

THE RELATIONSHIP BETWEEN THE SERUM PHOSPHATASE AND TENSIN HOMOLOG (PTEN) AND TLR4 AND THE SEVERITY AND PROGNOSIS OF NEONATAL SEPSIS

POVEZANOST SERUMSKIH NIVOVA FOSFATAZE I TENZIN HOMOLOGA (PTEN) I TLR4 SA TEŽINOM KLINIČKE SLIKE I PROGNOZOM KOD NEONATALNE SEPSE

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Summary

Background: Neonatal sepsis is associated with severe systemic inflammation and high mortality. This study evaluated whether serum levels of phosphatase and tensin homolog (PTEN) and toll-like receptor 4 (TLR4) are associated with disease severity and prognosis in neonatal sepsis.

Methods: This study included 116 neonates with sepsis and 50 healthy controls. Based on SOFA scores, septic neonates were classified into mild sepsis and severe sepsis groups; severe cases were further divided into 8 deaths and 44 survivors. Serum PTEN, TLR4, procalcitonin (PCT), C-reactive protein (CRP), heparin-binding protein (HBP), and white blood cell count (WBC) were measured. Correlations and diagnostic/prognostic performance were assessed using Pearson correlation and ROC analysis.

Results: Inflammatory markers increased with disease severity. PCT rose from 0.12 ± 0.01 ng/mL in controls to 0.75 ± 0.14 in mild sepsis and 1.74 ± 0.23 in severe sepsis; CRP increased from 5.34 ± 0.36 to 28.84 ± 3.52 and 77.26 ± 6.49 mg/mL, respectively. PTEN declined from 3.05 ± 0.17 ng/mL in controls to 2.25 ± 0.15 in mild sepsis and 1.37 ± 0.11 in severe sepsis, whereas TLR4 increased from 0.74 ± 0.16 mg/mL to 1.35 ± 0.14 and 2.51 ± 0.20 . Among severe cases, non-survivors had higher PCT (4.39 ± 1.13 vs 1.63 ± 0.36 ng/mL) and CRP (123.58 ± 9.03 vs 68.34 ± 5.27 mg/mL) than survivors. Non-survivors also had lower PTEN (0.95 ± 0.16 vs 1.24 ± 0.18 ng/mL) and higher TLR4 (2.86 ± 0.20 vs 2.14 ± 0.18 ng/mL). ROC analysis showed strong predictive value for PTEN (AUC 0.846; sensitivity 89.23%; specificity 86.23%) and TLR4

Kratak sadržaj

Uvod: Neonatalna sepsa je povezana sa teškom sistemskom inflamacijom i visokom stopom mortaliteta. Ova studija je ispitivala da li su serumski nivoi fosfataze i tenzin homologa (PTEN) i »Toll-like« receptora 4 (TLR4) povezani sa težinom bolesti i prognozom kod neonatalne sepse.

Metode: U studiju je uključeno 116 novorođenčadi sa sepsom i 50 zdravih kontrolnih učesnika. Na osnovu SOFA skora, novorođenčad sa sepsom je klasifikovana u grupe blage i teške sepse; teški slučajevi su dalje podeljeni na 8 smrtnih ishoda i 44 preživela pacijenta. Određivani su serumski nivoi PTEN-a, TLR4, prokalcitonina (PCT), C-reaktivnog proteina (CRP), heparin-vezujućeg proteina (HBP) i broj leukocita (WBC). Korelacije i dijagnostičko/prognostičke performanse su procenjivane primenom Pironove korelacione analize i ROC analize.

