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"CLINICAL OUTCOME IN ISCHEMIC STROKE PATIENTS WITH HYPERGLYCEMIA"

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CERTIFICATE

This is to certify that the dissertation entitled "**CLINICAL OUTCOME IN ISCHEMIC STROKE PATIENTS WITH HYPERGLYCEMIA**" is a bonafide original work done by **Dr.ABDUL RAHIM.A**, in partial fulfilment of the requirements for M.D. GENERAL MEDICINE BRANCH-I examination of the Tamilnadu Dr.M.G.R Medical University to be held in May 2018, under my guidance and supervision in 2017.

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INTRODUCTION

INTRODUCTION

Stroke is one of the leading causes of death and long term disability in India. Stroke is an important cause of premature death and disability in low-income and middle-income countries like India, largely driven by demographic changes and enhanced by the increasing prevalence of the key modifiable risk factors.

Among all the neurological diseases of adult life, cerebrovacular accidents clearly ranks first in frequency of importance. Almost fifty percent of neurological diseases in general hospital are due to stroke.

Cerebro vascular accident includes ischemic stroke, hemorrhagic stroke, and cerebro vascular anomalies such as intracranial aneurysm, AV malformation and cortical venous thrombosis. Stroke after heart disease, is the second most common cause of death among non-communicable diseases [1].

With the introduction of effective treatment for hypertension, there has been a marked reduction in the frequency of stroke.

Diabetes mellitus by virtue of its association with micro vascular and macrovascular disease is an important risk factor in the genesis of stroke.[2]

Most of the diabetic patients with stroke have raised glycosylated hemoglobin indicating that most of them have uncontrolled diabetes. Diabetics and stress hyperglycemics have severe strokes resulting in poor outcome. Stroke is Twice more common in diabetics than in non diabetics. [3]

Hypertension is common in diabetes and accelerates atherosclerosis which promotes intracranial small vessel disease and heart disease leading to lacunar and embolic infarction respectively. There are several risk factors that determine the outcome of stroke.

Hyperglycemia, fever, neuroprotective agents are those which are widely studied.

AIMS AND OBJECTIVES

AIM OF THE STUDY

To measure the random blood glucose level in the early phase of ischemic stroke (within 24 hours of onset) in both diabetics and in non diabetics and to evaluate the severity and prognosis in both diabetics and non diabetics in relation to hyperglycemia.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

DEFINITION :

Stroke or cerebrovascular accident is a rapidly developing episode of focal and at times global deficit of cerebral function with symptoms lasting more than 24hours or leading to death with no apparent cause other than that of vascular origin.[4]

Acute ischemic stroke is caused by thrombotic or embolic occlusion of a cerebral artery.

Transient ischemic attack (TIA) is an acute loss of focal cerebral or monocular function with symptoms lasting less than 24hours.

Reversible ischemic neurological deficit (RIND) refers to neurological deficit that disappears within 7 days of onset.

EPIDEMIOLOGY

Cerebrovascular disease or stroke is the fifth commonest among premature deaths in adults and fourth leading cause of death of all cause mortality in India. With both death and disability combined i.e., disability-adjusted life years (DALYs) stroke occupies the fifth position among all causes.

According to the World Health Organization (WHO), 15 million people suffer stroke worldwide each year. Of these, 5 million die, and another 5 million are left permanently disabled.

RISK FACTORS [5]

NON-MODIFIABLE RISK FACTORS

Age :

Increasing age is most powerful risk factor for cerebral infarction, intracerebral hemorrhage and subarachnoid hemorrhage as well as TIA

Sex :

men are more at risk for ischemic stroke than woman up to 75 years of age.

Race :

The risk is more in Blacks than Whites

Hereditary :

There is an increased incidence of stroke in individuals who have a first degree relative affected with stroke or who have paternal or maternal history of death or disability due to stroke and family history of TIA.

History of migraine headaches :

Is associated with all types of stroke more common among women.

Fibromuscular dysplasia:

Is more common among female patients.

MODIFIABLE RISK FACTORS

Hypertension :

Hypertension is a major risk factor for stroke. Hypertension is associated with an increased incidence of both haemorrhagic, ischaemic and lacunar stroke. It is an important predisposing factor not only for cerebral hemorrhage but also for infarction. Both systolic and diastolic pressures contribute to the risk though there is no critical level above which it operates. The reduction of BP by 10-12mmHg systolic and 5-6mmHg diastolic was found to be associated with 38% reduction in stroke incidence.

Diabetes mellitus :

It is an independent risk factor for stroke. It increases the susceptibility to coronary, femoral, and cerebral atherosclerosis. The relative risk increases two to fourfold in diabetics patients with diabetic complications like retinopathy and autonomic neuropathy have a higher incidence of ischemic stroke

Hyperglycemia And Stroke :

Diabetes mellitus is an independent risk factor for stroke and one of the important risk factors causing strokes at younger ages. The mechanism is believed to be accelerated atherosclerosis, which can Affect vessels in many distributions, including small and large vessels.

Cardiac involvement may predispose to embolic strokes as well. In addition, patients with diabetes may have any of several lipid abnormalities.

Elevated levels of triglycerides, low-density lipoproteins (LDL), and very low-density lipoproteins (VLDL), along with lower than normal levels of high-density lipoprotein (HDL), are common findings in the lipid profiles of patients with diabetes.

The combined effect of these factors results in promotion of atherosclerosis and thrombosis. Elevated blood glucose is common in the early phase of stroke. The prevalence of hyperglycemia, defined as blood glucose level more than 126 mg/dl has been observed in two third of all ischemic stroke subtypes on admission. [6]

Extensive experimental evidence in stroke models support that association between blood glucose and functional outcome has been found in increasing number of clinical studies.

Causes of Acute Hyperglycemia :

Although up to one third of acute stroke patients have either diagnosed or newly diabetic, probably a major proportion of patients have stress hyperglycemia, mediated partly by the release of cortisol and nor epinephrine. It is also a manifestation of relative insulin deficiency, which is associated with increased lipolysis even in non diabetic patients; stress

hyperglycemia may be a marker of glucose regulation in individuals with insulin resistance and developing diabetes.[7]

Hypercholesterolemia :

It is a secondary risk factor indirectly affecting the risk of stroke. Reducing high cholesterol levels decreases the incidence of coronary artery disease which is the main cause of mortality in patients with cerebro vascular disease.

Non valvular atrial fibrillation :

It is common in the age group of 65 - 85years and attributes to a five fold increase in the incidence of embolic stroke especially in those patients who have recent heart failure or thrombo embolism.

Cigarette smoking :

It increases the risk of infarction in men and women by predisposing to carotid atherosclerosis. Smokers experience a reduction in stroke risk only after 5 years following cessation of smoking.

Alcohol :

Light to moderate intake reduces the risk by increasing the HDL concentration, whereas heavy drinking increases the risk. More than one drink per day for women and more than two per day for men increases the BP, obesity and triglycerides level thereby increasing the risk.

TIA :

Three times greater risk for subsequent stroke or death due to vascular causes, especially those with hemispherical TIA. Patients with a previous history of stroke are at risk for a subsequent stroke. The risk of stroke recurrence is increased by the presence of dementia.

Carotid artery stenosis :

Asymptomatic Carotid artery stenosis less than 75% carries a risk of 1.3% annually whereas risk increases to 10.5% per year if the stenosis is greater than 75%. Ulcerated .echoluscent and heterogeneous plaques with a soft-core are at higher risk for embolism.

Blood factors :

Elevated haematocrit, hemoglobin and viscosity of the blood is associated with increased risk of ischemic stroke. Higher mean levels of plasma fibrinogen, factor VIII, von willebrand's factor, anti-thrombin III and lower mean levels of protein C is associated with increased risk. The Antiphospholipid antibodies is associated with increased risk of ischemic stroke. Serum folate concentration less than or equal to 9.2 nmol/L alone may be risk factor for ischemic stroke.

Hormones :

High dose estrogen oral contraceptives increases the risk of stroke in young women, while postmenopausal estrogen supplementation reduces the risk. The risk of cerebral infarction is increased in the first 6 weeks following delivery.

Others :

Abdominal or truncal obesity, physical inactivity, habitual snoring are associated with increased risk of ischemic stroke.

PATHOPHYSIOLOGY

Stroke is 80% to 90% ischemic and 10 % hemorrhagic.[8] Abrupt disruption of focal cerebral blood flow causes acute ischemic stroke. Acute ischemic strokes result from vascular occlusion secondary to thromboembolic disease. Ischemia causes cell hypoxia and depletion of cellular adenosine triphosphate (ATP). Without ATP, there is no longer the energy to maintain ionic gradients across the cell membrane and cell depolarization. Influx of sodium and calcium ions and passive inflow of water into the cell lead to cytotoxic edema. The causes of decreased cerebral blood flow includes abrupt occlusion of small penetrating arteries arterioles, single or multiple arterial stenosis, arteritis, arterial dissection, venous occlusion, and profound anemia.

An acute vascular occlusion produces heterogeneous regions of ischemia in the affected vascular territory. Local blood flow is limited to any residual flow in the major arterial source plus the collateral supply.

Affected regions with cerebral blood flow of lower than 10 mL/100 g of tissue/min are referred to collectively as the core. When cerebral blood flow falls below this then aerobic mitochondrial metabolism fails and anaerobic metabolism leads to lactic acidosis. These cells are presumed to die within minutes of stroke onset.

Zones of decreased or marginal perfusion (cerebral blood flow < 25 mL/100g of tissue/min) are collectively called the ischemic penumbra. Tissue in the penumbra can remain viable for several hours because of marginal tissue perfusion. When cerebral blood flow falls below a critical value of 20ml /100g/min there is a loss of neuronal electrical function which is a reversible.

As a sequel to this sodium and water enters the cell and potassium leaks out of the cell due to failure of energy dependent intracellular homoeostasis leading to irreversible cell death.

Based on these facts the concept of ischemic penumbra was formulated. It is an area of brain that has reached the reversible stage of electrical failure but has not yet passed into the irreversible stage. Thrombolytic agents are used in this time window to salvage the ischemic penumbra zone.

HOW ELEVATED GLUCOSE INJURES THE ISCHEMIC BRAIN

By provoking anaerobic metabolism, lactic acidosis and free radical production, hyperglycemia may exert direct membrane lipid per oxidation and cell lysis in metabolically challenged tissues. Moderately and severely increased blood glucose has been found to further lower the mitochondrial function in the area and ischemic penumbra.[9] Insulin resistance is a known risk factor for the onset of stroke acting through a

number of intermediate vascular disease risk factors (i.e. thrombophilia, endothelial dysfunction and inflammation) [10].

The evolution of acute infarction may be explained by the very same vascular factors, explaining why ischemic time seems to fly faster in patients with diabetes or grave hyperglycemia. Relative insulin deficiency liberates circulating free fatty acids, which together with hyperglycemia, diminishes vascular reactivity [11,12].

