

Association of C-Reactive Protein with Parameters of Early Onset Sepsis and Blood Culture

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ABSTRACT

Background: Blood culture is a gold standard technique to diagnose neonatal sepsis but the C-reactive protein (CRP) is also an important biomarker of acute phase reaction. CRP has a role in humoral immunity against infection, leading to inflammation. Very few of the data is available to conclude the diagnostic accuracy of CRP in association with parameters of early stage neonatal sepsis in pre-term or low birth weight babies. So the aim of current study was to find out the association of C-reactive protein with parameters of early onset sepsis and blood culture in pre-term and low birth weight babies.

Methods: A cross-sectional study was conducted at the Pediatric Medicine department of Maternal and Child Health Center (MCH), Shaheed Benazirabad during August 2022 to January 2023. Early onset sepsis was diagnosed on the basis of maternal factors, prenatal history and clinical examination. Blood sample was collected and sent to the pathology laboratory of Peoples University of Medical and Health Sciences for Nawabshah for measurement of C-reactive protein, white blood cell count and culture and sensitivity testing. Data was analyzed by using the Statistical Package for Social Science (SPSS) version-20. p-value less than 0.05 was considered as significant.

Results: A total of 120 patients of neonatal sepsis were enrolled in the study out of them 52 were positive for C-reactive protein. The mean age of the study participants was 1.6 ± 0.69 days. Male participants were predominant (63.5%) over their female counterpart. Majority cases of septicemia (57.7%) were having birth weight less than 2.5kg. Odd ratio of C-reactive protein was estimated at 95% confidence interval and the results found that age had significant association with positive C-reactive protein. Birth weight less than 2.5kg also showed significant negative association with C-reactive protein but the term of birth found no any significant association. Patients having positive blood culture and those who had WBC count more than $25000/\text{mm}^3$ reported strongly significant association with C-reactive protein.

Conclusion: It can be concluded that the C-reactive protein is significantly associated with parameters like age, WBC count more than $25000/\text{mm}^3$ and blood culture but no association has been found with maturity of neonate i.e. term or pre-term babies. The birth weight less than 2.5kg is negatively associated with the C-reactive protein.

Keywords: Neonatal sepsis, C-reactive protein, Pre-term

INTRODUCTION

Despite of technological advancement the neonatal sepsis is still a life threatening condition worldwide and its cure is becoming a challenge for pediatricians because of variations in presenting symptoms and poor outcome. Neonatal intensive care unit has been very well-developed in the recent years but the neonatal sepsis related mortality rate is still very high that is around 1.5% in term babies while more than 40% in low birth weight babies (1). It is very difficult for the pediatricians to diagnose early stage of neonatal sepsis when the disease is at sub-clinical stage. Because of poor practice of antibiotics administration during initial infection resulting in development of resistance (2).

Blood culture is a gold standard technique to diagnose neonatal sepsis but the C-reactive protein (CRP) is also an important biomarker of acute phase reaction. CRP has a role in humoral immunity against infection, leading to inflammation (3). It is produced from the liver as a result of infection specially those caused by bacteria that is why it is non-specific but when it is done in combination with other screening markers like white blood cell count (WBC), erythrocyte sedimentation rate (ESR), interleukin (IL) and Procalcitonin, the diagnostic accuracy increases up to 10 times (4). Decrease concentration of CRP has been found in the blood test drained from umbilical cord and in the serum of neonates. The low concentration of CRP in association with clinical signs and symptoms can be a predictor of neonatal septicemia as a result of pot-natal infection (5).

Literature revealed that either preterm babies or babies having low birth weight shows negligible increase in CRP because of their liver immaturity resulting in failure to synthesize significant amount of CRP. Researches are going on to identify the role of CRP during neonatal septicemia, its prognostic value, association with gestational age, birth weight and sub-clinical stage of sepsis (6). Very few of the data is available to conclude the diagnostic

accuracy of CRP in association with parameters of early stage neonatal sepsis in pre-term or low birth weight babies (7). So the aim of current study was to find out the association of C-reactive protein with parameters of early onset sepsis and blood culture in pre-term and low birth weight babies.

MATERIAL AND METHODS

A cross-sectional study was conducted at the Pediatric Medicine department of Maternal and Child Health Center (MCH), Shaheed Benazirabad during August 2022 to January 2023. The sample size was calculated by using the OpenEpi calculator and was 120. Those neonates who were admitted in the Neonatal Intensive Care Unit (NICU), with the signs and symptoms of early onset sepsis, were included in the study while those were excluded who were either admitted with late-onset sepsis or died soon after admission. The non-probability consecutive sampling technique was used for sample collection. Early onset sepsis was diagnosed on the basis of maternal factors, prenatal history and clinical examination. Blood sample was collected and sent to the pathology laboratory of Peoples University of Medical and Health Sciences for Nawabshah for measurement of C-reactive protein, white blood cell count and culture and sensitivity testing.

Data was analyzed by using the Statistical Package for Social Science (SPSS) version-20. All the categorical variables are presented in frequency and percentage while numerical variables in Mean with standard deviation. Chi-square test was used to find the association between C-reactive protein and multiple neonatal factors like age, gender, birth weight, term/preterm, positive blood culture, WBC count and symptoms including apnea, vomiting, feed reluctance, hypothermia and APGAR score ≤ 6 . Logistic regression model was used for the estimation of Odd ratios at 95% confidence interval while p-value less than 0.05 was considered as significant.

