CLINICAL OUTCOME OF STROKE IN RELATION TO ADMISSION DAY GLYCEMIC STATUS

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CERTIFICATE

This is to certify that the dissertation entitled **"CLINICAL OUTCOME OF STROKE IN RELATION TO ADMISSION DAY GLYCEMIC STATUS"** is the bonafide work of **Dr. K.S. RAGHAVAN,** in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for M.D General Medicine Branch I examination to be held in April 2012.

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DECLARATION

I, **Dr. K.S. RAGHAVAN,** solemnly declare that, I carried out this dissertation **"CLINICAL OUTCOME OF STROKE IN RELATION TO ADMISSION DAY GLYCEMIC STATUS"** is a bonafide record of work done by me at the Department of General Medicine, Govt. Rajaji Hospital, Madurai, under the guidance of **Dr. Moses K Daniel, MD** Professor, Unit Chief, Department of General Medicine, Madurai Medical college, Madurai.

This dissertation is submitted to The Tamil Nadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of M.D Degree General Medicine Branch-I examination to be held in April 2012.

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CONTENTS

1. INTRODUCTION

Among all the neurological diseases of adult life, cerebrovascular accidents clearly ranks first in frequency of importance. Atleast fifty percent of neurological diseases in general hospital are due to stroke. Cerebrovascular accident includes ischemic stroke, hemorrhagic stroke, and cerebrovascular anomalies such as intracranial aneurysm, AV malformation and cortical venous thrombosis. Stroke, after heart disease and cancer, is the third most common cause of death (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 complications is an important risk factor in the genesis of stroke(2). Most of the diabetic patients with stroke have raised glycosylated haemoglobin 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 at presentation, hypertension, hypothermia, fever are those which are widely studied.

2. REVIEW OF LITERATURE

DEFINITION :

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

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

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.

Family history: 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.

MODIFIABLE RISK FACTORS

Hypertension: It is the most 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 diabetic patients with diabetic complications like retinopathy, nephropathy and autonomic neuropathy have a higher incidence of ischemic stroke.

Hyperglycemia and Stroke : Elevated blood glucose is common in the early phase of stroke. The prevalence of hyperglycemia defined as blood glucose level more than 6.1mmol/l has been observed in two third of all ischemic stroke subtypes on admission and in atleast fifty percent in each subtype including lacunar stroke(6). Exclusive experimental evidence in stroke models support that association between blood glucose and functional outcome has been found in increasing number of clinical studies.

Dyslipidemia: 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 fivefold increase in the incidence of embolic stroke especially in those patients who have recent CCF, arterial hypertension and prior thromboembolism.

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.

Common Causes	Uncommon Causes
Thrombosis	Hypercoagulable disorders
Lacunar stroke (small vessel)	Protein C deficiency
Large vessel thrombosis	Protein S deficiency
Dehydration	Antithrombin III deficiency
Embolic occlusion	Antiphospholipid syndrome
Artery-to-artery	Factor V Leiden mutation
Carotid bifurcation	Systemic malignancy
Aortic arch	Sickle cell anemia
Arterial dissection	Thalassemia
Cardioembolic	Polycythemia vera
Atrial fibrillation	Systemic lupus erythematosus
Mural thrombus	Homocysteinemia
Myocardial infarction	Thrombotic thrombocytopenic purpura
Dilated cardiomyopathy	Disseminated intravascular coagulation
Valvular lesions	Dysproteinemias

Common Causes	Uncommon Causes
Mitral stenosis	Nephrotic syndrome
Mechanical valve	Inflammatory bowel disease
Bacterial endocarditis	Oral contraceptives
Paradoxical embolus	Venous sinus thrombosis
Atrial septal defect	Fibromuscular dysplasia
Patent foramen ovale	Vasculitis
Atrial septal aneurysm	Systemic vasculitis [PAN, granulomatosis with polyangiitis (Wegener's), Takayasu's, giant cell arteritis]
Spontaneous echo contrast	Primary CNS vasculitis
	Meningitis (syphilis, tuberculosis, fungal, bacterial, zoster)
	Cardiogenic
	Mitral valve calcification
	Atrial myxoma
	Intracardiac tumor
	Marantic endocarditis
	Libman-Sacks endocarditis
	Subarachnoid hemorrhage
	Drugs: cocaine, amphetamine
	Moyamoya disease
	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 – thromboembolism 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 (7)

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 legs

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 contralateral 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

Pathophysiology of stroke

Stroke is 90% ischaemic and 10% hemorrhagic(8). Ischemic stroke occurs because of a loss of blood supply to the brain, initiating the ischemic cascade. Brain tissue stops its function if lack of oxygen for more than 60 to 90 seconds and after several hours will endure irreversible damage possibly leading to death of the tissue, i.e., infarction. Atherosclerosis may interfere the blood supply by causing the shaping of blood clots in the vessel, or narrowing the lumen of blood vessels, or releasing showers of small emboli through the disintegration of atherosclerotic plaques. Embolic infarction takes place when emboli formed anywhere else in the circulatory system, especially in the heart as a result of atrial fibrillation, or in the carotid arteries. These break-offs, get into the cerebral circulation, then lodge in and block brain blood vessels.

