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Microbiological Etiology and Short-Term Outcome of Meningoencephalitis Patients Admitted in a Tertiary Care Hospital -50 Cases

Ananta Kumar Kundu*[1], Ahmed Hossain[2], Md. Nur A Alom Khan[3], Md. Abul Kalam Azad[4], Md. Daharul Islam[5], Akramumuzaman[6], Chandra Shekhar Bala[7]

Abstract

Introduction with Objective: *The aim of the present study was to evaluate the etiology and short-term outcome of Meningoencephalitis.* ***Materials and Methods:*** *A hospital-based observational study was conducted in the Department of Medicine, Sir Salimullah Medical College Mitford Hospital, from July 22 to June 2023. 50 Patients enrolled within the study period with features of Meningoencephalitis fulfilling the inclusion and exclusion criteria. Ethical clearance for the study was obtained from the Ethical Review Committee. A detailed history, clinical examination was carried out. In addition to the routine blood test, CSF samples were collected as soon as possible from all patients unless contraindicated and sent for cytological, biochemical, and microbiological tests. Data were collected in the pre-formed standard data collection form, recorded in separate case records and analyzed by SPSS 26.0.* ***Results:*** *Our results demonstrate the most of the cases (24, 48%) was tubercular meningoencephalitis, followed by (15, 30%) bacterial meningoencephalitis and (11,22%) viral meningoencephalitis. Gram positive diplococci found in 5 (33%) participants, 1 (6%) participant detected to had S. pneumoniae in PCR in the bacterial meningoencephalitis group. 1 (9%) participant detected to had Herpes simplex and 1 (9%) Varicella zoster in PCR among viral meningoencephalitis group. MTB detected in 8 (33%) participants in the tubercular meningoencephalitis group. Most of the participants 7 (46%), 18 (75%) who was diagnosed with bacterial and tubercular meningoencephalitis were severely disabled respectively, 7 (63%) who was diagnosed with viral meningoencephalitis had good recovery. Mean ± SD of the duration of hospital stay of the tubercular meningoencephalitis was highest (31.91 ± 12.46 days). Most of the participants who had a poor outcome presented with headaches, GCS<8 (OR 9.84),increased ESR, decreased Glucose (mg/dl) in CSF, abnormal CT/MRI Findings, low GOS- E score, increased duration of hospital stay between the participants who had a poor outcome, were statistically significant ($p<0.05$).* ***Conclusion:*** *In this study tubercular meningoencephalitis was the most common microbiological etiology of meningoencephalitis and most of the patients 18 (75%) were severely disabled, 3 (12.5%) died.*

Keywords: *Meningoencephalitis, GCS, Short-term outcome, GOS-E.*

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*1. **Corresponding Author:**
Dr. Ananta Kumar Kundu
Assistant Registrar
Medicine Unit-1, Kushtia Medical College Hospital
Kushtia, Bangladesh.
Email:kunduananta7@gmail.com
Contact:017455-72103

2. **Prof. Dr. Ahmed Hossain**
Professor
Ex-departmental Head of Medicine
Sir Salimullah Medical College Mitford Hospital
Dhaka, Bangladesh.

3. **Prof. Dr. Md. Nur A Alom Khan**
Professor, Head of the Department of Medicine
Sir Salimullah Medical College Mitford Hospital
Dhaka, Bangladesh.

4. **Prof. Dr. Md. Abul Kalam Azad**
Professor & Chairman
Department of Internal Medicine
Bangladesh Medical University
Shahbag, Dhaka, Bangladesh.

5. **Prof. Dr. Md. Daharul Islam**
Professor, Department of Medicine
Sir Salimullah Medical College Mitford Hospital
Dhaka, Bangladesh.

6. **Dr. Akrammuzaman**
Associate Professor, Departmental Head of Medicine
Kushtia Medical College Hospital
Kushtia, Bangladesh.

7. **Dr. Chandra Shekhar Bala**
Assistant Professor, Department of Medicine
Sir Salimullah Medical College Mitford Hospital
Dhaka, Bangladesh.

