

Pattern of Change of C-Reactive Protein and Serum Ferritin after Antibiotic Therapy in Neonatal Sepsis: A Prospective Study

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Abstract

Background: Neonatal sepsis remains one of the most serious causes of newborn morbidity and mortality, particularly where early diagnosis is difficult because of nonspecific clinical signs and the limitations of blood culture. Serial measurement of inflammatory biomarkers offers a practical way to monitor treatment response, but the dynamics of C-reactive protein (CRP) and serum ferritin after antibiotic therapy in term septic neonates need further prospective evaluation.

Methods: In this prospective observational study, 120 full-term neonates aged 1–28 days with clinical features suggestive of sepsis admitted to a tertiary care hospital were enrolled after informed consent. Venous blood was collected at admission (baseline), before antibiotics, and again at 24 and 48 hours after initiation of empirical antibiotic therapy for estimation of CRP and serum ferritin. Continuous variables were expressed as mean±standard deviation, comparisons were made with the paired t-test, and $p < 0.05$ was considered statistically significant.

Results: Of the 120 neonates, 63 (52.5%) were male and 57 (47.5%) female, with a slight predominance of cases in the first ten days of life (45.8%). Hypothermia (56.6%) and refusal to feed (44.1%) were the most frequent clinical manifestations. Mean CRP fell progressively from 24.15 ± 9.40 mg/L at admission to 16.30 ± 8.60 mg/L at 24 hours and 10.39 ± 9.30 mg/L at 48 hours ($p < 0.001$ for all pairwise comparisons), corresponding to reductions of 32.3% at 24 hours and 56.6% at 48 hours. Mean serum ferritin declined from 421.88 ± 88.18 ng/mL at baseline to 310.25 ± 63.77 ng/mL at 24 hours and 293.13 ± 94.92 ng/mL at 48 hours ($p < 0.001$ for admission versus 24 h and 48 h; $p < 0.01$ for 24 h versus 48 h). Overall, 100 neonates (83.3%) survived and 20 (16.6%) expired; the majority (53.3%) required a hospital stay of 6–8 days.

Conclusion: CRP and serum ferritin decline significantly within 48 hours of appropriate antibiotic therapy in term neonates with sepsis, and serial measurement of these biomarkers, combined with clinical assessment, is a useful, inexpensive tool for monitoring therapeutic response and guiding antibiotic duration.

Keywords: Neonatal Sepsis; C-Reactive Protein; Serum Ferritin; Biomarkers; Antibiotic Therapy; Treatment Response; Neonatal Outcomes.

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Introduction

Neonatal sepsis continues to be one of the most serious and life-threatening conditions affecting newborns, mostly in economically weaker nations. It is recognized by a systemic inflammatory reaction elicited by bacterial, viral, or fungal infections during the first 28 days of birth [1-3]. In spite of advances in neonatal intensive care, early diagnosis and timely treatment remain major clinical challenges, because newborns have an

immature immune system, limited physiological reserves, and a poor ability to localize infections, which makes them highly vulnerable to rapid disease progression. As a result, neonatal sepsis is linked with high rates of morbidity, prolonged hospitalization, long-term neurodevelopmental impairment, and mortality, and it remains a primary cause of newborn deaths in many developing regions [13-16]. The clinical presentation of sepsis

in newborns is often subtle, variable, and nonspecific, especially in the early stages. Poor feeding, lethargy, respiratory difficulty, temperature instability, apnea, and feeding intolerance may also be observed in noninfectious conditions, which makes clinical prognosis difficult and sometimes unreliable [19-22]. Blood culture still acts as the cornerstone for confirming sepsis, but it requires technical expertise, takes 48–72 hours for results, and may yield false-negative findings because of a low bacterial load or prior antibiotic exposure; waiting for culture reports before initiating treatment can be life-threatening [23-28]. Clinicians therefore often start empirical antibiotic therapy based on clinical suspicion alone, which increases the risk of unnecessary antibiotic use, antimicrobial resistance, altered gut microbiota, and increased healthcare costs [27,39].

