

Accuracy of C - Reactive Protein (CRP) for the Diagnosis of Neonatal Sepsis Having Blood Culture as Gold Standard

Accuracy of C -
Reactive Protein
(CRP) for the
Diagnosis of
Neonatal Sepsis

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ABSTRACT

Objective: To assess the diagnostic accuracy of C - reactive protein (CRP) for the diagnosis of neonatal sepsis while having blood culture as gold standard.

Study Design: A descriptive / cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Pediatrics, Bahawal Victoria Hospital, Bahawalpur, from December 2018 to May 2019.

Materials and Methods: A total of 160 full term neonates with suspicion of sepsis fulfilling the inclusion and exclusion criteria were included in the study. Detailed physical and clinical examination was done, and baseline investigations as per hospital criteria were asked. Sensitivity, Specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of CRP in relation to blood culture were calculated.

Results: There were 107 (66.9%) male and 53 (33.1%) female, showing a male to female ratio as 2.01:1. Mean age of the study participants was 5.26 days with a standard deviation of 3.1 days. Blood culture confirmed the presence of sepsis in 77 (48.1%) cases while 82 (51.3%) neonates were found as CRP positive. Sensitivity, specificity, PPV and NPV of CRP in relation to blood cultured for neonatal sepsis were calculated as 81.8%, 77.1%, 76.8%, 82.1% respectively while accuracy of CRP was found as 79.4%.

Conclusion: CRP was found to be a precise indicator of sepsis. In neonates who are suspected for sepsis should always be tested for CRP which will help in early prediction and management of such neonates.

Key Words: neonatal sepsis, CRP, blood culture, sensitivity.

Citation of articles: Haq HMA, Anjum AA, Bharo MA, Bhatti IA. Accuracy of C - Reactive Protein (CRP) for the Diagnosis of Neonatal Sepsis Having Blood Culture as Gold Standard. Med Forum 2019;30(8):55-58.

INTRODUCTION

Neonatal sepsis is known as a clinical syndrome described by signs and symptoms related to infection in the infants aged ≤ 28 days. Neonatal sepsis exhibits itself in the shape of systemic signs linked to infection.^{1,2} Infections are estimated to be the commonest cause of neonatal morbidity and mortality while neonatal sepsis is one of the major cause contributing to it.^{3,4} In Pakistan, exact numbers affected with neonatal sepsis are not known but global estimates of neonatal sepsis are calculated as 2202 / 100000 live births with mortality ranging 11 to 19%.⁵⁻⁷ It is also estimated that more than 40% of deaths under 5 years of age are noted in the neonatal period.⁸

Neonatal sepsis affects all regions of the world and more than 30 million neonates are affected with it while among these, it is estimated that around 2.7 million neonates die.^{8,9} In South Asia, around 25% of neonatal deaths are associated with neonatal sepsis. Those who survive from neonatal sepsis are left with increased chances of short as well as long term neurodevelopment diseases.^{6,10} Mortality rate associated with neonatal sepsis increase if the condition is not diagnosed and treated properly so with non specific presentation at early stages, special attention is advised to be given by the clinicians to such neonates for good outcome.⁵

For diagnosing neonatal sepsis, blood culture and sensitivity test are considered as gold standard.¹¹ In Pakistan, it has been shown that pathogens like E. coli, klebsiella pneumonia, staphylococcus aureus as well as some of the group B streptococci are commonly found in cases of neonatal sepsis.¹² It is also a fact that 48 to 72 hours are consumed in blood culture and sensitivity analysis.¹³ Researchers around the world are always trying different diagnostic options to diagnose a fatal condition like neonatal sepsis at the earliest. There is a need for a diagnostic test that has good sensitivity along with a reliable negative predictive value (NPV). Different laboratory parameters have been tried and tests like leukocyte count has been found showing a sensitivity of 35% and specificity as 77%, increased /

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Received: June, 2019

Accepted: July, 2019

Printed: August, 2019

decreased neutrophil count having sensitivity as 35% and specificity as 74%, low platelet count showing sensitivity as 61% and specificity as 82% and C-reactive protein (CRP) showing sensitivity as 23% and specificity as 84%.¹³ Other markers like procalcitonin, acute phase reactants as well as bacterial genomes and inflammatory cytokines are also being evaluated around the world.⁶ CRP is considered to be an easy and simple investigation and aim of this study was to assess its diagnostic accuracy for the diagnosis of neonatal sepsis while having blood culture as gold standard.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted at the department of Pediatrics, Bahawal Victoria Hospital, Bahawalpur, from December 2018 to May 2019. A total of 160 full term neonates with suspicion of sepsis were included in the study. Suspicion of sepsis at the time of presentation was described⁵ as drowsiness, unwillingness to feed, hypothermia as less than 35 °C, fits or having difficulty while breathing, mothers of presenting neonates who were having high grade fever or those who had foul smelling discharge during delivery. All those neonates who were noted to receive oral or injectable antibiotics, whose mothers had taken any narcotic analgesic during labor or those neonates who were having congenital heart disease, were not enrolled.

