RESEARCH ARTICLE

# The value of routine blood parameters, serum amyloid A and C-reactive protein in the diagnosis of respiratory tract infections in pregnant women

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**The diagnosis of respiratory tract infections in pregnant women is particularly challenging due to the limitations of radiographic imaging and the urgency to avoid unnecessary antibiotic exposure. Biomarkers that can reliably indicate infection etiology are highly needed. This research investigated whether a combination of routine blood parameters, serum amyloid A (SAA), and C-reactive protein (CRP) could serve as an effective diagnostic tool for this vulnerable population. The study compared the differences in routine blood parameters, SAA, and CRP between pregnant women infected with influenza virus and *Mycoplasma pneumoniae* and identified evidence for the differential diagnosis of respiratory infections during pregnancy. A total of 300 clinical cases of pregnant women aged 21 - 40 years with respiratory infections, who were admitted to Shandong Provincial Maternal and Child Health Care Hospital from October 2023 to May 2024, were collected and retrospectively analyzed. Patients were categorized into first trimester group (n = 93), second trimester group (n = 128), and third trimester group (n = 79) based on gestational age, and further divided into influenza group (n = 98), *Mycoplasma pneumoniae* group (n = 34), and influenza and *Mycoplasma pneumoniae* co-infection group (n = 168) according to pathogen type. Differences in hematological parameters, SAA, and CRP were compared across groups. The results showed that, with the increase in gestational weeks, leukocyte (WBC), neutrophil (N), and CRP significantly increased, while platelet count (PLT) decreased ($P < 0.05$). The co-infection group exhibited younger maternal age, a higher peak body temperature ($P < 0.05$), the lowest absolute lymphocyte count (L), and the highest levels of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and CRP ($P < 0.05$). Receiver operating characteristic (ROC) results demonstrated that N, NLR, and PLR had higher diagnostic efficacy for influenza, while L, PLR, and CRP had significant diagnostic value for *Mycoplasma pneumoniae*, and the combination of L, N, NLR, PLR, and CRP improved diagnostic accuracy for co-infections. Hematological and inflammatory markers in pregnancy-related respiratory infections correlated with gestational age and pathogen type. Combined detection of SAA, CRP, and routine blood parameters could aid early differential diagnosis.**

**Keywords:** influenza; *Mycoplasma pneumoniae*; routine blood parameters; Serum Amyloid A; C-Reactive Protein.

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## Introduction

Respiratory tract infections (RTIs) during pregnancy are a common clinical issue affecting maternal and fetal health. Due to alterations in

physiological state, pregnant women are more susceptible to respiratory pathogens. Various pathogens including the influenza virus and *Mycoplasma pneumoniae* can cause these infections. Influenza, an acute highly contagious respiratory illness caused by the influenza virus, is characterized by abrupt onset and significant symptoms, while *Mycoplasma pneumoniae* is primarily transmitted through respiratory droplets with an incubation period ranging from 4 days to 3 weeks [1]. *Mycoplasma pneumoniae* infection of the respiratory tract can lead to acute upper respiratory tract infections, acute bronchitis, bronchiolitis, community-acquired pneumonia, and exacerbations of bronchial asthma [2]. Untimely diagnosis or inappropriate management may lead to severe complications such as pneumonia and acute respiratory distress syndrome (ARDS) and even increase the risk of adverse pregnancy outcomes including preterm birth and low birth weight infants.