Due to collateral circulation, there is a spectrum of severity within the region of brain tissue affected by ischemia. Therefore, part of the tissue may die in a short time while other parts may only be damaged and could potentially recover. The ischemic area where tissue might get recovery is called the “ischemic penumbra”(9).

As glucose or oxygen becomes exhausted in ischemic brain tissue, the production of high energy phosphate compounds such as ATP fails, resulting in the failure of energy-dependent process necessary for tissue cell survival. This sets off a set of co-related events that bring about cellular injury and

death. A main cause of neuronal injury is the release of excitatory neurotransmitter, glutamate. The concentration of glutamate outside the cells of nervous system is normally in a low amount as a result of so-called uptake carriers. However, stroke cuts off the supply of glucose and oxygen. Therefore the transmembrane ion gradients run down, and glutamate transporters reverse direction, releasing glutamate into the extracellular area. Glutamate works on receptors in nerve cells, producing an influx of calcium which activates enzymes that digest the proteins, lipids and nuclear material of the cells. Calcium influx can cause the failure of mitochondria as well, which may lead further to energy depletion and can trigger cell death out of apoptosis.

Ischemia may also induce production of oxygen-free radicals and other reactive oxygen species. These react with and injure a quantity of cellular and extracellular elements. Damage to the blood vessel endothelium or lining is of importance. Actually, many antioxidant neuro protectants such as NXY-059 and uric acid, work at the level of the endothelium instead of in the brain per se, as well free radicals initiate elements of the apoptosis cascade in a direct way by ways of redox signalling.

In addition to injurious effects of brain cells, ischemia and infarction can lead to loss of structural integrity of brain tissue and blood vessels, partly through the release of matrix metalloproteases, which are zinc and calcium-dependent enzymes that may break down hyaluronic acid, collagen, and other

elements of connective tissue. Other proteases contribute to this process as well. The loss of vascular structural integrity leads to a breakdown of the protective blood brain barrier which contributes to cerebral edema, which may cause secondary progression of the brain injury.

As is the case with any kind of brain injury, the immune system is activated by cerebral infarction and may under some circumstances exacerbate the injury caused by the infarction. Inhibition of the inflammatory response has been shown to reduce tissue injury due to cerebral infarction in the experiment, but this has not been testified in clinical studies.

Hemorrhagic stroke

Hemorrhagic stroke leads to tissue injury by causing compression of tissue from an expanding hematoma. The pressure may cause a loss of blood supply to affected tissue with infarction, and the blood released by brain hemorrhage appears to have direct toxic effects on vasculature and brain tissue.

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.

Pathophysiology of hyperglycemia:

Overview of glucose metabolism

In healthy individuals without DM, the regulation of blood glucose concentration is maintained through hormonal, neural, and hepatic auto regulatory mechanisms (Robinson & van Soeren, 2004)(10). Under normal circumstances, a postprandial increase in blood glucose concentration stimulates the release of insulin from the pancreas, specifically the beta cells. Insulin mediates peripheral glucose disposal and suppresses glucogenesis in the liver. This process maintains blood glucose homeostasis. After uptake into the skeletal muscle, glucose either is directed to glucagon formation (pathway for carbohydrate storage) or glycolysis (used in the Kreb's cycle, resulting in energy production). Excess glucose also can be stored in the liver or converted to fatty acids for storage in adipose tissue.

Altered glucose metabolism in critical illness:

Critical illness induces a number of adaptive changes in human physiology; the most prominent are changes in the neuroendocrine function (Ferrando, 1999)(11). An increase in counter regulatory hormones, such as glucagon, epinephrine, norepinephrine, and growth hormone, results in increased hepatic glucose production and decreased peripheral glucose uptake, subsequently inducing a hyperglycemic state (Montori, Bistrian, & McMahon, 2002)(12). In addition, critical illness exacerbates the circulation of abnormal

levels of cytokines-particularly tumor necrosis factor, alpha, and interleukin—further elevating serum glucose (McCowen, Malhotra, & Bistrian, 2001)(13). Patients with DM exhibit a greater response to counter regulatory hormones, and may not increase insulin secretion as a compensatory response to needed levels, resulting in even higher glucose levels (Montori et al., 2002).

Effects of exogenous insulin:

In global ischemia (e.g., anoxic brain injury and encephalopathy), insulin acts directly on brain parenchyma to reduce neuronal necrosis in the brain cortex, striatum, and hippocampus (Auer, 1998)(14). Animal data indicate that the direct mechanism is mediated by insulin-like growth factor-1 receptors. The direct effect appears to predominate in global ischemia. In focal ischemia, unlike global ischemia, the effect of insulin is predominantly via peripheral hypoglycemia because neuroprotection largely is annulled by coadministration of glucose (Auer, 1998). Insulin also has been shown to improve cell membrane stability, assisting with cerebral edema resolution (American Association of Clinical Endocrinologists, 2003)(15).

