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Original Research Article

A Cross-Sectional Evaluation of C Reactive Protein in Children with Pyogenic Meningitis

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Abstract

Background and Objectives: Bacterial meningitis constitutes a significant global public health concern. C-reactive protein (CRP) serves as a suitable diagnostic marker to differentiate between bacterial and aseptic meningitis, particularly in cases with negative bacterial culture results in both blood and spinal fluid samples. This study aims to assess the serum level of CRP in pediatric meningitis cases of bacterial origin. The primary objective of this study was to estimate the serum CRP levels in pediatric meningitis cases caused by bacterial pathogens.

Materials and Methods: This hospital-based descriptive cross-sectional study was conducted at a tertiary care hospital located in India utilizing 250 samples. Cerebrospinal fluid samples were collected following standard guidelines. Bacterial identification and antimicrobial susceptibility testing were performed using automation. CRP levels were quantitatively estimated using a solid-phase, sandwich-format immunometric assay with a gold antibody conjugate.

Results: The median age of the cases was 4.1 years (1–5.3). Among the bacterial isolates, Escherichia coli was the most prevalent, followed by Klebsiella pneumoniae. Elevated serum CRP levels were observed in 29.33% of the participants. Significantly higher serum CRP levels were found in cases with Gram-negative bacterial etiology.

Conclusion: This study demonstrates a significant association between serum CRP levels and meningitis caused by Gram-negative bacteria. The findings suggest that elevated serum CRP may serve as a potential diagnostic marker for identifying bacterial meningitis cases with a Gram-negative etiology.

Keywords: Meningitis, C - reactive protein, Gram-Negative Bacteria, Child.

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Introduction

Bacterial meningitis (BM) remains a significant global public health concern, particularly in low-income countries, where the etiology of the causative bacterial isolates can vary based on age group and geographical location [1]. Despite advancements in antibiotic therapies and critical care, BM continues to present challenges in clinical medicine. Mortality rates, although reduced with effective antibiotics, can still reach up to 34%, and approximately 50% of survivors may suffer from long-term complications [2-4]. In the context of diagnosing BM, C-reactive protein (CRP) plays a vital role, especially when bacterial culture results are negative in blood and spinal fluid samples [5, 6]. CRP is a pentameric protein found in blood plasma, and its levels rise in response to inflammation. It is an acute-phase protein primarily produced by the liver in response to interleukin-6 secretion by macrophages and T-cells. CRP binds to lysophosphatidylcholine, present on the surface of dying cells and certain bacteria, thereby activating the complement cascade [8]. Normal CRP levels increase with aging, and higher concentrations are observed in conditions like advanced pregnancy, mild inflammatory states, viral infections (10-40 mg/L), active inflammation and bacterial infections (40-200 mg/L), and severe bacterial infections and burns (>200 mg/L) [10].

Although the diagnostic and prognostic value of CRP in bacterial and aseptic meningitis has been explored, its association with BM in the pediatric age group, particularly in low-income settings, lacks

extensive documentation. Therefore, this study aimed to estimate the elevation of CRP levels in pediatric meningitis patients, specifically those with bacterial etiology. The CRP assay represents a cost-effective and potentially valuable diagnostic and prognostic marker, which could be employed to guide empirical antimicrobial therapy in suspected cases of BM. The primary objective of this study was to estimate the serum CRP levels among pediatric meningitis cases with a bacterial etiology.

Material & Methods

The present investigation represents a hospital-based descriptive cross-sectional study conducted at a tertiary care center in India, spanning a duration of four months. The study's inclusion criteria encompassed patients meeting specific clinical, demographic, geographical, and temporal parameters. Instances, where the data's integrity could be compromised, were deliberately excluded from the analysis. To obtain cerebrospinal fluid (CSF) samples, aseptic lumbar puncture was performed following established guidelines, with the samples being collected in wide-mouth sterile universal containers and promptly transported for processing [1,11]. A total of 250 samples were meticulously selected for this study. These collected samples were subjected to inoculation on nutrient agar (basal media), MacConkey's agar (selective and differential media), blood agar (enriched media), and chocolate agar (enriched media, especially beneficial for Haemophilus influenzae). Subsequently, the inoculated culture plates were incubated aerobically at 37°C for 18-24 hours. For the isolation of capnophilic microorganisms, the candle jar technique was employed [12,13].

Phenotypic identification, along with antimicrobial susceptibility testing of bacterial species, was conducted using an automated system. The determination of Minimum Inhibitory Concentration (MIC) values was performed in accordance with the guidelines set by the CLSI-Clinical Laboratory Standard Institute [14]. Biochemical analysis necessitated the collection of 2 mL of venous blood from the study participants, which was then placed in a clot-enhancing tube devoid of any anticoagulant. Quantitative estimation of C-reactive protein (CRP) was carried out on the separated serum using a solid-phase, sandwich-format immunometric assay, employing a gold antibody conjugate, as per the manufacturer's instructions [15].

