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Original Article

The value of inflammatory factors and red blood cell immune indices in predicting perinatal infection in hypertensive women after cesarean section

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Abstract: Objective: This study was conducted to explore the predictive value of inflammatory factors and red blood cell (RBC) immune indices in perinatal infection of women with pregnancy-induced hypertension after cesarean section. Methods: Eighty women with pregnancy-induced hypertension and perinatal infection after cesarean section were enrolled as the study group. Another 80 pregnant women with hypertension but without perinatal infection during cesarean section were included as the control group. The two groups were compared in terms of interleukin-1β (IL-1β), IL-6, IL-10, transformation growth factor-β (TGF-β), tumor necrosis factor-α (TNF-α), γ-interferon (IFN-γ), immune adhesion inhibitor (FEIR), immune adhesion promotion factor (FEER), and immune complex rosette (RBC-ICR) levels. The mothers in the study group were grouped according to the level of white blood cells, and the differences in related indicators of women in different inflammatory states were compared. Finally, the correlation between inflammatory factors and RBC-related immune indices was calculated. The differences in inflammatory factors and RBC-related immune indices were evaluated among different infection types. The ROC curve of IL-1β, IL-6, IL-10 and FEIR, FEER, RBC-ICR for infection prediction was plotted. Results: The study group showed significantly higher maternal levels of inflammatory factors and FEIR and lower FEER and RBC-ICR than the control group ($P<0.05$). There was a significant correlation between inflammatory factors and RBC-related immune indices ($P<0.05$), and there was little difference in inflammatory factors and RBC-related immune indices among different infection types ($P>0.05$). Inflammatory factors and RBC-related immune indices exhibited good predictive value for perinatal infection of women with pregnancy-induced hypertension. Conclusion: Prior to perinatal infection, the inflammatory factors and the RBC indices of women with hypertension and cesarean section are significantly altered. Monitoring these indicators can be used to evaluate maternal prognosis.

Keywords: Inflammatory factors, RBC indices, gestational hypertension, cesarean section, perinatal infection, predictive value

Introduction

With the opening of China's two-child policy in recent years, the birth rate of newborns shows a gradual upward trend, and cesarean section, which refers to the birth of a baby through incisions in the abdomen and uterus, is one of the most important surgeries in the field of obstetrics, and is of irreplaceable significance to save the life of the critically ill fetuses and improve the pregnancy outcomes [1]. However, clinical practice also indicates that women who undergo cesarean section have a slower postpartum recovery and a higher incidence of complications than those who deliver vaginally [2]. Perinatal infections are common complications of pregnancy, and women are more susceptible to pathogens and inflammatory lesions due to reduced immune function [3]. Perinatal infections can seriously affect postpartum recovery, not only prolong hospitalization and increase treatment costs, but also induce sepsis and shock in severe cases that endanger life and health of the parturient [4]. Some scholars have found that women with hypertension during pregnancy have a higher rate of perinatal infection compared with healthy controls, which may be related to the effect of hypertension

on immune system [5], thus the prevention and monitoring of perinatal infection are of great importance for women with hypertension during pregnancy undergoing cesarean section.

Red blood cell (RBC) immunity is a defense mechanism of the body. RBC contains a variety of immune-related substances, which is closely related to T-lymphocytes, B-lymphocytes, NK natural killer cells and phagocytes [6]. It has been found that RBCs also have a complement receptor protein on their surface, which is able to adhere to immune complexes and is widely involved in a variety of inflammatory processes. Therefore, RBCs are often used as a biomarker to assess the inflammatory states [7, 8]. A study of infected women during the puerperium showed that the FEER of infected women was 23.50±3.10%, which was lower than that of healthy pregnant women (35.20±3.20%), and correlation analysis showed a negative correlation between FEER and IL-6 levels [9].

The aim of this study was to investigate the predictive value of inflammatory factors and RBC count on perinatal infections in pregnant hypertensive women after cesarean section, thus to provide clinical reference for the formulation of interventions to improve maternal prognosis.

Materials and methods

Baseline data

Eighty women with pregnancy-induced hypertension and perinatal infection after cesarean section admitted to our hospital from January 2019 to December 2019 were selected as the study group, and another 80 pregnant women with hypertension but without perinatal infection during the same period were enrolled as the control group.

Inclusion criteria: (1) all subjects met the diagnostic criteria [10] for gestational hypertension and underwent cesarean section; (2) aged between 20 and 40 years; (3) singleton pregnancy; (4) full-term pregnancy; (5) the study was approved by the Ethics Committee of Liaocheng Dongchangfu District Maternity and Child Health Hospital; (6) the study subjects signed the informed consent form.

