Original Article

ANALYSIS OF CEREBROSPINAL FLUID ANALYTES IN BACTERIAL AND TUBERCULOUS MENINGITIS

Noreen Samad, Sadia Jabeen, Iqra Zulfiqar

Department of Biochemistry, Bahauddin Zakariya University, Multan, Pakistan

ABSTRACT

Objective: Meningitis is the severe and lethal infection spread worldwide. The most common forms of meningitis are viral and bacterial meningitis caused by Neisseria meningitides and other species. Tuberculous meningitis (TBM) is the most mortal form of *Mycobacterium tuberculosis* infection, which has a high rate of neurological complications and sequelae. The best method for diagnosis of meningitis is cerebrospinal fluid analysis (CSF). The purpose of present study is to determine the CSF examination (glucose and protein levels) of subjects with bacterial meningitis (BM) and TBM and their comparison with healthy individuals.

Study Design: Cohort Study.

Place and Duration of study: The study was conducted in Children Medical Complex Hospital Multan, during February 2016 to June 2016.

Materials and Methods: The data of 75 children (25 of TBM, 25 of BM and 25 of normal) with age <5 years was collected. The analysis of CSF protein and glucose levels was done by standard methods. The data was statistically analyzed by using SPSS software (version 20).

Results: Results showed that levels of glucose in CSF were decreased in BM and TBM than normal individuals, whereas, in TBM glucose levels were more decreased than BM. On the other hand, the levels of protein were high in both diseases bacterial meningitis and TBM than normal individuals.

Conclusion: It is concluded that, poverty, sneezing, coughing, low nutritional quality of meals and unhygienic conditions are responsible for meningitis. Earlier diagnosis can might prevent the disease but severe form of this disease need effective antibiotic treatment. Vaccination also plays an efficient role in prevention of meningitis.

Keywords: Meningitis, BM, TBM, CSF analysis, Glucose, Protein.

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INTRODUCTION

Meningitis is an inflammation of the meninges (membranes that enclose the brain and spinal cord) disturbing the pia, arachnoid, and subarachnoid space in retort to bacteria and bacterial products [1]. It becomes the main apprehension of World Health Organization (WHO), now days. There are elevated risks of meningitis in individuals and they suffer neurologic complications. A large variety of newer and more potent antibiotics are available, but still the outcomes of meningitis and TBM are substandard [2].

BM associated neurologic sequalae account for an estimated 171,000 deaths worldwide every year [3]. In several areas of Africa and Asia, the annual rate of tuberculosis (TB) infectivity for all ages is about 2% and about 15% to 20% of these cases occur in children [4]. In Nigeria, it accounts for about 7.8% to 14% of all cases of TBM [5]. TBM is rare in developed countries with about 100 to 150 cases occurring annually in the United States. An earlier study reported BM fatality rate of 16% in children. According to the (WHO), Pakistan ranks 8th amongst the countries with highest burden of TBM in the world [7].

The main causes of meningitis are microorganisms that may be viruses and bacteria [8]. Almost, all microorganisms that are pathogenic to human beings have the ability to cause meningitis, but a relatively small number of pathogens streptococcus, Escherichia coli, Listeria monocytogenes, Haemophilus influenzae type b [Hib], Staphylococcus pneumonia, and Neisseria meningitidis account for most cases of bacterial meningitis. Meningitis-causing pathogens cross the blood–brain barrier transcellularly, paracellularly, or by means of infected phagocytes [9].

Meningitis is further characterized as bacterial and viral meningitis with bacterial meningitis further differentiated into acute bacterial meningitis and TBM [10]. Acute bacterial meningitis causes sudden onset of neurologic sequelae while chronic bacterial meningitis is tuberculosis meningitis, the

Correspondence: Dr. Noreen Samad, Assistant Professor, Department of Biochemistry, Bahauddin Zakariya University, Multan, Pakistan.

Email: **noreen.samad@bzu.edu.pk**

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most severe form of tuberculosis caused by Mycobacterium tuberculosis. It can also be caused by different type of drugs such as non-steroidal anti-inflammatory drugs, immunoglobulins and some antibiotics [10].

