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Assessment of Procalcitonin and C-Reactive Protein as a Sepsis Marker in Children

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ABSTRACT

Sepsis is a major cause of morbidity and mortality in children admitted in intensive care unit. Blood culture considered as a gold standard test for diagnosis of sepsis but C-reactive protein (CRP) and procalcitonin (PCT) were the early diagnostic markers of sepsis. The objective of this study is to evaluate the serum CRP and PCT levels as reliable marker of sepsis in children. This cross sectional hospital based study conducted in the department of the paediatrics in a tertiary care hospital, central India. Children <16 years of age with clinically suspected sepsis was enrolled in this study. Patients were divided into two groups. Culture positive confirmed sepsis and culture negative probable sepsis. C.R.P. and P.C.T. level was measured in all the suspected patients. A total of 120 patients were enrolled of which 40 belonged to confirmed culture positive group and 80 were probable sepsis group. The mean age of the confirmed sepsis patients was 4.67±1.35, predominantly male children (60%). Longer duration of ICU stay significantly associated with the sepsis. Staph aureus was the most common isolated recovered from culture positive sepsis patients CRP and PCT levels were significantly higher in culture positive confirmed sepsis children as compared to culture negative probable sepsis children. Both CRP and PCT are highly effective diagnostic and prognostic markers of sepsis but PCT is earlier to rise and more reliable than CRP. Sepsis, CRP, PCT, sepsis markers, children.

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Key Words
Sepsis, C.R.P., P.C.T., sepsis markers, children

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INTRODUCTION

Blood stream infections are the most common cause of morbidity and mortality among children. Sepsis is characterized by generalized systemic inflammation and organ dysfunction leading to hypotension or septic shock. This pathological condition impacting a large proportion of ICU patients and unfortunately have poor outcomes[1,2]. Early diagnosis, identification of the causative organism and prompt starting of appropriate treatment measures are shown to be beneficial effects for reducing sepsis morbidity and mortality[3,4]. Early diagnosis and management of sepsis also decreases the prolong hospital stay ultimately reduces the health care cost burden[5]. Detection of sepsis in children is very difficult in routine practice may be due to vague non specific clinical manifestation and sometimes false culture negative report could be due to antibiotics administration before taking the culture samples[6,7]. Thus, early recognition of blood stream bacterial infections could guide the treatment needed, reduce unnecessary administration of antibiotics and control the development of drug-resistant strains[8]. Blood culture is the most reliable and gold standard test for diagnosing sepsis but time consuming and false-positive results often occur due to contamination or no culture growth[9]. There are several sepsis biomarkers have been investigated, including Procalcitonin (PCT) C-reactive protein (CRP) IL-6 and IL-1. CRP and PCT are considered the best sepsis markers because of they have advantages of short time and high sensitivity[10]. PCT is a pro-peptide of calcitonin, secreted from the C-cells of the thyroid gland and CRP is an acute-phase reactant, synthesized by the liver, mainly in response to injury or infection. The serum PCT is more superior than CRP level because PCT differentiate between bacterial and viral infections unlike CRP, PCT level rise during bacterial infections but are unchanged during viral infections[11]. The combined use of common clinical biomarkers PCT, CRP and IL-6 with others such as WBC, fever, age and gender may increase sensitivity and specificity of these tools for sepsis diagnosis.

Aims and objective: The objective of this study is to evaluate the serum PCT and CRP level as a diagnostic marker of sepsis in children in central India.

MATERIALS AND METHODS

This was a prospective cross sectional study conducted in the department of paediatrics in a tertiary care hospital, central India. All the suspected children of sepsis admitted in our hospital during the study period were enrolled.

Inclusion criteria:

- Children <16 years of age
- Children admitted in PICU
- Children whose parents or their guardian provide consent for the study

Exclusion criteria:

- More than 16 years of age
- Known cases of chronic inflammatory disorder and immunodeficiency
- Those parents or their guardian not provide consent for the study

We have categorized all patients into two groups: confirmed diagnosed cases of sepsis and suspected cases of sepsis.

Confirmed diagnosed cases of sepsis: At least 03 sepsis-related clinical sign or symptoms. More than two positive sepsis-related blood test results and positive blood culture test.

Suspected cases of sepsis: At least 03 sepsis-related clinical sign or symptoms. More than two positive sepsis-related blood test results and negative blood culture test. Detailed history and clinical examination was done in all the patients. Blood sample was collected before the antibiotics given for the laboratory examination. All suspected patients performed following laboratory tests; PCT, CRP, WBC count, ESR and blood culture. Other relevant laboratory tests were also done depending on the patient's symptoms and physical examination. Blood culture was done by automated blood culture system (BACTEC-9050, BD). PCT was measured by enzyme-linked fluorescent assay using PCT kit (Bio Merieux) and CRP levels were measured by immunoturbidimetric analysis using a CRP reagent kit. The reference range of PCT and CRP levels was <0.05 ng mL and <10 mg L respectively. PCT and CRP levels were de ned within 6 hrs of receiving intensive care, with samples for bacterial culture obtained at the same time.

