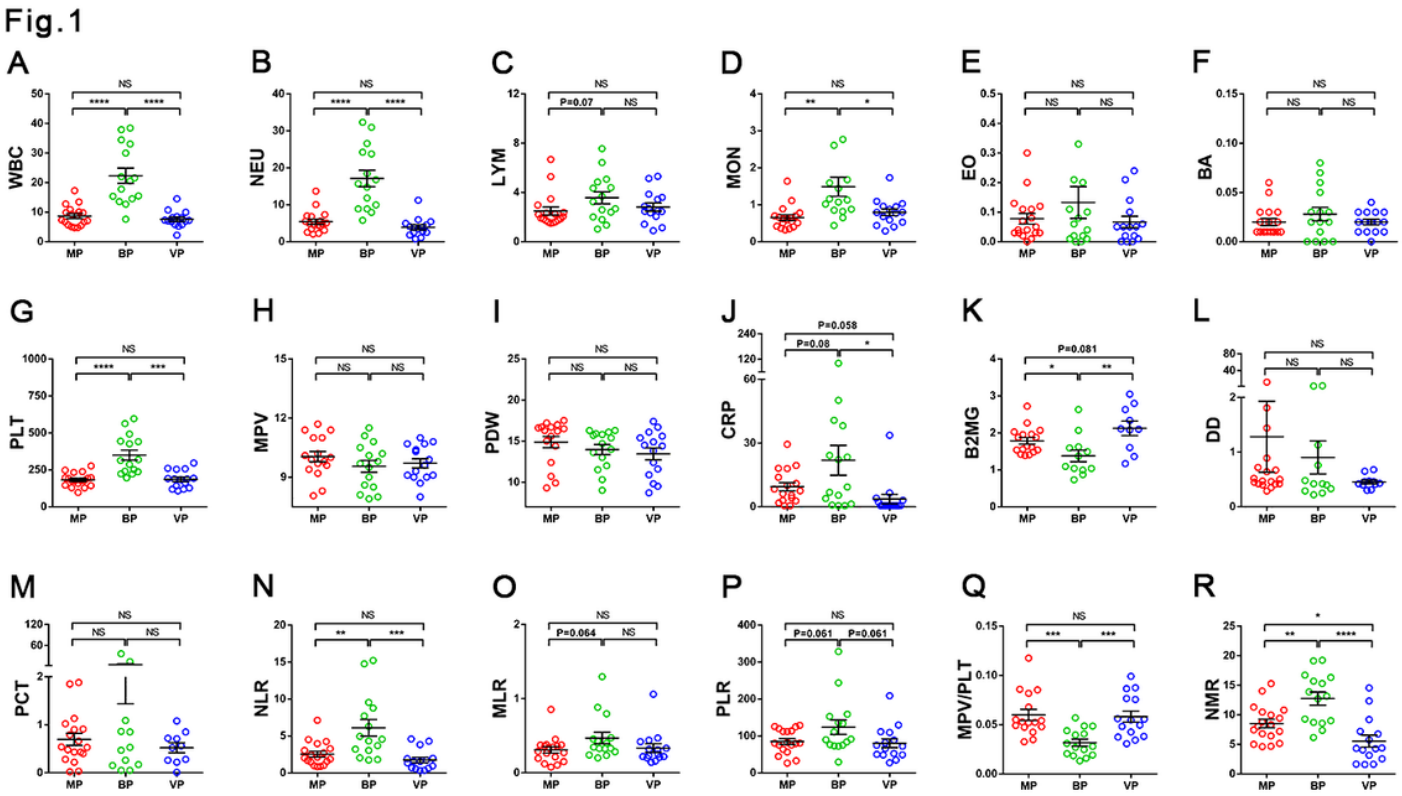

Figure 1

NMR levels were significantly different in children with MP, BP and VP

Fig.2