Signs and symptoms of meningitis are often slight in Children; thus, the findings of meningitis have to be made by CSF estimation [11]. The CSF assessment is very significant step for meningitis evaluation. There are number of biochemical parameters that are altered in these disorders. In meningitis, the major alteration takes place in CSF glucose and protein levels. White blood cells (WBC's) counts are also increased and red blood cells (RBC's) may also shows an abnormality. The glucose concentration is usually low, and the protein level is often high in meningitis, while CSF findings of TBM include increased white cell count, presence of RBC's, elevated protein, and decreased levels of glucose as compared to acute bacterial meningitis. CSF protein may be a biomarker of severe central nervous system infection for identifying patients for timely and intensive treatment.

The aim of the present study is to compare the CSF examination of glucose and protein levels in BM and TBM with healthy individuals.

MATERIALS & METHODS

This study was undertaken in children Medical Complex Hospital Multan, to assess the impact of TBM and BM on children. The permission was taken from the MS of children Medical Complex Hospital. These children belonged to Multan as well as other Southern Areas of Pakistan. We performed a prospective comparison of the presenting clinical features of 75 children (25 of TBM, 25 of BM and 25 of control). All cases aged <5years who were admitted to children Medical Complex Hospital were included in the study. Case histories of all patients were collected. At the time of admittance, a complete physical examination was performed.

CSF examination was done soon after admission of every child. Glucose and protein levels were determined in CSF.

Physical examination: Physical examination was done by "Bacterial Meningitis Score" (BMS) as described earlier [12]. The BMS was very helpful for rapid diagnosis of children at risk of bacterial meningitis (M). It is one of initial step of meningitis diagnosis, a scheme used for assessing the precision ranking of meningitis in children [13]. The Bacterial Meningitis Score is 0 in children who are at low risk of bacterial meningitis and 2 in children that who are at high risk of bacterial meningitis.

Protein estimation: Protein levels in CSF were determined by the method as described earlier [13].

Glucose estimation: Glucose levels in CSF were estimated by the method as described previously [14].

Statistical Analysis: The data were statistically analyzed using SPSS (version 20) by applying one-way ANOVA test. P-values less than 0.05 were considered as significant.

RESULTS

Basic characteristics of patients: Table-1 shows that 35 (40%) males and 40 (60%) females participated, in which, 9 (12%) were 9 months to 1 years, 15 (20%) 1 to 3 years,27 (36%) 3 to 4 years, 24(32%) 4 to 5 years.

Range of BMS score in control and test groups: Table-2 shows that BMS score for normal child was 0, while in BM it was less than or equal to 2 and in viral meningitis the BMS < 2.

CSF glucose levels among control, BM and TBM: Figure-1 shows the levels of glucose in control, BM and TBM. Data analyzed by one-way ANOVA ($F_{2,72}$=469.87 P<0.05) showed significant differences between test and control. Post HOC analysis by Tukey's test showed that levels of glucose were significantly decreased in BM and TBM. In addition, the levels of glucose were smaller in TBM than BM.

CSF protein levels among control, BM and TBM: Figure 2 shows the levels of protein in control, BM and TBM. Data analyzed by one-way ANOVA ($F_{2,72}$=265.17 P<0.05) showed significant differences between test and healthy individuals. Post hoc analysis by Tukey's test showed that levels of protein were significantly elevated in BM and TBM.

Table-1: Baseline characteristics of the patients (n=75)

	Frequency	Percentage (%)
Sex		
Male	30	40%
Female	45	60%
Total	75	100%
Age group		
9 months-1 year	09	12%
1 year-3 years	15	20%
3 years-4 years	27	36%
4 years -5 years	24	32%
Total	75	100%

Table-2: BMS score of healthy and test children.

