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Hypoglycorrhachia and Raised Total Protein Level in CSF, as Predictive Marker for Bacterial Meningitis

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ABSTRACT

Meningitis is an inflammatory condition in which protective layer of brain and spinal cord called meninges get inflamed. Among infectious meningitis, bacterial meningitis has higher morbidity and mortality rate, the aim of current study is to evaluate predictive marker of bacterial meningitis to initiate antibiotic therapy. Current study was conducted at department of central pathology, Allama Iqbal Teaching Hospital, Dera ghazi khan. The research was carried out on total of 188 CSF samples received from different wards of above mention hospital from September 2024 to September 2025. For the measurement of CSF glucose and total protein, Cobas pure 6000 fully automation biochemistry analyzer was used. For bacterial cultivation, samples were sent to Pak city diagnostic center located in Dera ghazi khan. Among these 188 specimens, 25(13.29%) samples met exclusion criteria. From remaining 163 samples, 91(55.8%) were diagnosed with meningitis against previously set criteria of cerebrospinal fluid cell count >5/uL. Biochemical analysis reveals that out of 91 sample, 32(35.16%) were diagnosed with hypoglycorrhachia (CSF glucose level <45mg/dl) and significantly raised CSF total protein level. The mean glucose level in these thirty-two specimens was 33 mg/dL and mean total protein level was recorded 218 mg/dL. Considering these abnormal parameters as an indication of bacterial meningitis, the sample with hypoglycorrhachia and elevated protein level were sent to microbiological laboratory for bacterial culture. Among these 32 samples, 26(81.25%) cultures were found positive for bacterial growth. Significantly reduction in CSF glucose level and elevation of CSF total protein are predictive marker for bacterial meningitis and antibiotic therapy can be initiated on the basis of these parameters.

Keywords: Cerebrospinal fluid, Meningitis, Bacterial meningitis, Hypoglycorrhachia, Total protein.

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INTRODUCTION

Meningitis is an inflammatory condition in which protective layer of brain and spinal cord called meninges get inflamed. The infectious meningitis is caused by bacteria, virus, fungi and parasite. According to World Health Organization, over 2500000 people around the globe reported with meningitis and encephalitis per year and resulting in 500000 people deaths in the world (1). It has been observed that morbidity and mortality rate of bacterial meningitis is significantly high in low- income countries and middle-income countries. Pakistan is included in top 10 countries with higher meningitis related mortality rate. Due to lack of medical history and data, the etiology of meningitis remains uncertain in Pakistan (2). As bacterial meningitis has higher morbidity and mortality rate then viral meningitis and if remain untreated, the death rate can reach up to 70%, so bacterial meningitis need urgent assessment and treatment. It is also reported that survivors may developed permanent neurological disorder as well. Number of laboratory diagnostic parameters like biochemical tests, culturing, bacterioscopy and polymerase chain reaction are available to identify the cause of ongoing meningitis. There are number of bacteria that can cause meningitis like streptococcus agalectae, streptococcus pneumonae, Hemophilus influenza, Nasieria meningitides and listeria monocytogenes. Virus related meningitis has an increased incidence rate as compare to bacterial meningitis but has low mortality rate. The main virus that cause viral meningitis are retrovirus group and other viruses may be include varicella zoster virus, cytomegalovirus and herpes simplex virus (3).

Although, the patients with bacterial meningitis show a variety of clinical sign and symptoms includes severe headache, nausea and vomiting, fever and stiffness of neck and patient with advance stages of meningitis may develop more severe clinical presentation like motor disorder, agitation, convulsion, torpor and even coma (4), but it is still observed that medical history and clinical sign and symptom of bacterial meningitis do not differ from viral meningitis and these sign and symptoms are more nonspecific in newborn, elderly patient with diabetes, and immunocompromised individual. As microbiological tests take more time to reveal exact etiology of meningitis, delay in administration of medicine can be life threating for the patient, therefore predictive marker like procalcitonin, inflammatory marker CSF/serum glucose ration and lacte should be performed on urgent bases to distinguish between bacterial and viral meningitis to reduce the outcome of disease (5).

