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A Study Of Clinical Profile In Patients With Febrile Illness And Altered Sensorium

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Abstract

Introduction

Acute febrile encephalopathy describes patients in which altered mental status either accompanies or follows a short febrile illness. Utmost cognizance of all these confounding factors is to be kept in mind while dealing with such patients. This study was aimed at studying the clinical profile of patients presenting with fever and altered sensorium to MICU at tertiary care hospital and to assess the conditions causing fever and altered sensorium in these patients.

Patients And Methods

Patients with fever and altered sensorium at the time of admission were enrolled. The following data was collected from them: Clinical presentation, FOUR score, CBP, malarial parasite, HIV, HBsAg, serum electrolytes, blood urea, serum creatinine, RBS, CSF, CXR-PA view, CT brain, MRI brain.

Results

100 patients were recruited. 32 patients had FOUR score < 8 and 68 patients had FOUR score > 8. Mortality was increased when FOUR score scale was < 5. Those patients having FOUR score in range of 7 to 10 had higher morbidity. Residual deficits were seen with patients having FOUR scores in the range of 7 to 10. Better outcome was seen with scores > 10. Based on these time interval between fever and altered mentation, cases were classified as acute (46 cases), sub-acute (46 cases) and chronic (8 cases).

Conclusion

Tuberculous meningitis was the most common etiology among subacute and chronic meningitis cases. FOUR scale score helped us to assess the condition at the admission and can be used as prognostic factor for outcome.

Keywords: Encephalopathy; altered sensorium; febrile illness; FOUR score; Tuberculous meningitis

Introduction

Febrile encephalopathy is a common condition leading to hospitalization in India (1,2). CNS infections are the commonest cause of non-traumatic coma (3,4). Acute febrile encephalopathy (AFE) is a term used to describe patients in which altered mental status either accompanies or follows a short febrile illness (1). Encephalopathy is a diffuse disease of brain that alters its structure or function. It is caused by variety of infective, metabolic, toxic, ischemic/hypoxic, nutritional causes or trauma. In febrile illness, encephalopathy may result from pathogenic mechanisms affecting nervous system directly or systemic complications like hypoglycemia, hypovolemia, hyperpyrexia, hypoxia, anemia, hepatic/renal failure and bleeding may contribute to its pathogenesis (5,6).

Considering the fact that confusion is a key sign of encephalopathy, this symptom accounts for around 2% of the patients in emergency departments (7,8). The list of differential diagnosis of the clinical syndrome of febrile encephalopathy is long and timely differentiation between these disorders is very important because correct diagnosis and treatment have a significant impact on morbidity and mortality. This diagnostic challenge is especially important in dealing with patients with multiple chronic medical conditions.

The profile of febrile encephalopathy varies on the basis of demographic and geographical characteristics of the study population (4). It is important to determine the etiologic spectrum of febrile encephalopathy syndrome, with an emphasis on the CNS infection by focusing on epidemiology and age groups (9). Patients presenting with fever and altered sensorium should be treated as a medical emergency. Early recognition, efficient decision making, and early institution of therapy are the key elements to saving the life of the patient. The presence of fever by itself is not sufficient to make a diagnosis of infective etiology, and therefore careful evaluation is required to exclude the clinical mimickers of infection. In addition, encephalopathy can be precipitated by systemic infections/sepsis without cerebral infection. Hence, utmost cognizance of all these confounding factors is to be kept in mind while dealing with such patients. Sepsis entails complications such as hypoglycemia, hyperpyrexia, hypovolemia, hepatic, or renal failure which can themselves cause altered sensorium.

Only a few studies have been done so far even though AFE is a common condition in India. Our study was aimed at studying the clinical profile of patients presenting with fever and altered sensorium to MICU at a tertiary care hospital and to assess the conditions causing fever and altered sensorium in these patients.

Patients And Methods

This was a descriptive type of study, done in patients admitted in MICU of Gandhi Hospital for fever with altered sensorium during December 2017 to May 2019. Prior permission was taken from our institutional ethics committee. Patients were recruited into study based on the following inclusion and exclusion criteria:

Inclusion Criteria:

1. Age > 15yrs
2. Patients with fever and altered sensorium at the time of admission.
3. New onset seizures, focal neurological deficits along with fever and altered sensorium

Exclusion Criteria:

1. Known epileptics
2. Past History of CVA
3. Head trauma
4. Known Renal and Hepatic disorders (metabolic encephalopathy)
5. Patients on Immunosuppressive drugs
6. Drug abuse
7. HIV
8. Heat stroke

All participants and their relatives were explained the purpose and procedure of research. Their participation in study was voluntary and they had the knowledge about option to drop out of study at any point of time. Informed consent was taken on a document written in their understandable language. If patient or relative was illiterate then document was read out by an individual unconcerned with hospital or patient. Document was read out in presence of 2 witnesses related to patient. If patient was unable to comprehend then signature/thumb impression of relatives were taken. Entire process was videotaped.

Upon recruitment into study, the following data was collected from the patients:

1. Age
2. Sex
3. Educational qualifications: illiterate, primary school, secondary school or graduate.
4. Residence location: Urban / rural
5. Clinical presentation
6. FOUR score
7. Diagnostic investigations: CBP with ESR, Smear for malarial parasite, HIV, HBsAg, serum electrolytes, blood urea, serum creatinine, RBS, CSF analysis, CXR-PA view, CT brain, MRI brain

Results

100 patients were recruited in this study. 45 patients were in age group of 26-35 years, 30 patients were in age group of 36-45 years. 10 patients were in age

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group of 15-25 and 46-55 each. 5 patients were in age group of 56-65 years. Among total study population, 66 were males and 34 were females. [Table 1; Graph 1]

Among 66 males most of them (30.30%) had studied till primary school educational group, followed by graduates (28.78%) and illiterates (22.72%). Among 34 females, 44.11% were illiterates followed by secondary education (29.41%) and primary school (14.7%) [Table 1; Graph 2]. Rural population was more affected compared to urban population (61% vs 39%) [Table 1; Graph 3].

TABLE 1: BASELINE DEMOGRAPHICS OF STUDY PARTICIPANTS

	n	**%**
AGE GROUP (years)		
15 – 25	10	10%
26 – 35	45	45%
36 – 45	30	30%
46 – 55	10	10%
56 – 65	5	5%
GENDER		
Male	66	66%
Female	34	34%
EDUCATION		
Illiterate	30	30%
Primary	25	25%
Secondary	22	22%
Graduation	23	23%
RESIDENCE		
Rural	61	61%
Urban	39	39%