BMS score	Score range
Control (n=25)	0
Bacterial meningitis(n=25)	> or = 2
viral meningitis (n=25)	<2

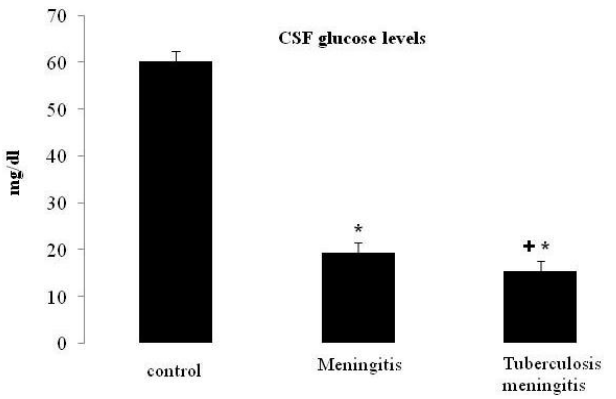

Figure-1: CSF levels of glucosen in healthy, BM and TBM individuals. Values are mean ± S.D.

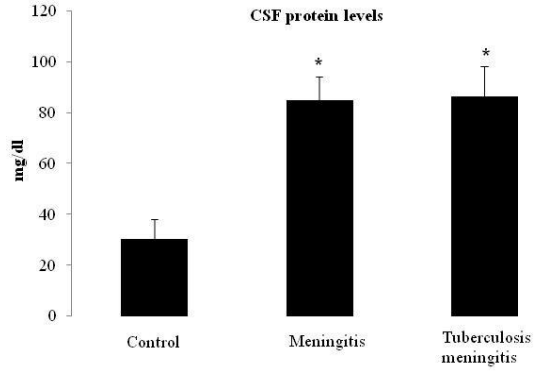

Figure-2: CSF levels of protein in healthy, BM and TBM individuals. Values are mean ± S.D.

DISCUSSION

Meningitis is a widespread disease across the world. It is a common disease in Pakistan. This is an inflammation of the outer protective layer of brain [15]. It was classified in to infectious (caused by viruses, bacteria, or other microorganisms) and non-infectious meningitis (caused by certain drugs) [16]. TBM is caused by *Mycobacterium tuberculosis* and is the most common form of central nervous system (CNS) TB. TBM is associated with a high frequency of neurologic sequelae and mortality if not treated promptly [17]. BM also becomes fatal if not diagnosed or treated at an early stage.

The most important predisposing factors for meningitis are head trauma, central nervous shunt, cerebro-spinal fluid fistula/leak, Immune suppressor, sickle cell disease and congenital defects.

In patients with meningitis the CSF appearance is cloudy, depending on the presence of white blood cells, red blood cells, bacteria, and/or protein [18]. The CSF glucose concentration is low in bacterial meningitis. Children are at high risk of meningitis and of resulting neurologic complications [19].

The important prognostic factor for meningitis is low levels of glucose. Our study revealed that the glucose levels were decreased during bacterial meningitis. Previous studies showed that CSF glucose levels are usually decreased in bacterial meningitis [20-22]. Furthermore, biochemical analysis shows significant decrease in glucose levels in TBM than BM which are consistent with previous studies. Studies have also suggested that children with bacterial meningitis have low glucose levels because of glycolysis because both white cells and the pathogen utilize glucose and impair CSF glucose transport [23].

The present study indicated that protein levels were decreased in BM and TBM patients than healthy individuals. Previously it is demonstrated that children suffering from BM have > 80 mg/dl protein levels in CSF [24]. In our study, it is observed that CSF protein levels are elevated significantly (Figure-2) in TBM compared to BM as reported previously [26]. The pathological condition decreases the CSF flow rate and increases protein concentrations in CSF up to 100-fold, through the inflammation in the arachnoid villi [27, 28].

CONCLUSION

It is concluded that, meningitis is a major concern of health for few decades. CSF analysis is a central investigative tool to discriminate BM and TBM. In addition, CSF analysis can give significant, quick and consistent analytic information with high sensitivity and positive predictive value and is very useful in distinguishing BM and TBM. It is for developing as well as underdeveloped countries. The major risk factors for severe meningitis are unhygienic conditions, lack of medical care, no vaccination; avoidance of timely hospital admissions. There is need to discover more potent antibiotics for the treatment of severe forms of meningitis.

AUTHORS CONTRIBUTION

Noreen Samad: Concept and overall supervision, manuscript writing.

Sadia Jabeen: Data collection, literature review; tabulation.

Iqra Zulfiqar: Data collection, literature review.

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