DISSERTATION OF

THE STUDY ON

A CLINICAL PROFILE OF COMA

This dissertation is submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

in partial fulfillment of the requirement of the award

for the degree of

M.D BRANCH 1

GENERAL MEDICINE

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CERTIFICATE

This is to certify that this dissertation entitled **`A CLINICAL PROFILE OF COMA'** submitted by **Dr.SATHYA A.C.** to **THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY, CHENNAI** is in partial fulfillment of the requirement of the award for the degree of M.D Degree[BRANCH 1] in GENERAL MEDICINE and is a bonafide research work carried out by her under direct supervision and guidance.

Signature of the Unit Chief **Signature of the HOD**

Signature of the Dean

DECLARATION

I solemnly declare that the dissertation titled, **'A CLINICAL PROFILE OF COMA'** was done by me at Stanley Medical College hospital during the year 2010 under the guidance and supervision of my unit chief **Prof. Dr.S.MAGESH KUMAR, M.D.**

The dissertation is submitted to **THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY** towards the partial fulfillment of the requirement of the award for the degree of **M.D Degree [BRANCH 1] in GENERAL MEDICINE.**

Place:

Date: **DR.SATHYA A.C.**

ACKNOWLEDGEMENT

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INTRODUCTION

Introduction

Impaired consciousness is among the most difficult and dramatic of clinical problems. The brain tolerates only limited physical or metabolic injury, so that impaired consciousness is often a sign of impending irreparable damage to the brain. Stupor and coma imply advanced brain failure, just as, for example, uremia means renal failure, and the longer such brain failure lasts the narrower the margin between recovery and the development of permanent neurologic injury. The limited time for action and the multiplicity of potential causes of brain failure challenge the physician. The physician must organize available information to anticipate as accurately as possible the likelihood that the patient will either recover or remain permanently disabled. Prospective studies of prognosis in adults and children indicate that within a few hours or days after the onset of coma, neurologic signs and electrophysiologic markers in many patients differentiate, with a high degree of probability, the extremes of no improvement or good recovery. Unfortunately, radiologic and biochemical indicators have generally provided less accurate predictions of outcome, with some exceptions.

AIM

OF THE

STUDY

Aim of the study

To determine the incidence,etiology,and outcome of coma,to determine the commonest causes of coma,to recognize unusual presentations and to assess the prognosis in these patients.

REVIEW

OF

LITERATURE

Coma and other altered states of consciousness

Coma, from the Greek ‘‘deep sleep or trance,’’ is a state of unresponsiveness in which the patient lies with eyes closed and cannot be aroused to respond appropriately to stimuli even with vigorous stimulation. The patient may grimace in response to painful stimuli and limbs may demonstrate stereotyped withdrawal responses,but the patient does not make localizing responses ordiscrete defensive movements.[(1)].The understanding of coma stretches from Baron Constantin von Economo's observations of brain-stem encephalitis in 1917, to Hans Berger's discovery of brain waves in the 1920s, to Giuseppe Moruzzi and Horace Magoun's experimental anatomical work of the 1940s.

Other acutely altered states of consciousness include,clouding of consciousness,stupor,delirium and locked-in-state.

Clouding of consciousness[(1)] is a term applied to minimally reduced wakefulness or awareness, which may include hyperexcitability and irritability alternating with drowsiness.

Stupor, from the Latin ‘‘to be stunned,’’ is a condition of deep sleep or similar behavioural unresponsiveness from which the subject can be aroused only with vigorous and continuous stimulation. Even when maximally aroused, the level of cognitive function may be impaired.

Delirium, from the Latin ‘‘to go out of the furrow,’’ is a more floridly abnormal mental state characterized by misperception of sensory stimuli and, often, vivid hallucinations. Delirium is defined by the (DSM-IV),8 as follows: ‘‘A. Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to

focus, sustain or shift attention. B. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia. C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.''

The locked-in syndrome describes a state in which the patient is de-efferented, resulting in paralysis of all four limbs and the lower cranial nerves. Although not unconscious, locked-in patients are unable to respond to most stimuli.

The vegetative state (VS) denotes the recovery of crude cycling of arousal states heralded by the appearance of ''eyes-open'' periods in an unresponsive patient. Very few surviving patients with severe forebrain damage remain in eyes-closed coma for more than 10 to 30 days. In most patients, vegetative behavior usually replaces coma by that time. Patients in the vegetative state, like comatose patients, showno evidence of awareness of self or their environment. Unlike brain death, in which the cerebral hemispheres and the brainstem both undergo overwhelming functional impairment, patients in vegetative states retain brainstem regulation of cardiopulmonary function and visceral autonomic regulation.

Brain death is defined as the irreversible loss of all functions of the entire brain,14 such that the body is unable to maintain respiratory and cardiovascular homeostasis.

The anatomy and physiology of coma

The maintenance of consciousness depends on interaction between the ascending reticular activating system (ARAS) and the cerebral hemispheres.In humans the ARAS lies in the paramedian tegmental region of the posterior part of the pons and the midbrain.It is a complex polysynaptic fiber system that extends from the superior half of the pons through the midbrain to the posterior portion of the hypothalamus and the thalamic reticular formation [(21)] .

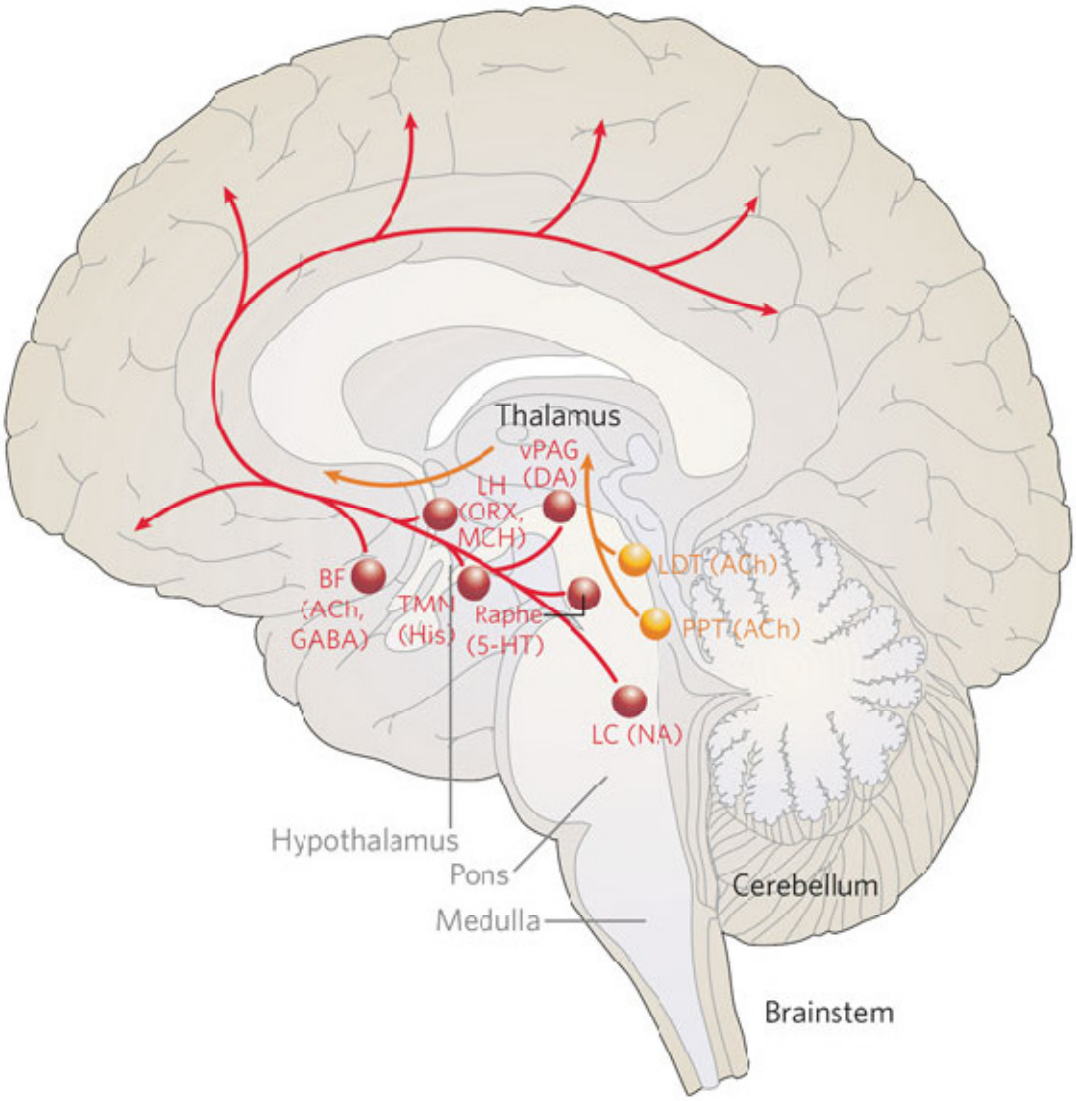
The thalamus is the source of diffuse thalamocortical projections that regulate and coordinate cortical activity. The medial longitudinal fasciculi and the oculomotor and trochlear nuclei lie amid the neurons of the ARAS.So ,when unresponsiveness is due to brain stem damage ,ocular motility is affected as well. Bilateral cerebral hemispheric lesions may cause transient coma,especially when the medial frontal lobe is involved.Large unilateral lesions of a dominant lobe may cause transient unresponsiveness even in the absence of a mass effect.

