Original Research Article

Cord C-reactive protein as a marker for early onset neonatal sepsis children

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Received: 15 December 2016

Accepted: 16 January 2017

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ABSTRACT

Background: Of the 2.8 million neonatal deaths, worldwide, 0.43 million is contributed by sepsis alone. The objective of this study was to determine the levels of umbilical cord C-reactive protein and assess the suitability of this test in diagnosing early onset sepsis in newborns born to mothers with no risk factors for intrapartum infection. To determine the influence of other factors such as parity, birth weight and mode of delivery on the levels of cord CRP.

Methods: CRP levels in cord blood were estimated for 103 consecutive newborns delivered at a tertiary care teaching hospital. These babies were monitored for signs of sepsis for 72 hours and were later followed up with serum CRP and blood cultures.

Results: A prospective cohort study of 103 consecutive newborns were taken of which 53.4% were male babies. Comparison of cord CRP levels of baseline characteristics revealed significant elevation in babies born to multipara mothers ($p = 0.0028$) and in low birth weight babies ($p = 0.05$), while there were no significant changes in different modes of delivery. The mean cord CRP of the study group was 0.694 ± 0.2979 . Out of 104 babies, 16 had elevated cord CRP (above 1.1mg/l) of these, 12 babies were later confirmed to have sepsis. The mean cord CRP level in babies with EOS was 1.3 ± 0.255 ($p = 0.001$). A sensitivity of 100%, specificity of 90.9%, positive predictive value of 75% and negative predictive value of 100% was determined.

Conclusions: This study confirms that cord CRP is an effective marker to predict EONS. An optimal concentration of cord CRP > 1.1 mg/L has maximal sensitivity and specificity to predict EONS.

Keywords: C - reactive protein, Neonatal sepsis

INTRODUCTION

Of the 2.8 million neonatal deaths worldwide, 0.43 million is contributed by sepsis alone. The risk of death due to sepsis in the early neonatal period is 34 times greater in settings with 30 neonatal deaths per 1000 live births.¹ The neonatal mortality rate in India being estimated to be 28 per 1000 live births in 2011 - 2015, India too falls in this category.²

Among this, Early Onset Neonatal Sepsis (EONS) remains a major cause for neonatal mortality and morbidity. The case fatality of EONS ranges from 16.7 - 19.4%.³

C-Reactive Protein (CRP) is the most extensively studied acute phase reactant so far, despite the ongoing rise and fall of new infection markers, it still remains the preferred index in many neonatal intensive care units⁴.

There is great interest in rapid diagnostic tests that are able to safely distinguish infected from uninfected newborns, especially in the early phase of the disease. CRP passes the placenta in very low quantities⁴ or not at all⁵ therefore, any elevation in the neonate always represents endogenous synthesis. Umbilical cord blood normally has low CRP (0.01-0.35 mg/l) but with intrauterine (foetal) bacterial infection, concentrations may be as high as 260 mg/l.⁶

Sensitive techniques like nephelometry are required to establish a cut off for standard values of cord CRP in normal as well as in early onset sepsis newborns.⁷

METHODS

Institutional ethical committee approval was obtained and informed consent was taken from the participants of the study. This is a prospective cohort study done in a tertiary care hospital on 103 consecutively delivered newborns. All newborns delivered between April 2015 to April 2016 at A. J. Hospital and Research Centre, Mangalore were included in this study and neonates less than 28 weeks of gestation and newborns that had lethal congenital abnormalities were excluded from the study.

Base line data was collected such as maternal age, parity, mode of delivery and birth weight was recorded. 5 ml of umbilical blood was collected in a plain vacutainer at birth and the sample was immediately processed by immunoassay method which was a quantitative method of CRP estimation. The included newborns were then monitored for signs of sepsis. Confirmation of sepsis was done by estimation of serum CRP or blood culture which was collected after doing venipuncture.

RESULTS

There were 103 babies eligible for the study. 46.6% (n = 48) were female and 53.4% (n = 55) were male.