In this context, laboratory biomarkers have gained increasing importance in the early confirmation and monitoring of sepsis. An ideal biomarker should be sensitive, specific, economically available, easily quantifiable, and capable of reflecting disease severity and treatment response [12,29-31]. Among the biomarkers investigated, C-reactive protein (CRP) and serum ferritin have attracted considerable attention due to their availability, affordability, and clinical usefulness in routine practice [1,4,7,9,32,33].

CRP is an acute-phase protein synthesized mainly by hepatocytes in response to interleukin-6 and other inflammatory mediators; it elevates within hours of tissue injury or infection and has consistently demonstrated elevation in bacterial sepsis and meningitis, although it is nonspecific [10,11,37,38,41,43,47].

Ferritin, the intracellular iron-storage protein, rises as an acute-phase reactant during infection and inflammation through iron-withholding defense mechanisms, and elevated ferritin has been linked to both diagnosis and prognosis of sepsis in neonates and children [2,5,7,32,33,35]. Serial monitoring of these two biomarkers could therefore provide an accessible, inexpensive framework for assessing the response to antibiotic therapy in settings where sophisticated diagnostics are unavailable [36,42,45,46]. The present prospective study was undertaken to evaluate the pattern of change of CRP and serum ferritin after antibiotic therapy in term neonates with sepsis at a tertiary care hospital in North India.

Materials and Methods

Study Design and Setting: This prospective observational study was conducted in the Department of Paediatrics, Darbhanga Medical College and Hospital (DMCH), Laheriasarai, Darbhanga, Bihar, after obtaining approval from

the Institutional Ethics Committee. The study was carried out in accordance with ethical principles for research involving human participants.

Study Population: A total of 120 full-term neonates aged 1–28 days admitted to the neonatal care unit with symptoms suggesting sepsis such as tachycardia, poor feeding, respiratory distress, apnea, hypothermia, hyperthermia, and vomiting were enrolled after written informed consent from their parents or guardians.

Exclusion Criteria: Preterm neonates, neonates discharged or leaving the hospital before completion of investigations, and neonates diagnosed with conditions other than sepsis during hospitalization were excluded.

Sample Size: The minimal sample size was estimated for a paired mean difference using the formula $n = Z^2 \times p \times q / d^2$, where $Z = 1.96$ for 95% confidence, p = expected prevalence from previous studies of 50%, and d = allowable error of 10%, yielding a sample of 120 full-term septic neonates. Baseline (pre-treatment) values constituted the control series and post-treatment values the study series for each participant.

Methodology: Detailed antenatal, perinatal, and clinical histories were recorded, followed by thorough physical examination at admission. Venous blood was collected under strict sterile conditions at the time of admission for estimation of baseline CRP and serum ferritin levels prior to initiation of antibiotic treatment. Empirical antibiotic therapy was started as per institutional protocol and modified when required based on clinical response. Blood was again collected on the first and second day after admission for serial CRP and serum ferritin measurement. All participants received appropriate supportive care during hospitalization, and clinical progress and laboratory findings were monitored regularly.

Statistical Analysis: Data were entered into a computerized database and analyzed using SPSS software version 25.0. Continuous variables such as CRP and serum ferritin concentrations were expressed as mean $\pm$ standard deviation, whereas categorical data were shown as frequency and percentage. Comparison of biomarker levels before and after antibiotic therapy was assessed using the paired t-test. Statistical significance was fixed at a p-value below 0.05.

Results

Study Population and Demographics: A total of 120 full-term septic neonates (age 1–27 days) admitted to the Pediatrics Department were enrolled in this prospective study. A total of 63 (52.5%) were male and 57 (47.5%) female,

showing a slight male predominance (Table 1, Figure 1).

