

# Coagulation parameters and Apgar score are associated with severity in preterm infants

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**Abstract. – OBJECTIVE:** Coagulation parameters are used to diagnose hematological diseases. The correlation between the coagulation parameters and Apgar score at 5 min is yet to be elucidated. The present study aimed at describing the neonatal coagulation parameters in preterm infants with a low Apgar score at 5 min.

**PATIENTS AND METHODS:** In this case-control study, 32 serious preterm infants were compared with 20 preterm infants, according to the Apgar score at 5 min. The prothrombin time (PT), thrombin time (TT), fibrinogen (Fbg), activated partial thromboplastin time (APTT), calculated international normalized ratio (INR), D-dimer (D2), fructose diphosphate sodium (FDP), and procalcitonin (PCT) values were recorded. The linear correlation between coagulation parameters and Apgar score at 5 min was analyzed by linear regression. The two groups were compared using GraphPad Prism 8 (LaJolla, CA, USA).

**RESULTS:** In the study, the mean coagulation parameters were significantly higher in the serious preterm infants with low the Apgar score at 5 min compared to the preterm infants with normal Apgar scores at 5 min ( $p < 0.05$ ). The correlation between coagulation parameters and Apgar score at 5 min was recorded (PT:  $R = 0.3984$ ; APTT:  $R = 0.3165$ ; INR:  $R = 0.4139$ ).

**CONCLUSIONS:** The coagulation parameters were significantly higher in serious preterm infants with a low Apgar score at 5 min. Also, the coagulation parameters and Apgar score at 5 min are associated with severity in preterm infants.

## Key Words:

Coagulation parameters, Apgar score at 5 minutes, Correlation.

## Introduction

The Apgar scoring system is relevant for the prediction of neonatal survival today as it was almost 50 years ago<sup>1</sup>. Apgar score at 5 min is used to assess the neonatal health status as a common clinical index after birth<sup>2,3</sup>. The test was performed 5 min after birth to identify the characteristics such

as color, heart rate, muscle tone, respiration, and reflex<sup>4,5</sup>. The 5-min Apgar score  $> 7$  indicated that the condition of infants was good to excellent<sup>6</sup>. Then, the doctors determined whether extra medical care or emergency care was required<sup>7</sup>. The Apgar score at 5 min was regarded as the optimal predictor of survival in infants<sup>8,9</sup>, with a controversial the value<sup>10,11</sup>. For example, administering of drugs to the mother produces low scores that do not reflect the condition of newborn infants<sup>12</sup>.

The serum had been isolated from preterm infant blood in the clinical laboratory. Compared to healthy newborns, preterm infants had a severe condition. In this study, we collected whole blood samples from preterm infants in neonatal wards and analyzed the following coagulation parameters: prothrombin time (PT), thrombin time (TT), fibrinogen (Fbg), activated partial thromboplastin time (APTT), calculated international normalized ratio (INR), D-dimer (D2), fructose diphosphate sodium (FDP), and procalcitonin (PCT). The comparison of these parameters revealed that the level of coagulation parameters and PCT differed, indicating that the Apgar score at 5 min was associated with coagulation parameters. Thus, coagulation parameters and Apgar score are associated with severity in preterm infants.

## Patients and Methods

This study was conducted in Chengdu Fifth People's Hospital, Sichuan Province, China, from June through December 2020. All preterm infants were born and inpatients in the newborn wards of the Chengdu Fifth People's Hospital. In this case-control study, 32 serious preterm infants were compared to 20 preterm infants with respect to the Apgar score at 5 min. Additionally, written consent was obtained from all the parents before any procedures were performed. The coagulation parameters were determined by testing the serum samples. A routine blood test was conducted, and

