(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 4, Issue 3, Page No: 917-925
May-June 2021

CT MRI study correlation with CSF analysis in patients admitted with febrile encephalopathy

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Type of Publication: Original Research paper
Conflicts of Interest: Nil

ABSTRACT

Background: Acute febrile encephalopathy (AFE) is a clinical term used to an altered mental state that either accompanies or follows a short febrile illness and is characterized by a diffuse and nonspecific brain insult manifested by a combination of coma, seizures, and decerebration. **Objective:** To study the CT MRI co-relation with CSF analysis in patients admitted with febrile encephalopathy**. Material and Methods:** A prospective observational study conducted among the 100 consecutive patients admitted in a Hamidia Hospital Bhopal during the period of 2 years 1st July 2018 to 30 June 2020 based on the following inclusion criteria: (1) Patients belonging to age of greater than15 years (2) Patients presenting with Fever with altered sensorium. A diagnosis of acute febrile encephalopathy, based on the following criteria: (i) fever (ii) acute depression of consciousness or mental deterioration for more than 12 hours with or without motor or sensory deficit and (iii) Total duration of illness at the time of admission 1 week or less. Exclusion criteria: (1) Patients with age below 15 years (2) Patients in who lumbar puncture is contraindicated. **Results:** The final study group comprised of 100 patients with mean age of 40.1 ± 16.4 years and male: female ratio of 1.4: 1. A diagnosis other than viral encephalitis was reached in 94 patients (62.3 %). Cerebral tuberculosis was the most common causes (31%) followed by acute bacterial meningitis (29%), and viral meningoencephalitis (28%) in the patient group of acute febrile encephalopathy. Other causes of acute febrile encephalopathy were cerebral malaria in 8% cases and brain abscess and Cryptococcal meningitis in 2% cases each. Mean age of patients with febrile encephalopathy was 40.1±16.4 years and majority of patients were males (59%). Most common diagnosis was CNS TB in 31% cases, followed by acute bacterial meningitis and viral meningoencephalitis in 29% and 28% cases respectively. Other caused included cerebral malaria (8%), brain abscess (2%), cryptococcal meningitis (2%). **Conclusion:** Acute febrile encephalopathy is one of the common cause of hospital admission among adults. The most common cause of acute febrile encephalopathy includes TBM followed by acute bacterial meningitis and viral meningitis. Our study was unique in assessing the correlation of various neurological findings with that of CSF examination. Neuroimaging is helpful in early diagnosis of various etiological causes of acute febrile encephalopathy. The diagnostic yield significantly increases when CSF and neuroimaging both are done simultaneously in cases with acute febrile encephalopathy.

Keywords: Acute febrile encephalopathy, Cerebral tuberculosis, Viral meningitis, CSF analysis

INTRODUCTION

The term "acute febrile encephalopathy" is used to describe conditions presenting with altered mental status with or following short febrile illness.[1] It is one of the most common clinical entity encountered by physician in emergency department. Most common causes of acute febrile encephalopathy

