ETIOLOGY, CLINICAL PROFILE AND OUTCOME OF NON - TRAUMATIC COMA

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CERTIFICATE

This is to certify that the dissertation entitled "**ETIOLOGY, CLINICAL PROFILE AND OUTCOME OF NON - TRAUMATIC COMA**" is a bonafide work done by **Dr. KANMANI.S.**, at Madras Medical College, Chennai in partial fulfillment of the university rules and regulations for award of M.D., Degree in General Medicine (Branch-I) under my guidance and supervision during the academic year 2009 -2012.

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DECLARATION

I solemnly declare that this dissertation entitled "**ETIOLOGY, CLINICAL PROFILE AND OUTCOME OF NON - TRAUMATIC COMA"** was done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, during 2009-2012 under the guidance and supervision of **Prof. E.DHANDAPANI, M.D.** This dissertation is submitted to the Tamil Nadu Dr .M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree in General Medicine (Branch-I).

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LIST OF ABBREVIATIONS

ABG – Arterial blood gas analysis

AIDS – Acquired immunodeficiency syndrome

CNS – Central nervous system

CNH – Central neurogenic hyperventilation

CSF – Cerebro spinal fluid

COPD – Chronic obstructive pulmonary disease

CT – Computed tomography

CMV – Cytomegalo virus

EEG – Electro encephalogram

GCS – Glasgow Coma Scale

HSV – Herpes simplex virus

HIV – Human immunodeficiency virus

IL – Interleukin

ICP – Intra cranial presssure

MRI – Magnetic resonance imaging

OCR – Oculo cephalic reflex

OVR – Oculo vestibular reflex

SAH – Sub arachnoid haemorrhage

TB – Tuberculosis

TBM – Tuberculous meningitis

TNF α – Tumor necrosis factor alpha

VZV – Varicella zoster virus

CONTENTS

INTRODUCTION

"And men should know that from nothing else but from the brain came joys, delights, laughter and jests, and sorrows, grieves, despondency and lamentations. And by this, in an especial manner, we acquire wisdom and knowledge, and see and hear and know what are fair, what sweet and what unsavoury……" - The Hippocratic writings[1].

Since the days of the Greeks, men knew that normal conscious behavior reckons on intact brain function and hence the disorders of consciousness are impliedas cerebral insufficiency. Impaired, reduced, or absent consciousness implies the presence of severe brain dysfunction and so demands immediate attention from the physician for expectation of potential recovery. Stupor and coma mean advanced brain failure, just as uremia means renal failure. If such brain failure lasts for a long time the margin between recovery and development of permanent neurologic injury becomes narrower[1].

In hospital neurology, the clinical analysis of comatose patients becomes a responsibility. There is always urgency in a need to determine the underlying disease process causing coma and the direction in which it is evolving and also to protect the brain against irreversible or more serious damage[2].

The terms stupor, confusion, unconsciousness, and coma have been endowed with many distinct meanings that it is almost not possible to avoid uncertainty in their usage. They are strictly not medical terms but literary, philosophic,and psychological ones as well[2].

Physicians, being practical and objective for the most part, give greater plausibility to patient's behaviour and response to overt stimuli than to what the patient says. So they usually give the term consciousness its commonest and simplest meaning – the state

ofpatient’s awareness of self and environment and his responsiveness to external stimulus and inner need. Unconsciousness has the just opposite meaning – a state of unawareness of self and environment or a suspension of those mental activities by which people are made aware of themselves and their environment, coupled with a diminished responsiveness to environmental stimuli[2].

AIMS AND OBJECTIVES

1. To evaluate 100 cases of non-traumatic coma and identify the various etiologies causing them.
2. To analyse the clinical profile of 100 cases of non-traumatic coma.
3. To analyse the outcome of 100 cases of non-traumatic coma.

REVIEW OF LITERATURE

DEFINITIONS

Consciousness:

Consciousness is the state of awareness of the self and the environment and coma is its opposite, i.e., the total absence of awareness of self and environment even when the subject is externally stimulated. Coma is a state of complete unresponsiveness to arousal, in which the patient lies with eyes closed[3].

Alterations in consciousness are conceptualized into two types. The first type involves cognitive and affective mental function, sometimes referred to as the "content" of mental function. Examples are dementia, delusions, confusion, and inattention[3].

The second type, alterations in arousal, though often referred to as altered levels of consciousness, do not actually form discrete levels but rather are made up of a continuum of subtly changing behavioural states that range from alert to comatose. These states are dynamic and thus may change with time. Four points on the continuum of arousal are frequently used to describe the clinical state of a patient: alert, lethargic, stuporous, and comatose[3].

Alert refers to a perfectly normal state of arousal. Lethargy lies between alertness and stupor. Stupor is a state of baseline unresponsiveness that requires repeated application of vigorous stimuli to achieve arousal[3].

Behavioural States Confused with Coma:

Several different states of impaired cognition or consciousness may resemble coma or might be confused with it. Furthermore, patients who survive the initial coma may advance to some of these syndromes after varying lengths of time. True coma is no longer presentonce sleep-wake cycles become established. Discrimination of these states from true coma is important to allow disposition of appropriate therapy and to help determine prognosis.[3]

Locked-in syndrome: Patients are alert and aware of their environmentbut are voluntarily able only to move their eyes vertically or blink and are quadriplegic, with lower cranial nerve palsies resulting from bilateral ventral pontine lesions which involve the corticospinal, corticopontine, and corticobulbar tracts. The locked-in syndrome most often is observed as a consequence of pontine infarction due to basilar artery thrombosis. Other causes include central pontine myelinolysis and brainstem mass lesions[3].

Persistent vegetative state: It refers tothose who have lost cognitive neurological function but maintain vegetative or non cognitive neurological function like cardiac action, respiration, and maintenance of blood pressure. This state follows coma and is identified by the absence of cognitive function or awareness of the environment, in spite of preserved sleep-wake cycle. Spontaneous movements do occur and the eyes might open in response to external stimulus, but the patient does not talk or obey commands. A condition that has been estimated to be ten times more common than persistent vegetative state is the minimally conscious state, in which severe disability accompanies minimal awareness[3].

Akinetic mutism: It refers to a partially or fully awake state in which the patient is able to form impressions and think, as demonstrated by later recounting of events, but remains virtually immobile and mute. The condition results from damage in the regions of the medial thalamic nuclei or the frontal lobes or from extreme hydrocephalus[4].

Abulia: It describes a milder form of akinetic mutism characterized by mental and physical slowness and diminished ability to initiate activity. It is also usually the result of damage to the frontal lobes and its connections[4].

Catatonia: It may result in a state of muteness, with considerably decreased motor activity. The preservation of body posture, with conserved ability to sit or stand, distinguishes it from organic pathological stupor. It generally is a psychiatric manifestation but can be mimicked by frontal lobe disease or drug effect[4].

Pseudocoma: It is the term for a condition in which the patient appears comatose (that is, unresponsive, unarousable, or both) but has no structural, metabolic, or toxic disorder[3].

TABLE 1 :CAUSES OF COMA[3]

1. SYMMETRICAL-NONSTRUCTURAL

<table>
<tr>
<td><u>Toxins</u>
Lead
Thallium
Mushrooms
Cyanide
Methanol
Ethylene glycol
Carbon monoxide
<u>Drugs</u>
Sedatives
Barbiturates
Other hypnotics
Tranquilizers
Bromides
Alcohol
Opiates
Paraldehyde
Salicylates
Psychotropics
Anticholinergics
Amphetamines
Lithium
Phencyclidine
Monoamine oxidase inhibitors</td>
<td><u>Metabolic</u>
Hypoxia
Hypercapnia
Hypernatremia
Hyponatremia
Hypoglycemia
Hyperglycemic nonketotic coma
Diabetic ketoacidosis
Lactic acidosis
Hypercalcemia
Hypocalcemia
Hyperthermia
Hypothermia
Hypermagnesemia
Aminoaciduria
Reye’s encephalopathy
Wernicke’s encephalopathy
Porphyria
Hepatic encephalopathy
Uremia
Dialysis encephalopathy
Addisonian crisis</td>
<td><u>Infections</u>
Viral encephalitis
Bacterial meningitis
Postinfectious encephalomyelitis
Syphilis
Sepsis
Malaria
Typhoid fever
Waterhouse-Friderichsen syndrome
<u>Psychiatric</u>
Catatonia
<u>Other</u>
Postictal
Diffuse ischemia
Hypotension
Fat embolism
Hypothyroidism
Hypertensive encephalopathy</td>
</tr>
</table>

2. SYMMETRICAL-STRUCTURAL

Supratentorial	**Subarachnoid hemorrhage**	**Infratentorial**
• Bilateral anterior cerebral artery occlusion • Bilateral internal carotid occlusion	• Trauma—concussion, contusion, • Thalamic hemorrhage • Hydrocephalus	• Pontine hemorrhage • Basilar occlusion • Midline brainstem tumour

3. ASYMMETRICAL-STRUCTURAL

Supratentorial	**Subdural hemorrhage, bilateral**	**Subdural empyema**
• Thrombotic thrombocytopenic purpura • Disseminated intravascular coagulation • Nonbacterial thrombotic endocarditis (marantic endocarditis) • Subacute bacterial endocarditis • Fat emboli • Unilateral hemispheric mass (tumor, bleed) with herniation	• Intracerebral bleed • Pituitary apoplexy • Massive or bilateral supratentorial infarction • Multifocal leukoencephalopathy • Creutzfeldt-Jakob disease • Adrenal leukodystrophy • Cerebral vasculitis • Cerebral abscess	• Thrombophlebitis • Multiple sclerosis • Leukoencephalopathy associated with chemotherapy • Acute disseminated encephalomyelitis • Infratentorial • Brainstem infarction • Brainstem hemorrhage

PATHOPHYSIOLOGY OF NON TRAUMATIC COMA

Cerebrovascular causes:

Ischemic stroke: Acute occlusion of an intracranial vessel causes reduction in blood flow to the brain region it supplies. The magnitude of flow reduction is a function of collateral blood flow and this depends on individual vascular anatomy, the site of occlusion, and likely systemic blood pressure. A decrease in cerebral blood flow to zero causes death of brain tissue within 4–10 minutes; values <16–18 ml/100 g tissue per minute cause infarction within an hour; and values <20 ml/100 g tissue per minute cause ischemia without infarction unless prolonged for several hours or days[5].

Focal cerebral infarction occurs via two distinct pathways: (1) a necrotic pathway in which cellular cytoskeletal breakdown is rapid, principally dueto energy failure of the cell; and (2) an apoptotic pathway in which cells become programmed to die[5].

Hypertensive Intraparenchymal Hemorrhage: It usually results from spontaneous rupture of a small penetrating artery deep in the brain. The most common sites are the basal ganglia (especially the putamen), thalamus, cerebellum, and pons. When hemorrhages occur in other brain areas or in non hypertensive patients, greater consideration should be given to hemorrhagic disorders, neoplasms, vascular malformations, and other causes. The small arteries in these areas seem most prone to hypertension-induced vascular injury. The hemorrhage may be small or a large clot may form and compress adjacent tissue, causing herniation and death. Blood may dissect into the ventricular space, which substantially increases morbidity and may cause hydrocephalus[5].

Subarachnoid Hemorrhage: Excluding head trauma, the most common cause of SAH is rupture of a saccular aneurysm. Other causes include bleeding from a vascular malformation (arteriovenous malformation or dural arterial-venous fistula) and extension into the subarachnoid space from a primary intracerebral hemorrhage. Some idiopathic SAHs are localized to the perimesencephalic cisterns and are benign; they probably have a venous or capillary source, and angiography is unrevealing[5].

Metabolic coma:

Many systemic metabolic abnormalities cause coma by interrupting the delivery of energy substrates (e.g., hypoxia, ischemia, hypoglycemia) or by altering neuronal excitability (drug and alcohol intoxication, anesthesia, and epilepsy). The same metabolic abnormalities that produce coma may, in milder forms, induce an acute confusional state. Thus, in metabolic encephalopathies, clouded consciousness and coma are in a continuum[4].

Unlike hypoxia-ischemia, which causes neuronal destruction, most metabolic disorders cause only minor neuropathologic changes. The causes of the reversible effects of these conditions on the brain are not understood but may result from impaired energy supplies, changes in ion fluxes across neuronal membranes, and neurotransmitter abnormalities[4].

- **Hepatic encephalopathy:** The best-described neurotoxin involved in hepatic encephalopathy is ammonia, which is produced primarily in the colon and enters the portal circulation which under normal conditions, is metabolized and cleared by hepatocytes[4]. In cirrhosis and portal hypertension, reduced hepatocyte function and portosystemic shunting contribute to increased circulating ammonia levels. Increased permeability of the blood-brain barrier increases the uptake and

extraction of ammonia by the cerebellum and basal ganglia[7].Acute hyperammonemia appears to have a direct effect on brain edema, astrocyte swelling, and the transport of neurally active compounds such as myoinositol, and thereby contributes to hepatic encephalopathy[8].

- **Uremic encephalopathy:** It is an acute or subacute organic brain syndrome that regularly occurs in patients with acute or chronic renal failure when glomerular filtration rate declines below 10% of normal[9]. The mechanism of the encephalopathy of renal failure is not known. Unlike ammonia, urea does not produce CNS toxicity and a multifactorial causation has been proposed for the encephalopathy, including increased permeability of the blood-brain barrier to toxic substances such as organic acids and an increase in brain calcium and CSF phosphate content[4].

  In recent years, there has been considerable discussion of the possible role of parathyroid hormone as a uremic toxin. In uremic patients, both EEG changes and neuropsychiatric abnormalities are improved by parathyroidectomy or medical suppression of parathyroid hormone[10].

- **Hypoglycemic coma:** Hypoglycemic coma induces a purely neuronal lesion of the neocortex, the hippocampus and the dorsolateral crescent of the caudoputamen in rat brains[11]. The experimental neurochemical and morphological changes in hypoglycemic brain damage differ from those in transient forebrain or global brain ischemia even though both insults affect the whole brain critically, leading to energy failure and selective neuronal death in certain areas vulnerable to each insult[12]. In particular, intracellular acidosis accompanies cerebral ischemia but not hypoglycemia. Profound hypoglycemia causes tissue alkalosis resulting from the

ammonia formation from deamination of amino acids, the consumption of metabolic acids, and the absence of lactic acid formation[13].

The essential biochemical abnormality is a critical lowering of the blood glucose. At a level of about 30 mg/dL, the cerebral disorder takes the form of a confusional state and one or more seizures may occur; at a level of 10 mg/dL, there is coma that may result in irreparable injury to the brain if not corrected immediately by the administration of glucose. As with most other metabolic encephalopathies, the rate of decline of blood glucose is a factor in both the depression of consciousness and residual dementia[14].

- **Hypoxic ischemic encephalopathy**: This occurs from lack of delivery of oxygen to the brain because of hypotension or respiratory failure. Causes include myocardial infarction, cardiac arrest, shock, asphyxiation, paralysis of respiration, and carbon monoxide or cyanide poisoning. In some circumstances, hypoxia may predominate. Carbon monoxide and cyanide poisoning are termed histotoxic hypoxia since they cause a direct impairment of the respiratory chain. If hypoxia-ischemia lasts beyond 3–5 min, some degree of permanent cerebral damage usually results. A uniformly dismal prognosis from hypoxic-ischemic coma is conveyed by an absent pupillary light reflex or extensor or absent motor response to pain on day 3 following the injury. Long-term consequences of hypoxic-ischemic encephalopathy include persistent coma or a vegetative state, dementia, visual agnosia, parkinsonism, choreoathetosis, cerebellar ataxia, myoclonus, seizures, and an amnestic state, which may be a consequence of selective damage to the hippocampus[15].

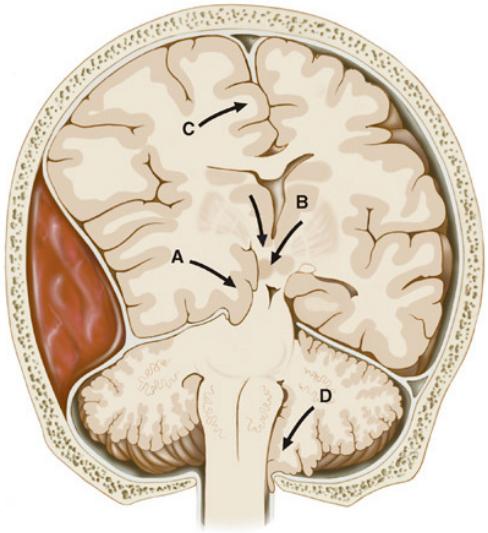
- **Others:** Coma and seizures are common accompaniments of large shifts in sodium and water balance in the brain. These changes in osmolarity arise from systemic medical disorders, including diabetic ketoacidosis, the nonketotic hyperosmolar state, and hyponatremia from any cause (e.g., water intoxication, excessive secretion of antidiuretic hormone, or atrial natriuretic peptides). Sodium levels <125 mmol/L induce confusion, and <115 mmol/L are associated with coma and convulsions. In hyperosmolar coma, the serum osmolarity is generally >350 mosmol/L. Hypercapnia depresses the level of consciousness in proportion to the rise in carbon dioxide tension in the blood. In all of these metabolic encephalopathies, the degree of neurologic change depends to a large extent on the rapidity with which the serum changes occur. The pathophysiology of other metabolic encephalopathies such as hypercalcemia, hypothyroidism, vitamin B12 deficiency, and hypothermia are incompletely understood but must also reflect derangements of CNS biochemistry, membrane function, and neurotransmitters[4].

Coma due to cerebral mass lesions and herniations:

Uncal transtentorial herniation: It refers to impaction of the anterior medial temporal gyrus (the uncus) into the tentorial opening just anterior to and adjacent to the midbrain. The coma that follows is due to compression of the midbrain against the opposite tentorial edge by the displaced parahippocampal gyrus. Lateral displacement of the midbrain may compress the opposite cerebral peduncle, producing a Babinski's sign and hemiparesis contralateral to the original hemiparesis (the Kernohan-Woltman sign). Herniation may also compress the anterior and posterior cerebral arteries as they pass over the tentorial

reflections, with resultant brain infarction. The distortions may also entrap portions of the ventricular system, resulting in hydrocephalus[4].

FIGURE 1: TYPES OF CEREBRAL HERNIATION



(A) Uncal (B) Central (C) Transfalcial (D) Foraminal

Central transtentorial herniation: It denotes a symmetric downward movement of the thalamic medial structures through the tentorial opening with compression of the upper midbrain. Miotic pupils and drowsiness are the heralding signs.