Furthermore, lowering glucose with insulin has been reported to reduce ischemic brain damage. [13]

The evolution of an infarction is accompanied by glutamate release mediating repeated waves of spreading depression (SD), another mechanism believed to propagate the necrosis of penumbral tissues. Although hyperglycemia alone did not trigger early response genes in cortical tissues of rats, in conjunction with induced SD, the expression of c-fos and cox-2 were substantially increased. [14]

This suggested that increased glucose may trigger untoward intracellular biochemical cascades also by altering early gene expression in metabolically challenged neurons.

The blood brain barrier is well known to be vulnerable to hyperglycemia, presumably through the liberation of lactic acid and free radicals.

The recent experimental study by Song et al in a rat model of collagenase induced intra cerebral hemorrhage add that hyperglycemia aggravates edema formation in zone surrounding the hemorrhage.[15] The study also documented increased cell death measured by TUNNEL staining. It is conceivable that hemorrhages are surrounded by a one of similarly challenged tissues as infarctions are where the availability of glucose influences the metabolic state.

COMMON CAUSES OF ISCHEMIC STROKE :

1.Thrombosis

Lacunar stroke (small vessel)

Large vessel thrombosis

Dehydration

2.Embolic occlusion

A. Artery-to-artery

Carotid bifurcation

Aortic arch, Arterial dissection

B. Cardio embolic

Atrial fibrillation

Mural thrombus

Myocardial infarction

Dilated cardiomyopathy

Valvular lesions

Mitral stenosis

Mechanical valve

Bacterial endocarditis

Paradoxical embolus

Atrial septal defect

Patent foramen ovale

Atrial septal aneurysm

Spontaneous echo contrast

UNCOMMON CAUSES :

1. Hypercoagulable disorders

   Protein C deficiency

   Protein S deficiency

   Anti thrombin III deficiency

   Antiphospholipid syndrome

   Factor V Leiden mutation

   Prothrombin G20210 mutation

   Systemic malignancy

   Sickle cell anemia

   Beta Thalassemia

   Polycythemia Vera

   Systemic lupus erythematosus

Homocysteinemia

Thrombotic thrombocytopenic purpura

Disseminated intravascular coagulation

Dysproteinemias

Nephrotic syndrome

Inflammatory bowel disease

Oral contraceptives

2. Venous sinus thrombosis
3. Fibro muscular dysplasia
4. Vasculitis
5. Systemic vasculitis

   (PAN, Wegner's, Takayasu's, giant cell arteritis)

   Primary CNS vasculitis

   Meningitis (syphilis, tuberculosis, fungal, bacterial, zoster)

6. Cardiogenic

   Mitral valve calcification

   Atrial myxoma

   Intra cardiac tumor

   Marantic endocarditis

   Libman-Sacks endocarditis

7. Subarachnoid hemorrhage vasospasm
8. Drugs: cocaine, amphetamine

9. Moyamoya disease
10. Eclampsia.

CLINICAL SYNDROMES [5]

TRANSIENT ISCHAEMIC ATTACKS

TIAs are abrupt in onset , brief in duration and recovery is possible in 24 hours. Recurrent TIAs can occur. Recognition and treatment is important as a complete stroke can be prevented.

Carotid TIAs

These are characterized by monocular blindness with recovery within Few minutes, visual field disturbance in the form of transient hemianopia and speech disturbance due to dominant hemispherical dysfunction. Hemi paresis and hemi sensory loss can occur both in vertebro basilar TIAs as well as carotid TIAs.

Vertebro Basilar TIAs

These are characterized by prominent visual symptoms like Diplopia, homonymous hemianopia and cortical blindness, transient vertigo dizziness, unsteadiness due to cerebellar dysfunction and transient lower cranial nerve symptoms like dysarthria, perioral numbness, nasal regurgitation.

Drop attacks occur without any warning .It is thought to be due to ischemia of relays in reticular systems which normally function as part of reflex antigravity mechanism.

Subclavian steal syndrome

This syndrome occurs when there is occlusion of the Subclavian artery proximal to origin of vertebral artery which results in retrograde flow of blood down the vertebral artery during exercising the arm thereby leading on to symptoms of hindbrain ischemia.

Mini Strokes

Mini strokes are characterized by episodic ischemic symptoms which recover within 24 hours but there are small infarcts or hemorrhage in CT and are as significant as the TIAs.

Stroke in evolution

Stroke in evolution refers to the slow progression of neurological deficit over several hours.

Major strokes

Major stroke are of sudden onset with loss of consciousness at the onset or soon after. It is very difficult to distinguish clinically between infarction or hemorrhage. Headache and vomiting if present, usually denotes hemorrhage especially if it is associated with rapid loss of

consciousness. Athero –thrombo embolism is suggested by the presence of bruit over the carotid arteries.

Unusual types of stroke

Multi-infarct dementia, watershed infarction.

Classification of stroke on the basis of oxford shire community stroke Sub classification [16]

Total anterior circulation syndrome (TACS)

Implies a large cortical stroke in middle cerebral or middle and anterior cerebral artery territories. it is characterized by a combination of new higher cerebral dysfunction Homonymous visual field defect an ipsilateral motor and / or sensory deficit involving at least two out of three areas of the face, arm or leg

Partial anterior circulation syndrome

Implies a cortical stroke in middle or anterior cerebral arterial territory. This includes patients with two out of three components of the Total anterior circulation syndromes or new higher cerebral dysfunction alone or motor / sensory deficit more restricted than those classified as a TACS.

Lacunar syndrome

Implies a sub cortical stroke due to a small vessel disease

- Pure motor stroke
- Pure sensory stroke
- sensory motor stroke
- ataxic hemi paresis

Evidence of higher cortical dysfunction or disturbance of consciousness excludes Lacunar syndrome.

posterior circulation syndrome

1. Ipsilateral cranial nerve palsy with contra lateral motor and sensory deficit,
2. Bilateral motor and or sensory deficit
3. Disorder of conjugate eye movement
4. Cerebellar dysfunction without ipsilateral long tract involvement
5. Isolated homonymous visual field defects

ANTERIOR CEREBRAL CIRCULATION SYNDROME

No	Signs and symptoms	Structures involved
1.	Paralysis of opposite foot and leg	Motor leg area
2.	Lesser degree of paresis of opposite arm	Involvement of cortical / corona radiata of arm fibers
3.	Cortical sensory loss over toes, foot and leg	Sensory area for foot and leg
4.	Urinary incontinence	Sensory motor area in Para central lobule
5.	Contralateral grasp reflex, suckling reflex, gegenhalten	Medial surface of the posterior frontal lobe
6.	Abulia, slowness, delay, intermittent interruption, lack of spontaneous whispering, reflex distraction to sights and sounds	Cingulate gyrus, medial inferior portion of frontal, parietal and temporal lobes
7.	Impairment of gait and stance (gait apraxia)	Frontal cortex near leg motor area
8.	Dyspraxia of left limbs, Tactile aphasia in left limbs	Corpus callosum

MIDDLE CEREBRAL CIRCULATION SYNDROME

No	Signs and symptoms	Structures involved
1	Paralysis of the contra lateral face, arm, and leg; sensory impairment over the same area (pinprick, cotton touch, vibration, position, two-point discrimination, stereognosis, tactile localization)	Somatic motor area for face and arm and the fibers descending from the leg area to enter the corona radiata and corresponding somatic sensory system
2	Motor aphasia	Motor speech area of the dominant hemisphere
3	Central aphasia, word deafness, anomia, jargon speech, sensory agraphia, acalculia, alexia, finger agnosia, right-left confusion (the last four comprise the Gerstmann syndrome	Central, suprasylvian speech area and parieto occipital cortex of the dominant hemisphere
4	Conduction aphasia	Central speech area (parietal operculum)
5	Apractognosia of the minor hemisphere (amorphosynthesis), anosognosia, hemiasomatognosia, unilateral neglect, agnosia for the left half of external space, dressing "apraxia," constructional "apraxia," distortion of visual coordinates, inaccurate localization in the half field, impaired ability to judge distance, upside-down reading, visual illusions (e.g., it may appear that another person walks through a table)	Non dominant parietal lobe (area corresponding to speech area in dominant hemisphere); loss of topographic memory is usually due to a non dominant lesion, occasionally to a dominant one)
6	Homonymous hemianopia (often homonymous inferior quadrantanopia)	Optic radiation deep to second temporal convolution
7	Paralysis of conjugate gaze to the opposite side	Frontal contraversive field or projecting fibers

POSTERIOR CEREBRAL CIRCULATION SYNDROME

Peripheral territory

No	Signs and symptoms	Structures involved
1	Homonymous hemianopia (often upper quadrantanopia)	Calcarine cortex or optic radiation
2	Bilateral homonymous hemianopia, cortical blindness, awareness or denial of blindness; tactile naming, achromatopia (color blindness), failure to see to-and-fro movements, inability to perceive objects not centrally located, apraxia of ocular movements, inability to count or enumerate objects, tendency to run into things that the patient sees and tries to avoid	Bilateral occipital lobe with possibly the parietal lobe involved
4	Verbal dyslexia without agraphia, color anomia	Dominant calcarine lesion and posterior part of corpus callosum.
5	Memory defect	Hippocampal lesion bilaterally or on the dominant side only
6	Topographic disorientation and prosopagnosia	Non dominant, calcarine, and lingual gyrus.
7	Simultagnosia, hemi visual neglect	Dominant visual cortex, contra lateral hemisphere
8	Unformed visual hallucinations, peduncular hallucinosis, metamorphosis, teleopsia, illusory visual spread, palinopsia, distortion of outlines, central photophobia	Calcarine cortex.
9	Complex hallucinations	Non dominant hemisphere.

POSTERIOR CEREBRAL CIRCULATION SYNDROME

Central territory

No	Signs and symptoms	Structures involved
1	Thalamic syndrome: sensory loss (all modalities), spontaneous pain and dysesthesias, choreoathetosis, intention tremor, spasms of hand, mild hemi paresis	Postero ventral nucleus of thalamus; involvement of the adjacent sub thalamus body or its afferent tracts
2	Thalamo perforate syndrome: crossed cerebellar ataxia with ipsilateral third nerve palsy (Claude's syndrome)	Dentatothalamic tract and issuing third nerve
3	Weber's syndrome: third nerve palsy and contra lateral hemiplegia	Third nerve and cerebral peduncle
4	Contra lateral hemiplegia	Cerebral peduncle
5	Paralysis or paresis of vertical eye movement, skew deviation, sluggish pupillary responses to light, slight miosis and ptosis (retraction nystagmus and "tucking" of the eyelids may be associated)	Supranuclear fibers to third nerve, interstitial nucleus of Cajal, nucleus of Darkschewitsch, and posterior commissure
6	Contra lateral rhythmic, ataxic action tremor; rhythmic postural or "holding" tremor (rubral tremor)	Dentatothalamic tract

DIAGNOSTIC EVALUATION OF ISCHAEMIC STROKE [17]

The diagnostic evaluation should include parallel assessment of the following.

