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Original Research Article

A Retrospective Study Assessing Association of C-Reactive Protein and Length of Antibiotic Treatment for Newborn Bacterial Infections

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Abstract

Aim: To study the correlation C-reactive protein and length of antibiotic treatment for newborn bacterial infections.

Material and Method: A total of 80 newborns were examined in the Department of Pediatrics, NMCH, Jamuhar, Sasaram, Bihar, India for one year. The research included neonates who were less than 28 days old and had a birth weight of more than 1500 grams, and were believed to have septicaemia. Neonates have had surgery as a result of a wound infection. Infants diagnosed with meningitis, which necessitates a prolonged course of antibiotics, were not included in the research. Following admission, the patient had blood culture and sensitivity testing, routine blood investigations, urine culture and sensitivity testing, chest x-ray, and CRP testing. The C-reactive protein (CRP) level was measured within 24-48 hours after the patient was admitted. Neonates were categorized based on their levels of C-reactive protein (CRP) in the bloodstream. Neonates were monitored for up to 48 hours after discontinuing the medications to see whether the symptoms of septicaemia reappeared.

Results: The study aimed to assess the efficacy of CRP levels as a measure for determining the duration of antibiotic treatment by calculating the negative predictive value (NPV) of CRP. Neonates with C-reactive protein (CRP) levels below 10 mg/L had the greatest negative predictive value (NPV) of 96%, suggesting that these neonates had the least likelihood of needing further antibiotic therapy. The negative predictive value (NPV) for newborns with C-reactive protein (CRP) levels between 10-20 mg/L was 93%, but it was 80% for those with CRP levels over 20 mg/L. This demonstrates that decreased levels of C-reactive protein (CRP) serve as robust indications of a successful course of antibiotic therapy, obviating the need for further treatment.

Conclusion: Our work conclusively shows that CRP levels play a crucial role in determining the appropriate length of antibiotic treatment for newborn bacterial infections. The findings align with previous research and strengthen the effectiveness of CRP as a dependable biomarker for forecasting treatment outcomes and the likelihood of recurrence. Additional investigation should examine the incorporation of CRP levels with other biomarkers to improve the accuracy of determining the duration of antibiotic treatment in newborns.

Keywords: CRP, Antibiotic, Bacterial infections

Introduction

Neonatal bacterial infection, sometimes known as sepsis, continues to be a major cause of illness and death among infants worldwide. The occurrence of neonatal sepsis in India varies between 11 and 25 occurrences per thousand live births, emphasizing the urgent need for efficient diagnostic and therapeutic approaches. Neonatal sepsis presents with a broad range of clinical presentations, including distinct symptoms like fever and inadequate feeding, as well as more subtle indicators like lethargy. This variability in symptoms poses a challenge for doctors in obtaining an accurate diagnosis. The lack of accuracy in diagnosis often results in the widespread use of antibiotics, hence exacerbating the escalating issue of antibiotic resistance. [1-3]

C-reactive protein (CRP) is a biomarker that is produced by the liver in response to inflammatory cytokines during the acute phase of an immune response. The levels of this substance may significantly rise during acute phase responses, and it has a very short half-life of about 19 hours. This characteristic makes it a potentially useful indicator for determining the appropriate length of antibiotic treatment. Through the surveillance of CRP levels, medical professionals may potentially ascertain the

appropriate time to cease administering antibiotics, hence minimizing inappropriate antibiotic use and its accompanying hazards. [4-7]

Neonates are often given antibiotics excessively due to non-specific symptoms and ambiguity in diagnosis. This not only raises the chances of antibiotic resistance but also leads to extended hospital stays and increased healthcare expenses. Hence, there is an urgent want for dependable biomarkers such as CRP to enhance the duration of antibiotic therapy, guaranteeing efficient treatment while minimizing negative effects and resource consumption. [8-10]

The objective of this research is to assess the significance of CRP in deciding the optimal duration of antibiotic therapy in newborns with suspected bacterial illnesses. Our objective is to analyse CRP levels within 24-48 hours of arrival and establish a connection between these levels and treatment results. This research aims to support the implementation of more precise and effective antibiotic use in newborn care.

Material and Method

80 neonates were studied in the Department of Pediatrics, NMCH, jamuhar, Sasaram, Bihar, India for one year. Neonates <28 days of life having birth weight more than 1500 grams with suspected septicaemia were included in the study. Neonates undergone surgery due to wound infection Neonates diagnosed as meningitis (because it requires longer treatment of antibiotics) were excluded from study. After admission blood culture and sensitivity, Routine blood investigations, urine culture and sensitivity, chest x-ray, CRP were done. CRP was estimated within 24- 48 hours of admission. Then neonates were classified as per the levels of CRP serum levels. Neonates were kept up to 48 hours after stopping the antibiotics to observe the recurrence of clinical features of septicaemia. If there is no recurrence of symptoms of septicaemia within four weeks of discharge or the baby required antibiotics for different diagnosis other than septicaemia. In the case of relapse the baby needed another course of antibiotics for suspected or proved septicaemia within 4 weeks after discharge. To estimate the value of CRP as a parameter for guiding the duration of antibiotic therapy, the negative predictive value with respect to further treatment was determined.

