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Comparison of Laboratory Profiles of Cerebrospinal Fluid among Bacterial and Viral Meningitis Patients

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Abstract

Background: Laboratory profiles are important markers for the detection of meningitis. **Objective:** The purpose of the present study was to compare of laboratory profiles of cerebrospinal fluid among bacterial and viral meningitis patients. **Methodology:** This cross sectional study was carried out in the Department of Microbiology at Mymensingh Medical College, Mymensingh, Bangladesh from July 2010 to January 2012 for around 2 years. Clinically suspected patients with meningitis from paediatrics wards of MMCH, Mymensingh, Bangladesh were included in this study. On the basis of cytological tests and biochemical tests of CSF the study subjects were categorized into three groups, which were identified as bacterial meningitis, viral meningitis and normal CSF. After collection of CSF, physical examination, routine bed side culture and appropriate biochemical tests were performed. Tests for protein and glucose of CSF specimens were performed. **Result:** A total 115 clinically and laboratory confirmed meningitis patients were enrolled in this study. The most of the cases of study population were in the age group 1 month to 5 years 97(84.3%) cases. Regarding the physical findings of CSF, purulent was found 21(60.0%) cases in bacterial meningitis and 14 (40.0%) cases were slightly turbid. The mean with SD of total count of WBC was higher in bacterial meningitis (1623.1±1708.06/mm3) than viral meningitis (56.0±73.83/mm3) (p=<0.001). Again the mean with SD of glucose was lowest in bacterial meningitis which was 21.0±9.77 mg/dL followed by viral meningitis which was 63.6±20.22 mg/dL. (p<0.001). Considering protein of CSF the mean with SD was highest in bacterial meningitis which was 242.8±188.09 mg/dL followed by viral meningitis which was 69.6±84.67mg/dL (p<0.001). **Conclusion:** In conclusion the WBC count, CSF glucose and protein are significantly differ in bacterial and viral meningitis. *[Journal of National Institute of Neurosciences Bangladesh, January 2021;7(1): 69-74]*

Keywords: Comparison; laboratory profiles; cerebrospinal fluid; bacterial meningitis; viral meningitis; meningitis

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Introduction

The high mortality and morbidity is resulting from bacterial meningitis; thus, rapid and accurate diagnosis is needed to increase the survival rate and decrease complications[1]. Therefore delay in diagnosis and initiation of proper antimicrobial therapy can result a

poor outcome. Bacterial meningitis cannot always be diagnosed on the basis of clinical sign and symptoms[2]. Therefore, laboratory support is essential for the rapid diagnosis of meningitis[3].

Conventional methods for diagnosis of bacterial meningitis is based on examination of CSF including physical, biochemical, cytological, Gram's staining and culture[4]. Though Gram's stain is simple, rapid and less expensive method for detecting bacteria but it has some limitations. Its sensitivity and specificity depends on skill hands with appropriate techniques. Gray and Fedorko[5] mentioned that in Gram's stains, concentrations less than 10^3 CFU/ml of CSF are associated with positive findings in 25.0% whereas concentrations of bacteria more than 10^5 CFU/ml of CSF lead to positive results in up to 97.0% of cases[6]. The "gold standard" for diagnosis of any infection including meningitis is the isolation and identification of the causative agent[7]. However, it requires a day or more for growth and can also give false result if not properly transported and stored as they are fastidious organisms[8]. Alamgir et al[9] from Bangladesh mentioned that positivity of Gram's stain and culture may decrease to 40.0 to 60.0% and less than 50.0% respectively in patients who have received prior anti-microbial therapy. Das et al[4] reported that the sensitivity of Gram's stain and CSF culture were 18% and 0% respectively in patients who have received antimicrobial therapy. Antibiotic therapy may cause alteration of CSF cytology, biochemical findings and also failure of detection of causative organism, so the diagnosis may be delayed[9]. Moreover, in primary level hospital culture facility is not available.

An alternative method for the diagnosis of bacterial meningitis is required which is rapid, reliable, less time consuming, easy to perform, sensitive and specific[10]. Latex agglutination test (LAT) may be an important diagnostic tool which fulfills the above criteria. LAT is sensitive and specific for *Streptococcus pneumoniae*, Haemophilus influenzae type b, group B *Streptococcus, Neisseria meningitidis* group *A, C, Y, W135, Neisseria meningitidis* B and *Escherichia coli* k1 antigen[11]. LAT has been proven to be useful but are not entirely satisfactory because of inadequate sensitivity and specificity. Reliable results are obtained only for samples containing more than 10^5 CFU per ml, but approximately 45.0% of patients with meningitis have less than 105 CFU per ml[12].