Hyperglycemia as a manifestation of the stress response is most evident after an ICU admission and may resolve as the underlying catabolic illness subsides (McCowen et al. 2001). Multiple factors have been associated with an increased risk of hyperglycemia in critical illness, including frequent administration of exogenous dextrose through intravenous drip, intravenous

medications and antibiotics in dextrose solutions, glucocorticoid medication, catecholamine vasopressors, total parenteral nutrition administration (TPN), as well as increased age and prolonged bed rest.

Some patients, particularly those with an untreated underlying process such as infection or ongoing injury, may demonstrate persistent metabolic disregulation and continued hyperglycemia (McCowen et al., 2001).

HbA1C:

HbA1C is structurally similar to hemoglobin A except for the addition of glucose Group to the terminal amino acid of the beta chain of the haemoglobin Molecule (glycosylation). Therefore HbA1C is a function of the exposure of the red blood cells to glucose. Since the glucose linkage to hemoglobin is relatively stable, HbA1C cumulates 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 HbA1C helps to monitor the overall degree of diabetic control achieved. The normal range of HbA1C is 3.8% to 6.4%

Hyperglycemic Effects on the Injured Brain

The effects of hyperglycemia on the injured brain have been studied in both animals and humans. Hyperglycemia has been associated with increased cerebral lactate resulting in local brain tissue acidosis (Kagansky, Levy, &

Knobler, 2001)(16). Brain tissue acidosis worsens mitochondrial function in the penumbra, the moderately ischemic tissue of the brain surrounding the injured core, and increases cerebral infarct size (Alvarez-Sabín et al., 2003)(17). In a study of 63 patients with sudden-onset focal neurological deficit consistent with hemispherical ischemic stroke who received serial MRI, hyperglycemia was shown to reduce penumbral salvage, resulting in greater final infarct size (Parsons et al., 2002)(18).

Hyperglycemia also adversely affects the ischemic brain by disrupting the blood-brain barrier and promoting cerebral edema. In their study of rats with hemorrhagic stroke and hyperglycemia, Song et al. (2003) found that hyperglycemia-induced brain injury resulted in increased free radical formation(19). In turn, the increased amount of free radical formation increased blood-brain barrier permeability and brain edema. The authors hypothesized that elevated glucose levels aggravated brain edema, which culminated in cell death surrounding hemorrhagic stroke tissue.

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 (20). 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(21). Furthermore, lowering glucose with insulin has been reported to reduce ischemic brain damage in an animal model(22).

The evolution of an infarction is accompanied by glutamate release which is believed to propagate the necrosis of penumbral tissues. Although hyperglycemia alone did not trigger early response genes in cortical tissues of rats the expression of c-fos and cox-2 were substantially increased (23)

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

Genome-wide association studies (GWAS)

Genome-wide association studies (GWAS) revealed both their promise and limitations as an approach to understand the genetic architecture of stroke. The promise of GWAS lies in their extraordinary power to detect novel biologic loci that, if replicated, can serve as markers for novel genes, proteins, and ultimately mechanisms of disease. In this regard, since our previously yearly review, new GWAS from 2009 suggested that loci on chromosomes 4q25 (*PITX2* gene, encoding a β-catenin–regulated transcription factor associated with atrial fibrillation), 16q22 (*ZFHX3* gene, encoding a homeodomain zinc-finger protein that has also been associated with atrial fibrillation), and 12p13 (*NINJ2* gene, encoding a protein that is upregulated by

nerve injury) could be added to the list of stroke-associated loci identified from earlier studies. The mechanistic basis for the associations with genetic markers across the spectrum of stroke-associated loci can now be explored and the genetic architecture of stroke.

Factors predicting poor outcome (24)

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 > 7mmol / l on admission.

    • 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(25). 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.

Good glycemic control seems warranted also in hemorrhagic stroke, although more clinical information is needed in this area. At least two clinical

trials have recently been initiated to examine the efficacy of early insulin therapy in acute stroke (26). Still there is no evidence to prove that the reversal of hyperglycemia improves the prognosis, as it has been demonstrated to do in acute myocardial infarction and in critically ill post surgical patients(27).

Hyperglycemia and Thrombolytic Therapy of Acute Ischemic Stroke

In several thrombolysis trials, hyperglycemia has been found to be associated with hemorrhagic events and was reconfirmed recently as well as in a re-analysis of the NINDS rt-PA trial. (28,29,30). In the latter study, an increase of admission glucose level was independently associated with decreased odds for neurologic improvement (odds ratio [OR]=0.76 per 100-mg/dL increase in admission glucose) and the OR for symptomatic ICH was 1.75 per 100-mg/dL increase in admission glucose (95% CI 1.11 to 2.78, *P*=0.02)(31). The relationship was weaker after excluding patients with ICH, suggesting that admission hyperglycemia may exert its hazards in part through hemorrhagic events. However, another recent study by Alvarez-Sabin et al found admission glucose >140 mg/dL (OR 8.4, CI 1.8 to 40.0) to be the sole independent predictor of poor functional outcome at 3 months in patients with recanalization within 6 hours, even after excluding the patients with symptomatic ICH. (31). The same was not true for the patients who did not recanalize, which leads to speculation that hyperglycemia might partially preclude the beneficial effect of rtPA and early reperfusion.

