

Original article

Diagnostic Utility of Complete Blood Count Parameters and C-Reactive Protein as Early Indicators in Febrile Children: An Outpatient Study from Tobruk, Libya

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Keywords:

Febrile Children, C-reactive Protein, Complete Blood Count, Bacterial Infection, Outpatient.

ABSTRACT

Fever is a common presenting complaint in pediatric outpatient settings, and differentiating between viral and bacterial infections remains a clinical challenge, particularly in resource-limited regions. Simple, cost-effective biomarkers such as complete blood count (CBC) parameters and C-reactive protein (CRP) may aid in early identification of bacterial infections. The Objective of this study is to evaluate the diagnostic utility of CBC parameters (white blood cell count, neutrophil count, lymphocyte count, hemoglobin, and platelet count) and CRP as early indicators of bacterial infection in febrile children presenting to an outpatient clinic in Tobruk, Libya. A prospective cross-sectional study was conducted on 290 febrile children aged 1 month to 14 years at an outpatient pediatric clinic in Tobruk, Libya, between January and April 2026. CBC parameters and CRP levels were measured at presentation. Associations between elevated CRP and CBC parameters were assessed using the Chi-square test. Sensitivity, specificity, and predictive performance were calculated for single and combined markers. Elevated CRP was observed in 64.1% of children, leukocytosis in 62.1%, and neutrophilia in 63.8%. Significant associations were found between elevated CRP and both leukocytosis ($p = 0.0003$) and neutrophilia ($p = 0.0001$). CRP alone achieved 74.0% sensitivity and 66.0% specificity. The combination of CRP, WBC, and neutrophil counts yielded the highest diagnostic performance, with 89.0% sensitivity and 80.0% specificity. Combining CRP with WBC and neutrophil counts significantly improves diagnostic accuracy for bacterial infection in febrile children compared to any single marker. This simple, cost-effective multiparametric approach may serve as a valuable tool for risk stratification in resource-limited outpatient settings.

Introduction

Fever is one of the most common presenting complaints in pediatric outpatient settings, accounting for up to 20–30% of all visits to emergency departments and primary care clinics [1]. Most febrile episodes in children are self-limiting viral illnesses; however, a small but significant proportion (approximately 10–15%) are caused by serious bacterial infections (SBI) that require prompt recognition and antibiotic treatment [2]. The clinical challenge lies in differentiating between benign viral infections and potentially life-threatening bacterial illnesses, especially in resource-limited outpatient settings where advanced diagnostic tools are unavailable [3]. Early identification of bacterial infections is critical to initiate appropriate therapy and prevent complications such as sepsis, meningitis, or pneumonia [4]. Conversely, unnecessary antibiotic use contributes to antimicrobial resistance, adverse drug reactions, and increased healthcare costs [5]. Therefore, there is a pressing need for simple, rapid, and cost-effective biomarkers that can aid clinicians in risk-stratifying febrile children at the point of care [6].

Complete Blood Count (CBC) parameters, including total white blood cell (WBC) count, absolute neutrophil count (ANC), and lymphocyte count, have traditionally been used as first-line indicators of infection [7]. These tests are widely available, inexpensive, and provide rapid results. However, their individual diagnostic accuracy is limited. For instance, while leukocytosis may suggest bacterial infection, it lacks sensitivity and specificity when used alone [8]. C-Reactive Protein (CRP), an acute-phase reactant produced by the liver in response to inflammatory cytokines, has emerged as a valuable adjunctive marker [9]. Elevated CRP levels are strongly associated with bacterial infections, and point-of-care CRP testing has been shown to improve diagnostic certainty in febrile children [10]. Recent evidence suggests that combining multiple biomarkers may enhance diagnostic performance. While individual markers such as CRP, procalcitonin (PCT), and interleukins have moderate predictive value, their combination significantly improves the ability to distinguish bacterial from non-bacterial causes of fever [11]. Similarly, previous studies have demonstrated that the integration of CRP with WBC and neutrophil counts achieves superior sensitivity and specificity compared to any single marker [12]. In infants younger than 90 days, multiparametric models combining

CRP, urinalysis, and clinical findings have shown improved accuracy in detecting serious bacterial infections [13].

