e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(6); 572-577

Original Research Article

Estimation Of Serum Levels of C - Reactive Protein in Pyogenic Pediatric Meningitis: A Cross-Sectional Study

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Received: 29-03-2023 / Revised: 24-04-2023 / Accepted: 20-05-2023

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Conflict of interest: Nil

Abstract

Background and Objectives: Bacterial meningitis represents a significant public health concern on a global scale. C-reactive protein (CRP) has proven to be a valuable diagnostic tool in distinguishing between bacterial and aseptic meningitis, particularly in cases where bacterial culture of the blood and spinal fluid yields negative results. The aim of this study was to assess and estimate the serum levels of CRP among pediatric patients diagnosed with meningitis of bacterial origin.

Materials & Methods: The observational cross-sectional study was conducted at a tertiary care medical teaching hospital located in central India. Patients who met the predefined inclusion criteria were carefully selected for participation in the study after obtaining their informed consent. Collection of cerebrospinal fluid samples followed standard guidelines. Phenotypic identification of bacteria, along with antimicrobial susceptibility testing, was carried out using automated techniques. The quantitative estimation of CRP was performed through a solid-phase, sandwich-format immunometric assay employing a gold antibody conjugate. Throughout the study, human rights, welfare, and autonomy of the participants were safeguarded in accordance with national ethical guidelines.

Results: Among the 170 cases included in the study, the median age was found to be 3 years. The most frequently isolated bacterium was Escherichia coli, followed by Klebsiella pneumoniae. Out of the total participants, 53 individuals (31.17%) exhibited elevated levels of serum CRP. Furthermore, it was observed that serum CRP levels were higher in cases associated with Gram-negative bacterial etiology. On average, cases attributed to Gram-negative bacteria demonstrated higher mean serum CRP levels.

Conclusion: Serum CRP levels were notably higher in cases of meningitis caused by Gram-negative bacteria.

Keywords: Meningitis, C - reactive protein, Klebsiella pneumoniae, Escherichia coli, Child.

Introduction

Bacterial meningitis (BM) poses a significant global public health challenge, particularly in low-income countries, where multiple bacterial etiologies contribute to its occurrence. The distribution of causative agents varies depending on age groups and geographical regions [1]. Despite advancements in antibiotics and enhanced critical care, BM remains an ongoing concern in the field of clinical medicine. Even though highly potent antibiotics are successful in eliminating bacteria, mortality rates still reach as high as 34% [2]. A considerable proportion of individuals who survive bacterial meningitis, approximately up to 50%, experience long-term complication [3,4].In differentiating between bacterial and aseptic meningitis, C-reactive protein (CRP) exhibits valuable diagnostic utility, particularly in situations where bacterial culture of the blood and spinal fluid yields negative results [5,6].Moreover, the use of CRP as a marker to assess treatment progress has also been examined [7].

CRP, an acute-phase protein of liver origin, is a pentameric protein present in blood plasma. Its circulating levels elevate as a response to inflammation. This increase is triggered by the secretion of interleukin-6 by macrophages and T-cells. The primary physiological function of CRP is to attach to lysophosphatidylcholine, which is present on the cell membrane of dying or dead cells, as well as certain bacterial species. By binding to lysophosphatidylcholine, CRP activates the complement cascade [8]. Normal CRP levels tend to increase with aging [9]. Elevated CRP concentrations are observed in various conditions, including advanced pregnancy, mild inflammatory and viral infections (ranging from 10 to 40 mg/L), active inflammation, bacterial infections (ranging from 40 to 200 mg/L), and severe bacterial infections or burns (exceeding 200 mg/L) [10].

However, there is a lack of comprehensive documentation regarding the association between CRP and bacterial meningitis (BM) in the pediatric age group, particularly in many low-income settings. Therefore, the primary objective of this study was to assess the extent of CRP elevation in pediatric patients with meningitis. The utilization of CRP as a diagnostic and prognostic marker proves to be cost-effective and can potentially guide empirical antimicrobial therapy in patients suspected of having BM.

Material & Methods

This was a cross-sectional observational study done in a tertiary care medical teaching hospital in Central India over a period of 6 months. Patients fulfilling the clinical, demographical, geographical, and temporal criteria were included in this study after obtaining informed consent. Cases with possibility to alter the quality of data were excluded from the study. Cerebrospinal fluid (CSF) sample was collected by aseptic lumber puncture as per standard guidelines in wide mouth sterile universal container and transported for processing as early as possible of sample collection [11]. The ethical guidelines were strictly adhered to in order to protect human rights, welfare, and autonomy throughout the study [12].

In the current study, a total of 170 samples were included for analysis. The collected samples were inoculated onto various types of agar media, including nutrient agar (as basal media), MacConkey's agar (as selective and differential media), blood agar (as enriched media), and chocolate agar (as enriched media, particularly useful for Haemophilus influenzae). The inoculated culture plates were then incubated aerobically at 37°C for a period of 18-24 hours. For the isolation of capnophilic organisms, the candle jar technique was employed [13, 14].

Phenotypic identification of bacterial species, as well as antimicrobial susceptibility testing, was performed using automation technology. The estimation of Minimum Inhibitory Concentration (MIC) values was conducted following the guidelines set forth by the Clinical Laboratory Standards Institute [15].

To conduct the biochemical assay, a total of 2 mL of venous blood was collected from the study participants and transferred into clot-enhancing tubes without any anticoagulant. The separation of serum from the collected blood samples was performed, following which quantitative estimation of C-reactive protein (CRP) was carried out in the biochemistry section. The estimation was conducted using the Nyco Card method (AXIS-SHIELD), in accordance with the manufacturer's instructions. This method employs a solid-phase, sandwich-format immunometric assay utilizing a gold antibody conjugate. The results were reported accordingly [16].