Statistical analysis: Data was tabulated in Microsoft Excel Sheet. SPSS software version 22 was used for

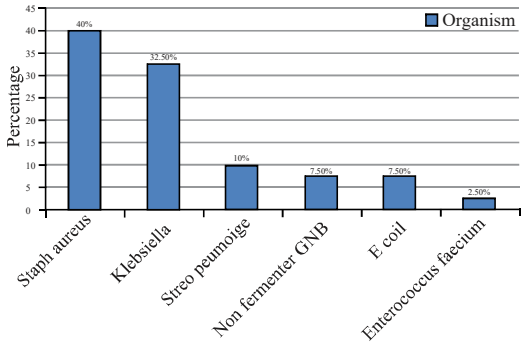

Fig. 1: Organisms isolated from positive blood culture sepsis patients

Table 1: Socio-demographic and clinical variables of confirmed and probable sepsis cases

Socio-demographic variables	Confirmed sepsis cases (n = 40)	Probable sepsis cases (n = 80)	p-value
Age group in years			
Mean age±SD	4.67±1.35	5.24±1.83	0.835
Gender			
Male	23	45	0.896
Female	17	35	
Body temperature			
≥37°C	32	67	0.610
≤ 37°C	8	13	
Residential status			
Rural	24	41	0.364
Urban	16	39	
Duration of illness			
Mean age ±SD	8.2±1.5	7.7±1.8	0.133
Length of ICU stay			
Mean age ±SD	6.8±1.6	5.7±1.3	0.001

Table 2: Comparison of laboratory markers between confirmed sepsis and probable sepsis cases

Laboratory sepsis markers	Confirmed sepsis cases (n = 40)	Probable sepsis cases (n = 80)	p-value
WBC $\times 10^9$ L (Mean±SD)	13,257±6281	11,877±5724	0.230
ESR mm h (Mean±SD)	39.6±30.4	33.7±26.8	0.279
CRP levels mg/l (Mean±SD)	65.14±38.39	25.42±17.23	<0.001
PCT levels ng/ml (Mean±SD)	18.62±11.39	4.54±3.39	<0.001

Table 3: Prognosis of patients with confirmed and probable sepsis cases

Outcome	Confirmed sepsis cases (n = 40)	Probable sepsis cases (n = 80)	p-value
Survival	26 (65%)	67 (83.7%)	0.020
Death	14 (35%)	13 (16.3%)	

analysis of data. Chi-square test was done and $p<0.05$ were considered statistically significant.

RESULTS

A total of 120 participants were enrolled in this study, out of them 40 were confirmed sepsis blood culture positive cases and 80 were probable sepsis compared to probable sepsis cases ($p<0.05$) Table 3 and Fig 1. Death rate was significantly high among confirmed sepsis patients (35%) as compared to suspected sepsis cases (16.3%).

DISCUSSIONS

Sepsis is the leading cause of mortality among critically ill children admitted in the intensive care unit. The probable regions of mortality in sepsis could be due to inflammatory responses induced tissue damage, body metabolic imbalance, organ failure, hypotension and septic shock[13,14]. Therefore, it is very important to early prediction of sepsis in intensive care unit may Mean age of presentation in our study among blood culture negative cases. The age Mean±SD of confirmed and probable sepsis cases was 4.67±1.35 and 5.24±1.83 respectively. Male children are predominant in both the group. Majority (60%) of the patients resided at rural area. No statistically significant difference between confirmed and probable sepsis cases in terms of age, gender, residential status, body temperature and duration of illness. Length of ICU stay was significantly higher in confirmed sepsis cases as compared to probable cases Table 1 and 2. Most common organism isolated from positive blood culture was staphylococcus aureus (40%) followed by Klebsiella (32.5%) and streptococcus pneumonia (10%).

Among laboratory markers of sepsis there are no significant changes in WBC and ESR level in confirmed sepsis and probable sepsis cases, whereas CRP and PCT was significantly higher in confirmed sepsis cases as appropriate control and treatment of sepsis rate. improve patient's quality of life and survival patients, The frequency of confirmed blood culture positive confirmed concordance with the Park *et al.*[15]. sepsis cases was 4.67±1.35 years. Corresponds to other study by Dominique *et al.*[16] and Rey *et al*.[17]. Early age group children are more susceptible to septicemia because of lower body immune defense mechanism. Current study reported that males children are predominant than females but statistically no significant difference, in agreement with the study conducted by Pecile *et al.*[18] and Simhachalam *et al* .[19].

In the present study ICU stay in hospital was significantly associate with the confirmed blood culture positive sepsis children, our finding correlate with the other studies. Park, *et al*.[20] and Yang *et al.*[21]. In our study WBC and ESR were increased in sepsis patients but not associated significantly, body temperature and WBC are the most frequently measured parameters of infection in ICU settings. However, several studies have found that WBC has a low diagnostic performance for evaluating sepsis. PCT and CRP are better markers of infection than temperature and WBC[22,23]. Staph aureus was the most common organism isolated from blood culture among sepsis patients, our results comparable to the Kumar *et al.*[24] and Hatherill, *et al.*[25]. In present study authors analyzed that acute phase reactants like CRP and PCT have significantly differentiating between culture positive

and culture negative sepsis group and also statistically significantly higher in culture positive confirmed sepsis group, similar finding observed by Simon *et al.*[26] Hong-Xiang *et al.*[27] and Pavare *et al.*[28]. The sensitivity and specificity of PCT was significantly more than that of CRP in differentiating between culture positive and culture negative sepsis cases. Mortality rate was significantly higher in confirmed sepsis cases as compared to probable sepsis cases, accordance to the LI and GONG *et al.*[29].

CONCLUSION

We have concluded that, CRP and PCT are the important diagnostic and prognostic markers of sepsis in children PCT was more sensitive and specific as compared to CRP, because its rises early in sepsis. Early detection and prompt treatment of sepsis may help to reduces children mortality.

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