It follows that the principal causes of coma are;

(1).Lesions that damage the ARAS or its projections.

(2).Destruction of large portions of the both cerebral hemispheres.

(3).Suppression of reticulocerebral function by drugs,toxins or metabolic derangements.



The cholinergic system, shown in yellow, provides the main input to the relay and reticular nuclei of the thalamus from the upper brainstem. This inhibits the reticular nucleus and activates the thalamic relay nuclei, putting them into transmission mode for relaying sensory information to the cerebral cortex. The cortex is activated simultaneously by a series of direct inputs, shown in red. These include monoaminergic inputs from the upper brainstem and posterior hypothalamus, such as noradrenaline (NA) from the locus coeruleus (LC), serotonin (5-HT) from the dorsal and median raphe nuclei, dopamine (DA) from the ventral periaqueductal gray matter (vPAG),and histamine (His) from the tuberomammillary nucleus (TMN); peptidergic inputs from the hypothalamus such as orexin (ORX) and melanin-concentrating hormone (MCH) both from the lateral hypothalamus (LH); and both cholinergic (ACh) and gamma-aminobutyric acid (GABA)-ergic inputs from the basal forebrain (BF).

Clinical presentation of coma inducing lesions

- Coma due to metabolic disorders
- Coma due to cerebral mass lesion and herniation
- Epileptic coma
- Toxic drug-induced coma
- Coma due to widespread cerebral hemispheric damage

Coma due to metabolic disorders

Systemic metabolic abnormalities cause coma by interrupting the delivery of energy substrates or by altering neuronal excitability.The same metabolic abnormalities may in a milder form induce widespread cortical dysfunction and an acute confusional state.

CBF is about 55 ml/100 g /min .Oxygen consumption is 3.5 ml/100g/min.Glucose utilization is 5 mg/100 g/min.Brain stores of glucose provide energy for about 2 min after interruption of blood flow and oxygen stores last 8-10 sec after blood flow cessation.Simultaneous hypoxia and ischemia can deplete stores very rapidly.The EEG rhythm becomes diffusely slowed,which is typical of metabolic abnormalities.

Unlike hypoxia-ischemia[12] ,other metabolic disorders cause only minor neuropathological changes.The reversible effects of these conditions on the brain are not understood.

Toxic prod0ucts of ammonia metabolism including putative false neurotransmitters have been proposed as causes of hepatic coma[20].Encephalopathy of renal failure is proposed to be due to increased permeability of the BBB to toxic substances .

Coma and seizures are a common accompaniment of any large shift in sodium and water balance in the brain.These changes in osmolarity arise from disorders includion DKA [7] ,NKHS and hyponatremia from any cause.

Hypercapnia depresses the level of consciousness in proportion to the rise in co2 tension in blood.

In all of these metabolic encephalopathies ,the degree of neurological change depends to a large extent on the rapidity with which the serum changes occur.

Coma due to cerebral mass lesions and herniations

Herniation refers to displacement of brain tissue into a compartment it normally does not occupy.Certain clinical configurations are characteristic of specific herniations.They are essentially false localizing signs since they derive from compression of tissue at a distance from the mass.

Supratentorial herniation:

1.Uncal herniation

2.Central herniation(transtentorial)

3.Cingulate herniation(subfalcine)

4.Transcalvarial herniation

Infratentorial herniation

1. Upward(upward cerebellar)
2. Tonsillar(downward)

Uncal transtentorial herniation

Refers to the impaction of the anterior medial temporal gyrus 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.In some cases ,displacement of the midbrain causes compression of the opposite cerebral peduncle resulting in contralateral hemiparesis as well(Kernohan-Woltman sign).The distortions may also cause regional hydrocephalus.

Central transtentorial herniation

Denotes a symmetric downward movement of the thalamic medial structures through the tentorial opening with compression of the upper midbrain.

Both uncal and central herniation cause progressive herniation of the brainstem from above downwards.The result is a sequence of neurological signs that corresponds to each affected level.

Cingulate herniation

In cingulate or subfalcine herniation, the most common type, the innermost part of the frontal lobe is scraped under part of the falx cerebri. Cingulate herniation can be caused when one hemisphere swells and pushes the cingulate

gyrus by the falx .cerebri. This does not put as much pressure on the brainstem as the other types of herniation, but it may interfere with blood vessels in the frontal lobes that are close to the site of injury (anterior cerebral artery), or it may progress to central herniation .Cingulate herniation may present with abnormal posturing and coma. Cingulate herniation is frequently believed to be a precursor to other types of herniation.

Upward herniation

Increased intracranial pressure in the posterioe fossa can cause the cerebellum to move up through the tentorial opening.The midbrain is pushed through the tentorial notch.

Tonsillar herniation

Also called foraminal herniation or coning ,downward forcing of the cerebellar tonsils into the foramen magnum,which causes compression of the medulla and respiratory arrest. 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 3-5mm is associated with drowsiness, 6-8mm with stupor and > 9mm with coma[23] .

Epileptic coma

The self-limited coma that follows seizures, termed the post-ictal state may be due to exhaustion of energy reserves or effects of locally toxic molecules that are the byproducts of seizures. The post-ictal state produces a pattern of

continuous generalized slowing of the background EEG activity similar that of metabolic encephalopathies.

Toxic drug induced coma

This class of encephalopathy is mostly reversible and leaves no residual damage provided hypoxia does not supervene. The combination of cortical and brainstem signs, which occurs in certain drug overdoses, may lead to an incorrect diagnosis of structural brainstem disease. Drugs with atropinic actions produce signs such as dilated pupils.

Coma due to widespread damage to cerebral hemispheres

This category comprises a number of unrelated disorders. This results from widespread structural cerebral damage, thereby simulating a metabolic disorder. Similar bihemispheric damage produced by disorders that occlude small blood vessels throughout the brain like cerebral malaria[22] , TTP and hyperviscosity. The presence of seizures and bihemispheric damage are sometimes an indication of this class of disorders.

Signs with localizing value in coma

- Respiratory patterns
- Pupillary response
- Eye movements
- Position or movements of the limbs

Respiratory patterns

The respiratory pattern of a patient in coma may be helpful in localizing the level of structural dysfunction in the neuraxis,but metabolic abnormalities may affect the respiratory centers of the pons(pneumotaxic and apneustic) and medulla(inspiratory and expiratory) and result in patterns resembling structural disease. Therefore thorough evaluvation of the metabolic status of the patient must guide the interpretation of respiratory changes.

Cheyne-Stokes respiration

This type of respiration consists of brief periods of hyperpnea alternating regularly with even shorter periods of apnea. It represents a more severe degree of posthyperventilation apnea in which the respiratory drive becomes more closely dependent on pCO_2.

It may follow bilateral widespread cortical lesions,bilateral thalamic dysfunction and with lesions of the descending pathways anywhere between the cortex and the upper pons. Metabolic disturbances,diffuse anoxia,heart failure often underlie this pattern of breathing.

Hyperventilation with brainstem injury

Patients with lesions of the midbrain and pons often have prolonged and rapid hyperpnea. Because most of these patients are relatively hypoxic despite the excessive ventilator effort,this type cannot be truly called as neurogenic hyperventilation.

