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COMPARISON OF C-REACTIVE PROTEIN WITH CULTURE AMONG CHILDREN WITH FEVER WITHOUT FOCUS BETWEEN 1 TO 36 MONTHS OF AGE

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Abstract

OBJECTIVE

To determine the frequency of raised C-reactive protein and positive culture, and to compare raised C-reactive protein with positive culture among children presenting with fever with and without focus.

METHODOLOGY

This cross-sectional study was carried out in Indus hospital Karachi and included 171 pediatric participants within the age range of 1 to 36 months who had presented with fever of 38°C or more in duration of 48-120 hours with no identifiable cause. A non-probability consecutive sampling strategy was utilized, and demographic, clinical, C-reactive protein (CRP) and culture data was methodically obtained. The quantification of CRP was carried out using the turbidimetric immunological methodology with cultures achieved on the standards basis. The data obtained was analyzed by SPSS version 26, where the acceptance level of the significance was at a P value of 0.05 or less.

RESULTS

The sample included 171 children aged between 1 and 36 months (the mean was 16.68 8.75 months; 48.5% were males). The percentage of the participants with an increased CRP (>6 mg/dL) was 26.3. There was no significant association with blood culture (p=0.863) and a significant association was noted with urine culture (p=0.009).

CONCLUSION

This research suggests that C -reactive protein is not closely related with blood culture outcomes but is significantly correlated with positive urine cultures in children between the ages of 1 month and 36 months presenting with fever without focus. Although not diagnostic in blood stream infections, CRP can still become an important early marker of urinary tract infections, which makes it an effective means of directing specific tests and enhancing the success of a diagnosis in cases of pediatric febrile illness.

INTRODUCTION

Fever without an apparent focus (FWF) stands among the most common clinical problems observed within pediatric emergency units, particularly, in children ranging between 1 to 36 months old [1,2]. The age is characterized by poor communication skill and non-matured immune system where, among this age group, it is very difficult to distinguish between benign viral infection and serious bacterial infection (SBIs) [3]. When SBI is missed or delayed and therefore not diagnosed early enough, significant morbidity and mortality can result in the event of sepsis, urinary tract infection (UTI), and occult bacteremia, to mention but a few [4]. A useful biomarker is the C-reactive protein (CRP), a sensitive acute-phase reactant which synthesis mostly occurs in hepatocytes, and which increases dramatically in case of inflammation and tissue damage [5]. The level of CRP normally starts increasing after 4-6 hours of a precipitating event, reaching its highest at 36-50 hours, and falling off sharply as inflammation clears [6]. Its action is to bind with phosphocholine on dead or dying cells and some bacteria stimulate classical complement pathway and opsonization [7]. In addition to its presence in innate immunity, CRP drives the continuum to adaptive immunity by liaising with the Fc y receptors on immune cells [8].

CRP is non-specific and yet has proved to be quite useful in the initial assessment of children who present with fever and do not have a definite focus of infection. High levels of CRP are very likely to indicate that there is a case of bacterial infection in case it is interpreted in concert with clinical impression and the culture findings [9,10]. Other than expecting to wait up to 72 h to detect whether blood or urine cultures are confirmed, CRP is a quick-to-obtain and relatively easy to measure indicator that has the potential to direct timely decision-making and cut the increasing misuse of antibiotics [11,12].

In a cross-sectional study conducted in India on febrile children aged 1–36 months, 40 of 140 cases were CRP positive, and a significant proportion of these had confirmed SBIs through blood or urine culture [13]. Such findings support the hypothesis that CRP may serve as a cost-effective triage tool in low- and middle-income countries (LMICs) where laboratory infrastructure may be constrained [14].

Pakistan, with its high burden of infectious diseases and over-reliance on empirical antibiotics, stands to benefit from such biomarker-based screening approaches [15]. However, local data evaluating CRP's predictive performance in febrile pediatric patients is limited. Moreover, confounding factors like age, nutritional status, and viral infections can affect CRP levels, emphasizing the need for context-specific evaluation [16].