1. Imaging of the infarct
2. Vascular studies
3. Cardiac evaluation
4. Hematological and other blood testing

Imaging

CT scan brain is done to differentiate hemorrhage from infarction. Investigations must be ordered based on the possible etiology. Cerebral arteriography is needed if intra arterial thrombolysis is contemplated. Angiogram is done if vascular stenosis is suspected and if it is negative or if posterior circulation is suspected then, Tran cranial Doppler is done.

CT versus MRI

1. Only a minority infarction demonstrated within 24 hours on CT. MRI documents infarct as early 6 hours
2. Anatomic extent and vascular distribution are better delineated in MRI. Small infarctions are easily seen and white matter better visualized.
3. Posterior fossa infarctions are better visualized in MRI.

CT scan changes in cerebral infarction [18]

Hyper acute infarct < 12 hours

normal (50 – 60%)

Hyper dense artery (25 – 50%)

- Obscuration of Lentiform nuclei

Acute infarct 12 to 24hours

- Low density basal ganglia
- Loss of grey white interfaces
- Sulcal effacement

1 to 3days

- Increasing mass effect
- Wedge shaped low density area that involves both grey&white matter
- Hemorrhagic transformation may occur (basal ganglia and cortex are common sites)

4 to 7days

- Gyral enhancement
- mass effect, edema persist

1 to 8 weeks

- Contrast enhancement persists
- mass effect resolves

months to years

- encephalomalacic changes
- volume loss
- calcification is rare

Clinical Correlation of Hyperglycemia and Infarct Progression

Although experimental studies have clarified several mechanisms by which hyperglycemia influences the destiny of ischemic brain issue, studies bridging the gap between clinical stroke and experimental models have been scare.

Recent advances in Magnetic Resonance Imaging techniques have permitted Correlation of loss of penumbral tissue with elevated blood glucose, which was linked to increased brain lactate production. [19] Using a subcutaneous glucose sensor for continuous monitoring up to seventy two hours, the sane group could reproduce the findings that the infarcts expanded more in hyperglycemic patients and that hyperglycemia was independently associated with the infarct volume change. [20] This suggests that increased glucose not only reflects the initial volume of infracted tissue in the acute stage but is one of the true determinants of early infarct progression in men.

Neurological Pearls In Prognosis

Factors predicting poor outcome [21]

1. age : more than 75 years
2. males : due to lack estrogen protective effect
3. risk factors : atrial fibrillation, DM, previous stroke
4. clinical findings
    - decreased consciousness at the onset
    - Presence of gaze deviation
    - Headache, nausea, vomiting in first 24 hours
    - Elevated systolic BP >180 mm Hg on first day
    - Hyperthermia on admission
    - NIHSS score of 16 or more
    - Large vessel disease
5. Laboratory findings
    - High glutamine in plasma > 200 micromol / L
    - CRP concentration > 10.2 mg / l within 72 hours
    - Hyperglycemia > 126mg / dl
    - Platelet count < 150000 due to increased bleeding
6. Neuro imaging studies
    - Hyper density in a major intra cranial artery
    - Early CT changes within 6 hours of onset

- >33 % of MCA territory involvement / multiple territory involvement with mass effect
- Hemorrhagic transformation on follow up CT / on intra cranial Doppler persisting MCA occlusion for hours
- No flow on SPECT perfusion patterns
- Carotid artery occlusion on conventional angiogram
- MCA , basilar artery occlusion on angiogram
- MRI – abnormal PWI in diffusion and perfusion weighted imaging
- MRA – absence of MCA is associated with poor prognosis

PROGNOSIS AND HYPERGLYCEMIA

Already ample literature has demonstrated that hyperglycemia on admission is associated with worsened clinical outcome as reviewed in a systemic overview of thirty three studies .[22] Glycemic control may be indicated also in non-diabetic patients, in which stress hyperglycemia was associated with a three fold risk of fatal thirty day outcome and 1.4 fold risk in of poor functional outcome.[23]

Preexisting hyperglycemia worsens the clinical outcome of acute stroke. Nondiabetic ischemic stroke patients with hyperglycemia have a 3-fold higher 30-day mortality rate than do patients without

hyperglycemia.[24] In diabetic patients with ischemic stroke, the 30-day mortality rate is 2-fold higher.[25]

TREATMENT

The first goal is to prevent or reverse brain injury. The second goal is to obtain an accurate understanding of the stroke mechanism so one can halt progression of brain injury or begin to prevent a second stroke

Treatments designed to reverse or lessen the amount of tissue infarction fall Within five categories:

1. Medical support
2. Thrombolysis
3. Anticoagulation
4. Antiplatelet agents
5. Neuroprotection

(1)Medical Support

1.When cerebral infarction occurs, the immediate goal is to optimize cerebral perfusion in the surrounding ischemic area

2. Preventing the common complications of bedridden patients like infections (pneumonia, urinary tract, and skin), deep venous thrombosis with pulmonary embolism.

3.Elevated BP should not be lowered unless there is malignant hypertension or concomitant myocardial ischemia. If the blood pressure

is low, raising it is advisable, using intravenous fluids or vasopressor drugs to enhance perfusion within the ischemic penumbra.

4. Treatment of cerebral edema if necessary

(2)Thrombolysis

The use of thrombolytic agents in acute cerebral infarction has been studied extensively. Angiography performed within a few hours of infarction frequently demonstrates arterial occlusions corresponding to patients presenting signs and symptoms. It is this association of arterial occlusion with acute neurological symptoms that prompted the study of thrombolytic agents in stroke patients.

Agent used for this purpose is intravenous recombinant tissue plasminogen activator (rtPA)

Indication [26]

Clinical diagnosis of ischemic stroke with clear symptom onset within 3 hours CT scan showing no hemorrhage or significant edema Age more than 18 years, Consent by patient or surrogate

Contraindication [26]

Sustained BP > 185/110

Platelets < 100,000; HCT< 25%; glucose < 50 or > 400

Use of heparin within 48 h and prolonged PTT, or elevated INR Rapidly improving symptoms Prior stroke or head injury within 3

months; prior intracranial hemorrhage Major surgery in preceding 14 days Minor stroke symptoms Gastrointestinal bleeding in preceding 21 days Recent myocardial infarction, Coma or stupor

Administration of rtPA [27]

Intravenous access with two peripheral IV lines (avoid arterial or central placement) Review eligibility for rtPA.

Administer 0.9 mg/kg intravenously (maximum 90 mg) IV as 10% of total dose by bolus, followed by remainder of total dose over 1 h. Continuous blood pressure monitoring.

No other antithrombotic treatment for 24 h.

For decline in neurological status or uncontrolled blood pressure, stop infusion, give cryoprecipitate, and reimage brain emergently

Avoid urethral catheterization for > 2 h.

(3)Anticoagulation

The role of anticoagulation in atherothrombotic cerebral ischemia is uncertain. Heparinization is generally accomplished by beginning an infusion without bolus and is monitored to maintain the activated PTT at approximately twice normal.

This regimen is maintained for 2 to 5 days. During this time the patient is monitored for hemorrhagic complications, the evaluation is

completed decision is made regarding the need for carotid endarterectomy, long-term anticoagulation, or an antiplatelet therapy.

If long-term anticoagulation is chosen, warfarin is administered and heparin discontinued when the international normalized ratio (INR) is in the range of 2 to 3.

(4)Antiplatelet Agents

Aspirin is the only antiplatelet agent that has been prospectively studied for the treatment of acute ischemic stroke. The use of aspirin within 48 h of stroke onset reduced both stroke recurrence risk and mortality minimally

(5)Neuroprotection

Neuroprotection is the concept of providing a treatment that prolongs the brain's tolerance to ischemia long enough to allow other measures to be employed to mitigate ischemia. Hyperthermia, Hyperglycemia are the agents which increases the size of the infarct, hence hypothermia and normalizing blood sugar are powerful neuroprotective agents.

HYPERGLYCEMIA AND THROMBOLYTIC THERAPHY OF ACUTE ISCHEMIC STROKE [28]

In several thrombolysis trials, hyperglycemia has been associated With hemorrhagic events [29] as well as in a re- Analysis of the NINDS rt-PA trial.[30]

In the latter study, as increasing admission glucose level was independently associated with decreased odds for neurological improvement (odds ratio, OR = 0.76 per 100 mg/dl increase in admission glucose) and the odds ratio for symptomatic intra cerebral hemorrhagic was 1.75 per 100 mg/dl increase in admission glucose (95 % CI 1.11 to 2.78, p = 0.02). The relationship was weaker after excluding patients with intra cerebral hemorrhage, suggesting admission hyperglycemia may exert its hazard in part through hemorrhagic events. However another recent study by Alvarez-Sabin et al found admission glucose more than 140 mg/dl (OR 8.4, CI 1.8 to 40.0) to be the sole independent predictor of poor functional outcome at three months in patients with recanalization within six hours, even after excluding the patients symptomatic intra cerebral hemorrhage.[31] The same was not true for the patients who did not recanalize, which leads to speculation that might partially preclude the beneficial effect of r-tPA and early reperfusion.

PRIMARY AND SECONDARY PREVENTION

Atherosclerosis Risk Factors

Hypertension is the most significant of the risk factors; in general, all hypertensives should be treated. Coronary artery disease is the most common cause of death in patients with cerebrovascular disease, treatment of hypercholesterolemia seems prudent for both the heart and brain. Tobacco smoking should be discouraged in all patients

Antiplatelet Agents

Platelet antiaggregation agent*s* can prevent atherothrombotic events, including TIA and stroke, by inhibiting the formation of intra-arterial platelet aggregates. These can form on diseased arteries, induce thrombus formation, and occlude the artery or embolize into the distal circulation.

The antiplatelet agents used most for this purpose are :

Aspirin, Clopidogrel, and

The combination of aspirin plus extended-release Dipyridamole

Anticoagulation Therapy

ATHEROTHROMBOTIC STROKE

There are few data to support the use of long-term warfarin for preventing atherothrombotic stroke, either intra cranially or extra cranially.

EMBOLIC STROKE

Several recent trials demonstrated that anticoagulation (INR range 2 to 3) in patients with chronic non valvular (non rheumatic) atrial fibrillation prevents cerebral embolism and is safe.

For primary prevention and for patients who have experienced stroke or TIA, anticoagulation with warfarin reduces the risk by about 65% and clearly outweighs the 1% per year rate of major bleeding complication.

Because of the high annual stroke risk in untreated rheumatic heart disease, primary prophylaxis against stroke has not been studied in a double-blind fashion. These patients generally receive long-term anticoagulation.

Anticoagulation also reduces the risk of embolism in acute myocardial infarction. Most clinicians recommend a 3-month course of anticoagulation when there is anterior Q-wave infarction, substantial Left ventricular dysfunction, congestive heart failure, mural thrombosis, or atrial fibrillation .Warfarin is recommended long-term if atrial fibrillation persists.

Thromboembolism is one of the most serious complications of prosthetic heart valve implantation. Anticoagulation has been proven effective for preventing strokes in this situation, while antiplatelet therapy alone has not.

However, coupled with warfarin anticoagulation, aspirin adds substantial benefit. A greater degree of anticoagulation (INR of 3 to 4, depending on valve type) is recommended for prosthetic heart valve patients.

