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 with MP and children with viral pneumonia (VP), the NMR level in children with MP was higher than that of children with VP, the NMR levels in the three groups of children were significantly different (\( P<0.05 \)). Combined with the NMR level, the children's age and pulmonary consolidation information, the AUC areas of MP, BP and VP had high accuracy for differential 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% of CAP worldwide [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 indicator for 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 PCR method 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 indicators of 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 Jiangning Hospital 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 “ZhuFutang Practice of Pediatrics (8th Edition)” [20];

(3) The children with positive mycoplasma pneumoniae nucleic acid were screened from the children who received the multiplex PCR nucleic acid detection of respiratory pathogens and were included as MP group;

(4) The positive cases of bacterial culture were screened from the children who received the sputum culture detection and were included as BP 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 who received the multiplex PCR nucleic acid detection of respiratory pathogens and were included as VP 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. The independent sample t-test or t’test was used to compare the blood cell indicators of various groups; the ranksum test was used to compare the non-normal distribution groups; the χ² test or Fisher’s exact probability test was used for the correlation analysis between the blood cell indicators and 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 CAP of which 26 cases received bacterial culture detection and 38 cases received multiplex PCR detection of 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 in VP group (31.25%). The 8 children with MP were positive for respiratory pathogen multiplex PCR detection but negative for the detection 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 with VP received the multiplex PCR detection of respiratory pathogens, and influenza A virus RNA was positive in 2 cases, influenza B virus RNA was positive in 8 cases, respiratory syncytial virus RNA was positive in 5 cases, adenovirus DNA was positive in 1 case, rhinovirus RNA was 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 (IQR 2–9), 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 MP included 12 cases (66.7%) of pulmonary consolidation, while the children with BP included 4 cases (26.7%) of pulmonary consolidation, but there was no significant difference between unilateral and bilateral pulmonary consolidation \( (P = 0.35) \).
| 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        |
| Gender (%)                      |            |            |            | 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)     |              |              |
| Vomiting n(%)                   | 4(22.2)    | 2(13.3)    | 0          | 0.711        | 0.108        |
| Diarrhea n(%)                   | 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 change n(%)             |            |            |            |              |              |

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

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 ~ | 0.88(0.85 ~ | 0.87(0.44 ~ |            |            |
|                 | 0.64)       | 1.44)       | 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 ~ | 1.16(0.44 ~ | 0.77(0.29 ~ |            |            |
|                 | 1.64)       | 4.20)       | 1.03)       |            |            |
| 7–12 years old  |             |             |             | 0.261      | /          |
| Mean ± SD       | 0.59 ± 0.19 | 0.82        |             |            |            |
| Median          | 0.59(0.32 ~ | 0.82        |             |            |            |
|                 | 0.89)       |             |             |            |            |
| 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       | < 182.2 ± 45.9 | 349.9 ± 132.6 | 185.8 ± 58.8 |          | 0.846      |
| Mean ± SD | 178.5 (97 ~ 276) | 314 (195 ~ 596) | 188 (108 ~ 296) |          |            |
| Median    | 9.55 ± 1.17 | 9.71 ± 0.91 |          |            |            |
| MPV       | 10.08 ± 1.00 | 9.7 (7.9 ~ 11.5) | 9.6 (8 ~ 11) | 0.226      | 0.345      |
| 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) |          |            |
| PDW       | 0.336 | 0.161 |          |            |            |
| 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) | 0.051      | 0.262      |
| 0–3 years old |          |           |           |            |            |
| 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 |          |           |           | <          | /          |
| Mean ± SD | 94.84 ± 26.38 | 243.69    |           | 0.0001     |            |
| 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 that the children with BP had significantly increased indicators than the children with MP. WBC was higher in the children with BP than 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 had significant difference. NEU was higher in the children with BP than 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 in the children with BP than in the children with MP (1.49 × 10^9/L vs. 0.65 × 10^9/L, P = 0.002), but each age group had no significant difference; PLT was higher in the children with BP than in the children with MP (349.9 × 10^9/L vs. 182.2 × 10^9/L, P < 0.0001); NLR was higher in the children with BP than in the children with MP (6.11 vs. 2.54, P =
0.003), and there was a significant difference in the 7–12-year-old group (15.23 vs. 2.94, \( P<0.0001 \)), while the 0–3-year-old group and the 3–7-year-old group had no significant difference; NMR was higher in the children with BP than in the children with MP (12.75 vs. 8.54, \( P=0.003 \)), and there was a significant difference in the 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 had no 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 had no significant differences in gender, dry cough or expectoration, vomiting, diarrhea, duration of disease and body temperature change; and had no significant differences in LYM, 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 (IQR 2–12) 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 (\( P=0.002 \)). The children with MP included 12 cases (66.7%) of pulmonary consolidation, while the children with VP included 2 cases (13.3%) of pulmonary 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 of the 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 value (7.48 (IQR 0.5–29.44)) of the children with MP was significantly higher than 0.5 (IQR 0.5–33.68) that of the children with VP (\( P=0.0586 \)).

The children with VP and MP had no 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 had no significant differences in WBC, NEU, LYM, MON, EO, BA, PLT, MPV, PDW, DD, B2MG, PCT, NLR, MLR, PLR and MPV/PLT.

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

The children with MP and BP had significant difference in the levels of WBC, NEU, MON, PLT, NLR and NMR (\( P<0.05 \)), with higher levels in the children with BP. The children with MP and BP had 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 VP had significant difference in the levels of WBC, NEU, MON, PLT, CRP, NLR and 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 VP had significant difference in the NMR level ($P < 0.05$), with higher level in the children with MP. In summary, the average levels of NMR in the children with MP, BP and VP were 8.54, 12.75 and 5.56, respectively, and showed significant difference between the children with MP and BP, between the children with MP and VP, and between the children with BP and VP ($P < 0.05$) (Fig. 1).

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

Next we analyzed WBC, NEU, LYM, MON, PLT, CRP, B2MG, NLR, MLR, PLR, MPV/PLT and NMR indicators for the differential diagnosis of MP, BP and VP. Only the area under the curve (AUC) areas of NMR diagnosis of MP, BP and VP was greater than 0.70, with good accuracy and diagnostic value. When MP was 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, children age, and pulmonary consolidation information, the AUC area of MP, BP and VP was all greater than 0.90, and had good accuracy and diagnostic value (Fig. 3).

Discussion

MP is an atypical bacterial infection pneumonia, 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 use of 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 significantly higher 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, the virulence of mycoplasma and viral infections is lower, and inflammatory response in human body depends on the virulence of the pathogen, bacterial infection leads to higher production of inflammatory factors in human body than mycoplasma and virus [23]. Among the indicators of blood cell analysis, NEU and MON are recognized inflammatory factors closely 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 generally elevated [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, and it is believed 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 difference in lymphocytes between children with MP and BP in the early stage of infection. Lymphocytes are 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 pneumoniae has no cell walls. Therefore, the antibiotics aiming 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 of medication" may be one of the reasons for repeated infections. In summary, because mycoplasma pneumoniae has no cell walls and antibiotic treatment is time-limited, it is easy to be colonized and causes repeated infections when the body's immunity is low. As the most phagocytic cells in blood cells, monocytes play 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 key reason for the differential diagnosis of MP, BP and VP by NMR.
According to the standard that the area under the ROC 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 may differentiate pneumonia caused by mycoplasma pneumoniae, bacterial and viral infections, which provides new 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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Figure 1

NMR levels were significantly different in children with MP, BP and VP
Figure 2

NMR may be used as an indicator for differential diagnosis of MP, BP and VP.
Figure 3

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