Rezultati: Informatorni markeri su se povećavali sa porastom težine bolesti. Nivo PCT-a je porastao sa $0,12 \pm 0,01$ ng/mL u kontrolnoj grupi na $0,75 \pm 0,14$ kod blage sepse i $1,74 \pm 0,23$ kod teške sepse; CRP je porastao sa $5,34 \pm 0,36$ na $28,84 \pm 3,52$ i $77,26 \pm 6,49$ mg/mL. PTEN je opao sa $3,05 \pm 0,17$ ng/mL u kontrolnoj grupi na $2,25 \pm 0,15$ kod blage sepse i $1,37 \pm 0,11$ kod teške sepse, dok je TLR4 porastao sa $0,74 \pm 0,16$ mg/mL na $1,35 \pm 0,14$ i $2,51 \pm 0,20$ mg/mL. Među teškim slučajevima, pacijenti sa smrtnim ishodom imali su više vrednosti PCT-a ($4,39 \pm 1,13$ prema $1,63 \pm 0,36$ ng/mL) i CRP-a ($123,58 \pm 9,03$ prema $68,34 \pm 5,27$ mg/mL) u poređenju sa preživelim. Takođe, pacijenti sa smrtnim ishodom su imali niže vrednosti PTEN-a ($0,95 \pm 0,16$ prema $1,24 \pm 0,18$ ng/mL) i više vrednosti TLR4 ($2,86 \pm 0,20$ prema $2,14 \pm 0,18$ ng/mL). ROC analiza pokazala je

(AUC 0.857; sensitivity 90.31%; specificity 86.16%).

Conclusion: Reduced PTEN and elevated TLR4 are associated with stronger inflammatory responses, greater sepsis severity, and poorer prognosis in neonates. These biomarkers may support early risk stratification and prognostic assessment.

Keywords: neonatal sepsis, serum PTEN and TLR4 expression, severity, prognosis

Introduction

Neonatal sepsis is a critical systemic infection characterised by an aberrant inflammatory response triggered by circulating microorganisms (1, 2). It occurs when pathogenic or opportunistic bacteria multiply in the newborn's blood and secrete toxins, resulting in systemic infection. This disorder is quite prevalent throughout the neonatal period and is linked to a significant risk of mortality. Due to the incomplete development of neonatal immune function, infants are exceedingly susceptible to infections, rendering timely diagnosis and efficient treatment particularly difficult.

Standard inflammatory markers, including white blood cell count, C-reactive protein, and procalcitonin, are frequently utilised for diagnosing and monitoring neonatal sepsis and may offer insights into illness severity. Nevertheless, these markers exhibit inadequate specificity for sepsis. They may not adequately represent the patient's status in the initial phase of infection. Consequently, identifying more sensitive and specific biomarkers is crucial for improving early diagnosis, prognostic evaluation, and clinical management of newborn sepsis.

In recent years, there has been increased attention on molecules involved in intracellular signalling pathways and immune regulation, particularly phosphatase and tensin homolog (PTEN) and toll-like receptor 4 (TLR4). PTEN is a tumour suppressor that is essential for regulating cell proliferation, apoptosis, and immune responses. PTEN largely regulates inflammatory and immunological processes by suppressing the PI3K/Akt signalling pathway, and alterations in PTEN expression are associated with the development of many diseases (3). Conversely, TLR4 functions as an essential pattern-recognition receptor enabling the host immune system to identify pathogens and initiate innate immune responses (4, 5). The activation of TLR4 triggers the release of inflammatory mediators. It enhances both cellular and humoral immune responses, hence supporting the host's defence against infection. Nonetheless, overactivation of TLR4 might lead to unregulated inflammation and worsen illness severity.

Given the critical roles of PTEN and TLR4 in inflammation and immune regulation, investigat-

snaznu prediktivnu vrednost za PTEN (AUC 0,846; senzitivnost 89,23%; specifičnost 86,23%) i TLR4 (AUC 0,857; senzitivnost 90,31%; specifičnost 86,16%).

Zaključak: Sniženi nivoi PTEN-a i povišeni nivoi TLR4 su povezani sa izraženijim inflamatornim odgovorom, većom težinom sepse i lošijom prognozom kod novorođenčadi. Ovi biomarkeri mogu doprineti ranoj stratifikaciji rizika i proceni prognoze.

