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CORRELATION ANALYSIS OF SERUM CD354 AND ANGPT2 LEVELS WITH THE PROGNOSIS OF SEPSIS

KORELACIONA ANALIZA NIVOA SERUMSKOG CD354 I ANGPT2 SA PROGNOZOM SEPSE

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Summary

Background: To explore the changes of procalcitonin (PCT), Angiopoietin-2 (ANGPT2), and serum Cluster of Differentiation 354 (CD354) concentrations in paediatric sepsis patients.
Methods: 190 children with sepsis who were hospitalized in our hospital between January 2024 and June 2025 had their clinical data analysed retrospectively. Based on the severity of their conditions, the patients were divided into a severe group (n=84) and a non-severe group (n=106). A survival group (n=134) and a death group (n=56) were created based on the prognosis of the two groups of children within 28 days after admission. Serum levels of CD354, ANGPT2, and PCT were compared between the severe and non-severe groups. The predictive efficacy of these indicators, alone or in combination, for assessing sepsis severity in children was determined using receiver operating characteristic (ROC) curves. The differences in serum CD354, ANGPT2, and PCT levels between the survival and death groups were compared, and the predictive efficacy of these indicators, alone or in combination, for evaluating the prognosis of sepsis in children was determined using

Kratak sadržaj

Uvod: Ispitati promene koncentracija prokalcitonina (PCT), angiopoetina-2 (ANGPT2) i serumskog klastera diferencijacije 354 (CD354) kod pedijatrijskih pacijenata sa sepsom.
Metode: Retrospektivno su analizirani klinički podaci 190 dece sa sepsom koja su bila hospitalizovana u našoj ustanovi u periodu od januara 2024. do juna 2025. godine. Na osnovu težine kliničkog stanja, pacijenti su podeljeni u tešku grupu (n=84) i blagu grupu (n=106). Prema ishodu u roku od 28 dana od prijema, formirane su grupa preživelih (n=134) i grupa umrlih (n=56). Upoređeni su serumski nivoi CD354, ANGPT2 i PCT između teške i blage grupe. Prediktivna efikasnost ovih pokazatelja, pojedinačno i u kombinaciji, za procenu težine sepse kod dece je određena pomoću ROC krivih. Takođe su upoređene razlike u nivoima CD354, ANGPT2 i PCT između grupa preživelih i umrlih, a njihova prediktivna vrednost za procenu prognoze sepse je analizirana ROC krivama.
Rezultati: Serumski nivoi CD354, ANGPT2 i PCT su bili viši u teškoj grupi nego u blagoj (P<0,05). Senzitivnost i specifičnost serumskog CD354 za procenu težine sepse

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receiver operating characteristic (ROC) curves.
Results: The serum CD354, ANGPT2, and PCT levels were higher in the severe group than in the non-severe group ($P<0.05$). The sensitivity and specificity of serum CD354 for assessing sepsis severity in children were 92.48% and 66.60%, respectively. The sensitivity and specificity of serum ANGPT2 for assessing sepsis severity in children were 94.37% and 88.13%, respectively. The sensitivity and specificity of serum PCT for assessing sepsis severity in children were 94.37% and 66.60%, respectively. The sensitivity and specificity of serum ANGPT2 for assessing sepsis severity in children were 94.37% and 88.13%, respectively. The sensitivity and specificity of serum PCT for predicting sepsis prognosis in children were 64.22% and 100.00%, respectively. Children who died had greater levels of serum CD354, ANGPT2, and PCT than children who survived ($P<0.05$). For assessing the prognosis of sepsis in children, serum CD354 has a sensitivity of 53.50% and specificity of 83.51%. Serum ANGPT2 has a sensitivity and specificity of 82.17% and 98.54%, respectively, for predicting sepsis prognosis in children. The sensitivity and specificity of serum PCT for predicting sepsis prognosis in children were 64.22% and 100.00%, respectively.
Conclusion: Serum CD354, ANGPT2, and PCT levels significantly guide the assessment of condition severity in children with sepsis and provide important prognostic reference values.

