DOI: https://doi.org/10.54393/pjhs.v5i06.1647

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
ISSN (P): 2790-9352, (E): 2790-9344
Volume 5, Issue 6 (June 2024)

Original Article

The Role of Cerebrospinal Fluid High-Sensitivity C–Reactive Protein (CSF hsCRP) in Distinguishing Bacterial Meningitis from Aseptic Meningitis

Umaira Ahsan[1*], Faiqa Arshad[2], Rao Shahzad Abdul Tawwab Khan[3], Muneeba Naz[4,7], Saima Pervaiz[5], Omer Shahzad Khan Rao[6] and Attiq ur Rehman[7]

[1]Department of Pathology, Abu Umara Medical and Dental College, Lahore, Pakistan
[2]Department of Pathology, Gujranwala Medical College, Gujranwala, Pakistan
[3]Wazirabad Institute of Cardiology, Wazirabad, Pakistan
[4]Chughtai Laboratories, Lahore, Pakistan
[5]Department of Immunology, University of Health Sciences, Lahore, Pakistan
[6]Al Aleem Medical College, Lahore, Pakistan
[7]School of Allied Health Sciences, Lahore, Pakistan

ARTICLE INFO

Keywords:
Cerebrospinal Fluid, Bacterial Meningitis, Aseptic Meningitis, C-Reactive Protein

How to Cite:
Ahsan, U., Arshad, F., Khan, R. S. A. T., Naz, M., Pervaiz, S., Rao, O. S. K., & Rehman, A. ur. (2024). The Role of Cerebrospinal Fluid High-Sensitivity C-Reactive Protein (CSF hsCRP) in Distinguishing Bacterial Meningitis from Aseptic Meningitis: Role of CSF hsCRP in distinguishing meningitis. Pakistan Journal of Health Sciences, 5(06). https://doi.org/10.54393/pjhs.v5i06.1647

***Corresponding Author:**
Umaira Ahsan
Department of Pathology, Abu Umara Medical and Dental College, Lahore, Pakistan
umairaahsan747@hotmail.com

Received Date: 1st May, 2024
Acceptance Date: 15th June, 2024
Published Date: 30th June, 2024

ABSTRACT

One of the most prevalent serious diseases in newborns and infants is meningitis. Aseptic meningitis is generally less severe than bacterial meningitis and often has a better prognosis. CRP level is the most useful criterion for diagnosing feverish children with significant infections. **Objective:** The present study aimed to determine the level of CRP in CSF of bacterial meningitis, and aseptic meningitis for early prediction of meningitis and remove the lapse in its treatment. **Methods:** This cross-sectional study was conducted at the Immunology Department of The Children's Hospital & the Institute of Child Health from Jan 2022 to Jan 2023. The present study enrolled patients who had meningitis symptoms (fever, headache, vomiting, and neck stiffness), aged between >2 years to 12 years, both male and female gender. The CRP levels of all patients were measured using the agglutination method. Data were analyzed using IBM-SPSS version 26.0. **Results:** Of the total 45 patients, 20 (44.4%) were males and 25 (55.6%) were females. The mean age of patients was 5.98+2.792 years. From total, 29 (64.4%) had bacterial meningitis while 16 (35.6%) had aseptic meningitis. The 09 (31.03%) bacterial meningitis patients had positive CRP (>3.0mg/L). The present study showed a statistically significant association between CSF-CRP results with bacterial and aseptic meningitis (p=0.003). **Conclusions:** While awaiting the results of other confirmatory tests, CSF-CRP can be utilized as an early diagnostic tool for the identification of bacterial and aseptic meningitis. Additionally, it could aid in the early diagnosis of aseptic vs bacterial meningitis.

