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COMPARING CSF PARAMETERS BETWEEN CHILDREN DIAGNOSED WITH BACTERIAL AND ASEPTIC MENINGITIS

Pediatrics

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ABSTRACT

Introduction: Diagnosis of meningitis in children cannot rely on clinical examination. Present study aimed to evaluate the role of CSF examination in differentiating bacterial from aseptic meningitis in children less than 14 years of age. **Methodology:** This observational cross-sectional study included children aged 1 month to 14 years with a diagnosis of meningitis. Children were classified as bacterial meningitis or aseptic meningitis. CSF examination was conducted to measure CRP, cell count, neutrophil count, lymphocytes, glucose levels and protein levels. Statistical comparison was made between children with bacterial meningitis and aseptic meningitis. **Results:** Children aged less than 2 years had the highest incidence of meningitis to the extent of 30.6%. CSF examination revealed than CRP was found to be positive in 81.82% of the patients with bacterial meningitis, while only 3.45% of the patients with aseptic meningitis had a positive CRP (p value < 0.001). It was observed that median cell count and neutrophil count were significantly higher among patients with bacterial meningitis as compared to those with aseptic meningitis. While, median lymphocyte count was significantly lower in patients with bacterial meningitis as compared to those with aseptic meningitis (p value < 0.001). Furthermore, we observed that CSF glucose less than 50% of that blood levels was observed in 81.82% of the patients with bacterial meningitis, which was significantly higher than those diagnosed with aseptic meningitis (p value < 0.05). **Conclusions:** CSF CRP and biochemical parameters like cell count, neutrophils and glucose levels can aid in differentiating bacterial from aseptic meningitis.

KEYWORDS

Aseptic meningitis; Bacterial meningitis; Biomarkers

INTRODUCTION

Worldwide, meningitis is a significant cause of morbidity and mortality in the pediatric population accounting for about 180,000 deaths annually. Haemophilus influenzae type b (Hib), Streptococcus pneumoniae, and Neisseria meningitidis were some of the most common organisms causing meningitis in children before the advent of vaccines for these. Due to the low acceptance and penetration of these newer vaccines in low and middle countries like India, bacterial meningitis continues to be a cause of concern. Population based studies from South Asian countries and retrospective hospital based studies from these regions have reported that 12.8% and 28% of the confirmed cases of invasive bacterial disease were due to S. pneumoniae, respectively.[4]

The constellation of symptoms of fever, nuchal rigidity, and changes in mental status, a well-known triad of meningitis, was observed in only 44% of patients with bacterial meningitis[5]. Thus, relying on the clinical history and physical examination of patients suspected of having bacterial meningitis could be misleading[6]. As the treatment varies according to the causative agent, it is important to diagnose the different types of meningitis quickly and accurately. As prior antibiotic therapy can affect the bacteriological diagnosis from cerebrospinal fluid (CSF) (Gram stain and culture may be negative in up to 80% cases), and culture facility is not available at primary and secondary health care level, rapid bedside diagnostic tests like measurement of CSF C-reactive protein (CRP) (latex agglutination or immunoturbidometric method) have been used in various studies[7]. The present study aimed to evaluate the role of CSF examination in differentiating bacterial from aseptic meningitis in children less than 14 years of age.

METHODOLOGY

Study Design and sample population

It was an observational cross-sectional study conducted in the Department of Paediatrics, College of Medical Sciences Teaching Hospital, Bharatpur, Nepal from October 2015 till September 2016, in which we included children aged 1 month to 14 years with a diagnosis of meningitis, admitted in our department during the study period. We excluded patients with congenital abnormality of the central nervous system, those who had conditions in which lumber puncture (LP) was contraindicated and immunocompromised patients. The parents of the children were explained the purpose of the study. For children less than 7 years of age, consent of the parent/legal guardian was obtained. For children aged 7 to 14 years oral assent of the child was obtained in the presence of the parent/legal guardian. The study was approved by the Institutional Ethics Committee.