Table 1: Gender of the selected infants (N=120)

Gender	Frequency (n)	Percent (%)
Male	63	52.5
Female	57	47.5
Total	120	100

Gender distribution (N=120)

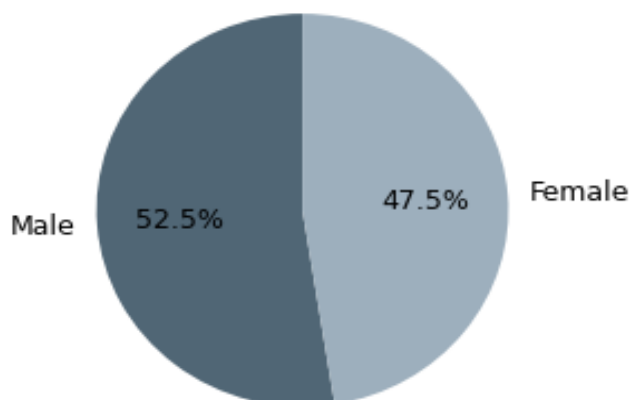


Figure 1: Gender of participants

Regarding age-wise categorization, the majority of neonates were in the 1–5 days (28, 23.3%) and 6–10 days (27, 22.5%) age groups, with mean ages of 2.14 ± 1.38 days and 7.74 ± 0.90 days, respectively. Additionally, 8 (6.7%) neonates were 11–15 days

old (13.5 ± 1.60 days), while 23 (19.2%) and 22 (18.3%) belonged to the 16–20 days and 21–25 days categories (19.71 ± 0.71 and 21.95 ± 0.65 days), and the remaining 12 (10.0%) were 26–30 days old (26.33 ± 0.49 days) (Table 2, Figure 2).

Table 2: Age of the participants (N=120)

Age (days)	Number (n)	Mean $\pm$ SD
01-May	28	2.14 ± 1.38
06-Oct	27	7.74 ± 0.90
Nov-15	8	13.5 ± 1.60
16-20	23	19.71 ± 0.71
21-25	22	21.95 ± 0.65
26-30	12	26.33 ± 0.49

Age-wise distribution of participants

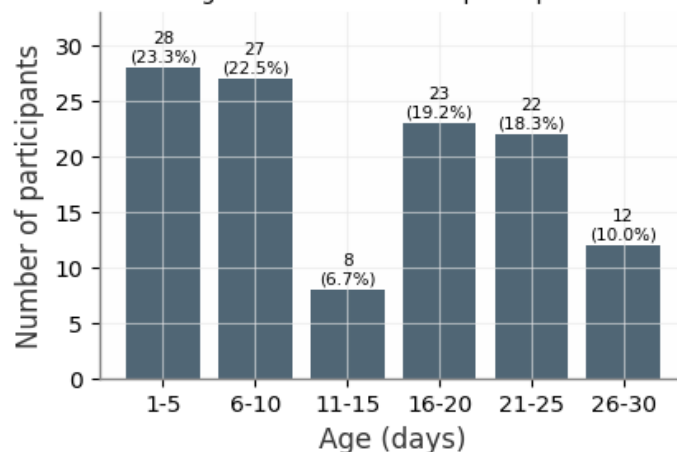


Figure 2: Age-wise distribution of participants

With respect to gestational age, the highest proportion of neonates were born at 40 weeks (37, 30.8%), followed by 37 weeks (36, 30.0%), 39 weeks (26, 21.6%), and 38 weeks (21, 17.5%), indicating that most neonates were delivered at term (Table 3, Figure 3).

