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ASSOCIATION OF LEVEL OF CSF SUGAR, PROTEIN AND CELLS WITH MORTALITY AMONGST CASES WITH BACTERIAL AND TUBERCULAR MENINGITIS.

Medicine

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ABSTRACT

Background- This study was conducted to assess the level of CSF sugar, protein and cells in patients with meningitis and correlate with mortality .
Methodology- This was prospective observational study conducted at tertiary care centre diagnosed with meningitis of bacterial and/or tubercular etiology for a period of 18 months. All patients were subjected to detailed clinical examination and laboratory investigation including CSF analysis.
Result-A total of 338 cases of meningitis were included.Tubercular meningitis was observed in 62.4% cases. We observed statistically significant association between elevated CSF protein(≥90 mg /dl) ,reduced CSF glucose(<35 mg/dl) with mortality for bacterial as well as tubercular meningitis ($p<0.05$). Elevated CSF ADA level(15 IU/l) and CSF cells(≥60 cells/ µl) was associated with mortality among tubercular meningitis patients.
Conclusion- Mortality was more common among the Tubercular and bacterial meningitis patients who had elevated CSF protein and low CSF glucose. Raised CSF ADA levels and CSF cellswas associated with poor outcome among the tubercular meningitis.

KEYWORDS

Meningitis, mortality, outcome, CSF protein, glucose, cells.

INTRODUCTION-

Meningitis is inflammation of meninges i.e. tissue surrounding the brain and spinal cord. In developing countries like India, meningitis still contribute to high incidence of morbidity and mortality among children as well as adults.[1] Risk factors that predispose individuals for meningitis include overcrowding, HIV infection, malnutrition, no immunization etc.[2] The most common etiology areviral andbacterial, including tuberculosis.

Meningitis due to bacterial causes are reported in approximately 1.2 million cases worldwide.[3] According to WHO, estimated incidence of TB each year was 10.4 million and of them TBM develop in approximately 1 lakh cases worldwide.[4] The severity of meningitis varies with the causative organism, such as bacterial meningitis can be highly fatal or may lead to severe residual disability amongst the survivors.[4] The complications which may be present in those who survive include cognitive impairment, hearing loss, behavioral problem, paralysis, seizure disorders etc.[5]

Prompt and appropriate treatment based upon the diagnosis is necessary for the survival of patients as well as to prevent long term sequel among them.[6]

CSF examination is helpful in establishing the etiological diagnosis of meningitis. The CSF examination include the measurement of protein, sugar, cell count etc. Apart from this, gram staining, culture sensitivity, acid fast staining, India ink preparation,viralpcr based upon clinical picture or differential diagnosis can be done.

With this background, the present study was conducted to assess the level of CSF sugar, protein and cells in patients with meningitis and correlate with mortality amongst cases with bacterial and tubercular meningitis.

METHODOLOGY-

The present study was conducted as prospective observational study at Department of General Medicine, Gandhi Medical College and associated Hamidia Hospital, Bhopal for a period of 18 months i.e. from 1st December 2017 to 30th May 2019. All the patients belonging to age group of more than 14 years diagnosed as case of meningitis of bacterial or tubercular etiology were included in the study whereas patients with altered mental sensorium with one or more derranged parameter like Hypoglycemia<50 mg/dl; Hypoxia, Hypercarbia> 50 mm of Hg, Hyponatremia < 120mg/dl or Hypernatremia >150 mg/dl; Serum Creatinine > 3 mg/dl; Patients having cerebral vascular accident followed by fever and Head Injury were excluded from the study.

All the patients were subjected to detailed evaluation with clinical history and systemic examination. Investigations such as CBC, urine routine microscopy , RFT, LFT along with CSF analysis was conducted in all the cases. Radiological Investigations and Non Contrast and Contrast Enhanced CT/ MRI were conducted in selected cases.

Statistical analysis:

All the data analysis were performed by using SPSS ver. 20 software. Frequency distribution and cross tabulation was performed to prepare the tables. Qualitative data were expressed as percentage and were analysed statistically using Chi-square test. Level of significance was assessed at 5%.

Result-A total of 338 cases of meningitis fulfilling the inclusion criteria, of them, 194 were females and 225 were males. In present study, most common diagnosis was tubercular meningitis observed in 211 (62.4%) cases whereas bacterial meningitis was observed in 127 (37.6%) cases.

Table-1: Distribution Of Meningitis With Outcome

Meningitis	Outcome			Total	P value
	Death	Discharged with no complication	Discharged with complication		
Bacterial	23 (27.1)	23 (19.2)	81 (60.9)	127 (37.6)	0.03
Tubercular	62 (72.9)	97 (80.8)	52 (39.1)	211 (62.4)	
Total	85 (100)	120 (100)	133 (100)	338 (100)	

Out of 338 patients, mortality was documented in 85 cases. Of them tubercular meningitis contributed to 72.9% death. However 60.9% cases with bacterial meningitis were discharged with some complication. Test of significance observed statistically significant difference in outcome in various etiologies ($p<0.05$). (Table 1)

Table-2: Association Of Outcome With Csf Findings Among Patients With Bacterial Meningitis