RESULTS

A total of 120 patients of neonatal sepsis were enrolled in the study out of them 52 were positive for C-reactive protein. The mean age of the study participants was 1.6 ±0.69 days and majority were from the age group of day one (44.2%) which has no statistical significance. Male participants were predominant (63.5%) over their female counterparts but results were non-significant. Majority cases of septicemia (57.7%) were having birth weight less than 2.5kg and the association with C-reactive protein was significant. There was no significant association either the neonate birth on term or preterm. About 46.2% cases of septicemia were positive for both C-reactive protein and blood culture and showed significant association. Majority of cases were having white blood cell count more than 25000/mm³ and significantly associated with C-reactive protein. Apnea, vomiting and feed reluctance were found in 88.5% of cases while Hypothermia, APGAR score ≤ 6 were present in 25% cases and all the symptoms were having significant association with the presence of C-reactive protein as mentioned in Table 1.

Table 1: Different parameters and their association with C-reactive protein

Parameters	CRP +ve n=52 (%)	p-value
Age		0.421
1 day	23 (44.2)	
2 day	17 (32.7)	
3 day	12 (23.1)	
Gender		0.75
Male	33 (63.5)	
Female	19 (36.5)	
Birth weight		0.04
≤ 2.5kg	30 (57.7)	
≥ 2.5kg	22 (42.3)	
Term	35 (67.3)	0.27
Preterm	17 (32.7)	
Positive Blood culture	24 (46.2)	0.000
WBC		
≤ 5000/mm ³	4 (7.7)	0.36
≥25000/mm ³	27 (51.9)	0.000
Apnea, vomiting, feed reluctance	46 (88.5)	0.001
Hypothermia, APGAR score ≤ 6	13 (25.0)	0.004

Odd ratio of C-reactive protein was estimated at 95% confidence interval and the results found that age had significant association with positive C-reactive protein. Birth weight less than 2.5kg also showed significant negative association with C-reactive protein but the term of birth found no any significant association. Patients having positive blood culture and those who had WBC count more than 25000/mm³ reported strongly significant association with C-reactive protein as shown in Table 2.

Table 2: Estimation of Odd ratio in CRP Cases

Parameters	Odd ratio	p-value
Age (days)	1.72 (1.01-2.92)	0.03
Birth weight ≤ 2.5kg	0.38 (0.17-1.0)	0.07
Term	1.72 (0.98-4.23)	0.25
Positive blood culture	8.4 (4.52-27.1)	0.001
WBC ≥25000/mm ³	4.65 (2.17-11.83)	0.000

DISCUSSION

Current study found that 41.7% cases of sepsis positive for C-reactive protein. The result is in accordance with another study conducted in Pakistan, found 44.1% positive C-reactive protein cases with diagnosis of neonatal sepsis (8). Majority were from the age group of day one (44.2%) which is an alarming situation and needs proper monitoring of maternal and perinatal care. Male participants were predominant (63.5%) over their female counterparts because in our setup male babies are always prioritized over the female babies secondly association of C-reactive protein to X chromosome and its role in immunoglobulin formation is not properly understood (9). The finding is also favored by Hisamuddin et.al (10).

Current study found that apnea, vomiting and feed reluctance were found in 88.5% of cases while hypothermia and APGAR score ≤ 6 were present in only 25% cases and all the symptoms were having significant association with the presence of C-reactive protein. On the other hand studies favored this finding up to some extent by reporting significant association with symptoms like apnea, vomiting and feed reluctance while a weak correlation with the hypothermia and APGAR score ≤ 6 (11). Same finding is also reported by Kheir et.al (12).

Current study found no significant association neonate maturity i.e. delivered on term or preterm. Age of neonate had significant association with positive C-reactive protein. Birth weight less than 2.5kg also showed significant negative association with C-reactive protein. Patients having positive blood culture and those who had WBC count more than 25000 reported strongly significant association with C-reactive protein. These findings are favored by other studies as well by reporting significant correlation of positive C-reactive protein with 1st day of life, WBC more than 25000/mm³ and maturity of neonate (13). On the other hand, Turner et.al found no association of positive C-reactive protein with the maturity of neonate because the preterm babies already have immature liver to synthesize significant amount of C-reactive protein. He studied on the association of C-reactive protein with the age of neonate and noticed that C-reactive protein was increased in term neonates and those who were having good birth weight as compared to preterm and low birth weight babies (14). Hengst et.al reported that the risk of neonatal sepsis increases with decreasing gestational age (15) because the newborns are not immunologically strong enough to fight against bacterial infections so require prolong hospital stay and serious intervention (16).

CONCLUSION

It can be concluded that the C-reactive protein is significantly associated with parameters like age, WBC count more than 25000/mm³ and blood culture but no association has been found with maturity of neonate i.e. term or pre-term babies. The birth weight less than 2.5kg is negatively associated with the C-reactive protein. C-reactive protein can be used as a diagnostic tool in early onset sepsis and treatment monitoring but very few of the studies have been done to reach a final conclusion so there is a need to perform study on larger scale as the current study limitation is the single centered study.

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