Currently, the diagnosis of respiratory infections relies on clinical symptoms, imaging examinations, and etiological testing. However, the application of radiological examinations such as computed tomography (CT) is strictly limited in pregnant women. While etiological tests like viral culture or nucleic acid amplification offer high specificity, they are often time-consuming or costly, which limits their applications in rapid clinical decision-making. Therefore, identifying rapid and reliable serological auxiliary diagnostic markers is crucial. Inflammatory biomarkers such as C-reactive protein (CRP) and serum amyloid A (SAA), which are key acute-phase proteins in the body's response to infection and inflammation [3], are widely used for the differential diagnosis of infectious diseases in non-pregnant populations. Concurrently, routine blood parameters such as white blood cell count (WBC), neutrophil percentage (NEUT%), lymphocyte percentage (LYMPH%), and platelet count (PLT) are also commonly used indicators for the preliminary clinical assessment of infection status. Novel inflammation markers derived from routine blood tests such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been found to reflect inflammatory status and disease progression, and these markers have been extensively studied clinically [4-6]. Although the value of those biomarkers has been widely validated in general patient populations, their diagnostic efficacy in the special demographic of pregnant women is not yet fully elucidated. The physiological inflammatory state of pregnancy and inherent changes in hematological indices may influence the response patterns and cut-off values of these markers during infection [7]. Furthermore, existing research predominantly focuses on single indicators, lacking a comprehensive evaluation and comparison of the combined use of routine blood parameters, SAA, and CRP in differentiating the etiological types of respiratory infections in pregnant women caused by bacterial, viral, or atypical pathogen infections.

This study aimed to systematically investigate the clinical value of routine blood parameters, SAA, and CRP in diagnosing respiratory tract infections in pregnant women with a focused analysis on the diagnostic efficacy of these indicators and their combinations in differentiating influenza, *Mycoplasma pneumoniae*, and co-infections. The research retrospectively included pregnant women diagnosed with respiratory tract infections and categorized them into influenza, *Mycoplasma pneumoniae*, co-infection, and control groups based on etiological test results. Routine blood parameters, SAA, and CRP levels were measured in all subjects. Receiver operating characteristic (ROC) curves were plotted, and the area under the curve (AUC) was calculated to assess the sensitivity, specificity, and optimal cut-off values for each indicator, thereby providing a comprehensive evaluation of their diagnostic value. The findings of this study would provide important evidence-based medical support for the early and rapid auxiliary diagnosis of respiratory tract infections in pregnant women. By validating the application value of a panel of readily accessible and rapidly measurable serological indicators, this study could assist clinicians in making more timely and accurate

etiological inferences and therapeutic decisions while avoiding unnecessary radiation exposure and antibiotic misuse, ultimately improving clinical outcomes for both mothers and fetuses.

## Materials and methods

### Study subjects

Clinical data of 300 pregnant women with respiratory infections who were admitted to the Shandong Provincial Maternal and Child Health Care Hospital from October 2023 to May 2024 were collected. The patients were divided into three groups based on the stage of pregnancy including first trimester group (n = 93), aged 21 - 39 years with a mean age of 29.29 ± 3.71 years; second trimester group (n = 128), aged 22 - 37 years with a mean age of 29.06 ± 3.30 years; and third trimester group (n = 79), aged 22 - 40 years with a mean age of 30.77 ± 4.40 years. Based on the type of pathogen, the patients were further divided into influenza group (n = 98), *Mycoplasma pneumoniae* group (n = 34), and influenza combined with *Mycoplasma pneumoniae* group (n = 168). The inclusion criteria were positive influenza antigen, nucleic acid test, or influenza virus culture; positive *Mycoplasma pneumoniae* antigen, antibody, nucleic acid test, or *Mycoplasma pneumoniae* culture. The clinical characteristics and routine blood parameters, SAA, and CRP levels were analyzed to explore the differences in these indicators between influenza and *Mycoplasma pneumoniae* infections. All procedures of this research were approved by the IRB Committee of Shandong Provincial Maternal and Child Health Care Hospital, Jinan, Shandong, China.

### Data collection

The general information of all enrolled patients was collected, and differences in clinical characteristics among different groups were analyzed. Clinical data including gestational age, body temperature, and clinical symptoms were documented at the time of patient enrollment. Peripheral venous blood samples were obtained from all patients prior to the initiation of any medication. Hematological parameters, SAA, and CRP tests were performed by the clinical laboratory of Shandong Provincial Maternal and Child Health Care Hospital (Jinan, Shandong, China). Various parameters of the complete blood count (CBC) were recorded, and the neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR) were calculated. The relationships between these indicators and gestational age as well as the types of infectious pathogens were analyzed.