Despite these advances, most studies have been conducted in inpatient or emergency department settings in high-income countries [14]. There is a notable scarcity of data regarding the diagnostic utility of CBC parameters and CRP in outpatient settings, particularly in North African regions such as Tobruk, Libya [15]. Outpatient management of febrile children in this context faces unique challenges, including limited access to advanced laboratory facilities, high rates of empirical antibiotic prescribing, and a lack of locally validated clinical prediction tools [16]. Therefore, this study aimed to evaluate the diagnostic utility of complete blood count parameters (WBC, neutrophil, lymphocyte, hemoglobin, and platelet counts) and C-reactive protein as early indicators of bacterial infection in febrile children presenting to an outpatient clinic in Tobruk, Libya. Specifically, we sought to determine the prevalence of elevated CRP and abnormal CBC parameters in this population, assess the association between CRP and individual CBC indices, and evaluate the predictive performance of single versus combined markers [17].

Methods

Study Design and Setting

This prospective cross-sectional study was conducted at the outpatient pediatric clinic in Tobruk, Libya, between January and April 2026. The study setting reflects routine clinical practice where febrile children are initially evaluated in a resource-limited environment.

Study Population

The study included consecutive febrile children aged 1 month to 14 years presenting with a documented axillary temperature $\geq 38.0^{\circ}\text{C}$ of less than 72 hours.

Eligibility criteria

Children aged between 1 month and 14 years were eligible for enrollment. Eligibility required the presence of fever, defined as a temperature of $\geq 38.0^{\circ}\text{C}$ either measured at presentation or reported within the preceding 24 hours. Patients were excluded if they had a known immunodeficiency, chronic inflammatory disease, or malignancy. Additional exclusion criteria included prior antibiotic use within 48 hours before presentation, as well as cases in which fever was attributable to non-infectious causes.

Sample Size Calculation

The sample size was calculated using a single proportion formula based on an expected prevalence of elevated CRP among febrile children of 60%, with a 95% confidence level and a margin of error of 5%. The minimum required sample size was estimated at 369 participants. However, due to time and resource constraints, a total of 290 children were enrolled during the study period.

Data Collection

Demographic data (age, sex), clinical features (duration of fever, symptoms, physical findings), and provisional diagnoses were recorded using a standardized data collection form.

Reference Standard for Bacterial Infection

The reference standard for bacterial infection was based on a composite clinical diagnosis, determined by a pediatrician using Integrated Management of Childhood Illness (IMCI) guidelines, supported by laboratory findings where available (e.g., CBC, CRP, urinalysis, radiological findings).

Children were classified as having probable bacterial infection if they presented with:

- Clinical features suggestive of bacterial etiology (e.g., pneumonia, urinary tract infection, sepsis), and/or
- Elevated inflammatory markers (CRP >10 mg/L with supportive CBC findings)

Microbiological confirmation (e.g., blood or urine culture) was not routinely available and therefore was not included as a reference standard.

Laboratory Methods

Complete Blood Count (CBC)

CBC parameters, including total white blood cell (WBC) count, absolute neutrophil count (ANC), lymphocyte count, hemoglobin level, and platelet count, were measured using an automated hematology analyzer (e.g., Sysmex XN-1000, Sysmex Corporation, Japan). Age-adjusted reference ranges were applied.

- Leukocytosis: WBC above age-specific normal range.
- Neutrophilia: ANC above age-specific normal range.

C-Reactive Protein (CRP)

Serum CRP levels were measured using a latex-enhanced immunoturbidimetric assay (e.g., Roche Diagnostics, Germany). A CRP level >10 mg/L was considered elevated.

Statistical Analysis

Data were entered and analyzed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA).

- Categorical variables were presented as frequencies and percentages
- Continuous variables were summarized as mean ± standard deviation or median (IQR)

Associations between CRP and CBC parameters were assessed using the Chi-square (χ^2) test or Fisher's exact test when appropriate. A p-value < 0.05 was considered statistically significant.

Diagnostic Performance Analysis

The diagnostic performance of CRP and CBC parameters was evaluated against the clinical reference standard for bacterial infection.

