



## Research Article

# C-REACTIVE PROTEIN AS PRIMARY LABORATORY INDICATOR OF INFECTION IN PEDIATRIC PATIENTS

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Received: June 26, 2019; Revised: July 24, 2019; Accepted: July 26, 2019; Published: July 30, 2019

**Abstract-** Introduction: C reactive Protein (CRP) is the acute phase reactant which is secreted from liver and its level rises within 12 hr of onset of initial stimulus of infective or inflammatory origin. Testing of CRP value has been widely used as indicator tool to detect early infection along with other laboratory tests.

Materials and Methods: This present study was aimed to analyze the different values of CRP in correlation with WBC count and blood culture in selected patients. Samples of pediatric patients aged less than 1 year were included in this study. Total 191 samples were analyzed retrospectively received in microbiology laboratory for CRP testing by standard methods. Data of CRP values were summarized on the basis of demographic variables and other laboratory tests.

Results: Out of 191 samples, CRP test was positive in 46 (24.08%) patients showed positive response with mean CRP value of 8.03mg/dl. Out of all age group, highest samples were from early neonate age group (0-7days) which shows 21.42% positive ratio. Out of positive samples majority of samples (22) were having CRP value 0.6-4.8 mg/dl. Majority of positive samples were having abnormal CRP value either in terms of leukopenia or leukocytosis. Out of 57 blood culture samples received, 23 shows positive bacterial growth.

Conclusion: Testing of CRP has been widely used as one of most sensitive indicator of infection detection. Serial measurement of CRP value can also be utilized as prognostic indicator to detect response of treatment. Rather than using single parameter, result should always correlate with other laboratory parameters.

**Keywords-** C reactive protein, WBC count, Blood culture, Neonate, Pediatric patients

**Citation:** Patel Purav, et al., (2019) C - Reactive Protein as Primary Laboratory Indicator of Infection in Pediatric Patients. International Journal of Microbiology Research, ISSN: 0975-5276 & E-ISSN: 0975-9174, Volume 11, Issue 7, pp.-1635-1637.

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## Introduction

C reactive protein is acute phase reactant which is an important laboratory marker as predictor for an infection. It is one of the best among all acute phase proteins because of regular use as marker of systemic inflammation in clinical setting. There are minimum 40 acute phase proteins are identified till date which is based on increase of 25% value from baseline after trigger of inflammation. C reactive protein was originally discovered in 1930 by William Tillett and Thomas Francis from the Rockefeller University and given its name because it is interacted with phosphorylcholine containing polysaccharide and lipoteichoic acid found on streptococcus pneumoniae. This protein was able to precipitate the "C" polysaccharide derived from the pneumococcal cell wall [1,2]. CRP consists of five identical, non covalently associated proteins arranged symmetrically around a central pore. The word pentraxins is being used to summarize the family of similar proteins with this structure. CRP can activate the classical complement pathway, bind to immunoglobulin receptors (Fc R) and can also stimulate the phagocytosis [3,4]. C-reactive protein (CRP) is synthesized in the liver and it is one of the most sensitive indicators of an acute phase reaction (increases in levels can be detected within 12 to 48 h), its levels in blood can be used to screen for many structural diseases and to monitor inflammatory and autoimmune disorders. CRP value has been widely used as to detect bacterial infection in children and neonatal sepsis [5]. Although various studies have been reported the good sensitivity and specificity of CRP for the diagnosis of various inflammatory conditions in ICU patients, definitive diagnosis would require correlation with other laboratory tests such as WBC total and differential count, culture, etc. This present study was aimed to analyze the different values of CRP in correlation with WBC count and blood culture in selected patients.

## Materials and Methods

This is a retrospective study comprising data analysis of laboratory samples of more than 190 pediatric patients up to 1 year in tertiary care teaching institute over a period of 6 months. All the samples received from pediatric unit aged up to 1 year, were subject to consideration for analysis. Among all different tests performed, data CRP were taken for evaluation in this study. Study results were compared with CBC result of same population along with blood culture results if it is received from same study subjects in same duration. A detailed history regarding clinical features suggestive of infection and other relevant complaints was obtained from the mother / guardian. Demographic details of the pediatric patients were recorded. Different samples were received for CRP, WBC, and blood culture testing. Sufficient blood samples were received in plain and EDTA tube for CRP and WBC study respectively. Sample was centrifuged and after serum separation, testing of CRP was carried out as per manufacturer's instructions. This test was done by using diagnostic kit for *in-vitro* detection of CRP in human serum by the rapid slide latex agglutination qualitative and quantitative method supplied commercially. A value of 0.6mg/dl was considered cut off value and above this value test was considered positive and titre value was measured then after. Data result of WBC count was also retrieved from hematology laboratory for comparison. Total of 57 samples were received for blood culture testing. CRP values of those samples were also included in this study. 3-5 cc of venous blood was collected by aseptic method for blood culture in BHI broth and incubated at 37°C for 7 days. Broth was inspected for any turbidity and hemolysis every day in sub cultures (nutrient agar, MacConkey agar and blood agar) were made on alternative day up to growth detected or till 7 days of incubation.[6] All the data was recorded and analysed.

