



ORIGINAL RESEARCH PAPER

Clinical Research

A CORRELATION OF C-REACTIVE PROTEIN AND FEVER OF UNKNOWN ORIGIN

KEY WORDS: Fever of unknown origin, CRP, ESR, Serious bacterial infection (SBI)

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ABSTRACT

INTRODUCTION: Fever without focus is termed when there is fever without localizing symptoms or signs, usually acute in onset and persists for less than one week. It is more common in children less than 36 months of age. C reactive protein level increases within hours of acute injury or onset of inflammation and reaches peak within 24 to 48 hours. CRP is elevated in all bacterial infections in acute stages
MATERIALS AND METHODS: A prospective hospital based descriptive study conducted between June 2018 and July 2019 in a tertiary care centre in South India with 76 children under 3 months of age included in the study. Investigations done predominantly included CBP with ESR & ANC, CRP, urine analysis, blood and urine cultures, chest radiograph.
RESULTS: CRP was a better indicator of serious bacterial infection (SBI) when compared to ESR and Leucocytosis when various predictive indicators like sensitivity, specificity, positive predictive value, negative predictive value were compared.
CONCLUSION: Semiquantitative CRP is useful in predicting occult serious bacterial infection (SBI) in children between 1 month to 36 months. CRP can also be considered a better predictive test than total white blood cell count and erythrocyte sedimentation rate.

INTRODUCTION:

Fever is a common manifestation of infectious diseases but is not predictive of severity⁽¹⁾. Most febrile episodes in a normal host can be diagnosed by a careful history and physical examination and require few if any laboratory tests⁽²⁾. Fever without focus is termed when there is fever without localizing symptoms or signs, usually acute in onset and persists for less than one week⁽¹⁾. It is more common in children less than 36 months of age. Fever in children in whom the cause could not be isolated even after 3 weeks of outpatient evaluation or 1 week of evaluation in hospital is called Fever of Unknown Origin⁽¹⁾. Approximately 20% to 30% of the children may have no identifiable cause of fever after history and physical examination⁽³⁾. Although most of these children will have a benign viral illness, children less than 3 years of age are at increased risk of clinically undetectable serious bacterial infection (SBI). These routinely include conditions like occult bacteremia (OB), UTI, occult bacterial pneumonia⁽⁴⁾. The not very common causes include infections such as bone and joint infection, meningitis, soft tissue infection or bacterial enteritis⁽⁵⁾.

C reactive protein was identified by Tilet and Francis in the year 1930. It is isolated from the plasma of patients with pneumonia. It was named because of its ability to bind and precipitate C polysaccharide of pneumococcus. It is synthesized by the liver and is present in trace amounts in serum (<0.3mg/dl)⁽⁶⁾. Its level increases within hours of acute injury or onset of inflammation and reaches peak within 24 to 48 hours. CRP is elevated in all bacterial infections in acute stages⁽⁷⁾. The kinetics of CRP metabolism seem to closely parallel the degree of injury and repair, there by supporting its value as an acute measure of disease activity. CRP has high positive predictive value, negative predictive value, sensitivity and specificity⁽⁸⁾.

MATERIALS AND METHODS:

STUDY DESIGN: A prospective Study of the evaluation of a diagnostic test (CRP)

STUDY PLACE: A tertiary health care centre in South India

STUDY PERIOD: June 2018 to July 2019

STUDY POPULATION: 76 children aged under 36 months

Inclusion criteria:

- a) Children aged 1-36 months
- b) Fever more than 12 hours up to 7 days⁽¹⁾
- c) Without obvious focus of infection on clinical examination.

Exclusion Criteria :

- a) Children who have received prior antibiotics and vaccines.
- b) Children with underlying immunological disease.

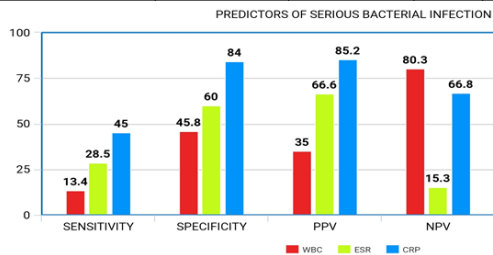
Children in the age group of 1-36 months presenting to the outpatient department and in the pediatric ward were screened for an axillary or rectal temperature of >102.2°C and who satisfied inclusion criteria were included in the study. Informed consent was obtained from parents or guardian. Investigations done predominantly included CBP with ESR & ANC, CRP, urine analysis, blood and urine cultures, chest radiograph. CSF analysis was done when necessary. A total of 76 patients were studied. Sensitivity, specificity, positive predictive value and negative predictive value of each of the predictors of SBI were determined at the cut off points.

