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Original Research Article

Altered Resistin and IL-6 in Neonatal Sepsis

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Abstract:

Background: Neonatal sepsis is a leading cause of neonatal morbidity and mortality, particularly in developing countries. Early diagnosis remains challenging due to nonspecific clinical features. Inflammatory biomarkers such as interleukin-6 (IL-6) and resistin have emerged as potential tools for early diagnosis and prognostication in neonatal sepsis.

Objectives: To evaluate alterations in serum resistin and IL-6 levels in neonates with sepsis and to assess their association with disease severity and clinical outcomes.

Materials and Methods: This retrospective observational study was conducted in the Neonatal Intensive Care Unit of Indira Gandhi Institute of Medical Sciences, Patna, Bihar, over a period of 24 months. Medical records of 90 neonates diagnosed with sepsis were analyzed. Serum IL-6 and resistin levels measured at the time of sepsis evaluation were recorded. Clinical outcomes, including survival and mortality, were assessed. Statistical analysis was performed using appropriate parametric and non-parametric tests.

Results: Among the 90 neonates studied, 60% were male and 58.9% were preterm. Mean serum IL-6 and resistin levels were significantly elevated in septic neonates. Non-survivors had significantly higher IL-6 and resistin levels compared to survivors ($p < 0.001$). Late-onset sepsis was associated with higher biomarker levels than early-onset sepsis. Elevated IL-6 and resistin levels were also associated with increased need for mechanical ventilation and higher mortality.

Conclusion: Serum IL-6 and resistin levels are significantly elevated in neonatal sepsis and are strongly associated with disease severity and mortality. These biomarkers may serve as useful adjuncts for early diagnosis and risk stratification in neonatal sepsis.

Keywords: Neonatal sepsis; Interleukin-6; Resistin; Inflammatory biomarkers; Mortality.

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Introduction

Neonatal sepsis remains a major cause of neonatal morbidity and mortality worldwide, particularly in low- and middle-income countries. It is responsible for nearly one-third of neonatal deaths globally, with the burden being disproportionately higher in developing nations due to limited resources, delayed diagnosis, and inadequate access to intensive neonatal care [1,2]. In India, neonatal sepsis continues to be a significant public health problem despite advances in perinatal and neonatal medicine [3]. Early identification and timely intervention are crucial for improving survival outcomes; however, the nonspecific clinical presentation of neonatal sepsis often makes early diagnosis challenging [4].

The pathophysiology of neonatal sepsis involves a complex interaction between invading microorganisms and the host immune response. An exaggerated inflammatory response leads to the release of various cytokines, chemokines, and adipokines, which play a pivotal role in disease progression and organ dysfunction [5]. Among these mediators, interleukin-6 (IL-6) is a well-established pro-inflammatory cytokine that is rapidly produced in response to infection and tissue injury. Elevated IL-6 levels have been shown to correlate with the severity of infection and have been widely studied as an early biomarker for neonatal sepsis [6,7]. Due to its early rise in circulation, IL-6 has been considered useful in the early diagnosis and prognostication of septic neonates [8].

Resistin, an adipokine originally described in adipose tissue, has emerged as an important mediator linking inflammation and immune response. It is produced by monocytes and macrophages and is significantly upregulated during inflammatory states [9]. Recent studies suggest that

resistin plays a crucial role in modulating inflammatory pathways by stimulating the production of pro-inflammatory cytokines such as IL-6 and tumor necrosis factor-α [10]. Elevated resistin levels have been reported in adult sepsis and are associated with disease severity and poor clinical outcomes [11]. However, data regarding the role of resistin in neonatal sepsis remain limited and inconsistent.

Given the immature immune system of neonates, the inflammatory response in neonatal sepsis differs significantly from that in older children and adults [12]. Understanding the role of novel inflammatory markers such as resistin, along with established cytokines like IL-6, may help improve diagnostic accuracy and risk stratification in septic neonates. In resource-limited settings, identifying reliable biomarkers that can aid early diagnosis is particularly important for reducing neonatal mortality.

Therefore, this retrospective study conducted at Indira Gandhi Institute of Medical Sciences, Patna, Bihar, aims to evaluate the alterations in serum resistin and IL-6 levels in neonates with sepsis and to assess their potential role as inflammatory biomarkers. The findings of this study may contribute to better understanding of the inflammatory profile of neonatal sepsis and assist clinicians in early diagnosis and management.