Both temporal and central transtentorial herniations have been considered causes of progressive compression of the brainstem, with initial damage to the midbrain, then the pons, and finally the medulla. The result is a sequence of neurologic signs that corresponds to each affected level[4].

Transfalcial herniation: It is the displacement of cingulate gyrus under the falx and across the midline[4].

Foraminal herniation: It is the downward forcing of cerebellar tonsils into the foramen magnum, which causes compression of the medulla, respiratory arrest, and death.

Lateral shift may be quantified on axial images of CT and MRI scans. In cases of acutely appearing masses, horizontal displacement of the pineal calcification of 3–5 mm is generally associated with drowsiness, 6–8 mm with stupor, and >9 mm with coma[4].

Infections and coma:

Bacterial meningitis: Bacterial meningitis is an acute purulent infection within the sub-arachnoid space. It is associated with a CNS inflammatory reaction that may result in decreased consciousness, seizures, raised intracranial pressure, and stroke. The meninges, the subarachnoid space, and the brain parenchyma are all frequently involved in the inflammatory reaction (meningoencephalitis)[16].

Release of bacterial cell wall components in the sub arachnoid space lead to production of inflammatory cytokines. This leads to vasogenic, cytotoxic & interstitial edema, alterations in cerebral blood flow and production of excitatory amino acids, reactive oxygen species &nitrogen species leading to cell injury and death. These factors result in raised intra cranial pressure and may lead to coma[16].

S. pneumoniae is the most common cause of meningitis in adults >20 years of age. The incidence of meningitis due to N. meningitidis has decreased with the routine immunization. Other causatives include enteric gram-negative bacilli, Group B streptococcus, S. agalactiae, L. monocytogenes, H. influenzae type b, Staphylococcus aureus and coagulase-negative staphylococci and local infections like otitis, mastoiditis and sinusitis due to various organisms[16].

Several characteristics that are significantly associated with an unfavorable outcome include advanced age, the presence of otitis or sinusitis, the absence of rash, a heart rate of more than 120 or below 60 beats per minute, hypotension (diastolic BP less than 60 mmHg), a low score on the Glasgow Coma Scale, seizures, pneumonia, an immune compromised state, a cerebrospinal fluid white-cell count of fewer than 1000 per cubic millimeter, a positive blood culture, an elevated erythrocyte sedimentation rate, and a reduced platelet count[17].

Viral meningitis and encephalitis: Immunocompetent adult patients with viral meningitis usually present with headache, fever, and signs of meningeal irritation coupled with an inflammatory CSF profile. Patients with viral meningitis often have mild lethargy or drowsiness; however, profound alterations in consciousness, such as stupor, coma, or marked confusion suggest the presence of encephalitis. Similarly, seizures or focal neurologic signs or symptoms or neuroimaging abnormalities indicative of brain parenchymal involvement are not typical of viral meningitis and suggest the presence of encephalitis or another CNS infectious or inflammatory process[16].

The common causative organisms include entero viruses, herpes simplex virus 1&2, varicella zoster virus, Epstein barr virus, HIV, arthropod borne viruses, west Nile virus, St.Loius encephalitis virus[16].

Viruses enter the CNS through several mechanisms. Many, such as enteroviruses, replicate outside the CNS and then invade by haematogenous spread. Viral particles pass directly across the blood–brain barrier, or are carried across in infected leukocytes (e.g. mumps, measles or herpesviruses), and then infect vascular endothelial cells. Other viruses invade through peripheral and cranial nerves, as for polio and HSV, respectively. Once within the

CNS, viruses may spread through the subarachnoid space in CSF, with consequent inflammatory response leading to meningitis. Viruses may also spread directly or via inflammatory leukocytes through neural tissue to neurons and glial cells[18].

Once CNS infection has taken hold, inflammatory cells, including lymphocytes specifically targeting the infecting virus, accumulate in the CNS. This is accompanied by the release of inflammatory cytokines such as interleukin (IL)-1β, IL-6 and tumour necrosis factor (TNF)-α as well as local immunoglobulin production by plasma cells. Inflammatory responses leading to increased permeability of the blood–brain barrier also permit entry of circulating immunoglobulins. Viruses may evade effective immune response either through immune tolerance or through escape of immune surveillance. T lymphocyte responses are an essential part of the immune response to some viruses, as illustrated by the increased frequency and morbidity associated with chronic cytomegalovirus (CMV) or varicella-zoster virus (VZV) meningitis in patients with impaired cell-mediated immunity. Viruses such as VZV may cause disease through a cerebral vasculitis, with immunocompetent patients usually developing a large-vessel vasculitis and immunocompromised patients developing a small-vessel, more diffuse vasculitis[18].

Neurological Tuberculosis: It is classified into tuberculous meningitis (TBM), tuberculoma and arachnoiditis. CNS TB is invariably secondary to TB elsewhere in the body.

It is generally believed that the critical event in the development of TBM is the rupture of a sub ependymally located tubercle (Rich focus), resulting in the delivery of infectious material into subarachnoid space[19].The pathology of TBM comprises of inflammatory meningeal exudate, ependymitis, vasculitis, encephalitis and disturbance of CSF circulation and absorption.

Hydrocephalus develops in the majority of patients with TBM who have been symptomatic for two to three weeks. In the majority, it is a communicating hydrocephalus due to the blockage of the basal cisterns by the exudate in the acute stage and adhesive leptomeningitis in chronic stage. Less frequently, the hydrocephalus is obstructive due to either narrowing or occlusion of aqueductby ependymal inflammation or a strategically placed brainstem tuberculoma, or at the outlet foraminae of fourth ventricle[20].

Tuberculoma is a mass of granulation tissue made up of a conglomeration of microscopic small tubercles. The centre of tuberculoma becomes necrotic, forming caseous material, while the periphery tends to be encapsulated with fibrous tissue. There may be liquefaction of caseous material resulting in the formation of TB abscess[21].

Brain abscess: A brain abscess is a focal, suppurative infection within the brain parenchyma, typically surrounded by a vascularized capsule. The term cerebritis is often employed to describe a nonencapsulated brain abscess[16].

A brain abscess may develop (1) by direct spread from a contiguous cranial site of infection, such as paranasal sinusitis, otitis media, mastoiditis, or dental infection; (2) following head trauma or a neurosurgical procedure; or (3) as a result of hematogenous spread from a remote site of infection. In up to 25% of cases, no obvious primary source of infection is apparent (cryptogenic brain abscess)[16].

Results of experimental models of brain abscess formation suggest that for bacterial invasion of brain parenchyma to occur, there must be preexisting or concomitant areas of ischemia, necrosis, or hypoxemia in brain tissue. The intact brain parenchyma is relatively resistant to infection. Once bacteria have established infection, brain abscess frequently

evolves through a series of stages, influenced by the nature of the infecting organism and by the immunocompetence of the host. The four stages include early cerebritis stage (days 1–3), the late cerebritis stage (days 4–9),early capsule formation (days 10–13), late capsule formation (day 14 and beyond)[16].

Prognosis worsens in delayed diagnosis, abscess rupture into ventricles, multiple abscess, or abnormal neurologic status at presentation[16].

Sub dural empyema: Subdural empyema is a collection of pus between the dura and arachnoid. It develops most commonly as a consequence of ear or sinus infection. Other causes include cranial osteomyelitis, penetrating head trauma or neurosurgery, infection of subdural effusions in childhood meningitis, and hematogenous spread from a remote source. Rapid disease progression before hospitalization, recurrent seizures, and depressed level of consciousness at admission are associated with poor prognosis[22].

Septic venous sinus thrombosis: It complicates meningitis or epidural or subdural abscesses or develop during the intracranial spread of infection from extracranial veins. Once established, infection and clot spread through the venous system, aided by the absence of valves in intracranial veins. The most common bacterial pathogens depend on the source of initial infection; with sinusitis they are Staphylococcus, aerobic and microaerophilic streptococci, gram-negative E. coli, or anaerobes, whereas S. aureus predominates when facial infection is the source. Otitis media or mastoiditis may be complicated by the development of the lateral sinus thrombosis[22].

Cerebral malaria: Severe malaria is a multisystem disease; cerebral involvement is one of the features. Cerebral malaria, renal failure, severe jaundice and adult respiratory distress syndrome are the main complications in severe malaria[23].

A conclusive pathophysiological model explaining the reversible coma of cerebral falciparum malaria does not exist. A central feature is the inhomogeneous obstruction of the cerebral microcirculation by sequestered parasitized erythrocytes causing dysoxia but no infarction of brain tissue, and resulting in net lactate production by the brain[24].

The clinical picture is that of a diffuse encephalopathy with unrousable coma; focal signs are relatively uncommon. In adults the onset in usually gradual, with high fever (mean duration of 5 days) and increasing drowsiness. Convulsions are present in about 15% of the cases. Even if optimal treatment is available, mortality rates remain high once the patient develops severe disease[25].

Septic encephalopathy: A diagnosis of septic encephalopathy requires evidence of extracranial infection and impaired mental state. Extracranial infection may be apparent from the history and examination, but blood cultures are positive in less than 50% of septic patients and a focus on infection may be difficult to find[26].

The systemic inflammation resulting from infection or other causes appears more likely to be the cause of septic encephalopathy. Inflammatory mediators released by leukocytes in sepsis have profound effects on endothelial cells and astrocytes; damage to these cells results in impaired neuronal function[26].

Encephalopathy is often the first manifestation of sepsis and septic patients with encephalopathy have a higher mortality than those without encephalopathy. These findings suggest that encephalopathy may be a cause of death in septic patients[26].

Toxic (Including Drug–Induced) Coma: This common class of encephalopathy is in large measure reversible and leaves no residual damage provided there has not been cardiorespiratory failure. Many drugs and toxins are capable of depressing nervous system function. Some produce coma by affecting both the brainstem nuclei, including the Reticular activating system, and the cerebral cortex. The combination of cortical and brainstem signs, which occurs in certain drug overdoses, may lead to an incorrect diagnosis of structural brainstem disease. Overdose of medications that have atropine like actions produces signs such as dilated pupils, tachycardia, and dry skin; opiate overdose produces pinpoint pupils <1 mm in diameter[4].

Epileptic Coma: Generalized electrical discharges of the cortex (seizures) are associated with coma, even in the absence of epileptic motor activity (convulsions). The self-limited coma that follows a seizure, the postictal state, may be due to exhaustion of energy reserves or effects of locally toxic molecules that are the by-product of seizures. The postictal state produces a pattern of continuous, generalized slowing of the background EEG activity similar to that of other metabolic encephalopathies[4].

APPROACH TO PATIENT WITH NON TRAUMATIC COMA

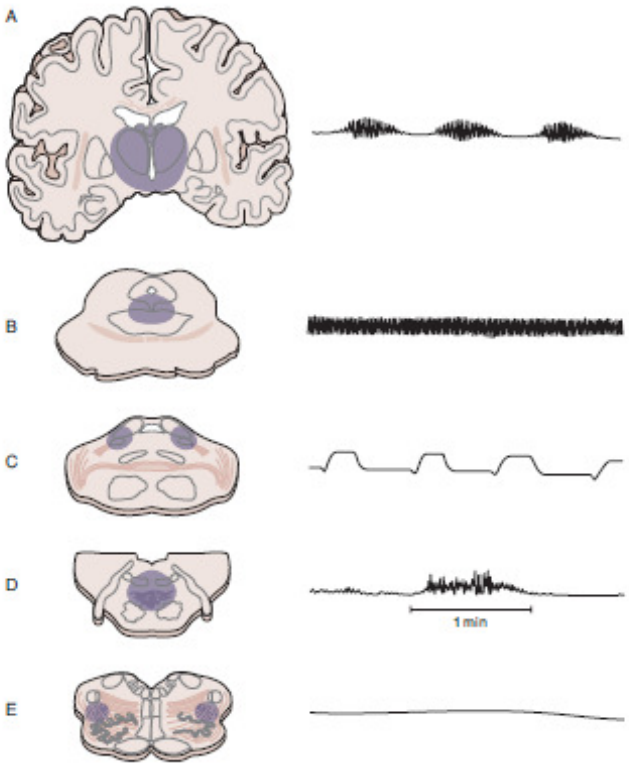
History: In many cases, the cause of coma is immediately evident (e.g., trauma, cardiac arrest, or reported drug ingestion). In the remainder, certain points are especially useful: (1) the circumstances and rapidity with which neurologic symptoms developed; (2) the antecedent symptoms (confusion, weakness, headache, fever, seizures, dizziness, double vision, or vomiting); (3) the use of medications, illicit drugs, or alcohol; and (4) chronic liver, kidney, lung, heart, or other medical disease[4].

General examination:

Temperature: Fever suggests a systemic infection, bacterial meningitis, encephalitis, heat stroke, neuroleptic malignant syndrome, malignant hyperthermia due to anesthetics or anticholinergic drug intoxication; only rarely is it attributable to a lesion that has disturbed hypothalamic temperature-regulating centres ("central fever"). A slight elevation in temperature may follow vigorous convulsions. Hypothermia is observed with exposure; alcoholic, barbiturate, sedative, or phenothiazine intoxication; hypoglycemia; peripheral circulatory failure; or extreme hypothyroidism. Hypothermia itself causes coma only when the temperature is <31°C (87.8°F)[4].

Respiration: Breathing is a sensorimotor act coordinated by nervous influences that arise from almost every level of the brain and upper spinal cord. Metabolically, respiratory control is primarily regulated by the classically known respiratory “centres” that lie in the reticulum of the lower brainstem inbetween the mid pons and the cervical-medullary junction[23].

FIGURE 2: ABNORMAL TYPES OF RESPIRATION SEEN IN COMA



(A) Cheyne – stokes breathing

(B) Central neurogenic hyperventilation

(C) Apneustic breathing

(D) Cluster breathing

(E) Ataxic breathing

Respiratory patterns that is helpful in localising the level of involvement -

1. **Cheyne-Stokes respiration:** Massive supratentorial lesions, bilateral deep-seated cerebral lesions, and mild metabolic disturbances give rise to altered patterns of breathing, particularly periods of waxing and waning hyperpnea alternating with a shorter period of apnea. This phenomenon has been attributed, to isolation of the brainstem respiratory centres from the cerebrum, rendering them more sensitive than usual to carbon dioxide (hyperventilation drive). The presence of Cheyne-Stokes breathing signifies bilateral dysfunction of cerebral structures, usually deep in the hemispheres or diencephalon, usually from intoxication or a metabolic derangement or occasionally, from bilateral structural lesions such as subdural hematomas[2].
2. **Central neurogenic hyperventilation:** Lesions of the lower midbrain-upper pontine tegmentum, either primary or secondary to transtentorial herniation gives rise to this type of respiratory pattern. It is characterized by an increase in the rate and depth of respiration to an extent that produces advanced respiratory alkalosis[2].
3. **Apneustic breathing:** Low pontine lesions, usually caused by basilar artery occlusion, cause this type of breathing, in which a few rapid deep breaths alternate with apneic cycles. There is a pause of 2 to 3 seconds in full inspiration[2].
4. **Cluster breathing:** It results from high medullary damage, comprises periodic respirations that are irregular in frequency and amplitude, with irregular pauses between clusters of breaths[2].

5. **Ataxic (Biot) breathing:** The rhythm of breathing is chaotic, being irregularly interrupted and each breath varying in rate and depth. It is caused by lesions of the dorsomedial part of the medulla[2].

Blood pressure: Marked hypertension suggests hypertensive encephalopathy, but it may also be secondary to a rapid rise in intracranial pressure (the Cushing response) most often after cerebral hemorrhage or head injury. Hypotension is characteristic of coma from alcohol or barbiturate intoxication, internal hemorrhage, myocardial infarction, sepsis, profound hypothyroidism, or Addisonian crisis[4].

Others: The funduscopic examination can detect subarachnoid hemorrhage (subhyaloid hemorrhages), hypertensive encephalopathy (exudates, hemorrhages, vessel-crossing changes, papilledema), and increased ICP (papilledema). Cutaneous petechiae suggest thrombotic thrombocytopenic purpura, meningococcemia, or a bleeding diathesis associated with an intracerebral hemorrhage. Cyanosis, reddish or anemic skin coloration are other indications of an underlying systemic disease responsible for the coma[4].

<u>Neurologic assessment:</u>

Observation without intervention:

Tossing about in the bed, reaching up toward the face, crossing legs, yawning, swallowing, coughing, or moaning reflect a drowsy state that is close to normal awakeness. Lack of restless movements on one side or an outturned leg suggests a hemiplegia. Intermittent twitching movements of a foot, finger, or facial muscle may be the only sign of seizures. Multifocal myoclonus almost always indicates a metabolic disorder, particularly uremia, anoxia, drug intoxication (especially with lithium or haloperidol), or a prion disease. In a

drowsy and confused patient, bilateral asterixis is a certain sign of metabolic encephalopathy or drug intoxication[4].

Posturing: Decorticate rigidity and decerebrate rigidity, or "posturing," describe stereotyped arm and leg movements occurring spontaneously or elicited by sensory stimulation. Flexion of the elbows and wrists and supination of the arm (decortication) suggests bilateral damage rostral to the midbrain, whereas extension of the elbows and wrists with pronation (decerebration) indicates damage to motor tracts in the midbrain or caudal diencephalon[4].

Level of Arousal: A sequence of increasingly intense stimuli is used to determine the threshold for arousal and the motor response of each side of the body. Tickling the nostrils with a cotton wisp is a moderate stimulus to arousal—all but deeply stuporous and comatose patients will move the head away and arouse to some degree. Pressure on the knuckles or bony prominences and pinprick stimulation are humane forms of noxious stimuli. Posturing in response to noxious stimuli indicates severe damage to the corticospinal system, whereas abduction-avoidance movement of a limb is usually purposeful and denotes an intact corticospinal system[4].

Pupils: The pupillary reactions, constriction and dilatation, are primarily controlled by the sympathetic and parasympathetic nervous system. The brainstem areas controlling consciousness are anatomically contiguous to those controlling the pupils and therefore pupillary changes are an important guide to the presence and location of brainstem lesions causing coma. Besides, because pupillary pathways are comparatively resistant to metabolic insult, presence or absence of the light reflex is the most essential physical sign potentially differentiating structural from metabolic coma[2, 27, 28].

The light reflex must be tested with a bright light, and if the pupils are small, a magnifying glass may be used to reveal any reflex constriction obvious to the naked eye[28].

Hypothalamic damage, principally in the posterior and ventrolateral portions, produces ipsilateral pupillary constriction, generally associated with ptosis and anhidrosis (Horner's syndrome). The significance of identifying hypothalamic dysfunction in comatose patients is that downward displacement of the hypothalamus with a unilateral Horner's syndrome is usually the first clear sign of developing transtentorial herniation. Crill had described five cases of supratentorial haemorrhage associated with ipsilateral Horner's syndrome[29].