## Results

This study was carried out in microbiology laboratory in tertiary care teaching hospital in Mehsana district. All the samples received in this laboratory in satisfactory condition from pediatric unit were subject to analysis. Age group below one year, were included in study and data of CRP value of these patients were recorded and analyzed. Total of 57 blood culture samples were also received in the same duration from this study group which were also subject to analysis and included in study data. Data of WBC count were also retrieved from cytology laboratory of the same study group and compared accordingly. Tabular representation of the study data is displayed in this article. [Table-1] represents the distribution of total and positive samples in this study. It shows that out of total samples received 46 samples shows positive CRP test which means value of CRP level was > 0.6mg/dl. 24.08% of total samples were positive and mean CRP value recorded among these positive samples, was 8.03mg/dl.

Table-1 Distribution of Total and positive samples

| Total samples | Positive samples | Percentage (%) | Mean CRP value in positive samples |
|---------------|------------------|----------------|------------------------------------|
| 191           | 46               | 24.08          | 8.03 mg/dl                         |

Different demographic variables were recorded and displayed in [Table-2]. Out of total study population, 102 were male and 89 were female. Out of 102 male patients 26 were positive for CRP and out of 89 female patients 20 were positive for CRP test which showed 25.49% and 22.47% positive ratio respectively. Majority of the study populations were below 1 month of age among them 98 were less than 7 days and 62 were between 8-30 days of age group. Remaining 31 patients were having age between 1 month to 1 year. In 0-7 days age group 21 samples were positive from 98 samples while in 8-30 days of age group total of 28 samples were positive among 62 samples. Both these age group showed 21.42% and 29.03% positivity ratio respectively. Age group of 1 month- 1 years showed 22.58 % positive ration which means out of total 31 samples, 7 were positive for CRP test.

Table-2 Demographic variables in study populations

| Study Variable  | Total | Positive | Percentage (%) |
|-----------------|-------|----------|----------------|
| Sex             |       |          |                |
| Male            | 102   | 26       | 25.49%         |
| Female          | 89    | 20       | 22.47%         |
| Age group       |       |          |                |
| 0-7 days        | 98    | 21       | 21.42%         |
| 8-30 days       | 62    | 18       | 29.03%         |
| 1 month- 1 year | 31    | 7        | 22.58%         |

[Table-3] shows ranges of CRP value among positive samples. Total of 22 samples were having CRP value in the range of 0.6 mg/dl to 4.8 mg/dl. Then after total of 15 samples were having CRP value in the range of 4.8 mg/dl to 19.2 mg/dl. A total of 9 samples were having high CRP value above 19.2 mg/dl.

Table-3 CRP values among positive samples.

| S. N. | CRP value range    | No of samples | Percentage (%) |
|-------|--------------------|---------------|----------------|
| 1     | 0.6 to 4.8 mg/dl   | 22            | 47.83          |
| 2     | >4.8 to 19.2 mg/dl | 15            | 32.61          |
| 3     | >19.2 mg/dl        | 9             | 19.56          |

[Table-4] represents the correlation of CRP value with WBC count in study population. Out of total 46 positive samples, 11 having normal WBC count while 19 and 16 showed leukopenia and leukocytosis respectively. While out of total 145 negative samples, 102 were normal WBC value, 17 showed leukopenia and 26 showed leukocytosis.

Table-4 correlation of CRP test result with WBC count in study population

| CRP value | WBC count |            |              |
|-----------|-----------|------------|--------------|
|           | Normal    | Leukopenia | Leukocytosis |
| Normal    | 102       | 17         | 26           |
| Positive  | 11        | 19         | 16           |

[Table-5] and [Table-6] shows the result of blood culture test among the study group. A total of 57 samples were received from pediatric unit. CRP test result has been compared with these blood culture results in [Table-5]. Among the 57 blood

culture samples, 23 showed growth of bacterial isolates. Among these 23 samples 4 were having negative CRP test while 19 were showed positive CRP test. Among the negative blood culture, 20 were positive and 14 were negative for CRP test. [Table-6] represents the details of bacterial isolates in this study. Of these 19 were showed growth of gram negative organisms. Different gram negative bacteria isolated were *E. Coli* (9), *Klebsiella* spp.(6) and *Acinetobacter* spp.(4). Out 23 positive isolates 4 were gram positive organisms all were *Staphylococcus aureus*.

