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USEFULNESS OF CRP AS A DIAGNOSTIC MARKER OF BACTERIAL VERSUS VIRAL ILLNESS IN CHILDREN

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Abstract

Background: Fever is one among the most cause for children ending up in visiting paediatric outpatient department . The most common cause of acute febrile illness is of viral origin. Clinical examination does not always rule out bacterial infection. There is no specific biomarker available to distinguish bacterial from non-bacterial infection, leading to a delay in starting antibiotics which can leads to serious complications. "C-Reactive Protein (CRP) can be a diagnostic tool to estimate the risk of serious bacterial infection (SBI) in febrile children**".** We aimed to identify infectious etiology in children with acute febrile illness using CRP levels.

Objective : To identify infectious etiology in children with acute febrile illness using CRP levels To determine usefulness of CRP for early initiation of antibiotics.

Materials and Methods: Data were collected from medical records of 250 children admitted at a tertiary care hospital. Children aged from 1month to 18 years who were admitted in the department of pediatrics from March 2022 to February 2023 with diagnosis of fever for evaluation were included . The collected data was analyzed with IBM SPSS 29. Correlation between CRP and total count, neutrophil, lymphocyte count, Pearson's correlation was used. Chi- square test was used to find the association between CRP and laboratory parameters The p-value <0.005 was considered as significant.

Results :We found those children diagnosed with bacterial infection were found to have elevated total counts and CRP was highly reactive .We found that there was positive correlation between reactive CRP and Total count (R^2 =0.102), Neutrophil(R^2=0.008) and negative correlation between reactive CRP and Lymphocytes (R^2=0.124).**Conclusion :** Most of the children admitted with Acute febrile illness had self-limited course without any evidence of SBI. CRP values were greater than 50 mg/L in most of the children with bacterial etiology and CRP values was nonreactive in children with viral etiology . Highly reactive CRP values with leukocytosis and neutrophilic predominance points to likelihood of bacterial etiology and this can guide appropriate management with antibiotics in children with acute febrile illness.

Keywords: Fever, C- reactive protein, pediatric age

Introduction :

One of the most prevalent diagnoses among paediatric patients under the age of five is fever without source (FWS).[1] In 30% of children , diagnosis is the main principal aim in identifying serious infection .[2-4] "Worldwide rates of severe bacterial illness have dramatically declined after the introduction of specialized vaccinations against Haemophilus influenzae *type b* and Streptococcus pneumoniae at the beginning of the century."[4-9] But this illness still raises questions, particularly for medical professionals and parents. Regarding the diagnosis and care of people with FWS, opinion differ. The utilization of invasive procedures, such as blood cultures and cerebrospinal fluid (CSF), typically causes discomfort in the patients.[10,11] In clinical practice, Fever of unknown origin(FUO) is difficult to manage and patient who consult with FUO are frequently prescribed antibiotics and unhelpful over the counter laboratory investigations. To diagnose FUO, there is no significant "gold standard" investigation.[11] Even in tropical countries where epidemiological characterization of fever in children is not exactly described .[12] Epidemiological data of the locality could be helpful in enhancing screening techniques, especially in low-resource settings where a lack of knowledge hinders the development of health policies.[13] Most of the children visiting paediatric clinic with acute febrile illness is of viral origin.[14] The clinical examination does not always rule out bacterial infection.[15] There is no specific biomarker available to distinguish bacterial from non-bacterial infection, leading to a delay in starting antibiotics which can leads to serious complications. Many biomarkers like CRP, Serum Ferritin, Procalcitonin, and Lactate helps in diagnosis of bacterial infection. "C-Reactive Protein is an acute phase reactant synthesized by liver is used as an marker of inflammation" In our study CRP is used as an marker to predict whether the etiological cause for acute febrile illness is bacterial or viral.[16] "CRP can be a diagnostic tool to estimate the risk of serious bacterial infection (SBI) in febrile children".

Objectives of the study:

1) To identify infectious etiology in children with acute febrile illness using CRP levels.

2) To determine CRP as an indicator for early initiation of antibiotics.

Methodology :

This is an observational study undertaken in the Department of Paediatrics at a tertiary care hospital, Chettinad Hospital and Research Institute for a period of 1 year from March 2022 to February 2023. The study design was approved by the institutional board of ethics (Ref no:IHEC-I/1760/23).