Apneustic breathing

Apneustic breathing is characterized by a long inspiratory pause ,after which air is retained for several seconds and then released. This abnormality appears with lesions of the lateral tegmentum of the lower half of pons.

Cluster breathing

Breathing with a cluster of breaths following each other in an irregular sequence may result from lower pontine or high medullary lesions.

Ataxic breathing

It is also called the atrial fibrillation of respiration.it is a completely irregular pattern in which inspiratory gasps of diverse amplitude and length are intermingled with periods of apnea. It follows damage of the dorsolateral medulla and heralds complete respiratory failure. The most common etiologies are cerebellar or pontine hemorrhage,trauma and posterior fossa tumour.

The pupils

Pupillary shape,size,symmetry and response to light provide valuable clues to brainstem and third cranial nerve function. The papillary light reflex is resistant to metabolic dysfunction. Various structural lesions causing coma and the associated papillary abnormalities are as follows:

- Diencephalic pupils are small pupils that react well to light.
- Unilateral hypothalamic damage induces miosis and anhidrosis on the ipsilateral side.
- Midbrain lesions may be either tectal or tegmental. Tectal lesions cause midsized pupils with loss of light reflex. Tegmental lesions involve the third nerve nucleus and cause unequal pupils with loss of light and ciliospinal reflex.
- Pontine tegmental lesions cause small pupils due to interruption of the descending sympathetic pathways. Pinpoint pupils are due to both sympathetic damage and parasympathetic irritation.
- Lateral pontine,lateral medullary and ventrolateral spinal cord lesions cause an ipsilateral Horner's syndrome.

Eye movements

In the absence of voluntary eye movements,assessment of ocular motility in coma relies heavily on reflex eye movements including the oculocephalic reflex and the oculovestibular reflex. Because

of the absence of cortical control of eye movements,the comatose patient lacks voluntary saccades,including the quick phase of nystagmus. Instead if the brainstem is intact,the eyelids are closed,the eyes slightly divergent,drift slowly from side to side(roving eye movements). Spontaneous blinking requires intact pontine reticular formation. The eyelids may remain tonically retracted because of failure of levator inhibition in some cases of pontine infarction(eyes open coma).

Spontaneous eye movements in comatose patients

- Periodic alternating gaze:cyclic horizontal rowing seen mostly with bilateral cerebral damage [(24)] .
- Repetitive divergence: There is slow deviation out with rapid return to primary. This is seen in metabolic encephalopathy.
- Nystagmoid jerking of single eye:The jerk may be vertical,horizontal or rotator.It is seen with middle or low pontine lesions.
- Status epilepticus:These are small amplitude vertical eye movements. It occurs with diffuse encephalopathy.
- Ocular bobbing:It consists of fast downward movement with slow upward drift.It may occur with pontine,extra-axial posterior fossa mass,diffuse encephalopathy.

- Reverse ocular bobbing:occurs with diffuse encephalopathy.
- Vertical ocular myoclonus:Pendular,vertical isolated eye movements associated with pontine lesions.

Abnormalities of lateral gaze

Conjugate gaze:

When both the eyes remain deviated to the same side in a comatose patient,the lesion may be in the cerebral hemisphere or pontine tegmentum. In a hemispheric lesion,the eyes look toward the lesion but can be overcome by oculocephalic maneuver,caloric testing or both. Unilateral lower pontine tegmental lesions cause the eyes to look to the hemiparetic side. Neither the oculocephalic maneuver nor the caloric test can overcome a pontine gaze palsy. Thalamic lesions cause forced deviation of the eyes to the side contralateral to the lesion(wrong-way eyes).

Disconjugate gaze

Isolated failure of ocular adduction,in the absence of papillary changes and with normal vertical eye movements,indicates a lesion of the MLF in the upper

pons ipsilateral to the eye that fails to adduct.MLF involvement is commonly bilateral in comatose patients. Rarely ,metabolic coma may induce a transient MLF syndrome.

Abnormalities of vertical gaze

Disconjugate vertical gaze in the resting position (skew deviation) may be seen with lesions of the brainstem,increased ICP,or with hepatic coma. Paresis of upward gaze is usually present with bilateral midbrain tectal damage. Downward gaze is preferentially affected by bilateral lesions of the superomedial perirubral region.

Motor activity of the body and limbs

Motor findings have a less clear-cut localizing value than similar findinds in alert patients. In light coma,the general motor responses may oscillate between lying quietly in bed and wildly thrashing about.when the level of coma deepens or a structural lesion affects the cerebral hemispheres and the diencephalon,decorticate rigidity may appear,contralateral to the hemispheric lesion.

Severe metabolic disorders or lesions of the upper brainstem give rise to decerebrate rigidity.

Differential diagnosis of coma

Diseases that cause no focal or lateralizing neurologic signs, usually with normal brainstem functions; CT scan and cellular content of the CSF are normal.

a. Intoxications: alcohol, sedative drugs, opiates, etc.

b. Metabolic disturbances: anoxia, hyponatremia, hypernatremia, hypercalcemia, diabetic acidosis, nonketotic hyperosmolar hyperglycemia,hypoglycemia, uremia, hepatic coma, hypercarbia, addisonian crisis, hypo- and hyperthyroid states, profound nutritional deficiency

c. Severe systemic infections: pneumonia, septicemia, typhoid fever,

malaria, Waterhouse-Friderichsen syndrome

d. Shock from any cause

e. Postseizure states, status epilepticus, subclinical epilepsy

f. Hypertensive encephalopathy, eclampsia

g. Severe hyperthermia, hypothermia

h. Concussion

i. Acute hydrocephalus

2. Diseases that cause meningeal irritation with or without fever, and with an excess of WBCs or RBCs in the CSF, usually without focal or lateralizing cerebral or brainstem signs; CT or MRI shows no mass lesion

a. Subarachnoid hemorrhage from ruptured aneurysm, arteriovenous malformation, trauma

b. Acute bacterial meningitis

c. Viral encephalitis

d. Miscellaneous: Fat embolism, cholesterol embolism, carcinomatous and lymphomatous meningitis, etc.

3. Diseases that cause focal brainstem or lateralizing cerebral signs, with or without changes in the CSF; CT and MRI are abnormal

a. Hemispheral hemorrhage (basal ganglionic, thalamic) or infarction

(large middle cerebral artery territory) with secondary brainstem

compression

b. Brainstem infarction due to basilar artery thrombosis or embolism

c. Brain abscess, subdural empyema

d. Epidural and subdural hemorrhage, brain contusion

e. Brain tumor with surrounding edema

f. Cerebellar and pontine hemorrhage and infarction

g. Widespread traumatic brain injury

h. Metabolic coma (see above) with preexisting focal damage

i. Miscellaneous: cortical vein thrombosis, herpes simplex encephalitis,

LABORATORY STUDIES AND IMAGING

The studies that are most useful in the diagnosis of confusional states and coma are:

- chemical-toxicologic analysis of blood and urine
- cranial CT or MRI
- EEG
- CSF examination

Arterial blood-gas analysis is helpful in patients with lung disease and acid-base disorders. The metabolic aberrations commonly encountered in clinical practice require measurements of electrolytes, glucose, calcium, osmolarity, and renal (blood urea nitrogen) and hepatic (NH3) function. Toxicologic analysis is necessary in any case of coma where the diagnosis is not immediately clear. However, the presence of exogenous drugs or toxins, especially alcohol, does not exclude the possibility that other factors, particularly head trauma, are also contributing to the clinical state.

The notion that a normal CT scan excludes anatomic lesions as the cause of coma is erroneous. Bilateral hemisphere infarction, small brainstem lesions, encephalitis, meningitis, mechanical shearing of axons as a result of closed head trauma, sagittal sinus thrombosis, and subdural hematomas that are isodense to adjacent brain are some of the disorders that may not be detected. Nevertheless, if the source of coma remains unknown, a scan should be obtained.

The EEG is useful in metabolic or drug-induced confusional states but is rarely diagnostic[(24)] , except when coma is due to clinically unrecognized seizures, to herpesvirus encephalitis, or to Creutzfeldt-Jakob disease. The amount of background slowing of the EEG is a reflection of the severity of any diffuse encephalopathy.