Table 3: Gestational age-based analysis (N=120)

Gestational age (weeks)	Number (n)	Percentage (%)
37	36	30
38	21	17.5
39	26	21.6
40	37	30.8

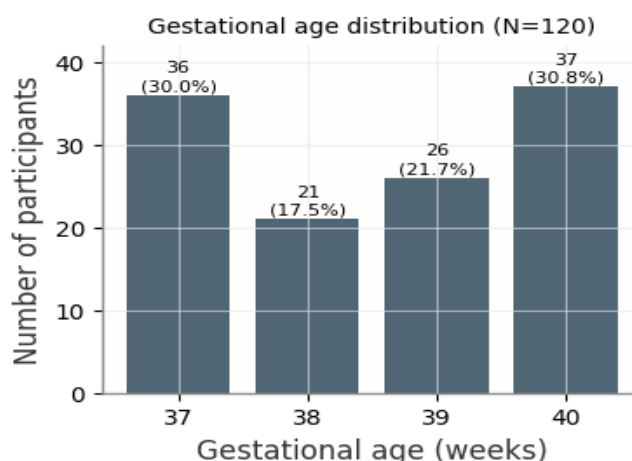


Figure 3: Percentage distribution of gestational age

In terms of birth weight, 37 (30.8%) neonates weighed 2.51–3.00 kg, followed by 35 (29.2%) in the 3.01–3.50 kg category, 25 (20.8%) at 3.51–4.00 kg, and 23 (19.2%) at 2.00–2.50 kg, with corresponding category means of 2.78 ± 0.14 ,

3.23 ± 0.14 , 3.64 ± 0.09 , and 2.34 ± 0.10 kg (Table 4, Figure 4). Overall, the study population predominantly consisted of term neonates with a birth weight between 2.51 and 3.50 kg and a nearly equal gender distribution.

Table 4: Birth weight of participants (N=120)

Birth weight (kg)	Number (n)	Mean $\pm$ SD
2.00 - 2.50	23	2.34 ± 0.10
2.51 - 3.00	37	2.78 ± 0.14
3.01 - 3.50	35	3.23 ± 0.14
3.51 - 4.00	25	3.64 ± 0.09

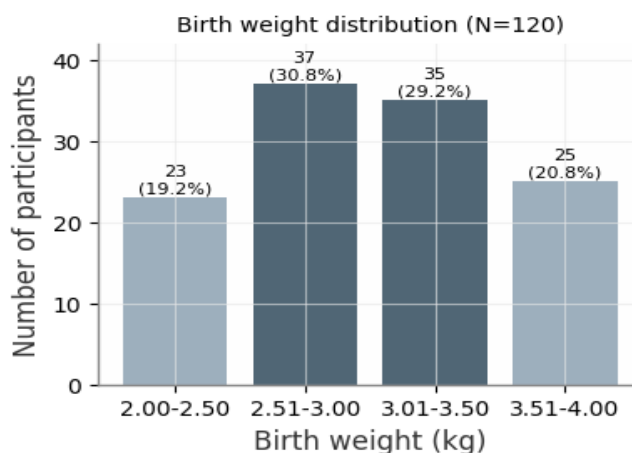


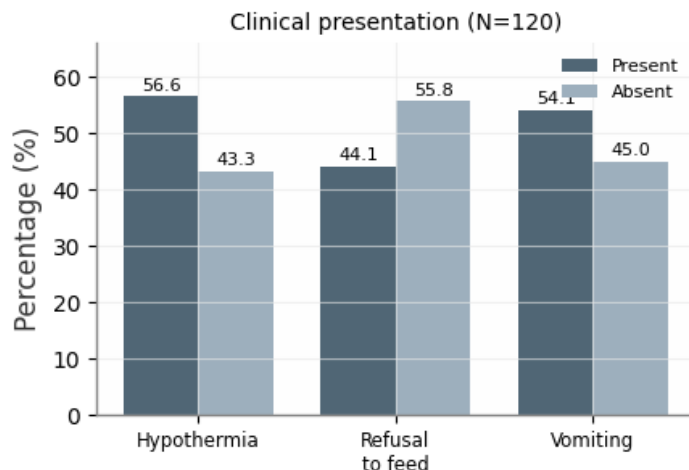
Figure 4: Birth weight distribution of participants

Clinical Presentation: The clinical presentation of neonatal sepsis in this cohort was characterized by multiple nonspecific signs at admission (Table 5, Figure 5). Hypothermia was present in 68 (56.6%) neonates, refusal to feed in 53 (44.1%), and vomiting in 65 (54.1%); the corresponding absent rates were 43.3%, 55.8%, and 45.0%.

