

Role of Cerebrospinal Fluid Pleocytosis and its Biochemical Parameters in the Diagnosis of Aseptic Meningitis

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ABSTRACT

Objective: To assess the role which CSF pleocytosis and its different biochemical parameters play in the diagnosis of aseptic meningitis,

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Frontier Medical College, Abbottabad from July 2017 to April 2018.

Materials and methods: All patients of both genders who were between the ages of 10 - 30 years and who were admitted with a suspected diagnosis of meningitis were included. All those patients who were suspected of suffering from fungal or tuberculous meningitis or who had traumatic lumbar puncture (LP) and those patients who were administered antibiotics prior to their LP were excluded. An experienced clinician made the diagnosis of meningitis considering history, physical examination as well as CSF results with significant emphasis laid on symptoms and signs of meningeal irritation (SOMI). CSF examination comprised of white blood cell count with quantification of neutrophil and lymphocyte counts, CSF protein & glucose levels and CSF Gram and ZiehlNeelsen (ZN) staining.

Results: There were 64 patients in this study. Out of which, 44 were male patients and 20 were female patients with a male to female ratio of 2.2:1. Fifty one patients, (79.69%), suffered from aseptic meningitis while 13 (20.31%) patients were suffering from bacterial meningitis. There were 51 patients who had aseptic meningitis and out of these, 37 patients were males while 14 patients were of female gender. Similarly, out of 13 patients who were diagnosed with bacterial meningitis, 07 patients were males while 06 patients were female. In patients with bacterial meningitis, white blood cell (WBC) count was distinctly higher and the predominant cell type was neutrophils while, on the other hand, lymphocytes were the chief WBC type in patients having aseptic meningitis. The mean protein levels were significantly raised in the CSF of patients who had bacterial meningitis in comparison to that of aseptic meningitis. Patients with bacterial meningitis exhibited distinctly lower levels of CSF glucose levels in comparison to those patients who had aseptic meningitis. Nearly all patients who were suffering from aseptic meningitis exhibited CSF lymphocytosis whereas 76.92% of patients who were suffering from bacterial meningitis had predominance of neutrophils.

Conclusion: Examination plays a pivotal role in the diagnosis of uncomplicated cases of meningitis. This is especially true when the CSF results were interpreted along with clinical findings in patients suffering from meningitis whether bacterial or viral. Nevertheless, advanced and more sophisticated laboratory tests should be carried out in complicated cases to make a correct and accurate diagnosis and to make a decision about the empirical drug therapy in these patients promptly

Key Words: meningitis, aseptic, CSF, pleocytosis

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INTRODUCTION

Meningitis is a serious medical disease which is associated with higher incidence of mortality.

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It is also associated with higher rate of debility especially in pediatric age group owing to permanent neurologic sequel.^{1, 2} It is estimated that more than one million cases of acute bacterial meningitis are reported annually and they primarily affect developing nations and certain geographical regions.^{3, 4} The term aseptic meningitis signifies a type of meningitis in which there is inflammation of meninges with predominance of lymphocytes in cerebrospinal fluid (CSF) and absence of bacteria.⁵ According to some, the term aseptic meningitis is considered tantamount to viral meningitis while others have a preference to call it lymphocytic meningitis.⁶ Therefore, these two terms can be used interchangeably. Clinical features and CSF findings

help to distinguish between these two types of meningitis.⁵

CSF examination is performed commonly in clinical practice. It yields invaluable information about the central nervous system (CNS), its status as well as its associated structures.⁷ Presence and type of white blood cell (WBC) in CSF, concomitant with its biochemical profile, aids in the identification of etiology well as to differentiate between different types of infections affecting the CNS as increased CSF leucocyte levels allude to an inflammatory process within CNS.⁸ Therefore, CSF examination and analysis is a vital part of workup of CNS disorders.

Bacterial meningitis constitutes a serious medical illness which needs prompt antibiotic therapy. Therefore, it is critical to distinguish it from other etiological causes of meningitis so as to make timely treatment decisions because any delay in starting drug therapy in these cases could lead to grave risk of debility and mortality.⁹ On the contrary, in patients who had aseptic meningitis, administering needless antibiotic treatment causes debility and greater economic expenditure.² Hence, timely, rapid and correct diagnosis of meningitis is crucial in such patients.¹ Therefore, this study is conducted to assess the role of CSF pleocytosis and its biochemical profile in the diagnosis of patients with aseptic meningitis.