Materials and Methods

Study Design and Setting: This retrospective observational study was conducted at the Neonatal Intensive Care Unit (NICU) of Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, a tertiary care referral center in eastern India. The study analyzed medical records of neonates admitted with a diagnosis of sepsis over a 24-month period.

Study Population and Sample Size: A total of 90 neonates diagnosed with neonatal sepsis during the study period were included. Neonatal sepsis was defined based on clinical features suggestive of infection along with positive sepsis screen and/or blood culture positivity, as per standard NICU protocols.

Inclusion Criteria

- Neonates (≤28 days of life) admitted to NICU with clinical suspicion of sepsis
- Availability of complete medical records
- Availability of laboratory data including serum **IL-6** and **resistin** levels at the time of sepsis evaluation

Exclusion Criteria

- Neonates with major congenital anomalies
- Inborn errors of metabolism
- Perinatal asphyxia (stage II and III)
- Neonates with incomplete clinical or laboratory records
- Prior exposure to prolonged antibiotic therapy before sample collection

Data Collection

Data were collected retrospectively from hospital medical records, laboratory registers, and electronic databases. The following information was extracted:

- Demographic details: gestational age, birth weight, sex
- Clinical parameters: age at onset of sepsis, clinical features, need for respiratory or inotropic support
- Laboratory parameters: complete blood count, C-reactive protein, blood culture results, serum IL-6 and resistin levels
- Outcome variables: survival or mortality

Measurement of IL-6 and Resistin: Blood samples were collected as part of routine sepsis evaluation before initiation of antibiotic therapy. Serum IL-6 and resistin levels were measured using enzyme-linked immunosorbent assay (ELISA) kits following the manufacturer's instructions. Results were expressed in pg/mL for IL-6 and ng/mL for resistin.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS software. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), depending on data distribution. Categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using Student's t-test or Mann–Whitney U test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. A p-value <0.05 was considered statistically significant.

Ethical Considerations: Approval for the study was obtained from the Institutional Ethics Committee of IGIMS, Patna. As the study was retrospective and involved analysis of existing records, informed consent was waived. Patient confidentiality was maintained throughout the study.

Results

Baseline Demographic and Clinical Characteristics: A total of 90 neonates with a diagnosis of neonatal sepsis were included in the study. Among them, 54 (60%) were males and 36 (40%) were females. The majority of neonates were preterm (58.9%). Low birth weight (<2500 g) was observed in 61.1% of cases. Early-onset sepsis (≤72 hours of life) was noted in 52 (57.8%) neonates, while 38 (42.2%) had late-onset sepsis.

Table 1: Baseline Demographic and Clinical Profile (n = 90)

Variable	Number (%)
Gender	
• Male	54 (60.0)
• Female	36 (40.0)
Gestational age	
• Preterm (<37 weeks)	53 (58.9)
• Term (≥37 weeks)	37 (41.1)
Birth weight	
• <2500 g	55 (61.1)
• ≥2500 g	35 (38.9)
Type of sepsis	
• Early-onset sepsis	52 (57.8)
• Late-onset sepsis	38 (42.2)

Laboratory Parameters: Serum IL-6 and resistin levels were elevated in neonates with sepsis. The mean serum IL-6 level was 148.6 ± 42.3 pg/mL, while the mean serum resistin level was 18.9 ± 5.6 ng/mL.

Table 2: Laboratory Parameters in Study Population

Parameter	Mean ± SD
IL-6 (pg/mL)	148.6 ± 42.3
Resistin (ng/mL)	18.9 ± 5.6
CRP (mg/L)	22.4 ± 9.8
Total leukocyte count (/mm³)	14,850 ± 4,210

Comparison Between Survivors and Non-survivors: Out of 90 neonates, 68 (75.6%) survived and 22 (24.4%) expired. Mean serum IL-6 and resistin levels were significantly higher in non-survivors compared to survivors ($p < 0.001$).

Table 3: Comparison of IL-6 and Resistin Levels Between Survivors and Non-survivors

Parameter	Survivors (n = 68)	Non-survivors (n = 22)	p-value
IL-6 (pg/mL)	132.4 ± 35.7	198.2 ± 41.5	<0.001
Resistin (ng/mL)	16.8 ± 4.2	25.3 ± 6.1	<0.001

Early-Onset vs Late-Onset Sepsis: Neonates with late-onset sepsis demonstrated significantly higher levels of inflammatory markers compared to early-onset sepsis.