Statistical Analysis

The statistical analysis was made in SPSS software version 21.

Results

The demographic data of the 80 neonates included in the study shows an equal gender distribution with 50% females and 50% males. The mean birth weight was 1800 grams with a standard deviation of 150 grams, indicating that the majority of the neonates were of similar weight. The average age at admission was 15 days with a standard deviation of 6 days, showing a relatively homogeneous age distribution within the cohort.

Poor Feeding was the most common clinical feature, present in 75% of the neonates. Among these, 33% had CRP levels <10 mg/L, 42% had CRP levels 10-20 mg/L, and 25% had CRP levels >20 mg/L. Fever was noted in 62.5% of the neonates, with a distribution of 30% having CRP levels <10 mg/L, 40% having CRP levels 10-20 mg/L, and 30% having CRP levels >20 mg/L. Lethargy was observed in 56.25% of the neonates, with 22% having CRP levels <10 mg/L, 44% having CRP levels 10-20 mg/L, and 34% having CRP levels >20 mg/L. Respiratory Distress occurred in 50% of the neonates, with 30% having CRP levels <10 mg/L, 38% having CRP levels 10-20 mg/L, and 32% having CRP levels >20 mg/L. Apnoea was seen in 37.5% of the neonates, evenly distributed among the three CRP level groups. Jaundice was present in 31.25% of the neonates, with the highest percentage (40%) in both the <10 mg/L and 10-20 mg/L CRP level groups, and 20% in the >20 mg/L CRP level group. Vomiting was noted in 25% of the neonates, with 25% having CRP levels <10 mg/L, 50% having CRP levels 10-20 mg/L, and 25% having CRP levels >20 mg/L. Seizures were the least common, present in 12.5% of the neonates, with 30% having CRP levels <10 mg/L, 50% having CRP levels 10-20 mg/L, and 20% having CRP levels >20 mg/L.

Neonates were categorized into three groups based on their CRP levels at admission: <10 mg/L, 10-20 mg/L, and >20 mg/L. The largest group consisted of neonates with CRP levels between 10-20 mg/L (37.5%), followed by those with CRP levels <10 mg/L (31.25%), and those with CRP levels >20 mg/L (31.25%).

The duration of antibiotic therapy varied according to the CRP levels at admission. Neonates with CRP levels <10 mg/L required an average of 5 days of antibiotic therapy, those with CRP levels between 10-20 mg/L required an average of 7 days, and those with CRP levels >20 mg/L required an average of 10 days. This indicates a correlation between higher CRP levels and longer durations of antibiotic therapy.

The recurrence of septicaemia symptoms within 4 weeks of stopping antibiotic therapy was highest among neonates with CRP levels >20 mg/L (20%), followed by those with CRP levels between 10-20 mg/L (7%), and lowest among those with CRP levels <10 mg/L (4%). This suggests that higher CRP levels at admission are associated with a higher likelihood of recurrence of septicaemia symptoms.

The negative predictive value (NPV) of CRP levels was calculated to determine the effectiveness of CRP as a parameter for guiding the duration of antibiotic therapy. Neonates with CRP levels <10 mg/L had the highest NPV (96%), indicating that these neonates had the lowest risk of requiring further antibiotic treatment. The NPV for neonates with CRP levels between 10-20 mg/L was 93%, while it was 80% for those with CRP levels >20 mg/L. This shows that lower CRP levels are strong indicators of a successful course of antibiotic therapy without the need for further treatment.

Table 1: Demographic Characteristics of Neonates

Characteristic	Number (%)
Gender	
Female	40 (50%)
Male	40 (50%)
Mean Birth Weight (grams)	1800 ± 150
Age at Admission (days)	15 ± 6

Table 2: Clinical Features and CRP Levels of Suspected Infected Neonates

Clinical Feature	Number of Neonates (%)	CRP Level <10 mg/L (%)	CRP Level 10-20 mg/L (%)	CRP Level >20 mg/L (%)
Poor Feeding	60 (75%)	20 (33%)	25 (42%)	15 (25%)
Fever	50 (62.5%)	15 (30%)	20 (40%)	15 (30%)
Lethargy	45 (56.25%)	10 (22%)	20 (44%)	15 (34%)
Respiratory Distress	40 (50%)	12 (30%)	15 (38%)	13 (32%)
Apnea	30 (37.5%)	10 (33%)	10 (33%)	10 (33%)
Jaundice	25 (31.25%)	10 (40%)	10 (40%)	5 (20%)
Vomiting	20 (25%)	5 (25%)	10 (50%)	5 (25%)
Seizures	10 (12.5%)	3 (30%)	5 (50%)	(20%)

Table 3: CRP Levels at Admission

CRP Level (mg/L)	Number of Neonates (%)
<10	25 (31.25%)
10-20	30 (37.5%)
>20	25 (31.25%)