### Statistical analysis

SPSS 23.0 software (IBM, Armonk, New York, USA) was employed to process and analyze the collected data. The normality of all continuous data was assessed using the Shapiro-Wilk test. The measurement data conforming to a normal distribution were expressed as mean ± standard deviation (x ± s), and t-tests were used for analysis. Differences between multiple groups were compared using one-way analysis of variance (ANOVA). Data not conforming to a normal distribution were expressed as medians and interquartile ranges and analyzed using rank-sum tests. Count data were expressed as percentages (%) and analyzed using chi-square tests. Receiver operating characteristic (ROC) curve analysis was performed to calculate the area under the curve (AUC) for each indicator and its ratio, thereby evaluating their diagnostic utility in differentiating influenza and *Mycoplasma pneumoniae* infections. *P* value less than 0.05 was set as statistical significance.

## Results

### Gestational stages and types of infectious pathogens

Based on gestational age, patients were categorized into three groups of first trimester, second trimester, and third trimester. Differences among the three groups regarding influenza infection, mycoplasma infection, and co-infection with both influenza and mycoplasma were compared. The chi-square value was 0.567

**Table 1.** Association between gestational stages and infection markers.

| Indicator | First trimester (n = 93) | Second trimester (n = 128) | Third trimester (n = 79) | *P* value |
|---|---|---|---|---|
| WBC (×10$^9$/L) | 7.21 ± 2.52 | 8.71 ± 2.86 | 9.21 ± 3.05 | 0.000 |
| PLT (×10$^9$/L) | 227.26 ± 52.67 | 216.63 ± 52.87 | 202.91 ± 50.26 | 0.010 |
| L (×10$^9$/L) | 0.91 ± 0.50 | 0.93 ± 0.52 | 0.90 ± 0.45 | 0.910 |
| M (×10$^9$/L) | 0.58 ± 0.19 | 0.75 ± 0.99 | 0.65 ± 0.25 | 0.165 |
| N (×10$^9$/L) | 5.67 ± 2.27 | 7.07 ± 2.61 | 7.59 ± 2.96 | 0.000 |
| NLR | 8.58 ± 8.61 | 10.50 ± 9.13 | 11.16 ± 9.22 | 0.137 |
| LMR | 1.71 ± 1.10 | 1.62 ± 1.08 | 1.58 ± 0.92 | 0.694 |
| PLR | 324.79 ± 226.37 | 305.85 ± 213.77 | 277.35 ± 152.23 | 0.313 |
| SAA (mg/L) | 55.01 ± 68.27 | 55.22 ± 80.43 | 71.08 ± 100.68 | 0.342 |
| CRP (mg/L) | 18.83 ± 18.08 | 23.23 ± 20.48 | 30.07 ± 27.76 | 0.004 |

with a *P* value of 0.967, indicating no significant difference in the types of infectious pathogens across different stages of pregnancy.

**Association between gestational stages and infection markers**

Patients were stratified based on gestational weeks to analyze differences in routine blood parameters, SAA, and the CRP levels across groups. The results demonstrated that, with advancing gestational weeks, leukocyte count, neutrophil count (N), and CRP levels significantly increased, while platelet count (PLT) markedly decreased with statistically significant differences ($P < 0.05$) (Table 1).

**Pathogen groups and clinical characteristics**

Based on the type of infectious pathogen, patients were divided into three groups of influenza, *Mycoplasma pneumoniae*, and influenza combined with *Mycoplasma pneumoniae* groups. Differences among the three groups in terms of gestational age, age, and body temperature were compared. The F-values were 0.182, 12.121, and 10.647 with corresponding *P* values of 0.834, 0.000, and 0.000, respectively. The results indicated that there was no significant difference in gestational age among the three groups. Patients in the influenza combined with *Mycoplasma pneumoniae* group were younger than those in the influenza only group and the *Mycoplasma pneumoniae* only group ($P < 0.05$). The peak body temperature in the influenza combined with *Mycoplasma pneumoniae* group was significantly higher than that in the influenza only group and the *Mycoplasma pneumoniae* only group ($P < 0.05$).

