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Original Research Article

Assessing the Diagnostic Utility of C- Reactive Protein (CRP) in Combination with Hematological Parameters of CBC in Detection Infections In Children

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Abstract

Aim: The aim of this study was to determine the diagnostic utility of C- reactive protein (CRP) in combination with hematological parameters of CBC as early diagnostic marker in detection infections in children.

Methods: The present study was a hospital based cross-sectional study which was carried out among the Children who presented to the Paediatric OPD or Inpatients attending Skmch, Muzaffarpur, Bihar, India. All the Children who presented to paediatric OPD or admitted to Paediatric ward with history suggestive of Infection were included in the study. The study included 500 children attending pediatric OPD / Inpatients.

Results: The study included 500 children attending pediatric OPD / Inpatients whose age ranged from birth to 17 years. Majority of the children 390 (78%) belonged to Under 5 age group. Out of 500, 275 (55%) were boys and 225 (45%) were girls. All the children underwent Widal test and 100 out of 500 were positive for it. The mean difference of all the components of Complete Blood Count was compared between Widal positive and negative children. It was observed that, there was mean difference observed between the groups of Widal positive children and Widal negative children for all the components of the Complete Blood Count and it was statistically significant for Packed Cell Volume, Eosinophil Count and Platelet Count. All the children blood sample was subjected to CRP testing and 180 out of 500 were positive for it. The mean difference of all the components of Complete Blood Count was compared between CRP positive and negative children.

Conclusion: In conclusion, the findings of the present study confirm that the serum levels of CRP in combination with WBC counts and other hematological parameters are better indicators of infection in the early diagnosis of sepsis in childhood than isolated use of CBC and it also aids in the evaluation of the response of the disease to the antibiotic therapy.

Keywords: Sepsis, CRP, CBC, Children.

Introduction

Fever in children is one of the most common reasons for parents to seek medical care which accounts to approximately 20% of all the cases in Pediatrics. [1] Children may present with fever as an initial/isolated symptom of a yet undifferentiated illness or with localizing signs that suggest an etiology such as pneumonia. A majority of children with fever without localizing signs will have a viral etiology which does not warrant laboratory evaluation and can often be managed with instructions for ensuring adequate hydration and use of antipyretics. [2] In one study it is estimated that up to 10% of febrile children, especially those 3 months of age and younger will have bacterial illnesses in the form of occult bacteremia, septicemia, bacterial meningitis, pneumonia, UTI, bacterial gastroenteritis, osteomyelitis, septic arthritis, and other general endemic tropical diseases. [3] India is a tropical country with a distinct spectrum of common tropical illnesses particularly seen in post monsoon season such as dengue, rickettsial infections, scrub typhus, malaria (usually due to Plasmodium falciparum), typhoid and leptospirosis. [4] The gold standard for sepsis diagnosis being the culture of microorganisms, which is diagnostic and treatment delay is inevitable. [5,6]

The present trend which is being applied for all the neonates who are suspected to have neonatal sepsis may lead to unnecessary and increased antibiotic consumption, a higher incidence of the side-effects due to their use, increased resistance to the antibiotics, a long hospitalization, the separation of the neonates from their mothers and increased health costs. C-Reactive Protein (CRP) is an acute phase protein primarily synthesized in the liver. [7] In response to an inflammatory stimulus, the CRP levels rise up to 50,000 times above normal, typically within 6 hrs and peak at 48 hours. [8] CRP is known to activate the classical complement cascade, stimulates phagocytic cells for phagocytosis. [9] In any infection, CRP secretion is induced by pro-inflammatory cytokines that are secreted by host mononuclear cells. [10] Though the primary function of CRP is conjugating pathogens and inducing their destruction by host complement system [11], its sustained release can also have adverse effects. [12,13] It is postulated that prolonged increased CRP levels could contribute to an imbalance in inflammatory response leading to a reduced control of parasitemia. [14,15]

The aim of this study was to determine the diagnostic utility of C- reactive protein (CRP) in combination with hematological parameters of CBC as early diagnostic marker in detection infections in children.

Materials and Methods

The present study was a Hospital based cross-sectional study which was carried out among the Children who presented to the Paediatric OPD or Inpatients attending Skmch, Muzaffarpur, Bihar, India. All the Children who presented to paediatric OPD or admitted to Paediatric ward with history suggestive of Infection were included in the study. The study included 500 children attending pediatric OPD / Inpatients.

