DISSERTATION ON

"A STUDY ON ETIOLOGY, CLINICAL FEATURES, DIAGNOSIS AND PROGNOSIS IN ACUTE FEBRILE ENCEPHALOPATHY"

Submitted in partial fulfillment for the Degree of

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BRANCH - I

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MADRAS MEDICAL COLLEGE

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CERTIFICATE

This is to certify that the dissertation titled "**A STUDY ON ETIOLOGY, CLINICAL FEATURES, DIAGNOSIS AND PROGNOSIS IN ACUTE FEBRILE ENCEPHALOPATHY**" is the bonafide original work of **Dr.JOTHILAKSHMI .V** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in APRIL 2016. The Period of study was from March 2015 to August 2015.

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DECLARATION

I, **Dr.JOTHILAKSHMI.V** solemnly declare that dissertation titled "**A STUDY ON ETIOLOGY, CLINICAL FEATURES, DIAGNOSIS AND PROGNOSIS IN ACUTE FEBRILE ENCEPHALOPATHY**" is a bonafide work done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 during 2015 under the guidance and supervision of my unit chief **Prof.Dr.S.G.SIVA CHIDAMBARAM M.D**, Professor of Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. DEGREE IN GENERAL MEDICINE BRANCH-I**.

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CONTENT

ABBREVATIONS

AFB	-	Acid fast bacilli
AIDS	-	Acquired Immunodeficiency syndrome
AMS	-	Altered Mental Sensorium
ART	-	Antiretroviral therapy
CM	-	Crytococcocal Meningitis
CrAg	-	Crytococcocal Antigen
CSF	-	Cerebrospinal Fluid
CBC	-	Complete Blood Count
CMV	-	Cytomegalovirus
DE	-	Dengue Encephalitis
ESR	-	Erythocyte Sedimation Rate
EBV	-	Epstein Barr Virus
EV	-	*Enterovirus*
JE	-	Japanese encephalitis
HIV	-	Human Immunodeficiency Virus
HSV	-	Herpes Simplex Virus
NA	-	*Not Applicable*
PCR	-	*polymerase chain reaction*
PMNL	-	*polymorphonuclear leukocyte*
LP	-	Lumbar Puncture
SE	-	Septic Encephalopathy
TBM	-	Tuberculosis Meningitis
VSV	-	*Varicella zoster virus*
ZN Stain	-	Ziehl -Nielsen Stain
WBC	-	White Blood count

INTRODUCTION

INTRODUCTION

Acute febrile encephalopathy is clinical terminology used for altered mental status that follows short febrile illness characterised by diffuse nonspecific brain insult with clinical manifestations of coma, seizures and decerebration. This can be caused due to meningitis or encephalitis. Despite several epidemiological reports and investigations, the clinical presentation with acute fever and altered sensorium has often remained a mystery in south Indian state of Tamilnadu. Encephalitis is acute inflammation of brain parenchyma and presents as a diffuse or focal neuropsychological dysfunction and is almost always manifested with inflammation of meningitis. Acute febrile encephalopathy is commonly caused by viral infection. The diseases is also caused by bacterial and protozoal infection.

AIMS

AND

OBJECTIVES

AIM & OBJECTIVES

To identify the etiology, clinical features, diagnosis and prognosis in patients with acute febrile encephalopathy above 13 years of age in a tertiary government general hospital in southern east India. Acute febrile encephalopathy is a important cause of morbidity and mortality in hospitalised patients with high mortality in undiagnosed or untreated patients. Various etiological causes such as viral encephalitis, cerebral malaria, bacterial meninigitis, fungal meningitis implicated in the etiology according to geographical location. A study was conducted in a tertiary centre at Rajiv Gandhi general Government hospital, Chennai Tamilnadu on etiology, clinical features and prognosis in patients presenting with acute febrile illness with encephalopathy.

Following investigation were done during the study period for the patients. Haemoglobin, total leucocyte count, differential leucocyte count, platelet count, peripheral blood smear,renal function test, serum electrolytes, dengue, widal test rapid diagnostic test for malarial parasite. Blood culture and urine culture were collected and any obvious site if sepsis was identified. Lumbar puncture was done in all of the patients and cerebrospinal fluid analysis for cytology, cell count, glucose, blood glucose ratio, gram stain and culture sensitivity for microbes, serology for herpes simplex virus, varicella zoster virus, cytomegalovirus, Epstein bar virus, Japanese encephalitis virus.

STUDY DESIGN:

A detailed history and clinical examination including neurological examination were done in all patients. Clinical examination included identification of maculopapular rashes, petechiae, purpura, vesicles, eschar, herpes labialis, lymphadenopathy, diarrhoea, vomiting, parotitis, myalgia, arthralgia.

Organomegaly, hypotension, shock. The investigation done in all patients included haemoglobin, blood counts, peripheral smear for malarial parasite Quatitative buffy coat for malarial (QBC) for plasmodium malaria, histidine rich protein based immuno chromatographic card test was done for patients in whom peripheral smear was negative for plasmodium falciparum malaria who were suspectable for complicated malaria. Serological test for dengue, hepatitis A,B,E and human immunodeficiency virus (HIV) leptospirosis antibody, blood culture and urine culture in sepsis cases and site of sepsis investigated. Cerebrospinal fluid examination for cytology, cell count, protein level, glucose level, gram stain, AFB stain, adenosine deaminase levels, India ink staining and culture and sensitivity. Chest x-ray, electrocardiography, ultrasonography of abdomen, electroencephalogram and constrast enhanced computerized tomography (CT scan) were done as and when required .Magnetic resonance imaging (MRI) of brain was done when required. Pyogenic meningitis was diagnosed on the basis of polymorphonuclear leucocytosis in CSF or positive gram stain or positive culture an sensitivity of CSF. Cerebral malaria was diagnosed in patients with febrile encephalopathy with positive peripheral smear or QBC for plasmodium falciparum. Outcome was assessed after 1month of follow up after discharge from hospital using modified Rankin scale (MRS).

Computed tomography (CT) brain non contrast and contrast enhanced of was done for all patients as a baseline imaging modality with AFE to rule out contraindications for lumbar puncture to study morphological changes. Magnetic resonance imaging (MRI) scan was done in particular cases where tubercular meningitis and fungal meningitis suspected. Appropriate treatment given to patient and follow up and outcome was studied in the patient. Magnetic resonance spectroscopy (MRS) was also done in when required.

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE

Definition and classification:
Acute febrile encephalopathy is fever less than 2 weeks duration with altered sensorium >12 hours with clinical manifestation of central nervous system infection.
Febrile encephalopathy is with <1week with alteration of consciousness.
Encephalopathy is diffuse disturbance of brain function with or without inflammation
Meningitis refers to inflammation of the leptomeninges and CSF within the subarachnoid space of the brain , spinal cord and the ventricular system.
Meningoencephalitis refers to inflammation of meninges and brain parenchyma
Encephalitis is dysfunction of brain associated with inflammation
Acute encephalitis syndrome is defined as a person of any age at any time of year with acute onset of fever and atleast one of one of
1.A change in mental status(confusion disorientation coma
2.New onset of seizures(excluding simple febrile seziures)
Bacterial / Pyogenic meningitis: Pyogenic bacteria detected on Gram stain or culture.
Tuberculous meningitis:AFB detected on smears and/or mycobacteria grown on culture of CSF
Aseptic mononuclear meningitis:no bacteria or fungi on microscopy or culture of CSF,with increased CSF WBC
Meningitis:Meningeal inflammation
Myelitis:Spinal cord inflammation
Radiculitis:Nerve root inflammation

SEPTIC ACUTE ENCEPHALOPATHY

Clinical course of brain abscess ranges from indolent to fulminant clinical manifestations with most of the clinical features depending on the size and location of a space–occupying lesion within the brain and the virulence of the infected microorganism.

SEPTIC ACUTE ENCEPHALOPATHY

SEPTIC ACUTE ENCEPHALOPATHY	
Sepsis	Acute Brain Dysfuction .
	Undiagnosed Complicated Infection Of CNS
Clinical Manifestation	Classic Triad Of Fever, Headache And Neurological Deficit Weakness, Fatigue To Confusion and Delirium
Sepsis Patients Associated	Increased Mortality
CT SCAN in brain abscess	hypodense center with peripheral uniform ring enhancement, surrounded by variable hypodense area of edema

INFECTIOUS CAUSES VIRAL/ BACTERIAL ENCEPHALITIS

INFECTIOUS CAUSES VIRAL ENCEPHALITIS	INFECTIOUS CAUSES OF BACTERIAL ENCEPHALITIS
Herpes simplex type ,type 2 Varicella zoster HSV Cytomegalovirus, CMV Epstein barr virus Arbovirus –japanese encephalitis,Dengue,chikungunya (mosquito borne) Rhabdoviruses-rabies (animal bites) HIV HSV	Meningitis Brain abscess Sepsis associated encephalopathy Leptospirosis (Infected dirty water) Typhoid M.tuberculosis (TB) Rickettsial (scrub typhus) Cerebral malaria

HISTORY OF ACUTE FEBRILE ENCEHALOPATHY

HISTORY	CLINICAL FEATURES
Fever with rashes	Maculopapular Petechiae/purpura Vesicles Eschar Herpes labialis
Respiratory symptoms	H1N1
Diarrhoea,vomiting	Enteroviruses
parotitis	HIV EBV
Myalgia,Arthralgia	Dengue,leptospirosis,chikun gunya
Cough,sputum	tuberculosis
Gum bleeding,melena	Dengue

VIRAL MENINGOENCEPHALOPATHY:

Chronic symptoms lasting more than 1 week suggest meningitis caused by viruses.

DENGUE ENCEPALOPATHY

Dengue(Break Borne Fever)	Single Stranded RNA Virus Of Flavivirus
Dengue Serotypes	Den-1 To Den 4 Are Heterogenous Endemic In Many Countries
	Bite Of Aedes Mosquito
Dengue Classical	Fever,Malaise,Headache Retroortibal Pain,Severe Myalgia, Arthralgia Face,Neck,Chest Erythema Maculopapular Rash
Dengue Haemorrhagic Fever Encephalopathy	Cerebral Anoxia Cerebral Edema Cerebral Haemorrhage, Hyponatremia, Hepatic Failure Toxicity
	NS 1 Antigen Dengue Igm antibody-5th day

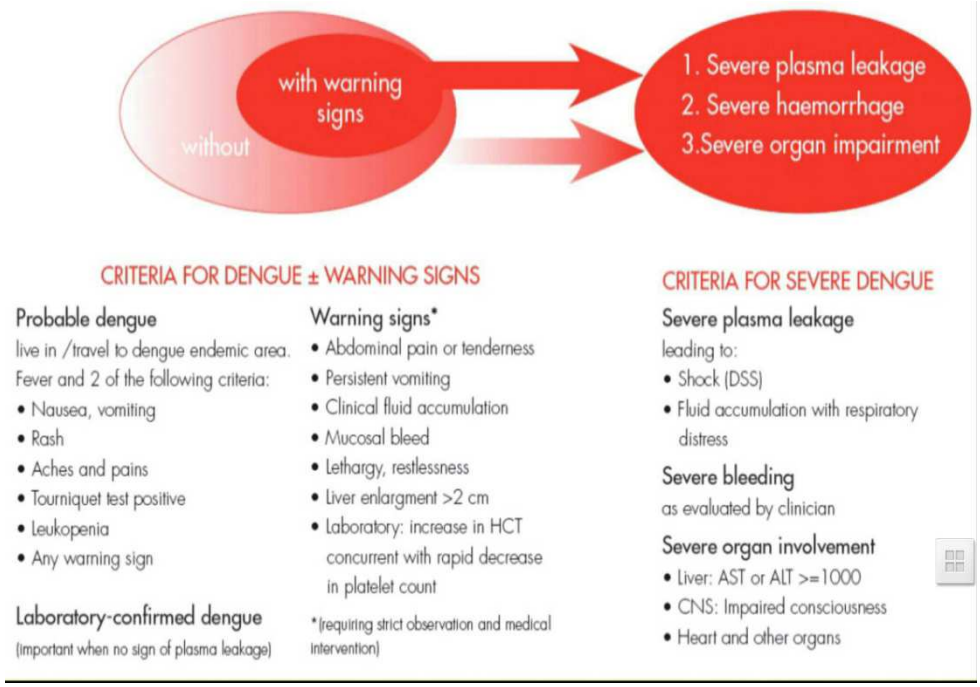
WHO CLASSIFICATION OF DENGUE VIRUS

DF/DHF	Grade	Symptoms	Laboratory
DF		Fever with two or more of following: Headache Retro orbital pain Myalgias Arthralgias	Leucopenia, occasionally thrombocytopenia may be present. No e/o plasma loss.
DHF	I	Above signs plus positive tourniquet sign	Thrombocytopenia < 100 000; Hct rise ≥ 20%
DHF	II	Above signs plus spontaneous bleeding	Thrombocytopenia < 100 000; Hct rise ≥ 20%
DHF*	III	Above signs plus circulatory failure (weak pulse, hypotension, restlessness)	Thrombocytopenia < 100 000; Hct rise ≥ 20%
DHF*	IV	Profound shock with undetectable BP and pulse	Thrombocytopenia < 100 000; Hct rise ≥ 20%

Who classification of Dengue fever

Asymptomatic or subclinical
Dengue fever
Dengue hemorrhagic fever
Dengue shock syndrome
Other (encephalopathy, hepatitis, myocarditis)

Highly suggestive	Confirmed
One of the following: 1. IgM + in a single serum sample 2. IgG + in a single serum sample with a HI titre of 1280 or greater	One of the following: 1. PCR + 2. Virus culture + 3. IgM seroconversion in paired sera 4. IgG seroconversion in paired sera or fourfold IgG titer increase in paired sera



CRITERIA FOR DENGUE & WARNING SIGNS

DENGUE SHOCK SYNDROME

DENGUE CLINICAL MANIFESTATION	
Uncomplicated Dengue Fever	Fever, Dehydration,Headache
Dengue Haemorrhagic Fever	Results Due To Secondary Infection .Vascular Leak , Coagulopathy Lead To Easy Brusing Bleeding Generalised Petechiae. Haemoconcentration,Serous Effusion And Hypoproteinemia
Dengue Shock Syndrome And Encephalitis	Multisystem Dysfunction In Severe Dengue Infection, Thrombocytopenia

Dyselectrolytemia

⇓

Shock Dehydration

⇓

LiverDysfunction (Thrombocytopenia Or Coagulopathy

⇓

Cerebral Hypoperfusion

⇓

Neurogenic C Shock

⇓

CerebralEdema Due To Vascular Leakage

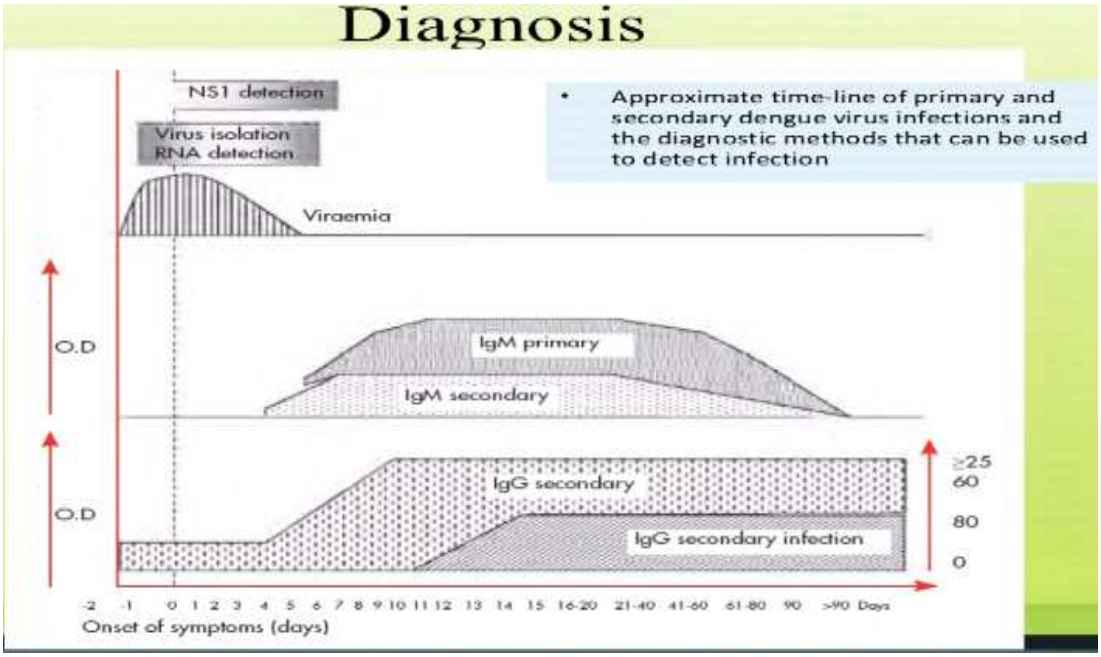
⇓

Dengue Encephalopathy

PATHOPHYSIOLOGY IN DENGUE ENCEPHALITIS

In recent times dengue encephalopathy is well recognised and common entity as a cause for acute febrile encephalopathy in patients presenting with thrombocytopenia. Increased intracranial bleeding (thrombocytopenia or coagulopathy). There is a increasing evidence in dengueviral neurotropism.Dengue neurotropism is a mechanism as patients with dengue IgM antibodies.

Dengue Haemorrhagic Fever	Acute Febrile Illness
Clinical Features	Dehydration, Thrombocytopenia With Altered Sensorium, Bleeding Gums, Melena, Hypotension, Shock, Headache, Altered Sensorium
Diagnosis	IGM Serology Was Positive
Dengue Encephalopathy	Lethargy To Overt Delirium



SEROLOGICAL VARIATION OF DENGUE

VARICELLA ZOSTER ENCEPHALITIS

VZV belongs to the herpesviridae family with 3 subfamilies α,β,γ herpesviridae with α-herpesvirruses neutrotropic and β, α are lymphotropic. α-βvirus herpesvirus VZV and is related closely to herpes simplex virus.

VARICELLA ZOSTER VIRUS INFECTION CLINICAL MANIFESTATIONS

TWO CLINICAL FORMS OF VARICELLA ZOSTER MANIFESTATIONS	
Primary infection varicella (chicken pox)	Characteristic vesicular lesion in different stages of development on the face trunk and extremities
Herpes zoster (shingles)	Reactivation of the endogenous latent VZV infection in the trigeminal sensory ganglion. painful unilateral vesicular lesion in the particular dermatomal distribution herpes labialis

In addition to subclinical reactivation of the viruses, subclinical reinfection that boosts the immune response also occurs. Neurological complications caused by VZV occurs in both primary and reactivated VZV both central and peripheral nervous system are affected CNS complications in chicken pox are most commonly cerebellitis, encephalitis.