RESULTS:

TEST	SBI positive	SBI negative	total
WBC			
WBC >15000	7	13	20
WBC <15000	11	45	56
TOTAL	18	58	76
ESR			
ESR >15 mm/1st hr	16	8	24
ESR < 15 mm/1st hr	12	40	52
TOTAL	20	56	76
CRP			
CRP => 6 mg/dl	15	4	19
CRP < 6 mg/dl	21	36	57
TOTAL	36	30	76

The table above denotes the various parameters studied and their comparison

	SENSITIVITY	SPECIFICITY	PPV	NPV
WBC >15000	13.4%	45.8%	35%	80.3%
ESR >5 mm/1st hr	28.5%	60.0%	66.6%	15.3%
CRP => 6 mg/dl	45.0%	84.0%	86.2%	66.8%



The above graphs shows the percentage of various predictors in comparison

WBC ≥15000 was observed in 7 children who had SBI giving rise to a sensitivity of 13.4%, 45 children who did not have SBI had WBC <15000 giving a specificity of 45.8%. Among the 21 children with WBC more than 15000 only 7 had SBI giving PPV of 35%. Among 118 children of WBC <15000, 45 cases did not have SBI giving a NPV of 80.3%.

ESR ≥ 15mm was observed in 16 cases of children who had SBI giving rise to sensitivity of 28.5%, 40 children who did not have SBI have ESR<15mm giving a specificity of 60%. Among 24 children with ESR more than 15mm 16 cases had SBI giving PPV of 66.6%. Among 42 children, 12 of the children with ESR<15mm did not have SBI giving a NPV of 15.3%.

CRP≥6mg/dl was observed in 15 cases of children who had SBI giving rise to sensitivity of 45.0%, 4 children who did not have SBI have CRP<6mg/dl giving a specificity of 84.0%. Among 19 children with CRP more than 6mg/dl 15 had SBI giving PPV of 85.2%. Among 57 children with CRP <6mg/dl 36 did not have SBI giving a NPV of 66.8%.

When fever was more 24 hours duration CRP was positive in 22% cases when compared 71% across CRP negative. However, duration of fever is insignificant. Among age more than 12 months 20% cases were CRP positive, when compared to 72 (80%) across CRP negative.

DISCUSSION:

The management of febrile young children without apparent source of infection remains controversial. Occult bacteremia, urinary tract infection and pneumonia are considered as serious bacterial infection in children(SBI). Because majority of febrile young children do not have SBI, laboratory tests and expectant antibiotic therapy of these children adds to cost, time, discomfort, parental anxiety and may contribute to antibiotic resistance. Recent prospective studies of febrile young children have found CRP to be a more sensitive and specific predictor of serious bacterial infection compared to WBC counts⁽⁹⁾. C reactive protein is a classic acute phase reactant. It is a serum protein which is synthesized in the liver. CRP levels are increased in the serum as a result of infection and inflammation. CRP estimation is a rapid diagnostic test. As CRP is easily available, less expensive, less time consuming and a better laboratory test in delineating children with and without SBI⁽¹⁰⁾, this study was conducted. The diagnostic utility of semiquantitative CRP is evaluated in this study.

CRP concentration is dependent on the duration of fever⁽¹¹⁾, suggesting that CRP is more reliable as an indicator of bacterial infection if fever has been present for more than 24hours⁽¹²⁾. However, significant number of cases were also negative for CRP in this study. CRP is one of the early marker for sepsis⁽¹³⁾. CRP concentration measured from blood is a

readily available⁽¹⁴⁾ inexpensive test. With recent availability of rapid CRP tests we can readily use in emergency settings⁽¹⁵⁾. CRP may become valuable diagnostic tool in the initial evaluation of febrile young children for occult serious bacterial infection and determine which children need additional diagnostic tests and antibiotic therapy.

CONCLUSION:

Semiquantitative CRP is useful in predicting occult serious bacterial infection (SBI) in children between 1 month to 36 months. CRP can also be considered a better predictive test than total white blood cell count and erythrocyte sedimentation rate.

CONFLICT OF INTEREST :NONE

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