Predominant high-voltage slowing or triphasic waves in the frontal regions is typical of metabolic coma[1] , as from hepatic failure, and widespread fast activity implicates sedative drugs (e.g., diazepines, barbiturates). A special pattern of coma, defined by widespread, variable 8- to 12-Hz activity, superficially resembles the normal rhythm of waking but is unresponsive to environmental stimuli. It results from pontine or diffuse cortical damage and is associated with a poor prognosis. Most importantly, EEG recordings may reveal clinically inapparent epileptic discharges in a patient with coma. Normal activity on the EEG also alerts the clinician to the locked-in syndrome or to hysteria or catatonia.

Lumbar puncture is performed less frequently than in the past because neuroimaging scans effectively exclude However,examination of the CSF is indispensable in the diagnosis of meningitis and encephalitis. intracerebral and subarachnoid hemorrhages that are severe enough to cause coma.

MATERIALS AND METHODS

Materials and methods

A total of 100 consecutive patients admitted in a comatose state to the IMCU/medical ward in Government Stanley Medical College , were enrolled in this study after prior written and informed consent.

PERIOD OF THE STUDY:FEBRUARY 2010 TO APRIL 2010

ETHICAL COMMITTEE APPROVAL: The present study was approved by ethical committee.

CONSENT: The relatives of the patient were informed about the nature of the study and those who were willing were included in the study after getting written informed consent.

Methodology:

A detailed case history was taken.Depression of consciousness was assessed by the GCS.A detailed clinical examination was done.Investigations were guided by the clinical presentation.Neurological outcomes were determined as intact(normal or no change from pre-morbid condition),impaired(alteration of tone,power or reflexes,cranial nerve dysfunction,ataxia,seizures,persistent vegetative state)or death.

Inclusion criteria:

Cases with coma &focal signs

Those without focal signs

Cases with coma &fever

Exclusion criteria:

Head injury

Toxin ingestion

OBSERVATION

AND

ANALYSIS

TABLE 1:ETIOLOGICAL CATEGORISATION OF COMA IN OUR STUDY

ETIOLOGY	No of cases
Vascular	35
Metabolic	24
Infectious	6
Seizures	8
Alcohol	18
Others	9

The most common etiology of coma in our study was a vascular event,either infarct or parenchymal hemorrhage.Metabolic causes followed them . Metabolic causes included hypoglycaemia,diabetic ketoacidosis,uremia and hepatic encephalopathy. Alcohol related causes accounted for a sizeable number of cases.One of them presented with corpus callosal demyelination,the Marchiafava Bignami disease. Seizures ,either presenting as status epilepticus or post ictal confusion were associated with coma.Infectious causes included cerebral malaria,meningitis and sepsis. Others included causes such as hypertensive encephalopathy,hypoxia induced coma in cardiac failure patients,co_2 narcosis, central pontine myelinolysis and myxedema coma .

GRAPH 1 :ETIOLOGICAL CATEGORISATION OF COMA IN OUR STUDY

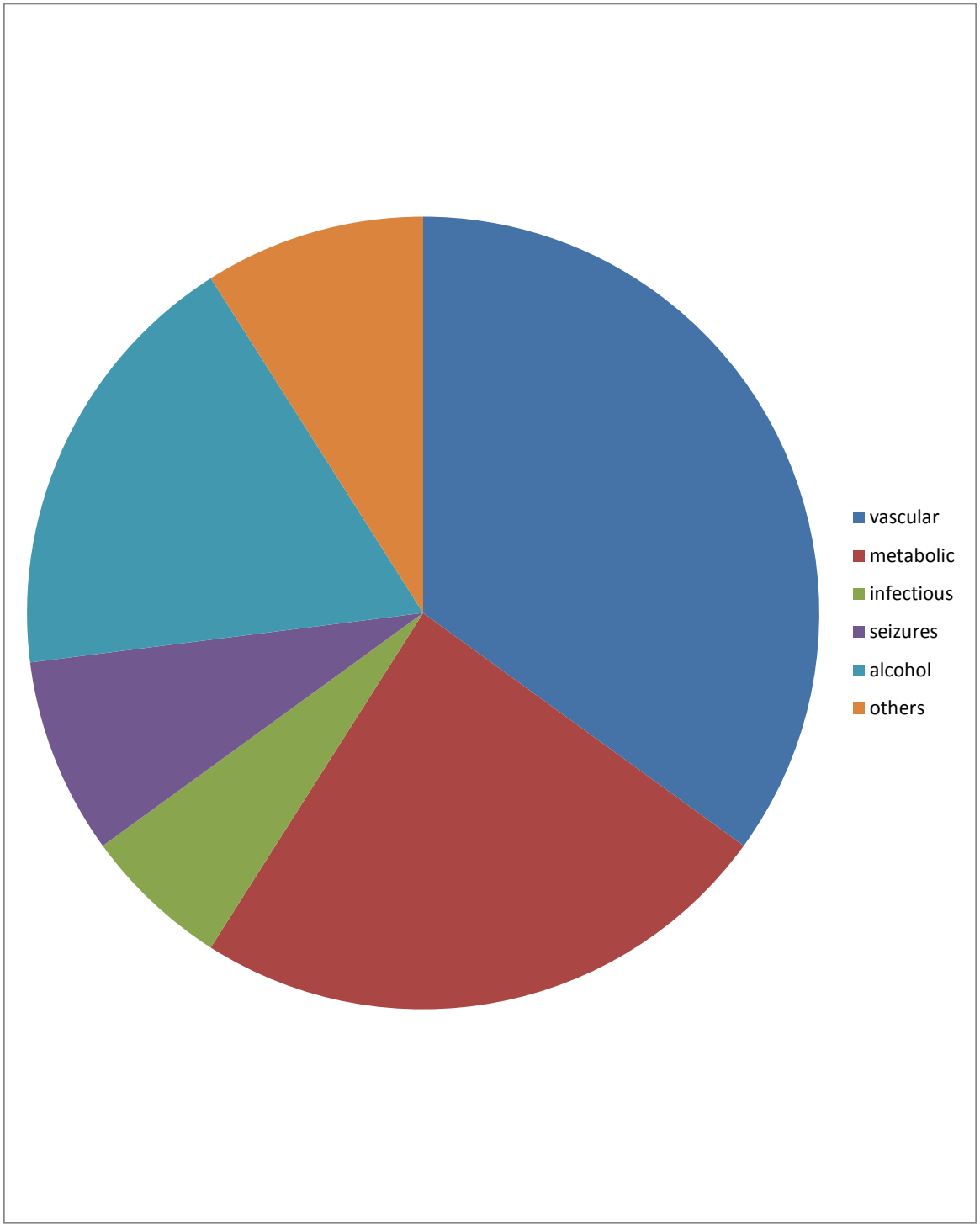


TABLE 2:GCS ON ADMISSION AND PROGNOSIS

GCS	TOTAL NO OF CASES	INTACT	IMPAIRED	DEATH
3/15	3	0	0	3
4/15	9	0	1	8
5/15	16	1	0	15
6/15	13	2	4	7
7/15	19	18	1	0
8/15	32	29	2	1
9/15	8	8	0	0

When the initial GCS was less than 5/15,the prognosis was uniformly fatal.Out of the 28 cases who presented ,only 2 survived.With GCS greater than 7/15 ,most of them survived.Out of the 59 cases there was only a single death.