THE NEUROPATHOGENEIS OF VZV INFECTION

Primary infection with VZV Lateny ↓ Reactivated diseases ↓ Spread of virus ↓ Afferent fibres of trigeminal ganglion ↓ Transaxonal transport ↓ Vasculopathy	Hamatogenous spread by T-cell mediated transport ↓ Transaxonal transport ↓ Afferent fibres innervating the afferent fibres infected ↓ Middle cerebral artery innervated by trigeminal ganglion is affected
Myelopathy	
Postherpetic neuralgia	
Retinal necrosis	
Cerebellitis	

Most Cranial Nerve Palsies Occur	Most Have Complete Recovery
Trigeminal Nerve Is The Cranial Most Commonly Affected In VZV Reactivation	The Optic Nerve,The Maxillary Nerve And The Mandibular Nerve Optic Nerve Ocular Disorders, Retinal Necrosis.
Ramsay Hunt Syndrome	Peripheral Facial Palsy Accompanied By Rash On The Ear (Zoster Oticus),The Vestibulocochlear Nerve If Involved Commonly
Reyes Syndrome	Disease With Encephalopathy And Liver Damage Associated With VZV Infection And Aspirin Intake
Cerebellitis	Completely Recovers Although Persistent Cerebellar Deficits Such As Cognitive Defects
Herpes Zoster Induced Encephalitis (Adults)	Residual Neurological Sequelae Common Increased Mortality Rate About 35% Without Treatment Neuropsychological Deficits - Subcortical Slowing Of Cognitive Process,Memory Impairment, Emotional,Behavioural Changes May Occur After A Latent Period Of 10 Yrs After Acute Infection.

In adults developing herpes zoster induced encephalitis residual neurological sequlae is common with increased mortality rate. Without treatment neuropsychological deficits such as subcortical slowing of cognitive process, memory impairment and emotional and behavioural changes may occur after a latent period of 10 yrs after acute infection. The Brain imaging modalities CT scan shows multifocal lesions at grey white matter junction, both ischemic and haemorrhagic lesions. Anterior, middle cerebral arteries and internal, external carotid artery are most commonly involved. Meningitis, vasculopathy and radiculitis are common.

HERPES SIMPLEX ENCEPHALOPATHY

HSE encephalitis	Cause-HSV-1 in adults and HSV-2 in neonates.
Commonly affects	Male:Female ratio:2:1.
AGE	Younger age group though older affected
More common	summer and rainy season
Spread	focal and severediseases causing acute necrotising encephalopathy
Onset	Insidious or violent
Common neurological manifestations	Altered sensorium ,seizures abnormal behaviour focal neurological deficit , ataxia, aphasia ,visual field defects , papilloedema. abnormal behaviour, marked cognitive impairment.
CSF analysis	Mononuclear pleocytosis, Raised proteins
Diagnosis	Serology test for HSV antibody in blood and CSF
CT scan	Bilateral asymmetrical frontotemporal lesion
MRIscan	bilateral asymmetric frontotemporal lesion and isolated temporal lesions
EEG	periodic lateralised epileptiform discharge (PLEDs) in the form of spike/sharp waves or slow waves from temporal lobe localization
Differential diagnosis	Herpes Simplex Encephalitis (HSE) Cerebral Vein Thrombosis ,Cerebral Malaria, Tubercular Meningitis,

PATHOGENESIS OF HERPES SIMPLEX VIRUS

HERPES SIMPLEX VIRUS HSV HERPES VIRIDAE FAMILY, ENVELOPED., DOUBLE-STRANDED DNA VIRUS	
Viral infection begins at point of entry Oral mucosa Genital mucosa Ocular conjunctival	Virus replicates locally ⇓ Tissue damage ⇓ Inflammatory response presents asvesicles ulcer

HERPES SIMPLEX ENCEPHALITIS DIAGNOSIS

HERPES SIMPLEX ENCEPHALITIS DIAGNOSIS
CSF analysis
WBC: 20-300cells /mm^3
Protein: 30-2500mg/dl
Glucose : Normal
EEG: spike an slow wave activity from temporal lobe.sensitivity 85%specificity 33%

TREATMENT OF VIRAL ENCEPHALITIS

TREATMENT OF VIRAL ENCEPHALITIS
Acyclovir IV 10mg/kg TDS
14 to 21 days course for confirmed HSE
Monitor renal functions
Antiobiotics if CSF analysis and imaging modalities delayed
Management of complications

ACUTE HEPATIC ENCEPALOPATHY

Acute hepatic encephalopathy in acute liver failure due to acute hepatitis failure (ALF) which clinically manifests as jaundice, coagulopathy and encephalopathy.

Hepatitis A virus is one of the common causes of Acute liver failure (ALF) in children and young adults besides Hepatitis B, D, E, Though Hepatitis A in common in children the possibilities of fulminant complications arises with age, peaking above age of 40yrs. Hepatitis A is a self limiting in most case though some present with fulminate hepatic failure. In ALF massive hepatocellular necrosis leads to Jaundice, coagulopathy and encephalopathy. ALF patients most of the patients recovered with only supportive therapy and adequate hydration. Acute hepatitis A virus infection was also cause of acute febrile encephalopathy in our study in 4% cases.

HIV-HUMANIMMUNODEFICIENCY VIRUS

HIV is the most common infection affecting the central nervous system. Upto 50% of HIV patients have clinically apparent neurological

diseases. 20% present first time with neurological manifestations.10 % to 15 present with only neurological symptoms. India has the second largest burden of HIV related pathology. Tamilnadu has the second largest burden of HIV related diseases .Neurological complications associated to HIV-1 infections are very common. The neuropathogenesis of HIV infection is direct HIV virus and its products or indirect opportunistic infections, HIV associated Neoplasms. Cells affected by HIV are perivascular macrophages, monocytes from blood, microglial cells and astrocytes

NEUROLOGICAL MANIFESTATIONS OF HIV INVOLVING THE BRAIN

Dementia	HIV Encephalopathy Progressive multiple Leucoencehalopathy (viral) Tuberculosis
Infective granulomas	Toxoplasmosis, Crytococcus Tuberculosis

CLINICAL STAGING OF HIV ENCEPHALOPATHY

STAGE	Mental Function	Motor Function
STAGE 0	Normal	Normal
STAGE 0.5	Absent, Minimal or Equivocal symtoms	Slowed ocular and extremity movements
STAGE 1	Able to perform all but the demanding aspects.Unequivocal func. and intellectual impairment	Unequivocal motor impairment Can walk without assistance
STAGE 2	Performs basic self care Cannot work or maintain demanding aspects of daily life	Ambulatory May require a single prop
STAGE 3	Major Intellectual incapacity	Major motor disability Cannot walk unassisted
STAGE 4	Intellect, social comprehension and output at rudimentray level	Paraparetic or paraplegic with bowel, bladder incontinence

CYTOMEGALOVIRUS ENCEPHALITIS

Cytomegalovirus is a double stranded linear DNA virus. Immuno competent host with CD4 counts < 50/cmm less than 2% of HIV infected patients develop CMV neurological symptoms. Crytococcal meningitis: Encapsulated yeast cells of C.neoformans detected in CSF by India Ink stain, positive CSF or serum cryptococcus Ag test

HIV ASSOCIATED CYTOMEGALOVIRUS ENCEPHALITIS

HIV ASSOCIATED CYTOMEGALOVIRUS ENCEPHALITIS	
GIT	Colitis,Esophagitis -,Diarrhoea,Fever And Abdominal Pain
Cardiovascular	Pericarditis, Myocarditis
Renal	Collapsing Focal Glomerulosclerosis
Eyes	Anterior uveitis –Iritis,Blurring Vision , Redness Of Eyes
CNS	Meningoencephalitis, Encephalitis Venticuloencephalitis, Radiculomyelopathy ,Peripheral Neuropathy In Less Than 1% Motor Deficit Localised Weakness Paraplegia Sensory Abnormalities Numbness, Hypoaesthesia, Paraesthesia, Dysaethesia, Disorientation, Confusion Apathy,Cranial Neuropathy,Nystagmus Transverse Myelitis

DRUG OF CHOICE, PROPHYLAXIS AND PROGNOSIS IN HIV ASSOCIATED CYTOMEGALOVIRUS ENCEPHALITIS

HIV ASSOCIATED CYTOMEGALOVIRUS ENCEPHALITIS	
Drug of choice is	Intravenous ganciclovir Second line- foscarnet
Oral valganciclovir	Long term prophylaxis
Highly active antiretroviral therapy therapy	Prevent CMV reactivation by reconstituting immune system
Prognosis	Without antviral therapy mortality 100%With antiviral therapy 50% recover

NONVIRAL CAUSES OF INFECTIOUS ENCEPALOPATHY

TUBERCULOSIS MENINGITIS

TUBERCULOSIS MENINGITIS (TBM)	
BACTERIA	Mycobacterium tuberculosis
PATHOGENICITY	Due to chronic reactivation bacillemia in older adults, Immune deficiency caused by aging, alchoholism, malnutrition, Human Immunodeficiency virus.
CNS COMPLICATION OF PRIMARY INFECTION.	
Tuberculosis Meningitis (TBM)	Spillage Of Tubercular Protein Into Subarachnoid Space Produces Intense Hypersensitivity Reaction, Vasculitis Leading To Thrombosis And Infarction
Common	HIV-Related TB Cases.
Meningitis	Stroke Syndromes Involving Basal Ganglia, Cerebral Cortex, Pons And Cerebellum
Communicating Hydrocephalus	Extension Of Inflammatory Process To Basilar Cisterns Impedance Of CSF Circulation
Clinical Manifestations	Headache , Fever, Altered Sensorium, Vomiting , Focal Neurological Deficit, Anorexia, Weight Loss, Positive Signs Of Meningeal Irritation, Other Cranial Nerve Palsy Facial Nerve, Hearing Loss ,.Speech, Memory Behaviour Disturbances ,Focal Signs – Hemiparesis,Sensory Impairment
Ophthalmoscopy	Choroid Tubercles
Gold Standard Diagnosis	Acid Fast Staining Of CSF Bacterial Culture
CSF Analysis	Increased Protein >500 mg/dl Low Glucose < 30mg/dl Lymphocytic Pleocytosis > 500cells Increased WBC Count >500 mm3. CSF Will Be AFB Smear Positive In 5% Culture Sensitivity In 50% PCR for TB positive
CT Scan Reliable Method For Diagnosis Of TBM	Multiple Ring Enhanced Lesions Basiliar Arachoiditis .Cerebral Edema ,Infarction, Vascular Enhancement,Ventricular Dilatation.
MRI Scan	
Antituberculosis Drugs (ATT Empirical Therapy	First line drugs Isoniazid (5mg/kg/day) Rifampicin(10mg/kg/day) Pyrazinamide (25mg/kg/day) Ethambutol 20mg/kg/day) supportive measures (Corticosteroids, Anticonvulsants ,Mannitol) started within 24-48 hours of admission
Treatment Of Complications	Corticosteriods In The Form Of IV Dexamethasone (0.6-1.2mg/Kg/Day In Three Divided Doses) X 7days Then Oral Prednisolone (2mg/Kg/Day In Three Divided Doses) Was Started In Patients With Hydrocephalus To Prevent The Progression Of Diseases,Ventriculoperitoneal Shunt For Hydrocephalus Liver Function Test Was Done Week- Detection Of ATT Induced Hepatotoxicity.
prognosis	Delayed treatment- high mortality and neurological complications.

CLINICAL CASE DEFINITION OF TUBERCULOSSIS MENINGITIS

Abnormal neurological signs and/or symptoms, and ≥ 2 of the following:

1. Discovery of adult source case with contagious tuberculosis who had significant contact with child
2. Presence of Mantoux (5 TU) skin test reaction ≥ 10 mm of induration, or ≥ 5 mm of induration if child had close contact with infected adult
3. CSF abnormalities without evidence of other infectious cause
4. Abnormalities on cranial CT consistent with CNS tuberculosis

CNS = central nervous system; CSF = cerebrospinal fluid; CT = computed tomography; TU = tuberculin units.

ANTITUBERCULOSIS DRUGS

Drug	Dose	Side-effects
INH (Isoniazid)	5-10 mg/kg per day	Hepatitis, hypersensitivity
Rifampin (RIF)	10 mg/kg per day (600 mg in adults)	Hepatic toxicity, red-orange staining, Drug interactions.
Pyrazinamide (PZA)	15 to 30 mg/kg per day(max 2g)	Peripheral neuropathy, abdominal pain
Streptomycin	15 mg/kg per day IM-1g in adults 20 to 40 mg/kg per day in children)	Deafness, dizziness
Ethambutol	25 mg/kg/day single dose	optic neuritis
Pyridoxine (VitB6)	50mg daily	

ACUTE BACTERIAL MENINGITIS

ACUTE BACTERIAL MENINGITIS (INFLAMMATION MENINGES & BRAIN)
Subarachnoid space surrounding meninges (Bacterialinvasion) enclosing the brain and the spine.
Infection andinflammatory response
Severe life threating diseases

The CSF which acts as a "shock absorber" for the brain and central nervous systemflows within it.

The three layers of the meninges:

The outer Dura mater

The Arachnoid membrane

The innermost Piamater.

Acute meningtitis (<1 day) duration is almost always a bacterial meningitis. Bacterial meningitis is caused by the presence of bacteria in the cerebrospinal fluid. Bacterial meningitis if not treated in time will cause damage to the meninges and central nervous system resulting in as partial or complete deafness (due to a sub-infection of the cochlea) and, particularly in younger victims, epilepsy or retardation. Bacterial meningitis remains untreated, leads to excessive damage to the brain or central nervous system. Symptoms of Bacterial Meningitis include fever, headaches, seizures, vomiting, impairment of consciousness and stiff neck and back. The most important symptom of bacterial meningitis for early recognition is that of stiffness of the neck on bending forward.

OVERVIEW OF BACTERIAL MENINGITIS

TYPICAL PATHOGENS INVOLVED IN BACTERIAL MENINGITIS

Neisseriameningitides,Streptococcus pneumonia Hemophilus influenzae	Most common pathogens
Staphlyococcus aureus,Staphlyococcus epidermis,(Various other Streptococci) *Escherichia coliKlebsiella enterobacter,*ProteusPseudomonas	Pathogens associated with complications due to Medical procedures on the nervous system such as neurosurgery, lumbar punctures, spinal anaesthesia and cranial trauma
Salmonella,Shigella,*Clostridium perfringensNeisseria gonorrheae*	Rare meningeal pathogens
Listeria monocytogenes	Mainly occurs in elderly>65 yrs age

BACTERIAL MENINGITIS

Pathogenesis: Three Major Pathways Exist By Which An Infectious Agent Bacteria, Virus Or Fungus Gain Access To The CNS From The Site The OrganismInvades The Submucosa By Circumventing Host Defense Mechanisms.

COMMON ORGANISMS OF BACTERIAL MENINGITIS ROUTE ENTRY

Organism	Mode of Entry
Neisseria meningitidis	Nasopharynx
Streptococcus pneumoniae	Nasopharynx or direct extension across skull fracture
Listeria monocytogenes	GI tract, placenta
Haemophilus influenzae	Nasopharynx
Staphylococcus aureus	Bacteremia, skin, or foreign body
Staphylococcus epidermidis	Skin or foreign body

These bacteria have a common mode of invasion into human body. Many are present on or in healthy humans as commensals, either on the skin or in the respiratory tract and as a result of trauma or weakness in the immune system invade the human body via the bloodstream. The bloodstream is their main route of infection to the meninges and cerebrospinal fluid. Once the bacteria enter the subarachnoid space intense host inflammatory response is triggered by lipoteichoic acid and other bacterial cell wall products. Bacterial meningitis can result from infections of the respiratory system, medical procedures, trauma to the nervous system or injury to the cranial region.

They result from infections of the upper respiratory tract or lungs (pneumonia leads to pneumococcal infections of the meninges). The type of bacteria responsible forparticular cases of meningitis is also dependent on age as detailed in the table below,

ETIOLOGY OF BACTERIAL MENINIGITIS WITH AGE VARIATION

BACTERIAL MENINIGITIS WITH AGE VARIATION	
BACTERIA	NO. OF CASES IN ADULTS AND CHILDREN
Neisseria meningitidis	10-30% in adults, 30-40% in children up to the age of 15
Streptococcus pneumonaie	30-50% in adults, 10-20% in children
Hemophilus influenzae	1-3% in adults, 35-45% in children
Listeria monocytogenes	Infants and elderly age group 10%

PNEUMOCOCCUS

Pneumococcus	Separate , paired or short chains of oval-shaped cocci, Cells enclosed by a polysaccharide envelope
Blood cultures	Pneumococci stain gram positive
Pathogenicity	Lobar pneumonia , Pleural,Empyhsema, Pericarditis, Endocarditis, Arthritis, Peritonitis. Middle ear infection (Cochlea) Bacterial meningitis (Hematogenous spread)
	Penicillin therapy reduces high mortality due to pneumococcal infections.

MENINGOCOCCUS (*NEISSERIA MENINGITIDIS*)

Meningococcus	Diplococcus Aerobic Bacteria Gram Negative Stain.Two Main Serogroups A And C Of Meningococcus Cause Epidemics . Humans Are Only Natural Host Of The Meningococcus . **Mortality Is High In Cases Of Meningitis Caused By N.Meningitidis,** Due To Rapid Release Of Large Amounts Of Bacterial Endotoxin Into Bloodstream Which Results In Toxic Shock And Hemorrhage In The Affected Areas.