Data was collected from medical records of 250 children who were admitted at tertiary care hospital. The data included children aged from 1month to 18 years who were admitted in the department of pediatrics from March 2022 to February 2023 with diagnosis of fever for evaluation. The following details were obtained such as Sociodemographic details, clinical history at the time of initial presentation (initial diagnosis), duration of hospital stay, laboratory findings "Complete blood cell count, CRP, Urine routine, Blood culture, urine culture, throat culture, swab culture, CSF culture and serology" and Treatment details (Choice of antibiotics , Duration of antibiotics) and Final diagnosis of the study participants. The collected data was analyzed with IBM SPSS 29. Descriptive statistics (frequency and percentage) was used for categorical variables and mean and SD was used for continuous variable. To assess the relationship between the CRP and total count, neutrophil, lymphocyte count, Pearson's correlation was used. "Chi- square test was used to find the association between CRP with total leukocyte count , neutrophils , lymphocytes , serology and diagnosis based on body fluid cultures . The p-value <0.005 was taken as significant.

Results :

The outcome of the study was to identify the etiology of fever in children and relationship of CRP with blood investigations and with positive cultures. This study explored the sociodemographic, clinical, lab parameters, association of CRP with blood count, culture findings among study participants who had fever and admitted in the pediatric ward. It also took forward whether to start antibiotics or not accordingly.

Table 1: Sociodemographic characteristics among study participants N=250

Age groups		Frequency	Percent
	Upto 2 yrs	86	34.4

	3 - 5 yrs	70	28.0
	6 - 10 yrs	46	18.4
	Above 10 yrs	48	19.2
Gender		Frequency	Percent
	Female	93	37.2
	Male	157	62.8

Table 1 outlines demographic characteristics of the study group. Among the study participants, 34.4% were children with age upto 2 years , 28 % between 3-5 years and 37.6 % were more than 6 years . Among them majority were male children (62.8%) and females 37.2 %.

Table 2: Distribution of Blood count and CRP value of the study participants N=250

Laboratory parameters (CBC)		**Frequency**	**Percent**
Total count		N	%
	< 4000	32	12.8
	4000 - 11000	124	49.6
	11001 - 20000	76	30.4
	> 20000	18	7.2
Neutrophils			
	< 40	66	26.4
	40 - 60	72	28.8
	> 60	112	44.8
CRP			
	Reactive	175	70.0
	Non- Reactive	75	30.0

Table 2 Describes various laboratory investigation done among the study participants, of which 12.8% of them had total count <4000 , 49.6% in the range between 4000 and 11000, 37.6 % more than 11000 . 44.8% of neutrophilic predominance with values above 60% had reactive CRP values . Lymphocyte predominance was about 34.4% and CRP non reactive .Among 250 children , CRP value was reactive among 175 (75%) study participants who presented with fever and in 25 % CRP was non reactive . This showed that majority of the study participants had raised CRP value.

Table 3 : Distribution of etiology of acute febrile children and comparison with CRP

			CRP		
			Reactive	Non reactive	Total
Diagnosis	Bacterial	Count	122	14	136
		%	69.7%	18.7%	54.4%
	Viral	Count	53	61	114
		%	30.3%	81.3%	45.6%
Total		Count	175	75	250
		%	100.0%	100.0%	100.0%

Among 250 children admitted 136 had fever of bacterial etiology , among them 69% CRP was reactive and 18.7 % CRP was non reactive and 175 children had fever due to viral etiology with CRP was 81.3% were non reactive and 30.3 was reactive .

Elevated Total count had significant (p=0.005) and has positive correlation with reactive CRP.The neutrophil count (P value - 0.005) and The lymphocyte did not have significant association with reactive CRP value.

We found that there was positive correlation between reactive CRP and Total count (R^2 =0.102), Neutrophil(R^2=0.008). “There was negative correlation between reactive CRP and Lymphocytes (R^2=0.124)”. (Figure 1,2 and 3)

