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Study of Etiological Pattern of Acute Meningo-Encephalitis Syndrome

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Abstract:

Background: *Acute meningo-encephalitis syndrome is a medical emergency which claim urgent management. So the objectives of the present study was to find out aetiological factors and differentiating parameter between different types acute meningo-encephalitis syndrome with minimum investigation.* ***Methods:*** *This hospital based observational study was carried out in medicine units of Chittagong Medical College. Fifty cases were studied who present with acute onset fever with central nervous system dysfunction.* ***Results:*** *In this study it reveals that hospital rate of bacterial meningitis was 26%, viral encephalitis was 34% and severe malaria was 26% among the patient with acute meningo-encephalitis syndrome. It shows that mean age (years) in viral encephalitis was 33.71, bacterial meningitis was 34.15 & in severe malaria was 27.92. It reveals that all patients of this series presented with acute onset fever (n=50,100%), maximum patients present with sign of meningeal irritation (n=44, 88%) & altered mental state (n=41,82%). Few patients was present with new onset seizure (n=11,22%) & neurologic deficit (n=1,2%). In Bacterial meningitis most patient was with low CSF glucose (n=10, 76.9%). In viral meningitis there were normal CSF glucose level (n=17,100%). High protein content in bacterial (n=13,100%) & Viral (n=15,88.2%) was found. It shows differential count of CSF WBC in different type of meningitis where in Bacterial meningitis it is neutrophils & in other type of meningitis it is the lymphocyte.* ***Conclusion****: CSF findings are hallmark of diagnosing various type of meningitis. CSF glucose and protein content found in this study significantly correlate with different etiology (p value = 0.000).*

Key word: *Acute, Meningo-encephalitis, Viral, Bacterial, Malaria*

Introduction:

Acute meningo-encephalitis syndrome is defined as acute onset fever with altered mental state or new onset seizure or with sign of meningeal irritation and neurologic deficit[1,2]. The most common types of acute meningitis are acute bacterial meningitis (70%) with incidence of 2.5 cases per 100000 population per year and aseptic meningitis (30%)[1,3]. Acute bacterial meningitis is a severe illness characterized by purulent CSF[1]. Aseptic meningitis is milder and typically self-limited, usually caused by viruses but sometimes by bacteria, fungi, parasites or non-infectious inflammation in systemic lupus erythomatosus, Behcet's disease, Sarcoidosis, malignancy & Mollaret meningitis with HSV-2[2,3]. In adult bacterial meningitis causative organism are Streptococcus pneumonia (~50%), Neisseria (~25%), Group-B streptococcus / S.agalactae (~15%), listeria (~10%), Haemophillus (<10%) and among virus 75-90% cause is HSV-2 & Arbo virus[1,3].

Many cases of infectious meningitis begin with a vague prodrome of viral fever. The classic meningitis triad of fever, headache and nuchal rigidity develops over hours or days. Brudzinski's and kernig's sign may also positive. According to Thomas KE et al, diagnostic accuracy of signs of meningeal irritation in patients with suspected meningitis showed nuchal rigidity, Kernig's sign & Brudzinski's sign sensitivity 30%, 5% & 5%, specificity 68%, 95% & 95%, positive predictive value 26%, 27% & 27%, negative predictive value 73%, 72% & 72%, positive likelihood ratio 0.94,

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0.97 & 1.0 and negative likelihood ratio 1.02, 1.0 & 0.97 respectively[11,12]. Meningococcal infection is associated with skin rash in 70% cases.[2,5] Although brain parenchyma is not typically involved early in meningitis. Lethargy, confusion, seizures and focal deficits may develop, particularly in untreated bacterial meningitis[3,4].

Acute meningitis is a medical emergency (mortality 20%, recovery rate with antibiotic 30%) [1]. So it requires a rapid diagnosis and treatment. After IV access and blood cultures are obtained lumbar puncture is done to obtain CSF for Gram stain, culture, cell count and differential and glucose and protein content. In bacterial meningitis CSF shows Polymorphnuclear pleocytosis in 90% cases, decreases glucose in 60% cases ,increased protein in 90% cases, increased pressure in 90% cases & in viral meningitis CSF pleocytosis in >95% cases[1-4].

Sometimes other investigation is needed to exclude cerebral malaria, metabolic, vascular & toxic causes of coma, electrolyte imbalance, organ failure, septicaemia & ICSOL. These tests must be done as rapidly as possible. However, patients with signs with mass effect (e.g, focal deficits, papilloedema, deterioration in consciousness, seizures) require head CT before lumber puncture because lumbar puncture can result in a shift of intracerebral contents downwards, towards and into the spinal canal. This process is known as coning, and is potentially fatal[5].