Hypoglycorrhachia is condition in which the glucose level of cerebral spinal fluid (CSF become reduced then its normal range. Literature has defined the term hypoglycorrhachia as reduction of CSF glucose level < 45 mg/dL or CSF to serum glucose ratio ≤ 0.6 (6). The studies have suggested that hypoglycorrhachia is always associated with pathophysiological condition. It may be occur due to bacterial presence in CSF, modified glucose transportation towards the cerebral spinal fluid or leukocyte mediated glycolysis. Hypoglycorrhachia has been seen in the patients of central nerves system pathologies with both infectious (microbial related) and noninfectious meningitis. Due to relationship among cerebral spinal fluid and serum glucose level, hypoglycorrhachia in CSF/serum glucose ratio is more informative in the diagnosis of CNS related condition like meningitis and encephalitis. CSF/serum glucose ratio has found to be significantly precise in diagnosis of bacterial meningitis and is an independent test to predict or indicate bacterial infection in meninges. The researcher has emphasized that ideally both CSF and blood sample must be taken in the same hour to get more reliable and precise CSF/serum glucose ratio (7).

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In normal circumstances, CSF contains a low level of protein because the higher molecular size of these proteins makes them unable to cross blood brain barrier. Studies have suggested that raised level of CSF protein is associated with infectious meningitis. To identify the infectious meningitis, initially physician suggests CSF cell count, glucose level, protein level, Gram staining and culture and sensitivity. Primarily, the treatment decisions are made on the basis of results of culture and sensitivity but these take more time may be 36 to 48 hours. Among these initial test, reduction in glucose level and elevation of protein are indicator for infectious meningitis more precisely bacterial meningitis. Abnormal result of these two biochemical parameters is may be great support to initiate antimicrobial treatment (8).

METHODOLOGY

Study Design

After the approval from ethical review committee, the current cross sectional experimental study was conducted at central pathology laboratory Allama Iqbal Teaching Hospital Dera Ghazi Khan. Study was consisting on total of 188 samples that were received from different wards of the above mention hospital like neurosurgery, medical unit-I, medical unit-II, medical emergency, surgical emergency, pulmonology ward, ICU and paeds ward.

Criteria

The patients who have clinical manifestation of meningitis with a total cell count of moe than 5 cell/ul were considered to have meningitis. Bacterial meningitis was defined as growth of any of bacteria on culture from the CSF or identification of any bacteria from the specimen of CSF with Gram stating (9). Initially we include all the CSF specimen that were received us at Central pathology department for cell count and biochemical analysis from September 2024 to September 2025. The mean age of studied patients was 37 years with range 15–78 years and there was a slight male predominance (61.7%). Patients that underwent for lumber puncture with known tuberous meningitis, insufficient medical history or data, carcinomatous meningitis and children under 15 years of age were excluded from the study.

Laboratory Examination

All the background and medical information like usage of medicine, history of hospital stay, mechanism of lumber puncture technique and history of diabetes were recorded by a laboratory expert. The entire specimen labeled accordingly with patient name lab ID and date. Physical examination of CSF was performed by one of laboratory scientist and the result like volume, color and appearance were recorded. For the measurement of CSF glucose and total protein, cobas pure 6000 fully automation biochemistry analyzer was used. Cobas pure 6000 is manufactured by Roche and work on the principal of spectrophotometry, by using the light of a specific wavelength to measure an analyte in given solution. The amount of light which is absorbed by solution is directly proportion to the concentration of analyte.

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Figure 1: Biochemistry analyzer

After biochemical analysis, all the samples were preceded for microbiological tests. The entire CSF specimens were streaked for cultivation on blood agar with the help of sterile wire loop. After streaking the petri plates were placed in an incubator at 37C for 24 hours and results were noted.

Figure 2: Microbial growth on blood agar

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RESULTS

Initially, a total of 188 patients who were undergone to lumber puncture technique were included in study. Among these 188 samples, a total of 25 (13.29%) specimens met the exclusion criteria (11 samples of newborn as they normally contain >20WBCs/mm, 6 with confirmed tuberculous meningitis, 4 with the history of diabetes, 4 with incomplete medical record/history) and were excluded from the study.