Approval from Institute's ethical and research committee was acquired for this study and informed written consent was taken from all the parents / guardians. In all neonates, detailed physical and clinical examination was done, and baseline investigations as per hospital criteria were asked. All the demographical information like name, age and gender were recorded. Under stringent aseptic technique, 10 ml of blood was drawn from all the study participants and sent to institute's central laboratory for CRP while blood culture were also asked to confirm the presence of neonatal sepsis. CRP was considered as negative with value < 5mg/dl and positive with a value above it.⁵

All the relevant information like age, gender, CRP, blood culture report and neonatal sepsis (yes/no) were noted on a predesigned proforma. SPSS version 20 was used for all kinds of data entry and analysis. Mean along with standard deviation were recorded for all quantitative variables while frequencies and percentages were calculated for qualitative variables. Sensitivity, Specificity, PPV, NPV and diagnostic accuracy of CRP were calculated in relation to blood culture.

RESULTS

Out of a total of 160 neonates, there were 107 (66.9%) were male and 53 (33.1%) female, showing a male to female ratio as 2.01:1. Mean age of the study participants was 5.26 days with a standard deviation of

3.1 days. Majority of the neonates, 78 (48.8%) were having age less than 1 week.

In all the 160 suspected sepsis cases, blood culture confirmed the presence of sepsis in 77 (48.1%) cases while others, 83 (51.9%) turned out to be negative. Amongst all neonates, 82 (51.3%) presented as CRP positive (Table No.1).

Sensitivity, specificity, PPV and NPV of CRP in relation to blood cultured confirmed sepsis were calculated as per formula given in Table number 2 as those values were found as 81.8%, 77.1%, 76.8%, 82.1% respectively while diagnostic accuracy of CRP was found as 79.4%.

Out of 77 neonates found having sepsis, E.coli (n=30, 39.0%), klebsiella pneumoniae (n=14, 18.2%) and S. aureus (n=12, 15.6%) were the commonest pathogens involved.

Table No.1: Findings of Blood Culture and CRP amongst All the Neonates

| | Blood Culture | CRP |
|----------|---------------|------------|
| Positive | 77 (48.1%) | 82 (51.3%) |
| Negative | 83 (51.9%) | 78 (48.7%) |
| Total | 196 | 196 |

Table No.2: Relation of CRP and Blood Culture amongst all the neonates

| CRP | Sepsis | | Total |
|-------------|-----------------------------------------------------------|----------|-------|
| | Positive | Negative | |
| Positive | 63 | 19 | 82 |
| Negative | 14 | 64 | 78 |
| Total | 77 | 83 | 160 |
| Sensitivity | $(a / a + c) \times 100 = 81.8\%$ | | |
| Specificity | $(d / b + d) \times 100 = 77.1\%$ | | |
| PPV | $(a / a + b) \times 100 = 76.8\%$ | | |
| NPV | $(d / c + d) \times 100 = 82.1\%$ | | |
| Accuracy | $\{(d + a) / \text{total patients}\} \times 100 = 79.4\%$ | | |

DISCUSSION

As we know that newborn babies have Newborns have a fragile immune system that make them more susceptible to infections. It is also seen that newborn babies get worse rapidly following infections and if diagnosis and treatment is delayed, worse outcomes are commonly seen.¹⁴ Proactive approach regarding diagnosis and treatment of neonatal sepsis has been found beneficial in researches conducted around the world so there is always a need of a diagnostic tool that can prove helpful in early diagnosis.

Neonatal sepsis commonly accompanies a presentation that is non-specific in nature so there is always a challenge in identifying neonates with and without sepsis. CRP is considered to be an easy to perform, time and cost effective test.⁵ We considered CRP through qualitative method, taking cut-off level value of 5mg/dl.