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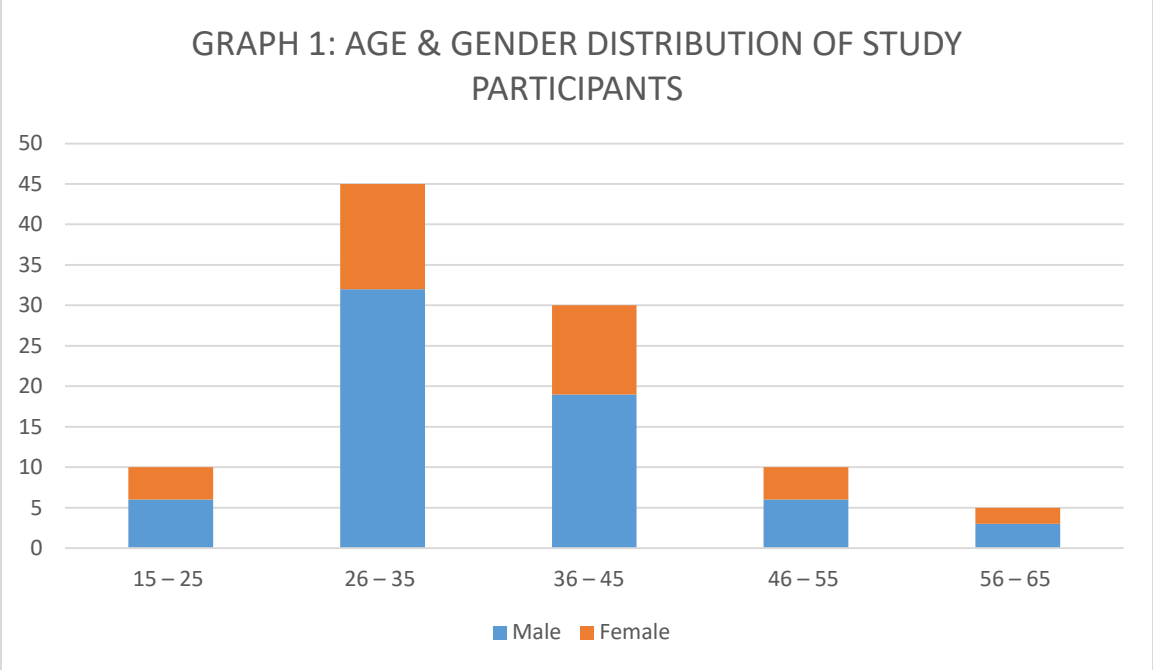

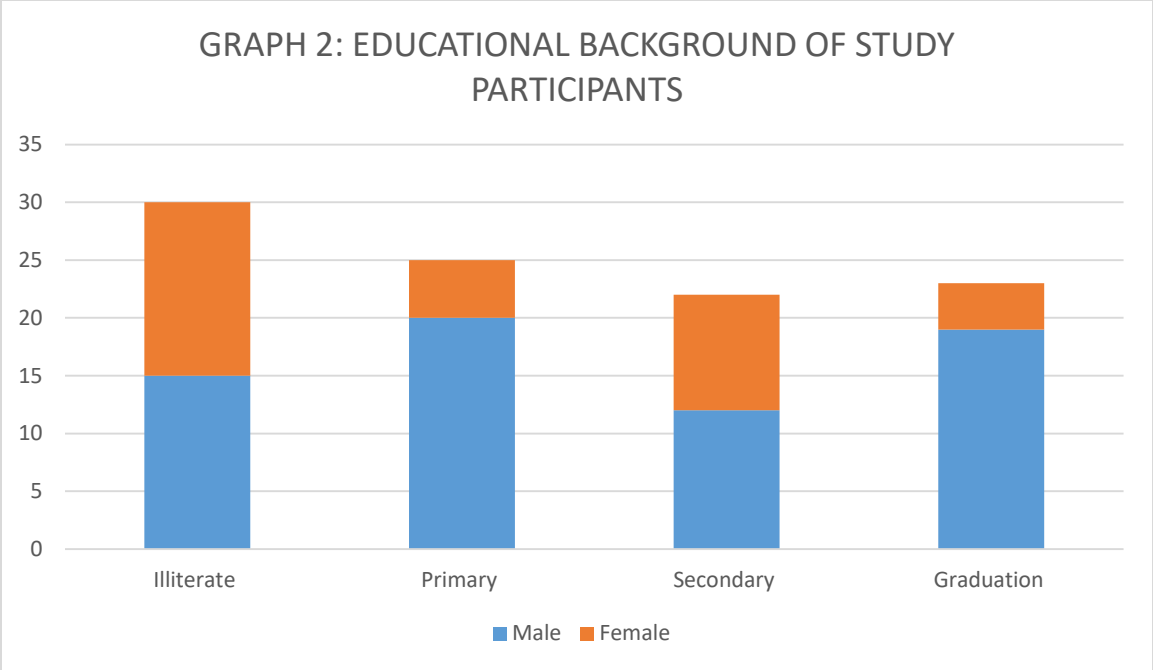

Fever and altered sensorium was the presenting feature in all patients. Altered sensorium ranged from drowsiness to deep coma which was assessed using FOUR score coma scale. Apart from fever and altered sensorium; headache, neck stiffness, vomiting, seizures, hemiparesis, cranial nerve palsy, speech disturbances, cognitive deficits were also noted in various patients. [Table 2; Graph 4]. Headache (74%) was the next most common sign observed after fever and altered sensorium. 12 patients had seizures during the course of illness. Among them, 10 patients had generalized tonic clonic seizures and two had focal motor seizures.

64 patients had neck stiffness. 36 patients did not have neck stiffness, even though there was meningeal involvement. Fundus examination showed papilledema in 10 patients. The meningeal signs Kernig's and Brudzinski's signs were positive in 35% and 54 % patients with neck stiffness respectively. [Table 2; Graph 4]

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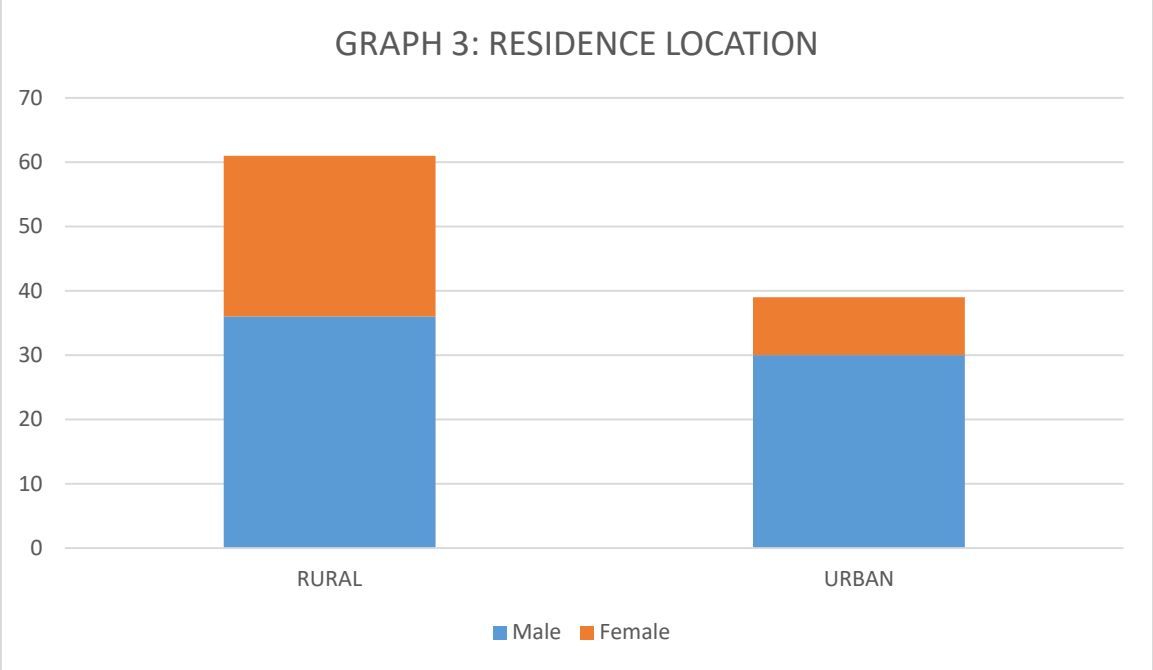

TABLE 2: CLINICAL FEATURES OF STUDY PARTICIPANTS		
	n	**%**
CLINICAL FEATURES		
Fever	100	100%
Altered sensorium	100	100%
Headache	74	74%
Neck stiffness	64	64%
Vomiting	48	48%
Seizures	12	12%
Hemiparesis	8	8%
Cranial nerve palsy	12	12%
Speech disturbance	4	4%
Cognitive deficits	2	2%
FOUR SCORE		
< 8	32	32%
> 8	68	68%
TIME INTERVAL BETWEEN ONSET OF FEVER AND ALTERED SENSORIUM		
≤1 day	10	10%