HAEMOPHILUS (*HEMOPHILUS INFLUENZAE*)

(Hemophilus influenzae)	*Obligate parasite, commonly live in the upper respiratory tract, lower genital tract, mouth and pharynx of humans.*
Clinical manifestations	*Bacterial meningitis, in young infants. conjunctivitis, Infection of the middle ear and secondary infections of the respiratory tract.*
Haemophilus infections	*Ampicillin most prevalent form of treatment.* *But as a result of developing resistance to this drug, Chloramphenicol and Tetracycline are more suitable and effective.*

MICROBACTERIAL THERAPY FOR ACUTE BACTERIAL MENINGITIS

Haemophilus inflenzae type B	3rd Generation cephalosporin
Neisseriameningitidis	Penicillin or Ampicillin
Streptoccus pneumonia	Vancomycin plus 3rd generation cephalosporin
Listeria monocytogenes	Ampicillin or Penicillin
Streptococcus agalactiae	Ampicillin or Penicillin

LEPTOSPIROSIS

Leptospirosis (Hemorrhagic Jaundice) Acute AnthropicZoonosis Infection	
Cause	Spirochaete Leptospira Interrogens
Common Victims	Agricultural Occupational Workers
Principle Source Of Infection.	Rats, Dog, Swine, Cattle
Infection Source	Leptospira Present In Water
Entry Into Body	Mouth-Nose, Conjunctiva ,Breaks In Skin
Incubation Period	7-13 Days
Leptospirosis Acute Severe Form	Weils Disease- Jaundice. Meningitis, Hepatitis, Nephritis,Rash And Produces Haemorrhage And Necrosis, Headache Neck Stiffness Continous Fever, Stupor, Coagulopathy Anemia In 3-6 Days Liver / Kidney - Infection Progressive, Fatal Septicemic Failure
Confirmatory Serological Test For Diagnosis	Microscopic AggutiationTest (MAT)
Other Test For Diagnosis	Serology Ellisa-Raised Igm Titers Positive Earlier Than MAT. PCR-Based DNA Fingerprinting Methods Available For Diagnosis
CSF Analysis	Pleocytosis

WEILS DISEASES CLINICAL MANIFESTATIONS AND COMPLICATIONS

Clinical features	Complications
Altered sensorium	Meningitis
Acute kidney failure-nephritis	Azotemia,oliguria, dysuria
Myocarditis and hypotension	Coagulopathy
Pulmonary haemorrhage-haemoptysis-respiratory failure	Hepatorenal failure
Acute hepatic failure-hepatitis	Gastroinstestinal bleed
Lymphadenopathy Hepatosplenomegaly Pancreatitis	Jaundice
Purpura	Thrombocytopenia , Anemia
Conjunctival effusion,heamorrhage	Chorioretinitis

TREATMENT OF LEPTOSPIROSIS

TREATMENT OF LEPTOSPIROSIS	
Drug of choice	Benzyl penicillin 5 mega units in a day for 5 days
Hypersensitive to penicillin	Erythromycin 250mg QID for 5 days Doxycycline 100mg BD for 7 days Tetracycline 500mg QID Ciprofloxacin 500mg BD Ampicillin and Amoxicillin are effective in the treatment.
Chemoprophylaxis	Doxycycline 200mg orally once weekly effective
vaccine	For 3 serotypes very effective

PATHOGENESIS OF BRAIN ABSCESS

MODE OF SPREAD	PRIMARY SITE OF INFECTION	SITE OF BRAIN ABSCESS
Haematogenous Spread	Lung Abscess, Empyema, Skin Infection Pelvic Infection Intra abdominal Infection, Bacterial Endocarditis, Cyanotic Congential Heart Diseases	Any Site Affected
Direct Transmission	Frontal Ethmoidal Sinusitis	Frontal Lobes
	Subacute Chronic Otitis Media,Mastoiditis	Inferior Temporal Lobe Cerebellum
	Dental Infections	Frontal Lobes

CRYPTOCOCCUS MENINGITIS

CRYPTOCOCCUS MENINGITIS

Cryptococcus meningitis	Major fungal meningitis in HIV related opportunistic infection.,10% of AIDS population.
Most common	Life threating infection of meninges mostly occurring in HIV patients with CD4 counts below 100
Most patients exposed	organism which is found in the soil contaminated by bird droppings, does not cause diseases in healthy

CRYTOCOCCAL MENINGITIS	
Clinical features	Fever, fatigue, nausea, vomiting, headache, confusion, personality changes visual, hearing impairment, progressive dementia
Untreated cases	Coma and death
Diagnosis	Cryptococcal antigen in CSF 1% CSF culture for cryptococcus 95 % India ink positive
Treatment	Antifungal drug amphotericin B 0.7mg/kg/day for 2weeks . Fluconazole is given daily prevents relapses.
Alternative drug	Flucytosine for 2 weeks. Fluconazole oral or IV 400mg qd for 6 weeks causes fewer severe side effects including rashes and liver enzyme abnormalities
Fluconazole Prophylaxis	CD4 count below 50mm3 can help prevent crytococcal meningitis. long time can cause drug resistent
Drug complications	Starting while treating cryptococcal meningitis increased the risk of (IRIS) immune reconstitution syndrome
HAART – Highly Active Antiretroviral Therapy, Iris-Immune Reconstitution Syndrome	

Confirmed etiotlogical agent among adult HIV infected patients.

NEUROCYSTERCOSIS

NEUROCYSTERCOSIS

NEUROCYSTICERCOSIS (NCC) MOST COMMON PARASITIC DISEASE OF THE CNS AFFECTING PEOPLE ALL OVER THE WORLD	COMMONEST CAUSE OF SMALL SINGLE ENHANCING CT LESION (SSECT)
CAUSE	TAENIA SOLIUM TAPEWORM
INTERMEDIATE HOST	PIGS
COMPUTED TOMOGRAPHY OF BRAIN OTHER INFECTIONS CAUSING RING ENHANCED LESIONS ARE	**RING ENHANCED LESIONS: CHARACTERISTIC NEUROCYSTICERCOSIS**
OTHER INFECTIONS CAUSING RING ENHANCED LESIONS ARE	**TUBERCULOMA** **TOXOPLASMOSIS** **CRYPTOCOCCOSIS** **HISTOPLASMOSIS** **CANDIDA ALBICANS**
VERY SIMILAR TO TUBERCULOMA	USUALLY SEIZURES, BUT FEVER ALSO CAN BE A PRESENTATION IN RARE CASES CLINICAL PRESENTATION
CLINICAL MANIFESTATION	SEIZURES, HEADACHE ALTERED SENSORIUM, MULTIPLE NONTENDER NODULAR
MRI	PUNCTATE ECCENTRIC HIGH DENSITY STRUCTURE IS PATHOGNOMONIC FOR DIAGNOSIS EXTENSIVE PARENCHYMAL NCC (**STARRY SKY APPEARANCE)** MOST COMMON SITE IN BRAIN PARENCHYMA CORTICOMEDULLARY JUNCTION
NCC- NEUROCYSTERCOSIS, ,SSECT SMALL SINGLE ENHANCING CT LESION	

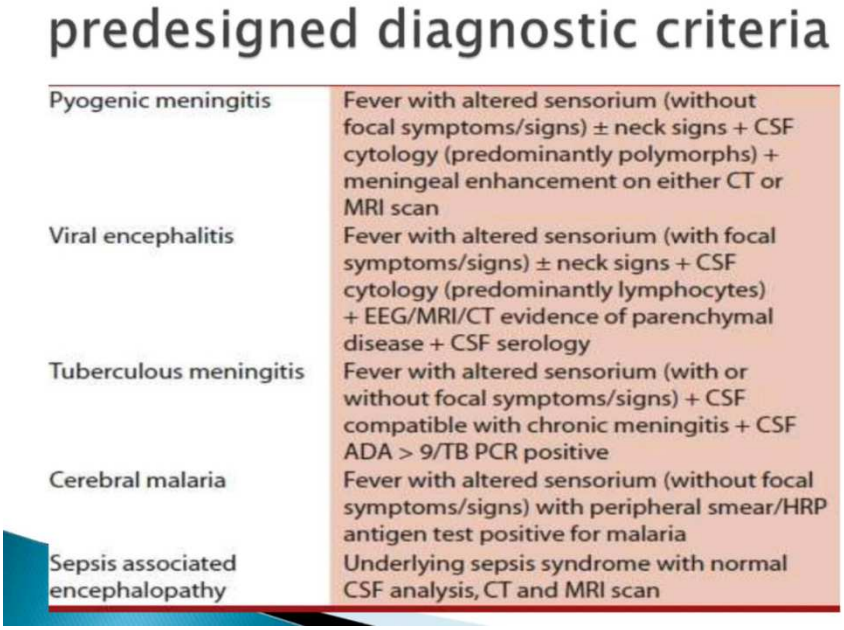
TREATMENT OF NEUROCYSTICERCOSIS

Mainstay treatment	➢ ***symptomatic***
Specific Antihelminthic	➢ ***Aldendazole 15mg/kg for 4 weeks*** ➢ ***Praziquental-50mg/kg for 15 days***
Anticonvulsants	➢ ***Seizures***
Cerebral odema or vasculitis	➢ ***Corticosteriods***
Surgical treatment	➢ **Hydrocephalus Gaint cyst (>10cm) with intracranial hypertension** ➢ **Cyst in fourth ventricle** ➢ **Cyst attached to middle cerebral artery (MCA)** ➢ **CSF diversion in obstructive hydrocephalus**

TUBERCULOMA VERSUS GRANULOMA

TUBERCULOMA	NEUROCYTICERCOSIS
➢ Usually Large >20mm,Multiple	➢ Smaller< 20mm May Be Single Or Multiple
➢ Severe Perifocal Oedema With Focal Neurological Deficit	➢ Cerebral Oedema No Midline Shift Or Focal Neurological Deficit
➢ MRI:Ring Enhanced Lesions	➢ MRI - A Punctate Eccentric High Density Structure Suggestive Of Scolex - Pathognomonic For Diagnosis.(44%) ➢ Multiple Ring Enhanced Lesions
➢ More Common In Posterior Fossa	➢ More Common At Grey- White Junction
➢ MR Spectroscopy Shows Lipid Peaks With Tuberculoma	➢ Ocular Manifestation ,Muscle Involvement Or Subcutanous Nodules
➢ Clinical Features Of TB Else Where –Lungs,Lymph Nodes	➢ Spontaneous Resolution Eventual Calcification More Common In NCC

DIAGNOSTIC CRITERIA USED FOR DIFFERENT ETIOLOGIES OF ACUTE FEBRILE ENCEPHALOPATHY



predesigned diagnostic criteria

Pyogenic meningitis	Fever with altered sensorium (without focal symptoms/signs) ± neck signs + CSF cytology (predominantly polymorphs) + meningeal enhancement on either CT or MRI scan
Viral encephalitis	Fever with altered sensorium (with focal symptoms/signs) ± neck signs + CSF cytology (predominantly lymphocytes) + EEG/MRI/CT evidence of parenchymal disease + CSF serology
Tuberculous meningitis	Fever with altered sensorium (with or without focal symptoms/signs) + CSF compatible with chronic meningitis + CSF ADA > 9/TB PCR positive
Cerebral malaria	Fever with altered sensorium (without focal symptoms/signs) with peripheral smear/HRP antigen test positive for malaria
Sepsis associated encephalopathy	Underlying sepsis syndrome with normal CSF analysis, CT and MRI scan

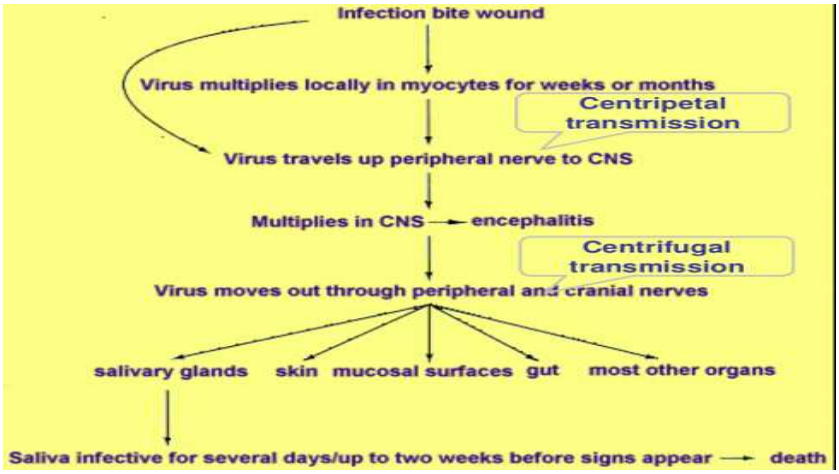
RABIES ENCEHALOPATHY

RABIES - HIGHLY FATAL DISEASE OF CNS CAUSE- LYSSAVIRUS TYPE 1	
Rabies Virus	Lyssavirus –Type 1,Bullet Shaped Virus
Transmission Route	Bites Of Rabid Animals
Most Common Affected	Young Adults
Affinity	Binding To Acetylcholine Receptors In Neural Tissue
Pathogenesis	Street Virus Found In Saliva Of Infected Animal Especially Dogs
Reservoir Of Infection	Dogs And Cats
	All Warm Blooded Animals Including Man Are Infected Rabies Is A Dead End
People At Risk	Lab Workers,Veterinarians,Dog Handlers,Hunters,Etc
Mode Of Transmission	Animal Bites,Licks,Aerosol,Person To Person.
Incubation Period	Depends On Severity Of Bite Number Of Wounds Amount Of Virus Infected Species Of Biting Animal Protection Provided By Clothing Treatment Taken.
Incubation Period	5 Days -6 Months
Common Affected	III,IV And Ixth Cranial Nerve Palsies Most Common
Clinical Manifestations In Man	Bizarre Behaviour, Agitation, Seizures, Difficulty In Drinking Headache, Fever, Sorethorat , Nervousness, Confusion, Pain Or Tingling At The Site Of The Bite , Hallucinations, Hydrophobia,Spasms Of Pharynx Produces Choking, Respiratory Paralysis, Coma And ***Death In 1-6 Days.***
Neurologic Phase Encephalitic Rabies -80%	Fever, Confusion, Hallucinations, Combativeness Muscle Spasms, Hyperactivity, Seizures. Autonomic Dysfunction Like Hypersalivation, Excessive, Perspiration, Gooseflesh, Pupillary Dilatation, Priapism, Hyperexcitability Followed By Periods Of Complete Lucidity ,Hydrophobia, Aerophobia, Foaming At The Mouth, Dysfunction Infected Brainstem- Severe Brainstem Damage,Coma, Death, Paralytic Rabies-20% Complicated Encephalitis , I Water Balance Disturbance, Cardiac Arrhythmia, Myocarditis.

TYPES OF CONTACT CATEGORY IN RABIES

Types of contact are:

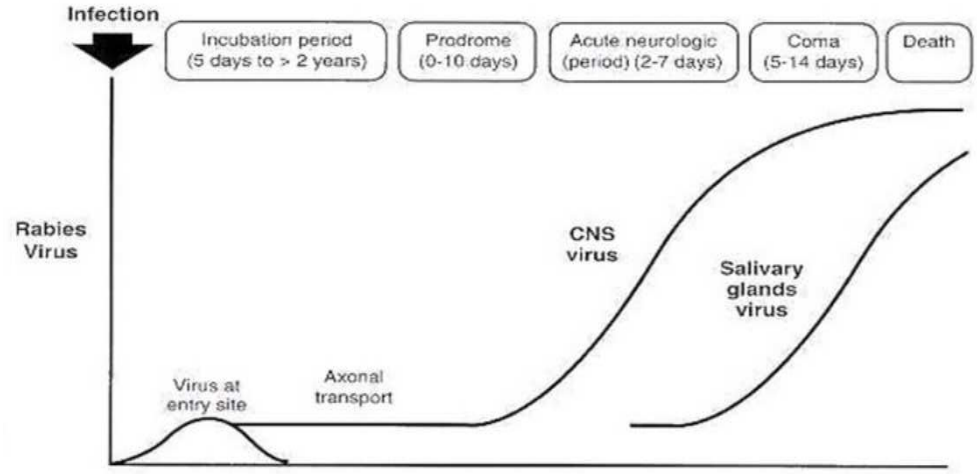
- category I – touching or feeding animals, licks on the skin
- category II - nibbling of uncovered skin, minor scratches or abrasions without bleeding, licks on broken skin
- category III – single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks; exposure to bat bites or scratches



PATHOGENESIS OF RABIES ENCEPALOPATHY

RABIES POST EXPOSURE PROPHYLAXIS

RABIES POST EXPOSURE PROPHYLAXIS
Rabies Immunoglobulin (RIG) single dose 20IU per kg of body weight indifferent parts of body and at site of bite and antirabies vaccination (RAPUR)intramuscular dosed of 1ml or 0.5ML given as 0,3,7,14,30 dose
Abbreviated multisite schedule 2-1-1 regimen,one dose right arm,one dose in the left arm on day 0 one dose on the deltoid muscle on days 7 and 21, the 2-1-1 schedule.if post exposure rabies immunoglobin is not given
Local treatment of wound , Tetanus toxoid vaccination



PROGNOSIS IN RABIES VIRUS WITH 100% MORTALITY

SCRUB TYPHUS ENCEPHALOPATHY

Due to rapid urbanization of rural and forested areas scrub typhus has become an emerging public health problem in India. Scrub typhus is a etiological factor for AFE, resulting in significant morbidity and mortality. Most common in patients from Tamil Nadu and Andhra Pradesh.

SCRUB TYPHUS ENCEHALOPATHY

Scrub Typhus (Bush Typhus)	
Cause	Orientia Tsutsugamushi Is A Zoonotic Disease
Pathogen	ObligateIntracellular Gram Negative Bacterium
Age Group	35-62 Years
Clinically Presents	Fever, Headache, Inoculation Eschar, And Lymphadenopathy.
Characteristic	Eschar Presence
Severe Form Manifestation	Pneumonia, Myocarditis, Azotemia, Shock, Gastrointestinal Bleed, And Meningoencephalitis
Central Nervous System Manifestation	Acute Encephalitis Syndrome (AES)
Complications	After 1 Week Of Illness -Jaundice, Renal Failure, Pneumonitis, ARDS, Septic Shock, Myocarditis, Meningoencephalitis, Respiratory Failure , Septic Shock Results In Multiorgan Failure, DIC,Mortality 7-30%
Diagnosis	Weil-Felix Agglutination Test Using Proteus OXK Strain Positive 50% During Second Week Of Illness Immunoglobulin M Enzyme Linked Immuno-sorbant Assay Positivity
CSF Analysis	
EEG Study	Bilateral Diffuse Cerebral Dysfunction With Epileptiform Discharges With No Specific Lateralization.
MRI	Diffuse Cerebral Edema, Hyperintense Lesions In Putamen & Thalamus In T2-Weighted & Fluid-Attenuated Inversion Recovery (Flair) Images.

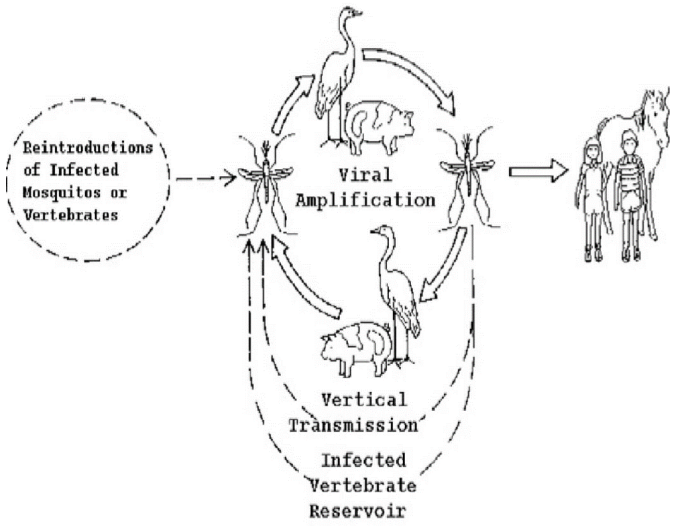
TREATMENT SCRUB TYPHUS ENCEPHALOPATHY

DRUG of choice	*Doxycycline 100 mg twice daily for a period of 7-10 days.*
Inadequate response to doxycycline	*Azithromycin given*
Multi-organ dysfunction syndrome (MODS) (>2 organ involvement)	*Multidisciplinary intensive care including ventilatory support and dialysis*

JAPANESE ENCEPHALITIS

JAPANESE ENCEPHALITIS

Japanese Encephalitis Zoonotic Disease Infecting Mainly Animals Incidentally Infects Man.	
Japanese Encephalitis Virus (JEV)	Mosquito Borne Flavivirus
	Virions - Spherical,Lipoprotein-Enveloped.Genome - Single Stranded Positive Sense RNA
Transmitted	Arboviruses (Abv) Endemic InTemperate And Tropical Asia.Epidemic In India
Domestic Animal Of JE	Horses Dead End Host
Amplifers	Domestic Pigs Virus Producing High Viremia Which Infect Mosquito Vectors
Reservoir	WildBirds Like Heron And Egret
Trasmission Of Je Virus Mosquitoes Principle Vector	Culex Tritaeniorhynchus (Oviposits In Flooded Fields (Fish Ponds, Rice Paddies And Ditches)
India Vector.	Culex Vishnui
Incubation Period	5 -15 Days
Pathogencity	Virus Multiplies At The Site Of Bite And In Regional Lymphnodes Viremia Spreads.
Neurological Disease	Life Threating Encephalitis, < 1% Cases Neuroinvasive Disease Severe High Case Fatality Rate
Diagnose	CSF Analysis Je Igm Antibodies
Prevention	Preventive Measures Adapted By Travellers Going To JVE Epidemic Areas.