In the present study, we noted the mean age amongst all the neonates as 5.26 days with a standard deviation of 3.1 days. Majority of the neonates, 78 (48.8%) were having age less than 1 week. Irshad M et al⁵ found the mean age of studied neonates as 4.5 days which is quite similar to what we observed while Anwer SK and Mustafa S¹⁵ found the mean age of studied neonates as 4 days while most of them were less than 1 week.

Majority of the neonates in our study, 107 (66.9%) were male. This is very consistent to previous findings where a predominant male prevalence has been found by earlier researchers.^{5,16} X linked immune regulatory gene factor could be the contributor to this finding in male gender.¹⁷

In the present work, blood culture confirmed the presence of sepsis in 77 (48.1%) cases. This is pretty near to what has been found by another local study done in Peshawar⁵ where 43% of neonates were found positive for sepsis while West BA et al¹⁸ and Anwer SK et al¹⁵ noted 43% and 42% of neonates positive for sepsis respectively which is again very close to our findings. Sriram R¹⁷ noted 50.4% neonates with the presence of sepsis in another study which is pretty consistent to the findings of this study.

In the current study, we noted 82 (51.3%) neonates as CRP positive. Another local study with a similar design from Peshawar⁵ found 48% neonates as CRP positive while Shirazi H et al¹³ noted 39% neonates with CRP positive which is lower than the current finding. As neonatal sepsis commonly accompany presentation that is non-specific in nature so there is always a challenge in identifying neonates with and without neonatal sepsis.

In this study, sensitivity, specificity, PPV and NPV of CRP in relation to blood culture were calculated as 81.8%, 77.1%, 76.8%, 82.1% respectively while diagnostic accuracy of CRP was found as 79.4%. In another local study from Lady Reading Hospital from Peshawar⁵ noted the sensitivity of CRP in relation to blood culture as 78 % while specificity was 74% and NPV as 81%. Our results are aligned with these findings and mean that around 3/4th of neonates who are found suspected having sepsis will be rightly diagnosed according to CRP estimation. This also mean that 1 out of every 4 neonates will have a chance of false negative results. Usually, neonates are reported to our setup with a history of antibiotics usage or mothers are administered antibiotics intrapartum, a CRP which is negative could give us a good lead to make a clinical decision to stop antibiotics usage. This can result in early discontinuation of hospitalization and could lead to cost effective treatment. West BA and coworkers¹⁸ noted that sensitivity of CRP as 74% while specificity was found as 74.1%, PPV as 68.4% and NPV of 79.0% which is very near to what was found in the current study. Anwer SK and colleagues¹⁵ got sensitivity, specificity, PPV and NPV of CRP in relation to positive blood culture for sepsis as 92.5%, 85.3%, 80.6% and

96.5% respectively which again shows the utility to CRP for the early prediction of sepsis in suspected neonates. Some researchers¹³ reported sensitivity of CRP in diagnosis of sepsis as low as 23% which is contrary to current findings while most others^{19,20} have got quite similar results in comparison to our findings. Variation in reported sensitivity of CRP in neonatal bacterial infection could be attributed to difference in diagnostic criteria labeled in the different studies and the span of infection studied.

In the present study, confirmed cases of neonatal sepsis through blood culture, E.coli (39.0%), klebsiella pneumoniae (18.2%) and S. aureus (15.6%) were found to be the commonest pathogens involved. It has been found earlier by local researchers^{5,12} that E. coli is the most common pathogen involved followed by k. pneumoniae.

In the current study, diagnostic accuracy of CRP was found to be 79.4% which means that CRP can be very helpful in predicting sepsis in suspected neonates while blood culture results are awaiting. With a high NPV 82.1%, it can also help immensely in excluding neonates having sepsis that could prevent unnecessary antibiotic usage and hospital stays.

This is the 1st study conducted at our center assessing the role of CRP as a diagnostic tool for neonatal sepsis having blood culture as gold standard. Studies having larger sample size, involving multiple health institutes and local population will certainly prove helpful in verifying the results of the current work.

CONCLUSION

CRP was found to be a precise indicator of sepsis. In neonates who are suspected for sepsis should always be tested for CRP which will help in early prediction and management of such neonates. CRP is an easy, quick and simple test. CRP can be highly helpful in resource constraint settings where blood culture is not always available.

Acknowledgement: We would like to thank Mr. Muhammad Aamir (aamir.chock@hotmail.com) for his assistance in statistical analysis.

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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