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ORIGINAL

EVALUATING THE UTILITY OF PROCALCITONIN AND COAGULATION FUNCTION TESTS IN ASSESSING INFECTIOUS DISEASE SEVERITY IN NEONATES: LESSONS FOR MANAGING INFECTIONS IN ATHLETES PATIENTS

Meng Tiantian[1], #, Huijuan Rong[2], #, Huimin Li[3], Pei Cao[4], Meng Li[5], Jiahui Guo[5], Luping Li[6]*

[1]Sensory Control Unit, fourth hospital, Shijiazhuang, Shijiazhuang 050000
[2]Nursing Department, Fourth Hospital, Shijiazhuang, Shijiazhuang 050000
[3]Sensitivity Control Division, fourth hospital, Shijiazhuang, Shijiazhuang 050000
[4]Sensory Control Division, fourth hospital, Shijiazhuang, Shijiazhuang 050000
[5]Sense and control department, Fourth Hospital, Shijiazhuang, Shijiazhuang 050000
[6]Emergency department, Fourth Hospital, Shijiazhuang, Shijiazhuang 050000
*Corresponding author: Luping Li
Email: sjzssygkk@126.com

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ABSTRACT

Infectious diseases present a considerable challenge in both neonatal and athlete populations, albeit with distinct clinical characteristics. This study seeks to bridge the gap between these two diverse cohorts by evaluating the applicability of procalcitonin (PCT) and coagulation function tests in assessing infectious disease severity in neonates and drawing insights that may be transferable to managing infections in athletes. Neonates, being immunologically vulnerable, are often susceptible to severe infections, whereas athletes, due to intense physical exertion, face an increased risk of infections that can impact their performance and overall health. To optimize healthcare strategies in both populations, it is essential to explore biomarkers that can aid in early diagnosis, disease monitoring, and treatment assessment. This study systematically reviews existing literature on PCT and coagulation function tests in neonates, highlighting their efficacy in differentiating infectious severity and guiding clinical decisions. Furthermore, it explores the relevance of these biomarkers in the context of infectious disease management in athletes, where rapid detection and prompt intervention are pivotal. The findings of this study underscore the potential utility of PCT and coagulation function tests as valuable tools for assessing infectious disease severity in neonates and

suggest their adaptation for use in athlete populations. By drawing lessons from neonatal medicine, this research offers insights that may enhance the healthcare strategies for athletes, promoting timely diagnosis, appropriate treatment, and optimized performance in the face of infectious challenges.

KEYWORDS: Disease management; Athlete health; Activated partial thromboplastin time; Neonatal infectious disease; Athlete immune response

1. INTRODUCTION

In the realm of sports, where peak physical performance is paramount, athletes are continually confronted with the challenge of maintaining their health and well-being. While athletes are trained to push their bodies to the limits, they are not immune to the threats posed by infectious diseases. From common respiratory infections to more severe conditions, such as bacterial or viral illnesses, infections can have a profound impact on an athlete's training regimen, competitive performance, and overall career trajectory. Consequently, the ability to swiftly and accurately assess the severity of infections in athletes is of utmost importance(Cantey & Lee, 2021). In this era of modern medicine, diagnostic tools play a pivotal role in the early detection and evaluation of infectious diseases. Among these tools, Procalcitonin and coagulation function tests have emerged as valuable biomarkers for assessing the extent and seriousness of infections (Akman, 2014). These tests provide clinicians with valuable insights into the body's response to pathogens and the degree of systemic inflammation, aiding in the determination of appropriate treatment strategies. However, their application in the context of athletes' health has not been thoroughly explored (Glaser, Hughes, Jnah, Newberry, & Harris-Haman, 2021; Russell et al., 2019). This article embarks on an in-depth exploration of the utility of Procalcitonin and coagulation function tests as diagnostic markers in assessing the severity of infectious diseases in athletes (ALSHAWY, Ibrahim, Hussein, & Lahlah, 2019).