Exclusion criteria: (1) patients with psychiatric disorders; (2) patients with prenatal infectious diseases; (3) patients with cognitive impairment; (4) patients with severe hepatic and renal dysfunction; (5) patients with chronic underlying diseases; (6) patients with autoimmune diseases; and (7) patients with hematologic disorders.

Intervention methods

Blood samples were collected from the veins in the morning, placed in vacuum tubes for 2 h, and centrifuged at 3000 r/min with a centrifuge. The supernatant was stored at -80°C. Flow cytometry was used to detect inflammatory factors, and enzyme-linked immunosorbent assay (ELISA) was used to determine RBC indices, with 3 rounds of tests for each index being averaged as the final result.

Observation indicators

The observation indicators were the differences of inflammatory factors and RBC-related immune indices between the study group and the control group and among different types of infections (distinguished as wound infections, urinary tract infections and other types). The women in the study group were divided into group A [leukocyte level of 11-15 × 10^9/L, n = 28], group B [leukocyte level of 16-20 × 10^9/L, n = 30] and group C (leukocyte level of >20 × 10^9/L, n = 22). The differences in inflammatory factors and RBC immune indices between different inflammatory states were investigated. Spearman correlation analysis was used to investigate the association between inflammatory factors and RBC indices. ROC curves were drawn to assess the predictive value of inflammatory factors and RBC immune indices for perinatal infection.

Statistical analysis

The collected data were stored using an EXCEL sheet. The statistical SPSS 22.0 was used to analyze the data. The normal distribution test was carried out on the collected data to see if the data were conformed to the normal distribution. The count data were expressed as [n (%)], and Chi-squared test was chosen for the analysis of the differences between groups. The measurement data were expressed as mean ± standard deviation, the t-test was used for the analysis of the differences between groups, and the correlation analysis was per-

Table 1. Comparison of baseline data between the two groups ($\bar{x} \pm sd$)/[n (%)]

Baseline data		Study group (n = 80)	Control group (n = 80)	t/X^2	*P*
Average age (years)		30.19±2.33	29.98±2.61	0.592	0.537
Average weight (kg)		71.28±3.22	71.43±3.01	0.781	0.304
Average week of pregnancy (weeks)		38.19±2.33	38.31±2.01	0.776	0.348
Average number of pregnancies		1.21±0.43	1.19±0.39	0.758	0.308
Education level	University and above	43	26	0.771	0.349
	High school	32	34		
	Lower secondary and below	5	10		
Monthly income	<1000 Yuan	51	46	0.234	0.871
	1000-5000 yuan	23	26		
	Over 5000 yuan	6	8		

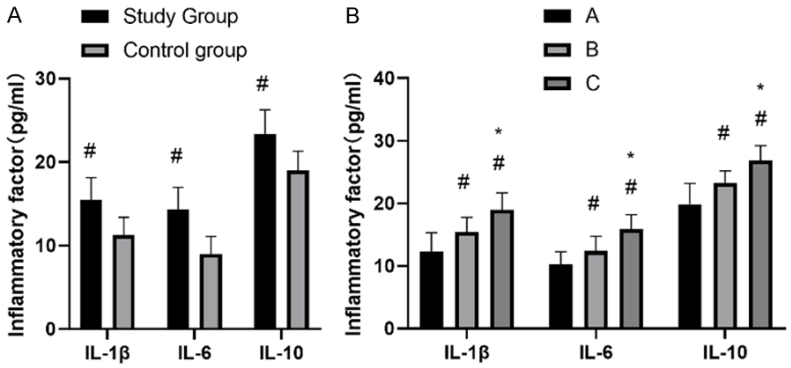

Figure 1. Differential comparison of IL-1β, IL-6 and IL-10 levels in different infection types. IL-1β, IL-6 and IL-10 levels in the study group were significantly higher than those in the control group ($P<0.05$) (A), #$P<0.05$ compared with the control group. There were significant differences in IL-1β, IL-6 and IL-10 levels between different groups (B), with #$P<0.05$ compared with group A, and *$P<0.05$ compared with group B.

formed using Spearman. $P<0.05$ indicated statistically significant difference [11].

Results

Comparison of the differences in clinical data

There was little difference in baseline data such as age, mean weight, mean gestational week, mean number of pregnancies, education level and family income ($P>0.05$), which were comparable (**Table 1**).