Damage to midbrainproduces clear-cut pupillary signs. Dorsal tectal or pretectal lesions interfere with the pupillary reflex, but may spare the response to accommodation. The result is midposition or slightly dilated (5 to 6mm in diameter); round and regular pupils that are fixed to light, but spontaneously alter in size and may show hippus& retain their ciliospinal reflex. Nuclear midbrain lesions almost always interrupt both the sympathetic and parasympathetic pathways of the eye. The resulting pupils are in midposition (4 to 5mm in diameter), fixed to light, usually a little irregular, and often unequal. Midposition fixed pupils are mostly a result of midbrain damage from transtentorial herniation, but can also occur when neoplasms, granulomas, haemorrhages, infarcts affect the midbrain[29].

Pontine lesions in the tegmentum interrupt descending sympathetic pathways and result in bilateral miotic pupils. Pinpoint pupils generally mean pontine haemorrhage provided no drugs have been taken or instilled in the eye. They are believed to result from parasympathetic irritation in combination with sympathetic disruption.

Lateral medullary and ventrolateral cervical spinal cord lesions cause an ipsilateral mild Horner's syndrome with slight ptosis and pupillary constriction, never abolishing the light reflex.

Pupils of comatose patients can be affected by peripheral lesions involving the third nerves or sympathetic pathways. The pupillary fibres in the third nerve are particularly liable to injury when uncal herniation compresses the nerve against the posterior cerebral artery or tentorial edge. Therefore in these instances, pupillary dilatation usually precedes extraocular motor abnormalities[2, 3, 4, 27, 29].

Eyelid and corneal reflexes: As in sleep, in most patients with stupor and coma, the eyes are closed by tonic contraction of the orbicularis oculi. Lifting the lids and releasing them helps in assessing their tone. In unconscious patients the eyelids slowly close after they are released. This movement cannot be mimicked voluntarily by a hysterical patient. Failure to close either lid or absence of tone suggests facial nerve dysfunction on the same side. Unilateral ptosis without pupillary changes occurs in medial pontine infarction, and bilateral ptosis results from rostral brainstem infarction[27].

Blinking either at rest or in response to a bright light, a loudsound or a threatshould be looked for in unresponsive patients. The occurrence of spontaneous blinking denotes that the pontine reticular formation is intact. If blinks can be triggered by sound or light, the related special sensory pathways must also be intact. Bilateral absence of blinking implies either structural or metabolic dysfunction of the reticular formation[27].

A stronger stimulus must often be used to elicit corneal reflex in unconscious patients than in alert patients. Bilateral positive response of eyelid closure along with upward deviation of

the eye (Bell's phenomenon) indicates normal functioning of the brainstem tegmental pathways from the midbrain (third nerve nucleus) upto the low pons (seventh nerve nucleus). In structural brainstem lesions above the midpons (trigeminal nucleus)Bell's phenomenon disappears, but the jaw may deviate to the opposite side (corneal pterygoid reflex). Presence of Bell's phenomenon with absent eyelid closure implies damage to the facial nerves or nuclei[27].

Ocular movements: It is clinically useful to look for both gross and subtle oculomotor abnormalities when evaluating patients in coma or stupor, since the pathways mediating the oculomotor reflexes lie adjoining to the brainstem areas necessary for consciousness[2,27].

A bilateral frontal lobe dysfunction impairs voluntary eye movements and also the fast phase of optokinetic and vestibular nystagmus. Parietal lobe dysfunction impairs smooth following responses towards the diseased hemisphere. Eyes turn inwardand down as a result of thalamic and upper midbrain lesions, typically with thalamic hemorrhage. Lesions of cerebellum result in disorders of saccadic eye movements (e.g., ocular flutter, ocular dysmetria, or opsoclonus) [2, 27, 28].

Conjugate horizontal ocular deviation to one side indicates damage to pons on the opposite side or a lesion in the frontal lobe on the same side. Eyes look towards a hemispherical lesion and away from a brainstem lesion[4].

"Ocular bobbing" describes a brisk downward and slow upward movement of the eyes associated with loss of horizontal eye movements and is diagnostic of bilateral positive damage usually from thrombosis of the basilar artery. "Ocular dipping" is a slower,

asymmetric downward movement followed by a faster upward movement in patients with normal reflex horizontal gaze; it indicates diffuse cortical anoxic damage[4].

Oculocephalic reflex: It is elicited by moving the head from side to side or vertically and observing eye movements in the direction opposite to the head movement. It depends on the integrity of the ocular motor nuclei and their interconnecting tracts that extend from the midbrain to the pons and medulla. These movements are normally suppressed in the awake patient. The ability to elicit them therefore indicates both reduced cortical influence on the brainstem and intact brainstem pathways, indicating that coma is caused by a lesion or dysfunction in the cerebral hemispheres. The opposite, an absence of reflex eye movements, usually signifies damage within the brainstem but can result infrequently from overdoses of certain drugs. Normal pupillary size and light reaction distinguishes most drug-induced comas from structural brainstem damage[4].

Oculovestibular response: Thermal, or "caloric," stimulation of the vestibular apparatus provides a more intense stimulus for the oculocephalic reflex but provides essentially the same information. The test is performed by irrigating the external auditory canal with cool water in order to induce convection currents in the labyrinths. After a brief latency, the result is tonic deviation of both eyes to the side of cool-water irrigation and nystagmus in the opposite direction. (The acronym "COWS" has been used to remind generations of medical students of the direction of nystagmus—"cold water opposite, warm water same.") The loss of induced conjugate ocular movements indicates brainstem damage. The presence of corrective nystagmus indicates that the frontal lobes are functioning and connected to the brainstem; thus functional or hysterical coma is likely[4].

GLASGOW COMA SCALE

Whenever there is an acute brain insult, either from head injury or non-traumatic events such as stroke or poisoning, it is necessary to assess the degree of brain dysfunction immediately. This provides a baseline from which progress towards recovery or complications may be judged and also determines what interventions are needed. Clinical assessment of the level of consciousness is the best measure of the overall brain dysfunction. This also gives an indication of the likely outcome – and the reliable measurement of this is essential both to discover the predictive value of early features and to validate comparisons made between alternative therapeutic regimes in the acute stage[30].

Before the Glasgow Coma Scale:

In Britain, Medical Research Council issued a glossary of psychological terms commonly used in cases of head injury during World War II. It claimed that its use would enable the interchange of information between various observers as injured men were handed over from one medical officer to other. The 16 terms included mild, moderate and severe confusion, coma and semicoma, as well as automatism and stupor. Unfortunately these terms were not easily defined and published reports regarding treatment of war injuries rarely referred to the severity of brain dysfunction. Post-war neurosurgical practice was rather concerned with elective surgery for aneurysms and tumors. There was a pessimistic attitude to head injuries – believing that apart from evacuating the occasional intracranial hematoma and elevating depressed fractures not much could be done to affect the outcome. However, as intensive care and resuscitation began to save the lives of many patients with head injury, neurosurgeons were challenged not only to assist in reducing

mortality, but also in saving as much of the damaged brain as possible in order to limit disability in survivors[30].

Furthermore pathological studies in Glasgow revealed that considerable mortality and persisting disability after head injury was possibly avoidable, as reflected in the title of one research paper 'Head injuries who talk and die'. Hence the inference was that if they had talked they had not incurred irreversible damage and should not have died. Failure to detect complications early enough for effective treatmentresulted in many avoidable deaths[30].

Scoring by Numbers:

Assigning numbers to the several response levels (the higher the number the better the response) was suggested a year later in a paper concerned with statistical estimates of outcome from the early coma score. This also enables communication among doctors who can readily report a patient's state as E2, M3, V2. Establishing the statistical association between the early responsiveness and the outcome rested onadding the scores to give an overall coma score, ranging from 3 to 14. 'Abnormal flexion' was includedthe next yearas an additional motor score and the score for fully alert became 15. Definition of coma was then proposed as no eye opening, not obeying commands and no recognizable words. According to this definition all patients scoring seven or less are in coma but only half of those scoring eight are in coma. When a patient's state is specified only by total score there is a loss of information compared with thosehaving the numbers for E, M and V. This is because for any given total score there can be various combinations of E, M and V. This was exemplified in an intensive care study, which showed that mortality ranged from 0-20% for patients scoring 7 with various permutations of E, M and V immediately after admission. Nonetheless the score is a useful tool in the triage for initial disposal; for guidelines that

indicate that patients above or below a given score should go to certain hospital facilities or should have particular investigations or therapeutic interventions[31].

Acceptance of the GCS:

A clinical tool that was devised for research soon became a part of everyday practice in many countries. Not only was it adopted by doctors and nurses in neurosurgical and intensive care units but also in other departments dealing with acute brain damage, traumatic and non-traumatic, as well as by the emergency personnel involved in retrieval of such patients. Its simplicity was attractive, and particularly nurseswelcomed it because marking the coma chart was similar to their routine recording of temperature, pulse and respiration. Actually there were two papers from Glasgow in a nursing journal within a year of the initial paper in the Lancet. It soon became a part of nurse training and as they outnumbered doctors by 10 to 1 and they played an important role in its dissemination as they moved around within and between hospitals. It was not long, before bodies sponsoring clinical research into traumatic and non traumatic coma required applicants to submit patient data using these scales. Some claims have also been made for medical negligence on the failure to use this coma scale as a bedside tool in the acute stage. More than 1000 publications referring to its use and university theses devoted to analysis of its application were done by the year 2000. Nonetheless,there was some skepticism, most of it regarded that GCS was very simple but the several proposed alternatives were in turn criticized by the Glasgow team. However, while assessing mildly injured patientsthere is benefit in adding the presence or absence of post-traumatic amnesia to the GCS score[30].

When to Assess the GCS for Prediction:

It is always better to assess the GCS soon after an acute insult for monitoring the progress. However,for predicting the likely outcome,the various changes in responsiveness that commonly occurs in the first 24 hours after an insultmust also be taken into account. Especially there might be rapid improvement as the effects of hypotension and shock, as well as of alcohol and other drugs decline. The most accurate time to assess GCS for prognosis is therefore after resuscitation and stabilization. But after resuscitation, many patients are often sedated and intubated; thereby making assessment on the full scale then becomes impossible. There is differenceof opinion in dealing with this, but the motor score alone may beuseful in such circumstances. The GCS score has been found to be more predictive of the outcome than any other single variable in the APACHE III scoring system which is used in general intensive care units[32].

Applications of the GCS:

GCS which was originally used for classifying injury severity in multicenter studies was then followed by its use in many clinical trials of agents and regimes believed likely to improve outcome after acute brain insults. This applicationhas obviously been restricted to the small number of units involved in such studies. Much more of its general use has been its adoption as a means of communicationbetween the different staff cadre caring for such patients from the scene of the insult through to the intensive care unit. Three grades of severity are recognized, severe (GCS 8 or less), moderate (GCS 9-12), and mild (GCS 13-15)[32].

The Glasgow Outcome Scale:

The aim was to have a restricted number of exclusive categories that summarized the social capacity of the patient rather than listing specific disabilities. The five categories were as follows:

Death - The only qualification to this relates to when the death occurs – usually it will be during the initial period in hospital, but it may be extended to those occurring within a specified time thereafter.

Persistent Vegetative State - Many patients who are vegetative at one month recover to a better category of outcome, emphasizing the need to state when the outcome has been assessed.

Severe Disability- This applies to a conscious patient who is dependent for daily support from another person by reason of mental or physical disability, usually a combination of both.

Moderate Disability - These patients have some disability such as dysphasia, hemiparesis or epilepsy and/or deficits of memory or personality but are able to look after themselves, do shopping and travel by public transport. They may be able to work when special arrangements are made.

Good Recovery - This implies a resumption of normal life with the capacity to work even if preinjury status has not been achieved. Some of these patients have neurological or psychological deficits[31, 32].

Glasgow Coma Scale with scores:

Eye opening

4. Spontaneous. Indicates arousal, not necessarily awareness.

3. To speech. When spoken to – not necessarily the command to open eyes.

2. To pain. Applied to limbs, not face where grimacing can cause closure.

1. None.

Motor response

6. Obeys commands. Exclude grasp reflex or postural adjustments.

5. Localises. Other limb moves to site of nail bed pressure.

4. Withdraws. Normal flexion of elbow or knee to local painful stimulus.

3. Abnormal flexion. Slow withdrawal with pronation of wrist, adduction of shoulder.

2. Extensor response. Extension of elbow with pronation and adduction.

1. No movement.

Verbal responses

5. Orientated. Knows who, where, when; year, season, month.

4. Confused conversation. Attends & responds but answers muddled/wrong.

3. Inappropriate words. Intelligible words but mostly expletives or random.

2. Incomprehensible speech. Moans and groans only – no words.

1. None.

LABORATORY INVESTIGATIONS AND IMAGING

Electrocardiography - The electrocardiogram is useful to show arrhythmia, myocardial infarction, bradycardia, conduction blocks or evidence of underlying atherosclerotic coronary vascular disease or hypertension. Hypercalcemia causes shortening of QT interval whereas hypocalcemia causes QT prolongation. In hypothyroid patients the heart rate is slow with low voltage QRS, flattened ST segments and flat or inverted T waves[3].

Electroencephalogram –It is helpful in many situations, asin patients too unstable to travel to a CT scan centres for confirming underlying cortical structural damage; partial complex seizures; post ictal states; non-convulsive status epilepticus, such as seen in comatose patients following anoxic ischemic damage. The earliest EEG changes to occur inmetabolic disorders are typically a decrease in the frequency of back-ground rhythms and the appearance of diffuse theta activity. It soon progresses to more advanced slowing with decreasing level of consciousness. Medium to high-amplitude, bilaterally synchronous and symmetric, broad triphasic waves, often with a frontal predominance, may be observed in hepatic encephalopathy. Herpes simplex encephalitis may be suggested by the presence of bilateral or unilateral periodic sharp waves with a temporal predominance[3].

Neuro-radiological imaging - Once the patient is treated and stabilized, after initial complete examination and necessary laboratory studies, the next investigation of choice is a non contrast CT scan of the brain, with 5-mm cuts of the posterior fossa. Alternatively, depending on the stability of the patient's condition and the clinical settings a MRI may be ordered. When structural disease of the brain stem is suspected, MRI provides excellent visualization of the posterior fossa and its contents. The value of the CT scan in demonstrating hemorrhage and mass lesions is unquestionable. Furthermore, it

alsodemonstrates features of brain herniation. The physician should be aware that the CT scan may miss an early infarction, isodense subdural hemorrhage and encephalitis. Special precautions are necessary in evaluating CT scan of comatose patients, especially prior to lumbar puncture, to rule out bilateral subdural hemorrhage or isodense subdural hemorrhage[3].

Others -

- Chemical -Toxicological analysis of blood and urine.
- CSF examination - Meningitis and Encephalitis.
- ABG - In patients with lung disease and acid base disorders.
- Serum electrolytes, glucose, Calcium, Osmolality, Renal and Hepatic function.

PROGNOSIS

The outcome of coma is related to the cause independent of the physical signs, depth of coma or length of coma. This is most important and shown most dramatically in coma caused by drug overdose. All such patients should be regarded as potentially salvageable and special attempts must be taken to avoid complications during the period of coma. Patients with drug overdose coma frequently appear deeply comatose with depressed brain stem reflexes because of the effects of the drugs upon the brain stem, yet may show disproportionately high levels of motor activity. In general, metabolic causes of coma have a better prognosis than anoxic–ischaemic causes. Cerebrovascular disease (subarachnoid haemorrhage or stroke) carries the worst prognosis of all .The likelihood of a good recovery is less than 5% in those who have suffered SAH or stroke, about 10% in those with hypoxic–ischaemic injury, but as high as 25% in those metabolic or infective causes of coma. Also hypoxic–ischaemic injury is the one most likely to result in the development of a vegetative state[33].

Even after 6 hours of coma patients with higher levels in the hierarchical scale have a better outcome. Within 6 hours of coma onset those patients who show eye opening have almost a one in five chance of achieving a good recovery whereas those who do not, have a one in 10 chance. Those who show no motor response have a 3% chance of making a good recovery whereas those who show flexion have a better than 15% chance. Those who make no noise have only an 8% chance of making a good recovery, while those who groan have a 30% chance of so doing[33].

The longer a patient remains in a coma the poorer his or her chance of recovery and the greater the chance that he or she will enter a vegetative state. By the third day the chance

of making a moderate or good recovery is reduced to only 7%, and by the 14th day is as low as 2%. By the end of the first week almost half of those patients who have not recovered consciousness are in a vegetative state[33].

The most important clinical signs in identifying those patients with a poor outcome are the brain stem reflexes, and the simple tests of corneal reflexes and pupillary responses. David bates et al., showed that none of the 90 patients who had absent corneal reflexes at 24 hours survived. There were 210 patients with anoxic ischaemic injury, 52 of whom had no pupillary reflexes at 24 hours and all died. By the third day 70 of these patients were left with a motor response poorer than withdrawal and all died. By the seventh day there were 26 patients who had absent spontaneous eye movements and all of those died. There are some clinical signs which predict a good outcome: the development of nystagmus on oculovestibular testing or the vocalisation of any recognisable word within 48 hours indicates a 50% likelihood of a good recovery and the presence of motor localising within the first 24 hours indicates a 20% chance of a good recovery[33].

Levy et al reported the outcome for a series of 210 patients who were comatose from cerebral hypoxic – ischemia. No single clinical sign is significant as an indicator of poor prognosis, but a combination of clinical signs may potentially improve the accuracy of prognosis. The most favourable sign was incomprehensible speech at the early time points. The following signs were associated with a 50% chance of independence if present on day 1: orienting spontaneous eye movements, confused or inappropriate speech, obedience to commands and normal oculocephalic or oculovestibular responses[34].

MATERIALS AND METHODS

PLACE OF STUDY: Institute of Internal Medicine, Rajiv Gandhi Government General Hospital, Chennai.

STUDY POPULATION:

The study was conducted on 100 cases of non - traumatic coma admitted in the medical wards of Rajiv Gandhi Government General Hospital, Chennai. They were diagnosed and evaluated by detailed history, clinical examination and relevant investigations.

STUDY DESIGN : Cross - sectional study

SELECTION CRITERIA:

Inclusion criteria-

1. Patients above age group 12 years.
2. Patients presenting in a comatose state for more than 6 hours.

Exclusion criteria-

1. History of trauma.
2. Transient unresponsiveness of syncope.
3. Transient post ictal unconsciousness.
4. Unresponsiveness of imminent death.