Recently CSF C-reactive protein with latex particle use in differentiating bacterial and non-bacterial meningitis & identification of a CSF inhibitors of macrophage Listecidal function as Interleukin-10.[35-37] Gram (-)ve bacterial meningitis 100% positive for Limulus amebocyte Lysate assay with the possibility of false positive result[3]. The best single test to differentiate bacterial meningitis from viral is rise of CSF lactic acid level (<2mmol/L in viral, 2-6mmol/L in partially treated case & >6 mmol/L in bacterial etiology).A normal CSF Lactic acid level could have eliminate need for unnecessary repeated lumbar puncture & also eliminate the need of empirical antibiotic coverage pending CSF culture result[5].

Methods:

It was an observational study done in the Medicine Department of Chittagong Medical College, Chittagong, Bangladesh among 50 cases suspected meningoenchephalitis during a period of one year. Patients who have history of fever less than 14 days and, and patients presented with one or more of the followings:- new onset seizure, altered mental state like coma, lethargy, confusion or agitation, neurologic deficit like focal sign of weakness, abnormal gait, involuntary movement or abnormal posture or abnormal tone of muscle, sign of meningeal irritation like nuchal rigidity, Brudzinski's sign or Kernig's sign and patient/Party who willing to take part in the study were included in the study and patients age <13yrs and patient who present with simple febrile seizure were excluded. All data were collected in individual case record form. This was done by taking history from patients or his or her attendants. All the cases were clinically examined including fundoscopy and then some routine first line investigation sent for all patients and second line investigation for selective cases. When there was sign of raised intracranial pressure (e.g, deterioration of level of consciousness with bradycardia, hypertension, irregular respiration, dilated poorly reacting pupils, sixth nerve palsy, decerebrate posture, papilloedema) brain imaging was done prior to Lumbar puncture.

All patients was managed properly and due nursing care (eg, management of unconscious patient) provided by duty nurse. All Lumbar puncture were done by duty doctors of medicine ward, examined in pathology & microbiology department of Chittagong Medical College and all Blood film for malarial parasite was done in Malarial Research Laboratory, CMC. Data was coded, edited and entered into computer and were analysed by using SPSS 12 and presented with tables, graphs keeping in view the objective of the study.

Results:

Table-I

Distribution of patients in relation with diagnosis among the patient of acute meningo-encephalitis syndrome (n=50).

	Viral encephalitis	Bacterial meningitis	Severe malaria	Not diagnosed
No of patient	17	13	13	7
%	34	26	26	14

It shows that in cases of acute meningo-encephalitis syndrome, viral encephalitis was 34%, bacterial meningitis 26%, severe malaria 26% & 14% cases there were no diagnosis.

Table-II

Distribution of patients in relation with age (n=50).

		Viral encephalitis	Bacterial meningitis	Severe malaria	Not diagnosed
Age (year)	Mean	33.71	34.15	27.92	47.29
	Range	17-55	19-48	18-38	38-55
	SD	12.282	8.952	7.729	6.726

It shows that mean age (years) in viral encephalitis was 33.71, bacterial meningitis was 34.15 & in severe malaria was 27.92.

Table-III

Distribution of patients in relation with CSF glucose level (n=50)

Diagnosis	CSF glucose(mg/dl)		Total
	Low(<40mg/dl)	Normal(≥40mg/dl)	
Viral meningo-encephalitis	0	17	17
Bacterial meningitis	10	3	13
Severe malaria	0	13	13
No diagnosis	2	5	7

It shows CSF glucose concentration among different types of meningitis. In Bacterial meningitis most patient was with low CSF glucose (n=10, 76.9%). In viral meningitis there were normal CSF glucose level (n=17,100%).

Table-IV

Distribution of patients in relation with CSF protein level (n=50).

Diagnosis	CSF protein(mg/dl)		Total
	normal(<45mg/dl)	Raised(≥45mg/dl)	
Viral meningo-encephalitis	2	15	17
Bacterial meningitis	0	13	13
Severe malaria	11	2	13
No diagnosis	7	0	7

It shows CSF protein content among different type of meningitis. High protein content in bacterial (n=13,100%) & Viral (n=15, 88.2%).

Table-V

Correlation of different clinical feature with viral, bacterial & malarial causes of acute meningo-encephalitis syndrome using one way ANOVA.