**Table I.** Clinical characteristics between the serious preterm infant group and preterm infant group.

Characteristics	Serious preterm infant group (n=32, Mean±SD)	Preterm infant group (n=20, Mean±SD)	p-value
Sex (males, females)	17,15	10,10	
Age (hours)	2.33±2.33	2.36±2.04	0.9624
Vaginal delivery	20	10	
Caesarean delivery	12	10	
Apgar score at 5 min	5.0±0.84	8.0±0.72	<0.0001
Increased oxygen requirement or respiratory support	32	0	
white cell (3.5-9.2×10 <sup>9</sup> /L)	12.18±4.67	6.48±1.73	<0.0001
Red cell (4.09-5.74×10 <sup>12</sup> /L)	4.82±0.58	4.73±0.35	0.5347
Hemoglobin (131-172 g/L)	172.04±30.24	136.30±11.78	<0.0001
Plate (85-303×10 <sup>9</sup> /L)	280.37±70.62	259.40±36.81	0.2263
PT (9.3-12.4 Second)	14.45±1.57	11.12±0.94	<0.0001
INR (0.86-1.15)	1.32±0.15	1.01±0.08	0.0003
Fbg (2-4 Second)	1.44±0.54	2.91±0.79	<0.0001
APTT (22.3-32.5 Second)	76.74±19.77	26.47±2.47	<0.0001
TT (16-21.6 Second)	20.65±1.81	18.75±1.86	0.0006
D2 (0-0.55 µg/ml)	3.24±2.93	0.34±0.10	<0.0001
FDP (0-5 µg/ml)	9.93±10.51	3.04±1.34	<0.0001
PCT (<0.05 ng/ml)	4.79±5.52	0.12±0.06	<0.0001
CRP (<0.5 mg/L)	<0.5	<0.5	

the PCT was determined using whole vein blood. The 5-min Apgar score <7 was considered for the serious preterm infant group, while that ≥7 defined the preterm infant group. Then, venous blood samples were collected and assessed for prothrombin time (PT), thrombin time (TT), fibrinogen (Fbg), activated partial thromboplastin time (APTT), calculated international normalized ratio (INR), D-dimer (D2), and FDP.

### Statistical Analysis

Data were analyzed using GraphPad Prism 8 (LaJolla, CA, USA) and represented as mean and standard deviation. The unpaired test was used to compare the two groups, and the correlation was compared using Pearson's correlation coefficient. The areas under the receiver operating characteristic (ROC) curves were computed for each coagulation parameter.  $p < 0.05$  indicated a statistically significant difference.

## Results

In the present study, we evaluated 52 preterm infants, including 32 serious preterm infants (Apgar score <7) and 20 preterm infants (Apgar score 7-10) born in the Chengdu Fifth People's Hospital, Sichuan Province, China. The clinical characteristics of these preterm infants were analyzed (Table I). Significant differences were detected in white blood cells (WBC)

and hemoglobin (HGB) in the two groups. The mean WBC in serious preterm infants (12.18±4.67×10<sup>9</sup>/L) was significantly higher than that of the control group (6.48±1.73×10<sup>9</sup>/L) ( $p < 0.0001$ ). The mean HGB in serious preterm infants (172.04±30.24 g/L) was significantly higher than that of the control infants (136.30±11.78 g/L) ( $p < 0.0001$ ).

The comparison between the serious preterm group and the preterm groups based on the coagulation parameters revealed significant differences in PT, APTT, INR, TT, D2, and FDP (Table I). The mean PT in the serious group (14.45±1.57 seconds) was significantly higher than that of the control group (11.12±0.94 seconds) ( $p < 0.0001$ ). The mean APTT in the serious group (76.74±19.77 seconds) was significantly higher than that of the control group (26.47±2.47 seconds) ( $p < 0.0001$ ). The mean INR in the serious group (1.32±0.15) was significantly higher than that of the control group (1.01±0.08) ( $p = 0.0003$ ). The mean TT in the serious group (20.65±1.81 seconds) was significantly higher than that of the control group (18.75±1.86 seconds) ( $p = 0.0006$ ). The mean D2 in the serious group (3.24±2.93) was significantly higher than that of the control group (0.34±0.10) ( $p < 0.0001$ ). The mean FDP in the serious group (9.93±10.51) was significantly higher than that of the control group (3.04±1.34) ( $p < 0.0001$ ). The mean PCT in the serious group (4.79±5.52) was significantly higher than that of the control group (0.12±0.06) ( $p < 0.0001$ ).

**Table II.** Correlation between Apgar score at 5 min and coagulation parameters.

	Apgar score at 5 min vs. PT	Apgar score at 5 min vs. APTT	Apgar score at 5 min vs. INR	Apgar score at 5 min vs. FBG	Apgar score at 5 min vs. TT	Apgar score at 5 min vs. PCT
Pearson r	0.6312	-0.5626	0.6434	-0.128	-0.2091	0.1037
95% confidence interval	0.5091 to 0.7285	-0.6730 to -0.4275	0.5257 to 0.7369	-0.4564 to 0.2310	-0.5199 to 0.1506	-0.2955 to 0.4721
R squared	0.3984	0.3165	0.4139	0.01639	0.04371	0.01075
p-value	<0.0001	<0.0001	<0.0001	0.485	0.2508	0.6142

Furthermore, a correlation was established between Apgar score at 5 min and coagulation parameters. As shown in Table II, a positive correlation was observed between Apgar score at 5 min and PT ( $R=0.3984$ ;  $p<0.0001$ ), a negative correlation was established between Apgar score at 5 min and APTT ( $R=0.3165$ ;  $p<0.0001$ ), and a positive correlation was established between Apgar score at 5 min and INR ( $R=0.4139$ ;  $p<0.0001$ ).