include central nervous system infections which can be due to virus (e.g. Japanese encephalitis), bacterium (bacterial meningitis, tubercular meningitis, typhoid encephalopathy), or a parasite (cerebral malaria).[2,3] The causes and profile of patients with acute febrile encephalopathy varies across different geographical location, or in different season in same geographical areas.[3] The exact incidence of acute encephalitis is not known but it has been estimated to be 0.42 per 1 lakh population in India.[4] The pathogenic mechanism underlying encephalopathy amongst patients with febrile illness could be due to direct effect of these agents on nervous system or may results secondary to systemic complications such as hypoglycemia, hypoxia, hypotension, hyperpyrexia, electrolyte imbalance or release of systemic chemical mediators.[5] Immediate and appropriate management of patients with altered mental status with fever is of utmost importance as it is associated with significant morbidity and mortality. Patient may also present with confusion in 2% cases and recognizing this sign is important for early identification of encephalopathy.[6] The treating physician has to be very meticulous as acute febrile encephalopathy results from various causes and the conditions may mimic other conditions. Majority of cases if correctly diagnosed and treated timely show complete recovery. However, mortality or long term disability with neurological sequelae is high amongst cases not treated or inadequately treated. Thus it is important to make a definitive diagnosis. A detailed diagnostic work up is usually required for making the definitive diagnosis[7]. CSF examination is helpful in establishing the etiological diagnosis in majority of cases with acute febrile encephalopathy. However, it may not be helpful in establishing diagnosis in some cases. However, a study suggested that incidence of bacterial meningitis is uncommon among elderly and in such cases routine CSF examination may not be necessary until other infectious foci are obvious.[8] CT scan is most widely used imaging modality in patients with acute febrile encephalopathy. This modalities is particularly helpful in ruling out associated intracranial space occupying lesions, however, contrast enhancement of meninges may suggest meningeal involvement. However, meningeal enhancement is a nonspecific sign and may be observed in other causes such as carcinomatous meningitis, reactive meningitis, and inflammatory vascular diseases of CNS. Though it is often indicated in patients with acute febrile encephalopathy but its diagnostic yield may not be justified as screening tool.[9] Recently, MRI brain is most commonly used imaging modality as it is associated with no radiation hazard and provide high resolution images. MRI may show characteristic patterns which may be helpful in diagnosis of diseases such as Herpes simplex (HSV) encephalitis, Japanese encephalitis (JE), etc. However, MRI and CT usually underestimate severity in some cases and may show normal findings in cases such as severe cerebral malaria or septic encephalopathy[9]. With the above background, the present study was conducted to study the CT/MRI co-relation with CSF analysis amongst patients admitted with febrile encephalopathy at tertiary care centre Bhopal.

Material and Methods: The present study entitled "CT MRI study correlation with CSF analysis in patients admitted with febrile encephalopathy in Hamidia Hospital, Bhopal" was conducted at Department of Medicine, Gandhi Medical College and associated Hamidia Hospital Bhopal for a period of 2 years amongst patients presenting with fever and altered sensorium at the study area.

Study design- Prospective observational study

Study population-Patients with diagnosis of fever with altered sensorium reporting to Department of medicine, Hamidia Hospital, Bhopal.

Study area- Department of Medicine, Gandhi Medical College and associated Hamidia hospital Bhopal

Study duration- 2 years i.e. from 1st July 2018 to 30th June 2020

Study tool-

- Pretested semi-structured questionnaire
- CSF analysis
- CT/MRI

Sample size-100

Sampling- convenient sampling technique

Inclusion criteria

- Patients belonging to age of greater than15 years

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- Patients presenting with Fever with altered sensorium.

Exclusion criteria

- Patients with age below 15 years
- Patients in whom lumbar puncture is contraindicated.

Methodology: After obtaining ethical clearance from institute's ethical committee, all the participants fulfilling the inclusion criteria were enrolled and written consent was obtained from the relatives. Detailed data regarding socio-demographical variables such as age, gender, phone number, address etc. were noted at the time of admission in a pretested questionnaire. Detailed history regarding onset, duration and progression of symptoms was obtained. Past history of similar episodes if any was also noted. History pertaining to comorbid conditions such as diabetes, hypertension or other medical or surgical history was obtained from the relatives of the patient. Further, all the patients were subjected to detailed general and systemic examination. Signs of neurological deficit if any were recorded. CNS examination was conducted in detail and signs of meningeal irritation such as Brudzinski and Kernig signs were assessed and findings were noted. All the patients were subjected to routine investigations i.e. CBC with platelets, RFT, LFT, RBS and Serum Sodium, Potassium, Calcium and Magnesium. In some cases following investigations were also done- Peripheral smear for malaria & HIV, HBsAg, HCV Viral Markers.

CSF sample was obtained using a spinal needle via lumbar puncture from L3-L4 space using sterile technique by the physician. CSF obtained was sent for CSF analysis. Further all the patients were subjected to CT scan or MRI of head to assess the radiological signs in cases with acute febrile encephalopathy. Data was entered in MS Excel sheet and analysis was done using IBM SPSS software version 20. Categorical data was expressed as frequency and percentage whereas numerical data was expressed as mean and standard deviation. Association between proportions was assessed using chi square test. P value <0.05 was considered statistically significant.