Table 4: Duration of Antibiotic Therapy Based on CRP Levels

CRP Level (mg/L)	Duration of Therapy (days) (Mean ± SD)
<10	5 ± 1
10-20	7 ± 2
>20	10 ± 3

Table 5: Recurrence of Septicaemia Symptoms After Stopping Antibiotics

CRP Level (mg/L)	Recurrence within 4 weeks (%)
<10	1 (4%)
10-20	2 (7%)
>20	5 (20%)

Table 6: Negative Predictive Value of CRP Levels

CRP Level (mg/L)	Negative Predictive Value (%)
<10	96%
10-20	93%
>20	80%

Discussion

The demographic statistics of the 80 neonates included in the research indicate a balanced gender distribution, with an equal proportion of girls and boys, each accounting for 50%. The average birth weight was 1800 grams, with a standard variation of 150 grams, suggesting that most of the newborns had a comparable weight. The mean age at admission was 15 days with a standard deviation of 6 days, indicating a very uniform age distribution

within the cohort. The demographic factors mentioned here are consistent with findings from previous research that investigate bacterial infections in newborns. These studies also observe comparable patterns in terms of gender, weight, and age. [11]

Poor feeding was the most common clinical feature, present in 75% of the neonates. Among these, 33% had CRP levels <10 mg/L, 42% had CRP levels 10-20 mg/L, and 25% had CRP levels >20 mg/L. Fever was noted in 62.5% of the neonates, with a distribution of 30% having CRP levels <10 mg/L, 40% having CRP levels 10-20 mg/L, and 30% having CRP levels >20 mg/L. Lethargy was observed in 56.25% of the neonates, with 22% having CRP levels <10 mg/L, 44% having CRP levels 10-20 mg/L, and 34% having CRP levels >20 mg/L. Respiratory distress occurred in 50% of the neonates, with 30% having CRP levels <10 mg/L, 38% having CRP levels 10-20 mg/L, and 32% having CRP levels >20 mg/L. Apnoea was seen in 37.5% of the neonates, evenly distributed among the three CRP level groups. Jaundice was present in 31.25% of the neonates, with the highest percentage (40%) in both the <10 mg/L and 10-20 mg/L CRP level groups, and 20% in the >20 mg/L CRP level group. Vomiting was noted in 25% of the neonates, with 25% having CRP levels <10 mg/L, 50% having CRP levels 10-20 mg/L, and 25% having CRP levels >20 mg/L. Seizures were the least common, present in 12.5% of the neonates, with 30% having CRP levels <10 mg/L, 50% having CRP levels 10-20 mg/L, and 20% having CRP levels >20 mg/L. Comparatively, a study by Ng et al. reported similar distributions of clinical features among neonates with bacterial infections, particularly noting the prevalence of poor feeding, fever, and respiratory distress as common symptoms. This consistency in clinical presentation supports the generalizability of our findings. [12]

The duration of antibiotic therapy varied according to the CRP levels at admission. Neonates with CRP levels <10 mg/L required an average of 5 days of antibiotic therapy, those with CRP levels between 10-20 mg/L required an average of 7 days, and those with CRP levels >20 mg/L required an average of 10 days. This indicates a correlation between higher CRP levels and longer durations of antibiotic therapy. Similar findings were reported by a study conducted by Manzoni et al., which demonstrated that neonates with higher CRP levels needed extended antibiotic therapy compared to those with lower CRP levels. [13]

The recurrence of septicaemia symptoms within 4 weeks of stopping antibiotic therapy was highest among neonates with CRP levels >20 mg/L (20%), followed by those with CRP levels between 10-20 mg/L (7%), and lowest among those with CRP levels <10 mg/L (4%). This suggests that higher CRP levels at admission are associated with a higher likelihood of recurrence of septicaemia symptoms. These results are corroborated by research conducted by Kawakita et al., which found a similar trend in the recurrence of septicaemia in neonates with elevated CRP levels at the initial diagnosis. [14]

The negative predictive value (NPV) of CRP levels was calculated to determine the effectiveness of CRP as a parameter for guiding the duration of antibiotic therapy. Neonates with CRP levels <10 mg/L had the highest NPV (96%), indicating that these neonates had the lowest risk of requiring further antibiotic treatment. The NPV for neonates with CRP levels between 10-20 mg/L was 93%, while it was 80% for those with CRP levels >20 mg/L. This shows that lower CRP levels are strong indicators of a successful course of antibiotic therapy without the need for further treatment. These findings are supported by a study by Hofer et al., which highlighted the high NPV of CRP in predicting the resolution of infection in neonates. [15]

Conclusion

In conclusion, our study demonstrates the significant role of CRP levels in guiding the duration of antibiotic therapy in neonatal bacterial infections. The results are consistent with existing literature and reinforce the utility of CRP as a reliable biomarker for predicting treatment outcomes and recurrence risks. Further research could explore the integration of CRP levels with other biomarkers to enhance the precision of antibiotic therapy duration in neonates.

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