GRAPH 2:GCS ON ADMISSION AND PROGNOSIS

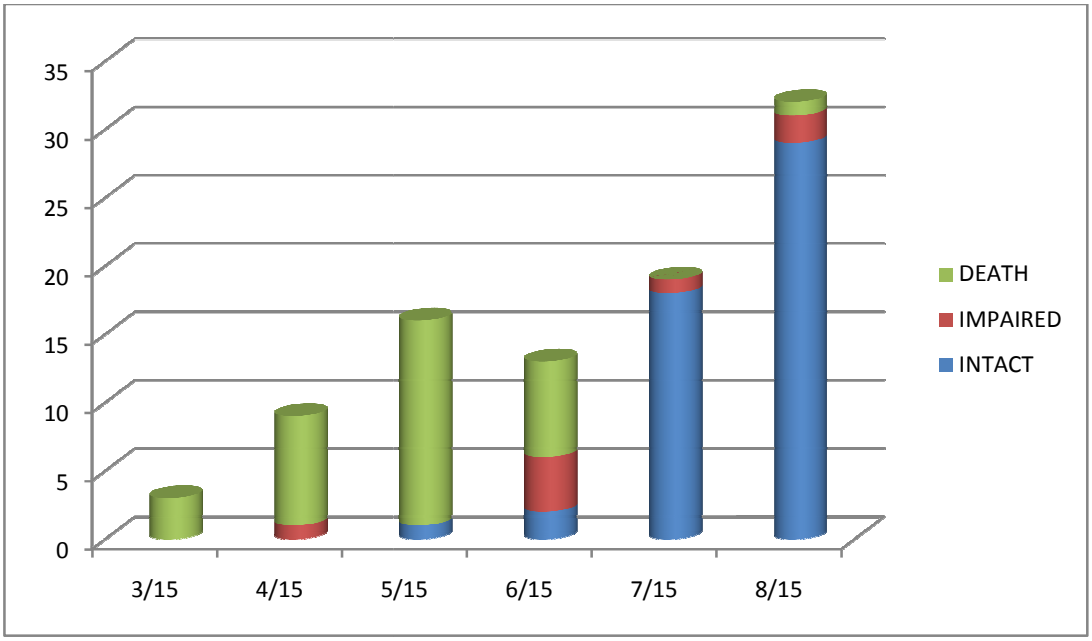


TABLE 3: ETIOLOGY OF COMA AND PROGNOSIS

ETIOLOGY	TOTAL NO OF CASES	INTACT	IMPAIRED	DEATH
ICH	16	1	0	15
INFARCT	18	10	1	7
METABOLIC	22	19	1	2
INFECTION	8	5	2	1
SEIZURES	8	5	2	1
OTHERS	28	18	2	8

Those presenting with coma and brain parenchymal hemorrhage had a grave prognosis.Out of the 16 cases which presented with ICH ,only one survived.CVA presenting with coma and an infarct had a better prognosis.Metabolic causes had the best prognosis in all.Out of 22 cases who were diagnosed to have metabolic coma,only 2 died .Seizures and infectious causes also had a better prognosis.only one out of 4 cases of hypoxic encephalopathy due to cardiac failure/arrest survived.The other fatalities were associated with myxedema coma in one case,central pontine myelinolysis and marchiafava-bignami disease.

GRAPH 3: ETIOLOGY OF COMA AND PROGNOSIS

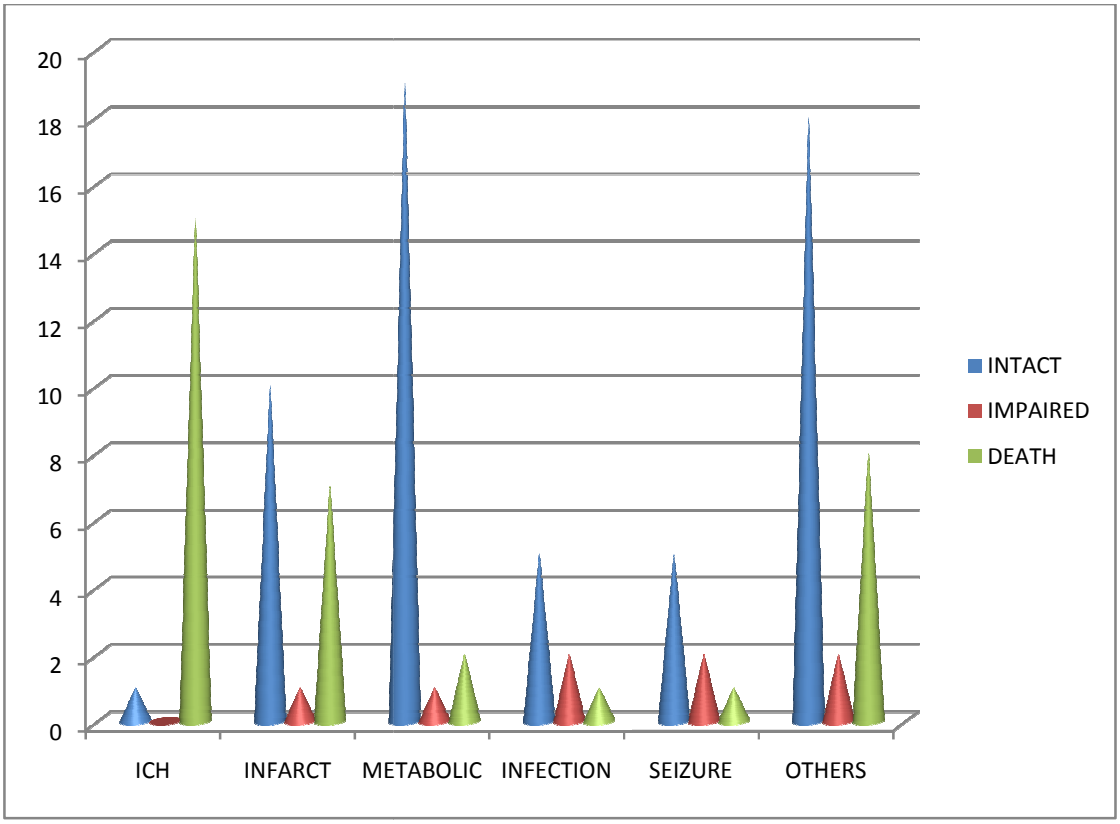


TABLE 4 : EYE SIGNS AND PROGNOSIS

PUPILS/EYE SIGNS	NO OF PTS SURVIVED	NO OF PTS EXPIRED
PRESENT	5	22
ABSENT	62	11

Out of the 27 cases who presented with pupillary /eye signs,only 5 survived.The death percent was 81.Coma was related to structural cause in most of them.

GRAPH 4 : EYE SIGNS AND PROGNOSIS

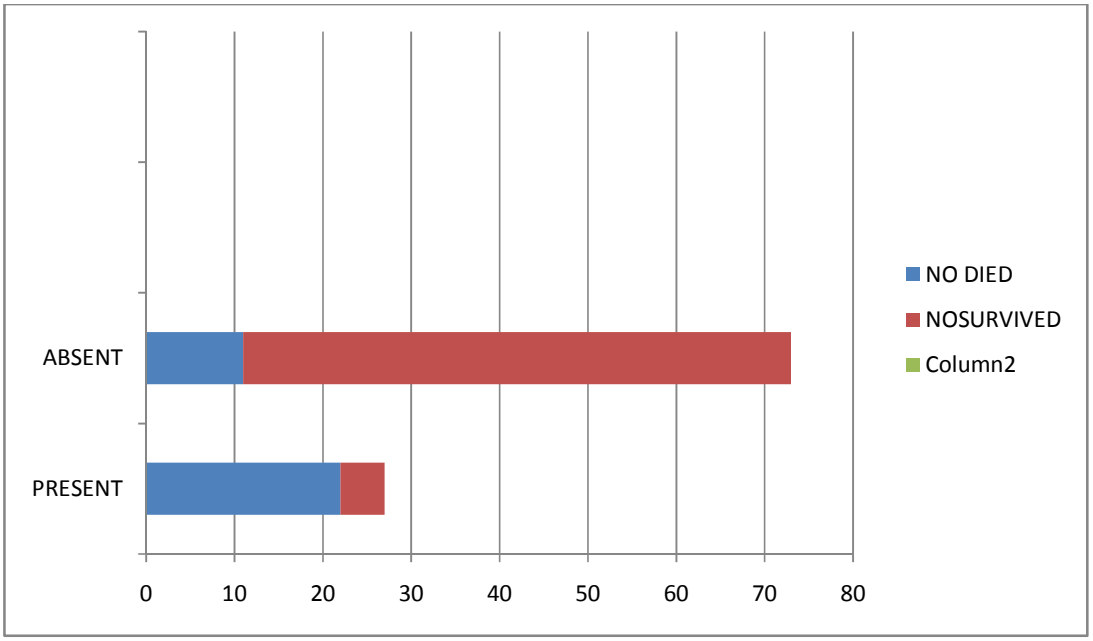


TABLE 5 : PREVALENCE OF RISK FACTORS IN COMA

RISK FACTORS	NO OF PATIENTS
HT	20
DM	17
ALCOHOL	23
SEIZURES	3
OTHERS	8
MORE THAN ONE RISK FACTOR	13

Alcoholism was the most prevalent risk factor.Hypertension ranked next followed by diabetes mellitus.Other risk factors included the presence of systemic disease such as DCLD,COPD,coronary artery heart disease.More than one risk factor was present in 13 of our patients.