This study aims to determine the frequency of raised CRP and positive culture results in children aged 1 to 36 months presenting with FWF and to compare CRP positivity with culture positivity. The findings may support more targeted diagnostic evaluation, optimized antibiotic use, and improved pediatric patient care in high-volume centers like Indus Hospital Karachi [17].

METHODOLOGY

This is a cross-sectional study that was carried out in The Indus hospital, Karachi. The sample of the study included the children between the ages of 1-36 months that presented with fever to the Pediatric Emergency Department, General Ward, Pediatric Intensive Care Unit (PICU), or High Dependency Unit (HDU). It was done using non-probability consecutive sampling and 171 subjects included. Operationally, fever was defined as an axillary temperature of 38 o C or above and lasting longer than 48 hours and less than 120 hours. On fever without focus Fever without focus was an acute febrile condition with no apparent source of infection determinable following careful history taking and physical examination. Infection was considered as the presence of the pathogenic organism which was diagnosed in laboratories by cultures. Any growth of microbes on regular blood or urine cultures media was considered a positive culture. High CRP was a CRP level in serum >6 mg/dl. Children were deemed ineligible upon the establishment of a recognized diagnosis of chronic inflammatory or autoimmune disorders (for instance, juvenile idiopathic arthritis or systemic lupus erythematosus), the existence of an underlying malignancy, the identification of any discernible source of fever during clinical assessment, or a recorded diagnosis of dengue fever or malaria as per laboratory findings.

Relevant demographic and clinical data of children were recorded after written informed consent of parents or legal guardians formulated on a predesigned structured proforma by trained research staff. Aseptic precaution was performed using 2 to 3 mL of venous blood that was collected to evaluate the CRP and blood culture. The turbidimetric immunoassay methodology was employed to evaluate serum concentrations of C-reactive protein utilizing the Alinity CI analytical platform (Abbott Laboratories). BACTEC automated system was used in blood cultures. The urine samples were either old by midstream clean-catch or under sterile catheterization followed by giving the urine specimen on blood agar media and MacConkey agar media to isolate the uropathogens. Analysis of all samples was performed in the central diagnostic laboratory of The Indus Hospital according to the standardized protocols and internal forms of quality control. The data was submitted into SPSS Version 26.0The continuous variables (e.g., age, CRP levels, WBC counts) were reported as mean ± standard deviation. The categorical variables (e.g., gender, CRP classification, culture outcomes) were expressed in terms of frequencies and percentages. Comparisons of CRP and culture outcome were done by the Chi-square test with p-value of 0.05 taken to be significant.

RESULTS

The study included a total of 171 participants with a mean age of 16.68 ± 8.75 months (95% CI: 15.36–18.01). The average duration of fever was 84.15 ± 20.37 hours (95% CI: 81.07–87.22). The mean C-reactive protein (CRP) level was 4.99 ± 4.45 mg/dL (95% CI: 4.32–5.66), while the mean white blood cell (WBC) count was 11,053.98 ± 2,061.55 cells/µL (95% CI: 10,742.77–11,365.18). The average platelet count was 305,489.35 ± 54,871.40 cells/µL (95% CI: 297,206.14–313,772.56). In terms of gender distribution, 83 (48.5%) of the participants were male and 88 (51.5%) were female (TABLE I).

Table I: Demographic and Clinical Characteristics of Study Participants (n=171)

Mean ± Standard Deviation		**95% Confidence Interval**
Age in months = **16.68 ± 8.75**		15.36–18.01
Duration of Fever in hours = **84.15 ± 20.37**		81.07–87.22
CRP Level in mg/dl = **4.99 ± 4.45**		4.32–5.66
WBC Count cells per/µL = **11053.98 ± 2061.55**		10742.77–11365.18
Platelet Count cells per/µL = **305489.35 ± 54871.40**		297206.14–313772.56
n (%)		
Gender	Male	83 (48.5)
	Female	88 (51.5)

The comparison of raised C-reactive protein (CRP) levels with blood and urine culture results among 171 participants revealed no significant association between raised CRP and positive blood culture findings (p = 0.863). Among those with a positive blood culture (n=28), 7 (15.6%) had raised CRP, while 21 (16.7%) did not. However, a statistically significant association was observed between raised CRP and positive urine culture results (p = 0.009). Of the 15 participants with a positive urine culture, 9 (20.0%) had raised CRP compared to only 8 (6.3%) among those without raised CRP (TABLE II).

