ACE JOURNAL OF PHARMACEUTICAL SCIENCES
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Research Article

Diagnostic Value of C-Reactive Protein in Patients with Acute Bacterial Meningitis in Iraqi Patients

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Key Words
C-reactive protein, acute bacterial meningitis, diagnostic accuracy, CSF biomarkers, sensitivity and specificity

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Received: 10th September 2024
Accepted: 11th November 2024
Published: 26th December 2024

Citation: Ali M. Al-Balkhi, Faris K. Khadir, Wameedh Q. Al Sammak and Ameen Al Alwany, 2024. Diagnostic Value of C-Reactive Protein in Patients with Acute Bacterial Meningitis in Iraqi Patients. Ace. J. Pharma. Sci., 4: 1-6, doi: 10.36478/ace pharma.2024.1.6

Abstract
Acute bacterial meningitis is a life-threatening infection of the central nervous system with significant morbidity and mortality worldwide. Rapid and accurate diagnosis is essential for initiating appropriate treatment. While cerebrospinal fluid (CSF) analysis remains the cornerstone of diagnosis, biomarkers like C-reactive protein (CRP) have been investigated as adjunctive tools to improve diagnostic accuracy. This study aimed to evaluate the sensitivity and specificity of CRP in diagnosing acute bacterial meningitis and its utility as a supportive diagnostic tool. A descriptive, prospective, cross-sectional study was conducted at Baghdad Teaching Hospital Emergency Room and Adult Neurology Outpatient Clinic from January to July 2023. A total of 33 patients aged 18-70 years presenting with fever and headache underwent lumbar puncture for CSF analysis. CRP levels were measured and compared to CSF culture results to determine their diagnostic utility. Other laboratory parameters, including CSF white blood cell counts, sugar levels and protein levels, were also evaluated. Statistical analysis included Student's t-test, Chi-square test and receiver operating characteristic (ROC) curve analysis. The mean CRP level among patients was 13.76±9.76 mg/L. Positive CSF cultures were observed in 63.6% of cases, with a CRP cut-off value of 8.60 mg/L yielding a sensitivity of 85.7% and specificity of 66.7%. Patients with positive CSF cultures had significantly higher CRP levels (17.20±10.32 mg/L vs. 7.76±4.67 mg/L, p=0.006), elevated CSF WBC counts (195.71±111.46 cells/mm³ vs. 45.50±47.59 cells/mm³, p=0.0001) and more frequent low CSF sugar levels (76.9% vs. 23.1%, p=0.002) and elevated CSF protein levels (77.8% vs. 22.2%, p=0.0001). The diagnostic accuracy of CRP was 78.8%, with a positive predictive value of 81.8% and a negative predictive value of 72.7%. CRP is a valuable adjunctive marker in the diagnostic work up of acute bacterial meningitis but is not definitive on its own. When combined with clinical findings and CSF analysis, CRP can improve diagnostic accuracy. The study is limited by its small sample size and single-center design, necessitating further multicenter research to validate these findings. Despite these limitations, CRP remains a practical and accessible tool for resource-limited settings.

INTRODUCTION

Acute bacterial meningitis remains a life-threatening infection of the central nervous system, associated with high morbidity and mortality worldwide despite advances in antimicrobial therapies and supportive care[1]. Rapid and accurate diagnosis is crucial to initiate appropriate treatment and improve patient outcomes[2]. However, differentiating bacterial meningitis from other causes of meningeal inflammation, such as viral or tuberculous meningitis, can be challenging due to overlapping clinical signs and symptoms[3]. Laboratory findings, including cerebrospinal fluid (CSF) parameters and pathogen identification techniques, are essential but not always definitive, often requiring additional supportive indicators to guide clinical decisions[4]. In this context, biomarkers have emerged as valuable adjuncts to routine diagnostic approaches[5]. Among these, C-reactive protein (CRP), an acute-phase reactant produced by the liver in response to inflammation, has attracted considerable attention for its potential role in improving the diagnostic accuracy of bacterial meningitis[6]. CRP levels typically rise rapidly in response to bacterial infections and are less markedly elevated in viral or other non-bacterial etiologies, suggesting that they could serve as a useful marker to discriminate between different types of meningitis[7]. CRP testing is relatively inexpensive, widely available and can be conducted rapidly, making it a practical tool for both developed and resource-limited healthcare settings[8]. Recent studies have sought to determine the specific added value of CRP in diagnosing bacterial meningitis, examining its sensitivity, specificity and predictive values when used alongside traditional diagnostic parameters such as CSF white cell counts, protein levels, glucose concentrations and advanced microbiological techniques[9,10]. Additionally, meta-analyses have reported promising results, indicating that CRP may significantly improve the ability to distinguish bacterial meningitis from non-bacterial causes, potentially reducing unnecessary antibiotic use and hospital admissions[11]. Despite these promising findings, there remains a need for further rigorous research. Variability in study populations, testing methods and diagnostic thresholds has led to inconsistent conclusions[12]. The purpose of this study was to evaluate the sensitivity and specificity of CRP in diagnosing acute bacterial meningitis and to determine its utility as a diagnostic tool.