		Sum of Squares	Df	Mean Square	F	Sig.
Gender	Between Groups	.008	2	.004	.015	.985
(male=1,)	Within Groups	10.271	40	.257		
female=2	Total	10.279	42			
Age category	Between Groups	1.991	2	.996	1.057	.357
(13-25=1, 26-35=2,	Within Groups	37.683	40	.942		
36-45=3,>45=4)	Total	39.674	42			
CSF protein	Between Groups	5.613	2	2.806	32.472	.000
(Normal<45mg/dl,	Within Groups	3.457	40	.086		
Raised ≥45mg/dl)	Total	9.070	42			
CSF glucose	Between Groups	5.367	2	2.683	46.512	.000
(Normal ≥40mg/dl,	Within Groups	2.308	40	.058		
Low <40mg/dl)	Total	7.674	42			
CSF WBC	Between Groups	6.494	2	3.247	76.744	.000
(Normal upto 5,	Within Groups	1.692	40	.042		
Raised>5/mm^3)	Total	8.186	42			

It shows there is CSF protein, CSF glucose & CSF WBC category significant difference of between viral, bacterial & malarial causes of acute meningo-encephalitis syndrome and p value respectively .000, .000 & .000. It also shows gender & age category were not differentiating criteria between viral, bacterial & malarial causes of acute meningo-encephalitis syndrome p value > 0.05.

Discussions:

Infection of central nervous system is a medical emergency. The incidence of bacterial meningitis is more than 2.5 per 100,000 people per year[3].The exact incidence of viral meningitis is very difficult to determine since most cases go unreported to public health authorities. There is no exact record yet in our country. About 400 patients admitted with meningitis in CMCH in medicine unit per year[6].

In this study, among the 50 patients with acute meningo-encephalitis syndrome, viral encephalitis was found 17 (34%), bacterial meningitis were reveals 23 (26%) severe malaria were found 13 (26%).In this study it was explored that severe malaria is an important cause among the patients with acute meningo-encephalitis syndrome since Chittagong is a malaria endemic zone.

A hospital-based study at Dhaka Medical College Hospital, Mymensingh Medical College Hospital, MAG Osmani Medical College Hospital, Rajshahi Medical College Hospital from June 2003 to July 2005 to investigate the etiologies of bacterial meningitis in Bangladesh were diagnosed with bacterial meningitis 136 (18%)[7].

In another prospective, hospital-based study to define the causes of encephalitis among patient admitted to Dhaka, Mymensingh and Rajshahi Medical College Hospitals in Bangladesh during 2003, viral encephalitis was found 25 (37.7%), bacterial meningitis was found 22 (34.9%)[8].

In study of consecutive patients (age's e"16) with aseptic meningitis or encephalitis treated in Turku University Hospital, Finland, during 1999 to 2003 where etiologic diagnosis was achieved by PCR were showing 43% of the patients with meningitis and 17% of those with encephalitis[9].

In this study, among the 50 patients with acute meningo-encephalitis syndrome, it shows there were an overall male preponderance with a male to female ratio was 1.6:1 (male=31,female=19).It also shows that mean age (years) in viral encephalitis was 33.71, bacterial meningitis was 34.15 & in severe malaria was 27.92.It reveals that maximum patients (n=29,58%) were between 26-35 & 36-45 years of age and all age groups were equally affected considering age less than 13 as an exclusion criteria.

According to Ridwanur Rahman, et al.,cerebral malaria was common for all the age group & highest mortality was found among the 51-60 age group[10].

A study at King George Hospital, India from June 2003 – December 2006, all patients with abnormal CSF findings were reviewed where 'meningitic' cases occurred in young immunocompetent patients aged between 17-32 years[11].

In this study, among the 50 patients with acute meningo-encephalitis syndrome, it reveals that average duration (days) before presentation in different type of acute meningo-encephalitis. In case of viral encephalitis it was 3.35 (1-6), bacterial meningitis 3.23 (1-6) & severe malaria 3 (1-5) & the area of the box also represent the no. of cases in individual category.Allthe patients of this series presented with acute onset fever (n=50,100%). Most of the patients presented with sign of meningeal irritation (n=44, 88%), altered mental state (n=41,82%). It also reveals that patients were presented with nuchal rigidity (n=39, 78.0%), Kernig's sign 24, 48.0%) & with confusion (n=22, 44.0%). Few patients was presented with new onset seizure (n=11, 22%), lethargy (n=11, 22.0%), coma (n=8, 16.0%), Brudzinski's sign (n=6, 12.0%), agitation (n=1, 2.0%) & abnormal tone (n=1, 2.0%). In this series no patient was presented with focal sign of neurologic deficit, abnormal gait, and involuntary movement.

A study of 104 cases of cerebral malaria (73 male, 31 female between July 1995 to June 1996 in Chittagong Medical College Hospital, revealed intermittent fever (83%), vomiting (80%), headache (75%), convulsion (60%) and history of travel or residence in malaria endemic area were important features noted in patients with cerebral malaria.[50] Most of the patients (69%) were admitted within 25 to 48 hours following unconsciousness[10].