Polymerase chain reaction (PCR) is also highly sensitive and specific technique for diagnosis of bacterial meningitis[13]. Reller et al[14] from New Zealand found sensitivity and specificity of PCR to detect pneumococcal meningitis 92.0% to 100% and 100.0% respectively in their study. PCR now can detect low number of pathogens in clinical specimens which does not require the presence of viable organisms[14]. Detection of *LytA* gene by PCR may be the alternate method to diagnose pneumococcal meningitis[13]. The purpose of the present study was to compare of laboratory profiles of cerebrospinal fluid among bacterial and viral meningitis patients.

Methodology

This cross-sectional study was carried out in the Department of Microbiology at Mymensingh Medical College, Mymensingh, Bangladesh. This study was conducted during the period of July 2010 to January 2012 for around 2 years. Clinically suspected patients with meningitis from paediatrics wards of MMCH, Mymensingh, Bangladesh were included in this study, due to limitation of budget, time and resource. Clinically suspected patients of meningitis with 0 to 18 years of age, high body temperature, feeding problems, vomiting, irritability, seizures or sluggishness, high pitched crying were included in this study. Patients treated with antibiotics after admission, patients above 18 years of age or with brain hypoxia and brain trauma were excluded from this study. Study population were divided into categories according to the criteria of CSF. On the basis of cytological tests and biochemical tests of CSF the study subjects were categorized into three groups, which were identified as bacterial meningitis, viral meningitis and normal CSF[15]. The protocol was approved by ethical review committee of Mymensingh Medical College Hospital. Informed written consent was taken from each patient or from their parents before his or her entry into the study after counseling the whole procedure in Bengali. After collection of CSF, physical examination, routine bed side culture in Blood agar, Chocolate agar medium and MacConkey agar media were performed. Tests for protein and glucose of CSF specimens were performed. The tests were done using by commercially available colorimetric reagent methods. It was done as per manufactures instructions. Protein estimation of CSF (DiaSys Diagnostic Systems GmbH & Co. KG, Germany). C-reactive protein (High sensitivity C-reactive protein Enzyme Immunoassay Test Kit (LumiQuick Diagnostics, Inc. U.S.A). Detection of bacterial antigen by latex agglutination test (LAT): (Remel Europe Ltd. UK). Statistical analysis of the study was done by computer software device as the Statistical Package for Social Science (SPSS) version

22.0. Confidence interval was considered at 95% level. The qualitative variables were expressed as frequency and percentage and the quantitative variables were expressed as mean with standard deviation. During analysis chi-square test was done to estimate the relationship or association between qualitative variables. P value less than 0.05 was considered statistically significant.

Results

A total number of eighty (80) patients of traumatic head A total 115 clinically and laboratory confirmed meningitis patients were enrolled in this study and the following tests were done from CSF includes cytology test, biochemical test, Gram's stain, culture, LAT, PCR and level of C-reactive protein. The most of the cases of study population were in the age group 1 month to 5 years 97(84.3%) cases. The age distribution among the bacterial meningitis (35) shows the maximum 17(48.5%) cases in the age group 1 month to 1 year followed by 11(31.4%) cases in the age of more than 1 year to 5 years (Table 1).

Regarding the physical findings of CSF, purulent was found 21(60.0%) cases in bacterial meningitis and 14 (40.0%) cases were slightly turbid. Clear CSF were found in 57(83.8%) cases in viral meningitis and 12(100.0%) cases in normal CSF (Table 2).

The mean with SD of total count of WBC was highest in bacterial meningitis which was 1623.1±1708.06/mm3 followed by viral meningitis which was 56.0±73.83//mm3. However, the mean with SD of total count of WBC in normal CSF was 0.25±0.87/ mm3. The difference of mean with SD of total count of WBC among bacterial and viral meningitis with normal CSF values were statistically significant (p<0.001). Again the mean with SD of glucose was lowest in bacterial meningitis which was 21.0±9.77 mg/dL followed by viral meningitis which was 63.6±20.22 mg/dL. However, the mean with SD of glucose in normal CSF was 74.2±20.80 mg/dL. The difference of mean with SD of glucose among bacterial and viral meningitis with normal CSF values were statistically significant (p=<0.001). Considering protein of CSF the mean with SD was highest in bacterial meningitis which was 242.8±188.09 mg/dL followed by viral meningitis which was 69.6±84.67mg/dL. However, the mean with SD of protein in normal CSF was 22.9±21.58 mg/dL. The difference of mean with