METHODOLOGY

All patients underwent full medical and neurologic clinical evaluation and Glasgow Coma Scale grading at the time of admission (time of admission to study was arbitrarily taken as

the time of first neurologic assessment). Laboratory investigations included complete blood count, renal function test, liver function test, urine routine examination. ECG and X-Ray chest were done for all patients. CSF examination (in suspected cases of meningo encephalitis), CT &MRI brain (in cases of cerebrovascular accident) and other investigations were done as required.

Patients were neurologically evaluated daily and the progression was monitored with Glasgow Coma Scale scoring. All patients were followed till discharge or the time of death in the hospital and their outcome was graded and recorded into 3 categories:

I - Death

II - Recovery with functional disability

III - Good recovery

The history, general examination, the neurological profile at the time of admission, important positive investigation findings, the diagnosis and outcome of all cases are presented in tabular form (master chart) and analysed.

OBSERVATION AND RESULTS

100 cases of non – traumatic coma formed the study group. In these cases age wise distribution, sex wise distribution and etiological distribution of coma was analysed.

Presence or absence of brainstem reflexes at admission and GCS score at admission were compared with the final outcome.The etiological factors were compared with outcome. Other independent variables were also entered into the comparison model. Appropriate statistical analysis was made.

TABLE 2: AGE AND SEX DISTRIBUTION

Age in years	Total	Male	Female
10-20	7	6	1
20-30	7	3	4
30-40	20	14	6
40-50	15	9	6
50-60	18	12	6
60-70	22	9	13
70-80	9	3	6
80-90	2	0	2

TABLE 3: AGE WISE ANALYSIS

Age distribution with outcome

Age in years	Total	I	II	III
10-20	7	1	2	4
20-30	7	2	1	4
30-40	20	7	4	9
40-50	15	3	4	8
50-60	18	8	4	6
60-70	22	9	4	9
70-80	9	7	1	1
80-90	2	2	0	0

The age group ranged from 17 years to 82 years. The mean age was 50.6 ± 17.9. Maximum cases were in the age group of 60 to 70 years. There was no significant relationship between age group and outcome ($p > 0.05$). Although patients with age more than 50 years were more likely to have a bad outcome compared other groups (Relative risk = 1.92). In the age group less than 50 years mortality was 26.5% while those more than 50 years mortality was 51%. Older patients had additional risk factors like diabetes mellitus, hypertension,coronary artery disease, old CVA which contributed to their increased mortality.

FIGURE 3: GRAPH SHOWING AGE WISE DISTRIBUTION

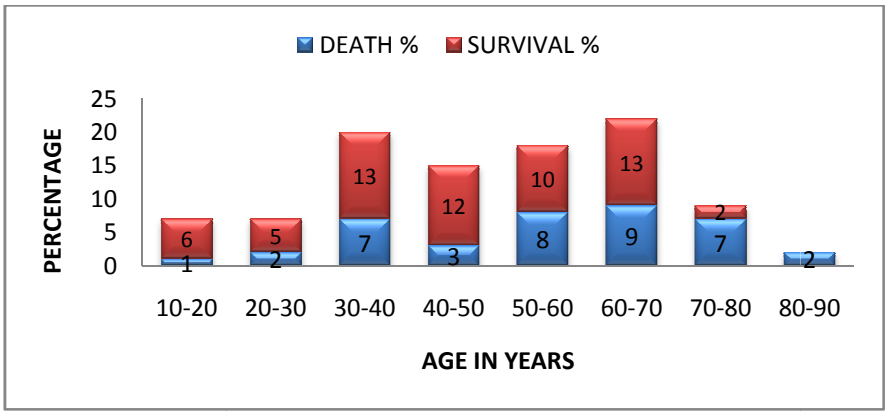


TABLE 4: SEX WISE ANALYSIS

Sex distribution with outcome

Sex	Total	I	II	III
Male	56	23	11	22
Female	44	16	9	19

There were 56 males and 44 females. The male to female ratio was 1.27:1. The difference in mortality among males and females was not statistically significant($p > 0.05$).

FIGURE 4: GRAPH SHOWING SEX WISE DISTRIBUTION

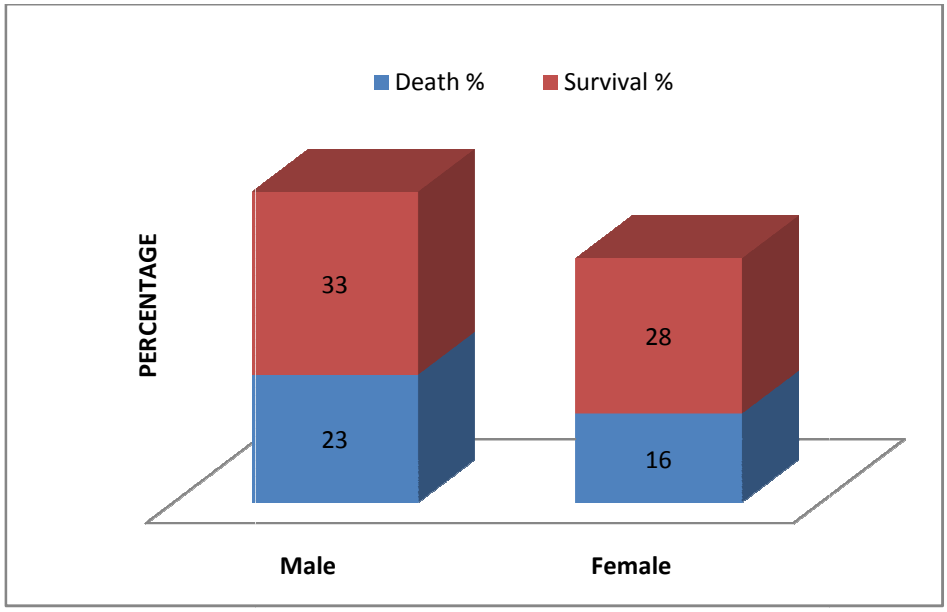
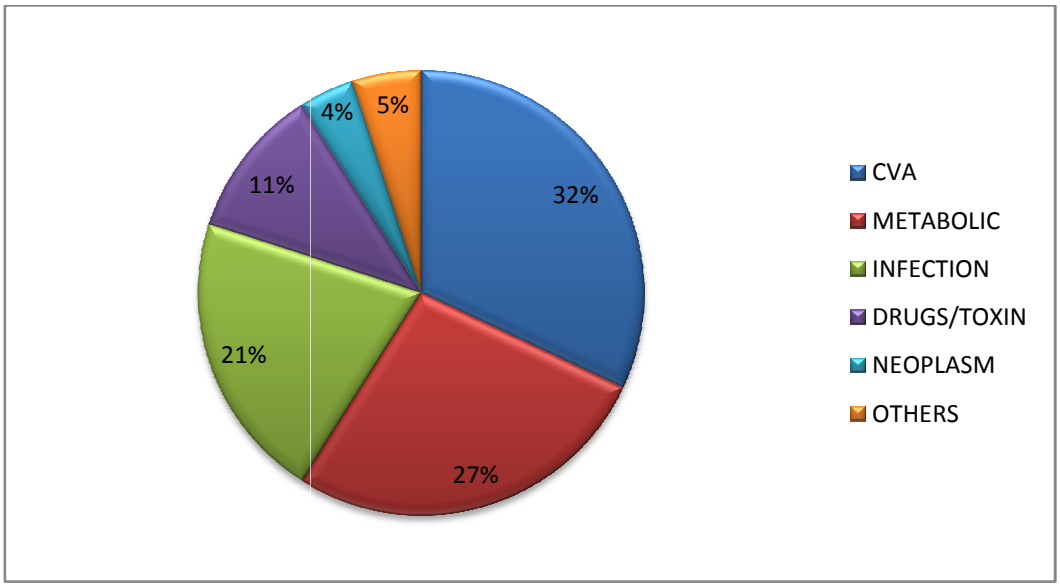


TABLE 5: ETIOLOGY OF COMA

Etiology	**Percentage**
1.Cerebro vascular accidents	32%
(a) Infarct	13%
(b) Intra cerebral haemorrhage	12%
(c) Subarachnoid haemorrhage	4%
(d) Cerebral venous thrombosis	3%
2. Metabolic	27%
(a) Hepatic coma	9%
(b) Uremic coma	6%
(c) Hypoglycemia	3 %
(d) Hypoxia	3%
(e) Hypercapnia	2%
(d) Hyponatremia	2%
3.Infection	21%
(a) Bacterial menigo encephalitis	6%
(b) Tuberculous meningitis	4%
(c) Cerebral malaria	4%
(d) Viral encephalitis	3%
(e) Others	4%
4. Drug over dosage and poisoning	11%
(a) Drug over dosage	5%
(b) OP poisoning	3%
(c) Snake bite	1%
(d) Others	1%
5. Intra cranial neoplasms	4%
6. Others	5%

Among the studied cases, cerebrovascular accidents stand the most common followed by others. Cerebral infarcts and hemorrhage dominate among cerebrovascular accidents. Next common are the metabolic causes among which the most common is hepatic coma. Bacterial meningo encephalitis is common among the infectious causes. Drug over dosage, poisoning, intracranial neoplasms are less common causes of coma in this study.

FIGURE 5: GRAPH SHOWING ETIOLOGY DISTRIBUTION

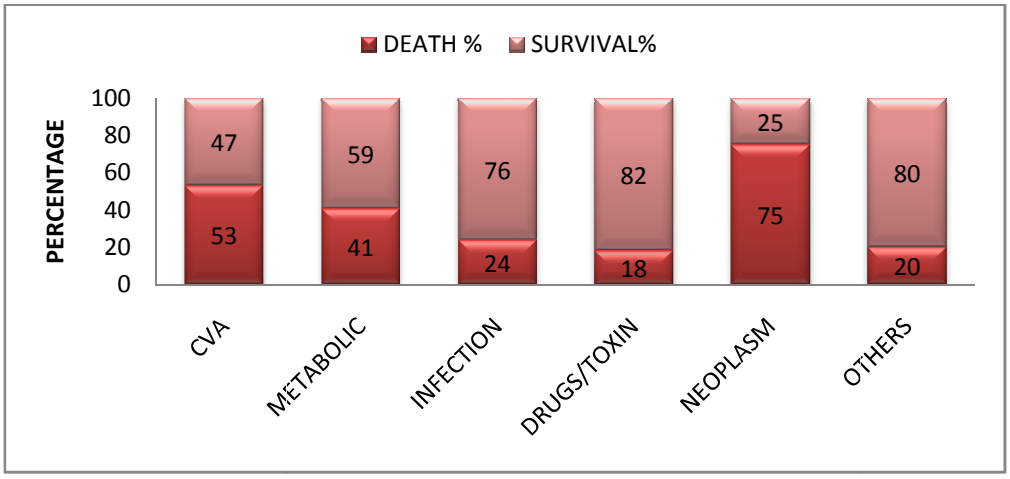


In the present study, metabolic and infectious causes of coma showed better survival while cerebrovascular accidents especially cerebral bleed and intracranial neoplasms were associated with poor outcome. Drug and toxin induced coma showed the best recovery. The patients who showed good recovery were anticipated to do so on 2nd or 3rd day itself based on clinical neurologic signs.

TABLE 6: ETIOLOGY AND OUTCOME

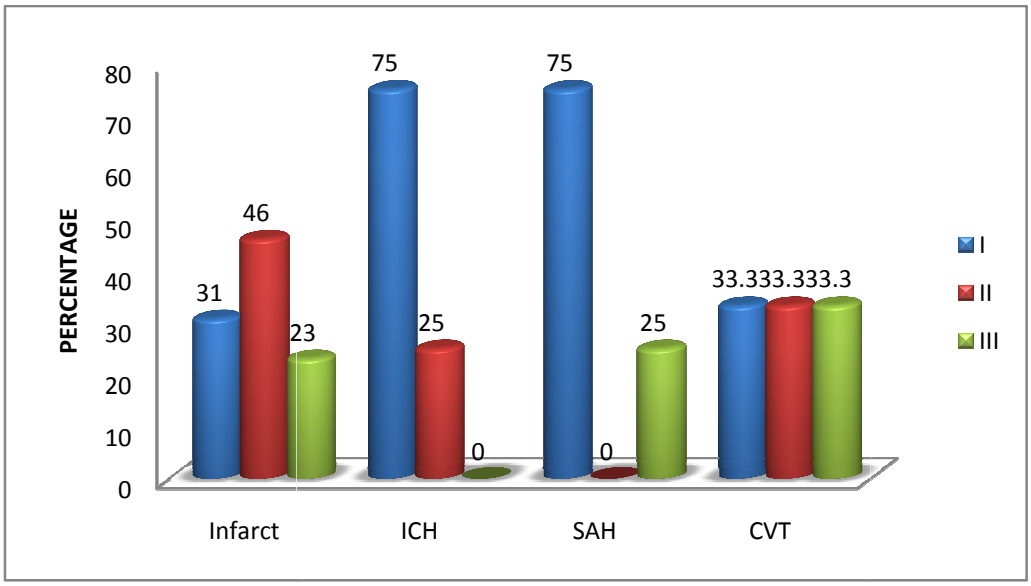
Etiology	Total	I	II	III
CVA	32	17	10	5
Metabolic	27	11	2	14
Infection	21	5	4	12
Drugs/toxin	11	2	2	7
Neoplasm	4	3	1	0
Others	5	1	1	3

FIGURE 6: GRAPH SHOWING ETIOLOGY OUTCOME DISTRIBUTION



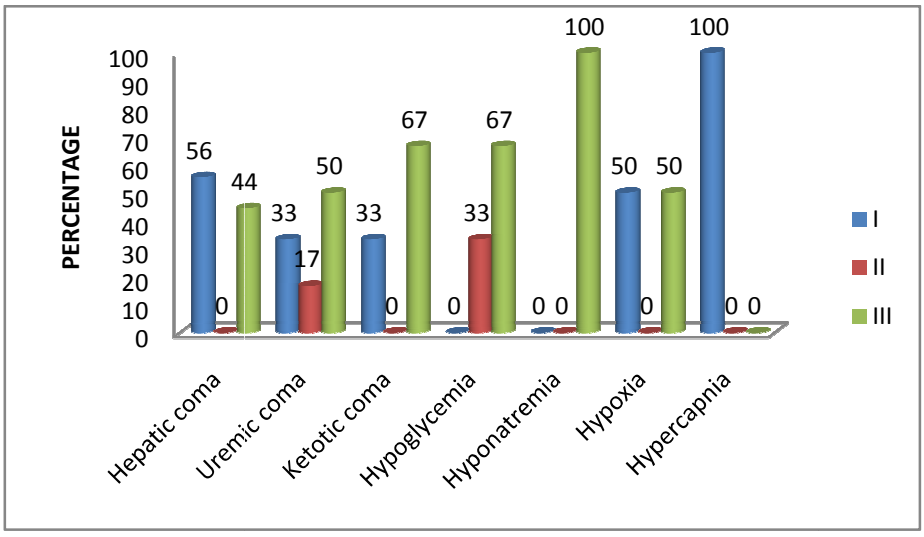
Among cerebrovascular accidents, patients with intra cranial haemorrhage and subarachnoid haemorrhage had 75% mortality. Most of the patients with cerebral infarcts were discharged with moderate disability. Those who died had massive infarcts usually with midline shift. There were 3 cases of cerebral venous thrombosis of which 2 were due to postpartum and 1 due to poly substance abuse. The patient who died was a postpartum female who presented to us with a very poor GCS at admission.

FIGURE 7: GRAPH SHOWING CEREBROVASCULAR ACCIDENTS AND OUTCOME



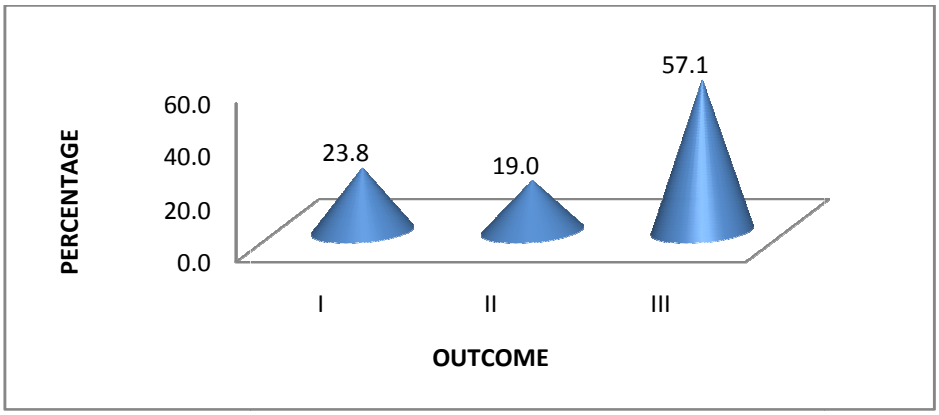
Among patients with metabolic causes, hepatic coma was the most common. 56% of patients with hepatic coma died and all of them were alcoholics. Patients with hypoglycaemia, hyponatremia and ketotic coma showed better survival. Both the patients with hypercapnia died. The outcome among those with hypoxia and uremia was mixed.

FIGURE 8: GRAPH SHOWING METABOLIC COMA AND OUTCOME



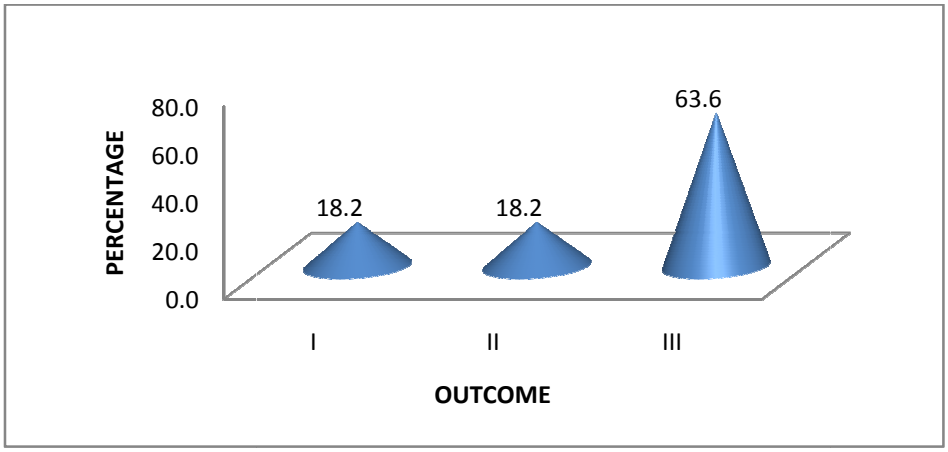
57.1% of patients with infectious causes of coma had good recovery. Both the patients who died of central nervous system tuberculosis were people living with HIV – AIDS. One patient had tuberculous meningitis and the other had multiple tuberculoma. The other patients who had bad outcome were bacterial meningo encephalitis, cerebral malaria and Weil's disease with disseminated intra vascular coagulation and multi organ dysfunction.