Table 5: Clinical presentation of neonatal sepsis (N=120)

Clinical manifestation	Yes (n)	No (n)	Yes (%)	No (%)
Hypothermia	68	52	56.6	43.3
Refusal to feed	53	67	44.1	55.8
Vomiting	65	54	54.1	45.0

Values as reported in the source thesis table.

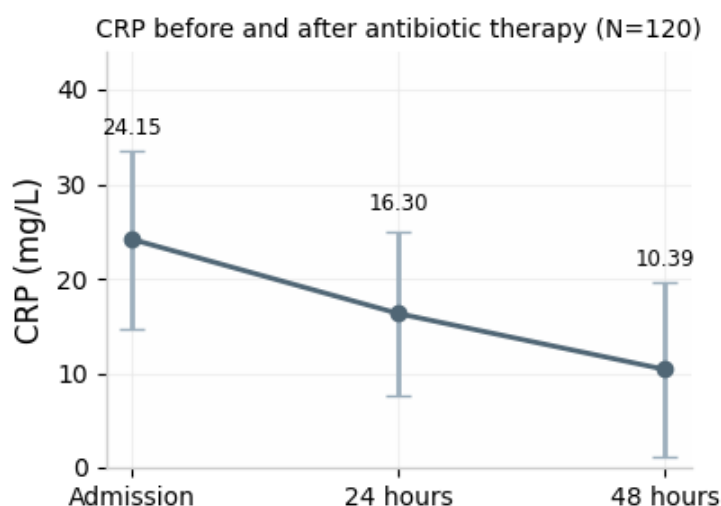
**Figure 5: Clinical presentation observed in neonatal sepsis**

C - reactive protein Levels and Temporal Changes: CRP was measured at three time points: at admission (baseline), 24 hours after admission, and 48 hours after admission (Table 6). At admission, levels ranged from 8.6 to 46.3 mg/L with a mean of 24.15 ± 9.40 mg/L. After 24 hours,

the range decreased to 4.3–42.7 mg/L with a mean of 16.30 ± 8.60 mg/L; by 48 hours, levels further declined to 1.6–40.5 mg/L with a mean of 10.39 ± 9.30 mg/L, demonstrating a progressive reduction over time (Figure 6).

Table 6: CRP concentrations at varied time frames (N=120)

Time frame	Range (mg/L)	Mean $\pm$ SD (mg/L)
Admission (baseline)	8.6-46.3	24.15 ± 9.40
24 hours	4.3-42.7	16.30 ± 8.60
48 hours	1.6-40.5	10.39 ± 9.30

**Figure 6: CRP before and after antibiotic therapy (mean $\pm$ SD)**

CRP Response to Antibiotic Therapy: The statistical analysis revealed statistically significant reductions in CRP levels with antibiotic therapy (Table 7). Differences between admission and 24 hours, admission and 48 hours, and 24 hours and 48 hours were all highly significant ($p < 0.001$).