Cljučne reči: neonatalna sepsa, serumska ekspresija PTEN-a i TLR4, težina bolesti, prognoza

ing their serum expression levels in neonatal sepsis and their association with disease severity and prognosis may provide valuable insights for clinical evaluation of this condition. Moreover, clarifying the link between changes in PTEN and TLR4 and the pathogenic progression of neonatal sepsis may aid in developing more accurate diagnostic techniques and targeted therapeutic strategies, thereby improving clinical outcomes in affected infants. This study seeks to evaluate blood levels of PTEN and TLR4 in neonates with sepsis and to investigate their link with disease severity and prognosis, thereby providing a scientific basis for early identification and tailored management of neonatal sepsis (6, 7).

Materials and Methods

General information

This study encompassed 116 neonates diagnosed with septicemia who were hospitalised to our hospital between March 2024 and June 2025. The patients' ages varied from 5 to 26 days, with a mean age of 22.54 ± 3.57 days. Of the total, 60 were male, and 56 were female. Utilising the SOFA scoring system, newborns with scores between 1 and 18 were classified as mild sepsis ($n=64$), while those with scores from 19 to 24 were classified as severe sepsis ($n=52$). In the severe sepsis cohort, 8 babies died and were classified as the death group, while the remaining 44 neonates survived and were labelled as the survival group. During the same research period, 50 healthy infants who had standard physical examinations were assigned to the control group. Written informed consent was obtained from the guardians of all participants before enrolment.

Inclusion criteria

The inclusion criteria were as follows: neonates aged 0–28 days post-birth, irrespective of sex, encompassing both full-term and premature infants; a diagnosis of neonatal septicemia in accordance with the Guidelines for the Diagnosis and Treatment of Neonatal Diseases or other established clinical protocols; manifestation of typical clinical signs, including abnormal body temperature, dyspnoea, poor

feeding, diminished activity, or irritability; laboratory confirmation of infection, evidenced by positive blood culture, elevated C-reactive protein levels, or abnormal white blood cell counts; and absence of antibiotic treatment within 72 hours before enrolment to prevent potential interference with blood sample results.

Exclusion criteria

Patients were excluded if they had a history of severe underlying diseases, hereditary conditions, congenital disorders, or metabolic disorders; concurrent severe infections, including significant viral or fungal infections; prematurity with low birth weight; severe dysfunction of major organs such as the heart, liver, or kidneys; or any other condition deemed by the research team as unsuitable for participation.

Ethical considerations

This study was reviewed and approved by the relevant ethics committee of our hospital before initiation. The study protocol was explained to the guardians of all eligible participants, and written informed consent was obtained before enrolment. All study procedures were conducted in accordance with applicable ethical standards and regulatory requirements.

Methods

Assessment of inflammatory indicators

The inflammatory status was assessed by enzyme-linked immunosorbent assay (ELISA) and automated blood cell analysis. Peripheral blood samples were collected from all participants, and serum was separated by centrifugation. Serum levels of procalcitonin (PCT), C-reactive protein (CRP) and heparin-binding protein (HBP) were analysed by ELISA according to the manufacturer's instructions.

Briefly, serum samples were added to 96-well microplates pre-coated with specific antibodies and incubated for 1–2 hours to permit antigen-antibody binding. After washing to remove unbound components, enzyme-conjugated secondary antibodies were added and incubated. The plates were washed again, and the chromogenic substrate was added to initiate the colour reaction. Finally, absorbance was measured with a microplate reader, and the concentrations of PCT, CRP, and HBP were calculated from the respective standard curves. An automated haematology analyser measured white blood cell count.

Detection of PTEN and TLR4 levels

Serum levels of PTEN and TLR4 were measured by enzyme-linked immunosorbent assay (ELISA). Fifty microliters of serum sample were added to antibody-coated wells and incubated to promote the formation of antigen-antibody complexes. The wells were later washed several times to remove unbound proteins. Enzyme-labelled secondary antibodies targeting PTEN or TLR4 were applied, incubated, and subsequently washed to remove excess antibody. Absorbance was measured at 450 nm with a microplate reader. The optical density measurements were converted into PTEN and TLR4 concentrations utilising the standard curves.