GRAPH 5 : PREVALENCE OF RISK FACTORS IN COMA

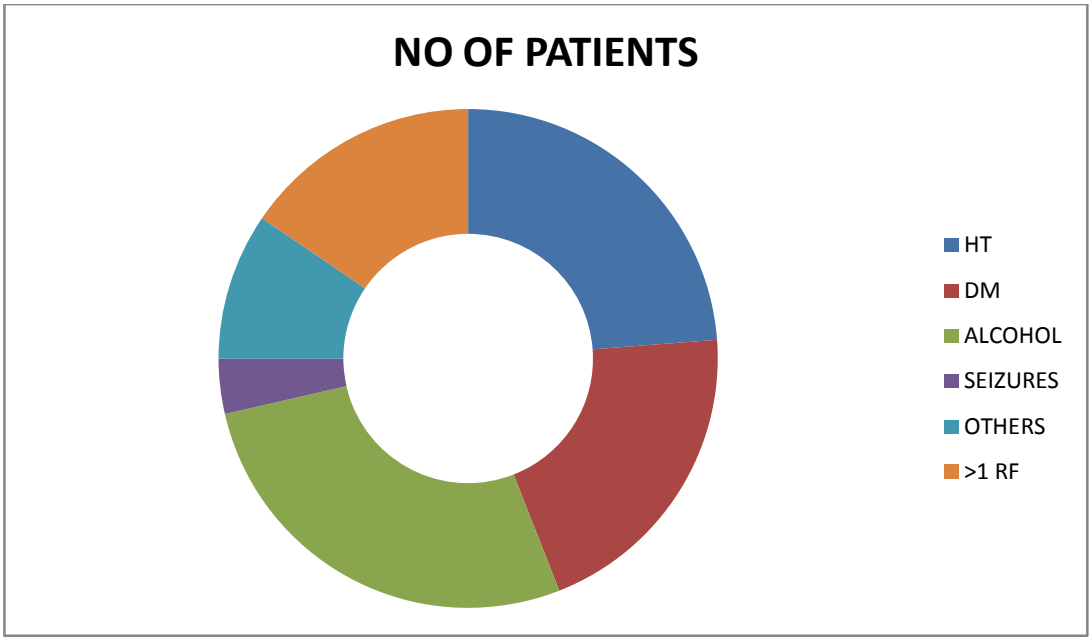
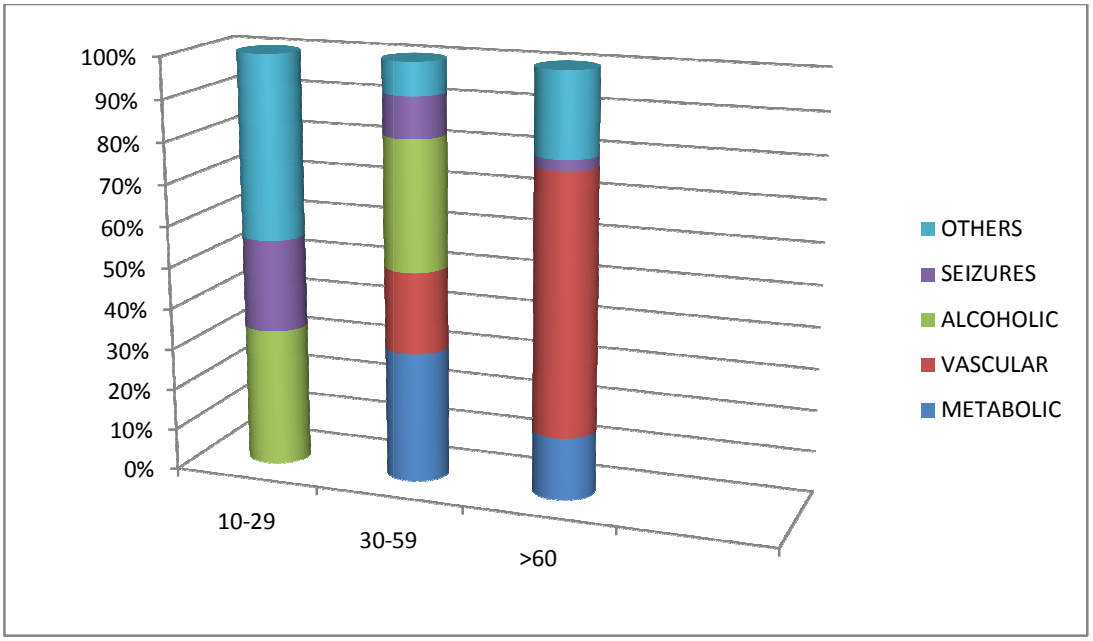


TABLE 6 : AGE GROUP-WISE CATEGORISATION OF ETIOLOGY

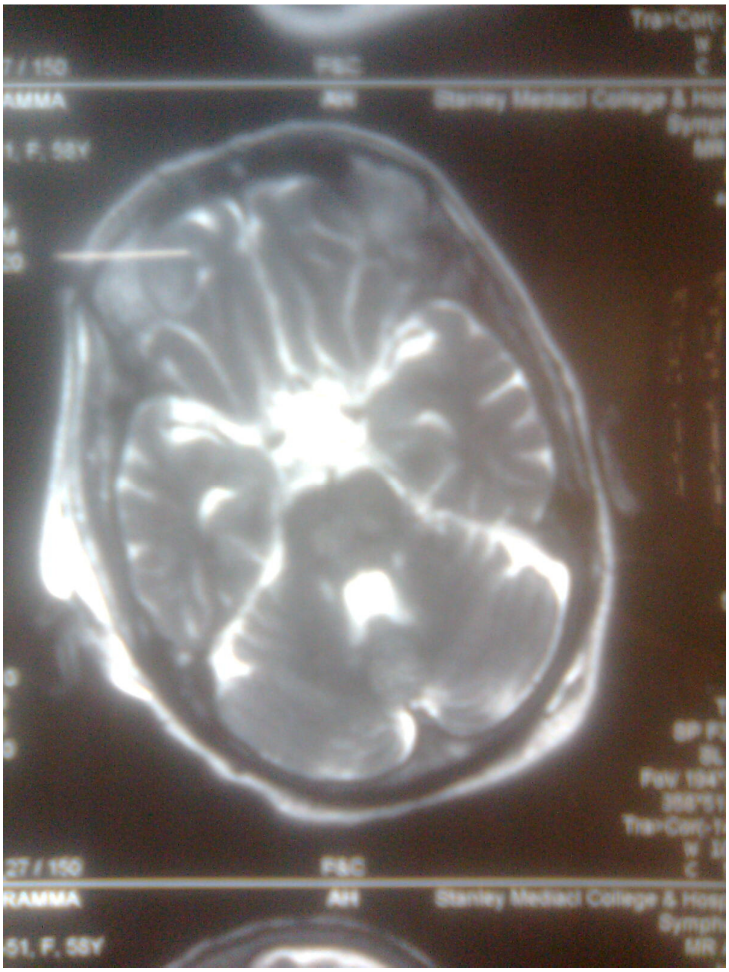
AGE	METABOLIC	VASCULAR	ALCOHOL	SEIZURES	OTHERS
10-29	0	0	3	2	4
30-59	16	10	16	5	4
≥60	6	25	0	1	8