SURGICAL THERAPY

Surgery for atherosclerotic occlusive disease is largely limited to carotid endarterectomy for plaques located at the origin of the internal carotid artery in the neck

Carotid endarterectomy is a proven effective prophylaxis against stroke and TIA.

Stroke Centers and Rehabilitation

Comprehensive stroke units that care for the acute patient followed by rehabilitation services have been shown to improve neurological outcomes and reduce mortality.

Proper rehabilitation of the stroke patient includes early physical, occupational, and speech therapy. It is directed toward educating the patient and family about the patient's neurological deficit, preventing the complications of immobility (e.g., pneumonia, deep vein thrombosis and pulmonary embolism, pressure sores of the skin, muscle contractures), and providing encouragement and instruction in overcoming the deficit. The goal of rehabilitation is to return the patient to home and to maximize

recovery by providing a safe, progressive regimen suited to the individual patient.

MORTALITY IN STROKE :

Early mortality (first thirty days) :

Generally death occurs with in first 1 days and is secondary to large infarction leading to cerebral edema and raised Intra cranial tension. These patients can be clinically identified by

1. Severe fall in level of consciousness.
2. Gaze paresis.
3. Hemianopia.
4. Dilated pupil on the infracted side.
5. Abnormal type of respiration.

In such patients CT scan will reveal large hemispherical infarct with edema and midline shift and or brain stem infarct.

Other causes after 10 days :

1. Aspiration pneumonitis.
2. Bed sores.
3. Infections.
4. Pulmonary embolism.

Late mortality :

Important causes are IHD and recurrent stroke.

SUMMARY OF EVIDENCE SUPPORTING A DETRIMENTAL ROLE FOR ELEVATED GLUCOSE IN STROKE

1. Experimental ischemic damage is worsened by hyperglycemia
2. Experimental ischemic damage is reduced by glucose reduction
3. Early hyperglycemia is associated with clinical infarct progression in brain imaging
4. Early hyperglycemia is associated with hemorrhagic conversion in stroke
5. Early hyperglycemia is associated with poor clinical outcome
6. Early hyperglycemia may reduce the benefits of recanalization
7. Immediate insulin therapy reported beneficial in acute myocardial infarction and surgical critical illness.

CONCLUSION

This recent evidence supports that acutely elevated, predominantly stress related hyperglycemia is associated with poor outcome such as dependent state or intra cerebral hemorrhage. Through different biochemical mechanisms, increased glucose in setting of cerebro vascular insults probably accelerates the course of ischemic injury, also in the boundary regions with milder perfusion deficit. Although admission hyperglycemia has been already demonstrated to be risk factor for symptomatic hemorrhage and worsened outcome after thrombotic

therapy, there is perhaps not enough evidence to withhold thrombolysis from hyperglycemic patients within the three hour time window. How ever restoration of normoglycemia as soon as possible should be encouraged, although conclusive evidence of decreased risk with this approach is lacking. Especially the non diabetic patients may be a risk of further brain damage if hyperglycemia prevails. The recent evidence summarized above urges corroboration in randomized controlled trial of the efficacy of immediate sugar control, and determination of where the level of target glucose concentration of relatively different current values in the published guidelines (EUSI < 10 mmol/l; ASA < 300 mg/dl) [7] should be set.

In the interim, we should fare well with adhering to good general stroke management, including control of blood glucose , normalization of body temperature, fluid balance and hemodynamics or we may otherwise risk the favorable outcome even in the patients with early recanalization.

MATERIALS AND METHODS

MATERIALS AND METHODS

Total of seventy of acute ischemic stroke patients admitted in the Institute of Internal medicine, Madras medical college & RGGGH, Chennai between February 2017 to september 2017 were studied. The Patients were selected on the following basis

INCLUSION CRITERIA:

1. Patients should be above the age of forty
2. Patients should have been admitted within twenty four hours of onset of symptoms
3. This should be the first cerebro vascular accident for the patient
4. Blood sugar recorded with in twenty four hours of the onset of stroke

EXCLUSION CRITERIA:

1. Patients admitted after twenty four hours of stroke
2. Those patients who received intravenous glucose before or during study period
3. Patients with reliable information about diabetes could not be obtained
4. Patients who died before it could be established whether or not they had diabetes
5. Illness presented with stroke like symptoms

Out of the seventy patients, ten were dropped as follow up could not be done.

Complete history was taken, clinical examination was done and clinical diagnosis for each patient was arrived.

Blood pressure measurement, blood sugar, urea, creatinine, electrolytes, hemoglobin, total count, differential count; urine sugar, albumin, deposits; electrocardiogram and chest X ray done for all patients

The severity of stroke for each patient is calculated based on NIH stroke scale, NIHSS [32] which takes the following clinical findings in to account and each criteria awarded specific points

1a Level of conscious

Alert	0
Drowsy	1
Stuporous	2
Comatose	3

1b LOC questions

Answers both correctly	0
Answers one correctly	1
Incorrect	2

1c LOC commands

Obeys both correctly	0
Obeys one correctly	1
Incorrect	2

2. Best gaze

Normal	0
Partial gaze palsy	1
Forced deviation	2

3. Visual

No visual loss	0
Partial hemianopia	1
Complete hemianopia	2
Bilateral hemianopia	3

4. Facial palsy

Normal symmetric	0
Minor paralysis	1
Partial paralysis	2
Complete paralysis	3

5. Best motor arm (right and left)

No drift	0
Drift	1
Some antigravity effort	2
No antigravity effort	3
No movement	4

6. Best motor leg (right and left)

No drift	0
Drift	1
Some antigravity effort	2

No antigravity effort	3
No movement	4

7. Limb ataxia

Absent	0
Present in one limb	1
Present in both limbs	2

8. Sensory

No sensory loss	0
Mild to moderate sensory loss	1
Total sensory loss	2

9. Best language

Normal, no aphasia	0
Mild to moderate aphasia	1
Severe aphasia	2
Mute, global aphasia	3

10. Dysarthria

Normal	0
Mild to moderate	1
Severe	2

11. Extinction/ inattention

No abnormality	0
Visual/ tactile/ spatial/ personal inattention	1
Profound hemi inattention	2

The points were added, with a maximum of forty two points.

NIHSS

Score	Stroke severity
0	No stroke symptoms
1-4	Minor stroke
5-15	Moderate stroke
16-20	Moderate to severe stroke
21-42	Severe stroke

Once clinical diagnosis of acute stroke is made venous blood sample is taken, with in twenty four hours of onset of symptoms, and sent to laboratory for glucose estimation.

In patients with blood sugar more than 6.1 mmol/l(110 mg/dl) [22] and without a history of diabetes , Hemoglobin A 1c was performed. (Hemoglobin A1c is structurally similar to hemoglobin A except for the addition of glucose

Group to the terminal amino acid of the beta chain of the hemoglobin Molecule (glycosylation). Therefore hemoglobin A 1c is a function of the exposure of the red blood cells to glucose. Since the glucose linkage to hemoglobin is relatively stable, Hemoglobin A1c accumulates through out of the life span of erythrocyte and its

concentration reflects the integrated blood glucose concentration over a period approximating to the half life of erythrocytes i.e. six to eight weeks. Therefore measurement of hemoglobin A 1c helps to monitor the overall degree of diabetic control achieved). The normal range of Hemoglobin A 1c is 3.8% to 6.4%.[33] Hence the patients can be classified into four groups

Blood sugar less than 6.1 mmol/l : **Non diabetic (euglycemic)**

History of diabetes : **Known diabetics**

Blood sugar more than 6.1mmol/l, no history of diabetes, and hemoglobin A1c more than 6.4% : **Newly detected diabetics**

Blood sugar more than 6.1 mmol/l, no history of diabetes, and hemoglobin A1c less than 6.4% : **Stress hyperglycemics**

Then computerized tomography, CT, of the brain was performed in all patients to :

Confirm the diagnosis

Detect the type of stroke

Detect the size of lesion (small < 5mm; Medium 5 – 10 mm;

Large > 10 mm or involving more than one vascular territory)

Locate the site of lesion

Identify the presence of cerebral edema or midline shift

The patients were followed up for thirty days and outcome in the form of death ; poor, moderate and good improvement were recorded.

Patients who were unable to return to any form of work, [34] persistent

Disability,[35] need for residential placement ,[36]dependent in activities of daily

Living , [37]and stable deficit with no recovery [38] were classified as those with poor outcome. Patient whose symptoms improved, who were independent in attending day to day activities, improvement in motor function and aphasia and no persistent disability were grouped as patients with good outcome. Patients who fared in between these two groups were grouped as those with moderate outcome.

OBERVATION AND RESULTS

OBSERVATION AND RESULTS

SEX DISTRIBUTION

SEX	Frequency	Percent
MALE	30	60.0
FEMALE	20	40.0
Total	50	100.0

AGE WISE DISTRIBUTION

Age	Frequency	Percent
40-50 YEARS	9	18.0
51-60 YEARS	15	30.0
61-70 YEARS	14	28.0
71-80 YEARS	12	24.0
Total	50	100.0