Statistical analysis

Data were expressed as mean $\pm$ standard error. Continuous variables were examined with ANOVA. Pearson's correlation analysis was performed to investigate the relationship between regularly distributed variables. In contrast, logistic regression was used to evaluate multiple factors. The diagnostic efficacy of each index for severe pneumonia severity was evaluated by ROC curve analysis. Statistical analysis was performed using Sigma Stat Version 3.1 (Systat Software, Inc., Chicago, IL). P values below 0.05 were considered significant.

Results

Demographic and baseline clinical characteristics

In this study, 116 neonates with sepsis and 50 healthy neonates were included. The septic neonates ranged in age from 5 to 26 days, with a mean age of 22.54 ± 3.57 days. Out of the septic neonates, 60 were males, and 56 were females. According to the SOFA score, 64 neonates were categorised into the mild sepsis group and 52 neonates into the severe sepsis group. Among the neonates with severe sepsis, 8 died, and 44 survived. There were no significant differences between the groups on basic demographic variables, suggesting they were comparable for subsequent analyses.

Inflammatory indicators in neonates with sepsis

The severity of the illness had a positive correlation with the rise in inflammatory markers. Neonates with mild and severe sepsis exhibited significantly elevated levels of PCT, CRP, HBP, and WBC count relative to the control group. Furthermore, inflammatory markers were significantly elevated in the severe sepsis group compared with the mild sepsis group, demonstrating a strong correlation

Table I Analysis of inflammatory indices in children.

Groups	PCT (ng/mL)	CRP (mg/mL)	HBP (ng/mL)	WBC (×10 ⁹ /L)
Control group (n=50)	0.12±0.01	5.34±0.36	12.35±2.11	7.14±1.22
Mild septicemia group (n=52)	0.75±0.14	28.84±3.52	37.41±4.38	13.65±2.36
Severe septicemia group (n=64)	1.74±0.23	77.26±6.49	76.22±6.05	17.52±3.51
variance ratio	11.556	16.382	13.024	17.338
P value	0.001	0.001	0.001	0.001

Table II Comparison of serum PTEN and TLR4 levels in children.

Groups	PTEN (ng/mL)	TLR4 (mg/mL)
Control group (n=50)	3.05±0.17	0.74±0.16
Mild septicemia group (n=52)	2.25±0.15	1.35±0.14
Severe septicemia group (n=64)	1.37±0.11	2.51±0.20
variance ratio	17.224	11.613
P value	0.012	0.007