Results

A total of 250 children were enrolled in the study, and their demographic characteristics revealed a median age of 4.1 years with an interquartile range of 1 to 5.3 years. A slightly higher number of female cases were included in the study compared to male cases, although this difference was not statistically significant.

Among the 250 samples analyzed, 82 (32.80%) tested positive for bacterial growth in culture. Notably, there was a significantly higher frequency of Gram-negative bacteria isolated from the samples. Polymicrobial involvement was not observed in any of the cases. Escherichia coli was the most frequently isolated bacteria, followed by Klebsiella pneumoniae and Haemophilus influenzae. The prevalence of E. coli was significantly higher than that of Klebsiella species. Among the Gram-positive isolates, Streptococcus pneumoniae was the predominant pathogen, followed by Streptococcus agalactiae. [Table 1].

Table 1: Etiology of BM in children

Organisms isolated	Frequency	%
Gram Negative		
Escherichia coli	38	15.20
Klebsiella Pneumoniae	22	8.80
Haemophilus influenzae	3	1.20
Total	63	25.20
Gram Positive		
Streptococcus pneumoniae	12	4.80
Streptococcus agalactae	7	2.80
Total	19	7.60
Culture Negative	168	67.20

Quantitative assay of C-reactive protein (CRP) was performed, and it was found that 29.33% of the children had positive CRP levels. Tables 2 and 3 present additional details related to the findings. Through the Fischer exact test, it was observed that the serum levels of CRP were significantly elevated in participants with meningitis caused by Gram-negative bacteria compared to those with infections caused by Gram-positive bacteria [Table 3].

Table 2: Etiology wise distribution of CRP levels

Organisms isolated	CRP mg/dl (Mean ± SD)
Gram Negative	
Escherichia coli	52.77 ± 11.34
Klebsiella Pneumoniae	64.58 ± 17.51
Haemophilus influenzae	46 ± 21.21
Total	56.33 ± 14.96
Gram Positive	
Streptococcus pneumoniae	24.80 ± 4.21
Streptococcus agalactae	18.5 ± 2.12
Total	23 ± 4.69

Table 3: Elevated CRP in children with Gram-negative BM (Fischer exact test)

	Gram-negative BM	Gram-positive BM	Row total	F Value	P Value
Elevated CRP	60	12	72	0.0185	<0.05
Normal CRP	3	7	10		
Column total	63	19	82		

Discussion

In summary, this study involved a total of 250 enrolled children diagnosed with bacterial meningitis (BM). Among them, only 82 (32.8%) cases were culture positive, indicating that the majority of cases were likely due to aseptic or viral meningitis. The most common isolate was E. coli (60.52%), followed by K. pneumoniae. Polymicrobial involvement was not observed in any case. Approximately 29.33% of participants had elevated serum C-reactive protein (CRP) levels, and CRP was found to be higher in cases with Gram-negative bacterial etiology. Mean serum CRP was also higher in Gram-negative cases. Similar findings have been reported in other global studies. McGill et al. enrolled 1126 patients and found that 57% had meningitis, with 36% being viral, 16% bacterial, and 42% of unknown cause [15-17]. On the other hand, Oordt-Speets et al. [18] reported that S. pneumoniae and Neisseria meningitidis were the predominant pathogens in various regions, causing 25.1% to 41.2% and 9.1% to 36.2% of BM cases, respectively. In this present study, S. pneumoniae was the most common Gram-positive bacterium (63%).

The mean serum CRP value for meningitis caused by Gram-negative bacteria in this study was 56.33 mg/L, and it was significantly higher compared to cases caused by Gram-positive bacteria. Other studies have also noted varying CRP levels in meningitis cases. For instance, Hansson et al. reported 12% of BM patients with serum CRP concentrations below 50 mg/L. In the current study, 28.66% of children had positive CRP on quantitative assay [19, 20]. The diagnostic role of serum CRP was highlighted in distinguishing Gram-negative BM from viral meningitis with high sensitivity, specificity, and negative predictive value, as suggested by Sormunen et al. [21] However, this study's limitation is the inability to identify viral and non-culturable etiologies. In conclusion, this research sheds light on the bacterial etiology of pediatric meningitis and emphasizes the diagnostic significance of serum CRP in guiding empirical antimicrobial treatment. Nonetheless, further investigations are needed to identify viral and non-culturable causes for a comprehensive understanding of meningitis etiology.

Conclusion

Among pediatric meningitis cases, Escherichia coli (E. coli) emerged as the most common bacterial etiology. Additionally, it was observed that CRP levels were significantly elevated in children with BM caused by Gram-negative bacteria. These noteworthy findings have potential implications in guiding the adoption of empirical antimicrobial therapy for suspected cases of pediatric meningitis with bacterial etiology.

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