Table 1: Age distribution of the study population (n=115)

Age Group	Bacterial Meningitis	Viral Meningitis	Normal CSF	Total
Neonates (0-28 days)	2(5.7%)	4(05.8%)	0(0.0%)	6(05.2%)
1 month to 1 Year	17(48.5%)	26(35.2%)	6(50.0%)	49(42.6%)
1 to 5 Years	11(31.4%)	33(48.5%)	4(33.3%)	48(41.7%)
5 to 10 Years	5(14.2%)	5(07.3%)	2(08.3%)	12(10.4%)
10 to 18 Years	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Total	**35(100.0%)**	**68(100.0%)**	**12(100.0%)**	**115(100.0%)**

Table 2: Physical findings of CSF in the study population (n=115)

Physical Appearance of CSF	Bacterial Meningitis	Viral Meningitis	Normal CSF	P value
Purulent	21(60.0%)	0(0.0%)	0(0.0%)	
Slightly Turbid	14(40.0%)	11(16.1%)	0(0.0%)	
Clear	0(0.0%)	57(83.8%)	12(100.0%)	<0.05
Total	**35(100.0%)**	**68(100.0%)**	**12(100.0%)**	

Table 3: Comparison of Cytological and Biochemical Examination of CSF of the Study Population (Mean±SD)

Tests of CSF	Bacterial Meningitis	Viral Meningitis	Normal CSF	P value
TC WBC/mm3	1623.1±1708.06	56.0±73.83	0.25±0.87	<0.001
Glucose (mg/dL)	21.0±9.77	63.6±20.22	74.2±20.80	<0.001
Protein (mg/dL)	242.8±188.09	69.6±84.67	22.9±21.58	<0.001

SD of protein among bacterial and viral meningitis with normal CSF values were statistically significant (p<0.001) (Table 3).

There was a highly significant difference in total count of WBC (p=0.001), the level of glucose (p=0.001) and protein (p=0.001) in CSF among the bacterial meningitis, viral meningitis and normal CSF (Table 4).

Table 4: Multiple Comparisons with Post Hoc Test of Bonferroni

Variables	Tye of Infection			P value
Glucose	Bacterial	Vs.	Viral	<0.001
			Normal	<0.001
	Viral	Vs.	Bacterial	<0.001
			Normal	0.18
Protein	Bacterial	Vs.	Viral	<0.001
			Normal	<0.001
	Viral	Vs.	Bacterial	<0.001
			Normal	0.68
WBC	Bacterial	Vs.	Viral	<0.001
			Normal	<0.001
	Viral	Vs.	Bacterial	<0.001
			Normal	1.00

Discussion

A total of 115 clinically suspected meningitis patients age ranging from 0 day to 18 years were included in the study, CSF samples were collected and analyzed by the above mentioned tests for detection of bacterial meningitis during the period from July 2010 to January 2012.

In this study, on the basis of cytological and biochemical examination of CSF, the study population was categorized into three groups. It has found bacterial meningitis 35 (30.4%) cases, viral meningitis 68 (59.1%) cases and normal CSF 12 (10.4%) cases. Alamgir et al[9] from Bangladesh and Nussinovitch et al[16] from Israel also observed similar categories of the study populations in their study. Alamgir et al[9] in Bangladesh had observed identical categories of the patients having clinically suspected meningitis where they had observed bacterial meningitis 38 (25.34%), aseptic meningitis 94 (62.66%) and non-meningitis 18 (12.0%). This finding is consistent with the present study. Similarly, Narchi[17] in Saudi Arabia observed in his study that 35 (35.7%) were bacterial meningitis and 63 (64.3%) were aseptic meningitis, which are comparable with the present study. Similar findings were also reported by Nussinovitch et al16 from Israel, Gurley et al[18] and Chowdhury et al[19] from Bangladesh, where they found 19.74%, 24.0% and 20.0% of bacterial meningitis cases respectively.

In this study, the age of the study population ranges from 20 days to 10 years in case of bacterial meningitis, 14 days to 10 years in case of viral meningitis and 3 months to 8 years in case of normal CSF findings. Das et al[4] also observed parallel age range among the total study population, where they found the age ranges from 3 months to 13 years of age in their study. In the present study, majority of study population 42.6% were in the age range from 1 month to 1 year and 41.7% were in the age range from 1 year to 5 years. Chowdhury et al[19] from Bangladesh also found 49.6% cases in the age ranges from 1 month to 1year and 26.2% cases in the age ranges from 1 month to 5 years which are almost similar to the present study.