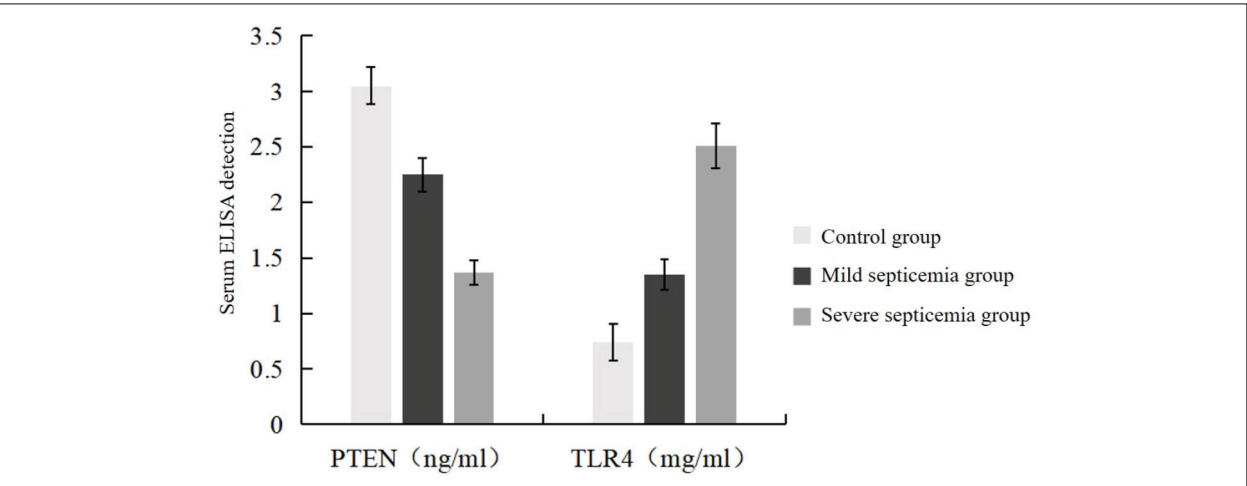


Figure 1 Detection of serum PTEN and TLR4 in children.

between systemic inflammation and sepsis severity. PCT levels rose from 0.12 ± 0.01 ng/mL in the control group to 0.75 ± 0.14 ng/mL in the moderate sepsis group and 1.74 ± 0.23 ng/mL in the severe sepsis group. CRP, HBP, and WBC count showed similar increasing trends, with all comparisons statistically significant at $p=0.001$ (Table I).

Comparison of serum PTEN and TLR4 levels in children

Serum PTEN levels decreased, while TLR4 levels increased, in correlation with the severity of

sepsis. PTEN levels were elevated in the control and mild sepsis groups, whereas they were decreased in the severe sepsis group. Conversely, TLR4 levels were minimal in the control group. They markedly increased in neonates with sepsis, particularly in cases of severe sepsis. PTEN levels diminished from 3.05 ± 0.17 ng/mL in the control group to 2.25 ± 0.15 ng/mL in the mild sepsis group and 1.37 ± 0.11 ng/mL in the severe sepsis group. TLR4 levels increased from 0.74 ± 0.16 mg/mL in the control group to 1.35 ± 0.14 mg/mL in the mild sepsis group and 2.51 ± 0.20 mg/mL in the severe sepsis group. The differences were statistically significant

Table III Analysis of inflammatory indices between the death group and the survival group.

Groups	PCT (ng/mL)	CRP (mg/mL)	HBP (ng/mL)	WBC ($\times 10^9$ /L)
Death group (n=8)	4.39 $\pm$ 1.13	123.58 $\pm$ 9.03	146.25 $\pm$ 10.55	20.36 $\pm$ 3.56
Survival group (n=44)	1.63 $\pm$ 0.36	68.34 $\pm$ 5.27	82.36 $\pm$ 6.32	15.27 $\pm$ 2.11
T value	15.386	9.021	16.522	11.115
P value	0.001	0.002	0.001	0.001

Table IV Analysis of PTEN and TLR4 levels in the death group and the survival group.

Groups	PTEN (ng/mL)	TLR4 (mg/mL)
Death group (n=8)	0.95 $\pm$ 0.16	2.86 $\pm$ 0.20
Survival group (n=44)	1.24 $\pm$ 0.18	2.14 $\pm$ 0.18
T value	10.522	13.631
P value	0.001	0.001