RISK FACTORS

HYPERTENSION

	Frequency	Percent
NO	18	36.0
YES	32	64.0
Total	50	100.0

DIABETES MELLITUS

	Frequency	Percent
NO	16	32.0
YES	34	68.0
Total	50	100.0

DYSLIPIDEMIA

	Frequency	Percent
NO	21	42.0
YES	29	58.0
Total	50	100.0

SMOKER

	Frequency	Percent
NO	34	68.0
YES	16	32.0
Total	50	100.0

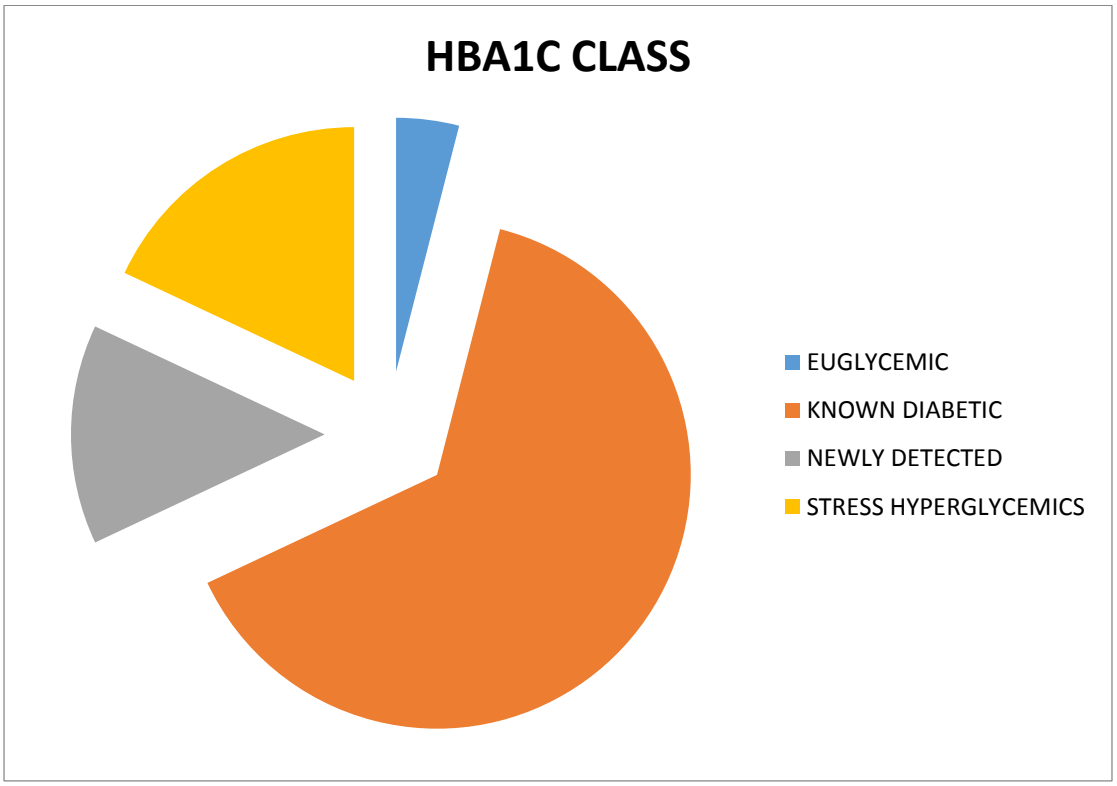
ALCOHOLIC

	Frequency	Percent
NO	36	72.0
YES	14	28.0
Total	50	100.0

GLYCEMIC STATUS

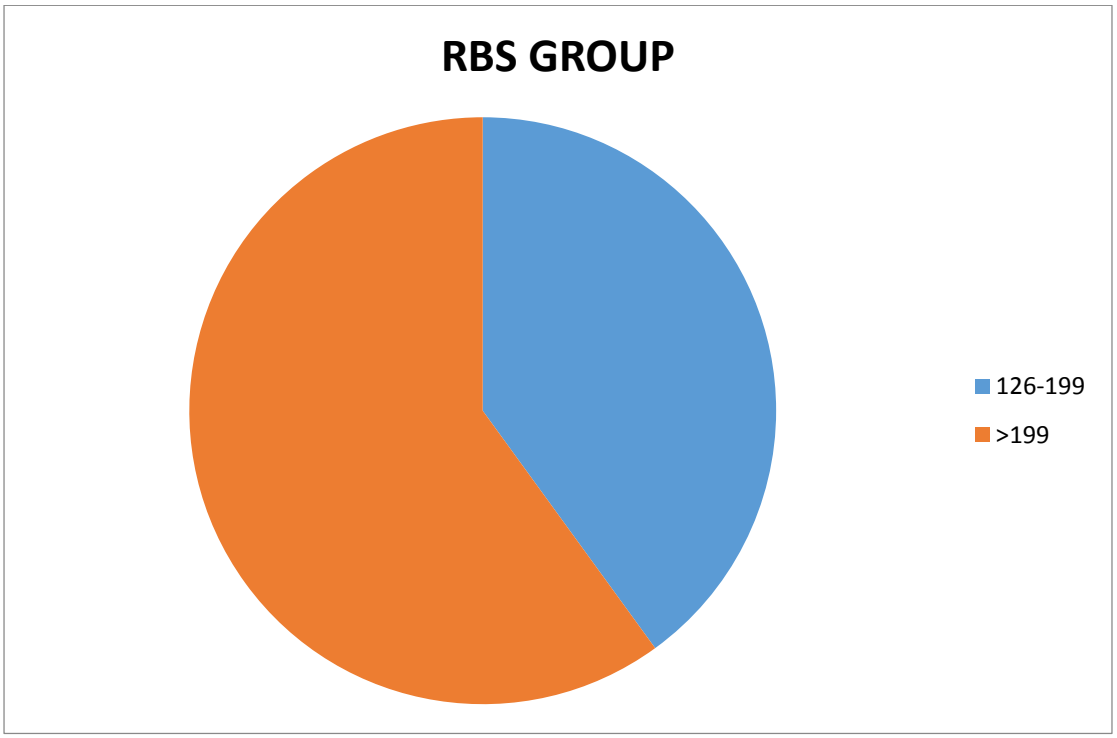
Based on HbA1c

	Frequency	Percent
EUGLYCEMIC	2	4.0
KNOWN DIABETIC	32	64.0
NEWLY DETECTED	7	14.0
STRESS HYPERGLYCEMICS	9	18.0
Total	50	100.0


HBA1C CLASS
EUGLYCEMIC
KNOWN DIABETIC
NEWLY DETECTED
STRESS HYPERGLYCEMICS

Based on random blood glucose

	Frequency	Percent
126-199	20	40.0
>199	30	60.0
Total	50	100.0


RBS GROUP
126-199
>199

STATISTICAL ANALYSIS :

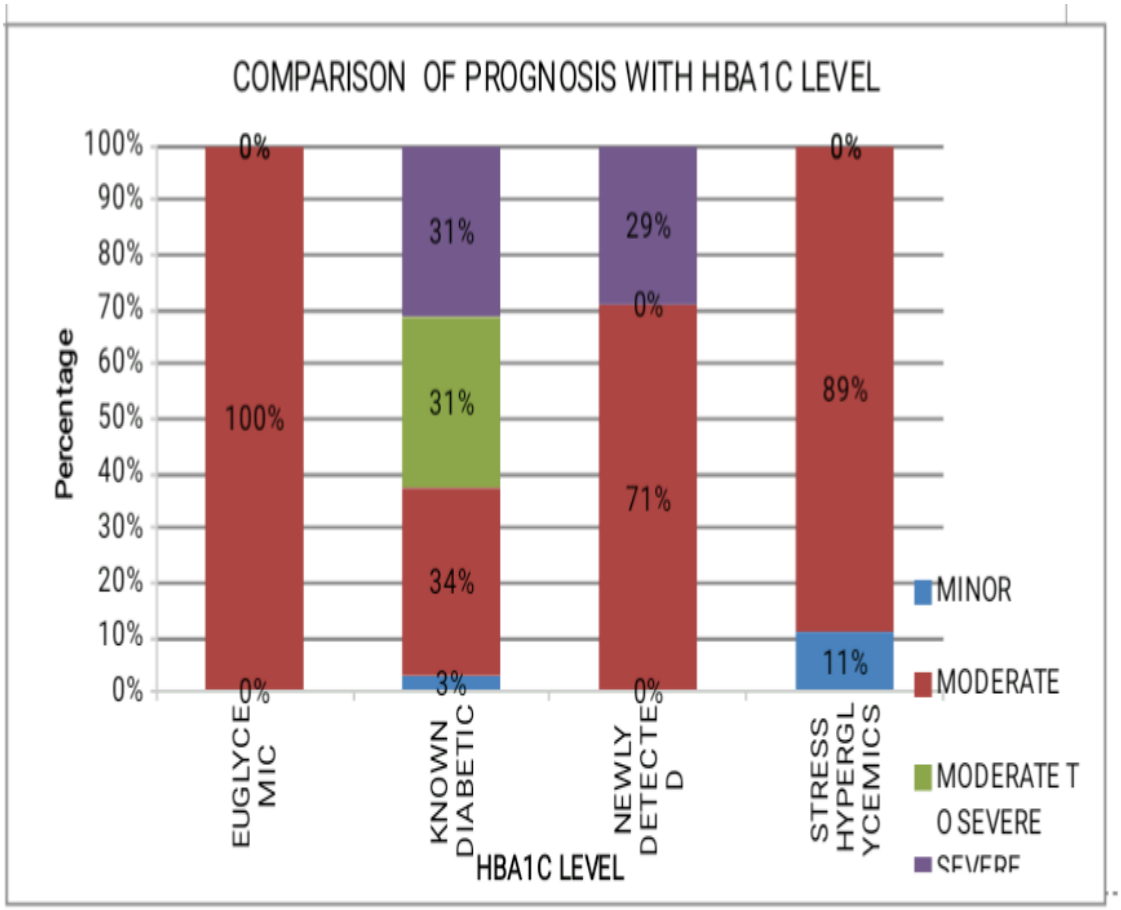
NIHSS is equated to stroke severity and clinical outcome of patient after stroke onset assessed in varying intervals

NIHSS vs HBA1C

NIHSS vs HBA1C							
Stroke severity			EUGLYCEMIC	KNOWN DIABETIC	NEWLY DETECTED	STRESS HYPERGLYCEMICS	
NIHSS CLASS	MINOR	Count	0	1	0	1	2
		% within HBA1C	0.0%	3.1%	0.0%	11.1%	4.0%
	MODERATE	Count	2	11	5	8	26
		% within HBA1C	100.0%	34.4%	71.4%	88.9%	52.0%
	MODERATE TO SEVERE	Count	0	10	0	0	10
		% within HBA1C	0.0%	31.2%	0.0%	0.0%	20.0%
	SEVERE	Count	0	10	2	0	12
		% within HBA1C	0.0%	31.2%	28.6%	0.0%	24.0%