Results

The study included a total of 170 children, with a median age of 3 years and an interquartile range of 1 to 4.5 years. There were slightly more female cases (95 out of 170) compared to male cases (75 out of 170), although this difference was not statistically significant.

Table 1 presents the culture results of the samples collected. Among these samples, 60 out of 170 (35.30%) tested positive for bacterial growth. Notably, in a significantly higher number of these culture-positive cases (78.33%, i.e., 47 out of 60), Gram-negative bacteria were isolated ($P < 0.05$ as determined by Binomial test calculation). It is worth mentioning that there were no cases of polymicrobial involvement, indicating the absence of multiple bacterial species in a single sample.Among the Gram-negative bacterial isolates, Escherichia coli accounted for the majority, with a prevalence of 63.82% (30 out of 47). Following E. coli, Klebsiella pneumoniae was the next most common isolate, representing 31.91% (15 out of 47) of the cases. The occurrence of E. coli was significantly higher compared to Klebsiella species ($P < 0.05$ as determined by Binomial test calculation). Among the Gram-positive isolates, Streptococcus pneumoniae was the predominant species, followed by Streptococcus agalactiae.

Table 1: Causative agents of bacterial meningitis in study population

Organism	Type	N	%	Total
Escherichia coli	Gram Negative	30	50.00	47
Klebsiella Pneumoniae		15	25.00	
Haemophilus influenzae		2	3.33	
Streptococcus pneumoniae	Gram Positive	8	13.33	13
Streptococcus agalactiae		5	8.33	
Total		**60**	**100**	

Table 2 shows that highest CRP levels were observed in cases of meningitis caused by Klebsiella Pneumoniae. Through the Fischer exact test, a statistically significant finding was observed, indicating that the serum levels of CRP were significantly higher in participants diagnosed with meningitis caused by Gram-negative bacterial isolates compared to those with Gram-positive isolates. This result is presented in Table 3.

Table 2: Organism wise CRP levels in study population

	CRP Levels	
Organism	**Mean**	**SD**
Escherichia coli	53.82	11.59
Klebsiella Pneumoniae	64.92	16.72
Haemophilus influenzae	44.00	21.21
Streptococcus pneumoniae	25.00	3.16
Streptococcus agalactiae	16.50	2.12

Table 3: CRP levels in bacterial meningitis cases (The Fischer exact test)

CRP levels	Bacterial Meningitis		Row Totals	P Value
	Gram Negative	Gram Positive		
Increased	42	9	51	< 0.05
Normal	5	4	9	
Column Totals	47	13	60	

Discussion

In summary, this study included 170 children with a median age of 3 years. There was a slightly higher number of female cases, although this difference was not statistically significant. Out of the 170 samples collected, only 32.67% were culture positive, indicating that the majority of cases were aseptic or viral meningitis. E. coli was the most common isolate, followed by K. pneumoniae. Approximately 30% of participants had elevated serum CRP levels, which were higher in cases caused by Gram-negative bacteria. The mean serum CRP level was also higher in Gram-negative cases.

The findings of this study are consistent with global studies, such as the one conducted by McGill et al. [17], which included 1126 patients enrolled between September 30, 2011, and September 30, 2014. In that study, 57% of the patients had meningitis, with 36% being viral, 16% bacterial, and 42% having an unknown cause. These similarities in findings suggest that the prevalence of different types of meningitis, including viral, bacterial, and unknown etiologies, is comparable across different studies conducted globally.

In this present study, Gram-negative bacteria, especially E. coli and Klebsiella pneumoniae, were significantly more frequently isolated compared to Gram-positive bacteria. No cases of polymicrobial involvement were observed. Among the Gram-positive isolates, Streptococcus pneumoniae was the predominant pathogen, followed by Streptococcus agalactiae. These findings differ from a study conducted by Oordt-Speets et al. [18], where Streptococcus pneumoniae and Neisseria meningitidis were the predominant pathogens in all age groups and regions, accounting for a significant proportion of cases. The prevalence of Streptococcus pneumoniae infection has been a growing concern, which aligns with the current study's finding of Streptococcus pneumoniae as the most common Gram-positive bacteria isolated [18, 19].

In the present study, the mean serum CRP value in meningitis caused by Gram-negative bacteria was 55.87 mg/L. This finding is in contrast to a study by Hansson et al., where they reported that 12% of patients with bacterial meningitis had serum CRP concentrations below 50 mg/L [20]. In this study, it was found that 30% of children had positive CRP on quantitative assay. The Fisher exact test revealed that the serum level of CRP was significantly higher in participants with meningitis caused by Gram-negative isolates compared to Gram-positive ones. According to the findings

of Sormunen et al., it has been noted that among the diagnostic tests investigated, serum CRP demonstrates the capability to differentiate Gram stain-negative bacterial meningitis (BM) from viral meningitis upon admission, exhibiting high sensitivity (96%), high specificity (93%), and a high negative predictive value (99%). The exclusion of BM based solely on conventional tests poses challenges. However, when combined with thorough physical examination and cerebrospinal fluid (CSF) analyses, the measurement of serum CRP provides significant assistance in the diagnostic process [21].

This study provides valuable insights into the bacterial causes of pediatric meningitis and highlights the diagnostic role of serum CRP in guiding empirical antimicrobial therapy. However, it is essential to acknowledge the limitation of this study, which is the incapability to identify viral and non-culturable etiologies.

Conclusion

The findings of this study indicate that E. coli is the most common bacterial cause of meningitis in the pediatric age group. Additionally, it was observed that children with meningitis caused by Gram-negative bacteria had significantly elevated levels of CRP. These findings have important implications for the selection of empirical antimicrobial therapy in suspected cases of pediatric meningitis with a bacterial etiology.

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