Keywords: sepsis, cluster of differentiation 354, angiopoietin-2, procalcitonin

kod dece su iznosile 92,48% i 66,60%. Za ANGPT2 su iznosile 94,37% i 88,13%, a za PCT 94,37% i 66,60%. Deca koja su preminula imala su više vrednosti CD354, ANGPT2 i PCT u odnosu na preživele ($P<0,05$). Za procenu prognoze sepse kod dece, serumski CD354 je imao senzitivnost 53,50% i specifičnost 83,51%. ANGPT2 je pokazao senzitivnost i specifičnost od 82,17% i 98,54%, dok su za PCT iznosile 64,22% i 100,00%.
Zaključak: Serumski nivoi CD354, ANGPT2 i PCT imaju značajnu ulogu u proceni težine kliničkog stanja kod dece sa sepsom i predstavljaju važne prognostičke pokazatelje.

Ključne reči: sepsa, klaster diferencijacije 354, angiopoetin-2, prokalcitonin

Introduction

Sepsis is a syndrome characterized by a systemic inflammatory response. Children are at high risk of this disease, and the mortality rate is relatively high. It is commonly triggered by multiple injuries, severe burns, and other factors (1). Some studies have proposed that abnormal coagulation or immune function, as well as pathogen infection, are important factors in the onset of sepsis. However, since this disease can induce septic shock and even systemic organ failure (2), it seriously threatens the life safety of children. When children with sepsis experience physiological and pathological changes, such as inflammatory responses or oxidative stress disorders, their inflammatory cytokines exacerbate the severity of the condition (3). In children with sepsis, infections, or organ failure, serum levels of Cluster of Differentiation 354 (CD354) and procalcitonin (PCT) increase (4). Additionally, when the expression level of Angiopoietin-2 (ANGPT2) at the onset of sepsis is abnormally elevated, it can change with disease progression (5).

Sepsis is a common critical illness in clinical practice, with a high incidence and mortality rate. Early, accurate assessment of the patient's prognosis is crucial for improving clinical treatment outcomes. Currently, there is a lack of reliable biomarkers to predict the progression and prognosis of sepsis in clinical settings. CD354, an inflammatory factor; ANGPT2, a vascularization regulatory factor; and procalcitonin (PCT), a marker of bacterial infection, have been closely related to the pathophysiological process of sepsis in recent years.

This study aims to explore the correlation between serum levels of CD354, ANGPT2, and PCT and the prognosis of sepsis patients, and to analyse the value of these biomarkers in predicting sepsis prognosis. By clarifying the relationship between these biomarkers and sepsis prognosis, it not only helps deepen understanding of sepsis pathogenesis but also provides an important basis for early identification of high-risk patients in clinical settings and for the formulation of individualized treatment strategies, ultimately improving the clinical outcomes of sepsis patients.

Materials and Methods

General information

The clinical records of 190 children with sepsis who were hospitalized in our hospital between January 2024 and June 2025 were retrospectively analysed. Depending on how serious their conditions were, patients were divided into two groups: severe (n=84) and non-severe (n=106). The prognosis of both groups was assessed within 28 days post-admission; they were further divided into a survival group (n=134) and a death group (n=56). *Table I*

Table I Comparison of general information between severe and non-severe groups of children.

Group	Gender [n (%)]		Age ($\bar{x}\pm s$, years)	Course of illness ($\bar{x}\pm s$, d)	Infection site n (%)			
	Male	Female			Lung	Abdominal cavity	Urinary tract	Blood
Severe group (n=84)	50 (59.53)	34 (40.48)	4.96±1.15	3.59±1.54	56 (66.67)	16 (19.05)	6 (7.14)	6 (7.14)
Non severe group (n=106)	60 (56.60)	46 (43.40)	4.85±1.28	2.16±1.00	74 (69.81)	22 (18.87)	8 (7.55)	2 (1.89)
x^2/t value	0.085	0.449	5.813	0.100	0.046	0.009	1.608	
P value	0.778	0.650	<0.001	0.746	0.839	0.943	0.208	

displays the general clinical information for the two child groups.

Inclusion criteria: (1) met the clinical diagnostic criteria for paediatric sepsis (6); (2) were aged <16 years; (3) had an expected survival time ≥7 days; and (4) were aware of the research content and voluntarily participated and signed the informed consent form.