FIGURE 9: GRAPH SHOWING INFECTION AND OUTCOME



63.6% of patients with drug over dosage and poisoning showed good recovery. Both the patients who died were due to toxic snake envenomation. One was due to neurotoxic snake envenomation which resulted in respiratory paralysis leading to death; other was due to hemotoxic snake envenomation with acute kidney injury. 2 patients with organophosphorous compound poisoning were discharged with moderate disability. Both of them had recovered from intermediate syndrome.

FIGURE 10: GRAPH SHOWING DRUG OVER DOSAGE/POISONING AND OUTCOME



Mortality among patients with intra cranial neoplasms reached 75% in this study.

FIGURE 11: GRAPH SHOWING INTRACRANIAL NEOPLASMS AND OUTCOME

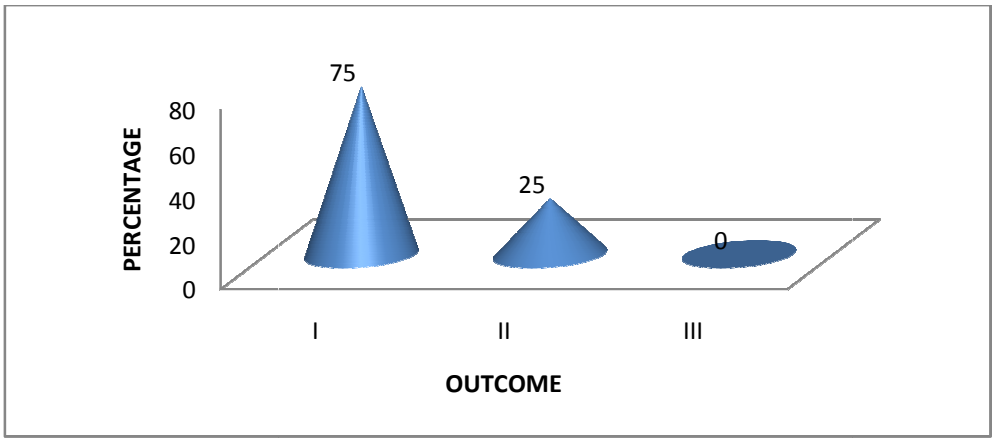
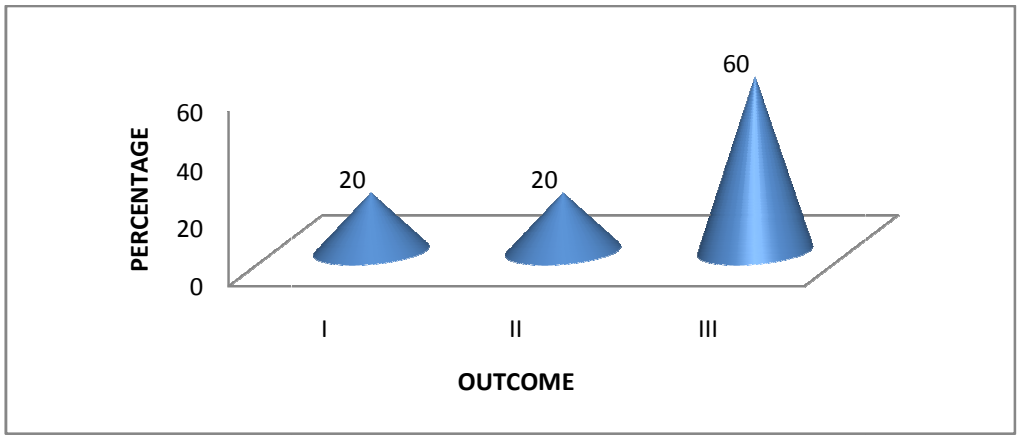


FIGURE 12: GRAPH SHOWING OTHERS AND OUTCOME



The miscellaneous causes of coma in this study were status epilepticus, hypertensive encephalopathy and myxedema coma.

TABLE 7: ONSET OF COMA WITH OUTCOME

Onset	Total	I	II	III
Abrupt	57	23	14	20
Gradual	43	16	6	21

Based on history, the onset of coma was classified into abrupt and gradual onset. Cerebrovascular accidents, drug over dosage & poisoning, hypoglycaemia, status epilepticus and some fulminant infections comprised abrupt onset of coma. Other metabolic causes, most infections and intra cranial neoplasms had more gradual onset of coma. Onset of coma is not statistically associated with coma ($p > 0.05$).

FIGURE 13: GRAPH SHOWING ONSET OF COMA WITH OUTCOME

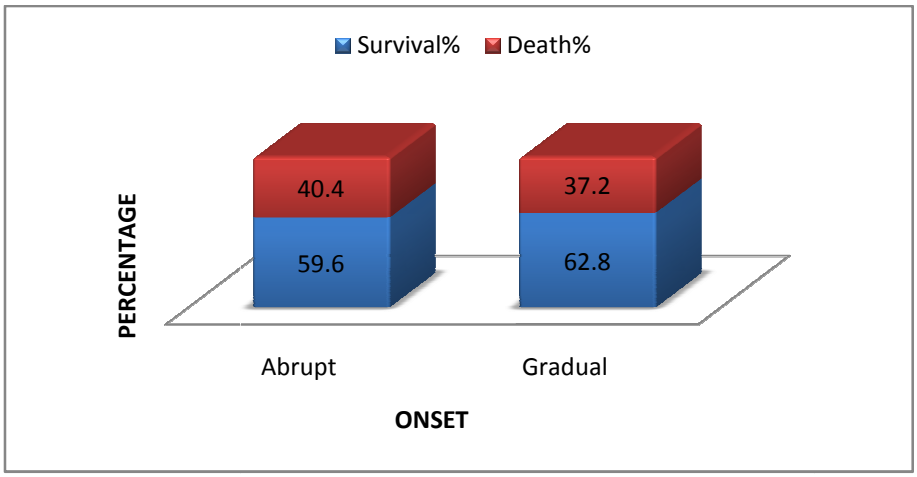


TABLE 8: PRECEDING COMPLAINTS

Preceding complaints	Percentage
Headache	53
Vomiting	73
Fever	36
Speech disturbances	12
Convulsions	19
Vertigo	14
Neck pain	8
Neuro deficit	28
Jaundice	16
GI Bleed	7

From the history of preceding complaints, headache and vomiting, which suggest raised intra cranial pressure, were the most common complaints in this study. Jaundice was present in most patients with hepatic coma. There were 19 patients presenting with convulsions, being more common in patients with infectious and cerebrovascular causes of coma. Neurodeficits were more common in patients with cerebrovascular accidents, who were discharged with some disability.

FIGURE 14: GRAPH SHOWING PRECEDING COMPLAINTS

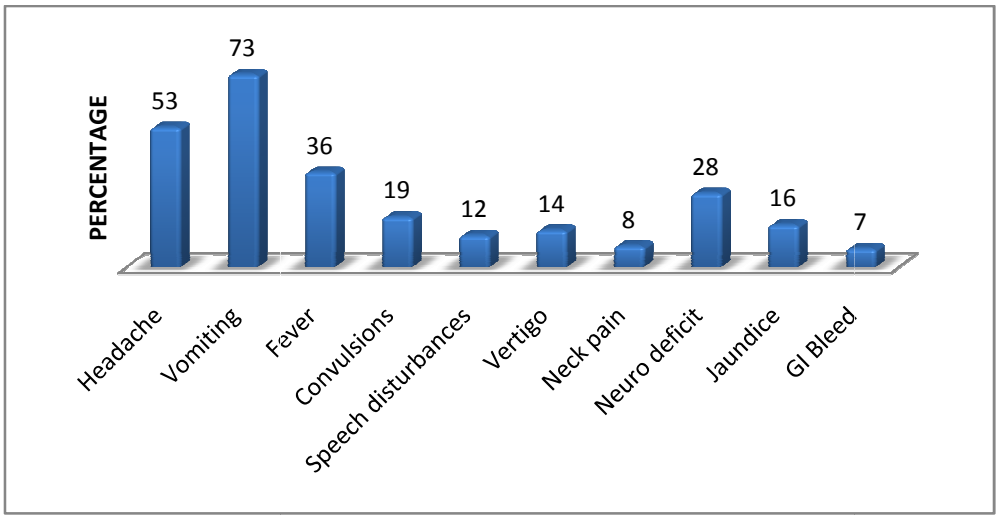


TABLE 9: OTHER DISEASES AND CONDITIONS ASSOCIATED WITH OUTCOME

Past history	Total	Death	Survival
Hypertension	26	12	14
Diabetes mellitus	27	10	17
Coronary artery disease	14	7	7
Dyslipidemia	23	9	14
Tuberculosis	6	3	3
COPD	8	6	2
Bronchial asthma	6	2	4
Epileptic	5	0	5
Previous CVA	9	5	4
Liver disease	11	7	4
Chronic kidney disease	7	2	5

The above table shows various diseases associated with outcome in patients with coma in this study. The most common diseases associated with patients of coma werediabetes mellitus and hypertension and hence being important risk factors for etiology of coma.

TABLE 10: RESPIRATORY PATTERN AND OUTCOME

Respiratory pattern	Total	I	II	III
Normal	41	1	15	25
Abnormal	59	38	5	16

Abnormal respiratory pattern was seen in total of 59 patients out of which 38 died. Presence of CNH resulted in 100% mortality. Therefore abnormal respiration was associated with significant mortality. ($X^2 = 39.05$, $p < 0.0001$)

FIGURE 15: GRAPH SHOWING ABNORMAL RESPIRATORY PATTERN AND OUTCOME

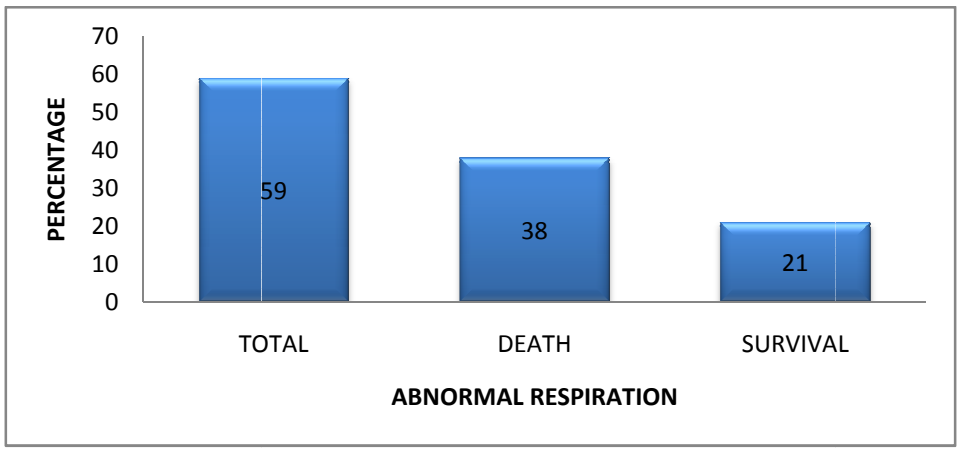


TABLE 11: SPONTANEOUS EYE MOVEMENT AND OUTCOME

Spontaneous eye movement	Total	I	II	III
Roving conjugate	59	13	9	37
Roving dysconjugate	1	1	0	0
Conjugate deviation to right	8	2	4	2
Conjugate deviation to left	11	3	7	1
Absent	20	20	0	0

20 patients had absent reflex eye movements and were associated with 100% mortality. Most of these patients had cerebrovascular events with intra cerebral haemorrhage being the commonest cause.

FIGURE 16: GRAPH SHOWING SPONTANEOUS EYE MOVEMENT AND OUTCOME

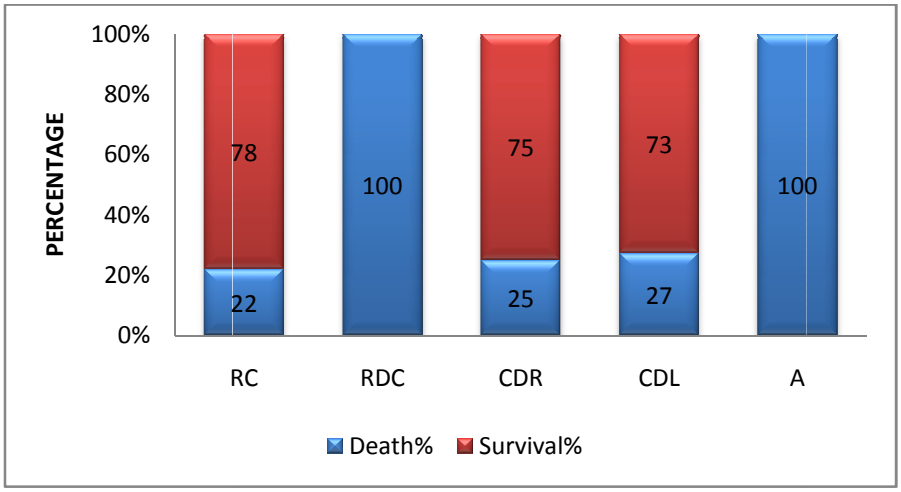


TABLE 12: FUNDUS AND OUTCOME

Fundus	Total	I	II	III
Normal	58	18	10	30
Diabetic retinopathy	9	2	2	5
Hypertensive retinopathy	11	5	3	3
Papilledema	22	14	5	3

On fundus examination papilledema was present in 22 patients in, out of which 14 died. Thus presence of papilledema is related to significant mortality. (X^2= 7.20, p = 0.0073)

The presence of brainstem reflexes in patients with coma at the time of admission predicts good outcome. It is apparent from the following tables and graphs that absence of any of these reflexes is a poor prognosis indicator. The absence of oculocephalic, pupillary and corneal reflexes suggested poor prognosis with a mortality of 95.8%, 92% and 88.5% respectively. p value was < 0.0001 for all the reflexes (X^2 = 42.88, 39.36, 36.13 respectively). In most metabolic and infectious etiologies the absent neuro ophthalmic signs initially showed signs of recovery with treatment which helped to continue the same line of management.

TABLE 13: OCULOCEPHALIC REFLEX AND OUTCOME

Outcome	Oculocephalic reflex			
	Absent		Present	
	No of cases	%	No of cases	%
I	23	95.8	16	21.1
II	0	0.0	20	26.3
III	1	4.2	40	52.6

FIGURE 17: GRAPH SHOWING OCULOCEPHALIC RELEX AND OUTCOME

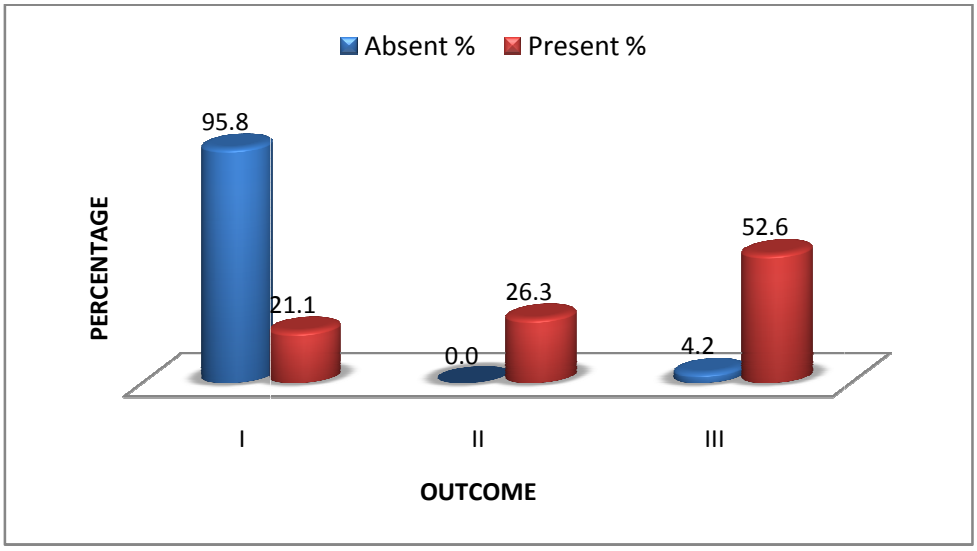


TABLE 14: PUPILLARY REFLEX AND OUTCOME

Outcome	Pupillary reflex			
	Absent		Present	
	No of cases	%	No of cases	%
I	23	92.0	16	21.3
II	0	0.0	20	26.7
III	2	8.0	39	52.0

FIGURE 18: GRAPH SHOWING PUPILLARY RELEX AND OUTCOME

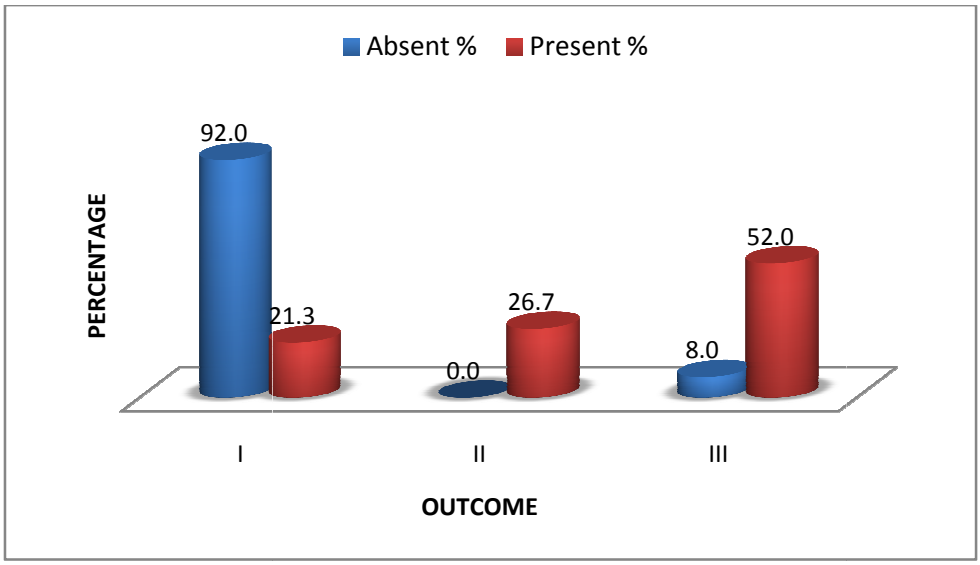


TABLE 15: CORNEAL REFLEX AND OUTCOME

Outcome	Corneal reflex			
	Absent		Present	
	No of cases	%	No of cases	%
I	23	88.5	16	21.6
II	0	0.0	20	27.0
III	3	11.5	38	51.4