TRANSMISSION CYCLE OF JAPANESE ENCEPHALITIS VIRUS

Diagnosis of acute febrile encephalopathy JE should be considered in patients who have returned from recent travel to JE epidemic areas. Disease is usually by serology examination.

TREATMENT, CHEMOPROPHYLAXIS & PREVENTION IN JAPANESE ENCEPHOPATHY

Drug Of Choice	**No Specific Drug Available**
Children Vaccination ≤ 15 Years In Endemic Areas	SA 14 -14-2 Japanese Encephalitis Vaccine Vaccination Children
Prevention	Avoid Mosquito Exposure By Using Bed Nets While Sleeping, Mosquito Repellants With Diethyltoluamide (DEET).Insecticides And Mosquito Killing Agents Should Be Used To Control Viral Spread, Larvivorous Fish Grown In Draining Rice Paddies

PATHOGENESIS OF JAPENESE ENCEPALITIS

Japanese encephalitis virus invasion into CNS

⇓

Microglia (resident immune cells of central nervous system)

⇓

Increased microglial activation

⇓

Increased cytokine secretion

⇓

(interleukin -1,tumor necrosis factor alpha)

⇓

Toxic effects on the brain

⇓

Activated microglia secrete

(Neurotoxins, excitatory neurotransmitters, reactive oxygen prostaglandin)

STAGES IN COURSE OF JAPANESES ENCEHALITIS IN HUMAN AND CLINICAL MANIFESTATION

Three Stages In Course Of Diseases	Clinical Manifestations
1.Prodromal Stage (1-6 Days)	Fever Headache Malaise
2.Acute Encephalitic Stage	Fever, Nuchal Rigidity,Focal Neurological Signs,Convulsions. Altered Sensorium Progressing To Coma.
3.Late Stage Of Sequelae	Fever Subsides, Serious Residual Neurological Deficit-Paralysis, Brain Damage –Deafness, Emotional Liability, Hemiparesis
Prognosis:	Average Period Between Onset Of Illness 5days Death In About 9 Days
Case Fatality Rate (CFR)	20-40% Humans - Mortality Rate 5-35%.
Serious Neurologic Sequelae	33-50%

CT scan shows oedema and congestion of brain and meninges, thalamus is severely affected. The differential diagnosis is meningitis, rabies, cerebral malaria, toxic encephalopathy

INVESTIGATION

LACTATE DEHYDROGENASE

Normally it is used in evaluation of many diseases conditions. LDH enzyme is found in all body cell and released into the serum when cells are damaged. LDH is thus a indicator of tissue and cellular damage. LDH also raises in other types of body fluids, the cerebrospinal and pleural fluid. In the presence of meningeal infections and diseases, like CSF to distinguish between viral, bacterial and fungal meningitis. LDH is evaluated in, If LDH is elevated more specific test like ALT, AST or ALP are further done to diagnosis a particular diseases.

LACTATE DEHYDROGENASE

Lactate Dehydrogenase (LDH)	Nonspecific
High Levels Of LDH In Cerebrospinal Fluid	Meningitis Is Bacterial In Origin
Low Or Normal Level	Viral
LDH Is Increased	Sepsis, Acute Liver Diseases, Meningitis, Encephalitis HIV.
LDH test is performed on body fluids	Peritoneal, pleural, pericardial fluid, Cerebrospinal fluid (CSF)

CSF LACTATE DEHYDROGENASE IN MENINGITIS

CSF ANALYSIS

CSF LACTATE DEHYDROGENASE IN MENINGITIS	
>35μ/dl	Bacterial Meningitis
25-35 μ/dl	Tubercular, Fungal Meningitis
>35 μ/dl	Viral Meningitis

CSF FINDING IN DIFFERENT TYPES OF MENINIGITS

Test	Appearance	Pressure	WBC/μL	Protein mg/dL	Glucose mg/dL	Chloride
Normal CSF	Clear	90 – 180 mm	0-8 lymph.	15-45	50-80	115-130 mEq/L
Acute bacterial meningitis	Turbid	Increased	1000 -10000	100 – 500	< 40	Decreased
Viral meningitis	Clear	Normal to moderate increase	5-300, rarely >1000	Normal to mild increased	Normal	Normal
Tubercular meningitis	Slightly opaque cobweb formation	Increased/ decreased, spinal block	100-600 mixed or lymph.	50-300 due to spinal block	Decreased	Decreased
Fungal meningitis	Clear	Increased	40-400 mixed	50-300	Decreased	Decreased
Acute syphilitic	Clear	Increased	About 500 lymph	Increased but <100	Normal	normal

NEUROIMAGING MODALITIES

COMPUTERISED TOMOGRAPHY (CT SCAN)

The Most Important Need For CT Scan	Rule Out Contraindication For Lumbar Puncture.
Rule Out Infection	Otorhinologic Structures Infection- Sinusitis, Mastoids To Locate Infection Causing Complications - Meningitis, Hydrocephalus, Subdural Effusion, Empyema, Cerebritis, Developing Abscess And Infarction
	Exclude Parenchymal Abscess ,Ventriculitis
Specific Findings In CT Scan	
Pyogenic Brain Abscess	Ring Enhanced Lesion
In Tuberculosis	Tuberculoma Multiple -Ring Enhanced Lesion Are Seen In CT scan

The diagnosis of acute bacterial meningitis should not be made on the basis of imaging studies alone. The diagnosis should rather be established by the affected patients history, physical examination findings and laboratory results of which lumbar puncture and CSF analysis is a the single most important diagnostic study. CT scan may reveal the cause of meningeal infection. Obstructive hydrocephalus occur in inflammatory changes in the subarachnoid space or ventricular obstruction. In acute meningitis CT scan may be normal in early stages of encephalopathy. So the results of an imaging scan do not exclude or prove the presence of acute meningitis. Computed tomography (CT) brain non contrast and contrast enhanced of the brain was done for all patient who presented with acute febrile encephalopathy.

MAGNETIC RESONANCE IMAGING (MRI)

Nonspecific Changes	Meningeal Enhancement Nonspecific Infections, Carcinomatous Meningitis. Reactive Meningitis, Inflammatory Conditions Sarcoidosis Collagen Vascular Diseases.
Magnetic Resonance Imaging (MRI) Scan	Detection Of Meningitis Complications Like Hydrocephalus, Cerebritis, Abscess, Cranial Nerve Lesions, Thrombosis, Infarction, Ventriculitis, Vasculopathy.
DENGUE Encephalitis	Bilateral Hyperintensities On Flair Sequences In Thalami (FLAIR Sequences)
Magnetic Resonance Spectroscopy	Useful To Distinguish An Abscess From Other Ring Enhancing Lesion-Tuberculoma, Neurocytisercosis, Glioma, Fungal

MATERIALS

AND

METHODS

MATERIAL AND METHODOLOGY

All patients above the age group of 13 years to 65 yrs who presented to the hospital with acute febrile encephalopathy with neurological manifestations and admitted in the department of medicine at Rajiv Gandhi hospital with fever of less than two weeks duration along with altered sensorium with or without seizures were enrolled in the study from March 2014 to July 2015. A prospective study was done from August 2014 to August 2015.a total of 100 case with acute febrile encephalopathy.

INCLUSION CRITERIA:

All children above the age of 13 years and all adults upto 65 years. Patients who presented to the medicine department with acute febrile illness with less than 2 weeks duration with any of the following clinical neurological manifestations of alteration of consiousness level, headache, disorientation, vomiting, focal neurological deficit, blurring of vision and with diarrhoea, vomiting chills rigors were enrolled in the study group. A total of 100 patients were taken for study.

EXCLUSION CRITERA :

Patients with non-infectious causes of unconsciousness who presented with Traumatic brain injury, chronic encephalopathy, Vascular (vasculitis, SLE, SAH, SDH, stroke, behcets) with past history of neurological disorders like seizures and in whom persistent altered mental status could be attributed to dearrgened Metabolic (hepatic renal failure ,diabetes) encephalopathy with metabolic parameters as hypoglycemia <50mg/dl , hypoxia (pao2 <60mmHg), hypercapnia (pco2 >50mmHg)

Dyselectrolytemia with hyponatremia (<120mg/dl) hypernatremia (>150mg/dl) space occupying lesion (SOL) or endrocinopathies like addison's, hypothyroidism hashimotos encephalopathy, Toxic (alcohol, drugs) encephalopathy patients were excluded from the study. Patient with previous psychiatric illness or previous drug treatment for any other neurological disorders were excluded from the study.

DEMOGRAPHY AND HOSPITAL STAY.

A total of 100 patients of the age group above 13 years were included in the study in which 50% were below 35 yrs of age .Males were common commonly affected. Male:female Ratio 2:1.

Patients admitted earlier with less clinical manifestation had good recovery and recovered after intensive treatment. For a duration of 7days or 14 days. patients who presented to the hospital after severe manifestations of Acute febrile encephalopathy and fever for more than a week duration had a longer course of treatment in the hospital in the intensive care unit and complications like acute liver failure was controlled in most patients. Patients with complications like acute respiratory distress, aspiration pneumonitis and disseminated intravascular coagulation would not be treated and mortality was high in these patients.

IDENTIFICATION OF COMPLICATING SIGNS IN ACUTE FEBRILE ENCEPHALOPATHY

Identification of deteriorating signs in Acute Febrile Encephalopathy	
Seizures Shock Sepsis	Raised ICT Papilledema Asymmetric pupils Posturing Absent Dolls eye movement

MANAGEMENT OF PATIENT WITH ACUTE FEBRILE ENCEHALOPATHY GCS<15

Assessment	**Oxygen therapy**	**Monitoring**
Airway Breathing Circulation Disability	If respiratory rate increased and inadequate for ventilation Ventilation O_2 saturation <92% despite high flow O_2 through venturi mask If GCS < 8 Signs of raised intracranial pressure Signs of shock despite fluid management	Heart rate Respiratory rate O_2 saturation Blood pressure Temperature ECG (hourly recorded or continuously monitored)

MANAGEMENT OF PATIENTS WITH RAISED INTRACRANIAL PRESSURE

Management of patients with raised intracranial pressure
Early intubation if GCS<8
Head end elevation of 15 -30^{o}
Avoid hypotonic solutions
Hypertonic saline -3% saline in Hypotension
Hypovolemia, serum osmolality >320mOsm//kg. Renal failure dose 0.1-1mg/kg/hr
Mannitol 20 % solution initial bolus 0.25-1g/Kg then 0.25-0.5g/kg,Q2-6h as requirement upto 48hours
Hyperventilation –$PaCO_2$ 30-35mmHg

EMPIRICAL TREATMENT OF ACUTE FEBRILE ENCEPHALOPATHY

EMPIRICAL TREATMENT OF ACUTE FEBRILE ENCEPHALOPATHY
IV cefotaxime 2 gm BD dose daily x 7 days
IV Acyclovir 500mg TDS daily x 7days
IV Artesunate 120 mg OD daily x7 days
Doxycycline 100mg oral BD daily x 7 days

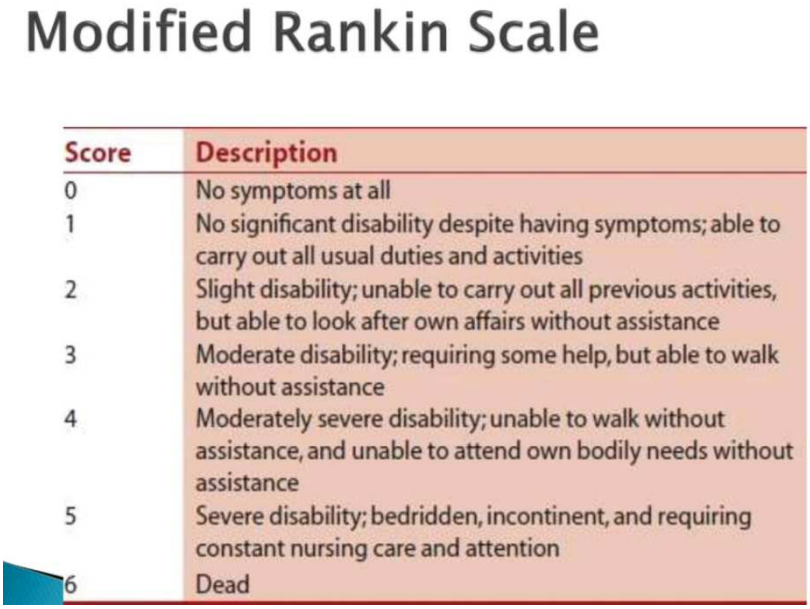
Then after Investigations Drug of choice continued or added

Most of the patients with acute febrile encephalopathy completely recovered without any neurological deficit. once the underlying etiology is diagnosed and the patient in treated with appropriate antivirals, antibiotics or even with empirical treatment. is. IV acyclovir is the treatment of choice for viral encephalititis. Respiratory complications like aspiration pneumonitis treated with higher antibiotic erythromycin, azithromycin, clarithromycin, symptoms resolved over several days to 2-3 weeks, Antibiotics are the most common form of treatment although some vaccines are available

PROGNOSIS

Prognosis was graded according to Modified rankin score. neurological sequelae like cognitive impairment, weakness, ataxia, seizure seen in 5%. The recent advent of newer antibiotics has reduced the mortality rate. Most cases of Bacterial meningitis have good prognosis provided the disease is diagnosed rapidly and treated appropriately. Condition such as alcoholism and high-dose steroid use reduce the chancesof a full recovery.

PROGNOSIS OF ACUTE FEBRILE ENCEPHALOPATHY ACCORDING TO MODIFIED RANKIN SCALE



Modified Rankin Scale

Score	Description
0	No symptoms at all
1	No significant disability despite having symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance, and unable to attend own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention
6	Dead

OBSERVATION

AND

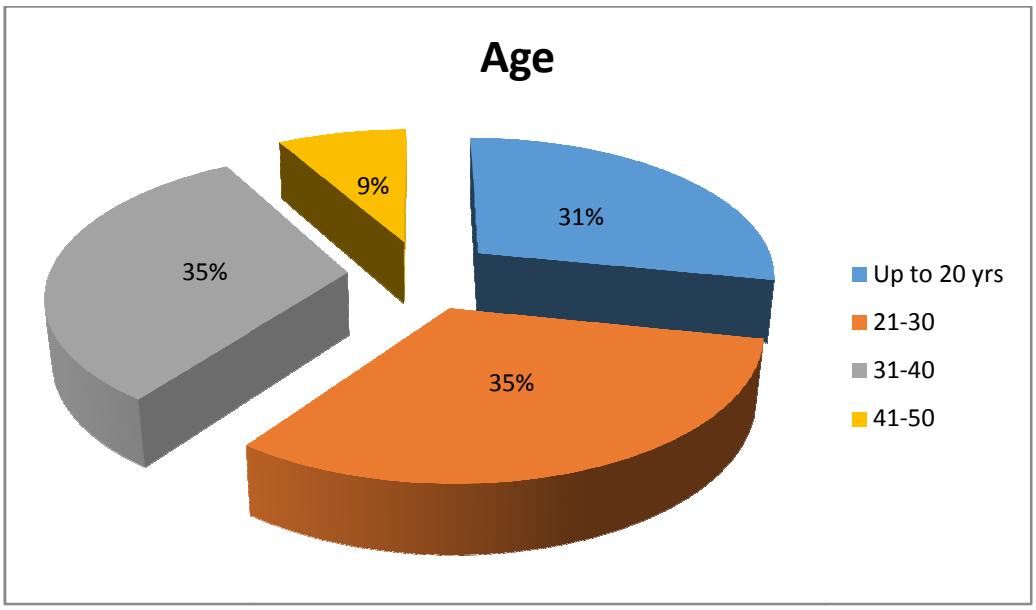
RESULTS

OBSERVATIONS AND RESULTS

Table 1: Age Distribution

AGE	FREQUENCY	PERCENT
Up to 20 yrs	31	31.0
21-30	35	35.0
31-40	25	25.0
41-50	9	9.0
Total	100	100.0

Chart 1 : Age Distribution

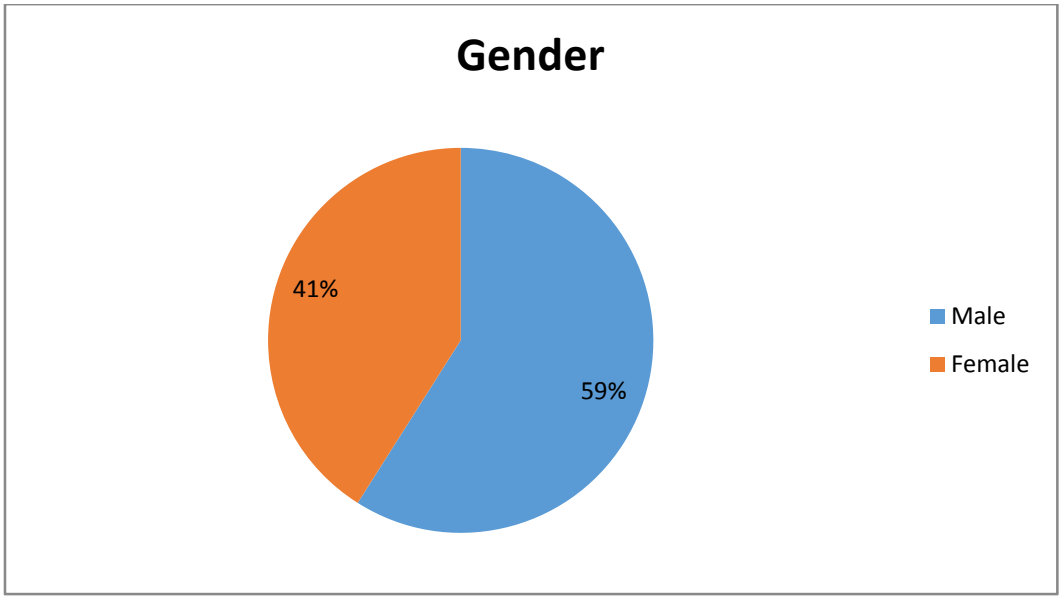


In our study 35% cases of acute febrile encephalopathy were most common in age group between 21-30 yrs

TABLE 2 : SEX FREQUENCY

SEX	FREQUENCY	PERCENT
Male	59	59.0
Female	41	41.0
Total	100	100.0

Chart 2 : Sex Frequency



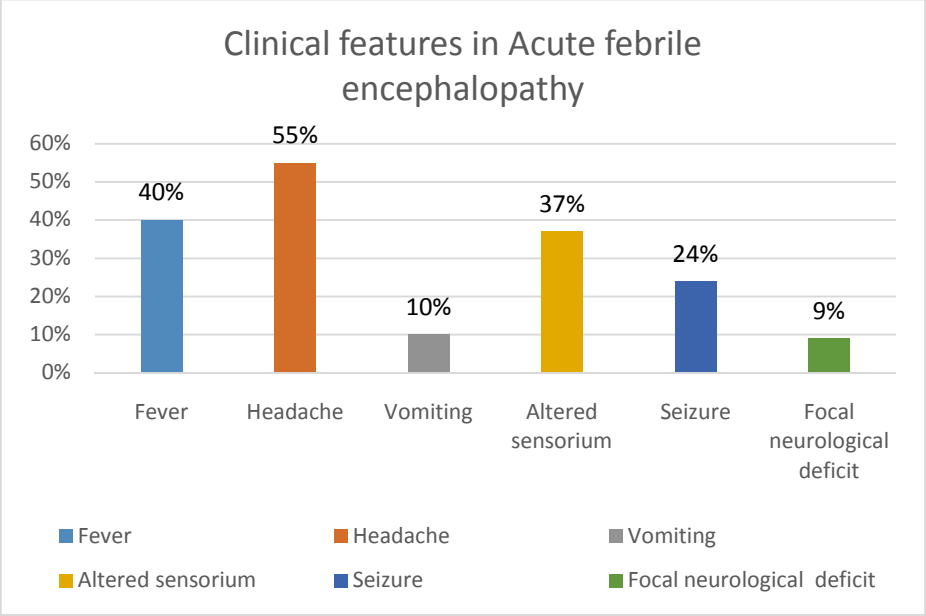
Male patients were more common in our study group about 59% cases.