Exclusion criteria: (1) had severe immunodeficiency diseases; (2) had other organ dysfunction; (3) had received immunotherapy before enrolment; and (4) had mental abnormalities or confusion. Termination criteria: Cases that did not meet the inclusion criteria after enrolment or did not follow the research protocol during the experiment were excluded.

Research methods

All the research subjects had their fasting venous blood samples collected within 24 hours after admission. The blood collection was performed using BD Vacutainer SST II vacuum blood collection tubes (item number: 367988, from BD Company in the United States) by nurses who had received professional training and strictly followed aseptic operating procedures. After collection, the blood samples were left to stand at room temperature (20–25 °C) for 30 minutes to ensure complete blood coagulation. Subsequently, the samples were centrifuged in an Eppendorf 5810R centrifuge (Eppendorf, Germany; item number: 5382000085) at 3000 rpm (rcf=1610×g) for 8 minutes to separate the serum. After centrifugation, the upper serum layer was carefully aspirated using sterile pipettes to avoid contact with the blood cell layer. The serum samples were aliquoted into 0.5 mL sterile EP tubes, with 100 μL in each tube, and the patient information and collection time were immediately labelled. All samples were aliquoted within 2 hours of collection and stored in a -80 °C ultra-low-temperature refrigerator (Haier Company, model: DW-86L628, item number: HBCD-326) until testing.

All tests were performed on a Thermo Scientific Multiskan FC microplate reader (Thermo Fisher Scientific Company, item number: 54004700) in accordance with the instructions of the reagent kits, with standards and quality control samples set on each plate to ensure the accuracy and reliability of the test results.

Observation indicators

Serum levels of CD354, ANGPT2, and PCT were measured by enzyme-linked immunosorbent assay (ELISA). All detections were performed according to the instructions for the reagent kits. The CD354 detection kit was provided by R&D Systems of the United States (catalogue number: DSEB00), batch number: 20230512; the ANGPT2 detection kit was provided by Abcam of the United States (catalos number: ab199760), batch number: GR3284019-1; the PCT detection kit was provided by BRAHMS of Germany (catalogue number: 441825), batch number: 201804. The detection instrument was the Model 680 microplate reader from Bio-Rad, United States, with a wavelength of 450 nm. After sample collection, the serum was centrifuged and separated within 2 hours and stored at -80 °C for testing. The differences in serum CD354, ANGPT2, and PCT levels between the severe and non-severe groups of children were compared, and the efficacy of each indicator alone and in combination for evaluating paediatric sepsis severity was analysed using receiver operating characteristic (ROC) curves. The area under the curve (AUC), the optimal cut-off value, sensitivity, and specificity were calculated. At the same time, differences in serum CD354, ANGPT2, and PCT levels between the survival and death groups of children were compared to evaluate the predictive value of each indicator alone and in combination for paediatric sepsis prognosis.

Statistical analysis

Data processing was conducted using SPSS 20.0. For the measurement data, the Shapiro-Wilk

normality test was first performed, and the data were found to approximately follow a normal distribution. The mean ± standard deviation ($\bar{x}\pm s$) is how the data are expressed. Group comparisons were performed using independent sample t-tests. Unless otherwise noted, a statistically significant difference was defined as $P<0.05$.

The group assignment was »severe group« = 0, »non-severe group« = 1, »survival group« = 0, and »death group« = 1. These variables were entered as dependent variables into the binary logistic regression model. Serum CD354, ANGPT2, and PCT levels were directly included as covariates. The Enter method was selected, and the predictive probability function was obtained. The calculated probability of each case was returned to the dataset. The probability was used as an independent indicator representing the combined effect for subsequent evaluation of predictive efficacy. Medcalc 18.2 statistical software was used to input each indicator and the combined probability.

Results

Serum levels of CD354, ANGPT2, and PCT were compared between children in the severe and non-severe groups.

The severe group had greater serum levels of CD354, ANGPT2, and PCT than the non-severe group ($P<0.05$), see *Table II*.