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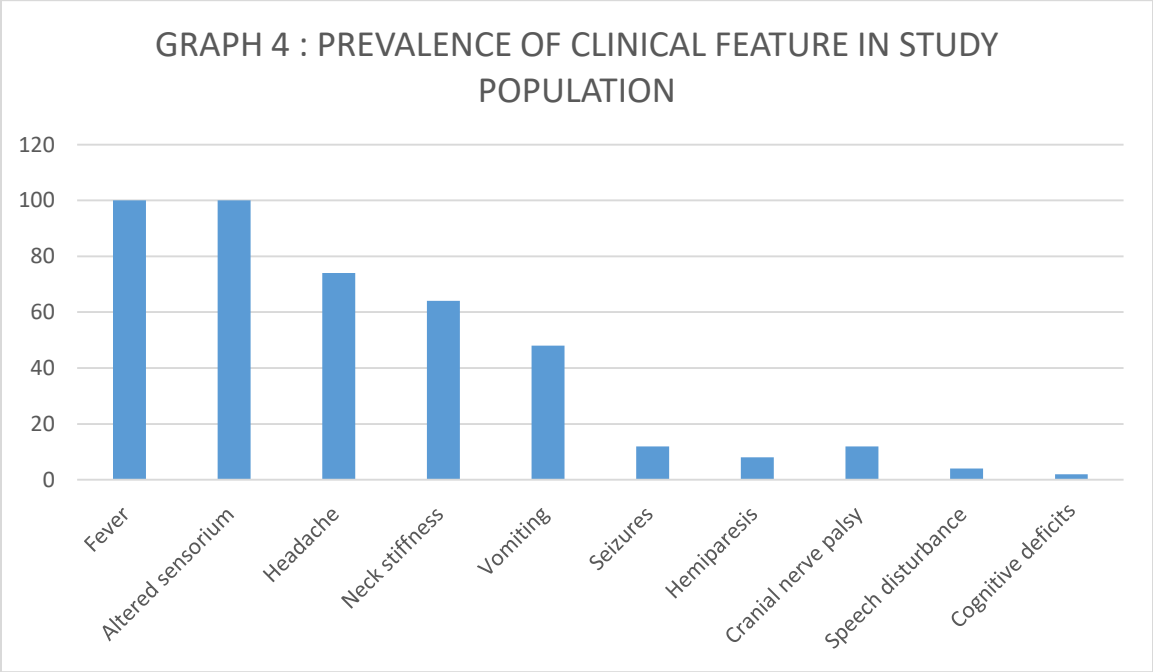
2-3 days	20	20%
4-8 days	33	33%
9 -15 days	27	27%
16-21 days	10	10%
MODE OF ONSET		
Acute	46	46%
Sub-acute	46	46%
Chronic	8	8%



FOUR score scale was used at the time of admission to assess mental status of the patient at presentation. In the current study; 32 patients had FOUR score < 8 and 68 patients had FOUR score > 8. In our study, we observed that mortality was increased when FOUR score scale was < 5. While those patients having FOUR score in the range of 7 to 10 had higher morbidity. Residual deficits were seen with patients having FOUR scores in the range of 7 to 10. Better outcome was seen with scores > 10. [Table 2]

Time interval between onset of fever to altered sensorium was different from patient to patient. In 33 cases, time interval was in the range of 4 to 8 days; in 27 cases time interval was in the range of 9 to 15 days; in 20 cases it was between 2 to 3 days; 10 cases were it was for 16 to 21days and in 10 cases it was for < one day. [Table 2; Graph 5]. Based on these time interval between fever and altered mentation, cases were classified as acute (<1 week), sub-acute (1-4 weeks) and chronic (>4 weeks). We had 46 acute cases, 46 sub-acute cases and 8 chronic cases. [Table 2; Graph 6].

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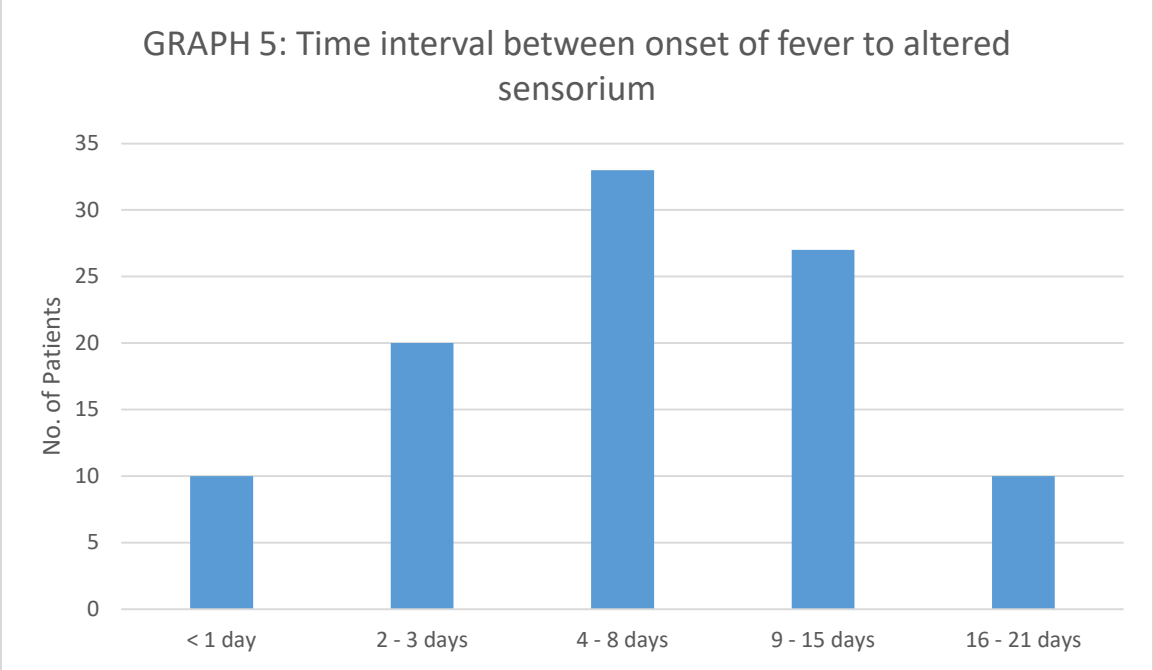