FIGURE 19: GRAPH SHOWING CORNEAL RELEX AND OUTCOME

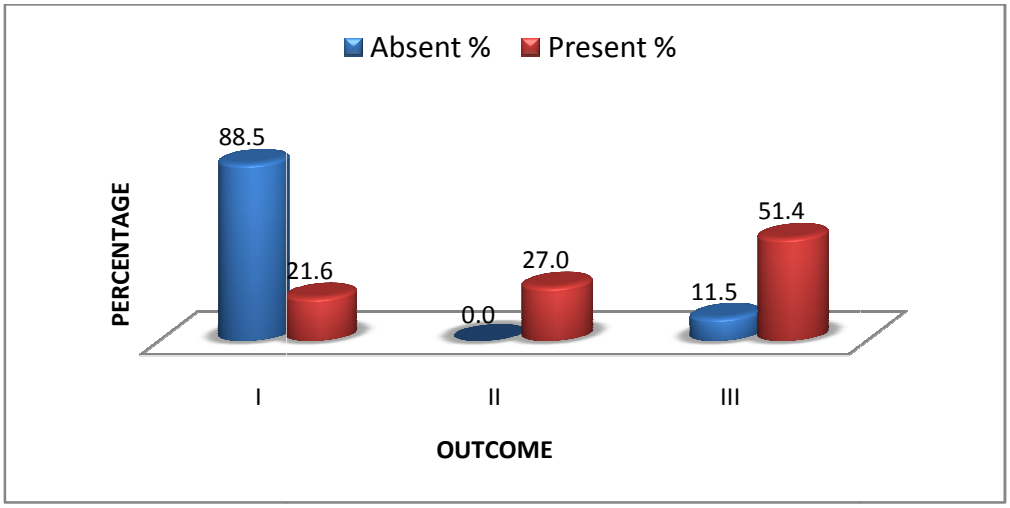
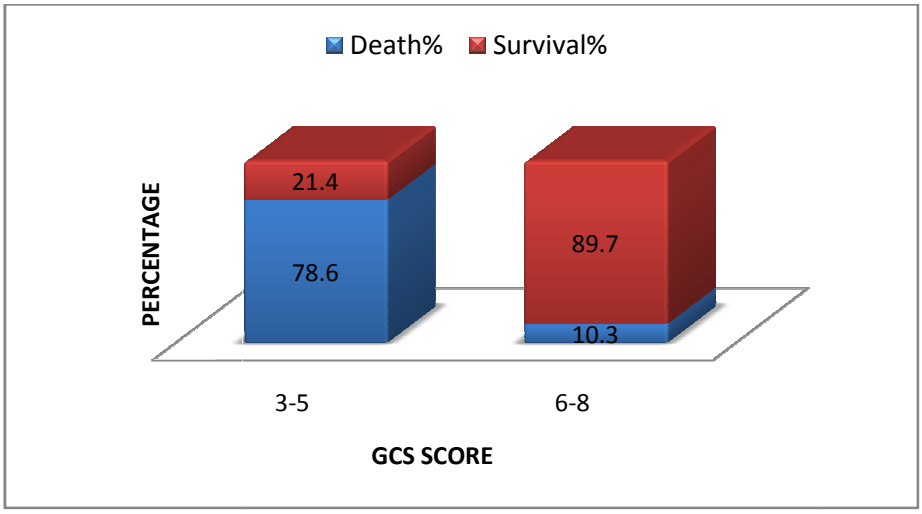


TABLE 16: GCS SCORE AND OUTCOME

GCS score	Total	I	II	III
3-5	42	33	2	7
6-8	58	6	18	34

This table shows the relation of GCS scores at the time of presentation to the outcome of coma. This has been divided into two groups: 3-5 & 6-8. The group of patients whose GCS score was 3 – 5 at admission suffered maximum mortality in comparison to the group of patients with a score 6 – 8. 78.6% of patients with GCS score 3 – 5 died in this study. Those who survived in spite of poor GCS score were due to hypoglycaemia, status epilepticus, sub arachnoid hemorrhage and drug over dosage/poisoning. p value was < 0.0001 for the association between poor GCS score and death (X^2 = 47.66).

FIGURE 20: GRAPH SHOWING GCS SCORE AND OUTCOME



DISCUSSION

Coma is one of the common problems in medical emergency ward. The overall prognosis of coma in any part of the world is generally poor as confirmed by several studies. Multicentre large prospective studies are being reported from developed countries to define the prognosis in coma and studies are being continued to determine the therapeutic interventions needed to improve the prognosis of coma.

AGE AND GENDER

Out of the studied 100 cases 56 were males and 44 were females. There was nostatistical significance in the difference in mortality rate among males and females.

Analysis of age group showed that majority of the cases appeared in the sixth decade. Age of the patient had no correlation with mortality. However, patients with age more than 50 years were more likely to have a poor outcome in comparison with other groups.

According to some studies, in coma due to head injury, age played an important determinant of outcome, but in studies on non-traumatic coma, age had no effect on outcome.

ETIOLOGY

While analyzing the etiology of coma, this study indicated that intracranial causes (57%) were the most common cause of non - traumatic coma followed by metabolic coma (27%). Drug and poisoning related coma comprised 11%. Miscellaneous causes contributed to 5%.

The present study is on par with Indian studies[36, 37, 38]in which intra cranial causes formed the majority of cases. However hypoxic ischemic was the commonest cause in the western studies[34,35].

TABLE 17: COMPARISON OF ETIOLOGY WITH PREVIOUS STUDIES AND PRESENT STUDY

Causes of Coma%	**Sharma et al** n=50	**Thacker et al** n=200	**Dhamija et al** n=75	**Sacco et al** n=169	**Levy D et al** n=500	**Plum & Posner** n=500	**Present Study** n=100
Intracranial	84.0	57.5	68.0	35.5	38.4	45.2	57.0
Metabolic	16.0	26.0	26.7	21.9	16.4	21.4	27.0
Drug/Poison	0.0	5.0	4.0	6.5	0.0	29.8	11.0

In the present study intracranial causes included cerebrovascular accidents (32%), neuroinfections (18%), neoplasms (4%) and status epilepticus (3%).

Out of 32 cases of cerebrovascular accidents 13 cases were due to infarction, 12 cases were due to intra cerebral hemorrhage, 4 cases due to sub arachnoid hemorrhage and 3 cases due to cerebral venous thrombosis.

Among the risk factors in patients with cerebrovascular accidents, 20 were hypertensives, 7 had diabetes mellitus, 11 had dyslipidemia and 6 of them had prior CVA.

There were 3 cases of cerebral venous thrombosis of which 2 were puerperium related and 1 due to poly substance abuse. Alain Ameri reported that CVT was more commonly

prevalent in women between 20-35 years. This is probably related to specific causes like pregnancy and oral contraceptive use in young women.

There were 18 cases of neuroinfections of which 6 cases had bacterial meningo encephalitis, 4 cases each of tuberculous meningitis and cerebral malaria, 3 cases of viral encephalitis and 1 case of neurocysticercosis.

There were 4 cases of intracranial neoplasms and 3 cases of status epilepticus.

Out of 27 patients with metabolic causes of coma 9 had hepatic coma. 7 of them had alcoholic liver disease and 2 had hepatitis B virus related liver disease. 6 patients with hepatic coma had prior upper gastrointestinal bleeding, hence it is one of the precipitating factors of hepatic coma.

Among 6 patients with uremic encephalopathy, 4 were due to diabetic nephropathy.1 patient had post renal failure due to hydroureteronephrosis secondary to carcinoma cervix and the other patient had SLE nephritis.

The other causes of metabolic coma were hypoxia, hypercapnia, hypoglycaemia, hyponatremia and diabetic ketoacidosis.

Among 11 patients with drugs and toxins as the cause for coma, 5 were due to drug overdosage – mostly sedatives, antidepressants, antipsychotics and antiepileptics.

The other causes of coma were due to sepsis, hypertensive encephalopathy and myxedema coma.

The high incidence of hepatic coma in our study is perhaps due to increased prevalence of alcohol consumption leading to alcoholic liver disease. The incidence of intra cranial

neoplasms being high when compared to other series probably reflects increased referral of such cases to our centre due to its tertiary level of care. CVA is the leading cause of non-traumatic coma in our study and also in various other studies.The present study is akin to Indian studies and the various causes of coma are comparable with Indian studies.

ETIOLOGY AND OUTCOME

The relation of cause of altered sensorium to outcome in the present series has been outlined in table showing etiology and outcome.There was higher mortality (42.1%) in patients with coma due to intracranial causes. Among the individual etiologies maximum mortality was in those with intra cranial neoplasms (75%) followed by CVA (53%); although the maximum number of patients who died was those with CVA especially hemorrhage since the incidence of CVA was much higher than neoplasms. The next etiology with higher mortality was metabolic coma (41%); much less than CVA and neoplasms. Coma due to infections (24%), drugs & toxins (18%) and others (20%) had less mortality.

Cerebrovascular Accident

Presence of any degree of altered sensorium substantially reduces the chance of a good outcome of patients with ischemic stroke and a poor chance of outcome in patients with cerebral hemorrhage.

Jones and Milliken noted that addition of altered sensorium with hemiplegiaincreased the mortality from 2 to 41%[39].Oxbury, Greenhall and Gainger found that any alteration in consciousness with ischemic stroke predicted at least 30% mortality[40].

In present series among 12 cases of cerebral hemorrhage 9 died with mortality of 75% and among 13 cases of ischemic stroke, only 4 died with mortality of 31%.

Level of consciousness is of major importance in anticipating outcome from subarachnoid hemorrhage. According to Richardson the mortality in the first 6 months is 29% for alert patients, 55% for drowsy patients, 71% for stuporous patients, and 90% for patients in coma. Age is important, young and alert patients have mortality one third that of elderly (McKissock et al)[40].In the present series, of the 4 patients who had SAH with altered sensorium at the time of presentation 3 died with a mortality of 75%.

Metabolic coma

Preserved pupillary light reflexes along with deep coma should alert the physician to a possible metabolic coma.In comparison with intracranial causesmetabolic coma carried better prognosis in our study.

Mortality among patients with metabolic causes of coma was intermediate between those with CVA and other causes (41%).Much of the mortality among metabolic causes was due to hepatic coma (45%).

In patients with cirrhosis and hepatic encephalopathy, the outlook is poor if the patient has ascites, jaundice and low serum albumin – all indicative of liver cell failure. The survival probability of cirrhotic patients after the first episode of acute hepatic encephalopathy is 42% at 1 year and 23% at 3 years[42].

Infections

Deep stupor or coma in infections like bacterial meningitis, viral encephalitis carries mortality of 50% or higher (Baird et al Dodge). But attention has to be given to the virulence of the organism and delay in beginning of effective treatment along with neurologic details. Correlations between altered state of consciousness, the presence of other neurological

abnormality, and outcome are difficult to deduce from published reports on fungal and viral infection of the nervous system[43].

In the present series among those with infections and coma the mortality was 24%. Among those who died were 2 patients who had tuberculous meningitis. Both of them were people living with HIV-AIDS.

Drugs and toxins

Best recoverywas noted in those with drug induced coma. So drug induced coma can be taken as an independent predictor of outcome. Sacco et al also found thatdrug related etiology of coma was an independent predictor of favourable outcome[35].

Among all etiologies this group had the lowest mortality being 18% in our study. Only 2 patients died in this group and both of them died due to poisonous snake envenomation. One was due to neurotoxic snake bite with respiratory paralysis and the other due to hemotoxic snake bite with acute kidney injury.

Levels of serum creatinine concentration on admission, vomiting, and neurotoxicity after the snake bite were strong predictors of mortality among in-hospital patients.In a study, of the 16 patients with an admission creatinine concentration of more than 2 mg/dl, eight died[44].

BRAINSTEM REFLEXES AND OUTCOME

Presence or absence of brainstem reflexesat admission is one of the most important variates found useful in the prediction of outcome of non-traumatic coma.

The relation of neuroophthalmologic signs like oculocephalic response, pupillary and corneal reflexes have been shown in table 13, 14 & 15. It is apparent from the tables that absence of any of these is a poor prognostic indicator .The absence of oculocephalic, pupillary and corneal reflexes suggested poor prognosis with a mortality of 95.8%, 92% and 88.5% respectively. 23 patients with absent oculocephalic, pupillary and corneal reflex had a mortality of 100%.

In Levi et al's series, 120 out of 500 had similar findings, and only one of them regained consciousness to die 2 weeks later. Thus the accuracy of predictability of death increases when combination of signs rather than when single clinical sign is used. Absent pupillary and corneal reflexes 6 hours after the onset of coma is associated with universal fatality[34].

In Sharma et al's study of prognosis in non- traumatic coma, 91% of patients with absent OVR died and 93% of patients with absent OCR died. None of the patients with absence of any two brain stem reflexesmade good recovery[37].

GCS SCORE AND OUTCOME

One among the useful guides to initial severity of coma is the depth and durationof coma, and it is to record this that the Glasgow coma scoring evolved. The severity of coma at the time of admission has been assessed by Glasgow coma scale in this study.The GCS scoring was done tilldischarge or the time of death in the hospital and their outcome was graded and recorded into 3 categories:I – Death, II - Recovery with functional disability, III - Good

recovery. The GCS score at the time of admission was between 3 and 8 in this study. As done in other studies the severity of comawas categorizedinto two groups, 3-5 and 6-8. The mortality among patients with GCS score of 3-5 was 78.6% while it was only 10.2% in those with 6-8. Thus there was an inverse relation of mortality to GCS score.

All 6 patients with a score of 3 died implying 100% mortality. 5 of these cases had an intra cerebral bleed and 1 was a case of cerebral venous thrombosis. In 18 cases with GCS score 4, two patients survived. Both the cases were due to drug over dosage. None of the patients in the CVA group could achieve recovery with low GCS.

In a study done by Sacco et al, patients with GCS score of 6 to 8 were 7 times more likely to recover than those with a score of 3 to 5.In the same study, the two week outcome for 88 patients with an initial GCS score of 3 to 5 was 85.2% death or in persistent coma. Among those with GCS of 6 to 8, 46.9% were dead or in persistent coma[35].

In another study on patients with acute meningitis (bacterial or unknown origin)96% of them with a GCS above 12 had a chance of complete recovery and only 15% in those with GCS less than or equal to 8[45].

The following table shows other studies with their results of outcome of coma in relation to GCS scoring which is similar to our study with 78.6% mortality in the group 3-5.

TABLE 18: GCS SCORE AND OUTCOME IN PREVIOUS STUDIES AND PRESENT STUDY

Studies	GCS score at admission	Death %	Survival %
1. Sacco RL	3-5	85.2	14.8
2. Dhamija	3-6	84.0	16.0
3. Thacker	<4	75.0	25.0
4. Present	3-5	78.6	21.4

CONCLUSION

- Out of 100 cases of non-traumatic coma, there were 56 males and 44 females. The difference in mortality among males and females was not statistically significant.
- The age group ranged from 17 years to 82 years. Maximum numbers of cases were in the age group of 60 - 70 years. Age group and the outcome of coma are not statistically significant. However, patients with age more than 50 years were more likely to have a bad outcome in comparison with the other groups. This may be due to increased occurrence of cerebrovascular accidents (CVA has high mortality in this study) and additional risk factors like diabetes mellitus, hypertension and coronary artery disease which contributed to higher mortality in patients of age more than 50 years.
- The onset of coma was divided into abrupt and gradual. Cerebrovascular causes, drug/toxin induced, status epilepticus and hypoglycaemia comprised most of the abrupt onset coma. Onset of coma is not statistically associated with outcome.
- Cerebrovascular accidents (32%) formed the majority of cases followed by metabolic causes (27%), infections (21%), drug/poisoning induced (10%) and intra cranial neoplasms (4%).In the present study 23 different etiologies causing non-traumatic comawere observed.
- Mortality was highest in intracranial causes group, which comprised of cerebrovascular causes, neuroinfections, intra cranial neoplasms and status epilepticus. Drug/ toxin induced coma carried the best prognosis and thus was an independent predictor of outcome.

- Absent brainstem reflexes, abnormalities of respiration and abnormal eye movements were significantly associated with poor outcome.
- The group of patients who had GCS score of3-5 at the time of admission suffered the maximum mortality, in comparison with the group of patients with GCS score of 6-8. Thus there was an inverse relationship of mortality with GCS score which was statistically significant.
- Results of this study demonstrate that an early indication of prognosis can be made from the combination of the GCS score, brainstem reflexes and etiologic subtype of coma. As the costs of intensive care have risen up dramatically, factors that provide early prognostic information can aid in decisions about the allocation of resources. Knowing the predicted probability of outcome may assist in clinical therapeutic decisions.