Drawing on the parallels between the athlete population and the neonatal population, where early diagnosis is crucial for effective treatment, we aim to unravel the potential benefits and limitations of these tests. By extrapolating lessons learned from neonatal medicine, we aspire to provide a comprehensive perspective on how these diagnostic tools can be harnessed to guide the management of infections in athletes (Darmody & Bendis, 2021; Fleiss et al., 2021; Velissaris et al., 2021). Furthermore, the unique challenges faced by athletes in managing infections, including the pressure to perform, the potential risks of overtraining, and the need for rapid recovery, necessitate a tailored approach to infection assessment. This article endeavors to bridge the gap between medical science and sports performance by synthesizing evidence-based insights and clinical experience. In doing so, we hope to equip healthcare professionals, coaches, and athletes themselves with the knowledge needed

to make informed decisions regarding infection management. Ultimately, our objective is to facilitate the swift and effective recovery of athletes, enabling them to return to the field, court, or track with confidence and vigor(Belov et al., 2021; Vain, 2020).

2 MATERIALS AND METHODS

2.1 General data

Seventy neonates with infectious diseases who received treatment in our hospital from July 2021 to March 2022 were retrospectively opted as the observation cluster (OG), and 35 neonates with non-infectious diseases admitted to our hospital during the same period were opted as the control cluster (CG).

Inclusion criteria (1) The data of enrolled children were complete; (2) The age of admission was 1-28 days; (3) There were different degrees of abnormal infection indicators or diagnosis of infection was established.

Exclusion criteria ： (1) Congenital platelet and coagulation factor abnormalities; (2) Maternal uteroplacental insufficiency; (3) Maternal thrombosis tendency or autoimmune diseases; (4) Maternal use of anticoagulant drugs, antiplatelet drugs, steroidal anti-inflammatory drugs or blood products in the third trimester of pregnancy.

2.2 Intervention Methods

Collect the blood test results of enrolled newborns, mainly PCT, APTT and PT, and then cluster them for Comparative and correlation analysis.

2.3 Outcome measures and evaluation criteria

(1) PCT, APTT and PT of newborns within the observation cluster and the control cluster were contrasted between clusters; (2) newborns within the observation cluster were divided into bacterial infection cluster and viral infection cluster according to the infection type area, and PCT, APTT and PT variances of newborns infected with different pathogens were contrasted;

(3) newborns within the observation cluster were divided into clusters according to the Neonatal Critical Case mark (NCIS) (Eschborn & Weitkamp, 2019) (< 70 divided into very risk cluster, 70-90 divided into risk cluster, and > 90 divided into non-risk cluster), and PCT, APTT and PT variances of newborns infected with different conditions were contrasted; (4) Pearson correlation analysis was used to analyze the correlation between neonatal NCIS marks and PCT, APTT, and PT within the observation cluster.

2.4 Statistical Methods

SPSS 24.0 software was used for statistical analysis. The measurement data obeying normal distribution and with equal variance were contrasted by t test and described as (mean ± standard deviation). The measurement data with skewed data or uneven variance were described by Mann-Whitney test (U test) in non-parametric test and median (upper and lower quartiles). The measurement data were contrasted by chi-square test and expressed as case (%). Pearson analysis was used for correlation analysis. P < 0.05 was considered remarkable(Nevoa et al., 2017).

3. RESULTS

3.1 Comparative of general data between the observation cluster and the control cluster

General data such as gender, gestational age, age, and birth weight were included and contrasted between the observation and control clusters, and the results showed that there was no remarkable variance in general data between the observation and control clusters (P > 0.05), Table 1.

Table 1 Comparative of general data between the two clusters ($\overline{x} \pm s$)/[n (%)]

General clinical data		Observation cluster（n=70）	Control cluster（n=35）	t/χ^2	P
Gender	Male	39	20	0.019	0.889
	Female	31	15		
Mean gestational age (weeks)		38.40±1.86	38.67±2.21	0.658	0.512
Mean age (d)		18.14±2.03	17.88±1.94	0.628	0.531
Mean birth weight (kg)		2.77±0.21	2.81±0.18	0.963	0.338

3.2 Comparative of PCT and coagulation function between the observation cluster and the control cluster

PCT, PT and APTT in observation cluster were remarkably upper than those in control cluster, and there was remarkable variance between the two clusters (P < 0.05), Table 2 and Figure 1.