Inclusion criteria

- 0 to 19 years age of either sex
- High suspicion of Infection in the Child by Clinician

Exclusion criteria

- Seriously ill Children
- Children already started on Antibiotics
- Not willing to take part

Study tool and variables: A pretested semi-structured questionnaire which included socio-demographic details, duration and type of illness and clinical features. Venous blood was drawn from all the children fulfilling Inclusion Criteria at the time of admission or at the time of Outpatient consultation.

Specimens and tests which were performed: The specimens of blood were obtained from each child prior to the commencement of the antibiotics for the sepsis work up, which included hematological parameters like the hemoglobin, total leukocyte count, packed cell volume, monocyte, neutrophil and eosinophil count, platelet count and red blood count. All the blood samples were simultaneously subjected to C-reactive protein (CRP) estimation and Widal test and the test results were obtained from the Laboratory.

Statistical analyses: Data were entered in Excel and analysis was done using SPSS version 22. Descriptive statistics were represented as frequencies, percentages, mean and standard deviation. Anova was used to find the difference between the groups.p value was considered statistically significant if it was less than 0.05.

Ethical considerations: A written informed consent was obtained from all the study participants. All the collected information was kept confidential, and is being used for research purpose only.

Results

Table 1: Distribution of children as per the Age Group

Age	Number	Percentage
< 1 year	20	4
1 – 5 year	370	74
6 – 10 year	100	20
11 – 17 year	10	2
Gender		
Male	275	55
Female	225	45

The study included 500 children attending pediatric OPD / Inpatients whose age ranged from birth to 17 years. Majority of the children 390 (78%) belonged to Under 5 age group. Out of 500, 275 (55%) were boys and 225 (45%) were girls.

Table 2: Descriptive statistics of the continuous variables used in the study

Variables	Minimum	Maximum	Mean	Std. Deviation
Age (in Years)	< 1	17	4.12	2.73
HB% (gm %)	6.90	16.80	12.09	1.31
PCV	25.10	47.20	36.42	3.15
TLC (thousands/dl)	1.14	36.80	9.16	5.04
Neutrophils	5	88	52.77	16.51
Lymphocytes	5	91	38.86	16.28
Monocytes	2	63	5.03	2.93
Eosinophils	1	8	3.58	1.16
RBC (million/dl)	3.12	6.90	4.71	0.43
PLT (lakhs/dl)	0.32	9.89	3.20	1.34

The table showed the descriptive statistics ie, Range, Mean and Standard deviation of Age, Hemoglobin, Packed Cell Volume, Total leucocyte count, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Red Blood Cells and Platelet Count. The mean values of all the children were within normal limits.

Table 3: Comparison of Mean and Standard deviation of various Investigations between Widal Positive and Negative Reports

Widal test		HB%	PCV	TLC	N	L	M	E	RBC	PLT
Negative (400)	Mean	12.08	36.11	9.34	53.05	38.50	4.93	3.65	4.70	3.27
	Std. Deviation	1.34	3.14	5.21	16.22	15.94	1.46	1.15	0.42	1.36
Positive (100)	Mean	12.16	37.67	8.42	51.56	40.37	5.45	3.27	4.73	2.92
	Std. Deviation	1.25	2.90	4.21	17.73	17.64	5.98	1.13	0.46	1.26
Total (500)	Mean	12.08	36.42	9.16	52.77	38.86	5.03	3.58	4.71	3.20
	Std. Deviation	1.31	3.154	5.04	16.51	16.28	2.93	1.16	0.43	1.34
*p value		0.580	< 0.001	0.108	0.423	0.310	0.114	0.003	0.60	0.021

All the children underwent Widal test and 100 out of 500 were positive for it. The mean difference of all the components of Complete Blood Count was compared between Widal positive and negative children. It was observed that, there was mean difference observed between the groups of Widal positive children and Widal negative children for all the components of the Complete Blood Count and it was statistically significant for Packed Cell Volume, Eosinophil Count and Platelet Count. So these three components of Complete Blood Count were significant predictors of Typhoid in the study Children.