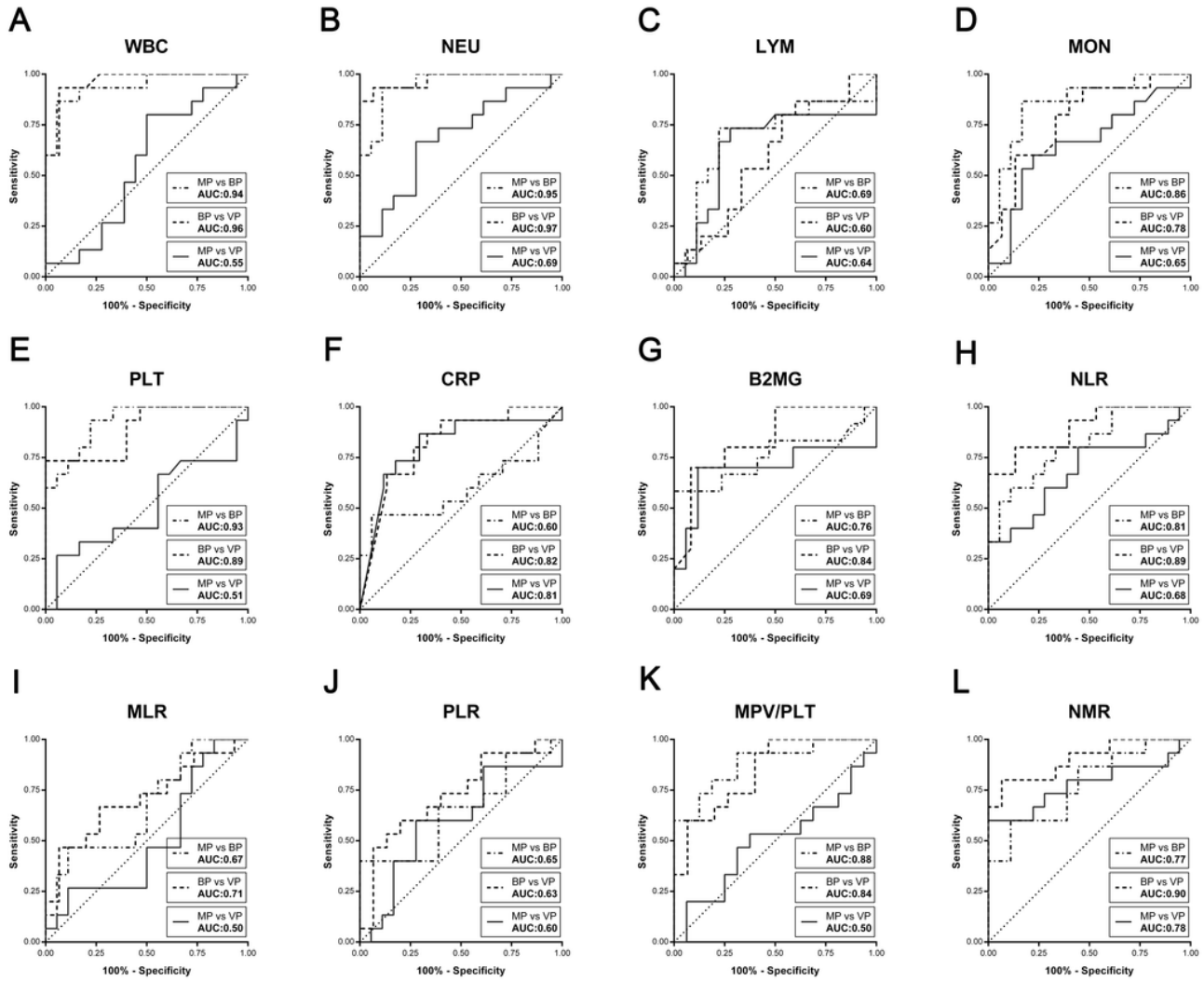

Figure 2

NMR may be used as an indicatorfor differential diagnosis of MP, BP and VP