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Introduction:

Acute nervous system infection is the leading preventable cause of neurological deficit around the globe. Meningoencephalitis is a medical illness that resembles both meningitis (infection or inflammation of the meninges) and encephalitis (infection or inflammation of the brain)[1]. These two disorders frequently overlap in clinical practice[2]. Skipping vaccinations, age (viral meningitis mostly affects children under five years old, and bacterial meningitis mostly affects people under 20), community settings (children in boarding schools and childcare facilities are at higher risk), and factors that may compromise the patients immune system, such as acquired immune deficiency syndrome (AIDS), use of immunosuppressant drugs, spleen removal, end stage renal disease, and others, are all risk factors for meningitis[3]. On the other hand, subacute or chronic ME is typically caused by Mycobacterium tuberculosis and fungus, such as Candida albicans, Cryptococcus neoformans. Acute CNS infection due to Naegleria fowleri, which ends in death within 2–7 days, is termed primary amoebic meningoencephalitis and is not related to immunodeficiency[2]. Despite rigorous diagnostic workup, one-third to two-thirds of encephalitis cases still have an unknown origin[4,5]. Meningoencephalitis remains the leading cause of childhood fatalities, as well as the leading cause of long-term neurological disability in children[6]. The meningococci bacteria are mostly responsible for these cases. There are considerable variances in the regional distribution of the etiological agents responsible for bacterial meningitis. For example, whereas N. meningitides groups B and C cause a substantial proportion of illness episodes in Europe, group A is present in Asia and continues to prevail in Africa, where it generates the majority of severe epidemics in the meningitis belt, accounting for around 80 to 85% of reported meningococcal meningitis cases[7,8]. Viral encephalitis is more common and has more severe long-term consequences and death, particularly for certain viral infections such as herpes simplex virus (HSV) and Japanese encephalitis virus. The use of Gram stain technique or methylene blue to stain the preparation of the CSF deposit allows for the differentiation of bacterial kinds - Gram-positive or Gram-negative - and determining their morphology: cocci, coccobacilli. The methods sensitivity is determined by the bacterial species. Latex tests are utilized for the rapid qualitative detection of antigens of alive and dead bacteria in CSF or urine, allowing for early etiology determination even after antibiotic therapy has begun[9]. Recently, CSF C-reactive protein containing latex particles was used to differentiate bacterial and non-bacterial meningitis, and Interleukin[10] was identified as a CSF inhibitor of macrophage Listecidal action. The best single test for distinguishing bacterial meningitis from viral meningitis is an increase in CSF lactic acid level (2 mmol/L in viral, 2-6 mmol/L in partially treated cases, and & ≥ 6 mmol/L in bacterial etiology)[10]. In the case of symptoms suggestive of intracranial pressure, a CT/MRI scan should be done[9]. A structured version of the Glasgow Outcome Scale Extended (GOSE) interview was developed in 1998 to help standardize scoring processes for both the GOS and GOSE[11]. The GOSE focuses on post-injury change but does not distinguish between changes related to brain damage and disability induced, for example, by injury to other areas of the body. The GOSE can be used to measure the repercussions of general trauma, including polytrauma, and all types of injury are considered. The goal of the study will determine whether to examine the overall impact of injury or focus on the impacts of brain injury[12]. The aim of this study is to evaluate the present Microbiological pattern of meningoencephalitis and its short-term outcome in a tertiary level hospital.

Materials and Methods:

This descriptive type of observational study was carried out in Department of Medicine, Sir Salimullah Medical College & Mitford Hospital (SSMC &MH) over a period of 12 months from July 2022 to June 2023. The Laboratory work C.S.F Routine and PCR for viral Meningitis panel was performed in the department of "Microbiology and Immunology" of Bangabandhu Sheikh Mujib Medical University, CSF for Bacterial Meningitis panel was done in Square Hospital, Panthapath, Dhaka, CSF for Gene-Xpert was done in ICDDR, B, Mirpur, Dhaka and other investigations were done in Sir Salimullah Medical College and Mitford hospital, Dhaka, Bangladesh. All patients with meningoencephalitis was admitted in the Department of Medicine within the study period.Total 76 patients were enrolled into the study among those 50 Meningoencephalitis patients within the study period who had fulfill the inclusion and exclusion criteria were taken and rest of 26 patients were required to have ICU support (7), died before doing lumbar puncture (5), refused to give consent (5), Urosepsis (2), ICSOL (2), Stroke with aspiration pneumonia (3), DKA (2) were excluded from the study. Sampling method was purposive sampling as per inclusion and exclusion criteria. Fifty Meningoencephalitis patient fulfilling inclusion and exclusion criteria. Inclusion Criteria were Hospital admitted patients in medicine wards with features suggestive of Meningoencephalitis, Patients age twelve years and above. Exclusion Criteria were Patients who refused lumbar puncture or died before doing lumbar Puncture, Patients of encephalopathy due to metabolic, endocrine and other infectious causes ex: UTI, aspiration pneumonia, Patients who have had recent head trauma, Stroke, SAH, CVST, known malignant lesions, Central nervous system neoplasm, connective tissue diseases, Critically ill patients required ICU support and Refused to give consent.

Sample Size Calculation

The sample size calculation was carried using the Fishers formula (Fisher et.al., 1998): n=z2 pq/d2

Where,

n= estimated sample size

Z= 1.96 (in 95% CI) value of standard normal distribution

P means prevalence of overall mortality = 11.5% (kafle et al. 2017)

q= 88.5%(100-P)
d= degree of accuracy or precision level is considered at 7%
So, n= (1.96)2x11.5x88.5/ (7)2
= 79.79 =80
Due to time constrain, we were able to collect 50 samples. So our sample was = 50

Results:

A total of 50 patients with meningoencephalitis were enrolled in the study. The mean age of participants was 33.86 ± 16.67 years, ranging from 12 to 70 years. The majority of patients (44%) were aged 25–50 years, while 40% were below 25 years and 16% were over 50 years. Female participants predominated, accounting for 60% of cases, giving a male-to-female ratio of 1:1.5. Most participants (70%) resided in urban areas, and 68% were married. Regarding socioeconomic status, 64% belonged to the lower socioeconomic class, whereas 36% were from the middle class (Table I). The etiological distribution revealed that tubercular meningoencephalitis was the most common cause, diagnosed in 24 (48%) patients, followed by bacterial meningoencephalitis in 15 (30%) patients, and viral meningoencephalitis in 11 (22%) patients (Table II).

Table I: Demographic Characteristics of Patients

Characteristic	Number (n=50)	Percentages
Age (mean ± SD)	33.86 ± 16.67	
Age <25 years	20	40
Age 25–50 years	22	44
Age >50 years	8	16
Gender Male	20	40
Gender Female	30	60
Urban Residence	35	70
Rural Residence	15	30
Middle class	18	36
Lower class	32	64

Table II: Etiological Distribution

Etiology	Number	Percentage
Tubercular	24	48
Bacterial	15	30
Viral	11	22

Clinical Features: Fever and altered mental status were universal across all etiologies. Headache was present in 75% of tubercular, 60% of bacterial, and 36.3% of viral cases. Vomiting occurred in 62.5% of tubercular, 46.6% of bacterial, and 36.3% of viral cases. New-onset seizures were frequent in viral (81.8%) and bacterial (73.3%) meningoencephalitis, whereas only 37.5% of tubercular cases had seizures (Table-III).

Table III: Clinical Features by Etiology

Symptom	Tubercular (%)	Bacterial (%)	Viral (%)
Fever	100	100	100
Headache	75	60	36.3
Vomiting	62.5	46.6	36.3
Altered mental status	100	100	100
Seizures	37.5	73.3	81.8

When outcomes were stratified by etiology, bacterial meningoencephalitis patients with poor outcomes frequently had extensor plantar reflexes and absent papilledema, with a significantly lower GCS (<8) (Table IV). In viral cases, poor outcomes were significantly associated with cranial nerve palsy, absent papilledema, extensor plantar reflex, and GCS <8 (Table IV). Among tubercular meningoencephalitis patients, neck rigidity, Kernig's sign, absent papilledema, and extensor plantar reflex were significantly associated with poor outcomes.