Table 2 Comparative of PCT and coagulation function between the observation cluster and the control cluster ($\overline{x} \pm s$)

Cluster	Cases	PCT（ng/ml）	PT（s）	APTT（s）
Observation cluster	70	0.17±0.02	13.84±0.92	41.13±3.03
Control cluster	35	0.07±0.01	11.88±0.91	34.12±2.08
t	-	37.844	10.328	12.300
P	-	<0.001	<0.001	<0.001

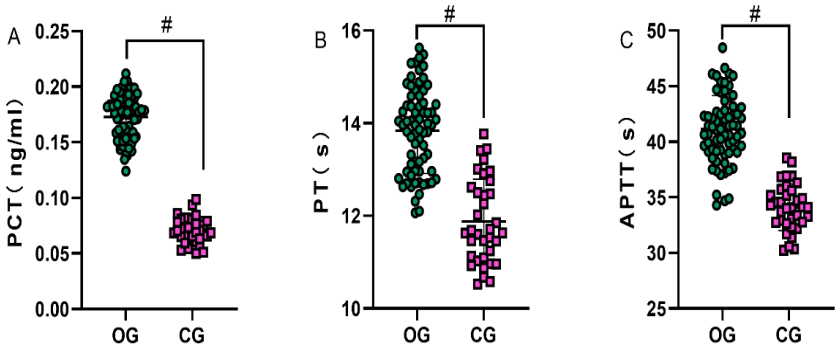

Figure 1 Comparative of PCT and coagulation function between the observation cluster and the control cluster PCT, PT and APTT within the observation cluster were remarkably upper than those within the control cluster, and the variance between the two clusters was remarkable (P < 0.05). # represents the variance between the same indicator clusters.

3.3 Variances in PCT and coagulation parameters in children infected with different pathogens

The observation cluster was divided into bacterial infection cluster (n = 41) and viral infection cluster (n = 39) according to pathogen infection type area. The PCT and coagulation parameters were contrasted between the two clusters. The results showed that the PCT level in bacterial infection cluster was remarkably upper than that in viral infection cluster (P < 0.05), but there was no remarkable variance in PT and APTT between the two clusters (P > 0.05). Table 3, Figure 2 and Figure 3.

Table 3 Variances in PCT and coagulation parameters in children infected with different pathogens ($\overline{x} \pm s$)

Cluster	Cases	PCT（ng/ml）	PT（s）	APTT（s）
Bacterial Infections cluster	41	0.18±0.02	13.80±0.91	41.54±3.13
Viral Infections cluster	29	0.16±0.02	13.88±0.95	40.54±2.83
t	-	4.121	0.356	1.369
P	-	<0.001	0.723	0.175

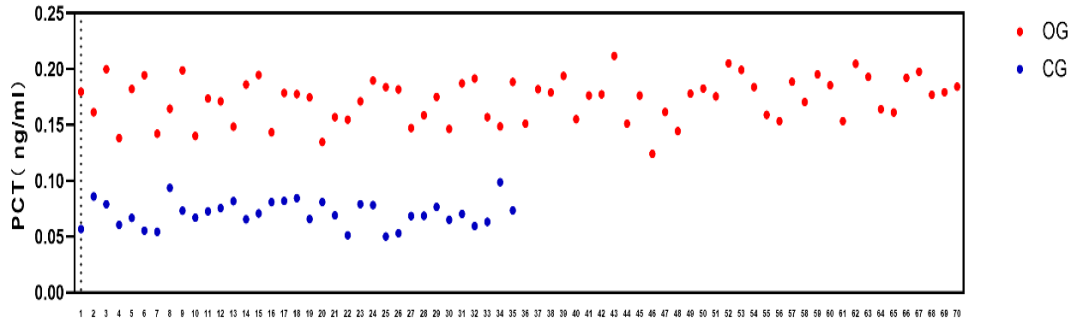

Figure 2 PCT levels in children infected with different pathogens The PCT levels in children infected with bacterial infection were remarkably upper than those in children infected with viral infection.