**Pathogen groups and laboratory parameters**

The results showed that the absolute lymphocyte count (L) was the lowest in the influenza combined with *Mycoplasma pneumoniae* group and the highest in the *Mycoplasma pneumoniae* group ($P < 0.05$). The absolute neutrophil count (N) was the lowest in the influenza group and the highest in the *Mycoplasma pneumoniae* group ($P < 0.05$). The NLR, PLR, and CRP levels were the highest in the influenza combined with *Mycoplasma pneumoniae* group, while the LMR was the lowest, and the differences were statistically significant ($P < 0.05$). (Table 2)

**Diagnostic value of laboratory indicators for influenza and mycoplasma pneumoniae infection**

Receiver operating characteristic (ROC) curves were plotted to calculate the area under the curve (AUC) and to evaluate the diagnostic value of each indicator for influenza, *Mycoplasma pneumoniae*, and co-infections. The results demonstrated that N, NLR, and PLR had high diagnostic value for influenza with sensitivity and specificity of 45.9% and 76.7%, 63.3% and 58.9%, 65.3% and 55%, respectively. L, PLR, and CRP had the highest diagnostic value for *Mycoplasma pneumoniae* with sensitivity and specificity of 55.9% and 67.3%, 44.1% and 82.3%, 47.1% and

**Table 2.** Pathogen groups and laboratory parameters.

| Group | Influenza (n = 98) | *Mycoplasma pneumoniae* (n = 34) | Influenza combined with *Mycoplasma pneumoniae* (n = 168) | *P* value |
|---|---|---|---|---|
| WBC ($\times10^9$/L) | 7.87 ± 3.10 | 9.06 ± 2.79 | 8.54 ± 2.81 | 0.070 |
| PLT ($\times10^9$/L) | 214.18 ± 54.74 | 221.21 ± 59.52 | 216.57 ± 50.37 | 0.797 |
| L ($\times10^9$/L) | 0.95 ± 0.45 | 1.13 ± 0.63 | 0.84 ± 0.48 | 0.006 |
| M ($\times10^9$/L) | 0.70 ± 0.74 | 0.60 ± 0.22 | 0.67 ± 0.69 | 0.778 |
| N ($\times10^9$/L) | 6.23 ± 2.84 | 7.27 ± 2.94 | 7.00 ± 2.55 | 0.045 |
| NLR | 7.80 ± 4.58 | 9.76 ± 9.58 | 11.47 ± 10.51 | 0.006 |
| LMR | 1.71 ± 1.04 | 2.12 ± 1.56 | 1.49 ± 0.88 | 0.004 |
| PLR | 272.99 ± 148.06 | 247.17 ± 130.41 | 333.98 ± 236.99 | 0.013 |
| SAA (mg/L) | 55.27 ± 79.46 | 50.10 ± 89.49 | 63.56 ± 83.76 | 0.580 |
| CRP (mg/L) | 19.87 ± 18.75 | 20.83 ± 27.11 | 26.46 ± 22.90 | 0.049 |

89.1%, respectively. L, N, NLR, LMR, PLR, and CRP had high diagnostic value for influenza combined with *Mycoplasma pneumoniae* with sensitivity and specificity of 44% and 97.73%, 41.1% and 73.5%, 60.7% and 61.4%, 20.8% and 92.4%, 45.8% and 75.8%, 45.2% and 75.8%, respectively.