Table 1: wards wise distribution of CSF specimen

Sr. No	Ward	Total No. of Sample	Excluded sample	Included sample
1.	Neurosurgery ward	43	02	41
2.	Medical unit-I	36	02	34
3.	Medical unit-II	29	01	28
4.	Pulmonology ward	26	06	20
5.	Medical emergency	21	02	19
6.	Surgical emergency	14	01	13
7.	Peads ward	11	11	0
8.	ICU,CCU	08	0	08
9.	Total	188	25	163

Among remaining 163 eligible subjects, 91(55.8%) were diagnosed with meningitis against previously set criteria of cerebrospinal fluid cell count >5/uL(9).

Biochemical analysis of current research reveals that out of 91 sample, 32(35.16%) were diagnosed with hypoglycorrhachia (CSF glucose level <45mg/dL) and significantly raised CSF total protein level. The mean glucose level in these thirty-two specimen was 33 mg/dL and mean total protein level was recorded 218 mg/dL.

There were 09 more sample with moderately elevated total protein level but their glucose level was found more than 45 mg/dL and was not sent for further investigation. In normal patients, the mean of CSF glucose level was 58 mg/dL and the mean of total protein level was 34 mg/dL.

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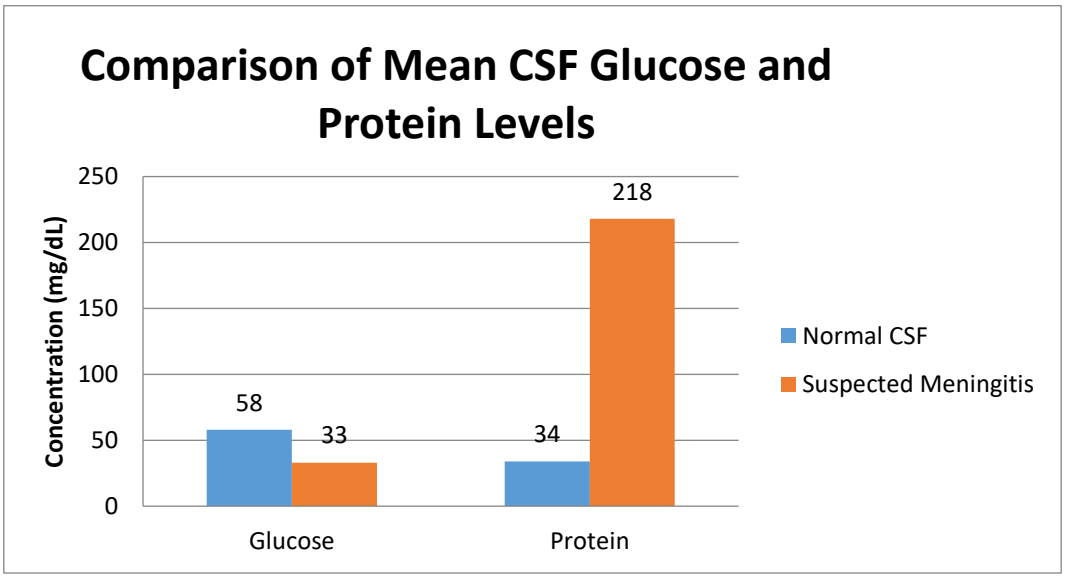
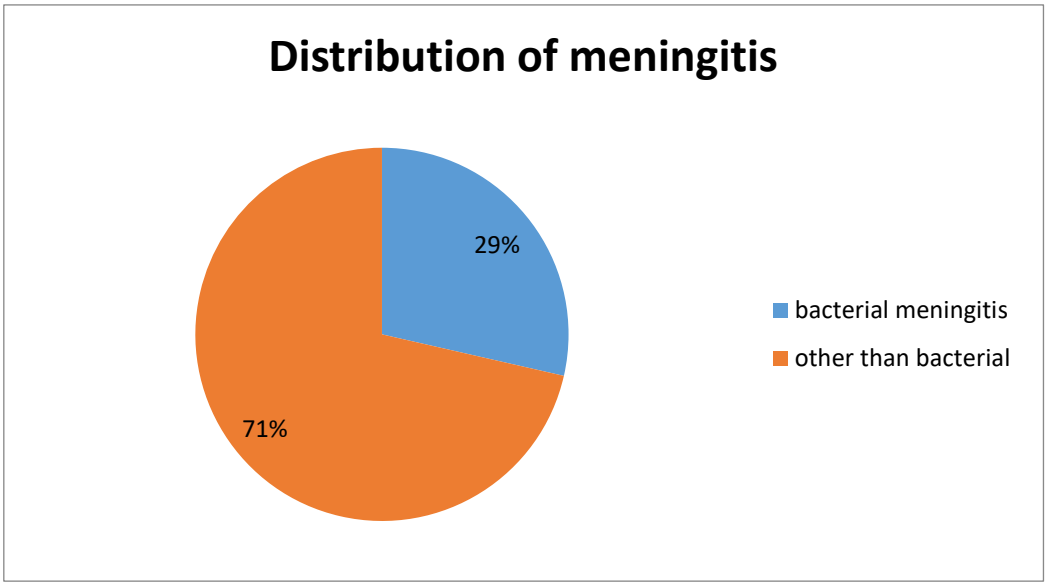


