

## Application of Arteriovenous Blood Gas Differences in Neonatal Sepsis

**Authors:** Hu Li, Yali Chen, Hu Zhenhong, Gao Fangjian, Nie Lili, Qiu Jianwu, Qiu Jianwu

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### Abstract

**Objective:** To investigate the clinical value of arterial-venous blood gas differences in neonatal sepsis and to provide a new objective indicator for early diagnosis.

**Methods:** This study enrolled neonates with sepsis hospitalized in the Neonatology Department of Yuebei People's Hospital from January 2022 to June 2024 as the observation group (n=22), and concurrently selected neonates with simple jaundice excluding infectious factors as the control group (n=23). By comparing multiple indicators in arterial-venous blood gas analysis between the two groups—including partial pressure of oxygen (PO<sub>2</sub>), oxygen saturation (SO<sub>2</sub>), pH value, partial pressure of carbon dioxide (PCO<sub>2</sub>), oxygen content (CaO<sub>2</sub>), and lactate (Lac)—and calculating arterial-venous partial pressure of oxygen difference (A-VPO<sub>2</sub>), arterial-venous oxygen saturation difference (A-VSO<sub>2</sub>), arterial-venous pH difference (A-VpH), arterial-venous partial pressure of carbon dioxide difference (A-VPCO<sub>2</sub>), arterial-venous oxygen content difference (A-VCaO<sub>2</sub>), and arterial-venous lactate difference, the clinical significance of these differences in early diagnosis of neonatal sepsis was explored.

**Results:** In comparisons of arterial-venous blood gas differences, the lactate difference in the observation group was significantly higher than that in the control group, while A-VCaO<sub>2</sub> was significantly lower in the observation group than in the control group, with statistically significant differences between the two groups (P<0.05). No statistically significant differences were observed between the observation and control groups in A-VPO<sub>2</sub>, A-VSO<sub>2</sub>, A-VpH, or A-VPCO<sub>2</sub> indicators (P>0.05).

**Conclusion:** A-VCaO<sub>2</sub> and lactate difference hold important reference value in the early diagnosis of neonatal sepsis.

## Full Text

### Clinical Utility of Arterial-Venous Blood Gas Differences in Neonatal Sepsis Diagnosis

Hu Li, Hu Zhenhong, Chen Yali, Gao Fangjian, Nie Lili, Qiu Jianwu\*

*Department of Neonatology, Yuebei People's Hospital Affiliated to Shantou University Medical College, Shaoguan, Guangdong, 512026, China*

*Correspondence author: Qiu Jianwu, Email: qiujianwu@yeah.net*

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#### Abstract

**Objective:** To explore the clinical application value of arterial-venous blood gas differences in neonatal sepsis and provide a new objective indicator for early diagnosis.

**Methods:** This study enrolled neonates with sepsis admitted to the neonatal department of Yuebei People's Hospital from January 2022 to June 2024 as the observation group (n=22). Concurrently, neonates with simple jaundice but without infectious factors were selected as the control group (n=23). We compared multiple parameters from simultaneous arterial and venous blood gas analysis between the two groups, including partial pressure of oxygen (PO<sub>2</sub>), oxygen saturation (SO<sub>2</sub>), pH, partial pressure of carbon dioxide (PCO<sub>2</sub>), oxygen content (CaO<sub>2</sub>), and lactate. We calculated the differences in arterial-venous oxygen partial pressure (A-V PO<sub>2</sub>), arterial-venous oxygen saturation (A-V SO<sub>2</sub>), arterial-venous pH (A-V pH), arterial-venous carbon dioxide partial pressure (A-V PCO<sub>2</sub>), arterial-venous oxygen content (A-VCaO<sub>2</sub>), and arterial-venous lactate to investigate their clinical significance in early diagnosis of neonatal sepsis.

**Results:** The lactate difference was significantly higher in the observation group compared to the control group, while A-VCaO<sub>2</sub> was significantly lower, with statistically significant differences between groups (P<0.05). No statistically significant differences were observed between the observation and control groups in A-V PO<sub>2</sub>, A-V SO<sub>2</sub>, A-V pH, or A-V PCO<sub>2</sub> (P>0.05).

**Conclusion:** A-VCaO<sub>2</sub> and the arterial-venous lactate difference demonstrate significant potential as reference indicators for early diagnosis of neonatal sepsis.