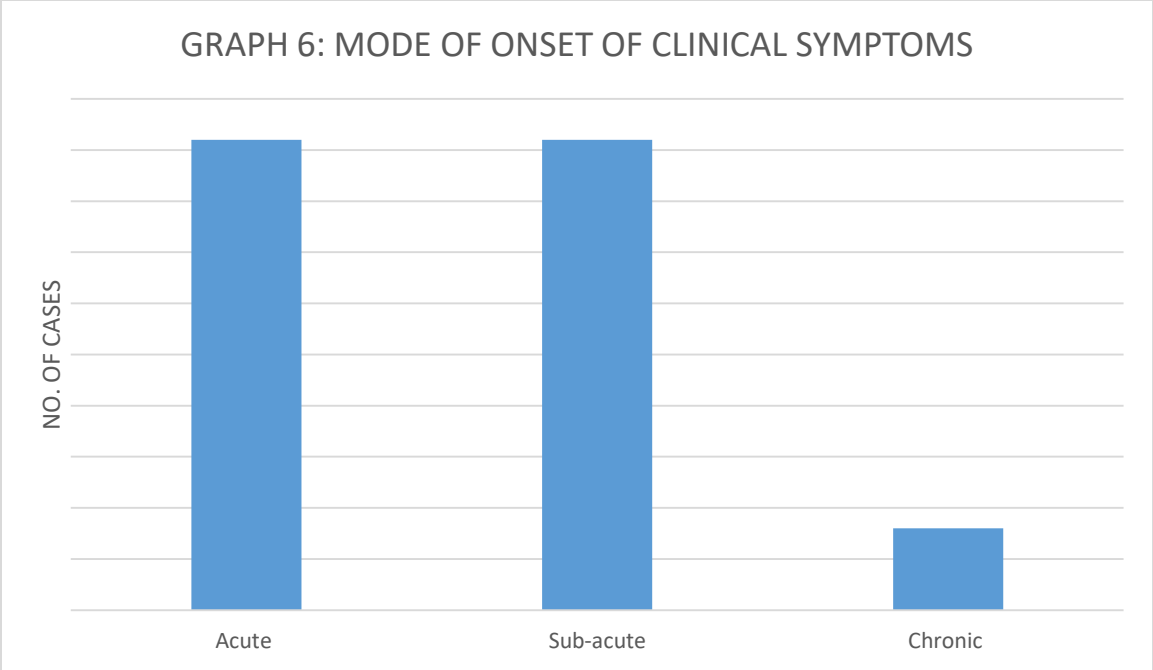

Blood Investigations revealed mean Hb 13.07±1.45 gm%, mean WBC 8898.97±1215.60, mean ESR 49.93±3.78, mean RBS 118±14.3 mg/dl and mean serum sodium 134.76±2.3. CSF analysis revealed mean sugar level of 33.06±17.1, mean protein level of 210.9±23.3 and mean cell count of 275.2±40.20. Radiological imaging revealed Meningeal Enhancement in 50 cases, Hydrocephalus in 12 cases, Granuloma in 10 cases, Vasculitic infarcts in 10 cases, Lobar enhancement in 6 cases, Brain Abscess in 2 cases and Cerebral edema in 2 cases. [Table 3]

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TABLE 3: INVESTIGATIONAL RESULTS OF STUDY PARTICIPANTS		
	MEAN±SD	
Hemoglobin	13.07±1.45 gm%	
WBC	8898.97±1215.60	
ESR	ESR 49.93±3.78	
RBS	118±14.3 mg/dl	
Serum Sodium	134.76±2.3	
CSF SUGAR	33.06±17.1	
CSF PROTEIN	210.9±23.3	
CSF Cell Count	275.2±40.20	
	n	**%**
Meningeal Enhancement	50	50%
Hydrocephalus	12	12%
Granuloma	10	10%
Vasculitic infarcts	10	10%
Lobar enhancement	6	6%
Brain Abscess	2	2%
Cerebral edema	2	2%

In our study, 55% cases recovered completely and 26% recovered with residual deficits and 19% deaths occurred. [Table 4; Graph 7]

TABLE 4: CLINICAL OUTCOME OF STUDY PARTICIPANTS		
	n	**%**
Cases Recovered	55	55%
Residual Deficits	26	26%
Deaths	19	19%

Among 100 patients, 58 patients were diagnosed as Tuberculous Meningitis, 16 patients were diagnosed as pyogenic meningitis, 14 patients were diagnosed as viral meningoencephalitis, 4 patients had cerebral Malaria. 4 patients had Sepsis associated encephalopathy (SAE), 2 patients had Brain abscess and 2 had Neuroleptic malignant syndrome. Among the 14 patients of viral meningoencephalitis, 4 patients were positive for dengue, 4 patients had positive HSV PCR in the CSF. No organism could be found in the remaining 6 patients. [Table 5; Graph 8].

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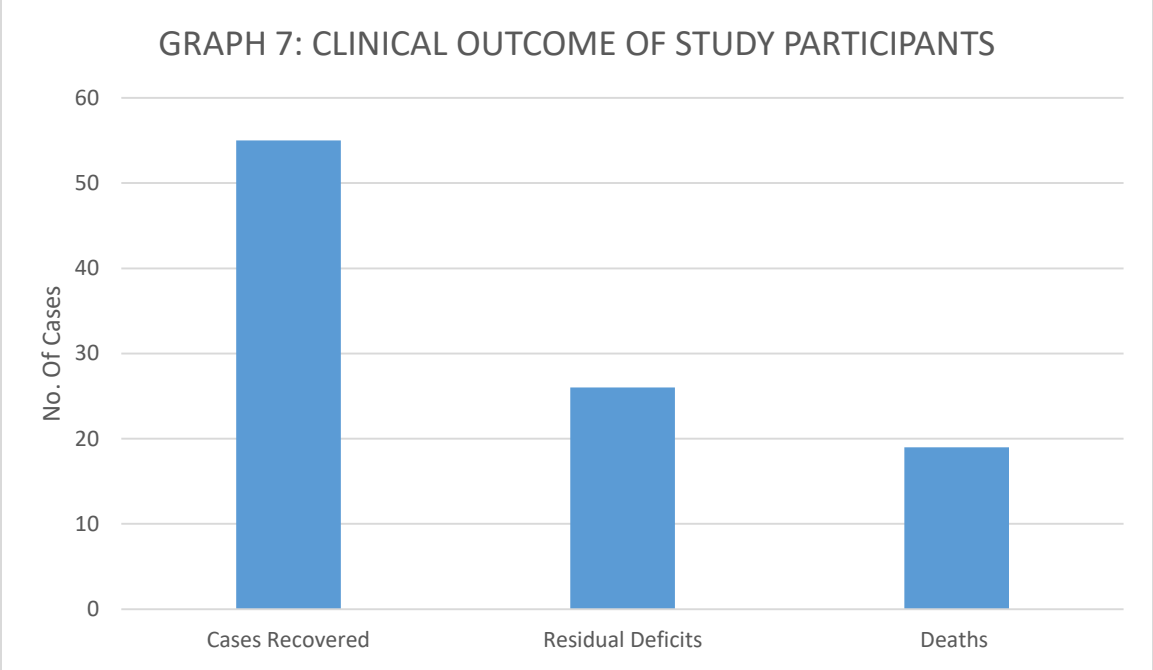

TABLE 5: ETIOLOGICAL DIAGNOSIS OF STUDY PARTICIPANTS

	n	**%**
Tuberculous Meningitis	58	58
Acute Pyogenic Meningitis	16	16
Viral Meningoencephalitis	14	14
Cerebral Malaria	4	4
SAE	4	4
Brain Abscess	2	2
NMS	2	2

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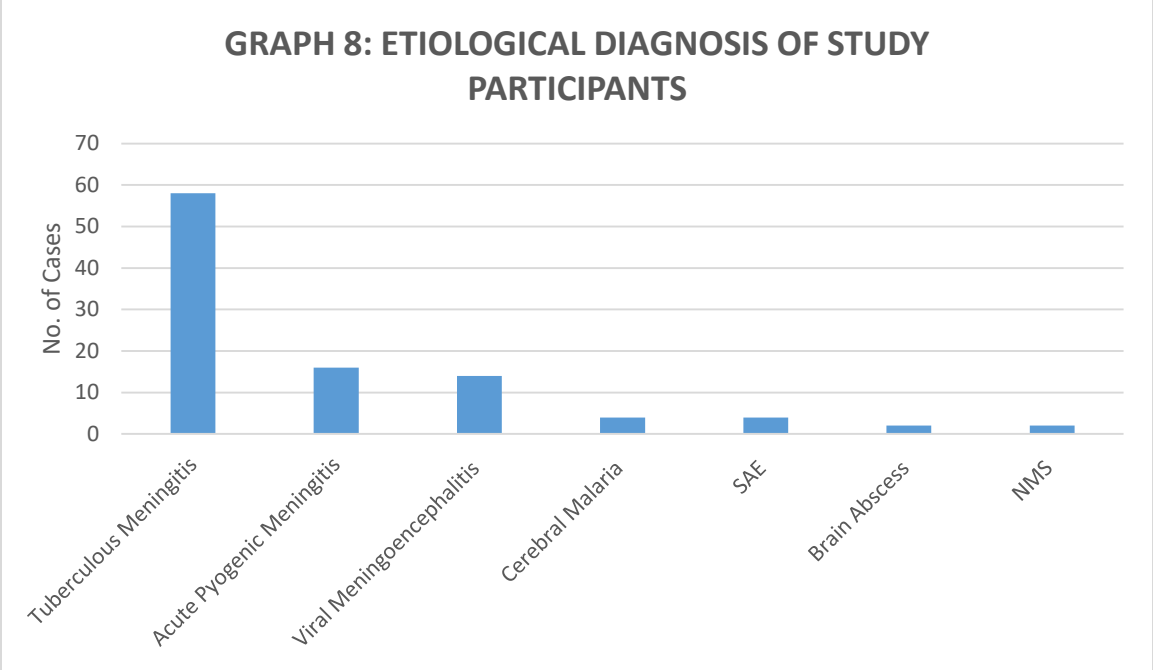