Pearson Chi-Square=21.714* P=0.010 significant

COMPARISON OF NIHSS & HBA1C LEVEL

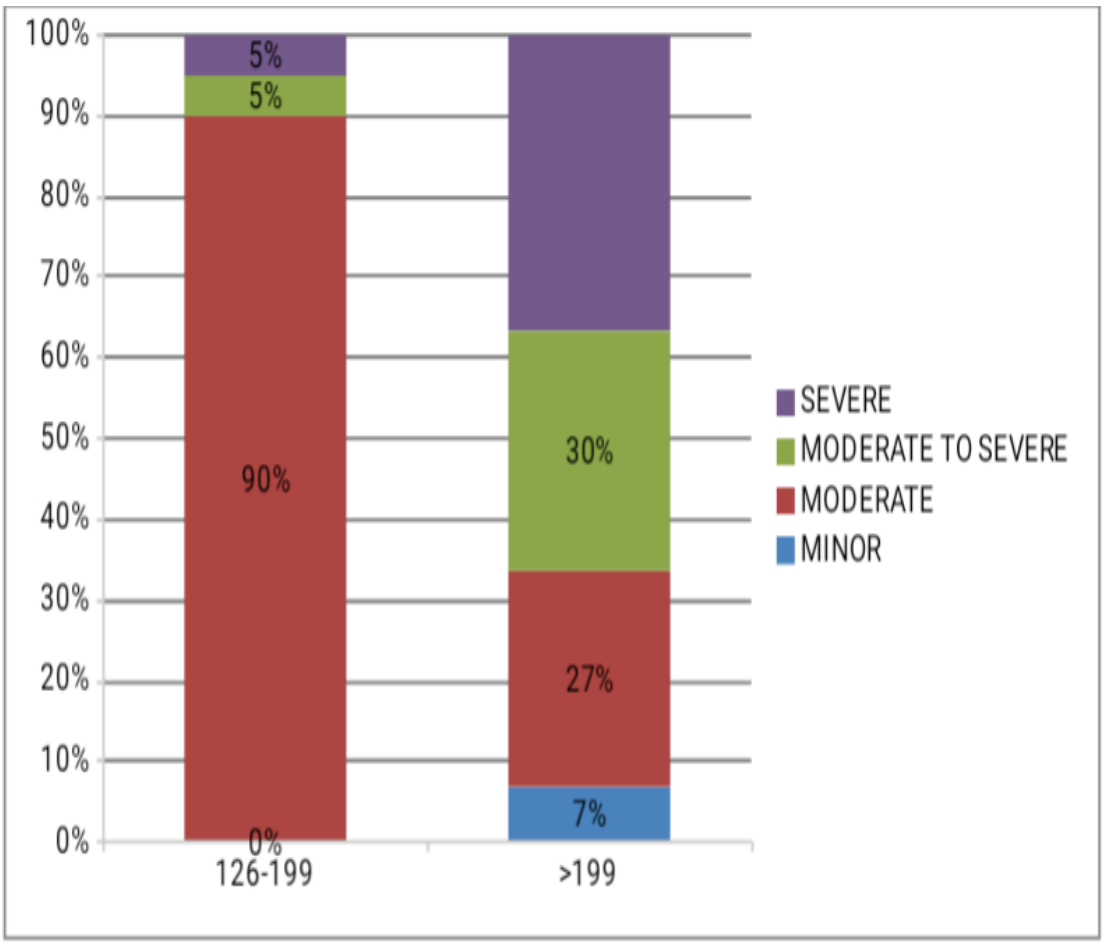


NIHSS VS RANDOM BLOOD SUGAR LEVELS

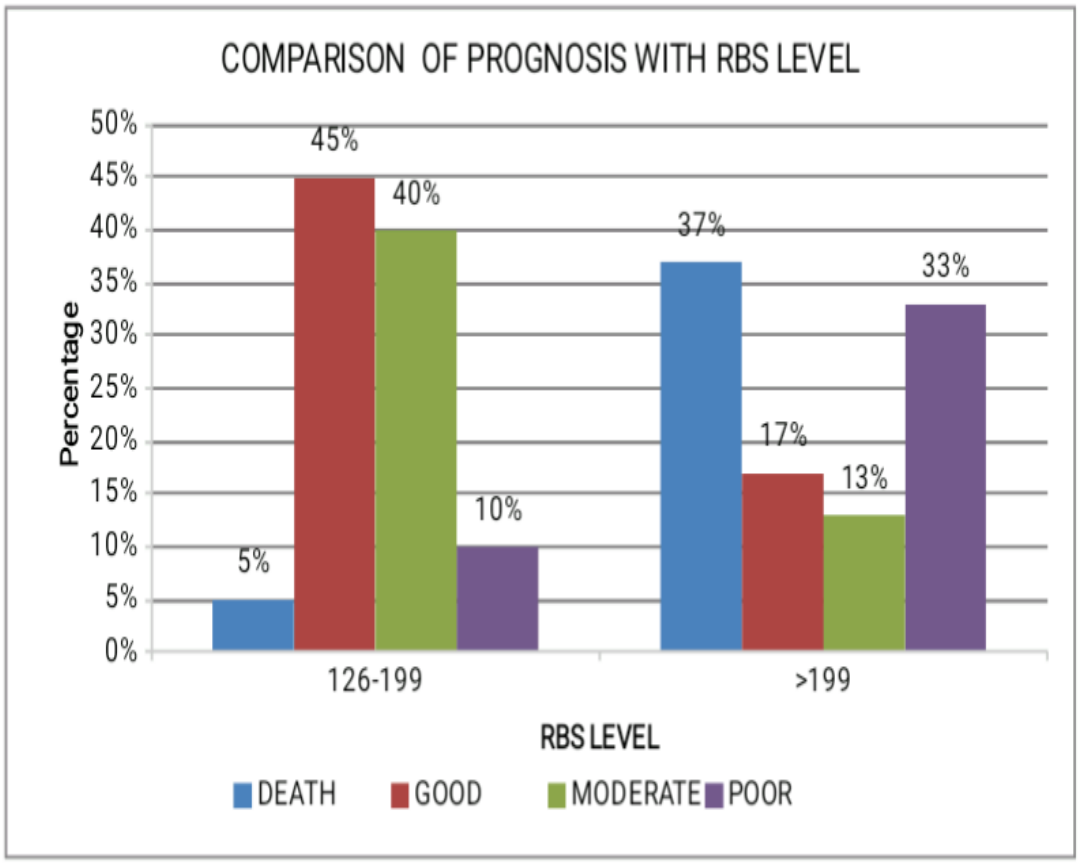
			RBS_GROUP		Total
			126-199	>199	
NIHSS	MINOR	Count	0	2	2
		% within RBS_GROUP	0.0%	6.7%	4.0%
	MODERATE	Count	18	8	26
		% within RBS_GROUP	90.0%	26.7%	52.0%
	MODERATE TO SEVERE	Count	1	9	10
		% within RBS_GROUP	5.0%	30.0%	20.0%
	SEVERE	Count	1	11	12
		% within RBS_GROUP	5.0%	36.7%	24.0%
	Total	Count	20	30	50
		% within RBS_GROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=21.819** P<0.0001 significant

COMPARISON OF NIHSS & RBS



COMPARISON OF CLINICAL OUTCOME & RBS



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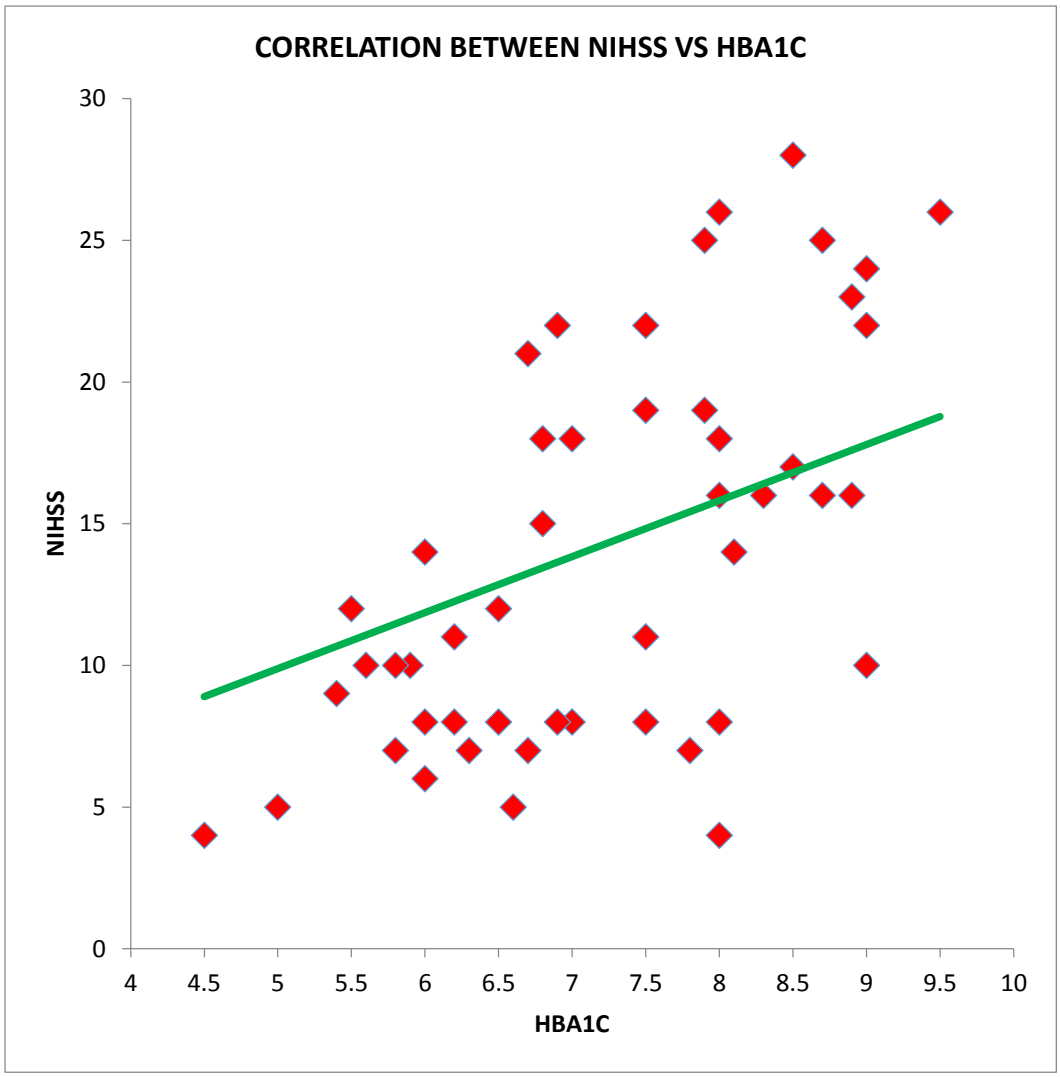
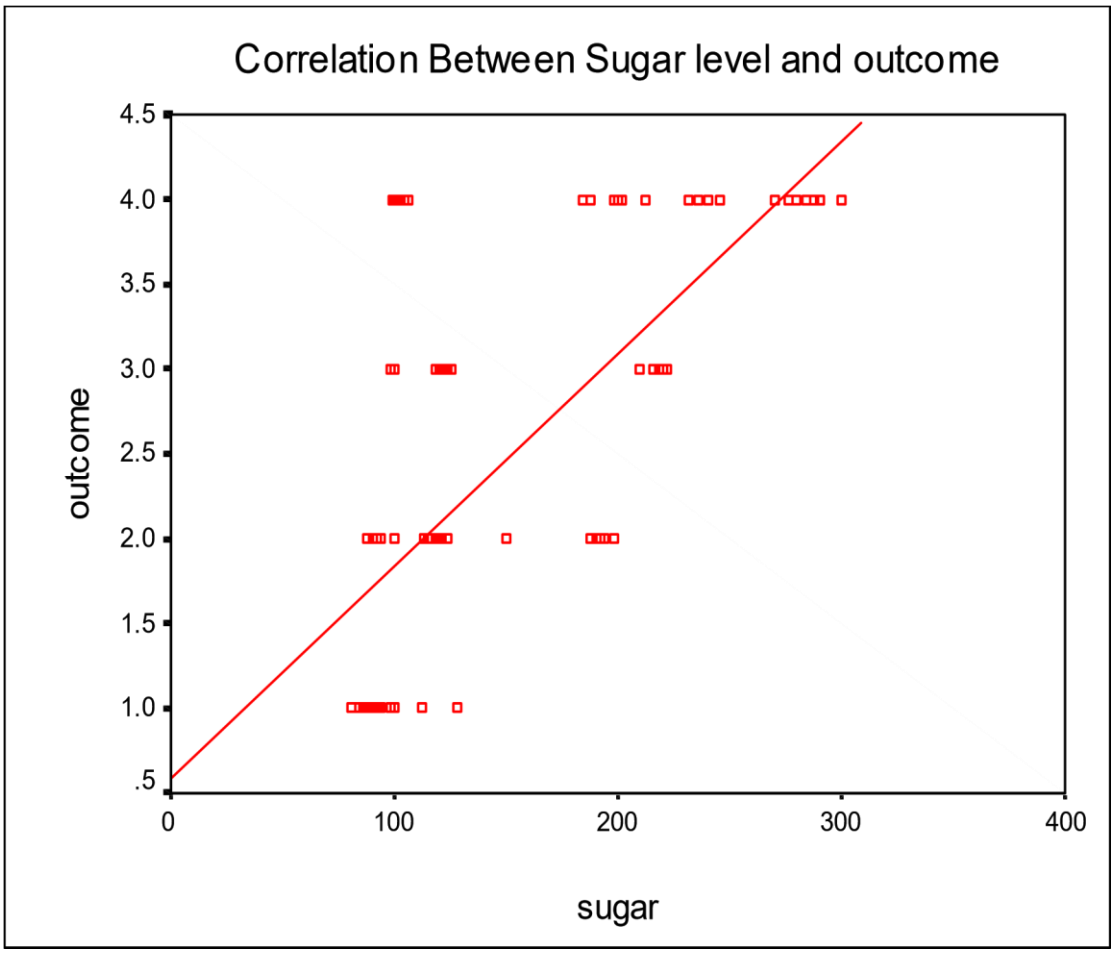