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ANNEXURES

KEY TO PROFORMA

DM – Diabetes mellitus

HT – Hypertension

CAD – Coronary artery disease

TB – Tuberculosis

COPD – Chronic obstructive pulmonary disease

TC – Total count

DC – Differential count

ESR – Erythrocyte sedimentation rate

PCV – Packed cell volume

RBC – Red blood corpuscles

AST – Aspartate amino transferase

ALT – Alanine amino transferase

ALP – Alkaline phosphatase

QBC – Quantitative buffy coat

ECG – Electrocardiogram

CT – Computed tomography

KEY TO MASTER CHART

M – Male

F - Female

P – Present

A – Absent

AB – Abrupt

GR – Gradual

STD – Sexually transmitted disease

HT – Hypertension

DM – Diabetes mellitus

CAD – Coronary artery disease

TB – Tuberculosis

VP – Ventriculo peritoneal

COPD – Chronic obstructive pulmonary disease

BA – Bronchial asthma

CVA – Cerebro vascular accident

CKD – Chronic kidney disease

RHD – Rheumatic heart disease

N - Normal

CNH – Central neurogenic hyperventilation

GCS – Glasgow Coma Scale

DCRB – Decerebrate

RC – Roving conjugate

RDC – Roving dysconjugate

CDR – Conjugate deviation to right

CDL - Conjugate deviation to left

HR – Hypertensive retinopathy

DR – Diabetic retinopathy

P – Papilledema

MS – Mitral stenosis

MR – Mitral regurgitation

PHT – Pulmonary hypertension

AF – Atrial fibrillation

Creps – Crepitations

CL – Clinical and by exclusion

CBC – Complete blood count

RFT – Renal function test

LFT – Liver function test

RBS – Random blood sugar

PT – Prothrombin time

INR - International normalised ratio

ABG – Arterial blood gas analysis

MP – Malarial parasite

QBC - Quantitative buffy coat

C/S – Culture and sensitivity

HBsAg – Hepatitis B antigen

HIV – Human immunodeficiency virus

ELISA - Enzyme linked immunosorbent assay

CSFA – Cerebro spinal fluid analysis

CT – Computed tomography

MRI – Magnetic resonance imaging

CXR – Chest X ray

USG – Ultrasonography

ECG – Electrocardiography

ECHO – Echocardiography

EEG - Electroencephalogram

MCA – Middle cerebral artery

PCA – Posterior cerebral artery

ICH – Intra cerebral haemorrhage

IVE – Intra ventricular extension

SAH – Sub arachnoid haemorrhage

CVT – Cerebral venous thrombosis

DCLD – Decompensated liver disease

OP – Organo phosphorous

HBV – Hepatitis B virus

PLWHA – People living with HIV - AIDS

TBM – Tuberculous meningitis

DCM – Dilated cardiomyopathy

HUN – Hydro urereronephrosis

DIC – Disseminated intra vascular coagulation

PT – Pulmonary tuberculosis

AKI – Acute kidney injury

PROFORMA

NAME:
AGE:
SEX:
IP NO:

ADDRESS:
OCCUPATION:
SOCIOECONOMIC STATUS:
EDUCATION:
DOA:
DOD/DEATH:

DIAGNOSIS:

OUTCOME: I/II/III

I – Death

II – Recovery with functional disability

III – Good recovery

HISTORY:

1. Loss of consciousness : Onset / Duration/ Progress
2. Preceding complaints :
   (a) Headache – Onset/ Duration/Site
   (b) Nausea & vomiting - Duration / Frequency/ Nature
   (c) Convulsions - Duration /Frequency/ Nature
   (d) Neck pain and stiffness
   (e) Visual disturbances - Photophobia/ Diplopia/Blurring of vision
   (f) Speech disturbances
   (g) Vertigo & dizziness
   (h) Focal weakness
   (i) Bowel & bladder disturbances
3. Psychiatric history :
4. Access to drugs & poisons :

5. Systemic illnesses :

   DM Seizures/ neurological disorder

   HT Renal disorder

   CAD Hepatic disorder

   Dyslipidemia Endocrine disorder

   TB / Bronchial asthma / COPD

6. Recent head injury
7. Others

PAST HISTORY: Any similar attacks

Any major illnesses

PERSONAL HISTORY: Diet – vegetarian/ mixed Marital status

Appetite Pre/extra marital contact

Sleep

Bowel

Micturition

Habits – Smoking/Alcohol/Tobacco/ Drug addictions/ Others

OBSTETRIC & GYNAECOLOGY HISTORY:

TREATMENT HISTORY:

FAMILY HISTORY:

CLINICAL EXAMINATION:

GENERAL EXAMINATION:

Appearance	Neck	Pallor
Built	Skin & nails	Icterus
Nutritional status	Evidence of trauma or drug ingestion	Cyanosis
Oral cavity	Others	Clubbing
Ear/ Nose/ Throat		Pedal edema
Eyes		Lymphadenopathy

VITALS:

1. Pulse
2. Blood pressure
3. Respiratory rate Pattern
4. Temperature

SYSTEMIC EXAMINATION:

CENTRAL NERVOUS SYSTEM:

1. HIGHER MENTAL FUNCTIONS – GLASGOW COMA SCALE

Verbal response		Eye opening		Motor response	
Oriented	5	Spontaneous	4	Obeying	6
Confused	4	To noise	3	Localizing	5
Inappropriate	3	To pain	2	Withdrawal	4
Incomprehensible	2	None	1	Flexor	3
None	1			Extensor	2
				None	1

2. CRANIAL NERVES

Oculo cephalic reflex	
Corneal reflex	
Pupillary reflex	
Spontaneous eye movements	
Fundus	

3. SPINO MOTOR SYSTEM

	Right	Left
a) Bulk		
b) Tone		
c) Power		
d) Deep tendon reflexes		
e) Superficial reflexes		
f) Primitive reflexes		
g) Involuntary movements		

4. SENSORY SYSTEM
5. CEREBELLUM
6. NECK STIFFNESS / RIGIDITY
7. SKULL
8. SPINE

OTHER SYSTEM EXAMINATION:

CARDIOVASCULAR SYSTEM

RESPIRATORY SYSTEM

GASTROINTESTINAL SYSTEM

INVESTIGATIONS

1. COMPLETE BLOOD COUNT:

    TC

    DC

    ESR

    Hemoglobin

    PCV

    Platelets

    RBC count

2. RENAL FUNCTION TEST:

    Sugar

    Urea

    Creatinine

    Electrolytes

3. LIVER FUNCTION TEST:

    Serum bilirubin

    Indirect bilirubin

    AST

    ALT

    ALP

    Total proteins

    Serum albumin

4. PERIPHERAL SMEAR OR QBC FOR MALARAIAL PARASITES:

5. URINE EXAMINATION :

    Albumin

    Sugar

    Deposits

    Ketone

    Bile salts / pigments

6. ECG
7. X ray chest
8. CT Brain
9. Cerebrospinal fluid examination
10. Others

SUMMARY OF CLINICAL AND LAB DIAGNOSIS:

FINAL DIAGNOSIS:

TREATMENT GIVEN:

FINAL OUTCOME:

MASTER CHART

Serial no	Name	Age	Sex	Onset	Headache	Vomiting	Fever	Convulsions	Speech disturbances	Vertigo	Neck pain	Neuro deficit	Jaundice	GI Bleed	Drug overdose/poisoning	Smoking	Alcoholism	Exposure to STD's	HT	DM	CAD	Dyslipidemia	TB	COPD	BA	Epileptic	Old CVA	Liver disease	CKD	RHD	Recently delivered	Fever	Icterus	Respiratory pattern	GCS on admission
1	Mrs.Savithiriammal	65	F	AB	P	P	A	P	A	A	A	P	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	CNH	3
2	Mr.Mani	58	M	AB	A	A	A	A	P	A	A	P	A	A	A	P	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	N	7
3	Mr.Senthil kumar	20	M	GR	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Post TBM on VP shunt	A	A	A	A	A	A	A	P	A	N	6
4	Mrs.Gnanammal	80	F	GR	A	P	A	A	A	A	A	A	A	A	A	A	A	A	P	P	P	P	A	A	A	A	A	A	P	A	A	A	A	Acidotic	4
5	Mr.Anbazhagan	50	M	GR	A	P	P	A	A	A	A	A	P	P	A	P	P	P	A	A	A	A	A	P	A	A	A	P	A	A	A	P	P	Periodic	4
6	Ms.Pavithra	17	F	GR	P	P	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	N	7
7	Mr.Kanagadurai	19	M	AB	A	A	P	A	A	A	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	Shallow	4
8	Mr.Gopi	42	M	AB	P	P	A	A	A	A	A	P	A	A	A	P	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	7
9	Mr.Lurdhraj	19	M	GR	P	P	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	N	7
10	Mrs.Dafnet	70	F	GR	A	P	P	A	A	A	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	P	A	A	A	A	P	A	N	6
11	Mr.Kumar	35	M	AB	A	P	A	A	A	A	A	A	A	A	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Shallow	6
12	Mr.Mari	45	M	AB	P	P	A	A	P	P	A	P	A	A	A	P	P	A	P	P	A	P	A	A	A	A	A	A	A	A	A	A	A	N	6
13	Mr.Balasubramani	60	M	AB	P	P	A	P	A	A	A	P	A	A	A	P	A	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	A	Periodic	4
14	Mr.Elumalai	60	M	GR	A	P	A	A	A	A	A	A	P	P	A	P	P	A	A	P	A	A	A	A	A	A	A	P	A	A	A	A	P	Periodic	4
15	Mrs.Kanaga	32	F	GR	P	P	P	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	N	7
16	Mrs.Gangammal	65	F	AB	P	P	A	P	P	A	A	P	A	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	Ataxic	5
17	Mrs.Manonmani	63	F	AB	A	A	A	A	P	P	A	P	A	A	A	A	A	A	P	P	A	P	PulmonaryTB	A	A	A	P	A	A	A	A	A	A	N	6
18	Mr.Balakrishnan	55	M	AB	P	A	A	A	A	A	A	P	A	A	A	P	P	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	A	N	6
19	Mr.Chengalrajan	70	M	AB	P	P	A	A	P	P	A	P	A	A	A	A	A	A	A	P	P	P	A	A	A	A	A	A	A	A	A	A	A	N	7
20	Mr.Subasridoss	44	M	GR	A	P	P	A	A	A	A	A	P	A	A	P	P	P	A	A	A	A	A	P	A	A	A	P	A	A	A	P	P	N	7
21	Mrs.Yasodhammal	63	F	GR	P	P	P	A	A	A	P	A	A	A	A	A	A	A	A	P	A	A	A	A	P	A	A	A	A	A	A	P	A	N	6
22	Mrs.Jeyalakshmi	58	F	GR	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	P	A	A	A	A	A	A	P	A	A	A	A	N	7
23	Mr.Sarangan	39	M	GR	P	P	A	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	7
24	Mr.Thanveer	18	M	AB	A	P	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Shallow	7
25	Mrs.Kala	62	F	AB	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	P	A	A	A	A	A	A	P	A	A	A	A	Periodic	5
26	Mr.Kuselan	47	M	GR	A	A	P	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	P	P	N	7
27	Mr.Gopal	65	M	AB	P	P	P	P	A	A	P	A	A	A	A	P	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	P	A	Periodic	4
28	Mrs.Thangamani	45	F	GR	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	N	7
29	Mrs.Lakshmi	65	F	GR	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	P	A	N	6
30	Mrs.Mary	80	F	AB	P	P	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	P	A	A	A	A	P	A	A	A	A	A	A	CNH	3
31	Mrs.Latha	35	F	AB	P	A	A	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	N	7
32	Mr.Manohar	59	M	AB	P	P	A	A	A	P	P	A	A	A	A	P	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	5
33	Mr.Jagan	39	M	AB	P	A	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	Hyperventilation	5
34	Mr.Arjunan	33	M	GR	P	P	P	P	A	A	A	A	A	A	A	P	P	P	A	A	A	A	PulmonaryTB	A	A	A	A	P	A	A	A	P	A	Periodic	4
35	Mrs.Manonmani	63	F	AB	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	P	A	A	A	A	P	A	A	A	A	A	A	Periodic	5
36	Mr.Sakthivel	25	M	AB	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	4
37	Mr.Subramani	70	M	AB	A	P	A	A	P	P	A	A	A	A	A	A	A	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	N	8

Serial no	Posturing	Oculo cephalic reflex	Corneal reflex	Pupillary reflex	Spontaneous eye movements	Fundus	Muscle tone	Deep tendon reflexes	Neck rigidity	CVS	RS	Abdomen
1	DCRB	A	A	A	A	HR	Decreased	Absent	A	N	Creps	N
2	N	P	P	P	CDR	N	Decreased	Sluggish	A	N	N	N
3	N	P	P	P	RC	P	Normal	Normal	A	N	Creps	N
4	N	P	P	P	RC	DR	Normal	Absent	A	N	Creps	N
5	DCRB	P	P	P	RC	N	Increased	Exagggerated	A	N	Rhonchi	Ascites, Splenomegaly
6	N	P	P	P	RC	N	Normal	Normal	P	N	N	N
7	N	A	A	A	A	N	Decreased	Absent	A	N	Creps	N
8	N	P	P	P	CDL	HR	Increased	Exagggerated	A	N	N	N
9	N	P	P	P	RC	N	Normal	Normal	P	N	N	N
10	N	P	P	P	RC	DR	Normal	Normal	A	N	Creps	N
11	N	P	P	P	RC	N	Normal	Normal	A	N	Creps	N
12	N	P	P	P	CDR	P	Decreased	Sluggish	A	N	Creps	N
13	N	A	A	A	CDL	P	Decreased	Absent	A	N	Rhonchi	N
14	N	A	A	A	A	N	Decreased	Sluggish	A	N	N	Ascites, Splenomegaly,dilated veins
15	N	P	P	P	RC	N	Normal	Normal	A	N	N	Splenomegaly
16	DCRB	A	A	A	CDL	P	Decreased	Sluggish	A	N	Creps	N
17	N	P	P	P	CDL	N	Increased	Exagggerated	A	N	N	N
18	N	P	P	P	CDL	HR	Increased	Exagggerated	A	N	Rhonchi	N
19	N	P	P	P	CDR	N	Decreased	Sluggish	A	N	N	N
20	N	P	P	P	RC	N	Increased	Exagggerated	A	N	Rhonchi	Ascites, Splenomegaly
21	N	P	P	P	RC	N	Normal	Normal	P	N	Rhonchi	N
22	N	P	P	P	RC	DR	Normal	Sluggish	A	N	Creps	Ascites
23	N	P	P	P	CDR	P	Normal	Normal	A	N	N	Hepatomegaly
24	N	P	P	P	RC	N	Normal	Normal	A	N	Creps	N
25	N	P	P	P	RC	DR	Normal	Sluggish	A	N	N	N
26	N	P	P	P	RC	N	Normal	Exagggerated	A	N	N	Ascites,Hepatomegaly, Splenomegaly
27	N	A	A	A	A	N	Normal	Exagggerated	P	N	Creps	N
28	N	P	P	P	RC	N	Normal	Normal	A	N	Creps	N
29	N	P	P	P	RC	DR	Normal	Sluggish	A	N	N	N
30	DCRB	A	A	A	A	P	Decreased	Absent	A	N	Creps	N
31	N	P	P	P	CDL	N	Increased	Exagggerated	A	MS,	Creps	N
32	N	P	P	P	RC	N	Normal	Normal	P	N	N	N
33	N	P	P	P	RC	N	Decreased	Sluggish	A	N	N	N
34	N	A	A	A	A	N	Normal	Normal	P	N	Creps	Hepatomegaly
35	N	P	P	P	RC	DR	Normal	Sluggish	A	N	N	N
36	N	P	A	P	RC	N	Decreased	Sluggish	A	N	N	N
37	N	P	A	A	CDL	N	Decreased	Sluggish	A	N	Creps	N

Serial no	Diagnostic investigations	Diagnosis	Outcome
1	CT - Brainstem hemorrhage	ICH	I
2	CT - Left massive MCA infarct	Infarct	III
3	CT - Hydrocephalus	Post TBM Sequelae - Shunt dysfunction	II
4	RFT,ABG	CKD - Uremic encephalopathy	I
5	LFT, USG	DCLD - Ethanol related - Hepatic encephalopathy	I
6	CSFA	Bacterial meningitis	III
7	CL	Snake bite - neurotoxic envenomation	I
8	CT - Right gangliocapsular hemorrhage	ICH	II
9	CSFA	Bacterial meningoencephalitis	III
10	RFT	Hyponatremia	III
11	Gastric lavage analysis,CL	OP poisoning	II
12	CT - Right massive MCA infarct	Infarct	II
13	CT - Right gangliocapsular hemorrhage/IVE	ICH	I
14	LFT, USG	DCLD - Ethanol related - Hepatic encephalopathy	I
15	MP QBC	Cerebral malaria	III
16	CT - Left massive MCA infarct,Midline shift	Infarct	I
17	CT - Right MCA infarct	Infarct	II
18	CT - Right gangliocapsular hemorrhage	ICH	II
19	CT - Right MCA infarct	Infarct	II
20	LFT, USG	DCLD - Ethanol related - Hepatic encephalopathy	III
21	CSFA,MRI	Viral meningoencephalitis	II
22	RFT,ABG	CKD - Uremic encephalopathy	III
23	CT,MRI	Left brain tumor - Astrocytoma	II
24	CL	OP poisoning	II
25	RBS	Hypoglycemic coma	III
26	LFT, USG,HBsAg	DCLD -HBV related - Hepatic encephalopathy	III
27	CSFA	Bacterial meningoencephalitis	I
28	RFT,ABG	CKD - Uremic encephalopathy	III
29	RFT,ABG,Urine acetone	Diabetic keto acidosis	III
30	CT - Brainstem hemorrhage	ICH	I
31	CT - Left MCA infarct,ECG - AF,ECHO	Infarct	II
32	CT,MRI	SAH	III
33	CL,EEG	Status epilepticus	III
34	CSFA,HIV ELISA	PLWHA,TBM	I
35	RBS	Hypoglycemic coma	II
36	CL	Drug overdosage - Antidepressants,Sedatives	III
37	CT,MRI - Right lateral medullary infarct	Infarct	III