DIAGNOSTIC EVALUATION OF ISCHAEMIC STROKE(32)

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.

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.

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

When cerebral infarction occurs, the immediate goal is to optimize cerebral perfusion in the surrounding ischemic area. Preventing the common complications of bedridden patients like infections (pneumonia, urinary tract, and skin), deep venous thrombosis with pulmonary embolism. 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. 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 (33)

- 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

Sustained BP > 185/110

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

Use of heparin within 48 hrs 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

Intravenous access with two peripheral IV lines (avoid arterial or central placement) Review eligibility for rtPA (34). 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 re image brain immediately. 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 hrs 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.

Primary prevention

1.Hypertension

Antihypertensive treatment is recommended for both prevention of recurrent stroke and prevention of other vascular events in persons who have had an ischemic stroke or TIA and are beyond the hyperacute period. Because this benefit extends to persons with and without a history of hypertension, this recommendation should be considered for all ischemic stroke and TIA patients. An absolute target BP level and reduction are uncertain and should be individualized, but benefit has been associated with an average reduction of ≈10/5 mm Hg, and normal BP levels have been defined as <120/80 mm Hg by JNC-7.

Several lifestyle modifications have been associated with blood pressure reductions and should be included as part of a comprehensive antihypertensive therapy. The optimal drug regimen remains uncertain; however, the available data support the use of diuretics and the combination of diuretics and an ACE. The choice of specific drugs and targets should be individualized on the basis of reviewed data and consideration of specific patient characteristics (eg, extracranial cerebrovascular occlusive disease, renal impairment, cardiac disease, and diabetes).

2. **Glycemic control**

More rigorous control of blood pressure and lipids should be considered in patients with diabetes. ACEIs and ARBs are more effective in reducing the progression of renal disease and are recommended as first-choice medications for patients with DM Glucose control is recommended to near-normoglycemic levels among diabetics with ischemic stroke or TIA to reduce microvascular complications and possibly macrovascular complications. The goal for hemoglobin A_{1c} should be $\leq 7\%$.

3. Cessation of smoking

All healthcare providers should strongly advise every patient with stroke or TIA who has smoked in the last year to quit. Avoidance of environmental tobacco smoke is recommended. Counselling, nicotine products, and oral

smoking cessation medications have been found to be effective in helping smokers to quit

4.Treatment of dyslipidemia

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

5.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 for this purpose are Aspirin and Clopidogrel.

6.Alcohol

Patients with ischemic stroke or TIA who are heavy drinkers should eliminate or reduce their consumption of alcohol. Light to moderate levels of no more than 2 drinks per day for men and 1 drink per day for nonpregnant women may be considered.

7. Obesity : Weight reduction may be considered for all overweight ischemic stroke and TIA patients to maintain the goal of a BMI of between 18.5 and

24.9 kg/m^2 and a waist circumference of <35 in for women and <40 in for men. Clinicians should encourage weight management through an appropriate balance of calorie intake, physical activity, and behavioral counselling

8. Exercise

For patients with ischemic stroke or TIA who are capable of engaging in physical activity, at least 30 minutes of moderate-intensity physical exercise most days may be considered to reduce the risk factors and comorbid conditions that increase the likelihood of recurrence of stroke. For those individuals with disability after ischemic stroke, a supervised therapeutic exercise regimen is recommended

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.

INTRA CEREBRAL HEMORRHAGE

Intra cerebral hemorrhage accounts for approximately 15%-25% of the strokes. The overall mortality for this type subtype of stroke is from 25 % to 60% In nearly 70% of patients Hypertension is the commonest cause of bleed.

The lipohyalinosis of the small intraparenchymal arteries is the leading cause of hemorrhage. The micro aneurysms of Charcot and Bouchard is uncertain, but they are found at anatomical sites preferentially affected by ICH.

Hyperglycemia and hemorrhagic stroke :

Incidence of hemorrhagic stroke is higher in diabetes either known diabetes or newly detected diabetes. This is due to the fact that blood brain barrier is disrupted by chronically elevated hyperglycemia which is dealt earlier in the topic ‘thrombolysis of ischemic patients with hyperglycemia’

The non hypertensive causes include following :

1. bleeding disorders, anticoagulant and fibrinolytic treatment
2. cerebral amyloid angiopathy

3. granulomatous angitis of the CNS

4. sympathomimetic agents

5. trauma

6. hemorrhagic infarction

7. vascular malformations

8. Intracranial tumors

Clinical features:

symptoms of increased ICT

symptoms that are specific for the location of the hematoma

focal neurological deficits

Imaging

The CT scan is sensitive to the high density fresh blood in the parenchyma while MRI can determine the time duration between the hemorrhage and the MRI examination common sites :

1 . Putamen - 35 %

2 . Lobar – 25 %

3 . Thalamus – 10-15 %

4 . Caudate nucleus – 5 %

5 . Pons – 5 %

6. Cerebellum – 5 – 10 %

Treatment

- Control of hypertension
- Air way maintenance if the GCS is less than 8
- Treatment of coagulation abnormalities
- Protamine sulfate is used if the hemorrhage is due to heparin
- Cryoprecipitate is used if the hemorrhage is due to heparin
- Measures for the prevention of further elevation of ICP

Routine anticonvulsants are not recommended in patients who do not have seizures at onset due to negligible risk of subsequent epilepsy in them. Patients with lobar hemorrhage and cerebellar hemorrhage can be managed surgically whereas the deep hemorrhages are managed medically.