CORRELATION BETWEEN NIHSS VS HBA1C
NIHSS
HBA1C
0
5
10
15
20
25
30
4
4.5
5
5.5
6
6.5
7
7.5
8
8.5
9
9.5
10


Correlation Between Sugar level and outcome
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
outcome
0
100
200
300
400
sugar

DISCUSSION

DISCUSSION

AGE, SEX AND RISK FACTORS:

In our study of fifty patients majority of them belonged to male sex showing a male preponderance which is commonly seen in most studies. Majority of the patients, fifteen were between the age group of 51 to 60. Among the fifty patients 32 had hypertension, 34 had diabetes, 29 had hypercholesterolemia, 3 had previous history of myocardial infarction, and one female patient had atrial fibrillation.

More than two third of the male patients were smokers and one half had history of alcohol intake. 36 patients had right sided weakness and 24 patients had left sided weakness.

GLYCEMIC STATUS :

Among the fifty patients in our study group, 30 patients had elevated admission day blood glucose level and 20 patients had normal blood glucose values. Diabetes was noticed in 32 patients and stress hyperglycemia in another 9 patients . Stress hyperglycemia amounted to more than one third of the patients

SEVERITY OF STROKE :

Severity of stroke was assessed with NIH Stroke scaling system. Admission day hyperglycemic patients had a higher score when

compared to Euglycemic patients , which was statistically significant with p = 0.0001. Among the admission day hyperglycemic patients. Uncontrolled diabetes patients had the highest mean NIHSS. Hence an elevated blood sugar at the time of stroke resulted in severe stroke.

SIZE OF STROKE:

The size of the lesion were analyzed with the help of CT scan brain. Most of the euglycemic patients had small sized infarcts whereas majority of the admission day hyperglycemic patients had large sized lesion with edema and midline shift. These data's were statistically significant with p = 0.001. Hyperglycemia by virtue of increased anaerobic metabolism, increased brain lactate, impaired mitochondrial function, vascular disease, increased free radical production, increased expression of c-fos and cox-2 causes severe brain injury and large sized infarcts. Hyperglycemia can disrupt the blood brain barrier resulting in large hemorrhage and hemorrhagic transformation of infarcts.

OUTCOME OF STROKE :

In this study of hundred acute stroke patients, euglycemic patients had a better outcome when compared to admission day hyperglycemic patients.

Euglycemic patients had a better recovery after acute stroke.

Seventeny two percent of euglycemic (patients including treated) had a good functional recovery. On the contrary only three percent of admission day hyperglycemic patients had good functional recovery at the end of thirty day follow up.

Early inpatient mortality was high in admission day hyperglycemic patients. Fifty percent of the admission day hyperglycemic patients died with in the first thirty days. In the euglycemic patients the early case fatality rate was only fifteen percent. Hence there was a three fold increased risk of early mortality in admission day hyperglycemic patients when compared to euglycemics. Poor outcome was noticed in thirty eight percent of admission day hyperglycemic patients and in three percent of euglycemic patients.

This study of fifty acute stroke patients shows that admission day elevated blood glucose level was associated with a high early mortality rate and an increased risk of poor functional recovery.

These data's were statistically significant with $\chi 2=21.819$ and $p=0.0001$.

In the ischemic stroke group early mortality rate was 2.07 % in euglycemic patients and 14.8 % in hyperglycemic patients. Poor outcome was noticed in 3.18 % in euglycemics and 38.3 % in hyperglycemics. Hence hyperglycemia was associated with an increased early mortality

rate and poor functional outcome in ischemic stroke group which was also statistically significant

Our study clearly shows a positive correlation (r = 0.71, p = 0.01) between admission day sugar value and the outcome of stroke. Higher admission day elevated blood glucose level has increased mortality and high risk of poor functional recovery.

COMPARISION WITH OTHER STUDIES :

According to Perttu J. Lindsberg and Risto o Roine [39] hyperglycemia was noted in two third (66%) of all ischemic stroke patients. In our study hyperglycemia was noticed in 60% of patients with ischemic stroke. In their study known diabetes and newly diagnosed diabetes contributed one third of cases (33%). In our study the same group contributed to 62 %.

A study published in European journal of Neurology, 2002 concluded that elevated glucose level after acute stroke is associated with higher stroke severity than those with normal level.[40]The mean NIHSS was 5.6 in euglycemics and 14.5 in hyperglycemic patients in our study.

In the journal of clinical endocrinology and metabolism, 2002 a study confirmed that patients with newly detected hyperglycemia had a significant higher early mortality and a lower functional outcome than

patients with a history of diabetes or normoglycemia.[41] Our study in hundred acute stroke patients had the same results.

Sarah E capes et al [22] analyzed thirty two similar studies and concluded that hyperglycemic patients had threefold increased early mortality than euglycemic patients. After ischemic stroke admission hyperglycemia was associated with three fold increased 30 day mortality than euglcemics. [22]

In our study, ischemic patients, who had elevated admission day glucose level experienced a three and a half fold increased early mortality than euglycemics.

Similar results were noticed in non diabetic patients. Non diabetic stress hyperglycemic patients with ischemic stroke had three and a half fold increased early mortality when compared to euglycemics. In the diabetic group since the sugar value before the onset of stroke was not known, the effect of stress in diabetic group could not be studied.

The study clearly shows an increased early mortality rate and poor functional recovery in patients with diabetes and stress hyperglycemia when compared to euglycemics.[22] Hence there is an urgent need to confirm the improvement in these patients by normalizing blood sugar. Several trails are now under way to improve the out come of Stroke by normalizing the blood glucose with human recombinant insulin. Stephan M. Vinychuk et al showed that administration of insulin to patients with

hyperglycemia improves functional recovery and vital activity of mild to moderate ischemic stroke patients. However, other clinical benefits of the insulin therapy remain to be determined.

CONCLUSION

CONCLUSION

There is a linear correlation between admission day hyperglycemia and ischemic stroke in its severity, size and outcome. The combined diabetes and stress hyperglycemics are found to have larger sized severe stroke and poor functional outcome in the form of increased mortality. There is a good correlation between admission day glucose level and the outcome in ischemic stroke. Admission day elevated glucose level was a significant predictor of mortality and poor functional outcome after acute stroke. Hence, restoration of normoglycemia as soon as possible should be encouraged. In the interim, we should fare well with adhering to good general stroke management, normalization of body temperature, fluid balance and hemodynamics or we may otherwise risk the favorable outcome even in the patients with normoglycemia.

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ANNEXURE

PROFORMA

NAME OF THE PATIENT :

AGE : SEX : IP NO :

ADDRESS : OCCUPATION :

CHIEF COMPLAINTS :

HISTORY OF PRESENTING COMPLAINTS :

PAST HISTORY :

HT / DM / TIA / PT / BA / COPD / CRF / CAHD / DCMP / RHD / AS / MVP / HEPATIC DISEASE / SEIZURES / PSYCHIATRIC DISORDERS

PERSONAL HISTORY : SMOKING, ALCOHOLISM, DIET

GENERAL EXAMINATION :

VITALS : BP, PULSE RATE, RESPIRATORY RATE AND PATTERN

CLINICAL EXAMINATION :

CENTRAL NERVOUS SYSTEM :

CARDIOVASCULAR SYSTEM :

RESPIRATORY SYSTEM :

ABDOMEN EXAMINATION :

SPINE AND CRANIUM :

CLINICAL DIAGNOSIS :

INVESTIGATIONS :

Blood sugar , urea , Serum creatinine

Serum electrolytes : sodium, Potassium

Blood hemoglobin , TC , DC, ESR

Urine albumin , sugar , deposits

Total cholesterol

Electrocardiogram

Chest X ray

CT scan brain

HBA1C

FINAL DIAGNOSIS :

PROGNOSIS (30 DAY FOLLOW UP) : Good / Moderate / Poor / Death

INFORMATION SHEET

We are conducting a study on **"CLINICAL OUTCOME IN ISCHEMIC STROKE PATIENTS WITH HYPERGLYCEMIA."** among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your co-operation to undergo relevant investigations as per need may be valuable to us.

The purpose of this study is to find the clinical outcome in ischemic stroke patients with hyperglycemia.

We are selecting certain cases and if you are found eligible, we would like to perform extra tests and you will be subjected to a non invasive procedure like CT –BRAIN and blood sugar levels.

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

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator

Signature/left thumb impression of Participant/Patient attender

Date :

Place :

ஆய்வு தகவல் தாள்

ஆய்வு தலைப்பு :

மூளையில் இரத்தக் குழாய் அடைப்பினால் பக்கவாதம் ஏற்பட்டிருக்கும் நபர்களில் அதிக சர்க்கரை அளவினால் ஏற்படும் விளைவுகள் பற்றிய ஆராய்ச்சி.

ஆய்வாளர் பெயர் : **மரு. அ. அப்துல் ரஹீம்.**

ஆய்வு நிலையம் : பொது மருத்துவப் பிரிவு,
சென்னை மருத்துவக் கல்லூரி, சென்னை-3.

இந்த ஆய்வில் தங்களை பங்கேற்க அழைக்கிறோம். இந்த தகவல் அறிக்கையில் கூறப்பட்டிருக்கும் தகவல்கள் தாங்கள் இந்த ஆராய்ச்சியில் பங்கேற்கலாமா வேண்டாமா என்பதை முடிவு செய்ய உதவியாக இருக்கும். இந்த படிவத்தில் உள்ள தகவல்கள் பற்றி உள்ள சந்தேகங்களை நீங்கள் தயங்காமல் கேட்கலாம்.