TABLE 6: DISTRIBUTION OF DEMOGRAPHICS AND CLINICAL FEATURES UNDER EACH ETIOLOGY

	male	female	age	fever	altered sensorium	head ache	neck stiffness	vomiting	seizures	hemiparesis	cranial nerve palsy	speech disturbances
TBM	36	22	35.5	58	58	44	44	35	7	8	8	2
VM	6	8	32	14	14	9	5	0	2	0	0	0
PM	10	6	29	16	16	14	15	13	2	0	4	2
CM	3	1	28.5	4	4	4	0	0	1	0	0	0
SAE	2	2	35	4	4	1	0	0	0	0	0	0
BA	2	0	30	2	2	2	0	0	0	0	0	0
NMS	2	0	17	2	2	2	0	0	0	0	0	0

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TABLE 7: VARIATION OF INVESTIGATIONAL PARAMETERS UNDER EACH ETIOLOGY

Etiology	WBC Count	Sodium	ESR
Tuberculous meningitis (N=58)	5602.08	133.3	66.22
Pyogenic meningitis (N=16)	14400.43	135.8	46.02
SAE (N=04)	10819.75	136.5	27.75
Cerebral malaria (N=4)	11075.5	137.5	7.25
Viral encephalitis(N=14)	13668.78	137.5	12.78
Brain abscess (N=02)	13561.5	135.5	35
NMS(02)	14251	137	13

CSF analysis was done to know the etiology of febrile encephalopathy; in our study this provided additional evidence for supporting the clinical features and history. ADA and CSF CBNAAT was performed to confirm tuberculous meningitis (TBM). CSF analysis along with imaging helped us to confirm the diagnosis. In our study the mean value of CSF in TBM for proteins, total cells and sugars were 263, 272.75 and 22.05 respectively; while that in pyogenic meningitis were 234.56, 421.18 and 23.5 respectively; and that in viral encephalitis were 114.68, 307.18 and 61.31 respectively. [Table 8].

TABLE 8: VARIATION OF CSF PARAMETERS UNDER EACH ETIOLOGY

	MEAN CELL COUNT	MEAN SUGAR LEVEL	MEAN PROTEIN LEVELS
Tuberculous Meningitis	272.50	22.05	263.00
Pyogenic Meningitis	421.18	23.50	234.56
Sepsis Associated Encephalopathy	3.25	66.25	21.00
Cerebral Malaria	4.50	65.75	26.00
Viral Encephalitis	307.18	61.31	114.68
Brain Abscess	7.50	71.00	30.00

MRI evidence of basal meningeal exudates, hydrocephalus, tuberculous granuloma in the brain helped to reach the diagnosis of tuberculous meningitis. CT was normal in some patients with tuberculous meningitis, but MRI revealed exudates and infarcts. Only 26 patients had neurological deficits. 12 patients had cranial nerve

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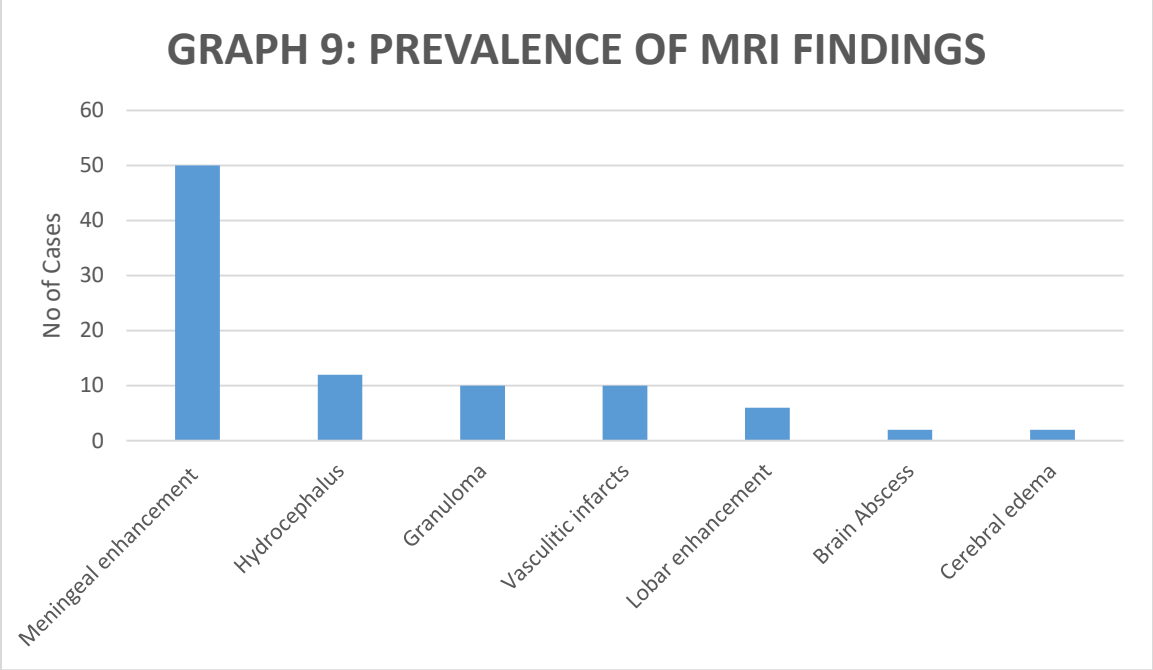
paralysis (lateral rectus palsy and facial weakness), most commonly involved nerves were 6th and 7th nerve, 8 patients had hemiparesis, 4 patients had speech disturbances and 2 patients had cognitive deficits. In our study we observed 8 patients with normal MRI/CT and remaining 92 patients had findings such as Meningeal Enhancement, Hydrocephalus, Granuloma, Vasculitic infarcts, Lobar enhancement, brain abscess and cerebral edema. [Table 9; Graph 9].

TABLE 9: PREVALENCE OF MRI FINDINGS

MRI FINDING	**n**
Meningeal enhancement	50
Hydrocephalus	12
Granuloma	10
Vasculitic infarcts	10
Lobar enhancement	6
Brain Abscess	2
Cerebral edema	2



Among 50 cases with Meningeal Enhancement, 10 patients were diagnosed with pyogenic meningitis followed by 40 cases of Tubercular Meningitis. 12 patients with tubercular meningitis showed hydrocephalus. 10 patients had granuloma. Among 10 patients with vasculitic infarcts, two had pyogenic meningitis and 8 had tubercular meningitis. 12 patients with tubercular Meningitis showed hydrocephalus. 10 patients had granuloma. Among 10 patients with vasculitic infarcts, 2 had pyogenic meningitis and 8 had tubercular meningitis. Among 14 patients with viral meningitis, 6 patients had MRI findings. Among 6 patients, 4 patients with HSV had lobar enhancement in frontal and temporal lobes and 2 patients with dengue had hyper-intensities in bilateral thalami, pons and left temporal lobe in MRI findings. Two patients had brain abscess in NMS. Serum CPK levels were increased which helped to diagnose their condition and they had a history of use of antipsychotics.