Table 3 : CLINICAL FEATURES IN ACUTE FEBRILE ENCEPHALOPATHY

CLINICAL FEATURES IN ACUTE FEBRILE ENCEPHALOPATHY	FREQUENCY	PERCENTILE
Fever	40	40%
Headache	55	55%
Vomiting	10	10%
Neck Rigidity	34	34%
Altered Sensorium	37	37%
Seizure	24	24%
Focal Neurological Deficit	9	9%

Headache 55% and fever 40% were the most common clinical manifestations. neck rigidity 34%, altered sensorium, 37%, seizures 24%, focal neurological deficit 9 % was least common

Chart 3 CLINICAL FEATURES IN ACUTE FEBRILE ENCEPHALOPATHY

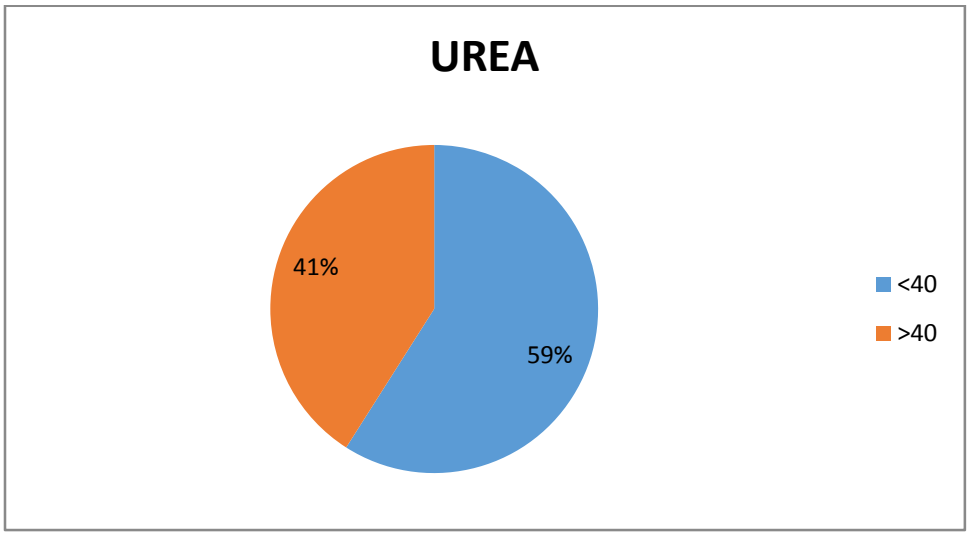


RENAL FUNCTION TEST

Table 4 BLOOD UREA LEVELS

UREA	FREQUENCY	PERCENT
<40 mg/dl	54	54.0
>40 mg/dl	46	46.0
Total	100	100.0

Chart 4 : BLOOD UREA LEVELS

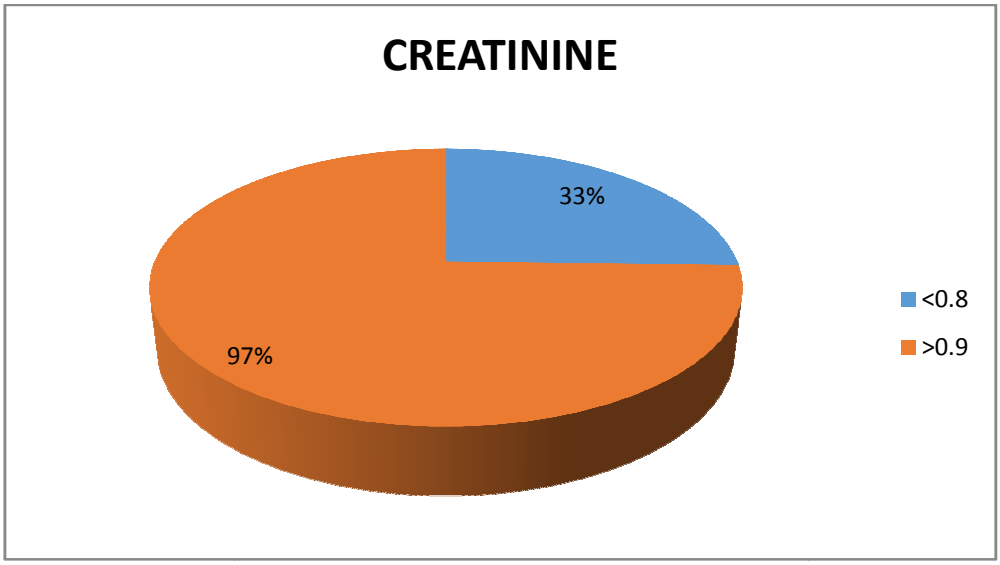


46% had raised blood urea values in our study in patients acute febrile encephalopathy

TABLE 5 : BLOOD CREATININE LEVELS

CREATININE mg/dl	FREQUENCY	PERCENT
< 0.8 NORMAL	33	33.0
>0.9 INCREASED	67	67.0
Total	100	100.0

Chart - 5 : BLOOD CREATININE LEVELS

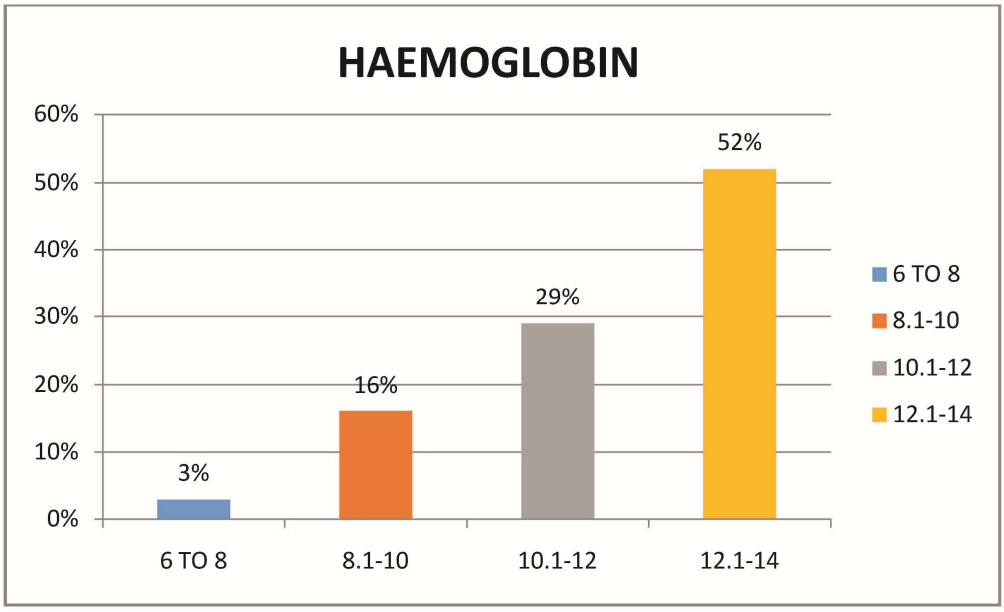


Creatinine was raised in 67% of cases in our study in acute febrile encephalopathy patient

TABLE 6 : BLOOD HEMOGLOBIN VALUE

HAEMOGLOBIN mg/dl	**FREQUENCY**	**PERCENT**
6-8	3	3.0
8.1-10	16	16.0
10.1-12	29	29.0
12.1-14	52	52.0
Total	100	100.0

Chart 6 : BLOOD HEMOGLOBIN FREQUENCY LEVEL

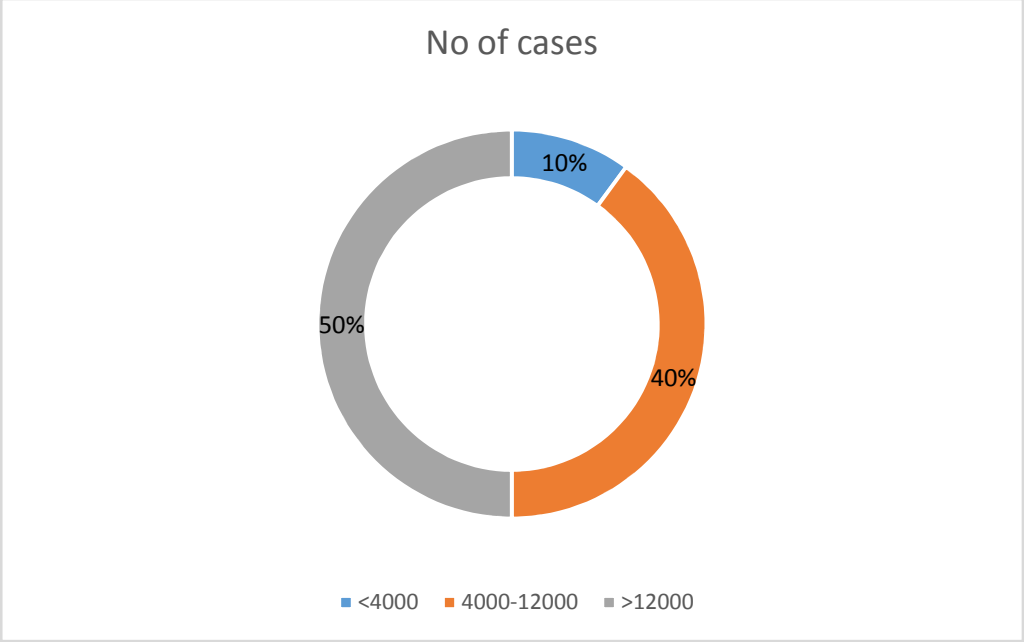


Hemoglobin was very low about 6-8 mg/dl in 3% of case with in our study and 52% had normal levels

TABLE 7 : Total leucocyte count

Total leucocyte count (cell/mm)	FREQUENCY	NO OF CASES
<4000	10%	10%
4000-12000	40%	40%
>12000	50%	50%

Chart 7: Total leucocyte count

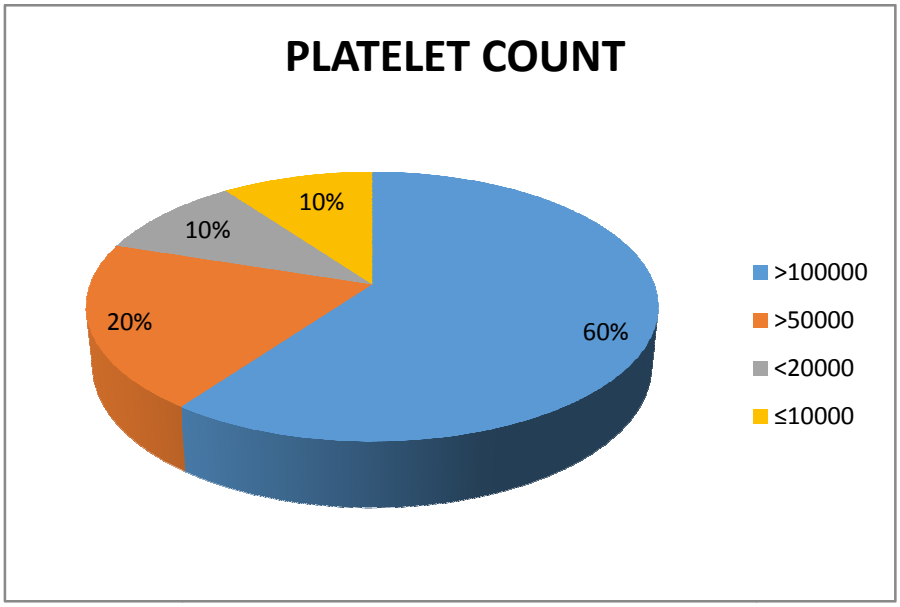


Total leucocyte count was raised in more90% cases in our study in acute febrile encephalopathy patient

TABLE 8: BLOOD PLATELET COUNT

PLATELET COUNT /ML	FREQUENCY	NO OF CASES
> 100000	60%	60%
> 50000	20%	20%
< 20000	10%	10%
≤ 10000	10%	10%

Chart 8 : BLOOD PLATELET COUNT



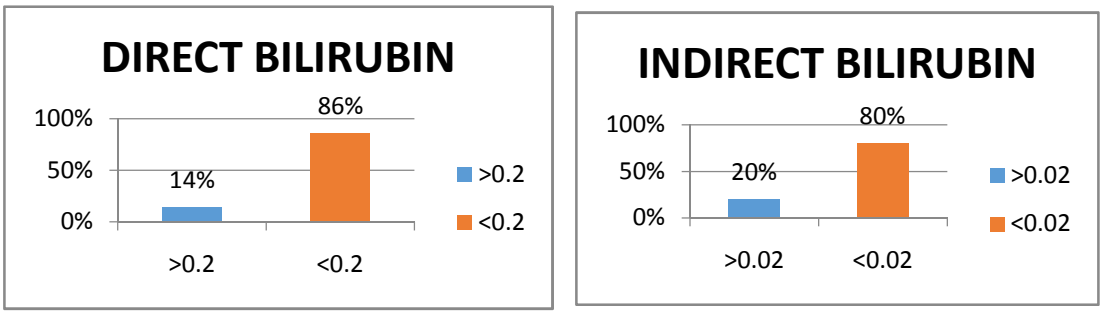
Platelet count was reduced in 50% of cases and 10% had very low levels and needed blood transfusion platelet transfusion in our study in patients with acute febrile encephalopathy.

TABLE 9 : LIVER FUNCTION TEST

DIRECT BILIRUBIN mg./dl	FREQUENCY	PERCENT
>0.2	14	14.0
<0.2	86	86.0
Total	100	100.0

INDIRECT BILIRUBIN mg./dl	FREQUENCY	PERCENT
>0.8	20	20.0
<0.8	80	80.0
Total	100	100.0

Chart 9. Liver Function Test

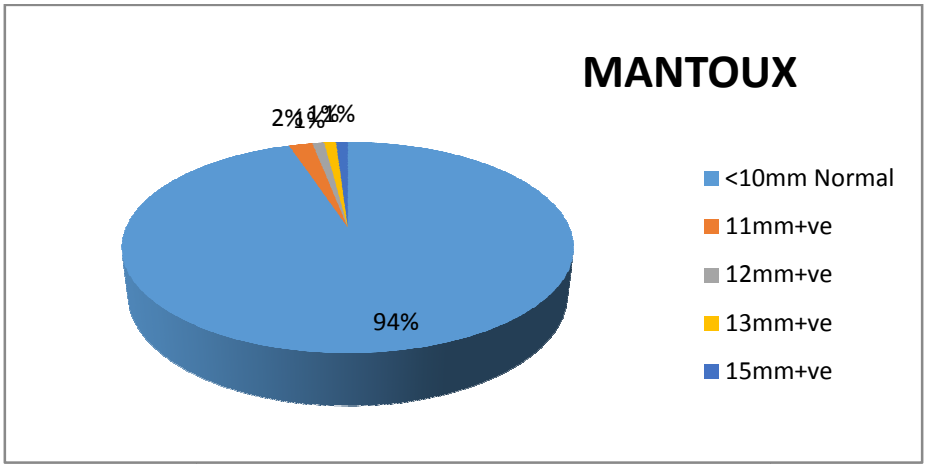


Liver function test was raised in 20 % of cases of patients with acute febrile encephalopathy due to hepatic complications.