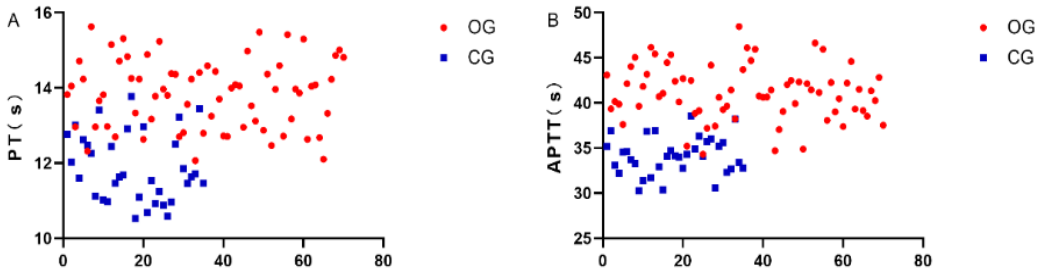

Figure 3 There was no remarkable variance in coagulation parameters between bacterial infection cluster and viral infection cluster.

3.4 Variances in PCT and coagulation parameters in children with different severities

The children within the observation cluster were divided into non-risk cluster, risk cluster and very risk cluster according to the disease condition. The comparative between the two clusters showed that the PCT, PT and APTT of the children in the very risk cluster were remarkably upper than those of the children in the risk cluster, and the PCT, PT and APTT of the children in the risk cluster were remarkably upper than those of the children in the non-risk cluster. The variance between the clusters was remarkable ($P < 0.05$). Table 4 and Figure 4.

Table 4 variances in PCT and coagulation parameters in children with different severities ($\overline{x} \pm s$)

Cluster	Cases	PCT（ng/ml）	PT（s）	APTT（s）
Noncritical recombination	27	0.19±0.01	14.94±0.37	44.75±1.55
Critical recombination	23	0.18±0.01	14.02±0.54	41.45±2.03
Critical recombination	20	0.15±0.03	13.47±0.12	40.07±0.12
t	-	29.285	85.535	60.730
P	-	<0.001	<0.001	<0.001

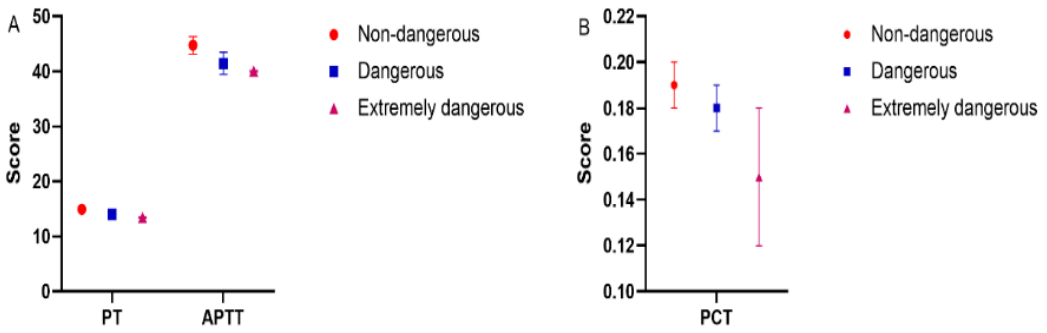

Figure 4 PCT and coagulation parameters in children with different severities were remarkably different between clusters in PCT (Figure B), PT and APTT (Figure A) levels ($P < 0.05$).

3.5 Correlation between PCT and coagulation parameters and NCIS mark within the observation cluster

The analysis showed that there was a remarkable negative correlation between PCT levels and coagulation parameters and their NCIS marks within the observation cluster (r = -0.6112, r = -0.9131, r = -0.8527, P < 0.0001), Table 5 and Figure 5.