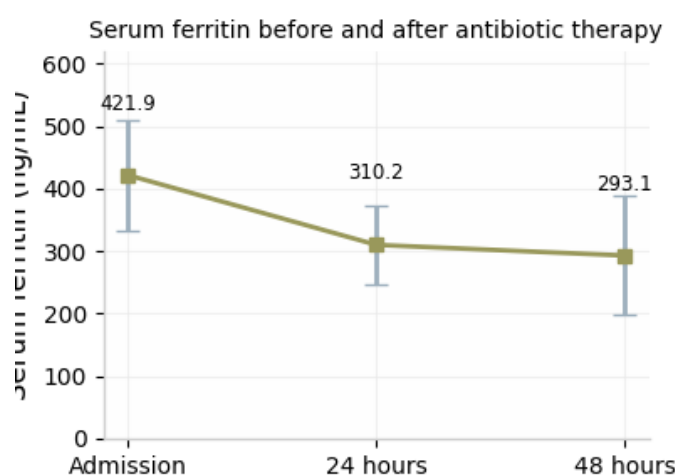
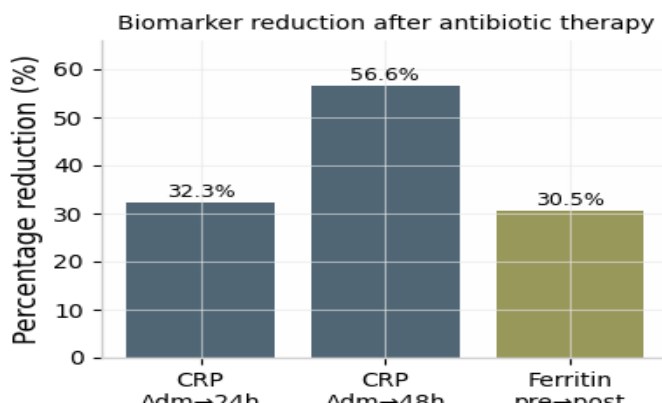
Table 7: Statistical computation of CRP reduction with antibiotic therapy

Comparison of CRP time points	p-value
Admission vs 24 h	<0.001
Admission vs 48 h	<0.001
24 h vs 48 h	<0.001

Serum Ferritin Levels and Changes: The mean serum ferritin level at admission (baseline) was 421.88 ± 88.18 ng/mL (range 261.9–613.9 ng/mL). At 24 hours, the mean decreased to 310.25 ± 63.77 ng/mL (range 230.6–590.2 ng/mL), and by 48 hours it further declined to 293.13 ± 94.92 ng/mL (range 120.5–586.3 ng/mL), demonstrating a progressive reduction over the 48-hour observation period (Table 8, Figure 7).

Table 8: Serum ferritin levels at varied time frames (N=120)

Time point	Range (ng/mL)	Mean $\pm$ SD (ng/mL)
Admission (baseline)	261.9-613.9	421.88 ± 88.18
24 hours	230.6-590.2	310.25 ± 63.77
48 hours	120.5-586.3	293.13 ± 94.92

**Figure 7: Serum ferritin before and after antibiotic therapy (mean $\pm$ SD)****Figure 8: Percentage reduction of biomarkers after antibiotic therapy**

Serum Ferritin Response to Antibiotic Therapy: Paired t-test analysis revealed that serum ferritin levels decreased significantly from admission to 24 hours ($p < 0.001$) and from admission to 48 hours ($p < 0.001$) following antibiotic therapy, while the difference between 24 hours and 48 hours was significant at $p < 0.01$, indicating that the maximum reduction in ferritin levels occurs within the first 24 hours of treatment initiation (Table 9).

Table 9: Statistical computation of serum ferritin reduction with antibiotic therapy

Comparison of serum ferritin time points	p-value
Admission vs 24 h	<0.001
Admission vs 48 h	<0.001
24 h vs 48 h	<0.01

Biomarker Reduction Summary: CRP levels showed a 32.3% reduction from admission to 24 hours, which increased to a 56.6% reduction from admission to 48 hours, while ferritin levels exhibited a 30.5% reduction following therapy compared to pre-therapy levels (Table 10, Figure 8).

Table 10: Summary of biomarker reduction after antibiotic therapy

Biomarker	Time period	Percentage reduction (%)
CRP	Admission to 24 h	32.3
CRP	Admission to 48 h	56.6
Ferritin	Before and after therapy	30.5

Clinical Outcomes: Out of the total 120 neonates, 100 (83.3%) survived, while 20 (16.6%) expired during the study period (Table 11, Figure 9).