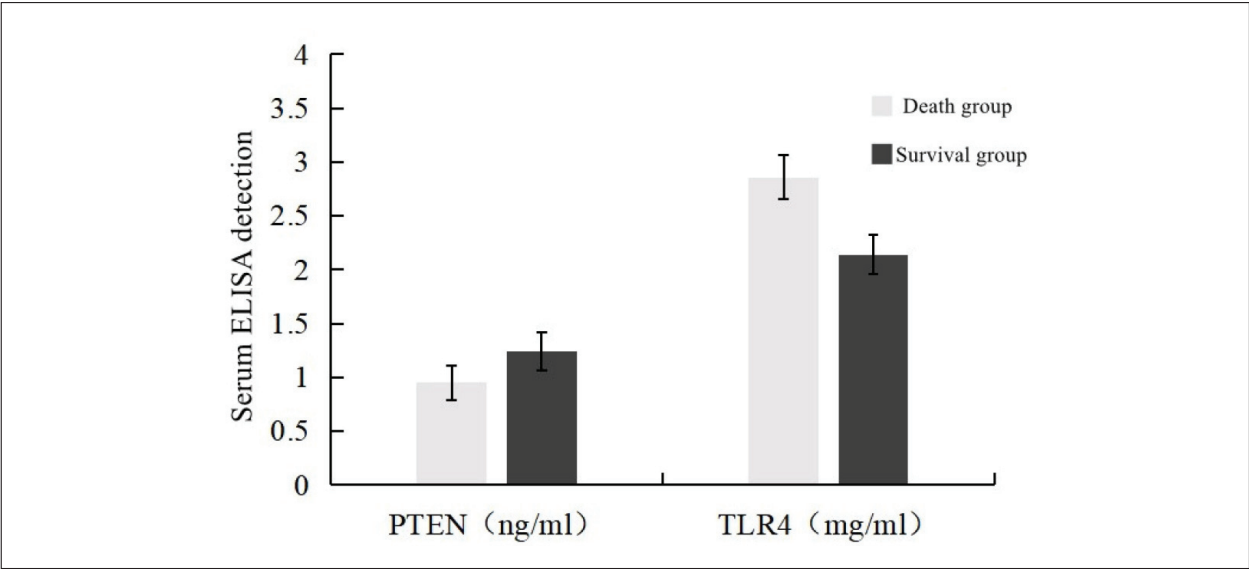


Figure 2 Detection of PTEN and TLR4 levels in the death group and survival group.

for both PTEN and TLR4 ($p=0.012$ and $p=0.007$, respectively) (refer to *Table II* and *Figure 1*).

Analysis of inflammatory indices between the death group and the survival group

Neonates with severe sepsis had significantly higher inflammatory responses in the mortality group relative to the survival group. The concentrations of PCT, CRP, HBP, and WBC count were significantly higher in neonates who expired compared to those who survived. PCT levels were 4.39 ± 1.13 ng/mL in the mortality group and 1.63 ± 0.36 ng/mL in the survival group, whereas CRP levels were

123.58 ± 9.03 mg/mL and 68.34 ± 5.27 mg/mL, respectively. The differences were statistically significant ($p=0.001$ for PCT, HBP, and WBC; $p=0.002$ for CRP) (*Table III*).

Comparison of serum PTEN and TLR4 levels between the dead group and the surviving group

Serum concentrations of PTEN and TLR4 showed significant differences between deceased infants and survivors. PTEN levels were significantly lower in the mortality group than in the survival group, whereas TLR4 levels were significantly high-

Table V Correlation analysis between PTEN, TLR4 levels and inflammation.

Index	PTEN		TLR4	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
PCT	-0.379	0.015	0.615	0.003
CRP	-0.226	0.002	0.524	0.004
HBP	-0.418	0.027	0.693	0.018
WBC	-0.355	0.014	0.227	0.005

Table VI Value analysis of PTEN and TLR4 levels in children’s condition and prognosis.

Index	AUC	sensitivity	specificity	P finger	95% CI
PCT	0.725	75.32	73.18	0.014	0.617–0.915
CRP	0.748	78.49	75.25	0.028	0.566–0.747
HBP	0.627	71.66	68.32	0.033	0.627–0.951
WBC	0.706	73.55	70.41	0.025	0.524–0.992
PTEN	0.846	89.23	86.23	0.002	0.632–0.879
TLR4	0.857	90.31	86.16	0.003	0.633–0.785

er in the mortality group. The PTEN concentration was 0.95 ± 0.16 ng/mL in the mortality group and 1.24 ± 0.18 ng/mL in the survival group. In contrast, TLR4 levels were quantified at 2.86 ± 0.20 mg/mL in the mortality group and 2.14 ± 0.18 mg/mL in the survival group. The two differences were statistically significant ($p=0.001$). The results suggest that diminished PTEN and increased TLR4 may be associated with adverse outcomes in neonates experiencing severe sepsis. The findings are elucidated in Table IV and Figure 2.