A study in sixty-eight parasitologically-confirmed adults admitted to the Chittagong Medical College Hospital showed the duration of present illness (6.96±3.24 days) before hospitalization and the duration of severe illness (2.31±1.96 days) were longer among those who died than among survivors[12]. In Thomas KE et al study in the diagnostic accuracy of Kernig's sign, Brudzinski's sign and nuchal rigidity in adults with suspected meningitis showed nuchal rigidity was present in 30% and Kernig's or Brudzinski's sign only in 5% cases of adults with meningitis[13].

In Raschilas F, Wolff M, Delatour F, et al multycentric study in outcome of and prognostic factors for herpes simplex encephalitis in adult patients showed eighty five (91%) of 93 adults with HSV-1 encephalitis were febrile on admission,14 disorientation (76%), speech disturbances (59%) and behavioral changes (41%) were the most common features, and one third of patients had seizures[14]. In a study in King George's Medical College, Lucknow, India on clinical features & prognostic indicators of Japanese encephalitis in children, a high incidence of fever (94.5%), coma (100%) and convulsions (84.7%) was seen. Focal neurological deficit was found in 29.3 per cent of patients and pleocytosis in the cerebrospinal fluid in 32.3 per cent. An extrapyramidal syndrome developed in 21.3 per cent patients during the convalescent stage[14].

In this study, among the 50 patients with acute meningo-encephalitis syndrome, it shows that mean CSF glucose (mg/dl) in viral encephalitis was 64.71,bacterial meningitis was 38.92 & in severe malaria was 66.85.Most of the patients with bacterial meningitis 10 (76.9%) revealed a low CSF glucose.

In this study, it shows that mean CSF protein (mg/dl) in viral encephalitis was 52.59, bacterial meningitis was 57.92 & in severe malaria was 35.All patient with bacterial meningitis 13(100%) & most patients with viral meningo-encephalitis 15(88.2%) revealed raised CSF protein.

In this study, it shows that mean CSF WBC (cell/mm3) in viral encephalitis was 22.59, bacterial meningitis was 676.92 & in severe malaria was 3.31. It also shows differential count of CSF WBC in different type of meningitis. In Bacterial meningitis it is neutrophils & in other type of meningitis it is the lymphocyte.

According to Simko et al, in encephalitis vs. meningitis; it showed CSF WBCs/mm3 202 (2-667) vs. 484 (58-1888), <10 CSF cells/mm3 19% vs. 12%, % of CSF Lymphocyte 76 (16-97) vs. 87 (43-100), CSF RBCs/mm3 2518 (0-27,566) vs. 54 (0-711) and CSF Protein(mg/dL) 73 (22-146) vs. 129 (75-281)15. According to Van DeBeek et al, predictors of bacterial etiology considering CSF glucose < 40, CSF protein > 60, CSF neutrophil count > 80%, CSF WBC count > 100, CSF: Serum glucose ratio < 0.23 showed that presence of any ONE of the above findings predicts bacterial etiology with > 75% certainty.[16]And considering CSF glucose < 34, CSF: Serum glucose ratio < 0.23, CSF protein > 220 mg/dl, CSF WBC count > 2000/mm3, CSF neutrophil count > 1180/mm3 showed presence of any ONE of the above findings predicts bacterial etiology with > 99% certainty[17].

Sometimes patients attendants fail to give adequate history. Patients were taking prior antibiotics which may alter the CSF findings. The study was carried out in low resource situation And the study may not represent the overall situation of Bangladesh, as only 50 cases were observed and the study was carried out in a particular period of time and in malaria endemic zone of Bangladesh.

Patient presents with acute fever and altered mental state with or without neurologic deficit & new onset seizure, particularly if there is signs of meningeal's irritation patient should be screened for acute meningo-encephalitis syndrome.

In our country laboratory facilities are very limited.PCR for virus and AFB is not always permissible due to poor economic status of patient. Even CSF culture and other serologic test are not readily available in most of the district town. So proper history taking & accurate clinical examination and minimum laboratory investigation to screen acute meningo-encephalitis syndrome like CSF study for biochemistry, cytology & Gram stain and blood film for malarial parasite in malaria prone zone. And sometime brain imaging and metabolic profile is recommended in selective cases if clinical data suggest.

Though fundoscopy was not included as differentiating parameter but during this study, it was observed that fundoscopy might be a good clinical tools to identify malarial retinopathy and to detect risk factors of stroke like hypertensive & diabetic retinopathy and to exclude mass effect or papillodema. Extra-neurologic sign like meningococcal skin rash, black water fever, and jaundice in severe malaria may also be used as differentiating parameter.

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