Table 4: Comparison of Mean and Standard deviation of various Investigations between CRP Positive and Negative Reports

CRP		HB%	PCV	TLC	N	L	M	E	RBC	PLT
Negative (320)	Mean	12.22	36.86	7.71	49.31	42.30	5.10	3.59	4.74	2.97
	Std. Deviation	1.36	3.22	4.06	16.56	16.45	3.58	1.16	0.44	1.18
Positive (180)	Mean	11.85	35.60	11.81	59.07	32.57	4.90	3.54	4.65	3.63
	Std. Deviation	1.18	2.85	5.57	14.48	13.96	0.99	1.15	0.41	1.51
Total (500)	Mean	12.09	36.42	9.16	52.77	38.86	5.03	3.58	4.71	3.20
	Std. Deviation	1.31	3.15	5.04	16.51	16.28	2.93	1.16	0.43	1.34
*p value		0.002	<0.001	<0.001	<0.001	<0.001	0.479	0.652	0.023	<0.001

All the children blood sample was subjected to CRP testing and 180 out of 500 were positive for it. The mean difference of all the components of Complete Blood Count was compared between CRP positive and negative children. It was observed that, there was mean difference observed between the groups of CRP positive children and CRP negative children for all the components of the Complete Blood Count and it was statistically significant for all its components except Monocytes and Eosinophils. So, all the variables were significant predictor of infection in the body.

Discussion

Sepsis is considered as one of the major causes of morbidity and mortality in ICUs. In order to avoid unnecessary treatment, development of multidrug resistance organisms, unwanted prolonged hospitalisation and economic burden, mainly in developing countries with poorly-equipped ICUs, an early, sensitive and specific laboratory test would be helpful. Decision-making based on symptoms of infection is often subjective. As such, detecting an infection or sepsis in hospitalised

patients remains a challenge, and there is a need for reliable biomarkers for this purpose, the acute phase reactants have been used as biomarkers of bacterial sepsis in adults and children. Biomarkers such as PCT, CRP, and ESR are known indicators of bacterial infection. Amongst them, CRP, which is an acute phase reactant produced by the liver has been used widely in many laboratories in diagnosing the onset of sepsis. [16]

Pulliam PN et al., demonstrated that CRP performs better in predicting severe Bacterial Infection in febrile children less than 36 months of age compared to leukocyte and neutrophil count. [17] Andreola B et al., demonstrated that CRP has a superior discriminatory power to total and differential WBC in detecting serious Bacterial Infection in children with fever without a source as it is more sensitive and specific. [18] The same results concerning the CRP and procalcitonin value in evaluating young children with bacterial or viral infection were demonstrated by the study of Olaciregui I et al. [19] In a recent study Kossiva L et al., evaluated the parameters complete blood count in combination with CRP and ESR to distinguish the presence from the absence of infection. [20] In the current study, CRP has a better discriminatory power with higher sensitivity and specificity as compared to WBC. In this study, a strong inverse relationship between increased CRP levels and decreased hemoglobin and RBC levels was observed.

As the sensitivity and the specificity of the individual tests may not justify their individual use in newborn infants and children, a significant improvement of diagnostic capability when used in various combinations, has been studied. An above 80% sensitivity by the combination of any 2 or more positive tests in culture positive Early Onset sepsis was also reported earlier from Indian studies. [21] In a study done at tertiary care hospital at Udaipur where both CRP and Hematological parameters were done for all the children, the sensitivity of the hematological screening parameters and CRP varied from 73.03-92.30%. [22] In a study done at Mangaluruto find out the relationship of CRP with Hematological parameters in Malaria Patients, a highly significant positive correlation was found between increase in parasitemia and C-reactive protein levels in P.falciparumand P. vivaxpatients. While a significant positive correlation was observed

between the increased parasitemia (%) and CRP levels, a significant negative correlation was observed between CRP and decreased hemoglobin, RBC, platelets and across various infecting species. [23]

Conclusion

In conclusion, the findings of the present study confirm that the serum levels of CRP in combination with WBC counts and other hematological parameters are better indicators of infection in the early diagnosis of sepsis in childhood than isolated use of CBC and it also aids in the evaluation of the response of the disease to the antibiotic therapy. Hence, the combination of total WBC count along with CRP could be a reliable diagnostic tool to detect the presence of Bacterial Infections in children. Routine ordering of CRP for detection of Bacterial Infection in febrile children is reasonably acceptable but further comparison of the performance of other diagnostic markers will be more meaningful to infer the diagnostic criteria for Bacterial Infection among children.

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