Correlation between serum PTEN and TLR4 levels and inflammation

The Pearson correlation analysis revealed a negative association between PTEN and TLR4 with PCT, CRP, HBP, and WBC ($P<0.05$). This suggests that an increase in PTEN levels may correlate with the reduction of the inflammatory response. A significant correlation was seen between TLR4 and PCT, CRP, HBP, and WBC ($P<0.05$). This suggested that as TLR4 levels increased, PCT, CRP, HBP, and WBC levels similarly increased (Table V).

Diagnostic and prognostic value of PTEN and TLR4

The ROC curve analysis demonstrated that PTEN and TLR4 had more predictive value than conventional inflammatory markers in evaluat-

ing the severity and prognosis of neonatal sepsis. The research indicated that TLR4 demonstrated the highest AUC value of 0.857, with a sensitivity of 90.31% and a specificity of 86.16% ($p=0.003$). PTEN demonstrated strong predictive capability, evidenced by an AUC of 0.846, a sensitivity of 89.23%, and a specificity of 86.23% ($p=0.002$). The AUC values of these surpassed those of PCT, CRP, HBP, and WBC count. The results suggested that PTEN and TLR4 may function as biomarkers for evaluating disease severity and prognosis in neonates with sepsis. The results of the ROC analysis are summarised in Table VI.

Discussion

Neonatal septicaemia is a common and potentially lethal condition in neonates, marked by a systemic inflammatory response and the presence of pathogens in the circulation. The neonate is susceptible to sepsis due to an immature immune system and reduced resistance to several pathogens. Prompt recognition and action for neonatal sepsis are essential in clinical practice, since delays in treatment can lead to swift organ failure and death. PTEN and TLR4 are two essential molecules in the pathogenesis of neonatal sepsis. PTEN is a multi-functional enzyme that influences cellular development, division, survival, and immune and inflammatory responses. PTEN has a protective role by negatively regulating inflammatory pathways, which

may be essential for alleviating excessive inflammatory responses and protecting tissues from damage. The expression and activity of PTEN may be altered in sepsis, potentially correlating with disease severity and prognosis (8–10). TLR4 is a pattern recognition receptor in the immune system that predominantly detects infections and activates the host's innate immune response (7). In sepsis, TLR4 recognises unique molecular patterns of pathogens, thereby triggering a series of signal transduction events that result in the production and release of inflammatory mediators (11, 12). The activation of TLR4 is essential for resistance to infection; nevertheless, excessive activation can lead to uncontrolled inflammation and organ damage (13). Thus, blood levels of PTEN and TLR4 may reflect the biological state and the immune response associated with neonatal sepsis. Evaluating these signs is advantageous for measuring sickness severity and may provide essential insights for forecasting therapeutic outcomes.

This study comprehensively investigated the correlation between serum PTEN and TLR4 expression levels and the severity and prognosis of neonatal sepsis. Inflammatory markers PCT, CRP, HBP, and WBC were significantly higher in children with severe and mild sepsis than in the control group, supporting the established view that these markers reflect the inflammatory state in newborn sepsis. The expression profiles of PTEN and TLR4 in neonatal sepsis are distinct. The significant reduction of PTEN in children with severe and mild sepsis indicates a protective role of PTEN in cellular inflammatory responses. PTEN typically has a substantial impact on cell proliferation and survival, while also significantly regulating inflammation. The PI3K/Akt pathway is known to regulate cellular responses to external stimuli; reduced PTEN activity can lead to excessive activation of this pathway, potentially resulting in an amplified immunological response and subsequent tissue damage (14, 15). This imbalance in immune response may be particularly consequential in severely ill children, who face an increased risk of severe inflammation and organ failure. The overexpression of TLR4 provides insights into the body's detection and response to septic germs, whereas the downregulation of PTEN provides insights into the body's response to septic germs. Increased TLR4 expression indicates activation of the host immune system and enhanced pathogen identification, serving as a natural defence mechanism to eliminate invasive infections (16–18). However, overactivation of TLR4 signalling may amplify inflammation and immunopathological damage, thereby increasing disease severity.