MORTALITY IN STROKE:

Early mortality (first thirty days) :

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

1. 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.

3. AIM AND OBJECTIVES

To measure the blood glucose level within twenty four hours of the onset of stoke in both diabetics and in non diabetics and to evaluate the severity and prognosis in both diabetics and non diabetics in relation to hyperglycemia.

4. MATERIALS AND METHODS

A total of hundred and eleven patients of acute stroke admitted in the department of medicine Government Rajaji Hospital Madurai between April 2011 and September 2011 were studied. The patients were selected on the following basis

INCLUSION CRITERIA:

1. Patients above 40 years
2. Patients admitted within twenty four hours of onset of symptoms
3. Patients should not be a known case of cerebro vascular accident
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 for whom 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 hundred and eleven patients, eleven 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, which takes the following clinical findings in to account and each criteria awarded specific points(35).

1a Level of conscious		**1b LOC questions**	
Alert Drowsy Stuporous Comatose	0 1 2 3	Answers both correctly Answers one correctly Incorrect	0 1 2
1c LOC commands			
Obeys both correctly Obeys one correctly Incorrect	0 1 2		
2. Gaze palsy		**3. Visual**	
Normal Partial gaze palsy Forced deviation	0 1 2	No visual loss Partial hemianopia Complete hemianopia Bilateral hemianopia	0 1 2 3
4 Facial palsy		**5 Best motor arm/ leg (right/left)**	
Normal symmetric Minor paralysis Partial paralysis Complete paralysis	0 1 2 3	No drift Drift Some antigravity effect No antigravity effect No movement	0 1 2 3 4
6 Limb ataxia		**7 Sensory**	
Absent Present in one limb Present in both limbs	0 1 2	No sensory loss Mild to moderate sensory loss Total sensory loss	0 1 2

8 Language		**9 Dysarthria**	
Normal, no aphasia Mild to moderate aphasia Severe aphasia Mute, global aphasia	0 1 2 3	Normal Mild to moderate Severe	0 1 2
10 Extinction/ inattention			
No abnormality Visual/ tactile/ spatial/ personal inattention Profound hemi inattention	0 1 2		

The points were added, with a maximum of thirty points. 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) and with out a history of diabetes, Hemoglobin A 1c was performed. Hence the patients can be classified into four groups (36).

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((37),

persistent Disability need for residential placement(38),

dependent in activities of daily

living and stable deficit with no recovery(39)

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.

Statistical Tools

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2010)** developed by Centre for Disease Control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

5. RESULTS AND OBSERVATION

Table - 1

Age distribution

Age group	**Cases**	
	No	**%**
40 - 49 years	12	12
50-59 years	34	34
60-69 years	36	36
70 years & above	18	18
Total	100	100
Range	40 – 80 years	
Mean	59.4 years	
SD	8.7 years	

Age group of patients included in the study ranged from 40 years to 80 years with a mean of 59.4 years.

AGE DISTRIBUTION

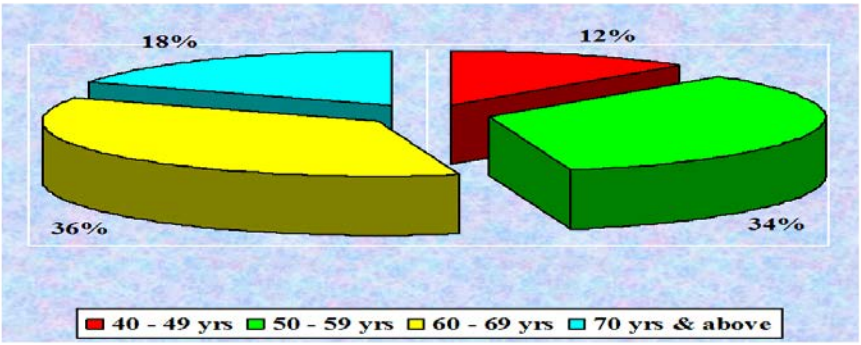


Table - 2

Sex distribution

Sex	Cases	
	No	**%**
Male	68	68
Female	32	32
Total	100	100

68% of cases included in the study were males and 32% were females.