INTRODUCTION

The medical disease known as meningitis is defined by the inflammation of membranes that shield the brain and spinal cord. One of the most frequent serious diseases among newborns (less than one month old) and infants (less than one-year-old) is meningitis. The frequency of bacterial meningitis in children varies depending on age group; the highest prevalence is seen in newborns under two months of age [1]. Meningitis is caused by various pathogens, including bacteria, viruses, and fungi. Bacterial meningitis is more severe while viral meningitis is more prevalent [2]. It is common for some bacteria, such as *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Streptococcus agalactiae*, to cause infectious meningitis. Group B *streptococcus* causes bacterial meningitis in newborns. These bacteria also cause other serious illnesses (sepsis and pneumonia) and

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account for almost half of the meningitis deaths that occur worldwide. If untreated, bacterial meningitis is lethal [3]. Between 5 to 20% children and 20 to 50% adults die every year with this condition [4]. Over time, the spectrum of organisms responsible for disease may change. The prognosis for bacterial meningitis has improved because of the availability of novel β-lactam antibiotics, vaccination against *Haemophilus influenzae, pneumococci,* and *meningococci,* better intensive care, and supportive therapy in developed countries [5]. These measures have also decreased the prevalence of bacterial meningitis. The main causes of childhood morbidity and death in developing countries are low vaccination rates, delayed seeking medical assistance, malnutrition, delayed diagnosis, and delayed starting proper antibiotic therapy in cases of bacterial meningitis [6]. Meningitis which is caused by viral infections as opposed to bacteria is known as aseptic meningitis. An inflammation of the meninges that results in pleocytosis of the cerebrospinal fluid, no growth on a standard bacterial culture, and a sudden onset of headache, fever, and stiff neck is known as aseptic meningitis. Common viruses that can cause aseptic meningitis include Enteroviruses, Herpesviruses, and the Mumps virus. Aseptic meningitis is generally less severe than bacterial meningitis and often has a better prognosis, as it tends to resolve on its own with supportive care [7-8]. C-reactive protein (CRP) is an acute-phase inflammatory protein. It has been included in screening tests for febrile children in recent decades [9]. Globally, CRP level is the most useful criterion for diagnosing feverish children with significant infections [10-11]. Due to many reasons, there is a delay in the diagnosis of meningitis patients. Because CSF culture sensitivity takes 48-72 hours for reporting which cause a delay in treatment.

The present study aimed to determine the level of CRP in CSF of bacterial meningitis, and aseptic meningitis for early prediction of meningitis and remove the lapse in its treatment.

METHODS

The present cross-sectional study was conducted at the Immunology Department of The Children's Hospital & the Institute of Child Health from January 2022 to January 2023, after getting ethical approval letter (Ref No.1459/SAHS dated 06 Dec 2021). The sample size of 45 children was calculated by taking positive bacterial meningitis children as 89%, taking 5% margin of error and 95% confidence interval [12]. The present study enrolled the patients who had meningitis symptoms (fever, headache, vomiting, and neck stiffness), aged between >2 years and up to 12 years, both male and female [13]. Patients of more than 12 years of age, and who had other types of brain infections (encephalitis/ brain tumors) were excluded. The lumbar puncture (LP) of suspected patients was performed by a neuro-physician. The CSF samples were received at the pathology laboratory for analysis. The physical examination, gram stain, protein, glucose, and cell count (total and differential leukocyte) were performed. Meningitis was classified as bacterial meningitis based on CSF examination results (increased protein >100 mg/dL, decreased glucose <40 mg/dL, and leukocyte count 100-5000/mm3 with polymorph nuclear leukocyte domination >80%), gram staining results, and/or positive bacterial culture. Conversely, viral meningitis was described as occurring when the bacterial culture was negative but the viral culture, serological tests, pleocytosis, or reverse transcriptase polymerase chain reactions were positive [14]. After the initial arrangements for diagnosis and treatment, and with informed consent about 05cc of blood was taken from each patient and transferred to the Pathology Laboratory. The samples were centrifuged at the speed of 3000 rpm for serum separation. Using the Dot Diagnostic Gmbh Germany Kit (Reference No. ASO/200607, Lot No. 200607), the CRP level of each patient was determined. The normal value of CRP was considered as <3.0mg/L. Data were analyzed using Statistical Package for the Social Sciences version 26.0 (IBM SPSS version 26.0). The quantitative variables were summarized as mean + standard deviation while the qualitative variables were expressed as frequency and percentages. A chi-square test/Fishers exact test was performed to evaluate the association between variables.

