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ORIGINAL RESEARCH

To study the role of C-reactive protein in determining the appropriate length of antibiotic treatment for newborn bacterial infections

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ABSTRACT

Aim: To study the role of C-reactive protein in determining the appropriate length of antibiotic treatment for newborn bacterial infections. **Material and method:** 80 neonates admitted at paediatric ward were studied. 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. **Results:** 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 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. **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.

Keywords: CRP, Antibiotic, Bacterial infections

INTRODUCTION

Neonatal bacterial infection, often known as septicaemia, continues to be a major contributor to illness and death among newborns worldwide. The prevalence of neonatal sepsis in India ranges from 11 to 25 cases per thousand live births. The clinical signs of this condition range from being very specific to being subtle, which might challenge the diagnostic abilities of a pediatrician.[1-4] The uncertainty about infection and the presence of non-specific symptoms in newborns have led to the extensive use of antibiotics, exacerbating the issue of antibiotic resistance. There is a growing need for thorough assessment of the reasons and length of treatment, which would subsequently reduce the time and expenses of hospitalization and minimize the negative effects and complications of antibiotics. C-reactive protein (CRP), an acute phase reactant, is produced in

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the liver in response to inflammatory cytokines.[5-8] Its levels may increase by more than 1000-fold during acute phase reactions. After effectively removing the microbial stimulus, it rapidly decreases owing to its very short half-life of 19 hours.[9,10] Therefore, C-reactive protein (CRP) may serve as a measure to determine the appropriate time to stop antibiotic treatment in cases of suspected newborn septicaemia. This was the main objective of the current research conducted on neonates less than 28 days.

MATERIAL AND METHOD

80 neonates admitted at paediatric ward were studied. 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

Different clinical features, CRP levels, micro organisms were classified with percentage. The statistical analysis was made in SPSS software. The ratio of male and female were 2:1.

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.Apnea 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.

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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%)	2 (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 data of the 80 neonates included in the study show 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. These demographic characteristics align with other studies focusing on neonatal bacterial infections, which also report similar distributions 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. Apnea 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

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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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