SEX DISTRIBUTION

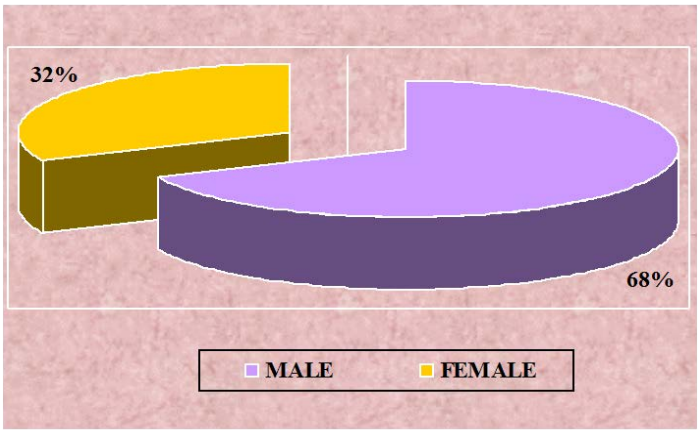


Table - 3

Type of diabetes

Type of diabetes	**Cases**	
	No	**%**
Euglycemia	47	47
Stress hyperglycemia	12	12
Known DM	22	22
Newly diagnosed DM	19	19
Total	100	100

Among the four types of diabetes cases in the study group, euglycemia was the most common type (47%).

TYPE OF DIABETES

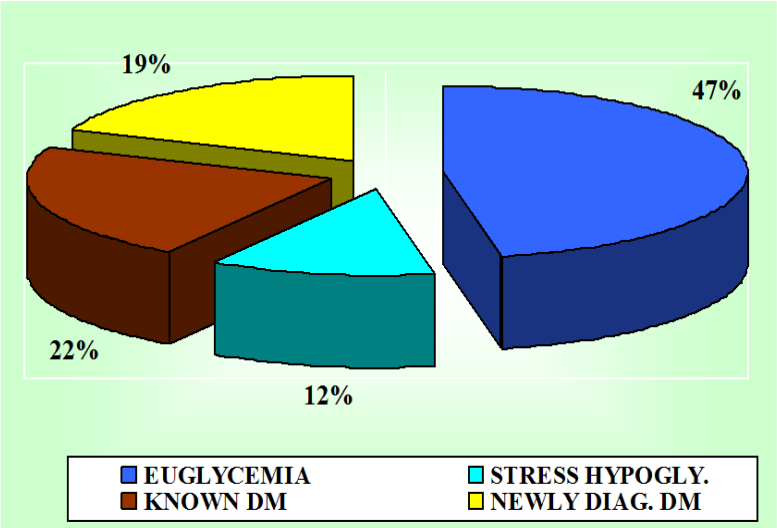


Table - 4

Prognosis

Prognosis	**Cases**	
	No	**%**
Good	34	34
Moderate	26	26
Poor	16	16
Death	24	24
Total	100	100

40% of the study cases had bad prognosis.

PROGNOSIS

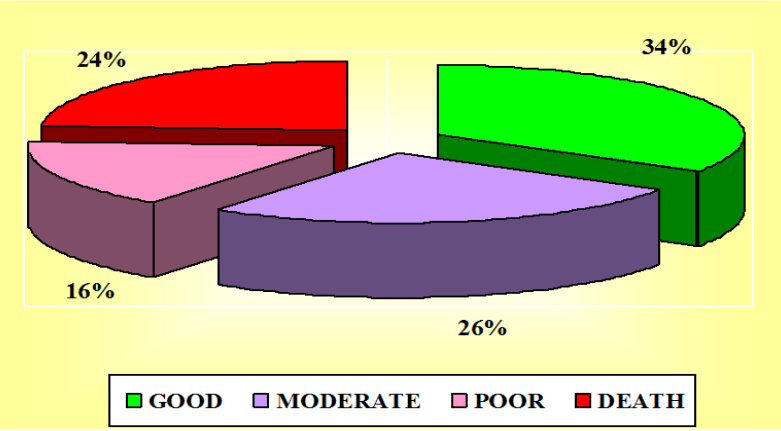


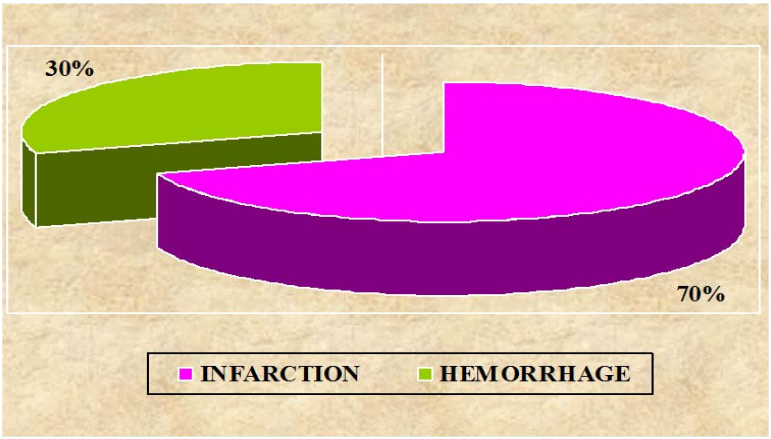
Table - 5

Type of stroke

Type of stroke	**Cases**	
	No	**%**
Infarction	70	70
Hemorrhage	30	30
Total	100	100

70% of cases had infarction and 30% had hemorrhage.