Comparison of IL-1β, IL-6 and IL-10 levels by infection type

The levels of IL-1β, IL-6 and IL-10 in the study group were significantly higher than those in the control group ($P<0.05$) (**Figure 1A**). Levels of IL-1β, IL-6, and IL-10 were significantly different among groups with different levels of leukocyte ($P<0.05$) (**Figure 1B**), and IL-1β, IL-6, and IL-10 levels tended to increase with the increase in the levels of inflammatory infection.

Comparison of TGF-β, TNF-α and IFN-γ levels among different infection types

The levels of TGF-β, TNF-α and IFN-γ in the study group were significantly higher than those in the control group ($P<0.05$) (**Figure 2A**). There were significant differences in the levels of TGF-β, TNF-α, and IFN-γ between groups with varying level of infection ($P<0.05$) (**Figure 2B**). The levels of TGF-β, TNF-α and IFN-γ increased with aggravation of the level of inflammatory infection.

Comparison of differential levels of FEIR, FEER, and RBC-ICR in different infection types

The FEIR and RBC-ICR levels in the study group were higher than those in the control group, and the FEER levels in the study group were lower than those in the control group ($P<0.05$) (**Figure 3A**). FEIR, FEER and RBC-ICR levels showed significant differences between groups with different levels of infection ($P<0.05$) (**Figure 3B**), i.e. the more severe inflammatory states indicated the higher serum FEIR and RBC-ICR levels and the lower FEER levels.

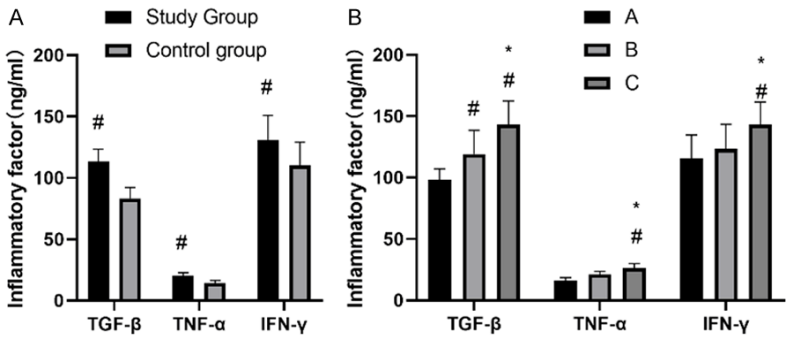

Figure 2. Differential comparison of TGF-β, TNF-α, and IFN-γ levels in different infection types. TGF-β, TNF-α, and IFN-γ levels in the study group were significantly higher than those in the control group (P<0.05) (A), with #P<0.05 compared with the control group. There were significant differences between groups in TGF-β, TNF-α, and IFN-γ levels (B), with #P<0.05 compared with group A, and *P<0.05 compared with group B.

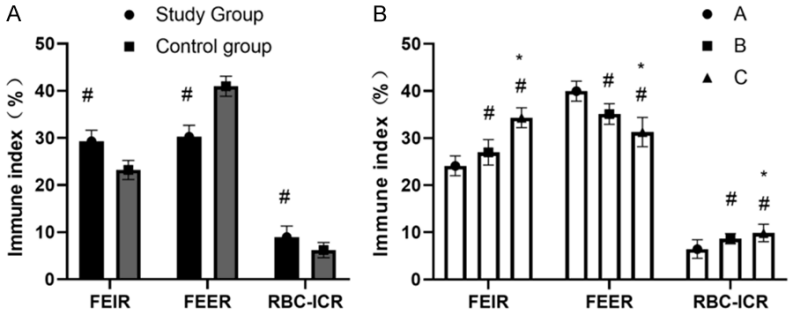

Figure 3. Comparison of the differences in FEIR, FEER and RBC-ICR levels between different infection types. #P<0.05 compared with the control group. There were some differences in the levels of FEIR, FEER and RBC-ICR between groups, with #P<0.05 compared with group A, and *P<0.05 compared with group B.