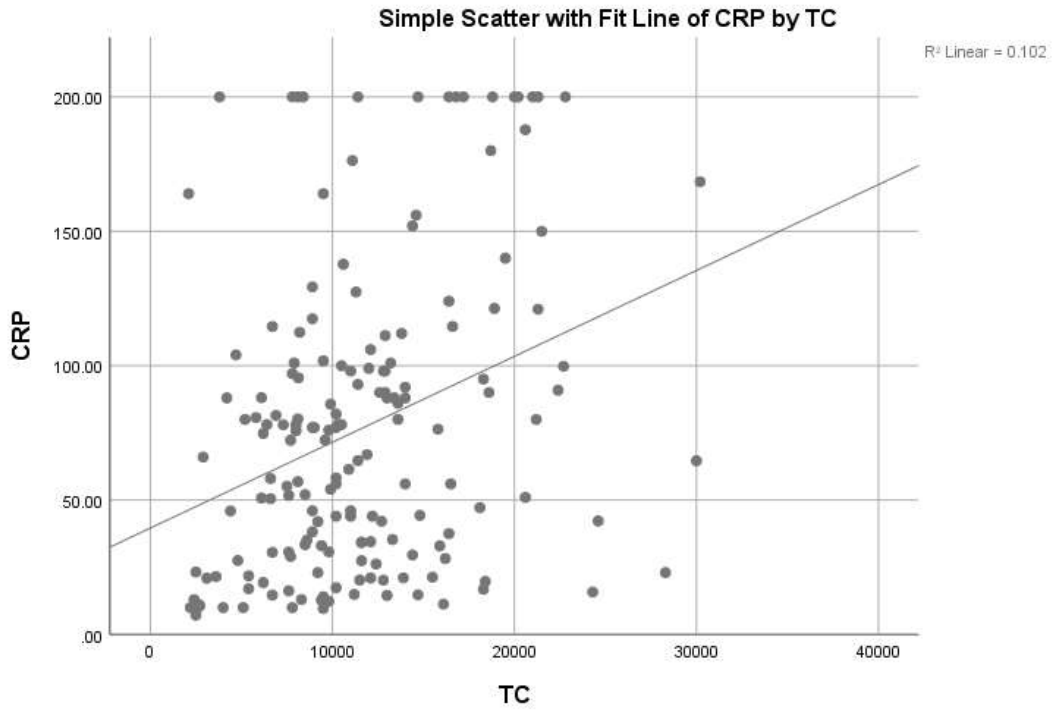

Figure 1: Scatter plot between CRP and Total count of the study participants

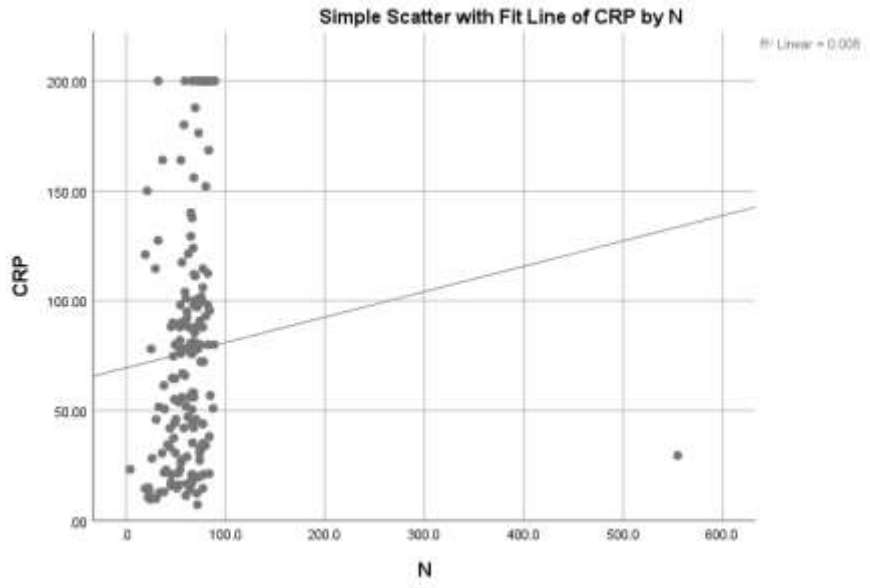

Figure 2: Scatter plot between CRP and Neutrophil among study participants

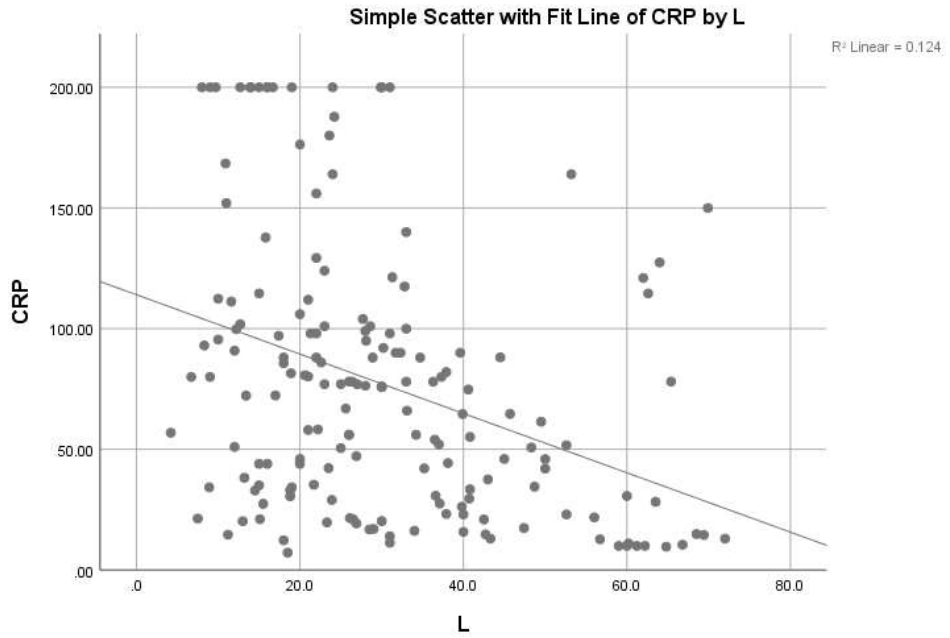

Figure 3: Scatter plot showing association between CRP and Lymphocyte count of the study participants

Various culture reports among study participants:

Blood culture done among 176 participants showed no significant growth (90%), 2.2% grew Salmonella typhi , 1.7% grew pseudomonas and less than 1 % grew other organisms such as Acinetobacter , Methicillin resistant staphylococcus aureus ,

The urine culture report among study participants found that majority of them didn't have any significant growth (48.4%), followed by 8% of Escherichia coli , 2.4% of Enterococcus and 1.2% of klebsiella. Less than 1 % were other organisms such as candida, proteus vulgaris, proteus mirabilis and pseudomonas.

The throat swab investigation done among 29 participants resulted in no growth (20.6%), COVID Negative (13.8%), H1N1 (6.9%). Other organisms such as Group A Beta hemolytic streptococcus, Klebsiella found less than 1% .

Discussion :

Our study illustrates the prevalence of SBI in vaccinated children where 41 out of 136 infants (29%) had SBI and the prevalence of this study was similar to a Latin study with slightly higher cases reported among developed countries.[5,15,16] About 45% of children had viral etiology with self -limiting course and without complications . "The most common cause among bacterial cause was urinary tract infection and "Escherichia coli" was the most frequent etiologic agent about 8% among of the cases".[17-19] This result emphasises the need, irrespective of clinical condition or medical history, to screen all FWS patients for UTI as it is the most common cause of infection in children.