TYPE OF STROKE



RELATIONSHIP BETWEEN PROGNOSIS AND OTHER PARAMETERS

Table - 6

Age and prognosis

Prognosis	**Age in years**	
	Mean	**SD**
Good	58.2	7.9
Moderate	61.1	10.6
Poor	60.3	9.7
Death	58.5	7.6
'p'	0.7439 Not significant	

Table - 7

Sex and prognosis

Prognosis	**Sex**			
	Males (68)		**Females (32)**	
	No	**%**	**No**	**%**
Good	23	33.8	11	34.4
Moderate	20	29.4	6	18.7
Poor	9	13.2	7	21.9
Death	16	23.5	8	25.0

Nearly 63% of the males and 53% of the females had favourable prognosis.

Table - 8

Prognosis and other quantitative variables

Prognosis	**Mean ±SD**				
	SBP	**DBP**	**Blood sugar**	**HbA1C**	**NIHSS**
Good	144.4 ±25.8	85.5 ±10	95.4 ±10	6.07 ±0.08	7.88 ±3.83
Moderate	154.5 ±24.8	88 ±11.9	140.9 ±49.7	6.95 ±1.5	10.73 ±4.34
Poor	154.4 ±25	90 ±12.6	183.1 ±46.4	8.06 ±1.58	14.56 ±4.27
Death	174.7 ±32.4	95.8 ±14.4	235.3 ±56.3	8.53 ±1.62	21.83 ±4.47
'p'	**0.0014 Significant**	**0.0436 Significant**	**0.0001 Significant**	**0.0001 Significant**	**0.0001 Significant**

Patients with adverse prognosis had higher B.P., blood sugar, HbA1C and NIHSS values than persons with better prognosis. This relationship was statistically significant ($p > 0.05$).

Hba1C & NIHSS & PROGNOSIS

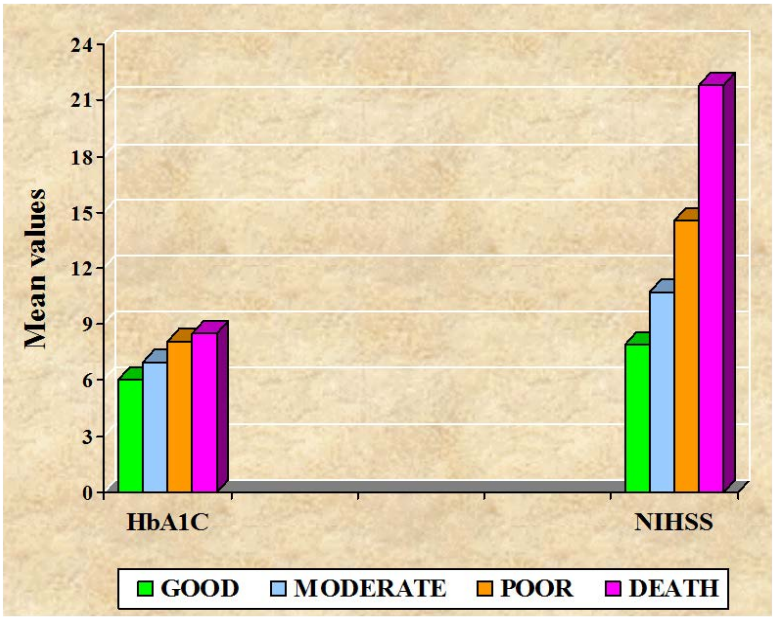


Table - 9

Prognosis and type of diabetes

Type of diabetes	Prognosis							
	Good		Moderate		Poor		Death	
	No	%	No	%	No	%	No	%
Euglycemia (47)	32	68.1	10	21.3	2	4.3	3	6.4
Stress hyperglycemia (12)	2	16.7	7	58.3	3	25	-	-
Known DM (22)	-	-	5	22.7	7	31.8	10	45.5
Recently diag. DM (19)	-	-	4	21.1	4	21.1	11	57.9

Percentage of death and poor prognosis were more in recently diagnosed and known DM cases than in the other two types of diabetes.

TYPE OF DIABETES & PROGNOSIS

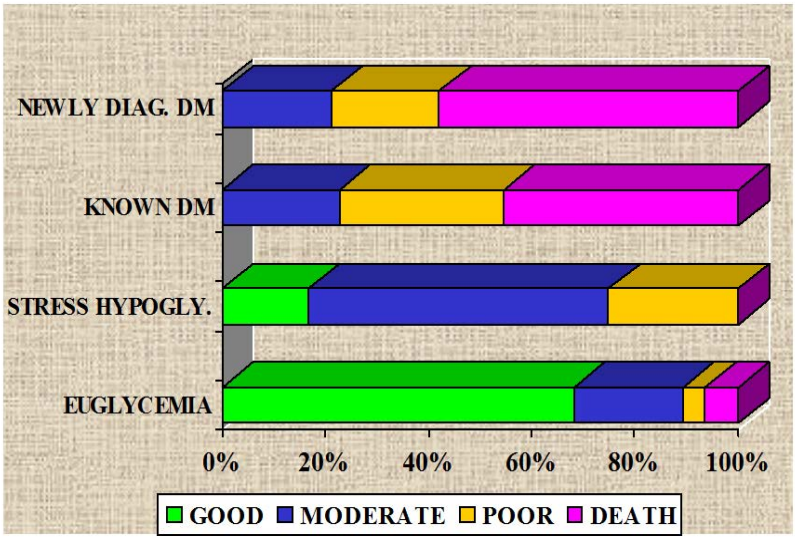


Table - 10

Prognosis and type of stroke

Type of stroke	Prognosis							
	Good		Moderate		Poor		Death	
	No	%	No	%	No	%	No	%
Infarction (70)	33	47.1	17	24.3	6	8.6	14	20
Hemorrhage (30)	1	3.3	9	30	10	33.3	10	33.3
'p'	**0.0008 Significant**							

More than 70% of infarction cases had favorable prognosis whereas this percentage was less than 35% in hemorrhage cases. This difference was statistically significant (p = 0.0008).