Table 5 Correlation between PCT, coagulation parameters and NCIS mark within the observation cluster

Indicators	NCIS	PCT	PT	APTT
NCIS	-	-0.6112	-0.9131	-0.8527
PCT	-0.6112	-	-	-
PT	-0.9131	-	-	-
APTT	-0.8527	-	-	-

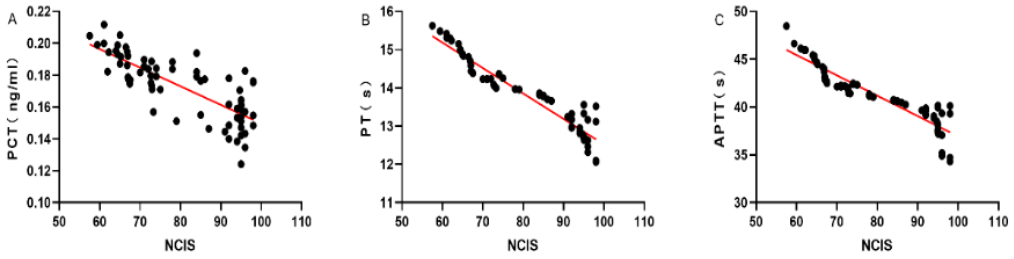

Figure 5 Correlation between PCT, coagulation indicators and NCIS mark within the observation cluster There was a remarkable negative correlation between PCT level (Figure A), PT (Figure B), APTT (Figure C) and NCIS mark within the observation cluster (r = -0.6112, r = -0.9131, r = -0.8527, P < 0.0001).

4. DISCUSSION

Data show that neonatal infection is currently a common and frequently-occurring disease in neonatal wards in China, and the incidence of neonatal infectious diseases in China is about 0.1% – 1.0%, with a mortality rate of about 15% – 50% (Gkentzi & Dimitriou, 2019; M. Zhang et al., 2021). Reports point out that about 1.6 million newborns die of infection each year worldwide, and surveys have also shown that about 8% – 80% of neonatal deaths are associated with infection, 42% of which will die within 1 week of birth (Hadfield & Cantey, 2021; Kutílek et al., 2019). Although high-grade antibiotics, fluid resuscitation, nutritional support, organ function support and other therapies are continuously applied in newborns with infectious diseases, severe infection is still one of the important causes of neonatal death. How to early identify, determine the severity of the disease, and timely carry out treatment has become the key to reduce the prognosis of newborns with infectious diseases (Ambalam et al., 2021; Liang et al., 2019). The predictive value of procalcitonin and coagulation parameters for the severity of neonatal infectious diseases was

analyzed by establishing a control cluster, and the results showed that the PCT, APTT and PT levels of newborns within the observation cluster of infectious diseases were remarkably increased contrasted with those of newborns within the control cluster of non-infectious diseases. A controlled study of 79 neonates with infectious diseases and 75 healthy neonates found that the mean PT time of neonates with infectious diseases was (13.89 ± 2.15) s, which was remarkably upper than that of the control cluster (12.98 ± 3.21) s, while the PCT level of neonates with infectious diseases was (0.13 ± 0.02) ng/ml, which was also upper than that of the control cluster (0.06 ± 0.01) ng/ml (Sewell, Roberts, & Mukhopadhyay, 2021). Another prospective study of 120 newborns showed that the PCT level and D-D level of newborns within the observation cluster of infectious diseases were upper than those of healthy newborns, and the above indicators were also closely related to the prognosis of newborns (Sabry, Ibrahim, & Khashana, 2021). These findings were similar to the conclusions of this paper.