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In this study, 34.48% of residual were seen in tuberculous meningitis, followed by 25% pyogenic meningitis. 25.86% deaths were in tubercular meningitis followed by 25% in cerebral malaria and SAE. Among the Tuberculous meningitis cases, 23 recovered, 20 had residual deficits and 15 deaths were seen. In Pyogenic meningitis, 10 cases recovered, 04 had residual deficits and two deaths were seen. In SAE, 03 cases recovered and one death occurred. In Cerebral malaria, 03 cases recovered and one death occurred. In Viral encephalitis, 14 cases recovered, no deaths occurred. In Brain abscess, two cases recovered and NMS, two cases recovered. [Table 10; Graph 10].

TABLE 10: TOTAL RECOVERIES, RESIDUAL DEFICITS AND DEATHS AMONG STUDY PARTICIPANTS

Etiology	Cases recovered	Residual deficits	Deaths
Tuberculous meningitis (N=58)	23 (39.65%)	20(34.48%)	15(25.86%)
Pyogenic meningitis (N=16)	10(62.5%)	04(25%)	2(12.5)
SAE (N=04)	03(75%)	00(0%)	01(25%)
Cerebral malaria (N=4)	03(75%)	00(0%)	01(25%)
Viral encephalitis(N=14)	14(100%]	00(0%)	00(0%)
Brain abscess (N=02)	02(100%)	00(0%)	00(0%)
NMS[N=02]	02[100%]	00(0%)	00(0%)

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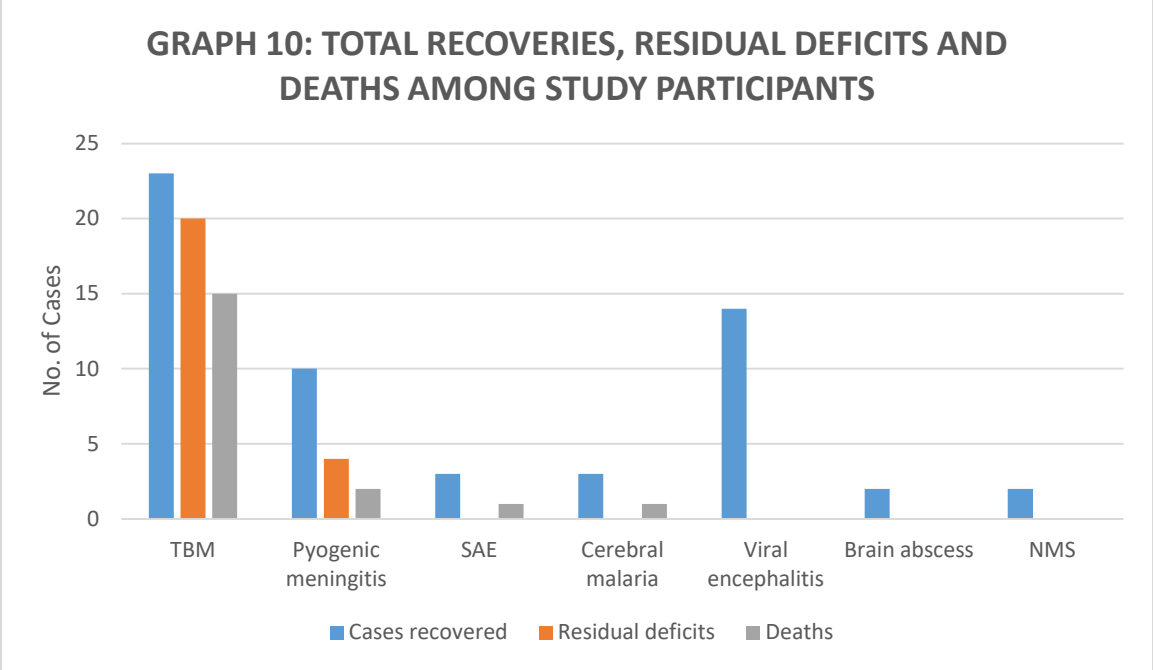

TABLE 11: RELATION OF FOUR SCORE TO OUT COME

FOUR SCORE	deaths	residual deficits	recovery
<5	TBM 1 PM 1	0	0
5--7	TBM 14 PM 1 SAE1	0	0
7--10	CM 1	TBM 20 PM 4	0
>10	0	VM 2	TBM23 PM10 VM14 NMS2 BA2 CM 3 SAE 3

In our study, 2% patients were found to have mild hyponatremia, 15% had moderate hyponatremia and 15% had severe hyponatremia. Among 15 patients with severe hyponatremia, 9 (60%) died. Among 10 patients with moderate hyponatremia 4 (40%) died. While 6 (8.2%) deaths occurred among those having normal sodium levels. Among 9 deaths in severe hyponatremia, 7 (77.78%) cases were of TB meningitis and 2 (22.22%) were of pyogenic meningitis.

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Among acute cases, 17.39% were of Tuberculous Meningitis, 34.7% were of Acute Pyogenic Meningitis, 34.7% were of Viral Meningoencephalitis, 8.69% were of Cerebral Malaria and 4.34% were of SAE. Among sub-acute cases, 91.30% were of Tuberculous Meningitis, 4.34% were of Cerebral Malaria and 4.34% wee of Brain Abscess. While among chronic cases, 100% were of tuberculous meningitis. [Table 12].

TABLE 12: ASSOCIATION OF MODE OF ONSET WITH DIAGNOSIS

ETIOLOGY CHRONIC Total	ACUTE	SUB ACUTE	CHRONIC	Total
Tuberculous Meningitis	8	42	8	58
Acute Pyogenic Meningitis	16	0	0	16
Viral Meningoencephalitis	14	0	0	14
Cerebral Malaria	2	2	0	4
SAE	4	0	0	4
Brain Abscess	0	2	0	2
NMS	02	0	0	02
Total	**46**	46	8	100

Discussion

In this study, we observed that according to age, majority of cases (45%) were between 26-35 years, 30% were in 36-45 years, 10% were in 15-25years, 10% were in 46-55 years and 5% were in 56-65years. 75% of cases who presented to the hospital were between the age groups of 26 - 45 years Although none of the CNS infections are known to have age distribution pattern in adult population, yet this apparent predominance in presentation to hospital in the age groups between 26 to 45 can be attributed to the working population in the society who gets preferential medical attention.

In our study, incidence was more in males (66%). In a study conducted by Bhalla A et al there was a male predominance with males constituting around 60% of the study population (1) and in another study by Elham Peidaee et al there were 60.8% males (7). Although none of the CNS infections are known to have a male predominance, yet this apparent male predominance can be attributed to the male dominated social system where a sick male gets preferential medical attention. Moreover males in our society indulge in outdoor activities more often due to work making them susceptible to vector-borne and infectious diseases.

Our study included the cases with the symptoms of fever, and altered sensorium. Among them, 74 (74%) presented with headache, 64(64%) patients presented with neck stiffness, 48(48%) patients presented with vomiting, 12(12%) presented with seizures, 12(12%) presented with cranial nerve palsies, 8(8%) presented

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with hemiparesis and 4(4%) presented with speech disturbances.

In the our study 64(64%) patients presented with neck stiffness and 36(36%) patients presented without neck stiffness .This indicates that absence of neck stiffness does not exclude the possibility of meningoencephalitis. Meningeal signs are reliable and usually present in awake patients. It may be absent in infants, elderly, sub-acute, chronic cases, immunocompromised and in patients with predominant encephalitis. The present study included non-infectious cases of febrile encephalopathy. 36(36%) patients without neck stiffness can be attributed to this.