RESULTS

In table 1, out of the total 45 patients, 20 (44.4%) were males and 25 (55.6%) were females. The patients had the ages between 02 years to 12 years old. The mean age of patients was 5.98+2.792 years. According to the CSF examination results, the patients were classified into bacterial meningitis and aseptic meningitis. From total, 29 (64.4%) patients had bacterial meningitis while 16 (35.6%) had aseptic meningitis.

Table 1: Demographic and Clinical Characteristics of Study Patients

Characteristics	Frequency (%)
Mean age (Y)	5.98+2.792
Age groups	
02 - 06 (Y)	27 (60.0%)
07 - 12 (Y)	18 (40.0%)
Gender	
Male	20 (44.4%)
Female	25 (55.6%)
Types of meningitis	
Bacterial meningitis	29 (64.4%)
Aseptic meningitis	16 (35.6%)

In figure1, out of a total of 29 bacterial meningitis patients, 13 (44.82%) were males and 16 (55.17%) were females, while from 16 aseptic meningitis patients, 07 (43.75%) were males and 09 (56.25%) were females.

DOI: https://doi.org/10.54393/pjhs.v5i06.1647

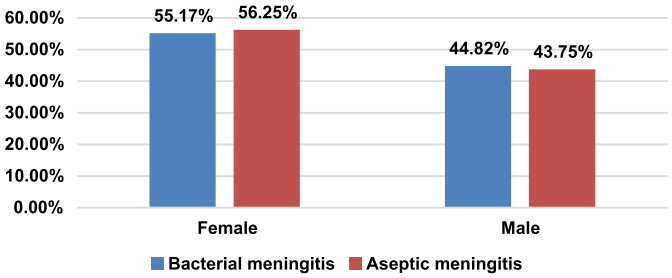

Figure 1: Gender Distribution of Bacterial and Aseptic Meningitis Study Patients

As illustrated in figure 2, according to the age groups, 18 (62.06%) bacterial meningitis, and 08 (50.0%) aseptic meningitis patients had an age between two to six years, while 11 (37.93%) bacterial meningitis and 08 (50.0%) aseptic meningitis patients had an age between seven to twelve years. The statistical association between gender, and age group with type of meningitis was estimated through the chi-square test. The present study found no statistically significant association between gender (p=0.597), and age groups (p=0.318) with types of meningitis. The p-value of <0.05 was considered statistically significant.

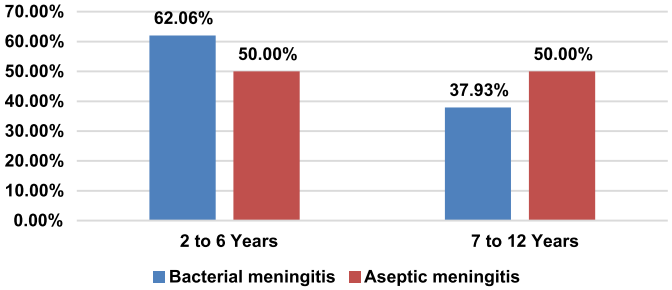

Figure 2: Age Group Distribution of Bacterial and Aseptic Meningitis Study Patients

Table 2 gives the picture of CRP values estimated in patients of bacterial and aseptic meningitis. The 20 (68.96%) bacterial meningitis and all aseptic meningitis patients had negative CRP (<3.0mg/L) while 9 (31.03%) bacterial meningitis patients had positive CRP (>3.0mg/L). The overall mean value of CSF-CRP was 2.216+1.697. The present study shows a statistically significant association between CSF-CRP results with bacterial and aseptic meningitis (p=0.003).