Table-5 Details of Blood culture result in study group.

| Blood culture result | CRP value |      | Total |
|----------------------|-----------|------|-------|
|                      | Normal    | High |       |
| Positive             | 4         | 19   | 23    |
| Negative             | 14        | 20   | 34    |

Table-6 Bacteriological profile in culture positive cases.

| SN                      | Microbial isolate            | Nos | Percentage % |
|-------------------------|------------------------------|-----|--------------|
| Gram negative organisms |                              |     |              |
| 1                       | <i>E. Coli</i>               | 9   | 39.13%       |
| 2                       | <i>Klebsiella</i> spp.       | 6   | 26.08%       |
| 3                       | <i>Acinetobacter</i> spp.    | 4   | 17.39%       |
| Gram Positive organisms |                              |     |              |
| 1                       | <i>Staphylococcus aureus</i> | 4   | 17.39%       |
| Total                   |                              |     | 23           |

## Discussion

This retrospective study was carried out in tertiary care teaching hospital in Mehsana district, Gujarat over a period of 6 months. Primary objective of this study to carry analysis of CRP values of different samples received in Microbiology laboratory from pediatric unit and also correlate the data result with results of WBC and blood culture testing. Many of these types of study with same objective have been carried out previously across the world as CRP still stands for one of the most sensitive indicators of infection and inflammations in early phases of illness. [7-11] In the present study, test results of total 191 samples for CRP test has been evaluated so far. Out of them 46 samples(24.08%) were having CRP values higher than 0.6 mg/dl which is similar to earlier study of deepali, et al.[8] In the context of demographic variables, male and female proportions were having minor difference in terms of positivity ratio. Also highest samples received in this study were less than 7 days old neonates which were 98 in number. After then 8-30 days age group having 62 nos. and 1 month to 1 year age group having 31 nos. of samples. Positivity ratio was highest in 8-30 days of age group which was 29.03% followed by almost same positivity ration for both remaining age group which was 21.42% for early neonates and 22.58% for up to 1 year age group. CRP values of study group ranges from 0.6 mg/dl to >19.2 mg/dl. Mean CRP value for this study in positive samples was 8.03 mg/dl. Among 46 positive samples, highest no.(22) of samples were having CRP value in the range of 0.6 to 4.8mg/dl followed by 15 and 9 samples having range of >4.8 to 19.2 mg/dl and >19.2 mg/dl respectively. Values of CRP were also correlated with results of WBC count of the same study group. It showed that out of 46 positive samples 11 were having normal WBC count, 19 were having low WBC count and 16 were having leukocytosis in laboratory results. Similar kind of study earlier showed that leukopenia and leukocytosis was associated with neonatal sepsis rather than normal WBC count [9,12]. Among this study group total of 57 blood culture samples were received in microbiology laboratory. Results of these samples were also included in this article to increase the scope of this article. Out of 57 samples 23 showed growth of pathogenic organisms of which highest number of isolates were *E.coli* (9) followed by *Klebsiella* spp.(6) and *Acinetobacter* (4) and *Staphylococcus aureus* (4). Among all these 23 positive samples, 19 were having high CRP value while only 4 samples were having CRP value in normal range. Out of 34 culture negative samples, 20 having high CRP value while 14 were having CRP value in normal range. In our hospital setup, CRP is prescribed routinely on pediatric patients presenting with clinical features suggestive of acute infection as a baseline test for infections. Currently it is best known that CRP values may rise in many reasons of inflammatory aitiology as well. Though it's widely considered as a primitive tool for early indicators of infection particularly in pediatric age group.

## Conclusion

From this study it is concluded that serum CRP level measurement is very sensitive tool to detect early infective or inflammatory changes in patients. But instead of prescribing as single tool of identification of infection, correlation with other laboratory test such as WBC study and bacteriological culture is always recommended.

**Application of research:** Study provides early indications of infection, but also serial measurement may be used as prognostic indicator also so that response to measurement can be assessed. This study is applied for analysis of day to day cases of pediatric patients admitted because of infective conditions.

**Research Category:** Medical microbiology

**Abbreviations:** CRP: C- reactive protein, ICU- Intensive care unit

**Acknowledgement / Funding:** Authors are thankful to GMERS Medical College, Vadnagar, 384355, Hemchandracharya North Gujarat University, Patan, 384265, Gujarat, India

**\*Research Guide or Chairperson of research: Dr Purav Patel**

University: Hemchandracharya North Gujarat University, Patan, 384265

Research project name or number: Clinical case study

**Author Contributions:** All authors equally contributed

**Author statement:** All authors read, reviewed, agreed and approved the final manuscript. Note-All authors agreed that- Written informed consent was obtained from all participants prior to publish / enrolment

**Study area / Sample Collection:** Pediatric unit, Gujarat University, Ahmedabad, 380 009, Gujarat

**Conflict of Interest:** None declared

**Ethical approval:** Ethical approval taken from GMERS Medical College, Vadnagar, 384355, Hemchandracharya North Gujarat University, Patan, 384265, Gujarat, India.

Ethical Committee Approval Number: Nil

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