In this study, of the biochemical and clinical markers studied , CRP was reactive in most of the children with bacterial etiology and levels were greater than 100 mg/L in most of the toxic children admitted with SBI . comparing to previous studies this study also showed that elevated CRP levels were associated to SBI.[19-23] In our study we have also studied duration of admission in all children and the approximate duration of antibiotic management was 5 to 7 days among the bacterial infection , in some patients with SBI duration of stay extended upto 10-14 days .[23]

As far as we are aware that any specific symptom , specific sign or biomarker has high specificity for identifying children with FWS , who may or may not have SBI[16,23] Hence SBI is diagnosed by detailed clinical history , physical findings and laboratory findings will guide the treating doctor for any further invasive investigations and to decide on initiation of antibiotic treatment.[21-23] This study emphasis on detailed history taking , basic blood investigations like complete blood count , urine routine , CRP can be used to identify the etiology of FWS is bacterial or viral . In our study, the common bacterial diagnosis among children admitted with FWS was UTI, Pneumonia , Acute pharyngotonsillitis and among viral etiology Bronchiolitis , dengue fever and lower respiratory infection secondary to influenza ,adenovirus .

Conclusion :

Most of the children admitted with Acute febrile illness had self-limited course without any evidence of SBI. "C-reactive protein levels greater than 50 mg/L in most of the children with

bacterial etiology and CRP values was nonreactive or reactive with levels < 50mg/L in children with viral etiology" . Highly reactive CRP values with leukocytosis and neutrophilic predominance points to likelihood of bacterial etiology and this can guide appropriate management with antibiotics.

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