The authors analyzed that due to immature development of various organ systems in newborns, when the body appears severe infection, a large amount of endotoxin in the body can stimulate mononuclear phagocytes and vascular endothelial cells to synthesize and secrete inflammatory mediators and cytokines, resulting in increased PCT levels (Fried et al., 2021; Z. Zhang et al., 2021). At the same time, the elevated inflammatory mediators and cytokines will promote the activation of endothelial cells and monocytes, so that the release of tissue factor increases, tissue factor can activate the exogenous coagulation system, and then affect the neonatal APTT and PT and other coagulation function indicators (Febro-Naga & Tinam-Isan, 2022). In this paper, it is found that there are also some variances in PCT levels in newborns infected with different pathogens. The analysis suggests that bacterial endotoxin is the main cause of PCT production, while viral infection will release infectin-γ from the body, and infectin-γ will block the synthesis of PCT to a certain extent. Therefore, the serum PCT level in newborns infected with viral infection will be lower than that in newborns infected with bacterial infection (Weitkamp, 2021). This result suggests that it is not advisable to use PCT alone to evaluate the condition of newborns infected with infectious diseases, because it is greatly affected by the type of infection. In order to verify the correlation between PCT, coagulation function and the severity of neonatal infectious diseases, it was finally found by clustering the newborns within the observation cluster that the neonatal serum PCT level, APTT and PT time would increase remarkably with the aggravation of the disease, and further correlation analysis confirmed this conjecture (Xu & Li, 2019). It has been pointed out that NCIS is a commonly used neonatal disease assessment index with high reliability and validity (Oligbu, Ahmed, Ferraras-Antolin, & Ladhani, 2021), and the results of this study found that neonatal NCIS marks in infectious diseases showed a negative correlation with PCT, APTT and PT. In this paper, the authors analyzed that infection will lead to increased release of inflammatory factors in the body, and

the entry of a large number of inflammatory factors into the blood will cause damage to vascular endothelial cells, while the consumption of coagulation factors and platelets caused by infection will induce secondary hyperfibrinolysis, and finally make the coagulation function of children appear abnormal, this process is closely related to the inflammatory state, the more severe the degree of infection, the more obvious the coagulation disorders, which is also the main reason for the results in this paper, this result also confirms the feasibility of PCT, coagulation function tests can be applied to the assessment of the severity of neonatal infectious diseases.

5. CONCLUSIONS

In the world of sports, where performance margins are often razor-thin, the effective management of infectious diseases in athletes is an imperative that cannot be underestimated. This article has delved into the realm of diagnostics, specifically the utility of Procalcitonin and coagulation function tests, as invaluable tools for assessing infection severity in athletes. Drawing inspiration from their applications in neonatal medicine, we have explored how these tests can be harnessed to provide insights into the health of athletes and guide their treatment.

As we conclude this examination, it is evident that Procalcitonin and coagulation function tests offer a promising avenue for evaluating infectious disease severity in athletes. These biomarkers can help clinicians differentiate between mild and severe infections, aiding in the timely initiation of appropriate treatments. By closely monitoring these markers, healthcare professionals can also track an athlete's response to therapy and make necessary adjustments, thereby optimizing the recovery process. However, it is crucial to recognize that the management of infections in athletes extends beyond the laboratory results. The unique demands of competitive sports, including the pressure to perform and the desire for rapid recovery, necessitate a holistic approach that encompasses physical, mental, and emotional aspects of an athlete's well-being. Coordinated efforts involving medical professionals, coaches, and athletes themselves are essential to navigate the complexities of infection management effectively. In conclusion, while Procalcitonin and coagulation function tests hold promise as valuable diagnostic tools for assessing infectious disease severity in athletes, their application should be integrated into a comprehensive strategy that considers the athlete's individual needs and circumstances. The lessons learned from neonatal medicine provide a valuable foundation upon which to build, but adaptation to the world of sports is crucial. With the right tools and a patient-centered approach, we can empower athletes to not only recover swiftly but also regain their competitive edge and continue to excel in their chosen disciplines. The intersection of medical science and sports performance is a dynamic field with much potential, and it is incumbent upon all stakeholders to explore and harness these possibilities for the benefit

of athletes worldwide.

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