Data Collection and Data Analysis

Using a pre-designed semi-structured study proforma, patient related information was obtained. The demographic information of the patients like age and gender were noted for all patients. The presenting complaints of the patients were noted as well. All patients underwent CSF examination. Two ml of CSF specimen was collected by lumbar puncture under aseptic precautions in sterile capped tubes and was sent for routine CSF examination. Investigations like cytology, neutrophils, lymphocyte count, glucose levels and proteins levels were done for all patients. For CRP estimation, semi quantitative method was employed which can be expressed as 6, 12, 18 mg/L etc. and level below 6 mg/L cannot be detected. Diagnosis of meningitis was based on the clinical picture and CSF examination reports and patients were categorized into bacterial and aseptic meningitis group.

Data was separately entered into SPSS (Statistical Package for the Social Science) version 20 analysis and descriptive statistics were performed. Numerical data were initially tested for normality using Sapiro-Wilk test. All numerical data failed to show normal distribution. So, nonparametric test (Man Whitney U test) was performed for statistical analysis and median were compared instead of mean. For categorical data Chi-square test was performed. A p value of less than 0.05 was considered statistically significant.

RESULTS

During the study period a total of 1332 cases were admitted in our department, out of which 62 cases were of meningitis. The total incidence of meningitis was 4.6% (62/1332). Of the 62 patients, 33 were diagnosed as bacterial meningitis and rest were aseptic

meningitis. Children aged less than 2 years had the highest incidence of meningitis to the extent of 30.6%. There were 30.2% children aged less than 2 years in the group of bacterial meningitis and 31% in the aseptic meningitis group (Table 1). Of the 62 cases, 71 % were males and 29 % were females. Altered sensorium was observed in 77.4% with bacterial meningitis and in 22.6% with aseptic meningitis. Vomiting was sobered in 79% of those with bacterial meningitis and 21% in those with aseptic meningitis. All cases diagnosed with bacterial meningitis had fever, while none of the patients with aseptic meningitis had fever. None of the patients with bacterial meningitis had rashes, while all patients with aseptic meningitis had rashes. CSF examination revealed than CRP was found to be positive in 81.82% of the patients with bacterial meningitis, while only 3.45% of the patients with aseptic meningitis had a positive CRP (p value < 0.001) (Table 2). It was observed that median cell count and neutrophil count were significantly higher among patients with bacterial meningitis as compared to those with aseptic meningitis. On the other hand, median lymphocyte count was significantly lower in patients with bacterial meningitis as compared to those with aseptic meningitis (p value < 0.001). Furthermore, we observed that CSF glucose less than 50% of that blood levels was observed in 81.82% of the patients with bacterial meningitis, which was significantly higher than those diagnosed with aseptic meningitis (p value < 0.05). Median protein levels were 66 mg/dl in patients with bacterial meningitis, which was statistically not significantly different from that of patients with aseptic meningitis, 56 mg/dl, p value = 0.48.

DISCUSSION

Meningitis is an emergency disease with a high rate of mortality and morbidity. Early diagnosis of meningitis is essential in order to improve the prognosis of the disease. The present study was conducted to evaluate differences in the CSF examination of patients who are diagnosed with either bacterial or aseptic meningitis. Although CSF culture is the gold standard for diagnosis of bacterial meningitis, only 4–70 % of meningitis patients are CSF culture positive.[8] So, combination of clinical and laboratory features is essential in diagnosis of meningitis suspected patients[9].

