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Identifying the Importance of Cerebrospinal Fluid C - reactive protein (CSF-CRP) in Establishing a Diagnosis of Acute Bacterial Meningitis

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Abstract **Original Research Article**

Introduction: Acute meningitis is a major cause of death and disability worldwide. Differentiating bacterial from nonbacterial meningitis is very important in deciding on treatment. Bacterial meningitis is a life-threatening neurological condition and needs prompt parenteral antibiotics, compared to viral and aseptic meningitis which carries relatively better outcomes. ***Aim of the study:*** The aim of the study was to identify the importance of the CSF-CRP test in diagnosing acute bacterial meningitis. ***Methods:*** This cross-sectional observational study was conducted at the Department of Pediatric Medicine, Dhaka Shishu Hospital, Dhaka, Bangladesh. The study duration was 6 months, from January 2017 to June 2017. A total of 100 children visiting the inpatient department of the hospital were selected for the present study following inclusion and exclusion criteria. ***Result:*** 57% were diagnosed as bacterial meningitis cases, while 43% were diagnosed with aseptic meningitis. Among the 57 cases of bacterial meningitis, 61.40% belonged to the youngest age group of 0-2 years, while among the aseptic meningitis cases, 37.21% belonged to the age group of 3-6 years. Total WBC and PBN were significantly higher among the bacterial meningitis cases. The sensitivity of CSF-CRP was 89.47%, specificity 90.69%, accuracy 90%, a positive predictive value of 92.72%, and a negative predictive value of 86.66% in diagnosing bacterial meningitis. ***Conclusion:*** The study findings conclude CSF-CRP to be an important prognostic factor and initial testing method in diagnosing acute bacterial meningitis. CSF CRP has high diagnostic accuracy in determining the incidence of acute bacterial meningitis.

Keywords: Meningitis, Bacterial, Infection, CSF.

INTRODUCTION

Acute bacterial meningitis is a pediatric emergency with a high mortality and morbidity rate that must be identified and treated as soon as possible. It is a potentially serious infection that occurs in infants and older children, and it is a significant cause of mortality and morbidity. Differentiating between the different types of meningitis cases is necessary for appropriate treatment, but it is often difficult to distinguish between bacterial and viral meningitis cases using basic symptoms and tests. Some inflammatory mediators, such as IL-6 and CRP, have been shown to help distinguish between bacterial and viral meningitis [1]. Bacterial meningitis has a high mortality rate worldwide, but the incidence rate is much higher in developing countries (15%-50%) than in developed countries (4%-5%) [2]. Even among survivors, neurological complications affect about 15% to 20% of patients [3]. Without treatment, meningitis patients are almost certain to die, and even with minimal antibiotics, the mortality rate among infants can be as high as 40% [2, 3]. Rapid and accurate diagnosis, combined with early appropriate therapy, is critical in reducing patient morbidity and mortality [4]. To differentiate between types of meningitis, various testing methods such as culture and sensitivity, Gram stain, cytology, and biochemistry of cerebrospinal fluid (CSF) samples are used [5]. Among these methods, proper culture is influenced by antibiotic therapy, transportation delays, and the length of time required to isolate the organism, whereas the gram stain method lacks specificity and can produce false positive results due to a variety of outside factors [6]. To address these deficiencies, several rapid diagnostic testing methods based on CSF have been developed to diagnose acute bacterial meningitis. The presence of nuclear polymorph leukocytes in the CSF is a good predictor of pyogenic meningitis. Leukocyte count in bacterial meningitis may be elevated to greater than 1000/mm^3