**Keywords:** Neonatal Sepsis; Arterial Blood Gas; Venous Blood Gas; Arterial-Venous Blood Gas Difference; Lactate

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## Introduction

Neonatal septicemia, also known as neonatal sepsis, is typically caused by bacteria, viruses, fungi, or other pathogens that trigger a potentially life-threatening systemic response in newborns [1]. Due to the distinct physiological and pathological characteristics of neonates compared to adults, clinical manifestations of sepsis are often insidious and nonspecific, with rapid disease progression that can easily lead to multiple organ failure and life-threatening complications. Consequently, early diagnosis and timely treatment are crucial for improving outcomes in neonatal sepsis. Global statistics indicate that approximately 4 million newborns die within 28 days of birth each year, with about one-third of these deaths attributable to sepsis [2].

The pathophysiological process of sepsis is frequently accompanied by severe tissue hypoxia, and oxygenation impairment represents a critical factor contributing to disease deterioration. Early fluid resuscitation and timely monitoring of oxygen delivery have been proven to be key measures for improving prognosis in sepsis patients [3]. However, traditional oxygen dynamics monitoring indicators—such as pH, arterial oxygen partial pressure (PaO<sub>2</sub>), arterial oxygen saturation (SaO<sub>2</sub>), venous oxygen saturation (SvO<sub>2</sub>), and lactate—have limitations in evaluating oxygen supply-demand status and tissue damage in sepsis patients due to influences from tissue perfusion, hemoglobin content, tissue oxygen delivery, and oxygen consumption [4]. In recent years, increasing attention has focused on the application of arterial-venous blood gas differences (such as differences in arterial-venous oxygen partial pressure and arterial-venous carbon dioxide partial pressure) in sepsis, particularly for assessing tissue oxygenation status, guiding fluid resuscitation, and monitoring sepsis progression. These indicators provide new objective evidence for clinical assessment by reflecting the balance between oxygen utilization and metabolism [5-7].

Although domestic and international studies have explored the application of arterial-venous blood gas differences in sepsis, research specifically addressing neonatal sepsis remains lacking. This study analyzes arterial-venous blood gas differences in neonates with sepsis admitted to our hospital from January 2022 to June 2024 to evaluate the clinical utility of these parameters in neonatal sepsis. We anticipate that this research will provide more objective and effective indicators for early diagnosis, treatment monitoring, and prognosis assessment of sepsis.

## Methods

**1.1 Study Population** We selected neonates diagnosed with sepsis who were hospitalized in the neonatal department of Yuebei People's Hospital from January 2022 to June 2024. Inclusion criteria comprised neonates clinically diagnosed with neonatal sepsis according to the diagnostic criteria in the 5th edition of *Practical Neonatology* [8]. Exclusion criteria included congenital heart disease and other congenital defects. Neonates who did not have simultaneous arterial

and venous blood drawn within the specified time or whose samples were unqualified were excluded from analysis. The control group consisted of neonates hospitalized in the neonatal department during the same period with simple jaundice but without infectious factors. This study was approved by the Ethics Committee of Yuebei People' s Hospital (Approval No.: KY-2021-241), and informed consent was obtained from all parents.

**1.2 Study Procedures** After confirming the clinical diagnosis, study subjects underwent simultaneous collection of 0.5 ml peripheral arterial and venous blood samples within a 3-minute interval. Blood gas analysis and internal environment testing were performed within 5 minutes using a GEM Premier 4000 automated blood gas analyzer. Operations were conducted by neonatologists according to the instrument manual, with detection reagents and quality control reagents being instrument-compatible products. We recorded arterial (A) and venous (V) blood gas parameters including  $PO_2$ ,  $SO_2$ , pH,  $PCO_2$ ,  $CaO_2$ , and lactate, then calculated the differences between arterial and venous parameters. By comparing differences in A-V  $PO_2$ , A-V  $SO_2$ , A-V pH, A-V  $PCO_2$ , A-V  $CaO_2$ , and lactate difference between the two groups, we analyzed their clinical significance and statistical relevance.

**1.3 Statistical Analysis** Data were analyzed using SPSS 22.0 statistical software. Normally distributed continuous variables were expressed as mean  $\pm$  standard deviation and analyzed using independent samples t-tests. Non-normally distributed continuous variables were expressed as median (25th percentile, 75th percentile) and analyzed using non-parametric rank-sum tests. Categorical data were expressed as counts and percentages and analyzed using chi-square tests.  $P < 0.05$  was considered statistically significant.

## Results

**2.1 Baseline Characteristics** This study enrolled 22 neonates in the observation group and 23 in the control group who met the inclusion criteria. The observation group included 15 males and 7 females, with a mean age of 5 days and mean birth weight of  $2822.73 \pm 716.93$  grams. The control group included 7 males and 14 females, with a mean age of 5 days and mean birth weight of  $2822.73 \pm 716.93$  grams. No significant differences were observed between the two groups in gender, age, or birth weight, indicating good comparability ( $P > 0.05$ ). Detailed baseline characteristics are presented in .