CSF		Outcome		Total	P value
		Death	Survived		
Protein	<90 mg/dl	0 (0)	21 (20.2)	21 (16.5)	0.013
	≥90 mg/dl	23 (100)	83 (79.9)	106 (83.5)	
Glucose	<35 mg/dl	18 (78.3)	55 (52.9)	73 (57.5)	0.04
	≥35 mg/dl	5 (21.7)	49 (47.1)	54 (42.5)	
Cells	≥60 cells/ µl	23 (100)	104 (100)	127 (100)	NA

The present study observed mortality in 23 (100%) cases of bacterial meningitis with raised protein whereas mortality was observed in 78.3% cases with reduced CSF glucose levels. The present study observed statistically significant association between elevated CSF protein and reduced glucose levels with outcome ($p<0.01$). However associationcould not be found between CSF cells and mortality in bacterial meningits as all had cell >60. (Table 2)

Table 3- Association Of Outcome With Csf Findings Among Patients With Tubercular Meningitis

CSF		Outcome		Total	P value
		Death	Survived		
Protein	<90 mg/dl	23 (37.1)	81 (54.4)	104 (49.3)	0.02
	≥90 mg/dl	39 (62.9)	68 (45.6)	107 (50.7)	
Glucose	<35 mg/dl	33 (53.2)	55 (36.9)	88 (41.7)	0.03
	≥35 mg/dl	29 (46.8)	94 (63.1)	123 (58.3)	
Cells	<60 cells/ µl	21 (33.9)	79 (53)	100 (47.4)	0.011
	≥60 cells/ µl	41 (66.1)	70 (47)	111 (52.6)	
ADA	<15 IU/l	26 (41.9)	90 (60.4)	116 (55)	0.014
	≥15 IU/l	36 (58.1)	59 (39.6)	95 (45)	

In present study, survival was significantly higher among the tubercular meningitis patients having CSF protein <90; CSF cells <60, CSF glucose ≥35 and CSF ADA levels <15 ($p<0.05$). (Table 3)

DISCUSSIONS

Meningitis is the one of the most prevalent CNS infection in our country. There is considerable urgency to establish an efficient diagnosis for these patients. Irreversible brain damage may result while waiting for confirming the diagnosis. Delay in diagnosis and treatment are regarded as a major contributing factors to the morbidity and mortality.[7]

In present study out of 338 patients, majority were diagnosed with tubercular meningitis (62.4%) whereas remaining 37.6% cases were diagnosed as bacterial meningitis. In line with that Bansal et al has indicated that TBM, pyogenic meningitis, and encephalitis together constitute more than 90% of the cases.[8] In another study, by Karmarkar et al pyogenic meningitis was the most frequent diagnosis (33.8%) followed by TBM (7.9%).[9]

In present study, out of 338 patients, 85 (25.1%) died, 120(35.5%) were discharged without complication whereas 133 (39.3%) were discharged with complications. When diagnosis distribution was compared with the outcome of the study it was found that majority of the patients who died had tubercular meningitis (72.9%). Similarly those who were discharged without any complications majority were diagnosed with tubercular meningitis (80.8%) whereas about60.9% cases with bacterial meningitis were discharged with some complications. Reports of Bhalla et al showed that of the total 127 patients, there were 21 deaths (16.5%). The maximum mortality was seen in patients with SAE with as many as 33% patients dying (6/18). Of the total number of 38 patients with meningoencephalitis, 7 succumbed to their illness (18.42%). Five patients out of 14 (35.7%) in whom no definitive diagnosis could be established succumbed to their illness.[10]

Biochemical analysis reveals a significant increase in protein concentration in the tuberculous and pyogenic meningitis.[11] In present study, raised protein, Cells and ADA level in CSF whereas reduced glucose levels were significantly associated with poor outcome in terms of survival ($p<0.05$). Albumin is principally produced by liver. Thus, its level in CSF give some integrated information about changes in the permeability of the blood-CSF barrier and CSF turnover.[12] A low cerebrospinal fluid glucose is also seen in other bacterial, fungal, parasitic, or neoplastic meningoencephalitis, and occasionally in few cases of viral meningitis. Typically, the CSF in cases of tubercular meningitis show a high CSF white cell count, which is predominantly lymphocytic, with a high protein and low CSF to blood glucose ratio.[13]

In cases with bacterial meningitis, the present study documented higher mortality among the patients with reduced glucose and raised protein levels. Cells in CSF were raised in all cases of bacterial meningitis independent of survival. In a study by Karmarkar et al studied 151 patients with mean age of 3.21 ± 2.9 (range of mth - 13 years) and male: female ratio of 1.71: 1 and reported that the mean CSF cell count in the patients was 27.40±70.885 (range: 0-520), median 10 cells.[9] The presence of a higher number of polymorphonuclear leucocytes in the cerebrospinal fluid after first 48 hours indicates bacterial meningitis as the likely etiology. Neutrophils can predominate, especially early in the disease and a high proportion of neutrophils in the CSF has been associated with an increased likelihood of a bacteriological diagnosis and improved survival.[13,14].

CONCLUSION-

Tuberculous meningitis (TBM) followed by bacterial meningitis is the most common form of central nervous system tuberculosis (TB) and has very high morbidity and mortality. Mortality was more common among the Tubercular and bacterial meningitis patients who had elevated CSF protein, increased CSF cells low glucose. Raised CSF ADA levels can also be a maker for the poor outcome among the tubercular meningitis. Thus, CSF analysis could be an important tool for predicting the outcome and should be done as early as possible after clinical judgment of the acute meningitis.

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