Table 2. Comparison of inflammatory factors and RBC immune indices between different infection types ($\bar{x}$ ± sd)/[n (%)]

Inflammatory factor	Wound infection	Urinary tract infection	Other infections	*F*	*P*
IL-1β	14.33±1.23	13.98±2.00	14.29±2.00	2.211	>0.05
IL-6	15.66±2.00	15.78±2.00	15.45±2.00	1.298	>0.05
IL-10	26.55±3.00	26.33±2.93	26.30±3.31	1.298	>0.05
TGF-β	90.44±5.10	92.00±4.59	93.01±4.11	2.119	>0.05
TNF-α	22.32±3.01	21.98±3.21	22.41±3.01	2.098	>0.05
IFN-γ	132.22±10.22	133.29±9.98	135.44±9.10	1.820	>0.05
FEIR	30.33±3.01	31.00±3.11	32.01±2.98	0.987	>0.05
FEER	34.11±2.31	35.19±3.98	36.01±3.19	0.283	>0.05
RBC-ICR	9.31±1.21	9.21±1.22	9.50±1.02	0.178	>0.05

Comparison of maternal inflammatory factors and RBC indices by type of infection

Women in the study group were grouped according to the type of infection: wound infection (n = 31), urinary tract infection (n = 41) and other (n = 8). The results showed that different infection types did not affect the levels of inflammatory factors and RBC indices (P> 0.05) (**Table 2**).

Assessment of the correlation between inflammatory and RBC indices

Spearman's analysis showed that inflammatory factors were positively correlated with both FEIR and RBC-ICR, and negatively correlated with FEER (P< 0.05) (**Table 3**).

Assessment of the predictive value of inflammatory factors and RBC-ICR indices for perinatal infection

The area under the curve (AUC) of inflammatory factors and RBC immune indices for infection were 0.6777 (95% CI = 0.5971-0.8682, P<0.05), 0.8281 (95% CI = 0.6745-0.9817, P<0.05), 0.9102 (95% CI = 0.8077-1.000, P<0.05), 0.9167 (95% CI = 0.8313-1.000, P<0.05), 0.8864 (95% CI = 0.7848-0.9881, P<0.05), and 0.8550 (95% CI = 0.6918-1.000, P< 0.05) (**Figure 4**), all of which showed a good predictive value.

Discussion

Gestational hypertension is a disease specific to women during pregnancy [12] and may have some adverse effects on pregnancy outcomes. Evidence has shown that fetal asphyxia and placenta previa may be significantly higher in women with gestational hypertension than in healthy controls, which are perinatal risk factors [13]. As a common means to

Table 3. Analysis of correlation between inflammatory factor levels and RBC immune indices

Inflammatory factor	FEIR		FEER		RBC-ICR	
	r-value	*P*-value	r-value	*P*-value	r-value	*P*-value
IL-1β	0.877	0.034	-0.891	0.026	0.726	0.034
IL-6	0.781	0.021	-0.778	0.023	0.873	0.033
IL-10	0.711	0.011	-0.872	0.043	0.767	0.023
TGF-β	0.822	0.043	-0.843	0.015	0.667	0.021
TNF-α	0.781	0.033	-0.789	0.021	0.781	0.019
IFN-γ	0.679	0.023	-0.911	0.022	0.871	0.023

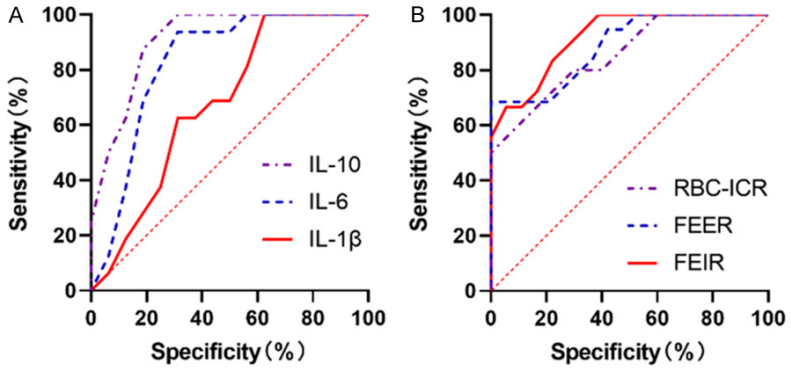

Figure 4. Predictive values of inflammatory factors and RBC immune indices for perinatal infection. The predictive AUC of IL-1β (A), IL-6 (A), IL-10 (A), FEIR (B), FEER (B) and RBC-ICR (B) for perinatal infection in pregnant hypertensive women underwent cesarean section was 0.6777 (95% CI = 0.5971-0.8682, *P*<0.05), 0.8281 (95% CI = 0.6745-0.9817, *P*<0.05), 0.9102 (95% CI = 0.8077-1.000, *P*<0.05), 0.9167 (95% CI = 0.8313-1.000, *P*<0.05), 0.8864 (95% CI = 0.7848-0.9881, *P*<0.05), and 0.8550 (95% CI = 0.6918-1.000, *P*<0.05), respectively.