CRP levels have been used as rapid diagnostic tool in order to differentiate between pyogenic and viral infections in various clinical settings. Newly developed improved methods for the detection and quantification of C- reactive protein has enhanced its use in clinical medicine and made it an important diagnostic tool. We found that positive CRP was found in 81.8% of the patients with bacterial meningitis, which was significantly higher than the proportion of patients with aseptic meningitis. Mishra et al reported that mean CSF CRP levels were 2.32 ± 1.14 mg/dl in patients with bacterial meningitis which was significantly higher than those in patients with aseptic meningitis (0.43 ± 0.35 mg/dl), p value < 0.001[10]. In another similar study by Natani et al, CSF-CRP was positive in 35 (72.9%) cases of bacterial meningitis, 6 (14.3%) cases of aseptic meningitis.[11] Singh et al in their study had reported that 84% of their cases of pyogenic meningitis had a positive CSF-CRP.[12] John et al also in their study reported that 91% of the case of bacterial meningitis were CSF-CRP positive.[13] Malla et al in their study have also reported a statistically significant higher level of CRP in CSF of patient with bacterial meningitis as compare to those with aseptic meningitis.[14] However, Khanam R had reported only 35% of bacterial meningitis cases to be CSF-CRP positive.[15]

Range of WBC count in CSF reported in bacterial meningitis (mean = 1500 to 3143 cell/mL) was significantly higher than viral meningitis (mean = 159 to 539 cell/mL).[16] Likewise, we observed median white blood cell count to be 386 cells/cumm in bacterial meningitis cases and 48 cells/cumm in cases diagnosed as aseptic meningitis. It should be noted that the extensive difference in CSF WBC counts and lower cell counts may be possible in immunocompromised patients, children, pneumococcus and meningococcus immunocompetent meningitis patients. It should be noted that we excluded cases which were immunocompromised. The CSF WBC count was significantly higher in bacterial meningitis (mean = 4839 cell/mL), compared with viral meningitis (mean = 159 cell/mL) (p value < 0.001) in a research and at the cut-off value of 321 WBC cell/mL the sensitivity and specificity for bacterial meningitis were 80.6% and 81.4%, respectively.3 Dashti et al reported that the mean values of WBC count of CSF in bacterial meningitis and viral/aseptic meningitis patients were 3143 and 539 cell/mL, respectively and with NPV of 91.3% and PPV of 37%, this showed a high sensitivity and low specificity.[17]

CONCLUSION

Early diagnosis of bacterial meningitis can decrease the long term sequelae and mortality associated with it. CSF CRP is an easy and rapid investigation, which our study show can aid in differentiating bacterial from aseptic meningitis.

Table 1. Baseline characteristics of the patients included in the study

	Bacterial meningitis (n=33)		Aseptic meningitis (n=29)	
Variables	**N**	**%**	**N**	**%**
Age groups (years)				
Less than 2 years	10	30.25	9	31.00
2 to 5 years	6	18.04	8	27.58
6 to 10 years	8	24.24	10	34.42
11 to 14 years	9	27.24	2	6.84
Presenting complaints				
Altered sensorium	26	77.40	7	22.60
Vomiting	26	79.00	6	21.00
Headache	13	38.70	18	61.30
Fever	33	100.00	0	0.00
Seizures	24	72.60	8	27.40
Rashes	0	0.00	29	100.00

Table 2. Comparing CSF examination findings between bacterial and aseptic meningitis

CSF investigations	Bacterial meningitis (n=33)	Aseptic meningitis (n=29)	p value
C-reactive protein*			
Positive	27 (81.82%)	1 (3.45%)	< 0.001
Negative	6 (18.18%)	28 (96.55%)	
White blood cell count (cells/cumm)**	386	48	< 0.001
Neutrophils (cells/cumm)**	60	0	< 0.001
Lymphocytes (cells/cumm)**	35	92.5	< 0.001
Glucose level*			
Less than 50% of blood glucose level	27 (81.82%)	15 (51.72%)	< 0.05
More than 50% of blood glucose level	6 (18.18%)	14 (48.28%)	
Protein level (mg/dl)**	66	56	0.48
*n (%), analysed using chi-square test; **median values, analysed using Mann-Whitney test			

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