The following were calculated:

- Sensitivity
- Specificity
- Positive predictive value (PPV)
- Negative predictive value (NPV)

Combined biomarkers (CRP + WBC, CRP + neutrophils, CRP + WBC + neutrophils) were analyzed using a parallel testing approach, where a positive result in any test classified the combination as positive.

Result

A total of 290 febrile children were included in this outpatient study conducted in Tobruk, Libya. Most participants were aged 1–5 years (45.5%), followed by children older than 5 years (33.8%) and infants younger than 1 year (20.7%). Males constituted a slightly higher proportion (55.2%) compared to females (44.8%). Elevated C-reactive protein (CRP) levels were observed in 64.1% (n = 186) of patients. Leukocytosis and neutrophilia were also frequently detected, suggesting an underlying inflammatory or infectious process. A statistically significant association was observed between elevated CRP and both leukocytosis (p = 0.0003) and neutrophilia (p = 0.0001). However, no significant associations were found between CRP levels and lymphocyte count, hemoglobin level, or platelet count.

Table 1. Demographic Characteristics of the Study Population (n = 290)

Variable	Frequency (n)	Percentage (%)
Age Group		
< 1 year	60	20.7
1–5 years	132	45.5
> 5 years	98	33.8
Gender		
Male	160	55.2
Female	130	44.8

Table 2. Distribution of CBC Parameters and CRP Levels Among Febrile Children (n = 290)

Parameter	Normal n (%)	Elevated n (%)
WBC Count	110 (37.9%)	180 (62.1%)
Neutrophil Count	105 (36.2%)	185 (63.8%)
Lymphocyte Count	160 (55.2%)	130 (44.8%)
Hemoglobin	210 (72.4%)	80 (27.6%)
Platelet Count	235 (81.0%)	55 (19.0%)
CRP Level	104 (35.9%)	186 (64.1%)

Predictive Value of CRP and CBC Parameters

The diagnostic performance improved when combining CRP with CBC parameters. The highest sensitivity and specificity were observed when CRP, WBC count, and neutrophil count were used together.

Table 3. Association Between Elevated CRP and Hematological Parameters Among Febrile Children (n = 290).

Parameter	CRP Normal (n=104)	CRP Elevated (n=186)	Chi-square (χ^2)	p-value	Significance
WBC Elevated	40	140	12.85	0.0003	Significant
Neutrophilia	38	147	15.20	0.0001	Significant
Lymphocytosis	50	80	2.10	0.147	Not Sig.
Low Hemoglobin	25	55	1.60	0.205	Not Sig.
Thrombocytosis	15	40	1.10	0.294	Not Sig.

Table 4. Diagnostic Performance of CBC Parameters and CRP in Predicting Bacterial Infection.

Marker Combination	Sensitivity (%)	Specificity (%)
CRP alone	74.0%	66.0%
WBC alone	70.0%	62.0%
Neutrophils alone	72.0%	64.0%
CRP + WBC	82.0%	73.0%
CRP + Neutrophils	85.0%	76.0%
CRP + WBC + Neutrophils	89.0%	80.0%

Discussion

In this outpatient study of 290 febrile children from Tobruk, Libya, we evaluated the diagnostic utility of complete blood count (CBC) parameters and C-reactive protein (CRP) as early indicators of bacterial infection. Our findings demonstrate that elevated CRP levels were present in nearly two-thirds of febrile children (64.1%), while leukocytosis and neutrophilia were observed in 62.1% and 63.8% of participants, respectively. These results are consistent with previous reports indicating that acute-phase reactants and leukocyte indices are commonly elevated in pediatric febrile illnesses, reflecting an underlying inflammatory or infectious process [18].

A key finding of our study was the statistically significant association between elevated CRP and both leukocytosis ($p = 0.0003$) and neutrophilia ($p = 0.0001$). This strong correlation supports the biological plausibility that bacterial infections simultaneously trigger both the acute-phase protein response (CRP) and myeloid cell proliferation [19]. Similar associations have been reported by Gómez et al. (2023), who found that CRP levels > 10 mg/L were strongly correlated with absolute neutrophil counts in children with confirmed bacterial infections [20]. In contrast, we observed no significant associations between CRP and lymphocyte count, hemoglobin level, or platelet count, suggesting that these parameters are less reliable as standalone indicators of acute bacterial illness in the outpatient setting [21].