Table 11: Clinical outcomes of neonatal sepsis following antibiotic therapy

Outcome	Number	Percentage (%)
Survived	100	83.3
Expired	20	16.6

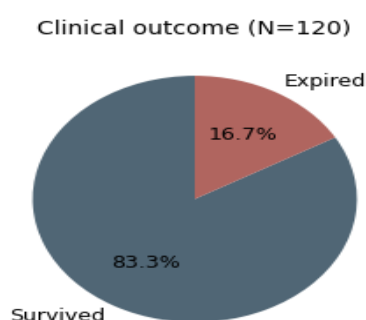


Figure 9: Outcome analysis

Hospital Stay Duration: Statistical calculation estimated a highly significant variation in the mean hospital stay duration among the groups ($p < 0.0001$) (Table 12, Figure 10). The majority of patients, 64 (53.3%), had a hospital stay of 6–8 days (mean 7.04 ± 0.65 days), followed by 39 (32.5%) who stayed 3–5 days (4.58 ± 0.67 days), 13 (10.8%) who stayed 9–11 days (10.00 ± 0.81 days), and 4 (3.3%) who stayed 12–13 days (13.00 ± 0.00 days).

Table 12: Mean hospital stay duration among the study groups

Hospital stay (days)	Number of patients	Mean $\pm$ SD
03-May	39	4.58 ± 0.67
06-Aug	64	7.04 ± 0.65
09-Nov	13	10.00 ± 0.81
Dec-13	4	13.00 ± 0.00

Overall $p < 0.0001$ as reported in the source thesis.

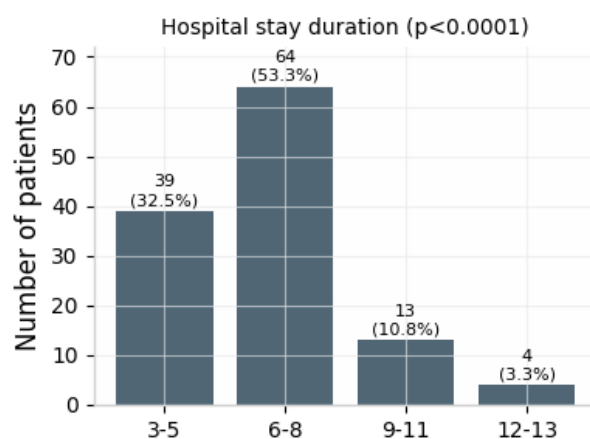


Figure 10: Hospital stay duration of patients

Discussion

Neonatal sepsis is among the primary causes of newborn morbidity and deaths worldwide, particularly in economically weaker nations where early diagnosis and prompt treatment remain challenging. The present study evaluated the demographic characteristics, clinical manifestations, inflammatory biomarkers, and clinical outcomes among 120 term neonates with sepsis, and highlights the role of CRP and serum ferritin in monitoring therapeutic response [3,13,16,20].

Demographic and Clinical Profile: The slight male predominance (52.5%) and the high concentration of cases within the first ten days of life (45.8%) reflect the common epidemiological pattern for early neonatal infections observed in previous literature, the male excess being attributed to the "male disadvantage" in early-life immunity [8,19,26]. The predominance of term births at 37–40 weeks and birth weights between 2.51 and 3.50 kg highlights that neonatal sepsis remains a significant threat regardless of favorable gestational age or birth weight [14,15,21]. Hypothermia (56.6%), refusal to feed (44.1%), and vomiting (54.1%) were the most prevalent manifestations — nonspecific signs that necessitate immediate diagnostic and therapeutic intervention, underscoring the critical role of temperature and feeding monitoring at admission [17,18,25,28,51].