Table- IV Neurological Examination vs Outcome in Meningoencephalitis (n=15)

Neurological Finding	Bacterial outcome Good	Poor	p-value	Viral outcome Good	Poor	p-value	Tubercular outcome Good	Poor	p-value
Neck rigidity	0 (0)	15 (100)	NS	3 (27)	2 (18.2)	NS	2 (8.3)	22 (91.7)	0.043*
Kernig's sign	5 (33.3)	10 (66.6)	NS	1 (9.1)	1 (9.1)	NS	2 (8.3)	14 (58.3)	0.038*
Cranial nerve palsy	0 (0)	1 (6.6)	NS	0 (0)	3 (27.3)	0.041*	1 (4.2)	11 (45.8)	NS
Papilledema (absent/present)	12 (80)	3 (20)	0.032*	6 (54.5)	0	0.029*	4 (16.6)	10 (41.7)	0.027*
Bilateral plantar extensor	2 (13.3)	8 (53.3)	0.021*	1 (9.1)	5 (45.5)	0.033*	5 (20.8)	11 (45.8)	0.031*
GCS <8	0 (0)	7 (46.6)	0.018*	0 (0)	4 (36.4)	0.012*	1 (4.2)	7(29.2)	NS

CSF Findings: Cerebrospinal fluid analysis revealed turbid CSF in all bacterial cases, with Gram-positive diplococci seen in 33.3% of samples. MTB was detected by GeneXpert in 33.3% of tubercular cases, and viral PCR identified Herpes simplex and Varicella zoster in 9.09% each of viral cases. Protein levels were highest in tubercular cases (194 ± 156 mg/dL), while cell counts were elevated in bacterial cases (528 ± 915.9/mm³). Lymphocyte predominance was seen in tubercular and viral meningoencephalitis, while neutrophilic predominance characterized bacterial cases (Table V). CSF parameters were associated with outcomes differently across etiologies. In bacterial meningoencephalitis, none of the CSF findings were significantly associated with poor outcomes (Table V). In viral meningoencephalitis, clear CSF and higher CSF glucose were significantly associated with favorable outcomes (p<0.01) (Table V). Interestingly, in tubercular cases, clear CSF was significantly associated with poor outcomes (p<0.001), while other parameters including glucose, protein, and ADA levels showed no significant association (Table V).

Table -V: CSF Findings vs Outcome in Meningoencephalitis (n=15)

parameter	Bacterial Good	Poor	P-value	Viral Good	poor	p-value	Tubercular Good	poor	P-value
Physical appearance									
– Turbid	6 (40)	9 (60)	NS						
– Clear	0 (0)	0 (0)	NS	8 (72.7)	3 (27.3)	<0.001*	0 (0)	24 (100)	<0.001*
Glucose (mg/dL)	2.0 ± 0.32	2.08 ± 2.43	NS	3.63 ± 1.16	1.23 ± 0.05	0.007*		1.76 ± 0.56	
Protein (mg/dL)	1.42 ± 0.40	2.08 ± 1.63	NS	1.03 ± 0.39	1.47 ± 0.43	NS		1.94 ± 1.56	
Cell count (mm³)	606.66 ± 1174.43	475.55 ± 773.46	NS	25.25 ± 18.29	7.33 ± 0.57	NS		100.91 ± 137.73	

parameter	Bacterial Good	Poor	P-value	Viral Good	poor	p-value	Tubercular Good	poor	P-value
Gram-positive diplococci	1 (7.1)	4 (26.7)	NS						
PCR (S. pneumoniae)	0 (0)	1 (6.6)	NS						
PCR (HSV)				1(9.1)	0 (0)	NS			
PCR (VZV)				0 (0)	1(9.1)	NS			
Gene Xpert (MTB detected)							8(33.3)	NS	
ADA (U/L)							8.43 ± 7.38	NS	

Glasgow Outcome Scale – Extended (GOS-E): Outcomes measured by GOS-E demonstrated that tubercular meningoencephalitis had the worst prognosis, with 75% severely disabled, 12.5% vegetative, and 12.5% deceased. In bacterial meningoencephalitis, 46.7% had poor outcomes, with 7 severely disabled and 2 vegetative, whereas viral meningoencephalitis showed the most favorable outcomes, with 72.7% achieving good recovery and only 27.8% experiencing poor outcomes (Tables VI).