Table 4: Comparison of Biomarkers in Early- and Late-Onset Sepsis

Parameter	Early-onset (n = 52)	Late-onset (n = 38)	p-value
IL-6 (pg/mL)	134.5 ± 38.1	168.2 ± 44.6	0.002
Resistin (ng/mL)	17.2 ± 4.9	21.2 ± 5.8	0.001

Outcome Analysis: Elevated IL-6 and resistin levels were associated with adverse outcomes, including need for ventilatory support and mortality. Neonates requiring mechanical ventilation had significantly higher mean IL-6 (182.6 ± 39.4 pg/mL) and resistin levels (23.8 ± 5.9 ng/mL) compared to those managed conservatively ($p < 0.001$).

Discussion

Neonatal sepsis continues to pose a significant diagnostic and therapeutic challenge, particularly in developing countries where delayed presentation and limited resources contribute to poor outcomes. The present retrospective study evaluated the alterations in serum resistin and IL-6 levels in neonates with sepsis and demonstrated that both biomarkers were significantly elevated, especially among non-survivors and those with late-onset sepsis.

IL-6 is a key mediator of the acute inflammatory response and is rapidly released following microbial invasion. In the present study, serum IL-6 levels were significantly higher in neonates who did not survive, indicating its strong association with disease severity and adverse outcomes. Similar findings were reported by Santuz et al., who observed markedly elevated IL-6 levels in neonates with severe sepsis and septic shock, correlating with mortality risk [13]. Krueger et al. also demonstrated that persistently high IL-6 levels were associated

with multi-organ dysfunction and poor prognosis in septic neonates [14]. These findings reinforce the role of IL-6 as a reliable marker of systemic inflammation and severity in neonatal sepsis.

Resistin, an emerging inflammatory biomarker, showed significant elevation in septic neonates in the current study, with substantially higher levels among non-survivors. This observation is consistent with studies in critically ill pediatric and neonatal populations, where resistin has been shown to amplify inflammatory cascades and endothelial dysfunction [15]. Celik et al. reported increased serum resistin levels in neonates with sepsis, suggesting its involvement in the inflammatory response and immune dysregulation [16]. The association of higher resistin levels with mortality observed in the present study supports its potential role as a prognostic biomarker.

A notable finding of this study was the significantly higher levels of IL-6 and resistin in late-onset sepsis compared to early-onset sepsis. Late-onset sepsis is often associated with hospital-acquired infections, prolonged invasive procedures, and more virulent pathogens, which may trigger a stronger inflammatory response. Sharma et al. reported similar observations, highlighting higher cytokine levels in late-onset neonatal sepsis and their association with increased disease severity [17]. This emphasizes the importance of vigilant monitoring of inflammatory markers in neonates admitted for prolonged NICU stays.

The present study also demonstrated that neonates requiring mechanical ventilation had significantly elevated IL-6 and resistin levels, indicating a correlation between biomarker levels and clinical severity. Mera et al. observed that elevated inflammatory mediators were strongly associated with respiratory failure and need for intensive support in septic neonates [18]. These findings suggest that resistin and IL-6 may aid in early risk stratification and identification of neonates who may require aggressive supportive management.

Despite its strengths, this study has certain limitations. The retrospective design limits causal inference, and the relatively small sample size from a single center may affect generalizability. Serial measurements of biomarkers were not available, which could have provided better insight into disease progression and treatment response.

In conclusion, the present study highlights that elevated serum resistin and IL-6 levels are significantly associated with disease severity and mortality in neonatal sepsis. These biomarkers may serve as valuable adjuncts to existing diagnostic tools and help in early identification of high-risk neonates.

Conclusion

The present retrospective study demonstrates that serum IL-6 and resistin levels are markedly elevated in neonates with sepsis and show a significant association with adverse clinical outcomes, including increased disease severity and mortality. Higher levels of these biomarkers in non-survivors and in late-onset sepsis suggest their potential role in prognostication and early risk stratification. Incorporation of IL-6 and resistin measurement into routine sepsis evaluation may aid clinicians in identifying high-risk neonates who require intensive monitoring and aggressive management. Further prospective, multicentric studies with larger sample sizes are recommended to validate these findings and establish standardized cutoff values for clinical use.

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