Serial no	Name	Age	Sex	Onset	Headache	Vomiting	Fever	Convulsions	Speech disturbances	Vertigo	Neck pain	Neuro deficit	Jaundice	GI Bleed	Drug overdose/poisoning	Smoking	Alcoholism	Exposure to STD's	HT	DM	CAD	Dyslipidemia	TB	COPD	BA	Epileptic	Old CVA	Liver disease	CKD	RHD	Recently delivered	Fever	Icterus	Respiratory pattern	GCS on admission
38	Mr.Adam Sheriff	65	M	AB	P	P	P	P	A	A	A	A	P	A	A	A	P	A	A	P	A	A	A	P	A	A	A	A	A	A	A	P	P	Acidotic	4
39	Mrs.Vanitha	25	F	AB	P	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	Hyperventilation	3
40	Mr.Vinayagam	35	M	GR	A	P	P	A	A	A	A	A	P	A	A	P	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	P	P	N	7
41	Mr.Malliga arjunan	35	M	AB	P	P	A	A	A	P	A	P	A	A	A	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	7
42	Mr.Ganesan	52	M	GR	P	P	P	A	A	A	A	A	P	A	A	A	P	A	A	A	P	A	A	A	A	A	A	P	A	A	A	P	P	Periodic	5
43	Mr.Velu	58	M	AB	A	P	P	A	A	A	A	A	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	Shallow	7
44	Mr.Manikathambi	80	M	AB	P	P	A	P	A	A	A	A	A	A	A	A	A	A	P	A	A	P	PulmonaryTB	A	A	A	P	A	A	A	A	A	A	CNH	3
45	Mr.Ramachandran	48	M	AB	P	P	A	P	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Hyperventilation	7
46	Mr.Selvam	28	M	AB	P	P	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Ataxic	4
47	Mr.Suresh	64	M	GR	A	P	P	A	A	A	A	A	A	A	A	P	P	A	A	P	P	P	A	A	A	A	A	A	P	A	A	P	A	Acidotic	5
48	Mr.Murugan	23	M	GR	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	P	A	N	7
49	Mr.Gurunathan	32	M	GR	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	Periodic	8
50	Mrs.Saradha	80	F	GR	A	P	P	A	A	A	A	A	A	A	A	A	A	A	P	P	A	P	A	A	P	A	A	A	P	A	A	P	A	Acidotic	6
51	Mrs.Andaal	50	F	AB	P	A	A	A	P	A	A	P	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	7
52	Mrs.Shantha	86	F	GR	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	P	A	A	A	A	A	A	A	P	A	Tachypneic	5
53	Mr.Ramesh	17	M	AB	A	P	A	A	A	A	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Shallow	7
54	Mr.Kumar	45	M	AB	A	A	A	A	A	A	A	P	A	A	A	P	P	A	P	A	P	P	A	A	A	A	A	A	A	A	A	A	A	CNH	6
55	Ms.Nithya	22	F	AB	A	A	A	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	Periodic	6
56	Mr.Chinnapaiyan	38	M	GR	P	P	P	P	A	A	A	P	A	A	A	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	Periodic	4
57	Mr.Perumal	60	M	AB	A	P	A	A	A	A	A	A	P	P	A	P	P	A	A	A	A	A	A	P	A	A	A	P	A	A	A	A	P	Periodic	5
58	Mrs.Manonmani	60	F	GR	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	Hyperventilation	5
59	Mrs.Saroja	43	F	GR	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	N	8
60	Mrs.Shahitha Begum	33	F	AB	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Shallow	5
61	Mrs.Sarojammal	73	F	GR	A	P	P	A	A	A	A	A	P	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	P	P	Acidotic	4
62	Mr.Ganapathi	54	M	AB	A	A	A	A	P	A	A	P	A	A	A	P	P	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	N	7
63	Mrs.Lakshmiammal	78	F	GR	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	P	A	N	6
64	Mrs.Mala	41	F	GR	P	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	Periodic	4
65	Mr.Jayaraman	70	M	AB	P	P	A	A	A	A	A	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	CNH	3
66	Mr.Durairaj	65	M	AB	P	P	A	A	A	A	A	P	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	Ataxic	5
67	Mrs.Ragammaal	65	F	GR	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	A	N	7
68	Mrs.Ramya	29	F	AB	P	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	P	A	A	N	7
69	Mr.Vembuli	70	M	GR	A	A	A	A	A	A	A	A	A	A	A	P	P	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	Shallow	6
70	Mrs.Selvi	63	F	AB	P	A	A	A	A	P	A	A	A	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	N	8
71	Mr.Kanagammal	54	F	GR	A	P	P	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	P	N	6
72	Mrs.Jeya	70	F	GR	A	P	A	A	A	A	A	A	A	A	A	A	P	A	A	P	P	P	A	A	A	A	A	A	P	A	A	A	A	Acidotic	7
73	Mrs.Gnanammal	82	F	AB	P	P	A	P	P	A	A	P	A	A	A	A	A	A	P	A	A	A	A	A	A	A	P	A	A	A	A	A	A	CNH	3
74	Mr.Unnikrishnan	40	M	AB	A	P	A	A	A	A	A	A	A	P	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Periodic	5

Serial no	Posturing	Oculo cephalic reflex	Corneal reflex	Pupillary reflex	Spontaneous eye movements	Fundus	Muscle tone	Deep tendon reflexes	Neck rigidity	CVS	RS	Abdomen
38	N	P	P	P	RC	N	Decreased	Sluggish	A	N	Rhonchi	Splenomegaly
39	DCRB	A	A	A	A	P	Decreased	Absent	A	N	N	N
40	N	P	P	P	RC	N	Normal	Normal	A	N	N	Ascites,Hepatomegaly
41	N	P	P	P	CDL	P	Normal	Normal	A	A	Rhonchi	N
42	N	A	A	A	A	P	Decreased	Sluggish	A	N	N	Ascites,Hepatomegaly
43	N	P	P	P	RC	P	Decreased	Sluggish	A	N	Creps	Tender hepatomegaly
44	DCRB	A	A	A	A	HR	Decreased	Absent	A	N	N	N
45	N	P	P	P	RC	P	Normal	Normal	A	N	N	N
46	DCRB	A	A	A	A	P	Normal	Sluggish	P	N	N	N
47	N	P	P	P	RC	DR	Normal	Normal	A	N	N	N
48	N	P	P	P	RC	N	Normal	Normal	P	N	Rhonchi	N
49	N	P	P	P	RC	N	Decreased	Sluggish	A	N	N	N
50	N	P	P	P	RC	DR	Normal	Sluggish	A	N	Rhonchi,creps	Ascites
51	N	P	P	P	CDR	HR	Increased	Exagggerated	A	N	N	N
52	N	A	A	A	RDC	N	Normal	Sluggish	A	N	BB,Rhonchi,Creps	N
53	N	P	P	P	RC	N	Decreased	Sluggish	A	N	Creps	N
54	N	P	P	P	CDR	HR	Normal	Exagggerated	A	S1 V	Creps	N
55	N	P	P	P	RC	N	Increased	Normal	A	N	N	N
56	DCRB	A	A	A	A	P	Decreased	Absent	A	N	Rhonchi,creps	Hepatomegaly
57	N	P	P	P	RC	N	Decreased	Absent	A	N	Rhonchi	Ascites, Splenomegaly
58	N	P	P	P	RC	N	Normal	Sluggish	A	N	Creps	N
59	N	P	P	P	RC	N	Normal	Normal	A	N	N	Splenomegaly
60	N	P	P	P	RC	N	Decreased	Sluggish	A	N	N	N
61	N	P	P	P	RC	N	Decreased	Sluggish	A	N	Creps,decreased breath sounds B/L bases	Ascites,Hepatomegaly,Splenomegaly
62	N	P	P	P	CDL	N	Decreased	Sluggish	A	N	N	N
63	N	P	P	P	RC	N	Normal	Normal	A	N	BB,Rhonchi,Creps	N
64	DCRB	A	A	A	A	P	Decreased	Absent	A	N	Creps	N
65	DCRB	A	A	A	A	HR	Decreased	Absent	A	A	Creps	N
66	N	A	A	A	A	HR	Decreased	Absent	A	Caro	N	N
67	N	P	P	P	RC	N	Normal	Normal	A	N	N	N
68	N	P	P	P	RC	P	Normal	Normal	A	N	Rhonchi	N
69	N	P	P	P	RC	N	Normal	Sluggish	A	N	Absent breath sounds	N
70	N	P	P	P	RC	HR	Normal	Normal	A	N	N	N
71	N	P	P	P	RC	N	Normal	Sluggish	A	N	Decreased breath sounds right base	Ascites, Splenomegaly
72	N	P	P	P	RC	DR	Normal	Sluggish	A	N	Creps	Ascites
73	DCRB	A	A	A	A	P	Decreased	Absent	A	Caro	Creps	N
74	N	P	P	P	RC	N	Decreased	Sluggish	A	N	Rhonchi	Hepatomegaly

Serial no	Diagnostic investigations	Diagnosis	Outcome
38	MP QBC	Cerebral malaria	I
39	CT,MRI	CVT - Postpartum	I
40	LFT,USG	Alcoholic hepatitis - Ethanol related - Hepatic encephalopathy	III
41	CT,MRI	CVT - Polysubstance abuse	II
42	LFT,USG,CT,Liver biopsy	Hepatocellular carcinoma - secondaries brain	I
43	CBC,RFT,LFT,ABG,USG,Pus C/S	Liver abscess - Sepsis	III
44	CT - Brainstem hemorrhage	ICH	I
45	CT,MRI	Neurocysticercosis	III
46	CT,MRI,CT Angiogram - SAH,Aneurysm PCA	SAH	I
47	RFT,ABG,Urine acetone	Diabetic keto acidosis	I
48	CSFA,MRI	Viral meningoencephalitis	III
49	CL	Drug overdosage - Antiepileptics,Sedatives	III
50	RFT,ABG	CKD - Uremic encephalopathy	II
51	CT - Right gangliocapsular hemorrhage	ICH	II
52	CXR,ABG	Pneumonia - Respiratory failure	I
53	CL	Organocarbamate poisoning	III
54	CT - Right MCA infarct,ECHO - Ischemic DCM,Severa LV dysfunction	Infarct	III
55	CL,EEG	Status epilepticus	III
56	CT,MRI	PLWHA,Multiple tuberculoma	I
57	LFT,USG	DCLD - Ethanol related - Hepatic encephalopathy	I
58	RFT,ABG,USG	Carcinoma cervix,HUN - Postrenal failure - Uremic encephalopathy	I
59	MP QBC	Cerebral malaria	III
60	CL	Drug overdosage - Antidepressants,Antipsychotics	III
61	CBC,RFT,LFT,ABG,USG,Fever profile	Leptospirosis - Sepsis,DIC	I
62	CT - Left MCA infarct	Infarct	II
63	RFT,ABG,CXR,Sputum C/S	Hyponatremia	III
64	CT,MRI,Biopsy from breast lesion	Carcinoma breast - secondaries brain	I
65	CT - Brainstem hemorrhage	ICH	I
66	CT - Bilateral medullary infarct, right cerebellar infarct	Infarct	I
67	CSFA	Bacterial meningitis	III
68	CT,MRI	CVT - Postpartum	III
69	CXR,ABG	COPD - Respiratory failure	I
70	CT,CL	HT Encephalopathy	III
71	LFT, USG,HBsAg,PT/INR	DCLD -HBV related - Hepatic encephalopathy,Coagulopathy	III
72	RFT,ABG	CKD - Uremic encephalopathy	III
73	CT - Brainstem hemorrhage	ICH	I
74	RBS,CL	Hypoglycemic coma - Alcohol related	III

Serial no	Name	Age	Sex	Onset	Headache	Vomiting	Fever	Convulsions	Speech disturbances	Vertigo	Neck pain	Neuro deficit	Jaundice	GI Bleed	Drug overdose/poisoning	Smoking	Alcoholism	Exposure to STD's	HT	DM	CAD	Dyslipidemia	TB	COPD	BA	Epileptic	Old CVA	Liver disease	CKD	RHD	Recently delivered	Fever	Icterus	Respiratory pattern	GCS on admission
75	Mr.Sigamani	60	M	GR	P	P	P	A	A	A	A	A	P	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	P	P	N	8
76	Mrs.Chinnamma	35	F	GR	P	P	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	7
77	Mr.Balu	48	M	AB	A	P	A	A	A	A	A	A	P	P	A	P	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	Periodic	4
78	Mr.Murugesan	38	M	AB	P	P	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Ataxic	5
79	Mrs.Lakshmi	39	F	AB	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	N	6
80	Mr.Thangarsu	60	M	GR	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	PulmonaryTB	A	A	A	A	A	A	A	A	P	A	Tachypneic	5
81	Mr.Sudakar	60	M	GR	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	Acidotic	7
82	Mrs.Estherammal	65	F	GR	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	P	A	N	7
83	Mrs.Saradha	58	F	GR	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	P	A	Shallow	5
84	Mr.Perumal	72	M	AB	P	P	A	A	A	A	A	A	A	A	P	P	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	CNH	4
85	Mr.Chandra	56	F	AB	A	A	A	A	P	A	A	P	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	N	7
86	Mrs.Alamelu	42	F	AB	P	P	A	P	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	Periodic	5
87	Mr.Rajith	19	M	AB	P	P	P	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	N	7
88	Mrs.Baby	60	F	AB	P	P	A	A	A	A	A	P	A	A	A	A	A	A	P	A	A	P	A	A	P	A	A	A	A	A	A	A	A	Ataxic	4
89	Mr.Nagaraj	48	M	AB	A	A	A	A	A	A	A	A	A	A	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Shallow	4
90	Mrs.Santhi	50	F	GR	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	P	A	Periodic	6
91	Mr.Dhanapal	75	M	AB	P	P	A	A	P	A	A	P	A	A	A	A	P	A	P	A	A	A	A	A	A	A	P	A	A	A	A	A	A	Hyperventilation	6
92	Mr.Vinayagamurthy	35	M	GR	A	P	P	A	A	A	A	A	P	P	A	P	P	P	A	A	A	A	A	A	A	A	A	P	A	A	A	P	P	Periodic	4
93	Mrs.Vennila	37	F	AB	P	P	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	Ataxic	5
94	Mr.Nizar Ahmed	61	M	AB	A	A	A	A	A	A	A	A	A	A	A	P	P	A	P	A	P	P	A	A	A	A	A	A	A	A	A	A	A	Hyperventilation	8
95	Mrs.Velammal	80	F	AB	P	A	A	P	A	A	A	P	A	A	A	A	A	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	Hyperventilation	6
96	Mr.Sekar	35	M	AB	A	P	A	A	A	A	A	A	A	A	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Shallow	7
97	Mr.Thangaraj	37	M	GR	P	P	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	6
98	Mrs.Vasantha	65	F	AB	P	A	A	P	A	A	A	P	A	A	A	A	A	A	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	Periodic	6
99	Mr.Ravi	35	M	AB	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Periodic	6
100	Ms.Radha	24	F	GR	P	P	P	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	PulmonaryTB	A	A	A	A	A	A	A	A	A	A	N	7

Serial no	Posturing	Oculo cephalic reflex	Corneal reflex	Pupillary reflex	Spontaneous eye movements	Fundus	Muscle tone	Deep tendon reflexes	Neck rigidity	CVS	RS	Abdomen
75	N	P	P	P	RC	N	Normal	Normal	A	N	N	Hepatomegaly,Splenomegaly
76	N	P	P	P	RC	P	Increased	Exagggerated	A	N	N	N
77	N	A	A	A	A	N	Decreased	Absent	A	N	BB,Rhonchi,Creps	Ascites,Splenomegaly
78	N	A	A	A	A	N	Decreased	Sluggish	P	N	N	N
79	N	P	P	P	RC	N	Decreased	Sluggish	A	N	N	N
80	N	P	P	P	RC	N	Normal	Normal	A	N	Decreased breath sounds right hemithorax	N
81	N	P	P	P	RC	N	Normal	Normal	A	N	N	N
82	N	P	P	P	RC	N	Normal	Sluggish	P	N	N	N
83	N	P	P	P	RC	N	Decreased	Absent	A	N	BB,Rhonchi,Creps	N
84	DCRB	A	A	A	A	HR	Decreased	Absent	A	N	Creps	N
85	N	P	P	P	CDL	N	Decreased	Sluggish	A	N	N	N
86	DCRB	P	P	P	RC	N	Decreased	Sluggish	A	N	N	N
87	N	P	P	P	RC	N	Normal	Normal	A	N	N	N
88	DCRB	A	A	A	A	P	Decreased	Absent	A	N	Rhonchi,Creps	N
89	N	A	A	A	RC	N	Decreased	Sluggish	A	N	N	N
90	N	P	P	P	RC	N	Normal	Sluggish	P	N	N	N
91	N	P	P	P	CDL	N	Decreased	Sluggish	A	N	N	N
92	N	A	A	A	A	N	Decreased	Absent	A	N	N	Ascites,Splenomegaly
93	N	P	P	P	RC	P	Decreased	Sluggish	P	N	N	N
94	N	P	P	P	P	HR	Normal	Normal	A	LVS3	Creps,Rhonchi	N
95	N	P	P	P	CDR	P	Decreased	Sluggish	A	N	N	N
96	N	P	P	P	RC	N	Decreased	Sluggish	A	N	Creps	N
97	N	P	P	P	RC	N	Normal	Normal	P	N	N	N
98	N	P	P	P	CDR	P	Increased	Exagggerated	A	N	Rhonchi	N
99	N	P	P	P	RC	N	Decreased	Sluggish	A	N	N	N
100	N	P	P	P	RC	N	Normal	Normal	P	N	N	N

Serial no	Diagnostic investigations	Diagnosis	Outcome
75	CBC,RFT,LFT,ABG,USG,Fever profile	Enteric fever - typhoid encephalothy	II
76	CT,MRI	Right brain tumour- Glioblastoma	I
77	LFT,USG	Alcoholic hepatitis - Ethanol related - Hepatic encephalopathy	I
78	CT,MRI	SAH	I
79	CL	Drug overdosage - Sedatives	III
80	CXR,CT chest,ABG	PT - Massive pleural effusion,respiratory failure	I
81	RFT,ABG,Urine acetone	Diabetic keto acidosis	III
82	CSFA	Bacterial meningitis	III
83	Thyroid function test	Myxedema coma	I
84	CT - Brainstem hemorrhage	ICH	I
85	CT - Left MCA infarct	Infarct	II
86	CL,EEG	Status epilepticus	II
87	MP QBC	Cerebral malaria	III
88	CT - Massive left MCA infarct with midline shift	Infarct	I
89	CL	Drug overdosage - Sedatives	III
90	CSFA,MRI	Viral meningoencephalitis	III
91	CT - Left MCA infarct	Infarct	I
92	LFT,USG	DCLD - Ethanol related - Hepatic encephalopathy	I
93	CT,MRI	SAH	I
94	CXR,ECHO	Acute pulmonary edema - respiratory failure	III
95	CT - Left gangliocapsular hemorrhage/IVE	ICH	I
96	CL	Organocarbamate poisoning	III
97	CSFA,HIV ELISA	PLWHA,Bacterial meningitis	III
98	CT - Left gangliocapsular hemorrhage/IVE	ICH	I
99	PT/INR,CL	Snake bite - hemotoxicenvenomation,AKI	I
100	CSFA,MRI	TBM	II

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No: 04425305301
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CERTIFICATE OF APPROVAL

To
Dr. Kanmani. S
PG in MD General Medicine
Madras Medical College, Chennai -3.

Dear Dr. Kanmani .S

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled "A study on etiology, clinical profile and outcome of Non-Traumatic coma"" No. 04042011.

The following members of Ethics Committee were present in the meeting held on 21.04.2011 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan, MD	-- Chairperson
2.	Prof. V. Kanagasabai MD Dean, Madras Medical College, Chennai-3,	-- Deputy chairman
3.	Prof. A. Sundaram, MD Vice Principal , Madras Medical College, Chennai -3	-- Member Secretary
4.	Prof R. Sathianathan MD	-- Member
5.	Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	-- Member
6.	Prof. Pregna B. Dolia MD Director , Institute of Biochemistry, MMC, Ch-3	-- Member
7.	Prof. C. Rajendiran .MD Director , Institute of Internal Medicine, MMC, Ch-3	-- Member
8.	Thiru. A. Ulaganathan Administrative Officer, MMC, Chennai -3	-- Layperson
9.	Thiru. S. Govindasamy . BA.BL	-- Lawyer
10.	Tmt. Arnold Soulina	-- Social Scientist

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

Sd /. Chairman & Other Members

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

Member Secretary, Ethics Committee