Table -VI: GOS-E Scores by Etiology

Outcome (GOS-E)	Bacterial n (%)	Viral n (%)	Tubercular n (%)
Good recovery	3 (20)	6 (57.14)	3 (12.5)
Moderate disability	5 (33.3)	3 (27.3)	5 (20.8)
Severe disability	7 (46.7)	2 (18.2)	18 (75)
Vegetative state	0	0	0
Death	0	0	3 (12.5)

Linear regression demonstrated a significant positive correlation between GCS and GOS-E, with 33% of the variation in GOS-E explained by GCS (R^2 = 0.334, B = 0.441, p=0.000) (Figure 1).

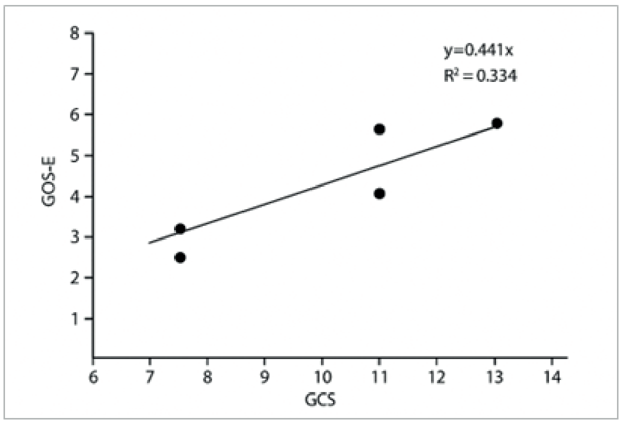

Figure-1: A significant linear regression between GOS-E and GCS.

Predictors of Outcome: Multivariate logistic regression identified several factors significantly associated with poor outcomes: presence of headache (OR 0.192, 95% CI 0.047–0.783, p=0.021), GCS <8 (OR 0.102, 95% CI 0.012–0.872, p=0.037), prolonged hospital stay (OR 0.778, 95% CI 0.650–0.930, p=0.006), elevated ESR (OR 0.893, 95% CI 0.819–0.974, p=0.011), low CSF glucose (OR 2.134, 95% CI 1.028–4.433, p=0.042), and abnormal CT/MRI findings (OR 0.065, 95% CI 0.008–0.558, p=0.013). Other variables such as CSF protein, ADA, and CRP were not statistically significant (Table VII).

In summary, tubercular meningoencephalitis was the most frequent etiology with the worst outcomes, bacterial cases had intermediate outcomes, and viral meningoencephalitis was associated with the most favorable prognosis. Neurological examination findings, CSF parameters, and imaging abnormalities were key determinants of short-term outcomes, and low GCS, headache, prolonged hospitalization, elevated ESR, low CSF glucose, and abnormal imaging were significant predictors of poor recovery.

Table-VII: Factors influencing the study outcome (N=50)

Factors	OR	95% CI Lower	Upper	p-value
Headache (no vs yes)	0.192	0.047	0.783	0.021^S
GCS (>8 vs<8)	0.102	0.012	0.872	0.037^S
Duration of hospital stay	0.778	0.650	0.930	0.006^S
ESR	0.893	0.819	0.974	0.011^S
CSF (clear vs turbid)	2.143	0.543	8.461	0.277^{NS}
CSF glucose	2.134	1.028	4.433	0.042^S
CT/MRI findings (normal vs abnormal)	0.065	0.008	0.558	0.013^S

Discussion:

Meningoencephalitis is a disorder of varied etiology and is now one of the leading cause of morbidity and mortality all over the globe. Meningoencephalitis is a disease of major public health importance due to its high epidemic potential, high case fatality rate (CFR), and sequalae among survivors. The present study had objectives to study various clinical features, find out possible etiologies and to determine outcome and effect of different prognostic markers in outcome of Meningoencephalitis at the time of end of hospital stay. A better understanding of presenting features, causes and outcome is essential to help to improve the approach and to plan rational management of Meningoencephalitis. In our study, most of the study participants 22 (44%) were aged between 25-50 years. The mean ± SD of the age of the study participants were 33.86 ± 16.67 years, which was almost similar to Zhao et al[13] conducted study. Most of the participants in our study 35 (70%) lived in urban areas and 32 (64%) belonged from lower socioeconomic class. Study conducted by De et al[14], found almost similar to this study. In our study, most of the study participants 30 (60%) were female. The male female ratio was 1:1.5, which was almost similar to study done by Ntagwabira15. In our study (5, 10%)

of participants were suffering from diabetes mellitus. Gabor et al[16], Vashisht et al[2] stated that diabetes was the most common co-morbid condition. In this study most of the study participants 24 (48%) had tubercular meningoencephalitis, followed by 15 (30%) had bacterial and 11 (22%) had viral meningoencephalitis, which was similar to study done by Paul Matthew Pasco et al[17], Borade et al[18] Among all study group, all the study participants 15 (100%) had fever and altered mental status as the presenting symptoms, which was almost similar to study done by De et al[14], Vasisht et al[19]. Among viral meningoencephalitis seizure was associated with poor outcome, similar to study findings by Zhao et al[13], De et al[14]. CNS examination findings among all study group found low GCS and extensor plantar were associated with poor outcome, similar to study by Kafle et al, Gabor et al[16], Van de beek et al[20], Modi et al[21]. Among the Viral meningoencephalitis study group investigations and CSF findings found high lymphocyte count in blood and low glucose content of the CSF was associated with poor outcome similar to study by Gabor et al[16]. CSF study among Viral meningoencephalitis found that clear color of fluid associated with good outcome but in Tubercular meningoencephalitis clear color of fluid was associated with poor outcome. Results were not similar with our study due to different etiology, agents, study group and methodology of study. Streptococcus pneumoniae was the etiological agents of Bacterial meningoencephalitis and Herpes simplex, varicella zoster was the etiological agents of Viral meningoencephalitis, similar to study by Vasisht et al[19]. Pelivanoglu, Kart Yasr et al found the most frequently identified cranial radiological findings were tuberculoma 37% of cases, which was similar to our study. Our findings shown that most of the participants 18 (75%) of Tubercular, 7 (46%) of bacterial meningoencephalitis were severely disabled and 3 (12%) died among Tubercular group, which was similar to study by Yerramilli et al[22], Borade et al[18]. Mean ± SD of the GOS-E in relation to poor outcome among bacterial meningoencephalitis was 3.44 ± 0.88, viral meningoencephalitis was 2.66 ± 0.57 and tubercular meningoencephalitis was 3.20 ± 1.10, respectively. Mean ± SD of the duration of hospital stay (days) in relation to poor outcome among Bacterial meningoencephalitis was 23.88 ± 15.38, Viral meningoencephalitis was 29.66 ± 5.03 and tubercular meningoencephalitis was 31.91 ± 12.46 respectively. Previous study by Sharma et al, Chen and Liu[23,24], Jakobsen et al[25], Weisfelt and others[26], In the DMC (derivation cohort), In the EDS (validation cohort), Outcome was graded using GOS and GOSE scoring denoted favorable/unfavorable. Findings were not similar to our study due to different etiology, agents, study group and methodology of study. Multivariate logistic regression was performed to assess the impact of factors on the overall study outcome. Table VII shown that, headache, low GCS, increased duration of the hospital stay, raised ESR, low glucose in CSF and abnormal CT/MRI findings of the participants were significantly associated with the poor outcome ($p<0.05$). Among the factors, glucose in CSF wass the strongest predictor of the poor outcome with an odds ratio of 2.134. In a previous study Sharma et al[23], Chen and Liu[24], Jakobsen et al[25], Weisfelt and others 26 found almost similar findings to our study.

Conclusion:

In the current study tubercular meningoencephalitis was the most common etiological agents of Meningoencephalitis. Most of the participants with tubercular and bacterial meningoencephalitis were severely disabled. Patients presented with headache, GCS<8, long duration of the hospital stay, increased ESR, decreased glucose in CSF and abnormal imaging findings of the participants were significantly associated with the poor outcome ($p<0.05$).

Conflict of Interest: None.

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