MATERIALS AND METHODS

This was a prospective study which was conducted from July 2017 to April 2018 at Frontier Medical College, Abbottabad. All patients of both genders who were between the ages of 10 -30 years and who were admitted with a suspected diagnosis of meningitis were included. All those patients who were suspected of suffering from fungal or tuberculous meningitis or who had traumatic lumbar puncture (LP) and those patients who were administered antibiotics prior to their LP were excluded. An experienced clinician made the diagnosis of meningitis considering history, physical examination as well as CSF results with significant emphasis laid on symptoms and signs of meningeal irritation (SOMI) i.e. headache, vomiting, photophobia, seizures, changes in the level of consciousness, presence or absence of focal neurological signs and Kernig's or Brudzinski's signs. Laboratory investigations included complete blood count (CBC), blood sugar and CSF examination. CSF examination comprised of white blood cell count with quantification of neutrophil and lymphocyte counts, CSF protein & glucose levels and CSF Gram and ZiehlNeelsen (ZN) staining.

SPSS (version 22) was used to manage, quantify and analyse data. Percentages and frequencies were used to characterize categorical variables while mean±standard deviation was used to characterize numerical variables.

Student's t-test was done for statistical significance and p-value <.05 taken as significant.

RESULTS

There were 64 patients in this study. Out of which, 44 were male patients and 20 were female patients with a male to female ratio of 2.2:1, Figure 1. Majority of patients had shown SOMI.

Fifty one patients, (79.69%), suffered from aseptic meningitis while 13 (20.31%) patients were suffering from bacterial meningitis, Figure 2.

Stratifying according to the gender and type of meningitis, there were 51 patients who had aseptic meningitis and out of these, 37 patients were males while 14 patients were of female gender. Similarly, out of 13 patients who were diagnosed with bacterial meningitis, 07 patients were males while 06 patients were female, Table 1.

Table No.1: Stratification of patients according to gender and type of meningitis, (n=64)

Variable	Aseptic Meningitis		Bacterial Meningitis	
	Number	%age	Number	%age
Male	37	57.82%	7	10.94%
Female	14	21.87%	6	9.37%
Total	51	79.69%	13	20.31%

Table No.2: CSF values in patients with aseptic and bacterial meningitis, (n=64)

Variable	Aseptic Meningitis		Bacterial Meningitis		P-value
	Mean ± SD	Median	Mean ± SD	Median	
WBC (cells/mm3)	14.20 ± 51.51	02	7872 ± 17443.54	1080	0.130
Neutrophils (%)	3.04 ± 6.74	00	65.38 ± 27.95	80	0.000*
Lymphocytes (%)	96.96 ± 6.74	100	33.08 ± 25.70	20	0.000*
Glucose (mg/dL)	64.82 ± 29.18	62	31.08 ± 25.44	25	0.001*
Protein (mg/dL)	33.39 ± 12.52	30	168 ± 84.97	176	0.000*

* p-value < 0.05

As per the type of leucocytes present in the CSF examination of meningitis patients, nearly all patients who were suffering from aseptic meningitis exhibited CSF lymphocytosis whereas 76.92% of patients with bacterial meningitis had predominance of neutrophils, Table 3.

Table 2 represents the different parameters of CSF examination. Median values were also cited as there

was wide variation and skewness in the data. In patients with bacterial meningitis, white blood cell (WBC) count was distinctly higher and the predominant cell type was neutrophils while, on the other hand, lymphocytes were the chief WBC type in patients having aseptic meningitis, as shown in Table 2 & 3. Patients with bacterial meningitis exhibited distinctly lower levels of CSF glucose levels as compared to those patients who had aseptic meningitis, Table 2. The mean protein levels were significantly elevated in the CSF of patients who had bacterial meningitis in comparison to that of aseptic meningitis (p value <.05), Table 2.

Table No.3: Leucocyte differential in CSF of patients, (n=64)

Cell count	Aseptic	Bacterial
Lymphocytes > 50%	100 %, n = 51	23.08 %, n = 03
Lymphocytes < 50%	00 %, n = 0	76.92 %, n = 10

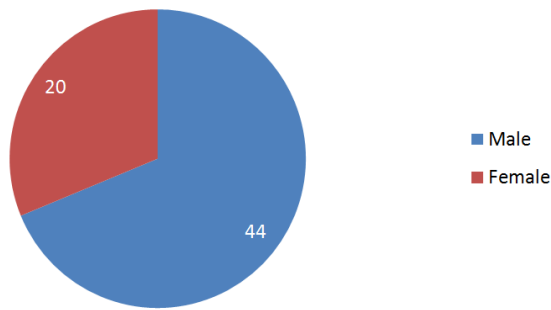


Figure No.1: Gender distribution of study patients, (n=64)