The receiver operating characteristic (ROC) curve and the area under the curve (AUC) of coagulation parameters and PCT between the serious preterm infant group and preterm infant group are shown in Table III.

### Discussion

The coagulation parameters and PCT showed clinical significance; however, the clinical significance of the coagulation test has recently gained interest<sup>13,14</sup>. Serious preterm infants were estimated by Apgar score at 5 min, which showed a lower score, indicating a serious condition that could result in increased oxygen requirement or respiratory support<sup>15,16</sup>. Thus, the coagulation abnormalities observed in serious preterm infants were directly linked to Apgar score at 5 min<sup>17</sup>.

The present study showed that the serious preterm infant group displayed significantly higher PT, APTT, TT, D2, and FDP than the preterm infant group (Table I). Also, the PCT estimations differed significantly between the two groups (Table I,  $p<0.0001$ ). The current analysis showed that APTT was negatively correlated (Pearson  $r=-0.5626$ ,  $R^2=0.3165$ ,  $p<0.0001$ ), PT was posi-

tively correlated (Pearson  $r=0.6312$ ,  $R^2=0.3984$ ,  $p<0.0001$ ), and INR was positively correlated with Apgar score at 5 min (Pearson  $r=0.6434$ ,  $R^2=0.41309$ ,  $p<0.0001$ ) (Table II). Thus, the change in PT, APTT, and INR was correlated with the Apgar score at 5 min, and these coagulation parameters could determine the severity of these serious conditions.

The ROC curve analysis revealed a satisfactory predictive value of the coagulation parameters (Table III). The AUC of PT and APTT between the serious preterm infant group and the preterm infant group was 0.9891 [95% confidence interval (CI): 0.9702-1.0] and 1.0 (95% CI: 1.0-1.0), respectively. The AUC of INR, FBG, TT, and PCT was 0.9891 (95% CI: 0.9703-1.0), 0.9297 (95% CI: 0.8489-1.0), 0.7625 (95% CI: 0.6302-0.8948), and 0.9731 (95% CI: 0.9365-1.0), respectively.

Therefore, a correlation was established in the current study between coagulation parameters and Apgar score at 5 min. The coagulation system is easily activated by inflammation and severe disease in humans.

### Conclusions

This study suggested that coagulation parameters and Apgar score are associated with severity in preterm infants; serious preterm infants may alter the coagulation parameters. Thus, the change in the coagulation system may be a cause of early significant serious conditions. Moreover, it might exhibit a pathogenic potential in preterm infants based on high PLT. Importantly, when the Apgar score at 5 min could not be applied to predict the

**Table III.** Comparison area under the ROC curve between the serious preterm infant group and preterm infant group.

	PT	APTT	INR	FBG	TT	PCT
AUC	0.9891	1	0.9891	0.9297	0.7625	0.9731
95% CI	0.9702 to 1.0	1.0 to 1.0	0.9703 to 1.0	0.8489 to 1.0	0.6302 to 0.8948	0.9365 to 1.0
p-value	<0.0001	<0.0001	<0.0001	<0.0001	0.0016	<0.0001

state of preterm infants, we used coagulation parameters to assess the severity in these infants.

### Ethics Approval

The study was approved by the Ethics Committee of Chengdu Fifth people's Hospital (2020066), China, and conducted according to the principles in the Declaration of Helsinki.

### Availability of Data and Material

Data are available upon request.

### Conflict of Interests

The authors have no conflicts of interest to declare.

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### Authors' Contribution

Zhou Fangye: conceived and analyzed data and drafted the manuscript; Yuan Li and Yupeng Luo: designed the experiments; Shenghang Zhen and Xiong Haoran: Collected the data and helped in data analysis; Min Huang: collected the data.

### Informed Consent

Written consent was obtained from all the parents before any procedures were performed.

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