## Discussion

Pregnant women experience a series of physiological changes and in a special physiological state with increased oxygen content, increased cardiac output, and accelerated heart rate, which make them more susceptible to various infections with respiratory infections being a common type, especially viral infections. The symptoms of infectious diseases are more severe in pregnant women, and acute respiratory viral infections increase the risk of adverse events such as preterm birth, miscarriage, and fetal malformation [8, 9]. Therefore, early diagnosis and treatment are of great significance for the outcomes of both the mother and the fetus. The results of this study showed that, as gestational age increased, infection indicators of WBC, N, and CRP gradually increased, while PLT levels gradually decreased. During pregnancy, the hematopoietic function of the bone marrow is enhanced, especially from the 16$^{th}$ week of pregnancy to the late stages of delivery. The number of mature cells and cell nuclei in the blood increases, and granulocytes also increase, leading to an increase in the total leukocyte count [10]. Generally, the white blood cell count in pregnant women is higher than that in non-pregnant women, starting to increase slightly from 7 - 8 weeks of pregnancy and peaking at 30 weeks, sometimes reaching 15 × $10^9$/L, mainly due to an increase in neutrophils. A previous study showed that, in 63 healthy pregnant women, WBC levels began to increase in early pregnancy, peaked in mid-pregnancy, and increased significantly during labor. The changes in NEUT were consistent with WBC, and both WBC and NEUT were higher than that in the normal population, even exceeding the normal reference range [6]. During pregnancy, blood volume increases significantly, starting from 6 - 8 weeks of pregnancy and peaking at 32 - 34 weeks, increasing by 30 - 45%, and then maintaining a steady level until delivery. The increase in plasma is greater than that in red blood cells, and the increase in blood cells and hemoglobin averages 25 - 30%, leading to hemodilution. In addition, the consumption and sequestration of platelets in the placental circulation are increased, leading to a decrease in platelet count [11]. In this study, the platelet count decreased with the progression of pregnancy, which might be related to hemodilution and was consistent with the previous findings [6]. Past studies suggested that normal pregnancy was also a chronic inflammatory response [12], and estrogen was considered to have a potential pro-inflammatory effect, stimulating the release of inflammatory factors such as CRP to some extent [13]. The results of this study demonstrated that the

distribution of respiratory pathogen types exhibited no statistically significant variations in pregnant women at different stages of pregnancy. Therefore, the changes in the above parameters during pregnancy were related to gestational age, excluding the influence of different pathogens. Further, this study showed that the age of patients in the influenza combined with *Mycoplasma pneumoniae* group was lower than that in the influenza only and *Mycoplasma pneumoniae* only groups. However, there is currently no direct evidence to show that pregnant women with influenza combined with *Mycoplasma pneumoniae* infection are younger than those with influenza or *Mycoplasma pneumoniae* infection alone. These results might be related to more pronounced immune modulation in younger pregnant women, their potentially higher levels of social activity, and consequently a higher risk of exposure to pathogens, while older pregnant women might have more immune exposure and immune memory, and they might pay more attention to health management during pregnancy. Such results might also be related to the sample selection in this study. The peak body temperature in the influenza combined with *Mycoplasma pneumoniae* group was significantly higher than that in the influenza only and *Mycoplasma pneumoniae* only groups, indicating that, in cases of co-infection, the inflammatory response was more intense due to the stimulation of multiple pathogens, and the condition was more severe, manifested by a significant increase in body temperature and obvious respiratory symptoms. CRP, a liver-synthesized protein, undergoes a significant increase during infection or tissue damage. It is an acute-phase inflammatory protein that can activate neutrophils and has a significant role in the complement system [14]. Influenza virus infection directly damages the immune function of patients, reducing the number of lymphocytes. The more severe the condition, the more pronounced the decrease in neutrophils. Cheng *et al*. found that the number of lymphocytes in children with influenza A was significantly reduced [15], and Wang *et al*. reported the same conclusion [16]. When *Mycoplasma pneumoniae* invades the human body, it is recognized as a foreign antigen, stimulating the production of corresponding antibodies and activating the immune response, leading to an increase in the number of lymphocytes. Simultaneously, the immune system attempts to fight the pathogen by increasing the number of white blood cells, but the increase is relatively small compared to the significant increase in white blood cells caused by bacterial infections. In this study, the absolute lymphocyte count (L) was the lowest in the influenza combined with *Mycoplasma pneumoniae* group and the highest in the *Mycoplasma pneumoniae* group. The absolute neutrophil count (N) was the lowest in the influenza group and the highest in the *Mycoplasma pneumoniae* group. The NLR, PLR, and CRP levels were the highest in the influenza combined with *Mycoplasma pneumoniae* group, while the LMR was the lowest. ROC curve analysis revealed that NLR, PLR, and LMR exhibited high sensitivity and specificity in diagnosing influenza co-infected with *Mycoplasma pneumoniae*, suggesting that NLR, PLR, and LMR could be used as markers to differentiate between different pathogen infections and provide a reference for the diagnosis of different respiratory infections.

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