Observation and results: The present study entitled "CT MRI study correlation with CSF analysis in patients admitted with febrile encephalopathy in Hamidia hospital, Bhopal" was conducted on a total of 100 patients who presented with fever with altered sensorium at Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal. The findings of present study are tabulated as under:

Table 1: Distribution of study participants according to their age and sex

Age (years)	Frequency (n=100)	Percent
≤20	17	17.0
21-40	35	35.0
41-60	41	41.0
>60	7	7.0
Total	100	100.0
Gender		
Male	59	59.0
Female	41	41.0
Total	100	100.0

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Table 2- Distribution of patients according to findings of blood investigations

Blood investigations		Frequency (n=100)	Percent
Hemoglobin (gm/dl)	<9	1	1.0
	9-9.9	12	12.0
	10-10.9	19	19.0
	11-11.9	19	19.0
	≥12	49	49.0
	Mean±SD	12.07±1.74	
Total leucocyte count (cells/cumm)	<4000	9	9.0
	4000-11000	85	85.0
	>11000	6	6.0
	Mean±SD	7900±2928.4	
Urea (mg/dl)	<20	6	6.0
	>20	94	94.0
	Mean±SD	38.85±24.24	
Creatinine (mg/dl)	<1.6	91	91.0
	>1.6	9	9.0
	Mean±SD	0.99±0.26	
Bilirubin (mg/dl)	<1	77	77.0
	>1	23	23.0
	Mean±SD	0.90±0.29	
RBS (mg/dl)	<200	98	98.0
	>200	2	2.0
	Mean±SD	122.9±29.5	
Sodium (mEq/L)	<135	22	22.0
	135-145	59	59.0
	>145	19	19.0
	Mean±SD	139.9±5.5	
Potassium (mmol/l)	<3.5	8	8.0
	3.5-5.5	85	85.0
	>5.5	7	7.0
	Mean±SD	4.6±1.15	

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Table 3- Distribution according to findings of CSF examination

CSF		Frequency (n=100)	Percent
Colour	Pale Yellow	6	6.0
	Reddish	2	2.0
	Straw Colored	1	1.0
	Turbid	1	1.0
	Watery	90	90.0
Cobweb	Present	6	6.0
	Absent	94	94.0
Cryptococcus (India Ink)	Positive	2	2.0
Glucose	<80	96	96.0
	>80	4	4.0
	Mean±SD	45.94±20.42	
Protein	<50	37	37.0
	>50	63	63.0
	Mean±SD	90.47±72.58	
ADA	<12	91	91.0
	>12	9	9.0
	Mean±SD	9.47±5.09	
Cells	Absent	2	2.0
	<5	10	10.0
	>5	88	88.0
	Mean±SD	188.7±336.2	
Neutrophils	Absent	42	42.0
	<80	42	42.0
	>80	16	16.0
	Mean±SD	25.9±34.29	
Lymphocytes	Absent	3	3.0
	<10	11	11.0
	>10	86	86.0
	Mean±SD	72.37±35.96	

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Table 4- Distribution of patients according to findings of CT/MRI

Neuroimaging	Frequency	Percent
Obstructive hydrocephalus	15	15
Diffuse meningeal enhancement	11	11
Hyper intensity fronto-temporal lobes	8	8
Basal exudates with basal meningeal enhancement	8	8
Communicating hydrocephalus with meningeal enhancement	1	1
Tuberculoma	4	4
Vasculitic acute infarct	4	4
Superior sagittal venous thrombosis	4	4
Acute infarct	3	3
Leptomeningeal enhancement in fronto-temporal lobes	2	2
T2 hyperintensity surrounded by hypointensity S/o brain abscess	2	2
Normal	38	38

Table 5- Correlation of CT/MRI findings with CSF in patients with acute febrile encephalopathy