and typically there is neutrophilic predominance (75%–95%) [7]. A CSF leukocyte count < 250/mm^3 may be present in as many as 20% of patients with bacterial meningitis [7]. However, the use of antibiotics may alter the CSF cytology from neutrophilic to lymphocytic predominance. Empirical antibiotic therapy is a commonly provided treatment. In such circumstances, the detection of C-reactive protein in CSF appears to provide a new dimension to the diagnosis of meningitis [8]. Blood or CSF analysis cannot distinguish all cases of aseptic from bacterial meningitis in young children with meningitis. As a result, patients with aseptic meningitis were often given expensive antibiotics for an extended period of time, putting financial strain on impoverished parents and extending hospital stays [9]. Serum CRP is an acute phase reactant used in the detection of newborn sepsis, urinary tract infection, pneumonia, and meningitis [10]. Carrol *et al*., used a latex slide agglutination test to detect CSF C-reactive protein, which was 100% sensitive and 94% specific in distinguishing bacterial meningitis from aseptic meningitis. CRP estimate can aid in the diagnosis of ABM patients more efficiently than culture [11]. Bangladesh is a developing country, with limited resources and a lack of skilled manpower, particularly in peripheral setup. An easy and comprehensive test to diagnose ABM would be an alternative tool to diagnose Acute Bacterial Meningitis (ABM). Routine use of CSF CRP in diagnosing ABM could be a reliable and easy method and can be done for rapid diagnosis of meningitis. It is not an alternative to CSF culture, cytology, and biochemistry, but for an initial quick assessment, it can be considered as the first line of investigation for suspected meningitis to differentiate ABM from aseptic cases in a rural or remote area where investigation facilities are limited. The test is also easily understood without the need for detailed training [12]. The present study was conducted with the goal of identifying the importance of cerebrospinal fluid C-Reactive Protein (CSF-CRP) in the diagnosis of acute bacterial meningitis.

OBJECTIVE

General Objective

- To observe the diagnostic accuracy of the CSF-CRP test in differentiating between different types of meningitis.
- To identify the importance of the CSF-CRP test in diagnosing acute bacterial meningitis.

METHODS

This cross-sectional observational study was conducted at the Department of Pediatric Medicine, Dhaka Shishu Hospital, Dhaka, Bangladesh. The study duration was 6 months, from January 2017 to June 2017. A total of 100 children visiting the inpatient department of the hospital were selected for the present study following inclusion and exclusion criteria. Informed written consent was obtained from the legal guardians of the children, and ethical approval was also obtained from the ethical review committee of the study hospital. A purposive sampling technique was used for the selection of the participants. Bacterial meningitis was defined as a CSF WBC count of 1,000-10,000/mm^3, while aseptic meningitis was defined as a CSF WBC count of around 1,000 mm^3, lymphocytic predominance, and glucose <40mg/dl. Data was collected using a pre-prepared questionnaire sheet through face-to-face interviews with the patient and guardian, and medical data were recorded in the same sheet after tests. Collected data was then analyzed using SPSS software v.20. The Chi-square test was used to analyze discrete variables. The statistical significance threshold was set to p-value≤0.05 (two-tailed). The confidence interval was set at a 95% level.

Inclusion Criteria

- Children between the age of 0-12 years
- Children presenting with fever and convulsions of short duration.
- Participants who had not received any antibiotics prior to admission and had characteristics of meningitis
- Children with bacterial /aseptic meningitis were diagnosed based on CSF findings.
- Patients whose guardians had given consent to participate in the study.

Exclusion Criteria

- Severely ill.
- Patients who had received antibiotics prior to admission in the study.
- Patients without bacterial or aseptic meningitis following operational definition.
- Unable or unwilling to answer the criteria question.
- Exclude those affected with other chronic diseases etc.

RESULTS

Table 1: Age Distribution of the participants (n=100)

Age in years	n	%
0-2	43	43.00%
3-6	27	27.00%
7-9	19	19.00%
10-12	11	11.00%

Among the total 100 participants, 43% were between the age of 0-2 years, 27% were from 3-6 years, 19% were from the age group of 7-9 years, and 11% were between the age of 10-12 years.

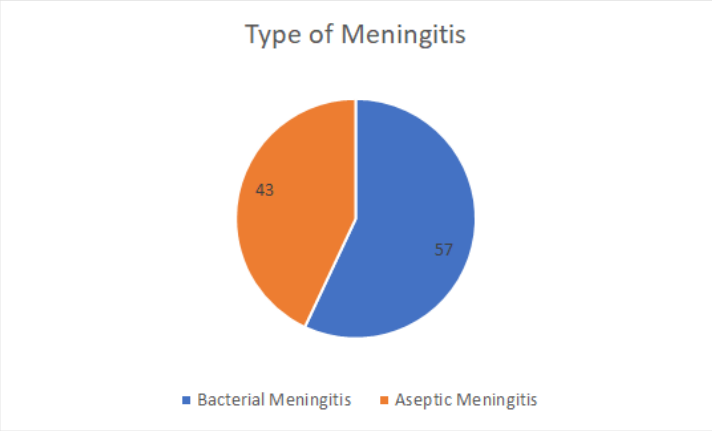

Figure 1: Distribution of the participants by type of meningitis (n=100)

Among the participants, 57% were diagnosed with bacterial meningitis cases, while 43% were diagnosed with aseptic meningitis.