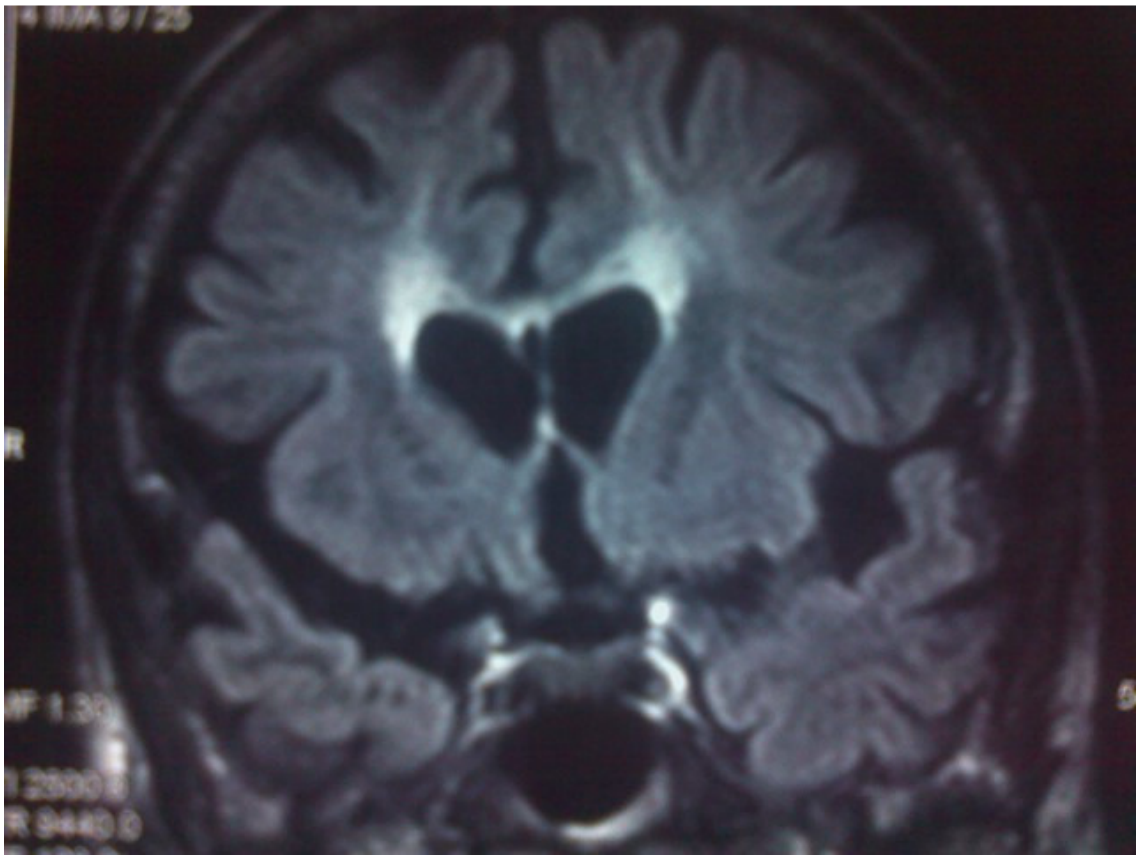
The most common etiology in those elder than 60 yrs was a cerebrovascular accident.In the younger age groups,metabolic and alcohol related causes were predominant.

GRAPH 6 : AGE GROUP-WISE CATEGORISATION OF ETIOLOGY



CT IMAGES


P&C
AH
Stanley Medical College & Hosp
F&C
AH
Stanley Medical College & Hosp



Interpretation of results

1.The most common etiology of coma was a cerebrovascular accident,parenchymal hemorrhage followed by infarct.

2.There was a significant positive correlation between initial high GCS and better functional outcome .

3.Intracerebral bleed had the worst prognosis followed by infarct.

4.Survival was better in patients with metabolic coma.

5.Abnormal pupillary size and reaction,abnormal EOM,abnormal respiratory pattern, at admission correlated significantly with mortality.

6.Hypertension,diabetes and alcohol were the most prevalent risk factors.

7.Alcohol was the leading cause of coma and altered sensorium in the age group 20-60 years.

8.Above 60 years,cerebrovascular accidents accounted for the majority of cases of coma.

DISCUSSION

Discussion

Our study had 100 patients of coma. The most common etiology were cerebrovascular accidents,either parenchymal hemorrhage or an infarct. Other major causes included metabolic causes such as hypoglycemia,diabetic ketoacidosis,uremic and hepatic encephalopathy. Alcohol intoxication was an important cause of altered consciousness.

The GCS was developed to describe consciousness level in head-injured patients. Now it is widely used for both traumatic and non-traumatic altered consciousness levels. In our study there was a positive correlation between initial high GCS and better patient outcomes. This has been supported by many studies.But a significant number of patients who had a low initial GCS in our study also had a better prognosis. This was true especially in patients with stroke and those with infectious causes.This is supported by the study done by C.J.Weir et al. As stroke may cause localized motor,speech and language deficits,the accuracy of GCS as a measure of conscious level may be affected. In turn the prognostic value may be impaired.

Teasdale and jennet have addressed the common pitfalls while recording GCS and account on how they should be avoided. Problems arise when the eyes are swollen shut(periorbital edema,ocular trauma) or paralyzed.The enforced eye closure should be recerded in these circumstances. Motor responses cannot be reliably monitored in the presence of splint or immobilization devices or in cases of spinal cord,plexus or peripheral nerve injury.

The presence of pupillary and other eye signs usually signify a grave prognosis. In our study . Out of the 27 cases who presented with pupillary /eye signs,only 5 survived.The death percent was 81.Coma was related to structural cause in most of them. But eye signs such as sluggish pupils were also present in alcoholics who presented in an obtunded state.Transient extra ocular

movement abnormalities do occur in metabolic coma. In a recent study better neurologic outcomes have been noted in post cardiac arrest patients who initially presented with an absent papillary/corneal reflex. Neurologic outcomes determined by GCS may no longer be accurate in post cardiac arrest patients according to Janis c. Kelly et al.Even in our study,the observed proportions might represent the lower limit of a confidence interval rather than the mean in which case the upper limit wll even be greater.

Also the initial GCS was deceptively low in alcoholics in our case. Most of them recovered to normal neurologic status . This could have been due to the depressant effects of alcohol.But GCS may not be statistically affected by the presence of alcohol until the BAL is 200 mcg/dl.

A multimodal work up including brain CT,MRI,EEG,somatosensory evoked potentials and the clinical examination to determine the prognosis might be the best approach.

A fundamental issue in determining the prognosis for any individual patient is the etiology . In our study,patients presenting with intracerebral hemorrhage had the worst prognosis in all.Out of 16 cases ,only one case survived. There were 7 females and 9 males. The mean age in females was 68.42. The mean age in males was 60 yrs.Generally ICH has a younger onset in males. The observation was the same in our study also. But the number of cases is limited. Also two of the males presented at extremely lower ages,one was a CKD and the other had no identifiable risk factors on initial evaluvation. This could have affected the mean.

The single most prevalent risk factor was hypertension. There was a significant proportion of alcoholics and smokers.Fogelholm and MIllios in a population based case control study did not find positive association between cigarette smoking and the risk of ICH. Also there is insufficient epidemiologic evidence to conclude whether recent alcohol use affects risk of either ischemic or hemorrhagic stroke.

In our study there were 18 cases of infarct who presented with obtundation . Out of them,7 cases died. Most of them massive anterior circulation infarcts.Prognosis of coma following stroke depends on the arterial territory affected by the stroke.Large proximal vessel occlusions causing diffuse hemispheric edema and midline shift carry a grave prognosis with a nearly 90% mortality when the shift of septum pellucidum was greater than 12 mm (Pullicino PM et al).Patients with coma caused by acute basilar occlusions may survive .

The most important metabolic causes in our study were hypoglycaemia,diabetic ketoacidosis,uremia and hepatic encephalopathy. We had 11 cases of hypoglycaemic coma. The median age was 60 yrs. All of them were known type II diabetics. All of them recovered without neurological deficit. Perhaps the time interval between dextrose administration and recovery differed in each case. There are also reports of persistent coma after adequate termination of hpoglycemia. The uniformly better outcome in our cases could have been due to earlier reporting to the hospital and early glucose administration.

One of our cases of hypoglycaemic coma had seizures. Many hypoglycaemic patients convulse as the blood sugar levels drop and some have only seizures as the manifestation of hypoglycaemia. Hypoglycaemia is a great imitator and it is better to check blood glucose in all comatose patients as an initial screening procedure.

In some cases there was difficulty in differentiating between hypoglycaemia and DKA . The great danger of delayed diagnosis is that the longer the hypoglycaemia lasts ,the more likely it is to produce irreversible neuronal loss. Patients with severe hypoglycaemia often have changes on MRI suggesting cerebral infarction. Specifically these lesions were found in the basal ganglia,cerebral cortex,substantia nigra and hippocampus.The absence of localized

haemorrhages on MR images in hypoglycaemic encephalopathy is in marked contrast to the presence of regional minor haemorrhages in post ischemic-anoxic encephalopathy.

There were 5 cases of diabetic ketoacidosis in our study.2 of them recovered without neurological deficit. One case had an impaired conscious at 48 hrs.Two other cases died.Both of them had an associated cerebrovascular accident –an infarct.DKA patients die from associated diseases.This view has been supported by DKA outcome study by Hamblin et al. The common associated morbidities were pneumonia,myocardial infarction,Cerebrovascular accident,bowel or lower limb ischemia.