இதில் மூளையில் இரத்தக் குழாய் அடைப்பினால் பக்கவாதம் ஏற்பட்டிருக்கும் நபர்களின் இரத்தத்தில் சர்க்கரை அளவு பரிசோதிக்கப்பட்டு, அதிக அளவு சர்க்கரையினால் ஏற்படும் விளைவுகள் பற்றிய ஆராய்ச்சி செய்கிறோம். அதற்கு இரத்தப் பரிசோதனை அவசியம், அதற்குத் தங்கள் ஒத்துழைப்புத் தேவை.

நீங்கள் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில்தான் இருக்கிறது. மேலும் நீங்கள் எந்த நேரமும் இந்த ஆராய்ச்சியில் இருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனையின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவில் தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம்

தேதி :

பங்கேற்பாளர் கையொப்பம் /
இடது கட்டைவிரல் ரேகை
தேதி :

PATIENT CONSENT FORM

Study Detail : " **CLINICAL OUTCOME IN ISCHEMIC STROKE PATIENTS WITH HYPERGLYCEMIA"**

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

In Patient Number :

Patient may check (√) these circles

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

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

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

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

e. I hereby consent to participate in this study. ❑

f. I hereby give permission to undergo detailed clinical examination and relevant investigations as required. ❑

Signature/thumb impression
Patient's Name and Address:

Signature of Investigator
Study Investigator's Name:
Dr.A.ABDUL RAHIM

ஆய்வு ஒப்புதல் படிவம்

ஆய்வு தலைப்பு :

மூளையில் இரத்தக் குழாய் அடைப்பினால் பக்கவாதம் ஏற்பட்டிருக்கும் நபர்களில் அதிக சர்க்கரை அளவினால் ஏற்படும் விளைவுகள் பற்றிய ஆராய்ச்சி.

பெயர் :
வயது :
பால் :

தேதி :
வெளிநோயாளி எண் :
ஆராய்ச்சி சேர்க்கை எண் :

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்துகொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் இரத்த சர்க்கரை அளவு பரிசோதிக்கப்படுகிறது என்பதை ஆராய்ச்சியாளர் கூற அறிந்துகொண்டேன்.

மேற்கண்ட பரிசோதனையின் போது ஏற்படக்கூடிய பின்விளைவுகளையும் முழுவதும் உணர்ந்து இந்த பரிசோதனைக்கு மனமார சம்மதிக்கிறேன்.

நான் ஆராய்ச்சியாளருடன் ஒத்துழைப்பேன் என்றும், எனக்கு ஏற்படக்கூடிய ஆசாதாரண நிகழ்வுகள் பற்றியும் உடனடியாக ஆராய்ச்சியாளரிடம் தெரிவிப்பேன் என்று உறுதி கூறுகிறேன். இந்த ஆய்விலிருந்து எப்போது வேண்டுமானாலும் எக்காரணமும் கூறாமல் என்னை விடுவித்துக்கொள்ளலாம் என்பதை அறிவேன்.

என்னிடம் இருந்து பெறப்படும் தகவல்களை அரசு, வரைமுறை அதிகாரிகள் ஆகியோர்களுடன் பகிர்ந்துகொள்ள ஆராய்ச்சியாளருக்கு அனுமதி அளிக்கிறேன். என்னுடைய சிகிச்சைக்கட்டுகளை பார்வையிட உரிமை உண்டு. என்னுடைய தகவல்களின் அடையாளம் இரகசியமாக வைக்கப்படும் என்பதை அறிவேன்.

இந்த ஆராய்ச்சியில் பங்கேற்க தன்னிச்சையாக முழு மனதுடன் சம்மதிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் / ரேகை

பங்கேற்பவர் பெயர்

இடம் :

தேதி :

ஆய்வாளர் கையொப்பம்

ஆய்வாளர் பெயர்

இடம் :

தேதி :

URKUND

Urkund Analysis Result

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Instances where selected sources appear:

27

CERTIFICATE – II

This is to certify that this dissertation work titled **"CLINICAL OUTCOME IN ISCHEMIC STROKE PATIENTS WITH HYPERGLYCEMIA"** of the candidate **ABDUL RAHIM.A** with registration Number **201511001** for the award of **M.D.** in the branch of **GENERAL MEDICINE**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **9 percentage** of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.A. Abdul Rahim
Post Graduate in MD General Medicine
Institute of Internal Medicine
Madras Medical College
Chennai 600 003

Dear Dr.A.Abdul Rahim ,

The Institutional Ethics Committee has considered your request and approved your study titled **"CLINICAL OUTCOME IN ISCHEMIC STROKE PATIENTS WITH HYPERGLYCEMIA " - NO.15012017 (II).**

The following members of Ethics Committee were present in the meeting hold on **19.01.2017** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.M.K.Muralidharan,MS.,M.Ch.,Dean, MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD., Prof.of Pharmacology.,MMC,Ch-3	: Member
5.Prof.A.Rajendran,MS, Prof. of Surgery,MMC,Ch-3	: Member
6.Prof.N.Gopalakrishnan,MD,Director,Inst.of Nephrology,MMC,Ch	: Member
7.Prof.Baby Vasumathi,MD.,Director, Inst. of O & G	: Member
8.Prof.K.Ramadevi,MD.,Director,Inst.of Bio-Che,MMC,Ch-3	: Member
9.Prof.R.Padmavathy, MD, Director,Inst.of Pathology,MMC,Ch-3	: Member
10.Prof.S.Mayilvahanan,MD,Director, Inst. of Int.Med,MMC, Ch-3	: Member
11.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
12.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
13.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

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

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

Member Secretary – Ethics Committee

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

NAME	AGE	SEX	HT	**DM**	DYSLIPIDIEMIC	SMOKER	ALCOHOLIC	BP	**RBS**	**HBA1C**	CT BRAIN	NIHSS	**PROGNOSIS**
parasuraman	75	M	Y	Y	Y	N	N	170/100	210	8.1	L FP	14	moderate
johnson	60	M	Y	N	Y	Y	Y	160/90	173	6.5	R cerebellar	8	good
boopathy	45	M	Y	Y	N	N	Y	130/80	203	8.5	L PT	17	poor
mathammal	80	F	Y	N	Y	N	N	180/100	197	6.9	R cerebellar	22	death
kantha	65	F	Y	Y	N	N	N	160/110	274	9	L FP	10	moderate
parvathy	78	F	Y	Y	N	N	N	160/90	322	8.7	L FTP	25	death
govindhan	72	M	Y	N	N	Y	Y	180/110	168	6.5	R GC	12	moderate
yuvaraj	70	M	N	Y	Y	Y	N	140/90	249	8.7	L PT	16	poor
lakshmi	50	F	Y	N	Y	N	N	178/110	146	5.8	L FP	7	good
perumal	81	M	Y	Y	Y	Y	Y	190/100	313	8.9	R FTP	23	death
elumalai	54	M	Y	N	N	N	N	210/130	289	4.5	L cerebellar	4	good
devaraj	60	M	Y	Y	Y	Y	N	190/110	254	8.5	R GC	28	death
saheedha	70	F	N	Y	Y	N	N	150/110	282	7.9	L PT	25	death
kurshith beevi	55	F	N	N	Y	N	N	190/100	222	6.7	L FTP	21	poor
lakshmanan	45	M	N	Y	Y	Y	Y	150/90	218	8	L thalamic	8	good
murugan	56	M	Y	N	N	Y	N	186/110	140	5.6	R GC	10	moderate
ramalingam	80	M	N	N	N	N	N	180/100	168	5	L FP	5	good
padmavathy	73	F	Y	N	N	N	N	160/86	151	6	R GC	14	moderate
chandra	65	F	Y	Y	Y	N	N	170/100	270	7.5	L GC	8	good
laxmibai	54	F	N	Y	N	N	N	130/80	232	8	R thalamic	4	good
srinivasan	55	M	N	Y	Y	Y	Y	190/110	320	9.5	L FTP	26	death
selvi	45	F	Y	Y	Y	N	N	160/90	198	6.7	L GC	7	good
lingammal	75	F	Y	Y	N	N	N	190/100	210	7	L GC	8	moderate
rajagopal	65	M	Y	Y	N	N	N	180/100	190	5.9	R FP	10	moderate
moheen ali	67	M	Y	Y	Y	N	N	180/110	163	6	R PT	6	good
anbu kannan	42	M	N	Y	Y	N	N	150/90	197	6.2	R GC	8	good
naguran	56	M	N	Y	Y	Y	Y	180/100	265	7.5	L GC	19	death
venkaaraman	54	M	Y	Y	N	N	N	170/80	189	6.6	R cerebellar	5	good
ayyadurai	55	M	Y	Y	Y	Y	Y	190/100	302	8	R GC	16	poor
kamala	70	F	N	Y	Y	N	N	180/110	442	9	L FTP	22	death
yakub sahib	72	M	Y	Y	Y	N	N	200/110	252	7.9	L GC	19	poor
damodharan	62	M	Y	Y	Y	Y	N	180/100	288	8	R GC	26	death
dilli babu	67	M	Y	N	N	N	N	160/90	168	5.8	R PT	10	moderate
ajay	50	M	Y	Y	N	Y	Y	190/110	312	7.5	L GC	22	death
solomon	55	M	Y	N	Y	N	Y	160/90	166	6.2	R FP	11	poor

deivanai	63	F	N	Y	Y	N	N	130/80	190	6.9	R GC	8	moderate
ponniyammal	71	F	Y	Y	Y	N	N	150/100	210	8	R FTP	18	poor
palani	44	M	N	N	N	Y	Y	180/100	148	5.5	L GC	12	moderate
gajendran	52	M	Y	N	N	N	N	150/110	183	6	R thalamic	8	good
chinnaponnu	68	F	N	Y	Y	N	N	130/80	210	6.8	L PT	15	poor
vijayan	49	M	N	Y	N	Y	Y	150/90	334	8.3	L GC	16	poor
yesuraj	61	M	Y	Y	N	N	N	190/100	281	7.5	R frontal	11	moderate
thayamma	77	F	Y	Y	Y	N	N	160/100	190	6.8	R cerebellar	18	poor
david	41	M	Y	N	N	Y	Y	150/90	222	7.8	R GC	7	good
krishnamoorthy	75	M	Y	Y	Y	N	N	180/100	301	9	L FP	24	death
anthonyammal	69	F	N	N	Y	N	N	130/80	130	5.4	R GC	9	moderate
gowri	63	F	Y	N	N	N	N	170/110	166	6.3	L PT	7	good
latha	59	F	N	Y	N	N	N	150/90	249	7	L GC	18	poor
vasantha	58	F	N	Y	Y	N	N	160/100	421	8.9	R GC	16	poor

HT-Hypertension ; DM – Diabetes ; S – Smoker ; A – Alcohol ;
Hb A1c – Glycosylated hemoglobin ; L – left ; R – right ; F – frontal infarct; FP – fronto parietal infarct;
PT – Parieto temporal infarct; THA – Thalamic infarct ; CEREBELAR – cerebellar infarct ;
F – Frontal ; FP – fronto parietal ; P – parietal ;
PT – parito temporal ; GC – ganglio capsular infarct ;