A significant correlation is observed between the considerable decrease in serum PTEN levels and the increase in TLR4 levels, alongside mortality rates in children with neonatal septicemia. These

findings may offer substantial biological insights to physicians, enabling more accurate assessment of children's disease risk and the formulation of more effective intervention strategies (19, 20). During the early stage of neonatal sepsis, a decrease in PTEN levels alongside an increase in TLR4 levels may alert the physician to the likelihood of worsening, necessitating modifications in treatment approaches, including intensified monitoring, prompt initiation of immunomodulatory therapies, or timely provision of life-support interventions. The rise in conventional inflammation markers, such as PCT, CRP, HBP, and WBC, indicates systemic inflammation and is associated with a poor outcome in patients with neonatal septicemia. Their levels may partially reflect the severity of the infection and the strength of the body's immunological response to it (21–23). Although conventional indicators are beneficial for preliminary disease evaluation, incorporating innovative biomarkers such as PTEN and TLR4 may provide a more refined assessment and is expected to yield more comprehensive insights for treatment decision-making. The simultaneous evaluation of these markers might enhance understanding of the immunological condition and clinical progression in children with neonatal septicemia, thereby improving the implementation of personalised treatment.

The Pearson correlation analysis revealed that PTEN was negatively associated with inflammatory markers, whereas TLR4 showed a positive correlation. The results yielded substantial insights into the roles of these two molecules in the inflammatory process. PTEN is typically recognised as a molecule that suppresses signalling pathways, and its down-regulation throughout the inflammatory process may indicate its vital role in modulating immune responses and averting excessive inflammatory damage (24). The increased level of TLR4, an immunological receptor, indicates the body's active involvement in pathogen detection and the initiation of inflammatory reactions (25). The presence of pathogens stimulates TLR4, triggering a series of inflammatory responses. This alleviates illness in the short term; however, it may also cause harm if left unchecked. The diagnostic importance of PTEN and TLR4 was quantitatively evaluated by ROC curve analysis. The AUC values for both markers are substantially higher than those of traditional inflammatory markers, suggesting their potential for early identification of neonatal sepsis and assessment of disease progression. A high AUC value for PTEN may indicate its protective role in prognosis, whereas a high AUC value for TLR4 may signal disease severity and progression rate. The discovery could enhance the development of novel diagnostic tools, allowing clinicians to detect high-risk youngsters earlier by monitoring changes in serum markers and to implement appropriate intervention measures.

This study sought to determine the relationship between blood PTEN and TLR4 expression levels and the severity and prognosis of neonatal sepsis. The expression level of PTEN decreased in children with sepsis, whilst TLR4 expression significantly increased; these changes are associated with the severity of the condition and the children's prognosis. Furthermore, PTEN showed a negative correlation with inflammatory markers, whilst TLR4 showed a positive correlation with the same indicators, thus confirming the critical functions of both molecules in the inflammatory process linked to neonatal sepsis. The ROC curve analysis revealed high AUC values for PTEN and TLR4, indicating their potential as biomarkers for diagnosing and prognosticating neonatal sepsis. This indicates that blood PTEN and TLR4 expression levels in children with severe sepsis may guide the formulation of evidence-based nursing strategies. Timely identification of sepsis is crucial. Caregivers must keep attentive to changes in the patient's vital signs, including body temperature, heart rate, respiratory rate, and blood pressure. Surveillance should be intensified for high-risk populations, including immunocompromised persons, postoperative or chemotherapy patients, and those

with suspected sepsis, who require thorough investigation. Sepsis is often precipitated by infection; therefore, timely infection control measures are essential. Caregivers must get a blood sample from the patient for bacterial culture to identify the infectious organism. Treatment was established using appropriate antibiotics informed by PTEN and TLR4 expression levels, along with bacterial culture and antimicrobial susceptibility test results.

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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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