Figure 1: Sex of babies.

There were 55 mothers who underwent LSCS, 44 had a normal vaginal delivery and 4 had a normal vaginal delivery with vacuum assistance. The mean cord CRP was 0.685 ± 0.297 mg/l in babies whose mothers underwent LSCS, 0.695 ± 0.264 mg/l in normal delivery and 0.8 ± 0.245 mg/l in those with normal delivery with vacuum assistance. These values on comparison did not show much significance between the groups (p = 0.735).

Figure 2: Mode of delivery.

Majority of the babies were having the birth weight between 3.0-3.5 kg (39.8%) while 34% (n = 35) fell between 2.5-3.0 kg, 11.7% (n = 12) of the babies less than 2.5 kg and 14.6% (n = 15) were >3.5 kg. The mean cord CRP in babies <2.5 kg was 0.833 ± 0.431 mg/l which was significantly higher than the other babies (p = 0.05).

Figure 3: Birth weight.

Cord CRP levels were compared in primipara and multipara mothers. 62 primipara and 41 multipara mothers were included. The mean cord CRP in babies born to primipara mothers was 0.645 ± 0.269 mg/l while in babies born to multipara mothers had a mean cord CRP of 0.768 ± 0.283 mg/l which was found to be a significant difference between the two groups (p = 0.028).

Figure 4: Parity.

The mean cord CRP was found to be 0.694 ± 0.279 mg/l with a minimum level of 0.2 mg/l and maximum value of 1.7 mg/l. 16 babies out of 103 babies were found to have an elevated level of cord CRP (>1.1 mg/l). 14 babies out of these 16 were confirmed to have sepsis within 24-48 hours. The mean cord CRP of those 14 babies was 1.3 ± 0.255 (p = 0.001).

In this study, the sensitivity of cord CRP to detect sepsis in newborn was found to be 100%, while specificity was

90.9%. The positive predictive value was found to be 75% and the negative predictive value was found to be 100%. The accuracy rate was 91.3%.

DISCUSSION

In this study, we evaluated the levels of cord CRP in newborns born to mothers who have low risk of contracting intra-partum infections.

CRP has been used in neonatology to assess the risk of neonatal sepsis because of inherent clinical difficulties in making a diagnosis of the same.⁸ The fetus is able to produce CRP and other acute phase reactants as early as four to five weeks of gestation. Paired mother and infant sampling showed that CRP does not cross the placenta.

In other studies, cord blood CRP was significantly elevated in primipara as compared to multipara.⁷ This is contrary to the findings in our study where we have found a significant elevation in the levels of cord CRP in multipara as compared to primipara.

Umbilical cord CRP concentrations were higher in low birth weight newborns as compared to normal and larger babies. This is in agreement with the study published by Tevisanuto et al.¹¹

This study showed cord CRP value ranging from 0.2 to 1.7 mg/l which is significantly lower than the established cut offs for cord CRP in other studies thus proving that by using more sensitive nephelometric method of estimated of CRP helps us in detecting and identifying values as low as 1.1 mg/l to be a significant indicator of sepsis in newborn.^{7,9}

The clinical significance of this study lies in the fact that if simple investigations like cord CRP can predict early onset neonatal sepsis, early administration of antibiotics can be warranted.

CONCLUSION

This study confirms that cord CRP is an effective marker to predict EONS even in the absence of intrapartum risk factors for infection in the mother. The clinical relevance of this observation is that CRP determination can be obtained on the same day and a value >1.1 mg/l can be used to highly suspect that the neonate has been exposed to a possible microorganism before birth. Umbilical cord blood sampling represents a simple, inexpensive and widely available test to determine whether a neonate has developed a fetal inflammatory response before birth.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Patrick R, Rajan A, Soans ST, Shriyan A. Cord C-reactive protein as a marker for early onset neonatal sepsis children. Int J Contemp Pediatr 2017;4:527-9.