**2.2 Comparison of Arterial-Venous Blood Gas Differences** No statistically significant differences were observed between the observation and control groups in A-V  $PO_2$ , A-V  $SO_2$ , A-V pH, or A-V  $PCO_2$  ( $P > 0.05$ ). However, the lactate difference was significantly higher in the observation group compared to the control group, with a statistically significant intergroup difference ( $P < 0.05$ ). Additionally, A-V  $CaO_2$  differed significantly between the observation and control groups, also reaching statistical significance ( $P < 0.05$ ). Detailed results are presented in .

## Discussion

Neonatal sepsis is a leading cause of infant mortality worldwide, affecting multiple organ systems with nonspecific and varied manifestations that can rapidly deteriorate, leading to severe consequences [9-11]. The definition of sepsis is based not only on microbial culture results but also on comprehensive evaluation of laboratory tests and clinical symptoms. Early symptoms and clinical manifestations of neonatal sepsis can differ from those in adult sepsis, complicating diagnosis and treatment. Timely identification and management are essential to reduce potential threats to neonatal health and decrease mortality and complication risks.

Blood gas analysis technology, primarily used to determine blood gas concentrations (e.g., oxygen and carbon dioxide), pH values, and other metabolic products, plays a crucial role in medical diagnosis and management of critically ill patients. In neonatal sepsis diagnosis and management, blood gas analysis is particularly vital. Arterial blood gas analysis serves as a key tool for evaluating neonatal sepsis by measuring pH, PaCO<sub>2</sub>, and PaO<sub>2</sub> to assess adequacy of ventilation and oxygenation, acid-base balance, and electrolyte status, thereby evaluating respiratory and circulatory function. Given the difficulty and potential risks associated with arterial blood sampling, numerous studies have explored using venous blood as an alternative. Venous blood gas analysis typically evaluates metabolic status and tissue perfusion by measuring pH, lactate, and base excess in venous blood. However, due to physiological differences between venous and arterial circulation, variations in patient clinical status, and non-uniform sampling procedures, studies have found significant heterogeneity and variability in the accuracy of using venous blood gas analysis as a substitute for arterial analysis [14]. Arterial and venous blood analysis results provide different clinical information that helps physicians comprehensively evaluate neonatal oxygenation status, ventilation function, acid-base balance, and physiological state. Understanding these parameters and their clinical applications is extremely important for improving neonatal outcomes. In neonatal sepsis evaluation, venous blood gas analysis can be combined with arterial analysis to provide a more comprehensive understanding of neonatal physiological status. In recent years, arterial-venous blood gas differences have emerged as novel monitoring indicators attracting increasing medical attention. Research demonstrates that these differences can more sensitively reveal tissue oxygenation status and metabolic disturbances, showing high predictive value particularly in sepsis patients [15].

Arterial-venous blood gas differences (such as A-V pH, A-V PCO<sub>2</sub>, A-V PO<sub>2</sub>, A-V SO<sub>2</sub>) provide critical information about neonatal circulatory and metabolic status, helping clinicians determine whether tissue perfusion insufficiency or metabolic disturbances exist.

In neonatal sepsis research, lactate has long been recognized as a marker of metabolic disturbance. Lactate is primarily generated in muscles and liver, while its clearance depends mainly on liver and kidney function. During sepsis, in-

flammatory cytokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6) inhibit liver and kidney function, reducing lactate clearance and causing elevated lactate levels [16]. Elevated lactate is typically associated with tissue perfusion insufficiency and poor oxygenation. In early sepsis stages, lactate response to infection can be observed even before C-reactive protein (CRP) elevation, making it valuable for early diagnosis and prognosis assessment [17]. One study reported that in clinical sepsis cases, venous blood lactate  $>2$  mmol/L at 6 hours after birth correlated with sepsis development ( $P=0.041$ ), and when the cutoff value was set at 3.38 mmol/L, sensitivity was 57.9% and specificity 68.5% ( $P=0.032$ ) [16]. Further research indicates that lactate levels are not only associated with sepsis occurrence but also closely related to patient prognosis; persistently elevated lactate typically requires more aggressive intervention [18].