Table 2: Distribution of the participants by types of meningitis according to age (n=100)

Age in years	Bacterial Meningitis (n=57)		Aseptic Meningitis (N=43)	
	n	%	n	%
0-2	35	61.40%	6	13.95%
3-6	11	19.30%	16	37.21%
7-9	7	12.28%	12	27.91%
10-12	4	7.02%	9	20.93%

Among the 57 cases of bacterial meningitis, 61.40% belonged to the youngest age group of 0-2 years, 19.30% were from the age group of 3-6 years, 12.28% were from the age group of 7-9 years and only 7.02% of the were from the oldest age group of 10-12 years. On the other hand, among the 43 aseptic meningitis cases, the majority (37.91%) belonged to the age group of 3-6 years, while 27.91% belonged to the age group of 7-9 years. Only 13.95% of the participants were from the youngest age group of 0-2 years.

Table 3: Laboratory Characteristics of CSF in studied patients

Parameters	Bacterial meningitis (n=57)	Aseptic Meningitis (n=43)	P value
	Range (Mean)	Range (Mean)	
Total WBC (mm^3)	70 – 22,000 (5021)	38 – 520 (158)	**<0.001**
PMN (%)	64 – 97(85)	0 – 56 (21)	**0.01**
Protein (mg/dl)	104 – 597 (316)	48 – 300 (112)	0.07
Glucose (mg/dl)	7 – 75 (28)	33 – 77 (54)	0.08

CSF findings of both bacterial meningitis and aseptic meningitis patients were measured comparatively in our study. Total White Blood Cell count was significantly higher in both range and mean value among the bacterial meningitis patients. The mean WBC count among bacterial meningitis patients was 5021 mm^3, and among aseptic meningitis cases, the mean was 158 mm^3. The mean polymorphonuclear leukocyte (PMN) count among bacterial meningitis cases was 85%, and among aseptic meningitis cases, it was 21%. The difference between them was statistically significant. The mean protein was 316 mg/dl and 112 mg/dl among bacterial and aseptic meningitis cases respectively. The difference between these values was not statistically significant. The mean glucose was 28 mg/dl and 54 mg/dl among bacterial and aseptic meningitis cases respectively, with no statistically significant difference.

Table 4: CSF C-Reactive Protein test results in study subjects

CSF CRP test Results (mg/L)	Bacterial meningitis (n=57)		Aseptic meningitis (n=43)		P value
	Number	Mean±SD	Number	Mean±SD	
CRP Positive	51 (89.47%)	21.7±10.9	39 (90.70%)	2.1±1.2 06	**<0.0001**
CRP Negative	6 (10.53%)		4 (9.30%)		
Total	**57 (100%)**		**43 (100%)**		

CSF CRP test was positive for 89.47% of the Bacterial meningitis cases, and 90.70% of the aseptic meningitis cases. The mean CRP was 21.7 mg/L among the positive cases of the bacterial meningitis group, while it was 2.1 mg/L among the CRP-positive cases of the aseptic meningitis group. This vast difference in the mean score was highly significant.