TABLE 10 : MANTOUX TEST

MANTOUX	FREQUENCY	PERCENT
<10mm	94	94.0
11mm+ve	2	2.0
12mm+ve	1	1.0
13mm+ve	1	1.0
15mm+ve	2	1.0
Total	100	100.0

Chart 10 : MANTOUX TEST



Mantoux was positive in our study in 5% cases with tuberculosis in of patients with tuberculosis encephalitis

TABLE 11 : SPUTUM CULTURE/SENSITIVITY& AFB

Sputum Culture/ Sensitivity& AFB	FREQUENCY	No of cases positive
Mycobacteria	5	5%

Sputum culture sensitivity seen in 5% cases in the study

CHART11: SPUTUM CULTURE/SENSITIVITY& AFB

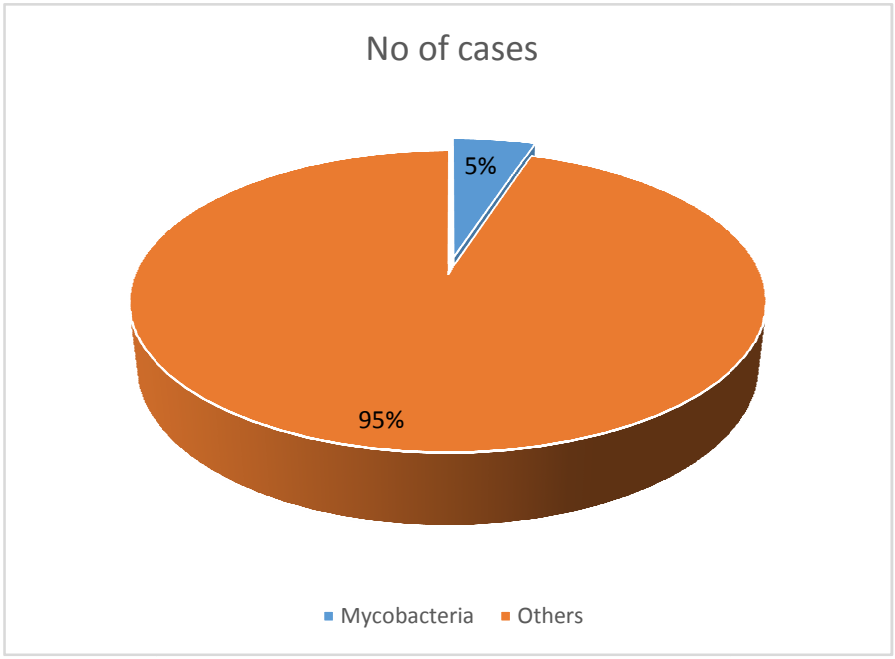
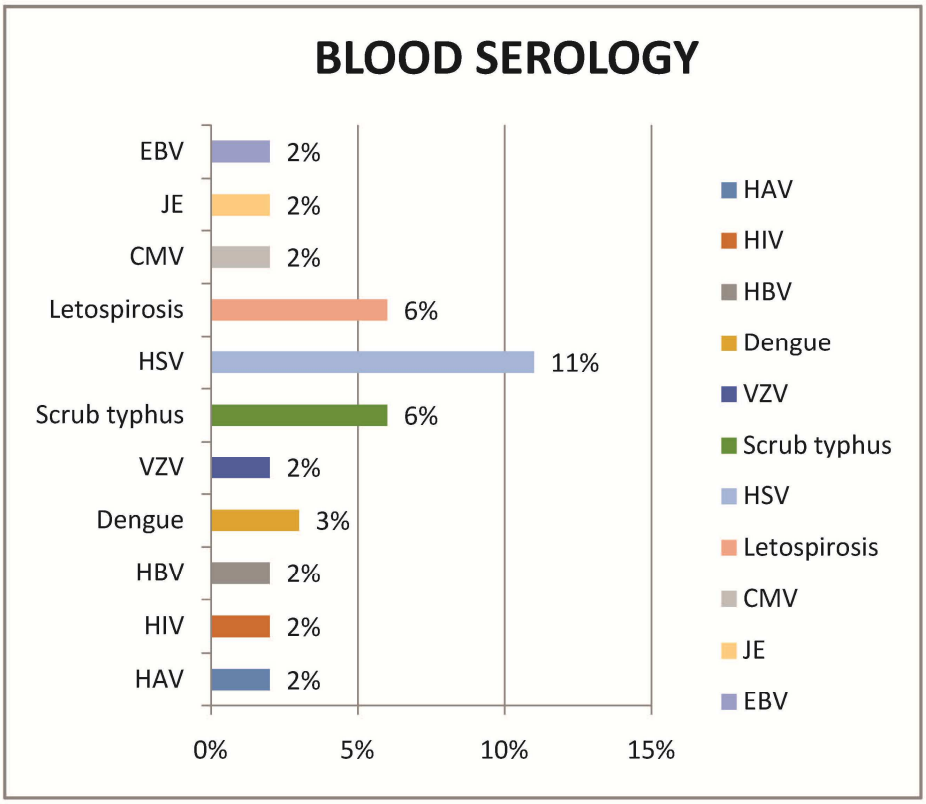


TABLE 12 : BLOOD SEROLOGY

BLOOD SEROLOGY	FREQUENCY	PERCENTILE
VIRAL		
HIV	2	2%
HBV	2	2%
DENGUE	3	3%
VZV	2	2%
SCRUB TYPHUS	6	6%
HSV	11	11%
LEPTOSPIROSIS	6	6%
HAV	2	2%
CMV	2	2%
JE	2	2%
EBV	2	2%

Herpes simplex virus was positive in 11%with maximum incidenceamong patients with positive IgM antibodies in serum cases in our study in acute febrile encephalopathy patient

CHART 12 : BLOOD SEROLOGY

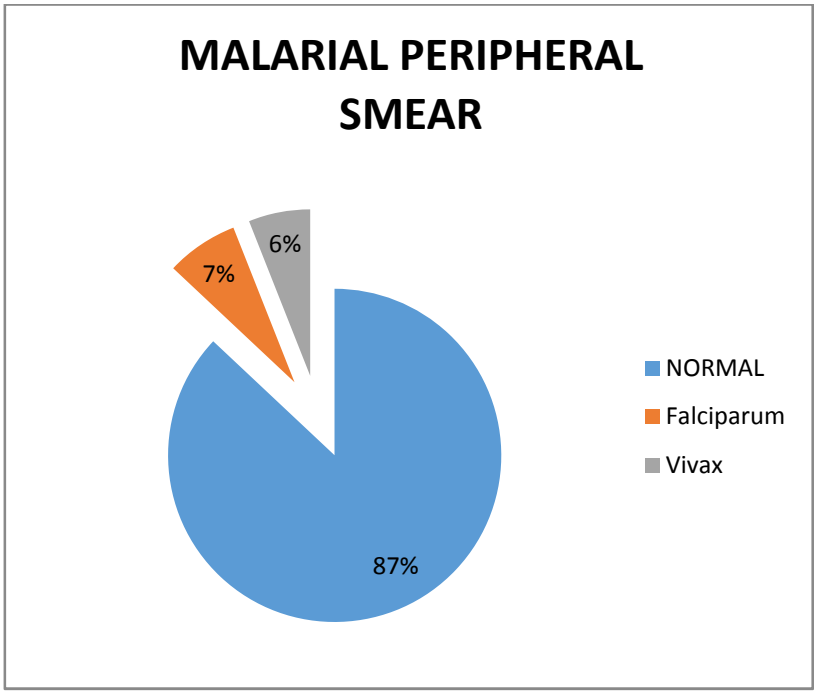


23% Viral encephalopathy was most common in 28% our case study

TABLE 13 : MALARIAL PERIPHERAL SMEAR

MALARIAL PERIPHERAL SMEAR	FREQUENCY	PERCENT
Falciparum	7	7.0
Vivax	6	6.0
Total	100	100.0

FIGURE 13 : MALARIAL PERIPHERAL SMEAR



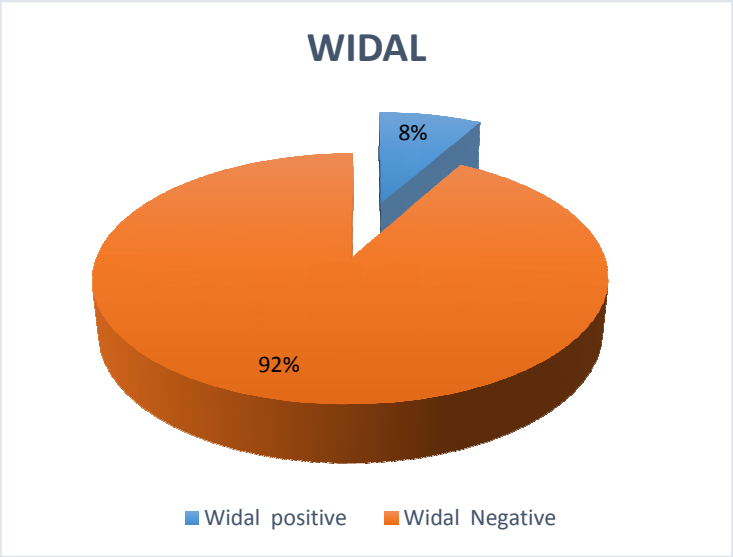
Malaria was positive in 13% cases in our study in acute febrile encephalopathy patient

WIDAL TEST

TABLE 14 : WIDAL TEST

WIDAL TEST	FREQUENCY	PERCENTILE
positive	8	8%

CHART 14 : WIDAL TEST



Widal positive in was 8% cases in our case study

TABLE 15 : BLOOD CULTURE SENSITIVITY

BLOOD CULTURE SENSITIVITY	FREQUENCY	NO OF CASES
Bacteria	16	16%
Fungus	6	6%
	Sputum C/S & AFB	
Mycobacteria	5	5%
Salmonella typhi	8	8%

BLOOD CULTURE & SENSITIVITY	Frequency	No Of Cases
Streptococcus	6	6%
Staphylococcus	4	4%
Streptococcus	6	6%
Pneumococcus	3	3%
Salmonella	3	3%

Chart 15 : BLOOD CULTURE SENSITIVITY

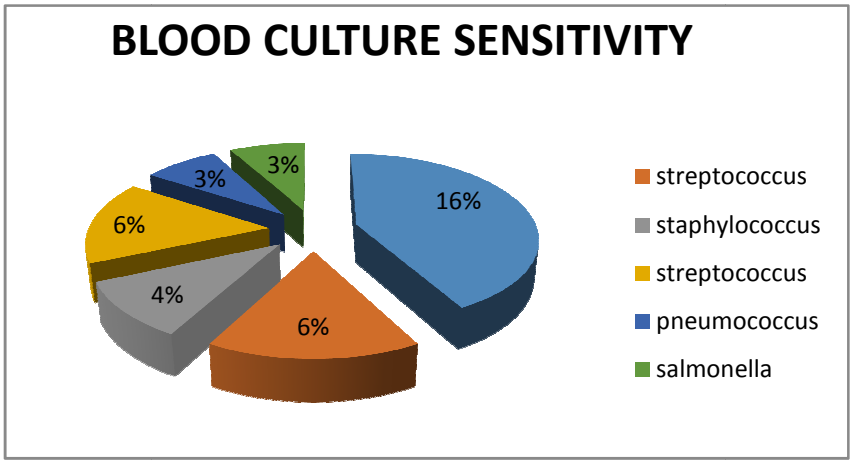


TABLE 16 : CSF PROTEIN AND SUGAR VALVES

PROTEIN(mg/dl)	FREQUENCY	CASES
<40	40	40%
40-100	40	40%
>100	20	20%
Sugar (mg/dl)		
≤40	60	60%
≥40	40	40%

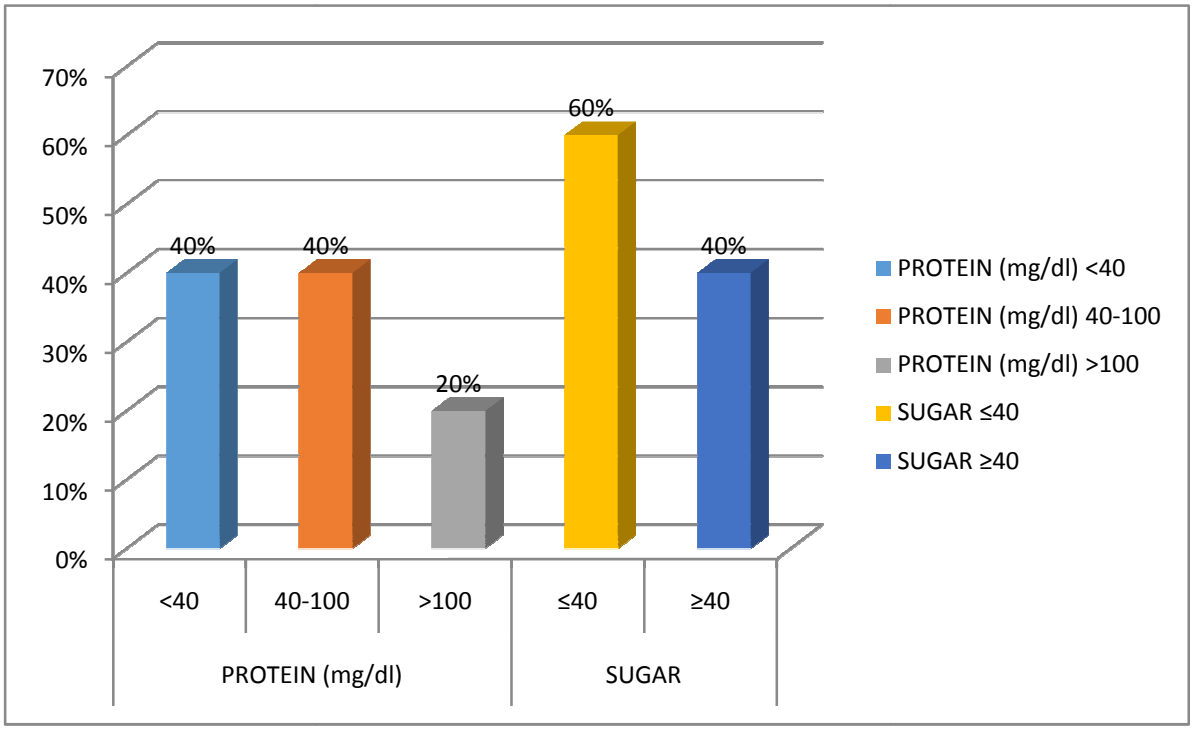


FIGURE 16 : CSF PROTEIN AND SUGAR VALVES

TABLE 17 : CSF BACTERIAL GRAM STAIN POSITIVITY

CSF BACTERIAL GRAM STAIN POSITIVITY	FREQUENCY	NO OF CASES
Streptoococi	4	4%
Staphylococci	2	2%
Mycobacteria Tuberculosis	5	5%
Pneumococcus	5	5%
Nesseriameningococcoi	1	1%
Gram negative Bacilli	1	1%
CSF Culture Sensitivity		
Bacteria	8	8%
Mycobacteria	6	6%
Fungus	1	1%
Cryptococcus	1	1%

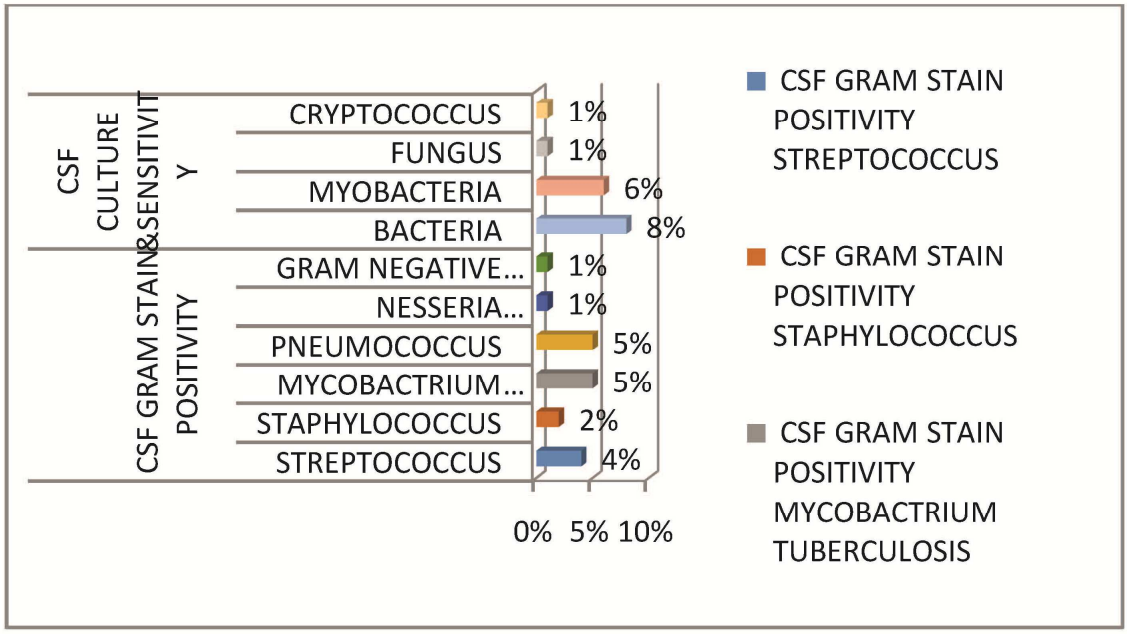


CHART 17 : CSF BACTERIAL GRAM STAIN POSITIVITY

Bacterial meningitis was seen in 16% of cases in our study

TABLE 18 : CSF VIRAL STUDY AND CULTURE&SENSITIVITY

CSF VIRAL STUDY	No Of Case
Herpes simplex virus	15%
Epstein barr virus	2%
Cytomegalovirus	2%
Japanesese encephalitis virus	1%
Varicella zoster virus	2%
Herpes zoster virus	2%

Herpes simplex virus was positive in 15% cases in our study

Chart 18 : CSF VIRAL STUDY AND CULTURE&SENSITIVITY

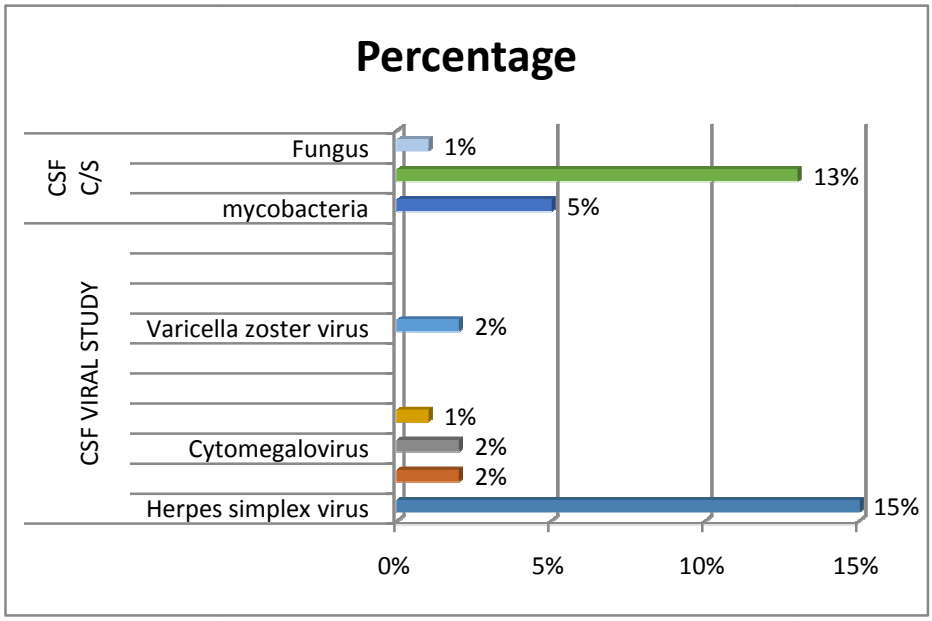


TABLE 19 : COMPLICATIONS IN PATIENTS WITH ACUTE FEBRILE ENCEPHALOPATHY

COMPLICATIONS IN PATIENTS WITH ACUTE FEBRILE COMPLICATIONS		FREQUENCY	Total No Of Patients/ 100
IMPROVED COMPLETEY WITHOUT ANY COMPLICATION OR NEUROLOGICAL DEFICIT		80	80
IMPROVED WITH NEUROLOGY DEFICIT	FOCAL NEUROLOGICAL DEFICIT	3	3
	VISUAL DEFICITS	2	2
	SENSORINEURAL DEAFNESS FOCAL NEUROLOGICAL DEFICIT	3	3
OTHER SYSTEM INVOLVEMENT	ARF-acute renal failure GIT-gastrointestinal PNEUMONIA ALF-acute liver failure	4 4 4 1	
DEAD	MODS-Multiorgan failure DIC-Disseminated intravascular coagulation ARDS-Acute respiratory distress syndrome	5 1 3	