We had 3 cases of hepatic encephalopathy in our series.All of them recovered. All the cases were chronic alcoholics and diagnosed cases of decompensated liver disease who had far advanced in their disease course. The presentation was different among them. One of them presented in a state of delirium and two others presented in an obtunded state. Hepatic encephalopathy excluding fulminant hepatic failure has the best chance of recovery among metabolic comas. But approximately 50 % of patients with cirrhosis die within one year of demonstrating encephalopathy(Pulver M et al). Focal neurologic signs were observed in none of them. Nystagmus on lateral gaze ,tonic conjugate downward or downward and lateral ocular deviation have been observed in hepatic coma. Decorticate and decerebrate posturing responses muscle spasticity and bilateral extensor plantar responses frequently accompany deep coma.

There were 4 cases of uremic encephalopathy in our series.The outcome was better in all except one. The level of BUN associated with uremic encephalopathy varied among patients. High levels of various uremic toxins such as guanidine compounds and advanced glycation end products as well as an excess of PTH are involved in the pathogenesis of uremic encephalopathy. The pH in ABG also had little correlation with the level of conscious.

All our cases presented in an obtunded state with hyperpnea. Delirium could be a more frequent presentation when uremia developed rapidly.This case series did not report delirious patients.The period of recovery following dialysis was variable. Tremor ,asterixis,muscle paratonia,convulsions or nonconvulsive status can occur in uremic patients.

We had 26 cases of alcohol intoxication in our series.All but 2 recovered. In one of them there was an associated cerebrovascular accident.The other patient had severely aspirated.Most of them presented in an obtunded state.A few presented in a delirious state.The major diagnostic problem in altered states of consciousness associated with acute alcohol intoxication lies in separating the potentially benign and spontaneously reversible signs of alcoholic depression from evidence of more serious injury.We had one such case who finally turned out to be a case of cerebrovascular accident.Alcohol intoxication acutely enhances platelet aggregation and activation of the clotting cascade, and rebound thrombocytosis . Mid dilated sluggishly reacting pupils were present in a significant proportion.

Only one out of 4 patients with hypoxic encephalopathy due to cardiac arrest survived.Data from 942 patients enrolled in the Brain Resuscitation Clinical Trials (1979-1994) demonstrated that loss of any of the cranial nerve reflexes following cardiac arrest significantly predicted poor outcome.One of our four patients had seizures. At the end of 48 hrs his conscious was impaired. With seizures and myoclonus,the prognosis is mostly agonal. But cases have been reported in literature with seizures and myoclonus following a cardiac arrest and late improvement,as late as 16 days after remaining at a GCS of 5 until that point(Golby et al).

There was one case of hypertensive encephalopathy who presented with seizures ,papilloedema and delirium. The patient succumbed to death.Renal parameters were normal in that patient on admission. The CT brain showed cerebral edema. When renal failure is also present along with the above manifestations then the contribution of each to coma would be questionable but the finding of posterior leukoencephalopathy on MRI would confirm the diagnosis of hypertensive encephalopathy.

Three of our cases presented with coma due to bacterial meningitis.one was a 20 yrs male who recovered. The other was a 27 yr old alcoholic who also recovered. The third patient was a 20 yr old female whose conscious was impaired after 48 hrs. she had seizures on admission and her initial GTCS was 6/15. Obtundation on admission,extremes of age,hypotension ,seizures within 24 hrs and CSF abnormalities are all associated with a bleak prognosis. In most cases the mortality was due to herniation.

In our study there were 9 cases of seizure disorder.There were 2 cases of tuberculoma,one case of neurocysticercosis. The rest were idiopathic seizures with a positive past history in two. Apart from the primary diagnosis seizures were also present in bacterial meningitis,hypertensive encephalopathy,focal seizures in a case with SOL,withdrawal seizures in alcoholics. Seizures at the time of initial presentation signifies a bad prognostic sign in cases of meningitis. Withdrawal seizures had no effect on the prognosis. All the post ictal cases ,despite the initial low GCS in a few recovered neurologic function at 48 hrs except two. Post ictal state can depress brain stem function and even flexor or extensor posturing can occur.

There were 3 cases of cerebral malaria in our study. Two of them recovered promptly with institution of antimalarials,one of those patients died. They were all confirmed by QBC. Decerebrate posturing was present in the case during the iniial 48 hrs.

other reported neurologig signs in cerebral malaria are,transient dysconjugate gaze,fixed jaw closure ,decorticate rigidity and ophisthoonus. Two of the patients who recovered had no neurologic dysfunction. Residual deficits are infact uncommon in adults compared to children. Also the fatality can be as high as 20 %.

We had one case each of myxedema coma,central pontine myelinolysis and marchiafava bignami disease.

The myxedema patient was a known hypothyroid on irregular treatment,who presented with hypothermia and obtundation. Her ABG showed carbondioxide retention and mild hypoxia. But the presence of hypothermia and other florid features of hypothyroidism made the diagnosis of myxedema as against carbondioxide narcosis. The prognosis in that patient was grave.

One of our patients ,a 50 year old male alcoholic presented with obtundation and a GCS of 4/15. The initial CT did not bring out an abnormality and a MRI brain was done.MRI showed hyperintensity on T2W of almost the entire corpus callosum.the features therefore were suggestive of type A MBD. Given the depth of coma,alcoholism and malnutrition ,the patient succumbed to the illness.

The other patient was a 55 yr old diabetic and CKD who was brought with unresponsiveness and weakness of all 4 limbs .she was treated outside with hypertonic saline. Her MRI showed subtle hyperintensities noted on both the sides of the pons,asymmetrical in T2W1,appeared hypointense in T1W1,no evidence of diffusion restriction.no enhancement of contrast,suggested central pontine myelinolysis ,isolated pontine lesion. At 48 hrs the pt remained in the same state. Recovery may take months in CPM but death is a common outcome.

CONCLUSION

Conclusion

The GCS ia a valuable tool but it may not account for the localized motor,speech and language deficits associated with a focal lesion and hence its accuracy may be affected which has an impact on its prognostic value. The presence of pupillary /eye signs may not portend a poor prognosis in all cases especially in hypoxic injury.

The initial GCS may be deceptively low in alcoholics.Caution is required while interpreting the clinical findings in alcoholics. There may be difficulties in differentiating the more serious injuries from reversible signs.

The presence of seizures in a comatose patient may not always signify a poor prognosis in all cases.

The limitations of our study are that it is an observational study and the number of patients analyzed may not be significant to apply the results to a larger population.The observed proportion might represent the lower limit of a confidence interval rather than the mean.Also, actual outcome from the illness in many instances could be worse than the best neurologic state because some patients who recovered temporarily (48 hrs) died of complications later.

A multimodal work up including brain CT ,MRI,EEG,somatosensory evoked potentials and clinical examination might be useful in predicting accurate prognosis than any of them alone.

ANNEXURES

PROFORMA:

1.Name:

2.Age:

3.Sex

4.Marital Status:

5.No Of Children:

6.Educational Status:

7.Occupation:

8.Address:

9.Height(M):

10.Weight(Kg):

11.Clinical Presentation:

12.Rapidity Of Symptoms:

13.Antecedent Symptoms:

14.Drugs:

15.Lung/Liver/Kidney/Heart Ds:

16.Hypertension:

Duration:

Treatment:

17.Diabetes:

Duration:

Treatment:

18.Hyperlipidemia:

Duration:

Treatment:

19. Promiscous Sex:
20. Alcoholism:
21. Smoking:
22. Menstrual History:
23. General Examination:
    - Gcs:
    - Anaemia
    - Jaundice
    - Cyanosis
    - Clubbing
    - Lymphadenopathy
    - Pedal Edema
    - Neurocutaneous Markers
24. Vital Signs:
25. Cns:
    - Gcs:
    - Posture:
    - Respiratory Pattern:
    - Eom:
    - Pupils:
26. Cvs:
27. Rs:
28. P/A:

Investigations:

1.Urine R/E:

Albumin:

Sugar:

Deposits:

2.Rft:

Urea:

Creatinine:

Electrolytes:

3.Cbc:

Tc Hb Esr

Dc Pcv Platelet

4.Cxr :

5.Ecg:

7.Csf Analysis:

8.Imaging:

9.Others(Abg,Lft,Tft,Nh3):

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