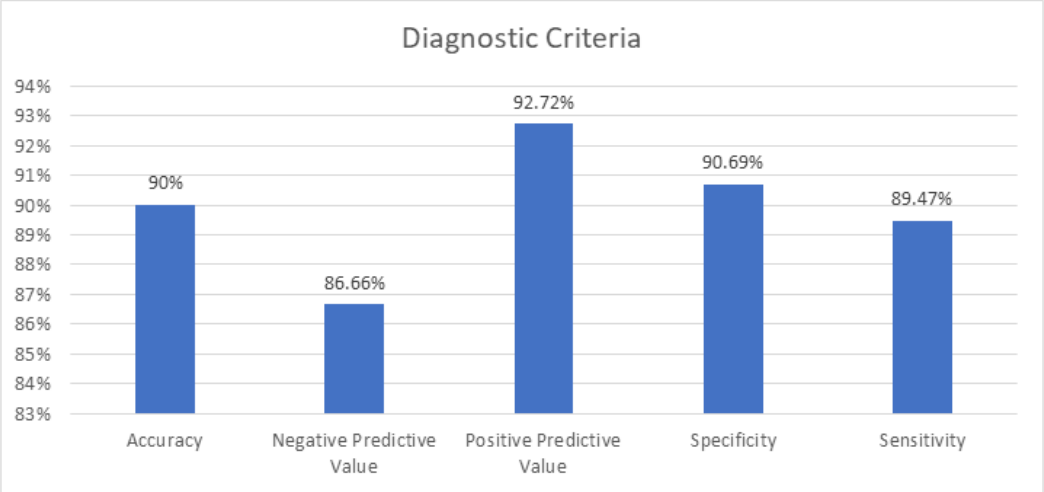

Figure 2: Sensitivity, Specificity, NPV, PDV & Diagnostic accuracy of the CSF-CRP test result

The sensitivity of CSF-CRP was 89.47%, specificity 90.69%, accuracy 90%, a positive predictive value of 92.72%, and a negative predictive value of 86.66% in identifying bacterial meningitis.

DISCUSSION

Bacterial meningitis is a potentially fatal disease. To decrease morbidity and mortality, early detection and adequate antibiotic therapy are critical. In poor nations such as Bangladesh, facilities for isolating blood- or CSF-borne pathogens are limited, and culture reports are time-consuming when they are available. To determine the etiology of meningitis at the bedside, a test that is simple, rapid, inexpensive, and reliable is required. CSF-CRP is a test that fits all of these criteria, and unlike CSF cytology and biochemistry, it does not need a high level of expertise to understand the data. Prompt recognition and early appropriate treatment are essential to reduce mortality and morbidity. The findings of the present study revealed that among a total of 100 cases, meningitis, in general, was more common among infants, with 43% of cases being under the age of 2 years, while another 27% were between the age of 3-6 years. Although different types of meningitis have different incident rates, some meningitis types are more common among the younger population [13]. Among the total 100 cases of the present study, 57 were diagnosed as ABM, while 43% were diagnosed as acute aseptic meningitis. Age-wise distribution of both these types of meningitis revealed that 61.40% of the bacterial meningitis cases had been from the age group of 0-2 years, compared to only 13.95% being among the aseptic meningitis cases. This was a considerable difference between the two groups. On the other hand, 12.28% of bacterial meningitis cases and 27.91% of aseptic meningitis cases belonged to the age group of 7-9 years. Bacterial meningitis cases observed a decrease as the age of the participants increased. This age distribution of both types of meningitis was similar to the findings of other studies [13, 14]. Among the different laboratory parameters, the total white blood cell count was between 70-22,000 among the bacterial meningitis cases, and between 38-520 among the aseptic meningitis cases. The mean WBC was 5021 mm^3 among the bacterial meningitis cases, and 158 mm^3 among the aseptic meningitis cases, and the difference between these factors was greatly significant. Similar findings in regards to WBC count have been observed in other studies as well, as bacterial meningitis patients tend to have increased WBC count regardless of age [15-18]. Similarly, a significant difference has also been observed in terms of leukocyte count (PMN), with mean PMN being 85% among bacterial meningitis cases and 21% among aseptic meningitis cases. Having a high PMN percentage can indicate the presence of infection in the patient body [18]. The mean protein count was also higher among the bacterial meningitis group, but this difference was not statistically significant. The mean glucose level was higher among the aseptic meningitis cases, compared to bacterial cases. In the present study, CSF-CRP was positive in 51 (89.47%) cases of Bacterial meningitis, and 3 (6.97%) cases of aseptic meningitis. The mean values of CRP (mg/L) were significantly higher among the bacterial meningitis cases, with a mean value 10 times higher among the bacterial meningitis cases. This was similar to the findings of multiple previous studies, where a high number of positive CSF-CRP tests was observed among bacterial meningitis patients [19-21]. Our study reported the CSF-CRP to have a Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Diagnostic Accuracy (DA) of 89.47%, 90.69%, 92.72%,

86.66%, and 90% respectively. This was also similar to the findings of other previous studies [19, 20].

Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

The study findings conclude CSF-CRP to be an important prognostic factor and initial testing method in diagnosing acute bacterial meningitis. CSF CRP has high diagnostic accuracy in determining the incidence of acute bacterial meningitis.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

RECOMMENDATION

The study was conducted within a short period. Further studies with larger sample sizes and more types of meningitis cases can be conducted to better understand the importance of CSF-CRP.

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