CHART 19 : PROGNOSIS AND COMPLICATIONS IN PATIENTS WITH ACUTE FEBRILE

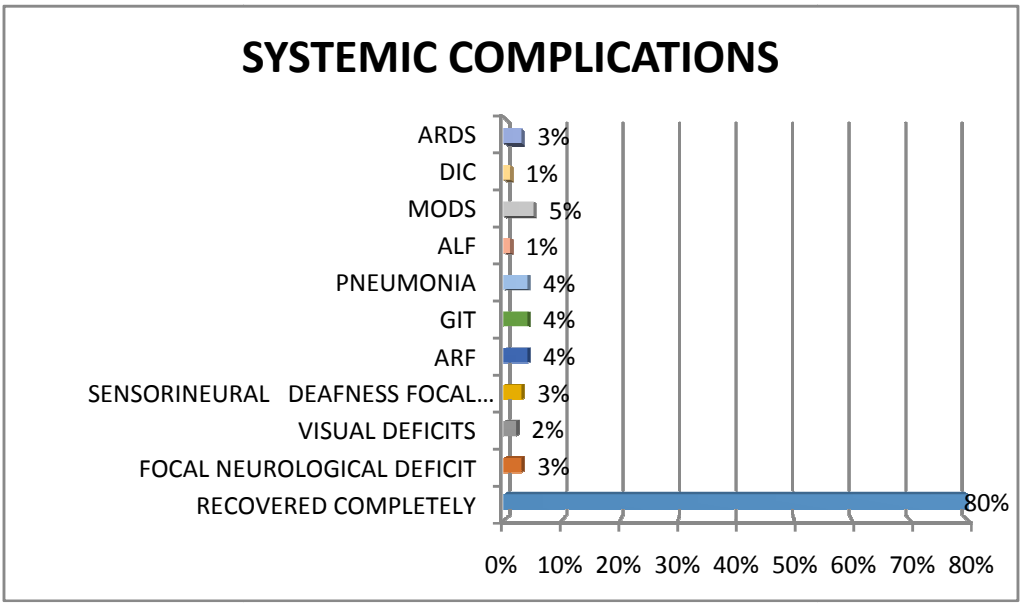


TABLE 20 : COMPLICATIONS IN PATIENTS WITH ACUTE ENCEPHALOPATHY IN PATIENTS

COMPLICATIONS IN PATIENTS WITH ACUTE ENCEPHALOPATHY IN PATIENTS	FREQUENCY	NO OF CASES
Respiratory failure	5%	5
Psychosis	2%	2
Peripheral circulatory failure	5%	5
Sepsis	6%	6
Hemiparesis	5%	5
Quadriparesis	5%	5
Pericardial effusion	4%	4
Drug reaction	3%	3

CHART 20: COMPLICATIONS IN PATIENTS WITH ACUTE ENCEPHALOPATHY IN PATIENTS

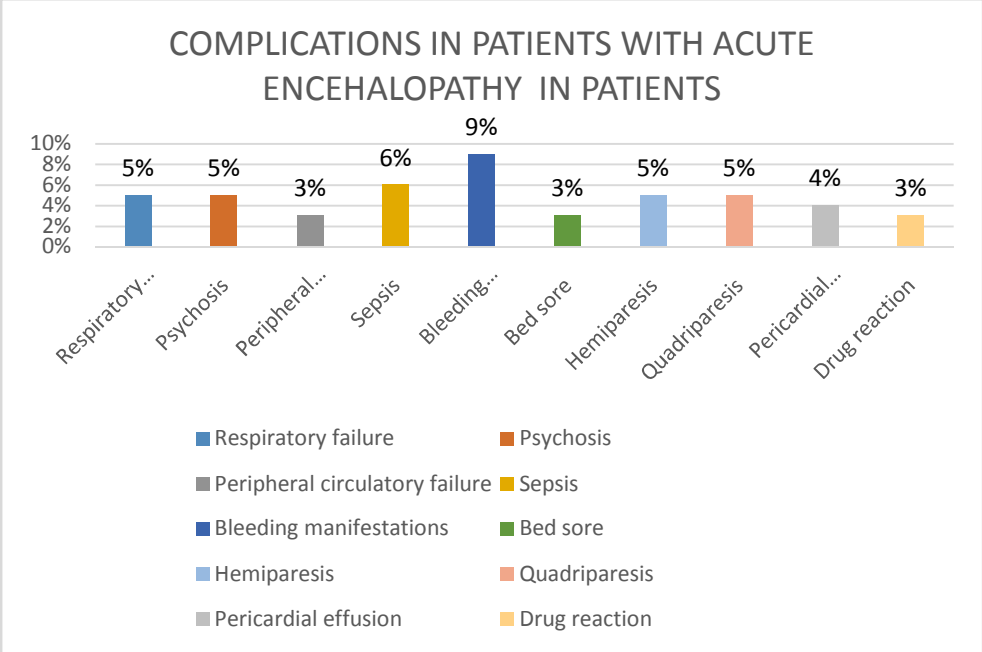


TABLE 21 : GENERAL AND SYSTEMIC EXAMINATION OF FINDINGS IN ACUTE FEBILE ENCEPHALOPATHY

General Examination finding of AES	FREQUENCY	NO OF CASES
Temperature(100 F)	60%	60
Tachycardia	40%	40
Bradycardia	6%	6
Tachypnea	8%	8
Anemia	25%	25
Hypotensive shock	10%	10
Icterus	18%	18
Edema	10%	10
Lymphadenopathy	5%	5
Cyanosis	3%	3
Clubbing	4%	4

CHART 21 : GENERAL AND SYSTEMIC EXAMINATION OF FINDING IN ACUTE FEBRILE ENCEPHALOPATHY

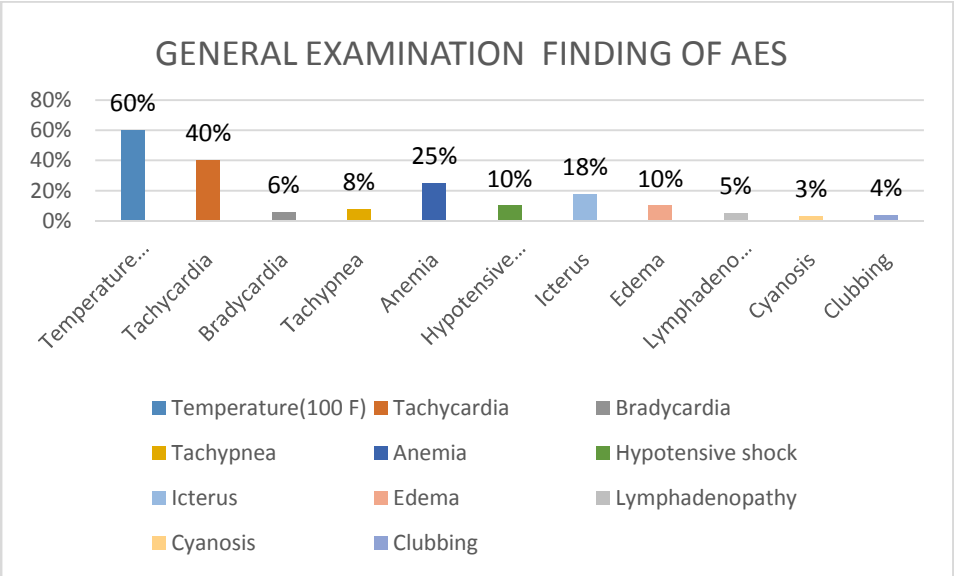
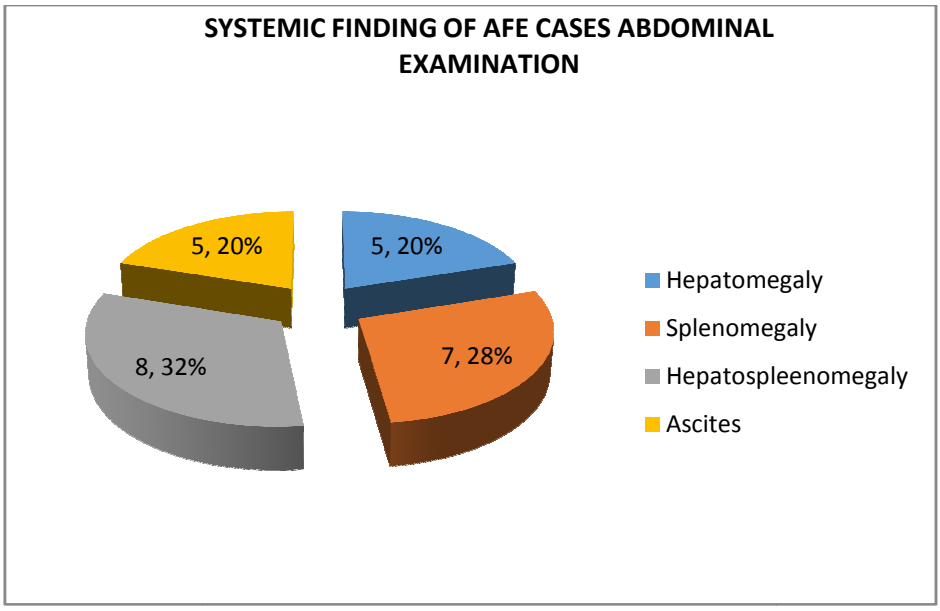


TABLE 22: SYSTEMIC FINDING OF AFE CASES / ABDOMINAL EXAMINATION

SYSTEMIC FINDING OF AFE	PERCENTILE	NO OF CASES
Abdominal examination		
Hepatomegaly	5%	5
Splenomegaly	7%	7
Hepatosplenomegaly	8%	8
Ascites	5%	5

FIGURE 22 : SYSTEMIC FINDING OF ABDOMINAL EXAMINATION

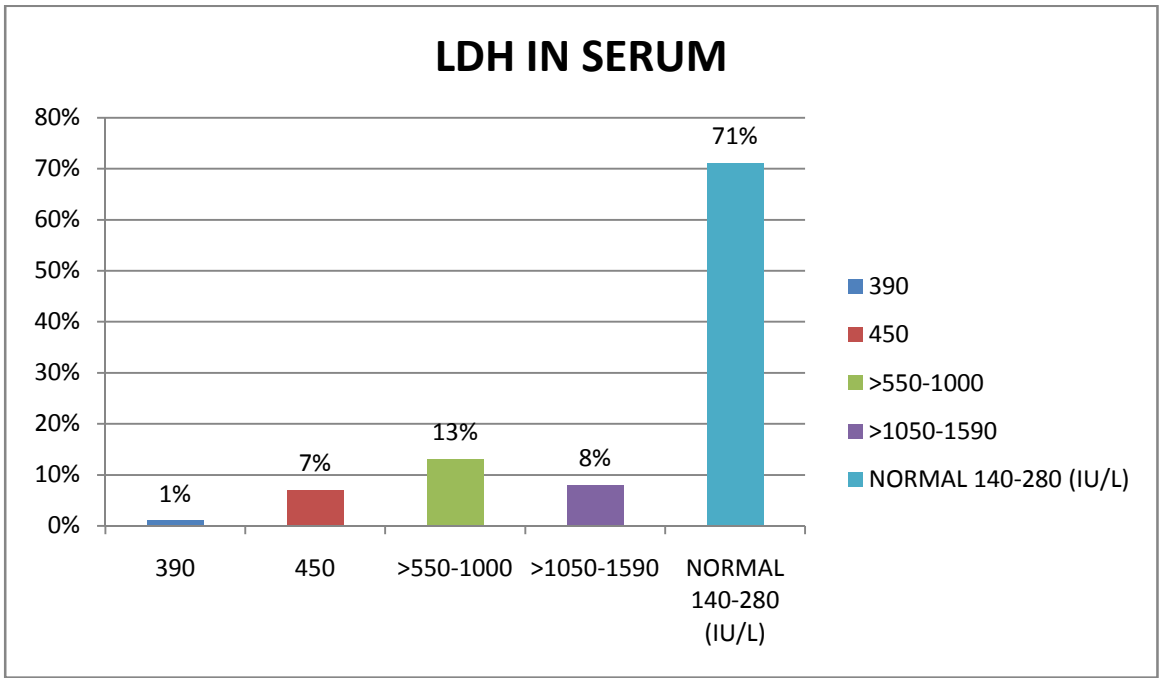


Abdominal examination showed 8% cases with hepatosplenomegaly and ascites 5% in of cases in our study in patients with acute febrile encephalopathy

TABLE 23 : LDH IN SERUM

LDH IN SERUM NORMAL 140-280 (IU/L)	FREQUENCY	PERCENT
390	1	1.0
450	7	7.0
>550-1000	13	13.0
>1050-1590	8	8.0
NO OF CASES TOTALLY INCREASED IN	29	29.0
NORMAL	71	71.0
Total	**100**	**100.0**

CHART 23 : LDH IN SERUM



Lactate dehydrogenase (LDH) levels raised in 28% cases in our study

DISCUSSION

DISCUSSION

- AGE - In our study 35% cases of acute febrile encephalopathy most common in age group between 21-30 years

- SEX - Male patients were more common in our study group about 59%

- ETIOLOGY-Viral aetiology of encephalopathy was more common in 28%, bacterial meningitis was seen in 16% cases of our study.

- CLINICAL FEATURES - Headache 55% and fever 40% were the most common clinical manifestations. Neck rigidity 34 %,altered sensorium 37%, seizures 24% & focal neurologicial deficit 9 % was least common

- SYSTEMIC EXAMINATION Abdominal examination showed 8% cases with hepatosplenomegaly and 5% with ascites in of cases in our study in patients with acute febrile encephalopathy

- RENAL PARAMETERS - 46% had raised blood urea values in our study in patients with acute febrile encephalopathy, Creatinine was raised in 67% of cases in our study.

- COMPLETE BLOOD COUNT - Hemoglobin was very low about 6-8 mg/dl in 3% of case with in our study and 52% had normal levels,Total leucocyte count was raised in morethan90% cases in our study in acute febrile encephalopathy patients

- PERIPHERAL SMEAR STUDY-Malaria was positive in 13% cases in our study

- WIDAL TEST - Widal positive was 8% cases in our case study

- CSF ANALYSIS - 23% Viral encephalopathy was most common in our case study

- PROGNOSIS - Most of the patients recovered with good prognosis focal neurological deficit was seen in 3% of patients. 80% of the patients recovered with good prognosis. Focal neurological deficit was seen in 3% of patients LDH levels raised in serum in 28 % of cases in our study suggestive of infectious etiology

- COMPLICATIONS - Respiratory system 5% ,peripheral shock 3%,sepsis, 6%,bleeding 9%

CONCLUSION

CONCLUSION

- Acute febrile encephalopathy is most common in age group between 21-30 yrs
- Male patients were more common
- Viral aetiology was more common cause of acute febrile encephalopathy and other aetiology like protozoal, fungal were rarely identified causes
- Headache and fever were the most common clinical manifestations.
- Raised blood urea, Creatinine values seen in few patients
- CSF analysis showed 23% Viral encephalopathy was most common cases
- Overall the Patients recovered with good prognosis

SUMMARY

SUMMARY

Viral aetiology was more common cause of acute febrile encephalopathy and other aetiology like protozoal, fungal were rarely identified causes. Males were more commonly affected. Headache and fever were the most common clinical manifestations, neck rigidity, altered sensorium, seizures, focal neurologicial deficit was least common

- Viral encephalopathy was most common in our case study
- Septic encephalopathy was second most common
- Most of the patients recovered with good prognosis and few complication
- Most common cause was viral meningitis-
- Herpes encephalitis, bacterial meningitis, cerebal malaria, tubercular meningitis, sepsis associated encephalopathy, typhoid encephalopathy, protozoal meninigitis were also seen

LIMITATIONS

THE LIMITATION OF THE STUDY

The limitation of the study were lack of estimation and CSF - DNA PCR estimation due to non availability.

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ANNEXURES

INFORMATION SHEET

We are conducting a study on

“A STUDY ON ETIOLOGY, CLINICAL FEATURES, DIAGNOSIS AND PROGNOSIS IN ACUTE FEBRILE ENCEPHALOPATHY”

among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is

1. Etiology clinical features, diagnosis and prognosis of patients with acute febrile encehalopathy.
2. Procedure all patient with febrile acute encephalopathy will be examined and evaluated for routine fever blood investigations ,if needed lumbar puncture will be done and CSF analysis will be done for viral serology ,CT scan if needed MRI scan will be done

We are selecting certain cases and if you are found eligible, we may be using your information which in any way do not affect your final report or management.

The privacy of the patients in the research will be maintained throughout the study. In the EVENT of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during study or to withdraw at any time; your decision will not result in any loss of benefits to which you are doing the study if anything is found abnormal which may aid in the management or treatment.

Signature Of Investigator Signature of Participant

Date:

Place

ஆராய்ச்சி தகவல் தாள்

இராஜீவ் காந்தி அரசு பொது மருத்துவமனைக்கு வரும் நோயாளிகளிடம் நோய்க்காரணிகள், நோய்கண்டறிதல், முன்கணிப்பு, கடுமையான காய்ச்சலால் ஏற்படும் மூளையழற்சி பற்றி ஆராய்வதே இந்த ஆய்வின் நோக்கமாகும்.

நாங்கள் உங்களிடமிருந்து பெறும் மாதிரிகள் முக்கியமானவை என்பதை தெரிவிக்கின்றோம்.

நீங்கள் இந்த ஆய்விற்கு தகுதியானவர்களாக இருக்கும் பட்சத்தில் தங்களிடமிருந்து 8 மி.லி. இரத்தம் எடுக்கப்பட்டு இரத்தப் பரிசோதனை செய்யப்படும். இடுப்பின் நடுப்பகுதி தண்டுவடத்திலிருந்து ஊசி மூலம் மூளை தண்டுவட திரவம் எடுத்து பரிசோதனை செய்யப்படும்.

சி.டி. ஸ்கேன் பரிசோதனை, தேவைப்பட்டால் எம்.ஆர்.ஐ. ஸ்கேன் எடுக்கப்படும்.

தங்களுடைய தனிப்பட்ட தகவல்களோ அல்லது தங்களின் உடல்நிலை பற்றிய குறிப்புகளோ எவ்வித வெளியீடாகவோ அல்லது அறிக்கையாகவோ வெளியிடப்படமாட்டாது என்பதை தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்ளலாம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

PATIENT CONSENT FORM

Study Detail : **"A STUDY ON ETIOLOGY, CLINICAL FEATURES, DIAGNOSIS AND PROGNOSIS IN ACUTE FEBRILE ENCEPHALOPATHY"**

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.
Patient's Name :
Patient's Age :
In Patient Number :

Patient may check (☑) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ❑

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that lumbar puncture will be done and CSF analysis will be done.8 ml venous blood will be drawn and given for investigation CT scan & MRI scan if needed will be done ❑

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethics committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms ❑

I hereby consent to participate in this study ❑

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ❑

Signature / thumb impression / parents

Patient's / parents Name and Address

Signature of Investigator / Study /

Investigator's Name:

Dr.JOTHILAKSHMI.V.