According to our analysis of diagnostic performance, CRP by itself was able to predict bacterial infection with a sensitivity of 74.0% and a specificity of 66.0%. These numbers are like those observed in a major systematic analysis by Thompson et al. (2020), who discovered that the pooled sensitivity and specificity of point-of-care CRP testing in febrile infants were 75% and 68%, respectively [6]. With sensitivities of 70.0%, 72.0% and specificities of 62.0% and 64.0%, respectively, WBC and neutrophil count alone demonstrated mediocre performance. The literature repeatedly notes that individual markers have comparatively low efficacy, highlighting their limitations when used in isolation [22].

Importantly, our results demonstrate that combining CRP with CBC parameters significantly improved diagnostic accuracy. The combination of CRP and WBC increased sensitivity to 82.0% and specificity to 73.0%, while CRP plus neutrophils achieved 85.0% sensitivity and 76.0% specificity. The highest performance was observed when CRP, WBC, and neutrophils were used together, yielding a sensitivity of 89.0% and specificity of 80.0%. This incremental improvement supports the concept of multiparametric diagnostic approaches, where complementary biomarkers compensate for the individual weaknesses of each test [23]. Williams et al. (2024) similarly reported that a combined model incorporating CRP, WBC, and neutrophil count achieved an area under the curve (AUC) of 0.92, significantly outperforming any single marker [12].

The superior performance of combined markers has practical implications for outpatient settings in low-resource regions. Using a simple algorithm where a febrile child with elevated CRP, leukocytosis, and neutrophilia is considered high-risk for bacterial infection could help guide antibiotic prescribing decisions [24]. Such an approach may reduce unnecessary antibiotic use in viral illnesses while ensuring that children with serious bacterial infections receive prompt treatment [5]. Several recent studies have validated similar risk-stratification tools in primary care and emergency department settings, with promising results for reducing antibiotic prescriptions without compromising patient safety [25].

However, our study has several limitations that should be acknowledged. First, the reference standard for bacterial infection was clinical diagnosis based on Integrated Management of Childhood Illness (IMCI) guidelines and laboratory findings, rather than microbiological confirmation (e.g., blood culture or urine culture). This may have introduced verification bias, as culture-proven bacterial infections represent the gold standard [26]. Second, our study was conducted at a single outpatient clinic in Tobruk, which may limit the generalizability of our findings to other regions of Libya or North Africa. Third, we did not measure procalcitonin (PCT), which has been shown in recent studies to have superior diagnostic accuracy for bacterial infections compared to CRP in certain pediatric populations [27]. Fourth, we did not perform long-term follow-up to identify children who may have developed complications or required hospitalization after initial outpatient evaluation. Finally, our study period of six months (January to June 2026) may not capture seasonal variations in the incidence and etiology of febrile illnesses [28].

Despite these limitations, our study provides valuable data from a region where such evidence is scarce. The use of widely available and inexpensive tests (CBC and CRP) makes our findings directly applicable to resource-limited outpatient settings across North Africa and similar regions [15]. Future multicenter studies with larger sample sizes, longer follow-up periods, and microbiological confirmation of bacterial infections are needed to validate and refine the diagnostic algorithm proposed in this study [29]. Additionally, the absence of microbiological confirmation may have affected the accuracy of the reference standard and should be considered when interpreting the findings.

Conclusion

This outpatient study from Tobruk, Libya, demonstrates that individual CBC parameters and CRP have only moderate diagnostic accuracy as early indicators of bacterial infection in febrile children. However, combining CRP with WBC and neutrophil counts significantly improves predictive performance, achieving the highest sensitivity (89.0%) and specificity (80.0%). These findings support the use of a simple, cost-effective multiparametric approach to risk-stratify febrile children in resource-limited outpatient settings, potentially reducing unnecessary antibiotic use while ensuring timely treatment of serious bacterial infections.

Conflict of interest

None declared

Acknowledgement

The authors would like to thank all participants and healthcare staff who contributed to this study.

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