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Original Research Article

A Hospital Based Cross Sectional Observation Study Assessing Diagnostic Utility of CRP and WIDAL Test with Hematological Parameters for Sepsis 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 for nine months. 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

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the 1st month of life. [1] It comprises various systemic infections such as septicemia, pneumonia, meningitis,

arthritis, osteomyelitis, and urinary tract infections. Superficial infections such as oral thrush, conjunctivitis are not included under neonatal sepsis. Blood culture is warranted as gold standard and distinguishes sepsis from noninfectious conditions; it lacks sensitivity and specificity as blood culture may yield false‐positive results because of contamination. Furthermore, it can remain negative despite generalized bacterial infection. There is a substantial time delay as the blood culture result is ready only after 24–72 h. [1]

In the recent days, large proportion of the ICU admissions ending in poor outcomes is impacted largely by pathological conditions like sepsis and septic shock. [2] Sepsis ensues following infection due to deregulated host response to infection leading to uncontrolled inflammation and organ dysfunction and potentially a hypotensive state known as septic shock. [3] In such cases, early diagnosis and appropriate therapy within the first hours of hospital admission plays a major role in improving patient outcome. [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 for nine months. 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 workup, 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	< .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
	SD	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
	SD	1.18	2.85	5.57	14.48	13.96	.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
	SD	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.falciparum and 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. [23,24]

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.

References

1. Kesavan R. Early diagnostic markers for neonatal sepsis: comparing procalcitonin and c-reactive protein with the gold standard culture method (Doctoral dissertation, Madras Medical College, Chennai).
2. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, Moreno R, Lipman J, Gomersall C, Sakr Y, Reinhart K. International study of the prevalence and outcomes of infection in intensive care units. Jama. 2009 Dec 2;302(21):2323-9.

3. Coelho FR, Martins JO. Diagnostic methods in sepsis: the need of speed. Revista da Associação Médica Brasileira (English Edition). 2012 Jul 1;58(4):498-504.
4. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M. Early goal-directed therapy in the treatment of severe sepsis and septic shock. New England journal of medicine. 2001 Nov 8;345(19):1368-77.
5. Garnacho-Montero J, Ortiz-Leyba C, Herrera-Melero I, Aldabo-Pallas T, Cayuela-Dominguez A, Marquez-Vacaro JA, Carbajal-Guerrero J, Garcia-Garmendia JL. Mortality and morbidity attributable to inadequate empirical antimicrobial therapy in patients admitted to the ICU with sepsis: a matched cohort study. Journal of Antimicrobial Chemotherapy. 2008 Feb 1;61(2):436-41.
6. Kumar G, Kumar N, Taneja A, Kaleekal T, Tarima S, McGinley E, Jimenez E, Mohan A, Khan RA, Whittle J, Jacobs E. Nationwide trends of severe sepsis in the 21st century (2000–2007). Chest. 2011 Nov 1;140 (5):1223-31.
7. Ansar W, Ghosh S. C-reactive protein and the biology of disease. Immunol Res. 2013;56(1):131-42.
8. Lima-Junior, J.D.C., Rodrigues-da-Silva, R.N., Pereira, V.A., Storer, F.L., Perce-da-Silva, D.D.S., Fabrino, D.L., Santos, F., Banic, D.M. and Oliveira-Ferreira, J.D., 2012. Cells and mediators of inflammation (C-reactive protein, nitric oxide, platelets and neutrophils) in the acute and convalescent phases of uncomplicated Plasmodium vivax and Plasmodium falciparum infection. Memórias do Instituto Oswaldo Cruz, 107, pp.1035-1041.
9. Dong Q, Wright JR. Expression of C-reactive protein by alveolar macrophages. J Immunol. 1996 Jun 15; 156 (12):4815-20.
10. Harpaz R, Edelman R, Wasserman SS, Levine MM, Davis JR, Sztein MB. Serum cytokine profiles in experimental human malaria. Relationship to protection and disease course after challenge. J Clin Invest. 1992;90 (2):515-23.
11. Chandrashekara S. C-reactive protein: An inflammatory marker with specific role in physiology, pathology, and diagnosis. Internet J Rheumatol Clinic Immunol. 2014 30;2(S1).
12. Gillespie SH, Dow C, Raynes JG, Behrens RH, Chiodini PL, McAdam KP. Measurement of acute phase proteins for assessing severity of Plasmodium falciparum malaria. J Clinic Pathol. 1991;44(3):228-31.
13. Hurt N, Smith T, Tanner M, Mwankusye S, Bordmann G, Weiss NA, et al. Evaluation of Creactive protein and haptoglobin as malaria episode markers in an area of high transmission in Africa. Trans R Soc Trop Med Hyg. 1994;88 (2):182-6.
14. Clark IA, Budd AC, Alleva LM, Cowden WB. Human malarial disease: a consequence of inflammatory cytokine release. Malar J. 2006; 5:85.
15. Utuk Eno-ObongEdet, I.E.E., Udo Jacob Jackson, Okpokowuruk Frances Samuel. Relationship between Serum C-reactive Protein Levels and Severity of Plasmodium falciparum Malaria in Children Seen in South Nigeria. Int J Trop Dis Health, 2014;4(10):1078-1087.
16. Lelubre C, Anselin S, Zouaoui Boudjeltia K, Biston P, Piagnerelli M. Interpretation of C-reactive protein concentrations in critically ill patients. BioMed research international. 2013 Jan 1;2013.
17. Pulliam PN, Attia MW, Cronan KM. C-reactive protein in febrile children 1 to 36 months of age with clinically undetectable serious bacterial infection. Pediat. 2001;108(6):1275-9.
18. Andreola B, Bressan S, Callegaro S, Liverani A, Plebani M, Da Dalt L.

Procalcitonin and C-reactive protein as diagnostic markers of severe bacterial infections in febrile infants and children in the emergency department. Pediatr Infect Dis J. 2007;26 (8): 672-7.
19. Olaciregui I, Hernández U, Muñoz JA, Emparanza JI, Landa JJ. Markers that predict serious bacterial infection in infants under 3 months of age presenting with fever of unknown origin. Arch Dis Child. 2009;94 (7):501-5.
20. Olaciregui I, Hernández U, Muñoz JA, Emparanza JI, Landa JJ. Markers that predict serious bacterial infection in infants under 3 months of age presenting with fever of unknown origin. Arch Dis Child. 2009;94 (7): 501-5.
21. Kossiva L, Gourgiotis DI, Douna B, Marmarinos A, Sdogou T, Tsentidis C. Composite bacterial infection index in the evaluation of bacterial versus viral infection in children: A single centre study. PediatTherapeut. 2014;4(2).
22. Bhat YR, Rao A. The performance of haematological screening parameters and CRP in early onset neonatal infections. J Clinic Diagnos Res. 2010 30;4 (6):3331-6.
23. Abhilasha Garg, Dr Chandan Kr. Agrawal, Dr Narendra Mogra, Pooja Kanwat, Dr AbhaPatni. Haemat ological Parameters in Neonatal Sepsis. J Med Sci Clinic Res 2015; 3(10):8102-8108.
24. Mahgoob, N., & Saber Ali, D. M. Acute Appendicitis Due to Missed Intrauterine Contraceptive Device/A Case Report and Literature Reviews. Journal of Medical Research and Health Sciences, 2022; 5(8): 2177–2181.