C-Reactive Protein Dynamics: CRP elevates in response to inflammation or tissue necrosis and, despite being nonspecific, has consistently demonstrated elevation in bacterial sepsis and meningitis [10,11,38,41,43]. A central finding of this study is the significant temporal decline of CRP in response to antibiotic therapy: a 32.3% reduction within the first 24 hours, reaching a 56.6% reduction by 48 hours, with highly significant differences between every pair of time points. This progressive decline confirms that CRP is an exceptionally sensitive indicator for monitoring the efficacy of antibiotic treatment in real time, consistent with surveillance data and efficacy-monitoring studies in early-onset neonatal sepsis [37,44,49,50]. The rapid fall in CRP also supports its role in determining the duration of antibiotic therapy, helping to limit unnecessary exposure [23,27,47].

Serum Ferritin Dynamics: Serum ferritin exhibited a 30.5% reduction following therapy, transitioning from a pre-treatment mean of 421.88 ng/mL to 293.13 ng/mL, with the maximum reduction occurring within the first 24 hours. The synchronized reduction of CRP and ferritin suggests that these biomarkers, used together, provide a robust framework for assessing treatment response; ferritin in particular has shown

prognostic value in neonatal and pediatric sepsis, with higher levels tracking organ dysfunction and mortality risk [1,2,5,7,32,33,35,46]. Dynamic changes in acute-phase reactants during the first 48 hours of therapy therefore mirror the resolution of the underlying inflammatory process [34,36,45].

Clinical Outcomes and Hospital Stay: The survival rate of 83.3% indicates that prompt initiation of therapy leads to favorable clinical outcomes for the majority of patients, although the 16.6% mortality rate is a reminder of the continued severity of this condition; this survival pattern is comparable to other regional studies focusing on full-term infants, who typically fare better than preterm populations [6,40]. The variation in hospital stay duration, with 53.3% of patients requiring 6–8 days, points toward the timeframe necessary for achieving clinical stability and aligns with standard practice recommending a minimum course of intravenous antibiotic therapy for confirmed sepsis in neonates [48]. These results collectively emphasize that integrating clinical symptom tracking with serial biomarker measurement is essential for effective management and successful recovery [31,39,42].

Strengths and Limitations: Strengths of this study include its prospective design, the use of paired pre- and post-treatment measurements within the same subjects, a uniform term population that minimized gestational-age confounding, and the use of two inexpensive and widely available biomarkers. Limitations include the single-center design, the relatively modest sample size, the absence of blood-culture-positive confirmation and organism-level analysis, the lack of a comparison biomarker such as procalcitonin, and the short follow-up limited to the hospital stay, which precludes assessment of long-term neurodevelopmental outcomes. Larger multicenter studies incorporating serial procalcitonin, interleukins, and host gene-expression signatures are needed to refine biomarker-guided antibiotic stewardship in neonatal sepsis [12,30,42,45].

Conclusion

Neonatal sepsis continues to be an important problem in newborn care owing to its rapid progression, ambiguous clinical symptoms, and risk of severe consequences; timely recognition and swift intervention are crucial for improving outcomes. In this prospective study of 120 term septic neonates, C-reactive protein declined by 32.3% within 24 hours and 56.6% within 48 hours of antibiotic therapy, and serum ferritin fell by 30.5%, with all changes statistically significant. Serial monitoring of CRP and serum ferritin, integrated with clinical assessment, provides a simple, inexpensive, and clinically useful tool for detecting neonatal sepsis, evaluating therapeutic

response, guiding the duration of antibiotic treatment, and identifying neonates who need additional supportive care. Comprehensive large-scale investigations are needed to strengthen the evidence supporting the use of these biomarkers and to refine diagnostic and therapeutic approaches that reduce the burden of neonatal sepsis.

Declarations

Ethics approval and consent to participate: The study protocol was approved by the Institutional Ethics Committee of Darbhanga Medical College and Hospital; written informed consent was obtained from parents or guardians. Consent for publication: Not applicable. Availability of data and materials: Available from the corresponding author on reasonable request. Competing interests: The author declares no competing interests. Funding: None. Acknowledgements: The author thanks the faculty and staff of the Department of Pediatrics, Darbhanga Medical College and Hospital, and the participating families.

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