protect hypertensive mothers and newborns, cesarean section has a high rate of clinical application. However, due to obvious trauma of cesarean section, the possibility of infections by pathogenic bacteria in postoperative incision, vagina and uterus is greater than that of vaginal delivery, and the risk of perinatal infection is also increased [14]. The causes of perinatal infection include decreased immunity, improper aseptic means during cesarean section, improper treatment during puerperium, *etc*. Infection can lead to high body temperature, abdominal pain, prolonged postnatal recovery and possibly death. Therefore, early intervention is highly recommended [15, 16].

Cytokines could be indicators of perinatal infection. Cytokines are sensitive to the inflammatory process induced by bacterial infections, and the level of cytokines is also correlated with the severity of the inflammatory response [17]. A survey of 80 cases of puerperium infected women showed that the serum levels of IL-6 and IL-10 were significantly higher than those of non-infected women. The scholars further analyzed 1 case of puerperia with sepsis and found that the cytokines were significantly increased [18]. RBC indices are also commonly used to reflect the immune states. A multicenter retrospective analysis found that women with cesarean section were under high stress caused by the incision, which had an impact on RBC indices. However, the authors did not analyze in depth the correlation between RBC markers and perinatal infections [19, 20].

This study analyzed the predictive value of inflammatory factors and RBC immune markers for perinatal infections. The results showed the inflammatory factors IL-1β, IL-6, IL-10, TGF-β, TNF-α, and IFN-γ levels in the study group were significantly higher than those in the control group. After further dividing the study group into groups A, B, and C according to the severity of infection, it was found that the levels of the above-mentioned inflammatory factors also showed an upward trend with the increase of the severity of inflammation. IL-6 and IL-10 are commonly used indicators of inflammation for disease monitoring and prognosis evaluation. Studies of some scholars have pointed out that IL-6 and IL-10 are commonly used indicators of inflammation in the body and are often used in disease monitoring and prognostic evaluation, and a survey of 90 high-risk pregnant women showed that an IL-10 level of >24.13 pg/ml had an accuracy of 98.89% in predicting the occurrence of maternal inflammation, which was similar to the results of this study [21]. The results showed that the FEIR and RBC-ICR levels of the study group were signifi-

cantly higher, and the FEER levels of the study group were significantly lower than those of the control group, and there were some differences in these indicators between women with different inflammatory states. A study on the correlation between RBC immune status and puerperal infection after cesarean section showed that the serum RBC immune indices of pregnant women with puerperal infection were significantly different from those of non-infected women, and the scholars believed that RBC immune factors were widely involved in the inflammatory response of the body, thereby better reflecting the body's inflammatory state [22]. The authors of this study speculated that RBCs were able to attach immune complexes to complement receptors on their own surface and carry them to the liver, spleen and other metabolic organs, and then rely on the phagocytosis of macrophages to remove inflammatory substances, therefore, as the inflammatory state of the body changes, serum RBC immune-related indices will also alter [23, 24].

The results of this study also showed that there was a significant relationship between inflammatory factors and RBC indices. IL-10 levels exhibited a significant positive correlation with FEIR and RBC-ICR, and a significant negative correlation with FEER, corresponding to the above-mentioned differences in RBC immune indices of pregnant women with different inflammatory states, which was similar to the results of other study [25]. We also found that IL-1β, IL-6, IL-10, FEIR, FEER, and RBC-ICR had good predictive value for perinatal infection in pregnant hypertensive women with cesarean section. A study on the prediction of lung infection in patients with cerebral infarction indicated that RBC immune indices were closely related to C-reactive protein, IL-6, IL-17, etc., and RBC had good predictive value for lung infection in patients with cerebral infarction, which was similar to the results of this study [26].

In summary, the inflammatory factors and RBC immune indices of pre-infection stage are significantly changed in women with hypertension during pregnancy, and their prognosis can be assessed by monitoring the above indicators. The innovation of this study lies in the use of inflammatory factors and RBC immune indices, the two commonly used clinical indicators for the diagnosis of perinatal infections, which provides a more refined clinical assessment tool for patients without increasing the number of laboratory tests and medical expenses. The limitation of this study is the simplification of the follow-up procedure for enrolled subjects, and it is proposed to conduct a clinical study with longer follow-up in the future.

Disclosure of conflict of interest

None.

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