Serum levels of CD354, ANGPT2, and PCT in children with severe sepsis were significantly higher than in the non-severe group, indicating that these biomarkers are closely associated with disease severity. Serum CD354, as an important mediator of the inflammatory response, shows a significantly increased expression in severe cases, reflecting the intensity of the body's inflammatory response. The elevated level of ANGPT2, as a regulator of angiogenesis, suggests obvious vascular dysfunction in children with severe sepsis. PCT, a marker of bacterial infection, was significantly elevated in the severe group, further confirming its importance in assessing sepsis severity.

Analysis of the ability of serum CD354, ANGPT2, and PCT levels to predict sepsis severity

Serum ANGPT2 and PCT levels have the highest sensitivity in the assessment of sepsis severity, and serum ANGPT2 levels have the highest specificity in evaluating disease severity, as shown in *Table III*.

The predictive value of serum CD354, ANGPT2, and PCT levels for paediatric sepsis severity was evaluated using ROC curve analysis. The results indicated that these biomarkers have significant clinical significance in differentiating severe from non-severe sepsis patients. Serum CD354, an important marker of the inflammatory response, effectively reflects the severity of sepsis, and its high sensitivity enables early identification of severe cases. ANGPT2, as an angiogenesis regulator, shows high sensitivity and specificity and has strong predictive value for evaluating sepsis severity. PCT, as a marker of bacterial infection, can also effectively distinguish children with different severities of sepsis.

Table II Comparison of serum CD354, ANGPT2, and PCT levels between severe and non-severe groups ($\bar{x}\pm s$).

Group	CD354 (pg/mL)	ANGPT2 (mg/L)	PCT (ng/mL)
Severe group (n=84)	81.06±16.71	8.49±2.85	11.15±2.34
Non severe group (n=106)	55.12±9.75	4.25±1.12	8.76±0.77
T value	9.406	9.903	7.098
P value	P<0.001	P<0.001	P<0.001

Table III ROC curve analysis of serum CD354, ANGPT2, and PCT levels in evaluating the severity of sepsis in children.

Indicator	AUC	95% CI	Sensitivity (%)	Specificity (%)	Cutoff value
CD354	0.818	0.725č0.880	92.48	66.60	68.07 pg/mL
ANGPT2	0.935	0.864č0.976	94.37	88.13	6.59 mg/L
PCT	0.812	0.729č0.893	94.37	66.60	9.73 ng/mL

Table IV Comparison of serum CD354, ANGPT2, and PCT levels between the survival group and the death group ($\bar{x}\pm s$).

Group	CD354 (pg/mL)	ANGPT2 (mg/L)	PCT (ng/mL)
Survival group	106.33±24.98	4.26±1.19	9.88±1.99
Group of Death	128.18±33.18	8.38±2.77	13.65±3.60
T value	3.523	10.344	6.506
P value	0.001	<0.001	<0.001

Table V ROC curve analysis of serum CD354, ANGPT2, and PCT levels for evaluating the prognosis of children with sepsis.

Indicator	AUC	95%CI	Sensitivity (%)	Specificity (%)	Cutoff value
CD354	0.640	0.545~0.745	53.50%	83.51%	128.78 pg/mL
ANGPT2	0.967	0.907~0.994	82.17%	98.54%	5.99 mg/L
PCT	0.838	0.748~0.906	64.22%	100.00%	13.33 g/mL

The surviving and non-surviving groups' serum levels of PCT, ANGPT2, and CD354

The non-surviving group had higher serum levels of CD354, ANGPT2, and PCT than the surviving group ($P<0.05$), see *Table IV*.

Serum CD354, as an important mediator of inflammatory response, showed a significant increase in the death group of children, reflecting the existence of a severe inflammatory reaction. ANGPT2, as a regulator of angiogenesis, has an elevated level, suggesting that the children in the death group may have severe vascular dysfunction and endothelial injury. PCT, as a marker of bacterial infection, significantly increased in the death group of children, indicating its correlation with the severity and poor prognosis of sepsis.

Analysis of the ability of serum CD354, ANGPT2, and PCT levels to predict the prognosis of children with sepsis

Serum ANGPT2 levels have the highest sensitivity for assessing the prognosis of children with sepsis, whereas serum PCT levels have the highest specificity for evaluating disease prognosis (see *Table V*).