Lactate difference refers to the concentration difference between venous and arterial lactate. Under normal conditions, arterial-venous lactate differences may be minimal. Animal experiments show arterial lactate is slightly higher than venous lactate without significant difference [19], while adult exercise studies demonstrate that arterial lactate is significantly higher than venous lactate initially, but the difference gradually narrows over time [20]. However, in sepsis states, arterial-venous lactate differences may change due to tissue hypoxia and microcirculatory disturbances [19]. During sepsis, microcirculatory 障碍 and tissue hypoxia increase lactate production while reducing clearance, potentially widening the arterial-venous lactate difference. Lactate levels positively correlate with sepsis severity and poor prognosis, and improving lactate clearance can enhance outcomes in septic children [21]. Increased arterial-venous lactate difference reflects the degree of lactate accumulation in tissues, indicating worsening tissue perfusion insufficiency and metabolic 障碍. In this study, the observation group showed significantly increased lactate difference compared to the control group ( $P<0.05$ ), indicating more severe metabolic disturbance in neonatal sepsis. During neonatal sepsis, microcirculatory 障碍 and tissue hypoperfusion increase lactate production while simultaneously reducing clearance due to microcirculatory impairment, resulting in significantly elevated venous lactate and consequently increased arterial-venous lactate difference. Lactate difference demonstrates high clinical value for early sepsis diagnosis, helping clinicians identify neonatal sepsis early even without obvious clinical symptoms, thereby enabling early intervention to improve oxygenation status and metabolic disturbances.

Research on blood oxygen content in neonatal sepsis primarily focuses on the impact of sepsis on oxygen delivery ( $QO_2$ ) and tissue oxygenation, and how these changes affect neonatal physiological and pathological status. Studies show that in neonatal GBS sepsis, metabolic acidosis is associated with tissue ischemia caused by reduced oxygen delivery [22]. By comparing piglets with similar systemic oxygen delivery reductions, researchers found differences in blood oxygen content reduction between sepsis and non-sepsis groups, which may relate to sepsis development and tissue oxygenation and metabolic status. Arterial-venous oxygen content difference is an important indicator for evaluating tissue oxy-

generation status, reflecting oxygen utilization in the microcirculation and closely relating to neonatal tissue oxygenation and oxygen supply-demand balance. A narrowed arterial-venous oxygen difference may indicate impaired tissue oxygen utilization, which in sepsis can lead to reduced oxygen extraction and a narrowed difference. A reduced arterial-venous oxygen content difference reflects insufficient oxygen uptake [23]. In this study, the arterial-venous oxygen content difference differed significantly between the observation and control groups ( $P < 0.05$ ), indicating poorer oxygenation status, higher tissue oxygen consumption, and inadequate oxygen supply or abnormal oxygen metabolism in the neonatal sepsis group. When used together with lactate difference, these parameters are particularly valuable for early sepsis identification. Since sepsis is often accompanied by microcirculatory 障碍 and poor oxygenation, arterial-venous oxygen content difference can serve as an indicator for early detection of oxygenation 障碍.

A-V  $PCO_2$  accurately reflects carbon dioxide metabolism and excretion, serving as an important indicator for evaluating tissue oxygen supply-demand status, cardiac output, and microcirculatory state, objectively reflecting tissue oxygenation. Increased A-V  $PO_2$  typically indicates more severe tissue hypoxia. A-V  $SO_2$ , as a key parameter for evaluating oxygenation status, often suggests 障碍 in oxygen transport when increased. In this study, A-V  $PO_2$ , A-V  $SO_2$ , A-V pH, and A-V  $PCO_2$  showed no significant statistical differences, possibly due to the limited sample size and the fact that study subjects were primarily early-stage sepsis patients. Future studies with larger sample sizes are needed to further validate these findings.

In the early diagnosis of neonatal sepsis, lactate difference and A-V  $CaO_2$  demonstrate significant application potential. These indicators can help clinicians more rapidly and objectively evaluate neonatal oxygenation and metabolic status, providing strong evidence for sepsis treatment decisions. Although A-V  $PO_2$ , A-V  $SO_2$ , A-V pH, and A-V  $PCO_2$  showed no statistically significant differences, these parameters provide valuable supplementary information for comprehensive assessment of neonatal oxygenation and acid-base status. Therefore, arterial-venous blood gas differences can serve as an auxiliary diagnostic tool for neonatal sepsis, offering clinicians more objective and accurate guidance. The development of bedside blood gas analyzers with diverse functions and micro-sampling capabilities, capable of detecting not only blood gases and internal environment but also hemoglobin, carboxyhemoglobin, bilirubin, and multiple other indicators [24,25], provides great convenience for timely neonatal testing and diagnosis. Future research with expanded sample sizes or combined with additional clinical indicators may further reveal associations between arterial-venous blood gas differences and prognosis in sepsis patients, thereby enhancing clinical diagnostic capabilities.

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#### Author Contributions:

Hu Li: Conceptualized the study, designed the research protocol

Hu Zhenhong, Gao Fangjian, Nie Lili: Collected experimental data

Hu Li, Chen Yali: Analyzed data and drafted the manuscript  
Qiu Jianwu: Revised the final manuscript version

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