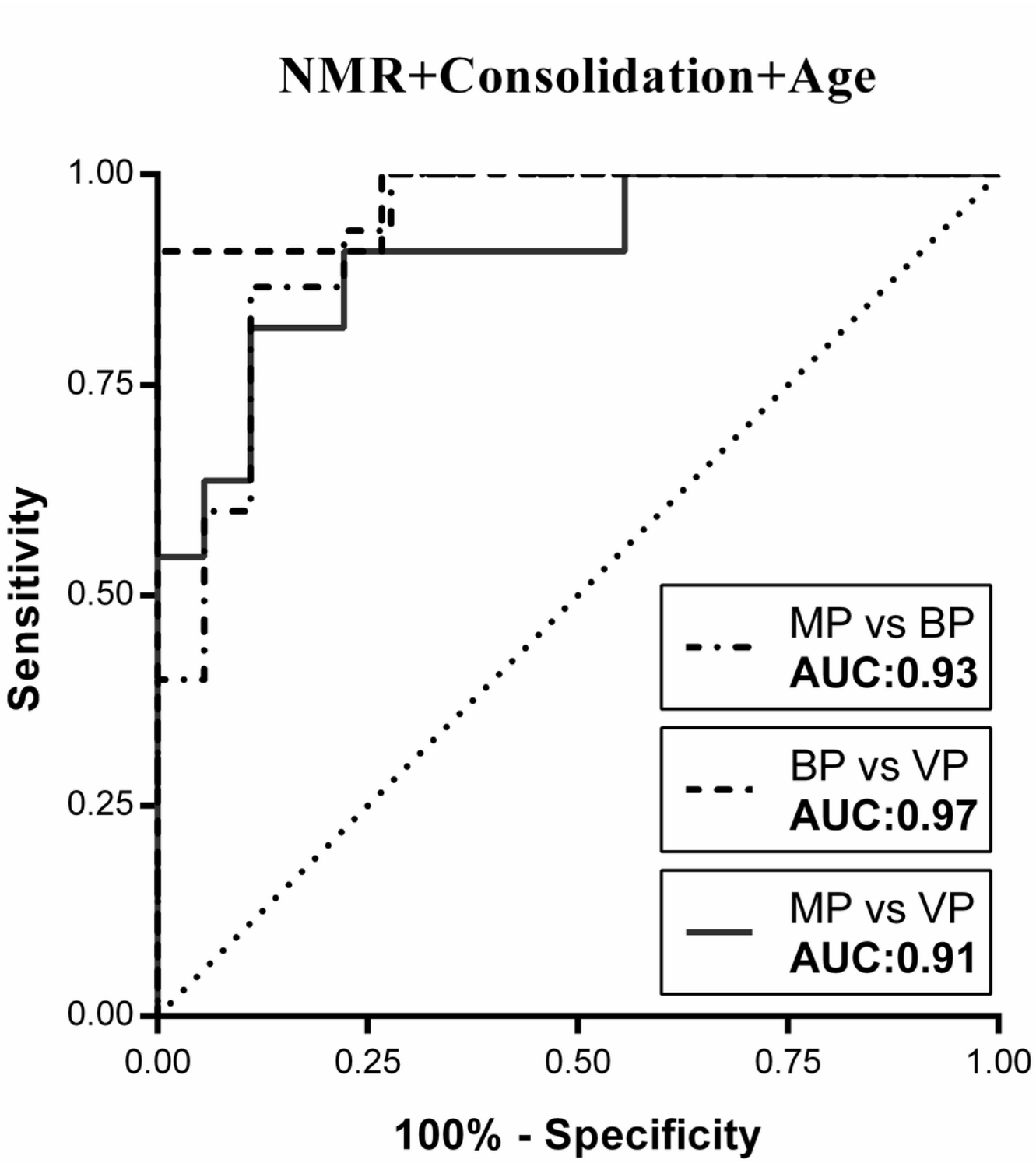

Figure 3

Effectivediagnosis of MP, BP and VP by combining NMR, children age, and pulmonary consolidation