MATERIALS AND METHODS

A descriptive, prospective, cross-sectional study was conducted at Baghdad Teaching Hospital Emergency Room and the Adult Neurology Outpatient Clinic over a six-month period from January 2023 to July 2023. A total of 33 patients presenting with fever and headache were enrolled. Inclusion criteria encompassed patients aged 18-70 years who presented with both symptoms and underwent lumbar puncture for cerebrospinal fluid (CSF) analysis. Exclusion criteria included patients with identifiable sources of fever, those outside the specified age range and those who had received antibiotics prior to presentation. Data were collected systematically for each participant and included demographic variables (age, sex), presenting symptoms, duration of symptoms and detailed laboratory findings. Clinical evaluations encompassed measurement of body temperature and the duration of fever. Laboratory investigations included serum C-reactive protein (CRP) levels, white blood cell (WBC) counts and platelet counts, alongside CSF analysis for WBC counts, sugar levels and protein levels. All CSF samples underwent culture to confirm bacterial growth. The primary aim of the study was to evaluate the sensitivity and specificity of CRP levels in diagnosing acute bacterial meningitis. Secondary objectives included identifying associations between CRP levels and CSF culture results and exploring additional laboratory parameters indicative of bacterial meningitis. Ethical approval was obtained from the institutional review board of the hospital. Written informed consent was obtained from all participants before enrolment, and all procedures adhered to the ethical standards of the Declaration of Helsinki. Data were analyzed using appropriate statistical methods. Continuous variables were expressed as mean±standard deviation (SD), while categorical variables were summarized as frequencies and percentages. Comparisons between groups (positive vs. negative CSF culture results) were performed using Student's t-test or Chi-square test as appropriate. Receiver operating characteristic (ROC) curve analysis was employed to identify the optimal CRP cut-off value for differentiating positive from negative CSF cultures. Diagnostic performance metrics, including sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), were calculated. A p-value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSIONS

A study was conducted at Baghdad Teaching Hospital Emergency Room and Adult Neurology Outpatient Clinic to evaluate the sensitivity and specificity of CRP in diagnosing acute bacterial meningitis. Females found to be the majority of the participants 20 (60.6%) as shown in (fig. 1). The mean age of participants was 39.58±14.79

years. All patients presented with headaches (100%), a mean body temperature of 38.50±1.10°C and a fever duration of 4.06±2.48 days. These demographic and clinical characteristics are detailed in (Table 1).

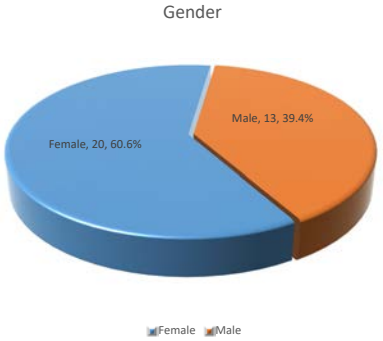

Fig. 1: Gender Distribution

Table 1: Demographic and Clinical Characteristics of Patients

Patients' variables	Mean	±SD
Age	39.58	±14.79
Headache (Yes) (No.) (%)	33	100%
Temp. (C^0)	38.50	±1.10
Fever duration (Days)	4.06	±2.48

The mean CRP level among patients was 13.76±9.76 mg/L, with elevated WBC counts observed in 27.3% of cases and elevated platelet counts in 12.1%. The mean CSF WBC count was 141.09±118.01 cells/mm³, while low CSF sugar levels and elevated CSF protein levels were found in 78.8% and 81.8% of patients, respectively. These findings are shown in (Table 2).

Table 2: Laboratory Investigations

Investigations	Mean	±SD
CRP	13.76	±9.76
WBC (elevated) (No.) (%)	9	27.3%
Platelets (elevated) (No.) (%)	4	12.1%
CSF WBC count	141.09	±118.01
CSF Sugar (Low) (No.) (%)	26	78.8%
CSF Protein (elevated) (No.) (%)	27	81.8%

Acute bacterial meningitis was diagnosed in 81.8% of cases, with 63.6% of these confirmed by positive CSF cultures. Other diagnoses included respiratory tract infections (15.2%) and urinary tract infections (3.0%). These diagnoses are summarized in (Table 3).