In this present study, among the bacterial meningitis, the male and female ratio was 65.7:34.2, in viral meningitis 54.4:45.5 and in normal CSF 58.3:41.6. As regards to the incidence of meningitis in male and female, Taskin et al[20] observed in their study, male and female ratio was 59.1:40.9 in bacterial meningitis, 72.7:27.3 in viral meningitis and 60:40 in normal CSF findings which are comparable with the present study. Similar findings were reported by Das et al[4] in India. The results of the present study closely resemble with the above mentioned study. No significant difference was found among the three groups regarding the sex incident in this study. The higher rate of positivity of bacterial meningitis in male subjects may be due to inclusion of higher number of male patients in this study population.

In the present study, all the cases of study population were presented with fever (100%). In In the present study, 7(20.0%) cases yielded positive by culture, 6(17.1%) cases positive in Gram's stain, increased WBC count in 35(100.0%) cases with neutrophilia, with low glucose contents and elevated protein level were in all cases (100%) of the bacterial meningitis. These findings of culture, Gram's stain and biochemical test in bacterial meningitis patients are almost similar to a study by Chowdhury et al[19] in Bangladesh. Ceyhan et al[21] in Turkey had observed similar findings in their study where cultures were positive in 10.0% of cases. Begum et al[11] in Bangladesh also found Gram's stain positive 13.3% in their study which were almost similar with this study. Alam et al[22] in Bangladesh and Das et al[4] in India reported in their research 13.7% and 06.0% bacterial isolation among bacterial meningitis cases respectively which are similar with this study.

Among the 68 viral meningitis cases it was observed that WBC count were more than 5 / mm^3 in all cases with predominant lymphocyte in all the cases 68(100.0%), protein level were less than 45 mg/dl in 42(61.7%) cases and glucose contents were less than 45 mg/dl in 10(14.7%) cases. It was observed that culture, Gram's stain, cytology and biochemical test were comparable with Saha et al[13] from Bangladesh, where they found negative CSF culture and Gram's stain with cell count 06-99 / mm^3 with lymphocytosis, normal protein and glucose level.

Among the 12 normal CSF cases it was observed that WBC count was ≤5 / mm^3 in all cases, where all the cells are lymphocytes 12 (100.0%), protein level were <45 mg/dl in 9 (75.0%) cases and glucose contents were more than 45 mg/dl in 11 (91.6%) cases. It was observed that culture, Gram's stain, cytology and biochemical test were analogous with Alamgir et al[9] in Bangladesh, where they found culture and Gram's stain negative with normal CSF cytology and normal protein and glucose level.

In this study, the total count of WBC (per cubic mm) was increased (1623.06 ±1708.06), the level of glucose (mg/dl) was reduced (21.04±9.77) and the level of protein (mg/dl) was elevated (242.77±188.08) in bacterial meningitis. Therefore, these findings proved that the conventional methods may also be a useful tool for categorizing the meningitis as bacterial meningitis, even in the absence of facilities for doing other methods. In this study it was observed that among the 35 bacterial meningitis cases Gram's stain, culture and LAT positive were in 15 (42.8%). Gram's stain negative, culture negative and LAT positive were in 9 (25.7%) cases. Gram's stain's negative, culture positive and LAT positive were in 1(02.8%) cases. The rate of detection of 35 bacterial meningitis cases by different methods showed that culture positive were in 7 (20.0%) cases, Gram's stain positive 6 (17.1%) cases and LAT positive were in 15 (42.8%) cases. In this study culture positive cases were more than gram's stain cases it may be due to less bacterial load in this CSF specimen. The results of the present study resemble with the Abro et al1 and Alamgir et al[9] where they also found gram's stain positivity was less than culture in their study. Alamgir et al[9] from Bangladesh also mentioned that Gram's stain and culture may decrease to 40.0 to 60.0% and less than 50% respectively in patients who have received prior anti-microbial therapy. In Gram's stains, concentrations less than 10^3 CFU/ml of CSF are associated with positive findings in 25% whereas concentrations of bacteria more than 105 CFU/ml of CSF lead to positive results in up to 97% of cases[23]. The low frequency of Gram's staining positive and culture positive in this study may be due to antibiotic intake in higher number of cases prior to CSF collection.

Conclusion

In conclusion highly significant difference is found laboratory profiles. The total count of WBC, glucose level and protein level in CSF are significantly different in bacterial, viral meningitis and normal CSF. A large scale study should be carried out in multi-centre basis to get the real scenario.

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