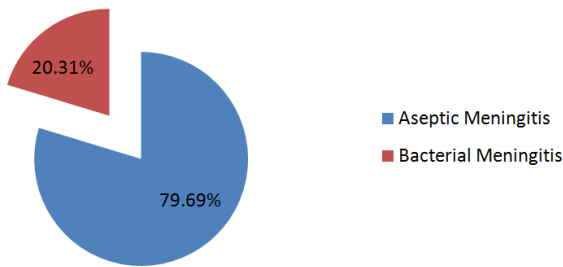


Figure No.2: Stratification of patients according to the type of meningitis, (n=64)

DISCUSSION

Meningitis is a CNS infection which is caused by a myriad of microorganisms. Amongst bacterial meningitis, the commonest bacteria causing meningitis are *N. meningitidis* and *S. pneumoniae* while amid aseptic meningitis, viruses and chiefly enteroviruses are responsible.^{2, 4, 10} Fever, vomiting, headache and neck rigidity characterizes meningitis. SOMI are frequently present in such cases.¹¹ However, CSF is required to make diagnosis and differentiate between different types of meningitis.

There was preponderance of male subjects, 68.75%, in our study. Similarly, there was a preponderance of male patients, 53%, as described by Egelund et al in their study.⁸ On the contrary, Agueda et al reported that the majority of their study subjects were females, 60.3%.² This discrepancy might be owing to the different regions in which these studies were conducted as Agueda et al performed their study in Portugal. Our study has reported the incidence of lymphocytic and bacterial meningitis to be 79.69% and 20.31% respectively. Equally, Amarilho et al stated that the frequency of aseptic and bacterial meningitis, amongst the confirmed cases of meningitis, was 89.65% and 10.35% respectively.¹² Contrarily, Abro et al reported a higher incidence of bacterial meningitis, 64.17%, as compared to aseptic meningitis, which was 35.82%.¹ Correspondingly, a higher rate of bacterial meningitis was described by Fouad et al whereas bacterial meningitis was responsible for 73.3% of cases and aseptic meningitis for 26.7%.⁴ This disparity of results among various studies could be due to variation in the place and timing of these studies as well as it might be owing to the difference in the vaccination status of the study participants.

CSF is a valuable laboratory test that aids considerably in the diagnosis and management of various CNS diseases. Presence or absence of leucocytes in CSF, their number and type has been regarded as a main criterion for the diagnosis of different CNS diseases.⁸ In this study, patients with aseptic meningitis had marked lymphocytosis while those with bacterial meningitis had discernible leukocytosis with predominant neutrophilia. Patients with bacterial meningitis had markedly raised CSF protein levels when compared with aseptic meningitis while their CSF glucose levels were characteristically lower as compared to aseptic meningitis. Our findings corroborated with other studies. Abro et al conducted their study in UAE. They have also reported a raised leucocyte count with predominance of neutrophils, elevated protein and lower glucose levels in the CSF of their patients with bacterial meningitis.¹ Equally, many other researchers have described markedly raised levels of CSF protein in patients with bacterial meningitis.^{12, 13} Likewise, many other investigators have reported neutrophilia with lower glucose levels in the CSF of patients with bacterial meningitis while predominant lymphocytosis and a normal glucose levels in patients with aseptic meningitis.^{2, 5, 8, 14, 15} We haven't performed advanced laboratory investigations e.g. polymerase chain reaction (PCR) as they were expensive laboratory procedures and concurrently being a developing state, they were only available at a very few advanced centers in our country. Aseptic meningitis can be differentiated from bacterial meningitis based on CSF analysis but this is not beyond limitations. In these patients, history and more sophisticated investigations e.g. viral culture, PCR,

considering for carcinomatous cells and fungal causes of CNS diseases like histoplasmosis, should be carried out to arrive at correct diagnosis. Likewise, other causes of aseptic meningitis e.g. malignancy, chemicals or drugs (baclofen, methotrexate, intravenous immunoglobulins), etc. should be considered while making diagnosis in such cases.^{6, 16}

CONCLUSION

CSF analysis plays a pivotal role in the diagnosis of uncomplicated cases of meningitis. This is especially true when the CSF results were interpreted along with clinical findings in patients suffering from meningitis whether bacterial or viral. Nevertheless, advanced and more sophisticated laboratory tests should be carried out in complicated cases to make a correct and accurate diagnosis and to make a decision about the empirical drug therapy in these patients promptly.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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