Table II: Comparison of Raised CRP with Blood Culture and Urine Culture (n=171)

Positive Culture, *n (%)*		**Raised CRP**		**95% C. I**	**P-Value**
		Yes (n=45)	**No (n=126)**		
Blood Culture	Positive (n=28)	7 (15.6)	21 (16.7)	0.363–2.340	0.863
	Negative (n=143)	38 (84.4)	105 (83.3)		
Urine Culture	Positive (n=15)	9 (20.0)	8 (6.3)	1.326–10.256	0.009*
	Negative (n=156)	36 (80.0)	118 (93.7)		

DISCUSSION

The present study assessed the role of C-reactive protein (CRP) as a diagnostic marker in febrile children aged 1 to 36 months presenting with fever without focus (FWF), a frequent and clinically ambiguous presentation in pediatric emergency settings. FWF in this age group is particularly challenging due to immature immunity and limited communicative ability, making it difficult to distinguish between benign viral infections and serious bacterial infections (SBIs) such as bacteremia and urinary tract infections (UTIs) [1,2,3]. In our study, children with fever of 48 to 120 hours duration and no identifiable clinical source were evaluated for CRP levels and culture positivity. The study found no significant association between raised CRP and positive blood cultures (p=0.863), but a statistically significant association between raised CRP and positive urine cultures (p=0.009), suggesting that CRP may have better predictive value for UTIs in children with FWF.

These findings are in line with prior studies, such as that by Chitra et al. [13], which found that 40 out of 140 febrile children with elevated CRP levels had confirmed bacterial infections, primarily UTIs. Similarly, Pulliam et al. [9] reported that CRP can aid in identifying occult bacterial infections, especially in settings where immediate culture results are unavailable. While CRP is a non-specific inflammatory marker, it is a rapid and cost-effective tool that may complement clinical judgment when laboratory infrastructure or time is constrained [5,6,10,14]. However, its utility appears to vary depending on the type of infection; as shown in our study and supported by Hengst [10] and Sorsa [12], CRP is more reliably associated with UTIs than with bloodstream infections in this age group. The strengths of this study include the clearly defined inclusion criteria, standardized CRP measurement methodology, and dual culture analysis (blood and urine), which enhance the validity and applicability of the findings. Moreover, it was conducted in a high-volume tertiary care center, reflecting real-world clinical settings in low- and middle-income countries like Pakistan [15].

However, the study has several limitations. Its cross-sectional design restricts longitudinal evaluation of CRP kinetics. The relatively small number of culture-positive cases, particularly in urine cultures, may limit statistical power. Furthermore, the lack of viral testing may have confounded CRP interpretation, as viral infections can also lead to elevated CRP levels [16]. Future studies should include serial CRP measurements and viral diagnostics to further clarify its predictive performance in febrile children without a clear source of infection.

CRP may not be a reliable standalone predictor of bacteremia in children with FWF, but it shows significant association with urinary tract infections. Therefore, CRP remains a valuable adjunct in the early evaluation of febrile children and may assist in guiding further investigations and antibiotic stewardship in resource-limited settings.

CONCLUSION

This research suggests that C -reactive protein is not closely related with blood culture outcomes but is significantly correlated with positive urine cultures in children between the ages of 1 month and 36 months presenting with fever without focus. Although not diagnostic in blood stream infections, CRP can still become an important early marker of urinary tract infections, which makes it an effective means of directing specific tests and enhancing the success of a diagnosis in cases of pediatric febrile illness.

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