சுய ஒப்புதல் படிவம்

ஆய்வின் தலைப்பு :

நோய்க்காரணிகள், நோய்கண்டறிதல், முன்கணிப்பு, கடுமையான காய்ச்சலால் ஏற்படும் மூளையழற்சி பற்றிய ஆய்வு.

ஆராய்ச்சி செய்பவரின் பெயர்: மரு. ஜோதிலட்சுமி.வி

ஆராய்ச்சி நிலையம் : பொது நல மருத்துவத்துறை,
இராஜீவ் காந்தி அரசு பொது மருத்துவமனை மற்றும்
சென்னை மருத்துவக் கல்லூரி,
சென்னை - 600 003.

பங்கு பெறுபவரின் பெயர் :
பங்கு பெறுபவரின் எண். :

பங்கு பெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்ஆய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்ஆய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம்..... இடம்..... தேதி
கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம்..... இடம்..... தேதி

ஆய்வாளரின் பெயர்.....

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.V.Jothilakshmi
Postgradaute M.D.(General Medicine)
Madras Medical College
Chennai 600 003

Dear Dr.V.Jothilakshmi,

The Institutional Ethics Committee has considered your request and approved your study titled **"A study on Etiology, Clinical diagnosis and Prognosis in patients with Acute Febrile Encephalopathy" No.04052015.**

The following members of Ethics Committee were present in the meeting held on 12.05.2015 conducted at Madras Medical College, Chennai-3.

1. Prof.C.Rajendran, M.D.,	: Chairperson
2. Prof.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.B.Vasanthi, M.D., Prof. of Pharmacology, MMC	: Member
5. Prof.P.Ragumani, M.S., Professor of Surgery, MMC	: Member
6. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
7. Prof.K.Srinivasagalu, M.D.,Director, I.I.M. MMC, Ch-3	: Member
8. Thiru S.Rameshkumar, B.Com., MBA	: Lay Person
9. Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
10. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

3/6/15

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

MASTER CHART

	AGE	SEX	CLINICAL FEATURES														investigation						RFT			LFT			serology	MICROBIOLOGY		
			HEADACHE	SEIZURES	ALTERSENSORIUM	NECK RIGIDITY	FOCAL NEUOROLOGICAL DEFICIT	PHOTOPHOBIA	ICTERUS	DIAHERRA	VOMITIG	DEHYDRATION	RASHES	LYMPHADENOPATHY	TEMPERATURE	SPUTUM	HYDROPHOBIA	HAEMOGLOBULIN	WBC COUNT	TOTAL LEUCOCYTE COUNT	PLATELETS	CD4 COUNT	UREA	CREATININE	SGOT	DIRECT BILIRUBIN	INDIRECTBILIRUBIN	MANTOUX	VIRAL	SRCB TYPHUS	DENGUE	MSAT
															F			mg/dl	cell/mm				meq/dl	meq/dl	SGOT	direct	indirect	mm				
1	14	M	+	+	+	+		+							100			13	8000		50000		30	0.9		mg/dl	mg/dl					
2	45	F				+			+		+	+	petechia		103			14	1000		100000		26	0.8		0.02	0.2				IgM+	
3	34	M			+										99			12	3000		250000		30	1.1		0.03	0.8					
4	35	M	+	+		+			+						99.9			14	34000		20000		34	0.8		0.13	0.6				IgM+	
5	15	M							+			+			100			10	23000		45000		13	0.9	250	1	0.8		HAV			
6	26	F	+									+			104			13			300000		40	1.2		0.02	0.9					
7	36	M	+	+		+		+					Eschar		101			14	4000		430000		30	0.89		0.03	0.8			IgM+		
8	32	M						+		+						++		8.6	4500	L	340000		26	0.86		0.9	4.5					
9	38	F	+	+	+	+		+			+				102			9.9	5000		230000		30	0.9		2	1					IgM+
10	27	M																12.5	6500		210000		39	1		0.05	0.6					
11	18	M	+			+												11.7			150000		23	1.1		0.03	0.4					
12	34	M	+			+				+		+		+	102			9	3000		14000	500	34	0.9	30	0.043	0.3		HIV		IgM+	
13	24	F	+									+			103			6.7	12000	p	23000		39	1.2		0.014	0.2				IgM+	
14	34	F					+	+	+	+	+							8.9	13000	p	43000		36	0.98		0.04	0.6					
15	45	M	+															10.1	240000		346000		29	0.876		0.053	1.2					
16	34	F	+		+	+											+	11.8	5000		245000		29	0.9		0.04	1.3					
17	23	F																13.2	4000		23000		36	1.1		3	1					IgM+
18	34	M	+		+								Vesicles					14	7000	L	340000		40	1.5		0.02	0.2	11mm+VE				
19	23	M												+	101			13.8	12000		21500		50	2		0.01	0.6		VZV			
20	45	F	+			+												11.3	5000		34000		68	1.5		0.02	0.2					
21	35	F													101			12.2	12000		45000		50	1.3		0.05	0.4					
22	48	M			+		+											14	4000	p	234500		40	1.1		0.035	0.6					
23	26	M	+								+							13.5	3000		23100		28	0.9		0.04	0.2					

24	17	F	+	+		+						+			99.9			8.9	2000		16000		30	1.9		0.9	1.2				IgM+	
25	24	M										+	petecl	+	100			11.9	4000		32000	90	35	1.2		0.34	0.7		HIV			
26	34	M			+													12.5	4500		45000		40	1.2		0.45	0.23					
27	25	M	+	+		+									101			13.1	2500		320000		28	1.1		0.9	2					IgM+
28	19	M	+		+	+		+		+					100			13	15000		54000		40	1.1		0.01	0.2					
29	23	F					+				+							10.5	20000	P	60000		58	1.3		0.03	0.5					
30	45	M	+	+		+												12.6	24000		320000		30	1.1		0.03	0.1					
31	16	M							+		+							13.3	4000		203000		45	0.8	450	0.08	0.3		HBV			
32	35	M	+		+	+	+					+		+	102			12.9	25000		45000		50	3		0.7	0.4					
33	31	F											Eschar					10.5	2000		23560		100	12		0.06	0.5			IgM+		
34	35	F	+	+	+													10.9	3400		365000		30	0.9		0.09	0.4					
35	45	M	+						+			+			101			12.5	3000		40000		34	1		1	0.9				IgM+	
36	25	M									+							13	12000		23340		67	2		0.04	0.2					
37	45	M	+	+	+	+												12.5	23000		210000		35	1.1		0.05	0.1					
38	36	F		+				+								++		10.3	5500		125000		30	1		0.08	1	12mm+ve				
39	28	F	+															9.9	2300		348900		45	1.2		0.08	0.8					
40	40	M						+							102			12.6	10000	P	245300		45	1.5		1	0.3					
41	19	M			+									+	101			9.7	2400		342500		45	1		0.09	3					
42	43	F	+	+	+	+		+										10.5	3000		56000		30	0.89		0.04	0.5					
43	31	F	+			+												11.5	4000		54000		34	0.9		0.07	0.7					
44	35	M																13.4	5000		145000		45	1		0.05	0.3					
45	18	M	+	+	+	+				+	+							13.7	35000	P	245800		40	1		0.02	0.8					
46	17	M						+										14	23000		234500		30	0.8		0.08	0.7					
47	36	F	+		+	+		+								+		8.6	14000	L	345060		123	14		0.03	0.6	15mm+VE				
48	16	F	+					+				+	petecl	+	104			10.3	3800		23410		34	1		1	0.9				IgM+	
49	15	M							+			+						13.7	14000	L	45000		25	0.9		0.07	2		HAV			
50	31	M							+						101			12	4500		345000		27	0.9		0.02	4	13mm+ve				
51	24	M	+		+	+		+							100			10.4	3800		243500		34	1.1		0.05	0.1					
52	34	F																13	3450		34500		26	0.9		0.03	0.2					
53	25	F									+		Eschar					11	70000		234100		74	3		0.05	0.2			IgM+		
54	34	M	+			+												12.6	2345	P	234500		80	4		0.05	0.1					
55	17	M	+		+										100			12.1	5600	L	45630		24	0.9		0.03	0.6					
56	26	F							+						101			10.9	14500		34500		54	2.5		0.02	2.3					
57	19	F	+		+	+		+	+						100			9.9	13000		25000		32	1.2		0.07	4.3					IgM+
58	21	M	+		+	+												11.6	4530		45000		54	1.5		0.04	0.7					
59	24	M																13	5400	P	234500		32	0.9		0.03	0.9					
60	32	F					+											10.8	2300		124500		134	10		0.06	0.5					
61	29	F	+	+	+	+					+	+	Vesicles					9.6	3450		23450		54	1.5		0.45	0.3		VZV			
62	16	M										+			102			10.4	12350		12500		23	0.9		0.08	4				IgM+	
63	15	M	+		+	+		+	+									12.7	5400		234100		45	1.6		0.067	0.8					
64	26	F													102			10.5	12000	L	456300	L	65	2.5		0.04	0.8					

65	34	M	+	+	+	+												13.5	5400		234500		29	0.9		0.09	0.2					
66	32	M							+			+			102			12.5	13500		123450		69	3		0.05	4			IgM+		IgM+
67	17	M	+		+	+	+	+							99			13.6	2340		32450		25	0.9		0.08	0.8					
68	28	F	+	+	+	+					+							10.6	4500		245000		45	2		0.07	0.3					
69	45	M										+			101			13	12350		234105		25	0.89		0.02	3					
70	29	M							+									10.7	3450		25000		19	0.7		0.04	5				IgM+	
71	18	F	+	+	+	+		+							100			13.5	12000	L	150050		26	0.76		0.03	0.2	11mm+ve				
72	32	F	+															13.6	3450		354250		54	3		0.05	0.4					
73	39	M			+		+								103			11.8	5430	L	345200		43	2		0.04	0.3					
74	35	M	++															12.6	13500		354290		54	3.5		0.01	0.8					
75	17	M										+	Eschar					9.8	5430		234500		32	1.2		0.05	0.2			IgM+		
76	23	F			+				+	+	+							12	4530		23450		43	1.5		0.03	0.4					
77	31	M	+			+		+										12.6	3240		23450		73	4		0.08	0.3					
78	38	M	+	+	+			+	+	+					101			12.6	12450	P	34500		35	0.9		0.05	3					
79	17	F																11.6	5640		14500		63	2.6		0.07	0.5					
80	19	M	+	+	+	+		+							100			14	4500		345000		34	1.1		0.04	0.9					
81	20	M							+						102			13.7	13000		324500		28	0.87		0.06	2.3					IgM+
82	35	F	+	+	+	+												11.1	6000		32100		24	0.76		0.03	0.3					
83	24	F																6.6	5600		23150		65	3.6		0.03	0.7					
84	18	M	+		+	+		+			+							10.9	4530		345200		190	14		0.03	0.3					
85	14	F					+	+	+			+			101			8.9	13500	P	24000		40	13		0.05	0.5	15mm+ve			IgM+	
86	25	F	+	+												+		9.7	5765	L	25640		36	0.9		0.9	2					
87	34	M													104			11.9	25000		254600		45	3		0.06	0.1					
88	32	F	+		+										102			8.7	35000		354200		69	4.5		0.07	0.3					
89	24	M													101			13.1	23000		235100		45	3		0.01	0.4					
90	18	M	+		+			+							102			12.8	2345		34500		123	15		0.05	3					
91	34	F	+	+	+	+						+		+				6	1000	P	43500		89	8		1	0.9		HIV			
92	35	F						+										12.5	7860		89000		34	0.9		0.04	0.3					
93	23	M	+								+				99.9	k		14.1	6540		356400		23	0.8		0.06	0.2					
94	17	M	+		++												+	13.9	5630		254300		34	1.4		0.03	0.1					
95	14	M	+	+			+	+	+			+			104			14.1	5640	P	34500		65	4		0.08	3				IgM+	
96	15	F	+	+	+													13.6	6700		453200		40	2		0.06	0.4					
97	18	M																12.7	14000		45300		60	3		0.08	0.5			IgM+		
98	18	M	+	+	++	++		+	+				Eschar		103			13.5	2340		345000		34	2		0.07	3					
99	20	F													101			13.3	5600	P	345600		39	2.5		0.04	0.4					
100	14	F	+						+		+	+						10	3000		100000		30	0.8		4	0.2		HBV			
										j																						

		sputum		BLOOD				CSF BIOCHEMII				CELL COUNT		CSF ANALYSIS				CSF SEROLOGY					
WIDAL	PERIPERAL SMEAR	CULTYRE & SENSITIVITY	AFB	CULTUR SENSITIVITY		AFB	LDH	sugar	protein	LDH	ADA	WBC	cytology	culture sensitivity		Gram stain	AFB	Rabies	JE	CMV	undentified	HSV1/2	PCR
								mg/di	mg/dl			cell/ʁL	P/L										
+																							
																						+	HSV+
																					+		
								450															
	falciparum								34	70				Streptococcus		GM+ve							
		mycobacteria	+			+	1250	20	100	110	16	100	L-550										TB
												600							IgM+				
+												135									+	+	HSV+
								30	60			1020											
+												1200								IgM+			CMV+
								30	200	96		145	P-550	pneumococcus		GM-ve							
				streptococcus								1250											
				staphylococcus			1257	25	65			1050											
																		IgM+ve					
																					+	HSV+	
							890			120				mycobactrium			+						
							650	20	186	100		1050	P-500	Streptococcus		GM+ve							
																					+	HSV+	
	falciparum							45	74	50		150									+	HSV+	
				streptococcus																			
																			IgM+				JE+

+																							+	HSV+
							450	25	89	106		250	p-590	cryptococcus		india ink +								
							1430	30	64	112	11	1000	L 450	mycobacterium										TB
				streptococcus								1590												
				pnuemocococcus				28	80			1200												
																						+		
												250										+	HSV+	
	falciparum						550	10	120	106		678	P-650	staphlococcous		GM+ve								
								40	70	40		80								IgM+				
								45	150	39		450												
																					+			
																						+	HSV+	
		mycobacteria	+				1050	30	130				L 650											
																							TB	
				streptococcus			450	20	90												+			
	vivax							25	150			1200	P-550	streptococcus		GM+ve								
																					+			
								35	85										IgM+					
				streptococcus			550	25	80	65		135										+	HSV+	
+				salmonella																				
		mycobacteria	+				1450	10	200	100	130		L 500	mycobac	n								TB+	
																						*		
							450	20	400	120	12	765	L 450	mycobacterium									TB+	
	vivax																							
							550	10	250	90		2000	P-560	pneumo	occus	GM-ve								
																						+		
							850	20	290	96				streptococcus		GM+ve								
				streptococcus																		+	HSV+	
							1590	15	300	130	16			mycobacterium									TB+	
	falciparum																							
							650	25	269	98		1400		streptococccus		GM+ve								
				staphylococcus			550																	
																						+		
								45	150	100		100	P-800											
							650	40	75			120		pneumococcus		GM-ve				IgM=+				
+				streptococcus																	+			

																						+	
	falciparum																						
							450	15	300	100		145	P-650	neisseria		GM-ve					+		
							550	10	450	jj		1430	P-550	pneumococus		GM-ve						+	
							1345	20	300	550	70	980	L 450	mycobacterium			+						TB+
				pneumococcus			550																
																						+	
	falciparum			salmonella			390																
																						+	
							650	24	295			1350	P-450	streptococcus		GM+ve							
								45	75											IgM+ve			CMV+
+																						+	
										450	75												
		mycobacteria		pneumococcus			1560	18	450					mycobacterium			+						TB+
																					+		
																						+	
							650	30	290	234		950	P-650	staphlococcus		GM+ve							
	falciparum																						
+																							
		mycobacberia																			+		
																		Rabies				+	
				staphlococcal			450	30	76				P-200	pnemococcus		GM-ve						+	
																						+	
	vivax																						
				salmonella			450	35	45				P-250										
								25	200			150	P-350										

VSV	EBV	IMAGING MODA CT SCAN						IMAGING MODA MRI SCAN					IMAGING MODA MAGNETIC IMAGING MO		PROGNOSIS					other system affected
		Odema	Focal	HYDROCEPHALI		TUBERULOMA		Focal		Basal exudate		DIFFUSE	MRS		IMPROVE	NEURODEFICIT		DEAD		
		+																		
																visual D				
		+		+		+														ARDS
								Temperoparital		+										
								REL				REL	neurocysticersosis							GIT
	+																	D		MODS
		+	subdural effusion													focal				
										+										
													tuberuloma+			SNHL				
				+		+				+										
+		+	Leptomenigitis																	
								temperoparital		+										

												REL								
		+																D		MODS
		+	+	+		+				+			tuberculoma							
																				GIT
		+																		
												REL	neurocystecercosis							
		+	Leptomenigitis					Abscess				REL	abcess			focal				ARF
																				ARF
							++			+								D		MODS
																				ARF
		+		+																
		+																		RS
		+																		
		+	Subdural effusion						+			REL	abscess							
																SNHL				
										+			neurocysticecosis							
							++											D		DIC
		+																		
				+																
				+						+										
		+				+														
										+										
		+										REL	Abscess							
	+																			
		+	Leptomenigitis					Abscess												
										+										
		+		+		+				+		REL								
		+								+						BLURRING VISION				
							++											D		ARDS
																				ARF
+																				
		+								+		REL	Abscess							
				+																

							++										D		MODS	
		+								+										
																visual D				
		+				+				+										
																				Pneum
			Meningitis													SHNL				
							++													
		+																		
			Abscess							+										
										+										
		DIFFUSE																		
												+	tuberculoma						RS	
		+	meningitis					Abcess		+						bluring of vision				
		+																		
			meningitis							+						focal		D		MODS

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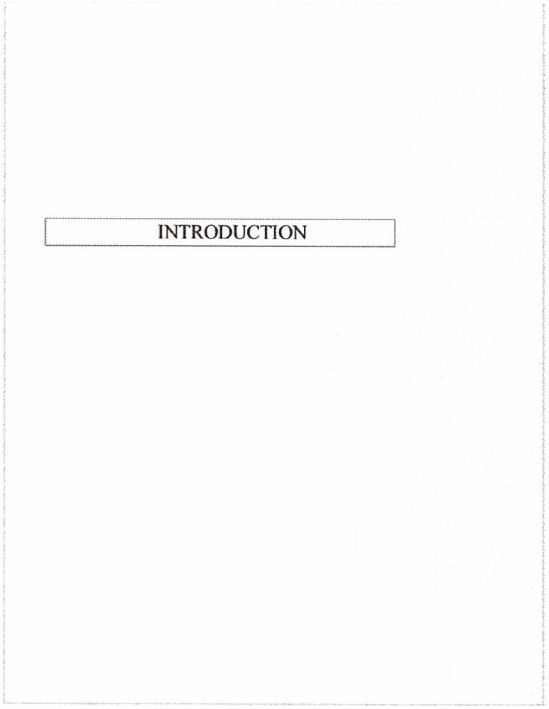
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