Table 3: Diagnoses of Patients

Diagnoses		No.	%
CSF Culture (Positive)		21	63.6
Final diagnosis	acute bacterial meningitis	27	81.8
	respiratory tract infection	5	15.2
	UTI	1	3.0

Patients with positive CSF cultures showed significantly higher CRP levels (17.20±10.32 mg/L vs. 7.76±4.67 mg/L, p=0.006), along with elevated CSF WBC counts (195.71±111.46 vs. 45.50±47.59 cells/mm³, p=0.0001), more frequent low CSF sugar levels (76.9% vs. 23.1%, p=0.002), and higher CSF protein levels (77.8% vs. 22.2%, p=0.0001), as detailed in (Table 4).

Table 4: Comparison of Variables Based on CSF Culture Results

Variables		CSF Culture				
		Negative		Positive		P value
Gender	Female (No.)(%)	6	30.0%	14	70.0%	0.346
Age	mean±SD	43.00	±17.863	37.62	±12.792	0.323
Temp.	mean±SD	38.092	±0.9671	38.748	±1.1303	0.102
CRP	mean±SD	7.758	±4.6697	17.195	±10.3180	0.006
WBC	elevated (No.)(%)	5	55.6%	4	44.4%	0.160
CSF WBC	mean±SD	45.50	±47.586	195.71	±111.464	0.0001
CSF Sugar	Low(No.)(%)	6	23.1%	20	76.9%	0.002
CSF protein	Elevated(No.)(%)	6	22.2%	21	77.8%	0.0001

The ROC curve was utilized to determine the optimal CRP cut-off value for differentiating positive from negative CSF cultures. The analysis identified a cut-off value of 8.60 mg/L, yielding a sensitivity of 85.7% and a specificity of 66.7%. Additionally, the positive predictive value (PPV) was 81.8%, the negative predictive value (NPV) was 72.7% and the overall diagnostic accuracy was 78.8%. These findings underscore the utility of CRP as a diagnostic marker for acute bacterial meningitis and are illustrated in (Fig. 2).

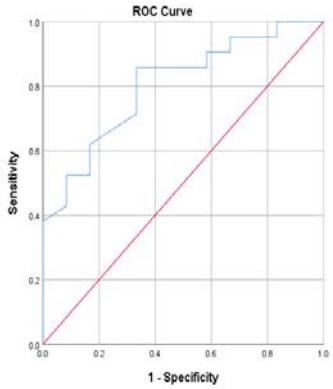

Fig. 2: ROC Curve of the CRP Value to Determined Acute Bacterial Meningitis

The study aimed to evaluate the diagnostic utility of CRP levels in identifying acute bacterial meningitis and differentiating it from other febrile conditions. The observed female predominance, accounting for 60.6% of participants, aligns with global observations of sex-based differences in bacterial meningitis outcomes. A study by Dias *et al.* (2017) reported that while males were more likely to experience adverse outcomes, females exhibited higher serum inflammatory parameters, which may influence the presentation and disease progression[13]. The mean age of participants in this study was