In our study, Kernig's and Brudzinski's signs were positive in 22(35%) and 35(54%) patients of neck stiffness (64 patients) respectively. This can be attributed to mechanism of genesis of Kernig's and Brudzinski's signs. The signs are based on the severity of inflammation of meningeal and nerve roots. Irrespective of the disease severity, these meningeal signs may be absent in infants, elderly patients, in immunocompromised or comatose patients (10). All these factors may account for absence of meningeal signs in the rest of the cases with neck stiffness. In our study, 12(12%) patients presented with seizures. Among them, 10 patients presented with generalized seizures and 2 patients presented with focal seizures. In the present study 7(12%) patients with tubercular meningitis presented with seizures. Among them 2(28%) patients presented with focal seizures and 5(72%) patients presented with generalized seizures. In a study conducted by Bang N D et. al., Among 100 patients of TBM cases, 39 cases had seizures (11). In our study, the incidence of TBM was less than the above study. This might be attributed to small sample size of the present study. The above mentioned study included only the tubercular meningitis which might have led to the variation.

In our study, 2 (12.5%) patients with pyogenic meningitis had generalized seizures. In a study conducted by Van de beek et. al., 15 % of cases with pyogenic meningitis presented with seizures, which is nearly consistent to our study (12). In our study, 2 (14.2%) patients with viral meningoencephalitis and 1 (25%) patient with malaria had seizures.

In the present study, 26 patients had neurological deficits of which 12 had cranial nerve palsies, 8 had hemiparesis, 4 had speech disturbances and 2 had cognitive problems. In our study, 8 (13.7%) patients with TBM had hemiparesis, 8(13.7%) had cranial nerve palsies and 2(3.4%) had speech disturbances. In a study conducted by Bang ND et. al., among TBM patients 20% had hemiplegia, 22% had sixth nerve palsy and 7% had seventh nerve palsy (11). In our study, among 8 cranial nerve palsies, 5 (62.5%) had 6th nerve palsy and 3 (37.5%) had 7th nerve palsy. The deficits can be attributed to vascular infarcts, tuberculomas and basal exudates seen in TBM. These can also lead to seizures in TBM. The more incidence of neurological deficits in the above study might attributed to the sample which included only TBM cases.

In our study, 4 (25%) patients had 6th nerve palsy and 2 (12.5%) patients had speech disturbances with pyogenic meningitis. In a study conducted by Van de beek et. al., 14 (3%) study patients had 6th nerve palsies and 24 (4%) had hemiparesis (12). The high incidence in our study might be attributed to the sample. The compared study contained exclusively cases of pyogenic meningitis. In our study we included all cases of different etiologies. The neurological deficits in pyogenic meningitis could be because of exudates and vascular infarcts.

In our study, it was observed that there was increased mortality with FOUR score scale < 5. Scores 7-10 had morbidity more than others. 18 deaths were observed with FOUR score < 7. One death was observed with a score between 7-10. Residual deficits were seen in 24 cases with scores between 7-10. Good outcome was seen in 57 cases with scores above 10. In a study conducted by Cornelis N. et al used both the FOUR and GCS scores on admission to predict the outcome in patients with bacterial meningitis. The predictive value of GCS for unfavourable outcome and mortality was driven only by the motor score, but for the FOUR score motor, brainstem and respiratory items were predictive. The FOUR score is more useful in the lower-score regions, where the brainstem and respiratory patterns are more likely to be affected. Cornelis N. et al compared the FOUR score with the Glasgow Coma Scale (GCS) score, they performed a receiver operator characteristic curve analysis, and calculated the area under the curve (AUC) of the FOUR and

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GCS scores for the prediction of unfavourable outcome and mortality. The median FOUR score on admission was 14 (interquartile range [IQR] was 12–16), and the median GCS score was 12 (IQR 9–14). The outcome was unfavourable in 135 of 427 (32%) patients, of whom 55 (13%) died. There was a strong correlation between the FOUR score and the GCS score ($r = 0.85$, $p < 0.001$). AUCs for the GCS and FOUR scores in the prediction of unfavourable outcome (both 0.64) and mortality (both 0.68) were comparable. Logistic regression analysis showed that the FOUR motor, brainstem and respiration items were individual predictors of unfavourable outcome and mortality. For the GCS score, only the motor component was predictive, while the FOUR score provided a spectrum of clinical abnormalities in patients with a GCS score of 3. The FOUR score adds considerably to the prediction of outcome in patients with severe meningitis by means of better testing of the brainstem reflexes and respiratory status. Future studies should consider incorporating the FOUR score into clinical assessment (13).

We observed that 8 patients had normal MRI/CT findings and remaining 92 patients had findings such as Meningeal Enhancement, Hydrocephalus, Granuloma, Vasculitic infarcts, Lobar enhancement, brain Abscess and cerebral edema. In a study conducted by Aniyang Modi et al CT scan brain was used as baseline imaging in all the patients of AFE. Only 34 patients had shown abnormalities on imaging, CT or MRI. Meningeal enhancement was seen in 41% patients with pyogenic meningitis (14). In the present study, 20% of pyogenic meningitis and 80% of TB meningitis had meningeal enhancement. This variation might be due to sample size.

A study conducted by Bang et al in TBM reported that Forty-three patients underwent cranial MRI before beginning treatment (42 with contrast enhancement). Abnormalities were detected in 86 % of patients. 26 (62%) had basal meningeal enhancement, 19 (44%) had hydrocephalus, 13 (30%) had infarctions and 6(14%) had tuberculomas. 35 of these 43 patients had repeat cranial MRI scans performed 60 days post randomization which found that 13 (37%) had basal meningeal enhancement, 10 (29%) hydrocephalus, 12(34%) had infarctions and 10 (29%) had tuberculomas. According to them, meningeal enhancement on MRI was seen in 8/22 patients with clinical evidence of pyogenic meningitis. Basal exudates were demonstrable on all six patients with tubercular meningitis on MRI. The presence of meningeal enhancement was also demonstrated in 4/48 patients with meningo-encephalitis. As many as 22 patients with meningitis (16 pyogenic and six tubercular) and 44 patients with meningo-encephalitis did not show meningeal enhancement on MRI. 95% case of meningo-encephalitis had parenchymal abnormalities on MRI implying that MRI was more useful in picking up parenchymal abnormalities in patients suspected of having encephalitis (11).

In a study conducted Modi A et al, 25 patients showed that MRI findings in HSV encephalitis had bilateral T2 weighted hyperintensities in the temporal lobes. In our study 4 patients with HSV encephalitis had temporal hyper intensities. This is suggestive of consistent results with above study.

In our study, 2 patients had cerebral edema on MRI, 1 (25%) patient with cerebral malaria showed cerebral edema diffusely on imaging. Patankar TF et al showed that 67% had diffuse cerebral edema (15). This variation might be attributed to small number of cases of cerebral malaria in the study and the above study being done in exclusively malarial study sample with febrile encephalopathy.

CT and MRI were done to analyse the etiology. MRI imaging was very helpful to diagnose cases which were normal on CT imaging. Meningeal enhancement, lobar enhancement and infarcts on MRI were very consistent with etiologies which were suspected. In our study, out of 100 patients, 58 patients were diagnosed with Tuberculous Meningitis, 16 patients were diagnosed with pyogenic meningitis and 14 patients were diagnosed with viral meningo-encephalitis. Among the 14 patients with viral meningoencephalitis, 4 patients had dengue and 4 patients had positive HSV PCR in the CSF. Another similar study conducted by Elham Peidaee et al reported that bacterial meningitis, viral encephalitis and SAE, followed by tuberculous meningoencephalitis cerebral malaria, leptospirosis and brain abscesses were the most common causes of febrile encephalopathy (7). In another study from India in which one-third of the participants were elderly, meningitis was responsible for more than half of the cases with acute encephalitis syndrome, followed by metabolic encephalopathy, alcoholic

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encephalopathy, cerebral malaria, brain abscesses, and SAE (1).