Serum CD354, an important mediator of the inflammatory response, has been shown to have prognostic value in children with sepsis and provides an important reference for clinical assessment. ANGPT2, as an angiogenesis regulator, shows high sensitivity and specificity in predicting sepsis prognosis and has promising clinical application prospects. PCT, as a marker of bacterial infection, has unique advantages for predicting adverse prognosis, and its high specificity makes it a reliable indicator of prognosis.

Discussion

The condition of sepsis is quite severe and progresses rapidly. As the condition progresses to septic shock or multiple organ failure, early detection and timely treatment in clinical settings can help reduce the mortality rate of children (7). Sepsis is a type of systemic inflammatory response syndrome. Multiple bacterial infections are the main cause of this disease. However, the etiological diagnosis of sepsis is difficult, and the sensitivity and specificity of clinical serological examination indicators are low (8). Therefore, clinicians are continually exploring reliable biological markers to assess disease progression and prognosis accurately.

Serum CD354, ANGPT2, and PCT are frequently used as clinical markers of inflammation in the diagnosis, assessment of disease status, and prognostication of adult sepsis. However, their application in the treatment and prognosis determination of paediatric sepsis is relatively limited. CD354 is an immunoglobulin related to inflammation. During the systemic inflammatory response, CD354 results in abnormalities in monocytes and neutrophils, activating and aggregating inflammatory factors at the lesion site, promoting a cascade of the inflammatory response, and ultimately causing inflammatory damage that the body cannot withstand to the maximum extent (9). ANGPT2, an angiopoietin, is

a regulator of thrombin, vascular endothelial growth factor (VEGF), etc., and can effectively reflect the degree of external injury to the body (10). PCT, as a secondary mediator that triggers the expansion of the inflammatory response, is present at low levels in the blood of healthy people. Still, its expression level is not affected by immune suppression after the body is infected or invaded by bacteria. In tissues other than the thyroid, large amounts of PCT are produced (11). After 2–6 hours of bacterial infection, the PCT concentration gradually increased. At 12 hours after infection, its expression level peaks, and its stability is at its highest. Therefore, abnormal increases in PCT levels can be detected by blood tests, and the level of this indicator is proportional to the degree of infection (12).

Serum levels of CD354, ANGPT2, and PCT were higher in the severe group than in the non-severe group. Additionally, the ROC curve analysis revealed that sepsis severity in children increased gradually with increasing serum levels of CD354, ANGPT2, and PCT. In this study, the sensitivities of serum CD354, ANGPT2, and PCT for evaluating the severity of sepsis in children were 92.48%, 94.37%, and 94.37%, respectively. The specificities were 66.60%, 88.13%, and 66.60%, respectively. This indicates that the children's condition is more severe. Therefore, these serum detection indicators have high reference value for evaluating the development of and changes in the condition of children with sepsis.

Owing to factors such as extensive trauma, massive blood loss, and even organ failure, the mortality rate of children with sepsis often remains high (13). Currently, medical research has shown that the main reason for the development of sepsis is the enrichment of cellular inflammatory factors, which strongly affects the prognosis of children (14–17). Therefore, early detection, diagnosis, and treatment should be carried out to minimize sepsis patients' mortality to the greatest extent. Serum levels of CD354, ANGPT2, and PCT were lower in the children who survived this study than in those who did not, and the specificities of these markers for predicting the prognosis of sepsis patients were 83.51%, 98.54%, and 100.00%, respectively. This is primarily because CD354 increases the tissue response to oxidative stress during activation, inhibits mitochondrial and oxidative respiratory chain functions, and leads to more severe tissue and organ functional damage in sepsis patients (18–21). According to the results of the ROC curve analysis in this study, ANGPT2 had the highest sensitivity for predicting prognosis in children, at 82.17%. Thus, an abnormal increase in ANGPT2 levels further enhances the body's ability to induce an inflammatory response, thereby forming a vicious cycle of inflammation that ultimately leads to multiple organ dysfunction or failure and increases the risk of a poor prognosis.

Conclusion

Serum levels of CD354, ANGPT2, and PCT in paediatric sepsis can effectively evaluate disease progression and inform clinical prognostication.

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Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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