CSF		Neuroimaging		χ^2	p value
		Normal	Abnormal		
Colour	Yellow	0 (0)	6 (9.7)	6.8	0.15
	Reddish	0 (0)	2 (3.2)		
	Straw	0 (0)	1 (1.6)		
	Turbid	0 (0)	1 (1.6)		
	Watery	38 (100)	52 (83.9)		
Cobweb	Present	0 (0)	6 (9.7)	3.9	0.04
	Absent	38 (100)	56 (90.3)		
Cryptococcus India ink	Seen	1 (2.6)	1 (1.6)	0.13	0.74
	Not seen	37 (97.4)	61 (98.4)		
Glucose	<80	35 (92.1)	61 (98.4)	2.4	0.12
	>80	3 (7.9)	1 (1.6)		
	Mean±SD	53.71±22.2	40.7±17.4		
Protein	<50	21 (55.3)	16 (25.8)	8.8	0.003
	>50	17 (44.7)	4 (74.2)		
	Mean±SD	69.5±59.5	104.7±77.5		

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Cells	Absent	1 (2.6)	1 (1.6)	13.03	0.001
	<5	9 (23.7)	1 (1.6)		
	>5	28 (73.7)	60 (96.8)		
	Mean±SD	99.9±230.3	248.8±382.2		
Neutrophils	Absent	20 (52.6)	22 (35.5)	2.8	0.24
	<80	13 (34.2)	29 (46.8)		
	>80	5 (11.9)	11 (17.7)		
	Mean±SD	24.8±34.3	26.7±34.5		
Lymphocytes	Absent	1 (2.6)	2 (3.2)	2.13	0.35
	<10	2 (5.3)	9 (14.5)		
	>10	35 (92.1)	51 (82.3)		
	Mean±SD	72.4±36.7	72.3±35.7		
ADA	<12	36 (94.7)	55 (88.7)	1.05	0.31
	>12	2 (5.3)	7 (11.3)		
	Mean±SD	7.62±3.75	10.7±5.52		

Discussion: The present study entitled "CT MRI study correlation with CSF analysis in patients admitted with febrile encephalopathy in Hamidia hospital, Bhopal" was conducted on a total of 100 patients presented with acute febrile encephalopathy with the aim to assess the correlation of the CT MRI findings with CSF analysis among these patients. Fever with altered mentation, also called acute febrile encephalopathy is one of the common symptom complex responsible for hospital admissions among both adults as well as children. Acute febrile encephalopathy may results secondary to acute bacterial meningitis, viral encephalitis, cerebral malaria, typhoid encephalopathy, cryptococcal meningitis etc.[2,3] Though, etiological diagnosis of acute encephalopathy could be made with the help of CSF examination, but in few cases, CSF may not yield definitive diagnosis.[8] Neuroimaging modalities such as MRI and CT scan are widely used among patients with acute febrile encephalopathy. These modalities is particularly helpful in ruling out associated intracranial space occupying lesions and associated contrast enhancement of meninges may suggest meningeal involvement. However, these imaging modalities underestimate the severity of disease in some cases. Neuroimaging may reveal normal findings in certain encephalopathy such as severe cerebral malaria or septic encephalopathy.[9]

The study included 100 adolescent and adult patients belonging to more than 15 years of age. The mean age of patients with acute febrile encephalopathy was 40.1±16.4 years and 41% patients belonged to 41 to 60 years of age. Advancing age is one of the most important physiological stage which is associated with impaired in cellular and humoral immunity as well as reduced cough reflex, and high susceptibility to infectious diseases.[10,11] Only 7% patients with acute febrile encephalopathy in our study belonged to >60 years of age group. Sen I et al (2017) analysed 50 patients of acute febrile encephalopathy with mean age of 35.06 years and most common age of patients with AFE was 31 to 40 years.[12] Similar to present study, mean age of patients with acute febrile encephalopathy in a study of Khan R et al (2015) was 33.89±17.31 years.[13] Acute febrile encephalopathy may affect patients of either gender. Our present study observed male preponderance with male:female ratio of 1.4:1. About 59% patients in present study. These findings were concordant with the findings of Karmarkar SA et al (2008) in which majority of patients were males and male: female ratio was