In a retrospective multinational study (n = 2583), it has provided information on the etiological spectrum of community acquired CNS infections from 37 referral centres in 20 countries. The most frequent infecting pathogens reported in this study were Streptococcus pneumoniae and Mycobacterium tuberculosis. (16).

In most of these studies, the most common causes of encephalitis were reported to be herpes viruses, especially HSV and VZV However, M. tuberculosis was reported as the most prevalent cause in a study in England and as the second leading cause of encephalitis in a study in France. The results of numerous studies that investigated the etiological spectrum of encephalitis syndrome differed according to the populations studied, the geographic regions, and diagnostic methodologies, as well as the "definition of case" used for encephalitis syndrome.

In our study, predominant cases were TBM (58%). This might be due to reason that we have conducted the study at a tertiary care centre. Another reason being increased prevalence of TBM in our country. Our study included all the cases of fever with encephalopathy irrespective of time duration. In the present study, the diagnosis of only around one-third of the patients with CNS infections was documented microbiologically. Similar to previous studies, the most prevalent pathogen of bacterial meningitis, as well as CNS infections, was S. pneumoniae. Despite the reported yields of 70–85% for CSF culture, as well as 50–90% for blood culture in bacterial meningitis, the yields in a study were only around 25% and 12% respectively (17).

In our study, mean value of CSF in TBM for proteins (263) total cells (272.5) and sugars (22.05) whereas in Pyogenic meningitis for proteins (234.56), total cells (421.18) and sugars (23.5). In case of CSF in Viral encephalitis for proteins (114.68), total cells (307.18) and sugars (61.31). Similar study conducted by Pinky Pandey et al., observed that out of 356 CSF samples processed, only 16(4.5%) samples showed growth on CSF culture45. A study conducted in Manipal Teaching Hospital Nepal from 2000 to 2005 demonstrated 4.58% growth on CSF culture. A similar study conducted from 2004 to 2008 showed 4.4% growth on CSF culture. Among the 13 bacterial meningitis cases confirmed by culture results, it was observed that TLC was greater than normal range and it was found to be in the range of 10-2000 cells/mm3 with predominantly neutrophils (73.8%). Protein levels were greater than normal values (89.4 mg/dL) and glucose contents were lower than normal range (28.8 mg/dL). Markedly decreased CSF glucose with markedly increased total protein, high WBC count with 89% neutrophils, and the presence of a large number of PMN leukocytes and bacteria in the Gram stained smear of the CSF sediment are the most striking laboratory results in bacterial meningitis (18).

Similarly, a study also mentioned that the examination of the CSF of a patient with acute bacterial meningitis characteristically reveals a cloudy fluid consisting of an increased white blood cell count and predominance of PMN leukocytes, a low glucose concentration in relation to serum value, a raised concentration of protein and positive Gram stained smear and culture for the causative microorganisms. During the bacterial infection, due to microbial physiology, proteins are released and thus the level of protein is increased in CSF. The change in protein level can be used to distinguish viral from bacterial meningitis. As in bacterial infection, the protein level is usually raised and in case of viral infection the level of protein remains mildly increased. Thus this finding in present study goes well with the established medical knowledge. The duration of onset between fever and altered sensorium varied in different kinds of meningitis. In viral meningoencephalitis the duration between fever and altered sensorium was 1-3 days, in cerebral malaria this duration was 4-5 days and in pyogenic meningitis the duration was 10-12 days and in TB Meningitis it was 7-21 days. The differences noted in the onset between fever and altered sensorium might be due to the different causative agents and various host factors.

In our study, the cases were classified by the mode of onset of the disease into 3 groups acute, subacute and chronic presentations. Etiologies in acute group were PM (16), VM (14), CM (2), NMS (2) and SAE (4). In sub-acute group most common aetiology was TBM (42) followed by CM (2) and brain abscess (2). In the chronic group all cases were TBM (8).The reason for this might be due to the fact that India is a developing country where the prevalence of TB is high. Due to

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drug resistance in TB and poor compliance to treatment there is high prevalence of TB cases.

In our study, large number of cases of viral meningitis and cerebral malaria were observed during the months of July - December, which suggested favorable environment for disease causation. However, variation in temperature patterns has also been considered a possible explanation. Rise in temperature in summer season also corresponds to an increase in the number of patients with encephalitis. The results from the present study are consistent with Modi et. al. who observed, the prevalence of cases throughout the year but observed the post monsoon surge in viral encephalitis and malaria, suggesting the seasonal occurrence of the disease (14).

In the current study, among 100 patients 27 were found to have hyponatremia. Based on the levels of Sodium they were classified as Mild hyponatremia (Serum Sodium levels 130-134 mEq/ lit), Moderate hyponatremia (Serum Sodium 126-129 mEq/lit) and Severe hyponatremia (Serum Sodium <125 mEq/ lit). Out of 19 deaths, 9/ 15 (60%) deaths were observed in severe hyponatremia patients and 4/ 10(40%) deaths were in moderate hyponatremia patients. No deaths were observed in mild hyponatremia patients. The present study also reported that 6 out of 73 patients died who had normal sodium levels (135 mEq / lit). 77% of deaths were due to TB meningitis and 33% of deaths were due to pyogenic meningitis. The reason for this might be due to the fact that the prevalence of TB is high in our region. The reasons for the hyponatremia in TBM might be, cerebral salt wasting and syndrome of inappropriate secretion of antidiuretic hormone. Our study did not identify the cause of hyponatremia in meningitis. The frequencies of hyponatremia in these studies have ranged between 35% and 71% (19). The reason for this difference in the results could be due to nature of studies, exclusion of other conditions such as nutritional deficiency (vomiting, low salt intake), drugs (diuretics, carbamazepine), other diseases such as thyroid, adrenal, heart, hepatic or renal failure.

In the present study out of 100 patients,19 deaths occurred. Out of which 15/58 (25.86 %) were due to TBM, followed by SAE 1/4 (25%), cerebral malaria constituting ¼ (25%) each and pyogenic meningitis 2/16 (12.5%). In a study done by Modi et al, out of 120 patients, 16 died. Among which 6 were due to AVE, 3 each due to PM and CM, and the rest 4 deaths were observed in cases of SAE (14).

During the study we faced some difficulty in diagnosing the cases of brain abscess (2%) with help of clinical features and investigations. Imaging modalities CT/MRI brain helped in diagnosing the cases. During the study we also faced problem in diagnosing 2 (2%) cases. In these two cases investigations used for the study were not conclusive .Imaging modalities were also inconclusive. Multiple histories revealed the use of antipsychotics in the patients and we could diagnose the cases as NMS. We further came to a conclusion with the help of serum CPK levels in the patient.

Conclusion

Meningoencephalitis affects mostly males in the age group of 26 to 35 years. Tuberculous meningitis is the most common etiology of meningoencephalitis in our region followed by viral meningoencephalitis and pyogenic meningitis.

Tuberculous meningitis was the most common etiology among subacute and chronic meningitis cases. Diagnosing tuberculous meningitis was challenging; clinical presentation, CSF studies, and brain imaging features helped to make a proper diagnosis. High number of TBM can be attributed to high prevalence of TB cases in our region. Hence, in all developing countries, TB should be properly supervised and treatment should be instituted at right time from the primary center level which can decrease the magnitude of the problem.

FOUR scale score helped us to assess the condition at the admission and can be used as prognostic factor for outcome.

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