Graph 1: Representing Comparison of Mean CSF glucose and protein level

Considering these both abnormal parameter as an indication of bacterial meningitis, the sample with hypoglycorrhachia and elevated protein level were sent to microbiological laboratory and were streaked on blood agar for possible bacterial growth. Among these 32 samples, 26(81.25%) cultures were found positive for bacterial growth and later confirmed with Gram-staining.



Graph 1.2: Representing distribution of meningitis

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DISCUSSION

Bacterial meningitis has more morbidity and mortality rate as compare to viral meningitis or those with non-infectious meningitis. There is list of bacteria that can cause meningitis around the globe, more common bacteria includes Streptococcus pneumonia, Listeria monocytogenes, Haemophilus influenzae and Neiserria meningitidis (10). Among infectious meningitis, bacterial meningitis cause characteristic changes in the composition of CSF such as markedly raised pleocytosis with predominance of neutrophils, raised total protein and reduction in glucose level. Lack or delay in treatment, bacterial meningitis can leads to sepsis and septic shock (11).

The current study was consisting on a total of 188 samples of CSF. The results of our study showed that among these 188 specimens, 25 samples met exclusion criteria. From remaining 163 samples, 91 were diagnosed with meningitis against previously set criteria of cerebrospinal fluid cell count >5/uL. Biochemical analysis reveals that out of 91 sample, 32 were diagnosed with hypoglycorrhachia (CSF glucose level <45mg/dl) and significantly raised CSF total protein level. The mean glucose level in these 32 specimen was 33 mg/dL and mean total protein level was recorded 218 mg/dL. Considering these abnormal parameters as an indication of bacterial meningitis, the sample with hypoglycorrhachia and elevated protein level were sent to microbiological laboratory for bacterial culture. Among these 32 samples, 26 cultures were found positive for bacterial growth. In a previously published study, the researcher has reveals that the hypoglycorrhachia is one of the independent predictor for bacterial meningitis (12).

CONCLUSION

The outcome of our study concluded that the significantly reduction in CSF glucose level (hypoglycorrhachia CSF glucose level <45mg/dl) and elevation of CSF total protein are predictive marker for bacterial meningitis and antibiotic therapy can be initiated on the basis of these two parameter without waiting of culture report because delay in treatment can lead to death of the patient.

DATA AVAILABILITY

The data supporting the findings of this study are not publicly available due to restrictions imposed by the institute and the supervising authority. As the corresponding author, I can provide the data upon reasonable requests, subject to approval from the relevant institutional authorities.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest regarding the publication of this manuscript. There are no financial, personal, or institutional relationships that could influence or be perceived to influence the work reported in this study.

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