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1.71:1[14]. Similar to present study, Sen I et al (2017) also documented male preponderance. Out of 50 patients, 32 patients were males and 18 patients were females[12]. Our study documented anemia in 51% cases (<12 gm/dl). Hemoglobin status represents nutritional status of the patients. However anemia could be associated with cerebral malaria and enteric encephalopathy. These findings were supported by findings of Jain B et al (2016) in which anemia was observed in 41.17% cases.[15] Rawat CS et al (2019) in also observed findings similar to present study.[16] In present study, most common cause of acute febrile encephalopathy was cerebral tuberculosis (31%), followed by acute bacterial meningitis (29%) and viral meningoencephalitis (28%). Other causes of acute febrile encephalopathy were cerebral malaria in 8% cases and brain abscess and cryptococcal meningitis in 2% cases each. Our study findings were supported by findings of Bansal A et al (2005), in which authors concluded that TBM, pyogenic meningitis, and encephalitis together constitute more than 90% of the cases of AFE.[1] However, Jain B et al (2016) observed acute bacterial meningitis as most common cause of meningitis (38.8%) followed by tubercular meningitis (17.7%). Cryptococcal meningitis was observed in 1.2% cases and malaria was noted in 11.8% cases.[15] The findings of present study were supported by findings of Bhalla A et al (2010), 70% patients with acute febrile encephalopathy had primary CNS infection. They observed bacterial meningitis in 25.2% cases, TBM in 7.87% and 29.9% cases had meningoencephalitis. Other causes included cerebral malaria, leptospirosis, and brain abscess.[17] Karmarkar SA et al (2008) also documented pyogenic meningitis as most common cause of acute febrile encephalopathy (33.8%), followed by tubercular meningitis (7.9 %) and cerebral malaria (5.2%). [14] The present study was conducted at tertiary care centre where patients especially of low socioeconomic status seek care. Incidence of TB is higher in population of low socioeconomic status. Also, compliance to ATT among these patients is poor. These may contribute to higher proportions of TBM cases in our study. Neuroimaging in present study revealed normal finding in 34.5% cases of ABM, 37.9% cases had diffuse meningeal enhancement whereas superior sagittal venous thrombosis, Acute infarct and communicating hydrocephalous was noted in 4, 3 and 1 cases respectively. In present study, CSF was watery in 100% cases with normal CT/ MRI findings, communicating hydrocephalus with meningeal enhancement and superior sagittal venous thrombosis. However, CSF was turbid or pale yellow in 36.5% cases of diffuse meningeal enhancement. Cobweb appearance was observed in 33.3% and 9.1% cases with Acute infarct and Diffuse meningeal enhancement respectively. CSF glucose was more than 80 mg/dl in 10% cases with normal CT/MRI whereas it was less than 80 mg/dl in all other cases of acute bacterial meningitis with abnormal CT/MRI findings. CSF protein was >50 in 50% cases with superior sagittal venous thrombosis. CSF cells were raised in almost all the cases of acute bacterial meningitis irrespective of neuroimaging finding. These findings were supported by findings of Nagra I et al (2011) in which, neuroimaging revealed hydrocephalus, subdural empyema, ventriculitis, venous thrombosis or infarction in few cases of patients with acute bacterial meningitis[18].

Conclusion: Acute febrile encephalopathy is one of the common cause of hospital admission among adults. The most common cause of acute febrile encephalopathy include TBM followed by acute bacterial meningitis and viral meningitis. CSF examination is helpful in establishing etiological diagnosis of cases with acute febrile encephalopathy but in few cases, diagnosis may be doubtful. Though, neuroimaging was normal in cerebral malaria and maximum cases of viral meningoencephalitis, it was useful in tubercular meningitis, bacterial meningitis as well as brain abscess. Our study was unique in assessing the correlation of various neurological findings with that of CSF examination. Neuroimaging is helpful in early diagnosis of various etiological causes of acute febrile encephalopathy. The diagnostic yield significantly increases when CSF and neuroimaging both are done simultaneously in cases with acute febrile encephalopathy.

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