39.58±14.79 years, emphasizing that acute bacterial meningitis predominantly affects middle-aged adults in this cohort. This is consistent with findings by Polkowska *et al.* (2017) in Finland, where the median age of bacterial meningitis patients has shifted towards older populations over the years[14]. Headache was a universal symptom among participants in this study (100%), corroborating its role as a consistent clinical feature of bacterial meningitis. This finding is supported by Bijlsma *et al.* (2016), who identified headaches as a critical diagnostic symptom across various populations[15]. Similarly, fever was another prominent feature, with a mean body temperature of 38.50±1.10°C, consistent with its status as an early indicator of bacterial meningitis. Studies such as those by Hsieh *et al.* (2021) reinforce the diagnostic value of fever in both adult and pediatric cases. The mean fever duration before seeking medical attention was 4.06±2.48 days, aligning with recent observational studies. Hsieh *et al.* (2021) reported an average fever duration of 3-5 days in bacterial meningitis cases, reflecting similar patterns in symptom progression before clinical intervention[16]. The elevated mean CRP level (13.76±9.76 mg/L) in the current study highlights its role as a critical marker in bacterial meningitis diagnosis. This finding aligns with the study by Aksoy *et al.* (2017), which demonstrated significantly higher CRP levels in bacterial meningitis compared to viral or chronic meningitis[17]. CSF biochemical analysis in this study revealed elevated protein levels (81.8%) and low sugar levels (78.8%), findings that are consistent with the study by Alnomasy *et al.* (2021). Their research highlighted the diagnostic power of combining serum PCT and CSF protein levels, which yielded high sensitivity and specificity for distinguishing bacterial meningitis from viral cases[18]. Similarly, Thakur *et al.* (2020) reported that elevated CSF CRP levels (>3.08 mg/dL) were strongly associated with bacterial meningitis severity, reinforcing the importance of this marker in diagnosis[6]. Elevated CSF WBC counts (141.09±118.01 cells/mm³) observed in the current study corroborate the findings by Almeida *et al.* (2023), who emphasized the diagnostic utility of elevated CSF WBC and protein levels. Almeida's study also identified CSF lactate and CRP as particularly useful biomarkers for differentiating bacterial from viral meningitis, showcasing their specificity and sensitivity in clinical settings[19]. The findings of the current study regarding the diagnostic utility of CRP levels, CSF WBC counts, CSF glucose and protein levels in acute bacterial meningitis are consistent with recent studies in the literature. These studies further reinforce the clinical significance of these biomarkers in differentiating bacterial meningitis from other CNS infections. Elevated CRP levels, as observed in this study, were significantly higher in patients with positive CSF cultures (17.20±10.32 mg/L vs. 7.76±4.67 mg/L, p=0.006). This is consistent with the findings of Aksoy *et al.* (2017), which highlighted CRP as a critical marker in distinguishing bacterial meningitis from other forms of meningitis. The study demonstrated that elevated CRP levels had strong diagnostic characteristics, enhancing the clinician's ability to differentiate bacterial from viral or chronic meningitis[17]. The significantly elevated CSF WBC counts in patients with positive cultures (195.71±111.46 cells/mm³ vs. 45.50±47.59 cells/mm³, p=0.0001) align with the study by Fouad *et al.* (2014), which emphasized the diagnostic role of cytochemical parameters, including CSF leukocyte counts. The study noted that increased CSF WBC is a reliable marker of CNS inflammation, particularly in bacterial meningitis cases with negative Gram stains[20]. Low CSF glucose levels, which were more frequently observed in patients with positive CSF cultures (76.9% vs. 23.1%, p=0.002), are a hallmark of bacterial meningitis. This finding is in agreement with Alnomasy *et al.* (2021), who demonstrated significantly reduced glucose levels in bacterial meningitis compared to viral cases. The study highlighted that hypoglycorrhachia reflects the consumption of glucose by pathogens and the immune response in the CSF[18]. The elevated CSF protein levels in this study (77.8% in positive cultures vs. 22.2% in negative cultures, p=0.0001) are consistent with findings by Thakur *et al.* (2020). Their study demonstrated that elevated CSF protein levels, often observed in bacterial meningitis, correlate positively with CRP and inversely with CSF glucose levels. These relationships further enhance the diagnostic utility of combining multiple biomarkers[6]. Moreover, the combination of CSF and serum markers, as suggested by Almeida *et al.* (2023), supports the use of multi-parameter approaches for improved sensitivity and specificity in bacterial meningitis diagnosis. The study underscored that combining serum PCT with CSF protein levels provides a more robust diagnostic framework than relying on single markers[19]. Our study identified a CRP cut-off value of 8.60 mg/L, yielding a sensitivity of 85.7%, a specificity of 66.7% and an overall diagnostic accuracy of 78.8%. These results align with findings from several other studies that have evaluated the role of CRP in the diagnosis of meningitis and other bacterial infections. For instance, the study by Santotoribio *et al.* (2018) reported that a CRP threshold of 14.0 mg/L demonstrated a

sensitivity of 100% and a specificity of 83.3% in differentiating bacterial from viral meningitis. This high sensitivity underscores the reliability of CRP as a marker for bacterial infections, consistent with the diagnostic strength observed in our study[21]. Additionally, Goldberg *et al.* (2020) found that repeating a CRP test within 12 hours of admission improved diagnostic reliability in bacterial infections. This approach could be particularly relevant in meningitis cases with equivocal CRP values at presentation, complementing the diagnostic approach outlined in our study[22]. Furthermore, Kumar *et al*. (2021) showed significantly elevated CRP levels in bacterial meningitis (mean 91.13 mg/L) compared to viral meningitis (mean 2.70 mg/L, $p<0.0001$). While the cut-off value identified in our study was lower, the conclusion regarding the diagnostic significance of CRP remains consistent, reinforcing its utility as a robust marker to differentiate bacterial from viral meningitis[23-25].

CONCLUSIONS

C-reactive protein (CRP) is a valuable adjunctive marker in the diagnostic work up of acute bacterial meningitis but is not definitive on its own. While elevated CRP levels showed significant sensitivity and specificity in identifying bacterial meningitis, its use should be interpreted in conjunction with clinical findings and CSF analysis. CRP levels, combined with other laboratory parameters such as CSF WBC counts, sugar levels and protein levels, can aid in differentiating bacterial from non-bacterial meningitis. However, CRP alone cannot confirm the diagnosis and its role remains supportive rather than conclusive. This study is limited by the small sample size and its single-center design, which may affect the generalizability of the findings. Future studies with larger, multicenter cohorts are needed to validate these results and further explore the diagnostic utility of CRP in diverse populations and clinical settings. Despite these limitations, CRP remains a practical and accessible tool that, when integrated with other diagnostic measures, can improve the accuracy of bacterial meningitis diagnosis.

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