Table 2: CSF C-Reactive Protein Test Results in the Study Patients

CSF CRP Test Results	Bacterial Meningitis (n=29)		Aseptic Meningitis (n=16)		p-value (Chi-square)
	N (%)	Mean + SD	N (%)	Mean + SD	
CRP <3.0mg/L	20 (68.96%)	2.697 ± 1.9390	16 (100.0%)	1.344 ± 0.4211	0.003*
CRP >3.0mg/L	09 (31.03%)		0 (0.0%)		

*p-value is considered statistically significant.

DISCUSSION

In addition to being a frequent and dangerous infection in infancy and childhood, bacterial meningitis is a major contributor to child mortality and morbidity [15]. To prevent this, it is essential to identify the condition early and start treatment with a suitable drug [16]. In a nation with few resources like Pakistan, where it can be challenging and time-consuming to isolate organisms appropriately, a simple, fast, affordable, and accurate test is required. The present study was conducted to estimate the values of CSF-CRP in bacterial and aseptic meningitis patients. According to this study, CSF-CRP may be used in situations when it is challenging to isolate microbes. The findings from this hospital-based study showed that the age group most vulnerable to acute bacterial meningitis was young children. Most of the patients (60.0%) belonged to the 02-06 years of age group and were affected with bacterial meningitis. A study by Rahman *et al.*, also showed similar results [17]. The present study had a female preponderance (55.6%). The results of Bhatta *et al.*, study showed the male preponderance of meningitis patients [18]. The difference in results may be due to the population, and geographical differences. The study patients were mostly infected with bacterial meningitis (64.4%) as compared to aseptic meningitis (35.6%). The study conducted by Rahman *et al.*, enrolled 100 patients and showed that most patients were infected with bacterial meningitis (57.0%) [16]. Another cohort study conducted by Mintegi *et al.*, concluded that more patients were infected with aseptic meningitis (88.86%) [11]. In the present study, (68.96%) bacterial meningitis and all aseptic meningitis patients had negative CRP (<3.0mg/L) while the 09 (31.03%) bacterial meningitis patients had positive CRP (>3.0mg/L). The study by Rahman *et al.*, showed that (89.47%) of patients of bacterial meningitis, and 04 (6.97%) patients of aseptic meningitis had positive CSF-CRP [17]. According to Jadavinia *et al.*, patients with bacterial meningitis had statistically significantly greater levels of CRP in their CSF than those with aseptic meningitis. CRP value was 0.95±0.68 mg/L in septic and 0.16±0.36 mg/L in aseptic with statistically significant p<0.001 [19]. As per Jablr PM *et al.*, the mean CSF CRP values in cases of viral and bacterial meningitis were 3.16 and 4.44. They concluded that there was no difference (p=0.39) in the mean CSF CRP levels between viral and bacterial meningitis [20]. The present study shows a statistically significant association between CSF-CRP results with bacterial and aseptic meningitis (p=0.003). The overall mean value of CSF-CRP was 2.216 + 1.697. The mean value of CSF-CRP of bacterial meningitis was 2.697 + 1.9390, while the mean value of CSF-CRP of aseptic meningitis was 1.344 + 0.4211. According to Panji M *et al.*, the mean CRP of CSF was 55.22 ± 3.11 mg/L for bacterial meningitis and 7.5 ± 1.18 mg/L for aseptic meningitis. They also reported a statistically significant

DOI: https://doi.org/10.54393/pjhs.v5i06.1647

association (p=0.001) between CRP and meningitis [21]. The agglutination technique was used in this study to measure the CSF-CRP. Improved laboratory facilities might reduce the study's limitations by enabling the detection of hs-CRP concentrations in CSF samples.

CONCLUSIONS

The present study concluded that the CSF-CRP is associated with bacterial and aseptic meningitis. While awaiting the results of other confirmation tests, it can be utilized as an early diagnostic tool for the diagnosis of bacterial and aseptic meningitis. The current study also found that, in contrast to aseptic meningitis, bacterial meningitis had a considerably higher CSF-CRP level. Therefore, it could also aid in the early diagnosis of aseptic vs bacterial meningitis.

Authors Contribution

Conceptualization: UA, RSATK
Methodology: FA, MN
Formal analysis: UA, SP
Writing-review and editing: FA, OSKR, AR

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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