TYPE OF STROKE & PROGNOSIS

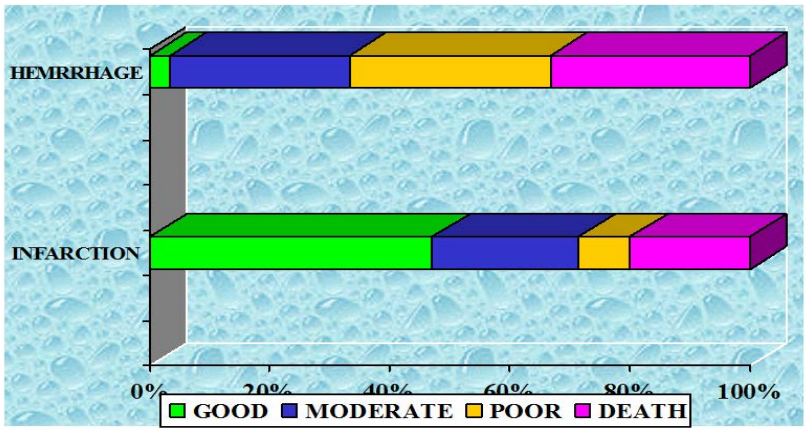


Table - 11

Type of diabetes and presence of risk factors

Type of diabetes	**Risk factor**			
	Present (83)		**Absent (17)**	
	No	**%**	**No**	**%**
Euglycemia	37	44.6	10	58.8
Stress hyperglycemia	22	26.5	-	-
Known DM	13	15.7	6	35.3
Recently diagnosed DM	11	13.3	1	5.9

Table - 12

Type of diabetes and other quantitative parameters

Type of diabetes	**Mean ±SD**		
	Blood sugar	**HbA1C**	**NIHSS**
Euglycemia	97.5 ±11.9	6.1 ±0.19	9.11 ±5.16
Stress Hyperglycemia	120.6 ±2.8	6.09 ±0.07	12.42 ±3.94
Known Diabetes mellitus	230.3 ±39.8	8.77 ±1.29	15.73 ±6.75
Recently diagnosed DM	231 ±32.9	8.93 ±1.41	20.05 ±5.04
P	**0.0001 Significant**	**0.0001 Significant**	**0.0001 Significant**

Mean B.P, blood sugar, HbA1C and NIHSS values were maximum in recently diagnosed DM cells followed by known DM cases. The values were lower in the other two types. The differences were statistically significant ($p < 0.05$).

BLOOD PRESSURE & SUGAR &

TYPE OF DIABETES

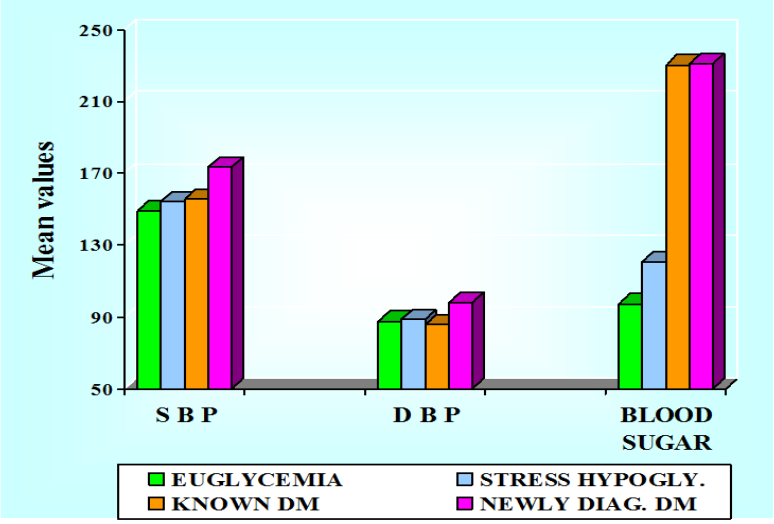


Table - 13

Type of diabetes and type of stroke

Type of diabetes	Type of stroke			
	Infarction		Hemorrhage	
	No	%	No	%
Euglycemia (47)	41	87.2	6	12.8
Stress hyperglycemia (12)	11	91.7	1	8.3
Known DM (22)	10	45.5	12	54.5
Recently diag. DM(19)	8	42.1	11	57.9

Nearly 90% of euglycemia and stress hyperglycemic cases had infarction whereas less than 50% of known and recently diagnosed DM cases had hemorrhage.

TYPE OF DIABETES AND TYPE OF STROKE

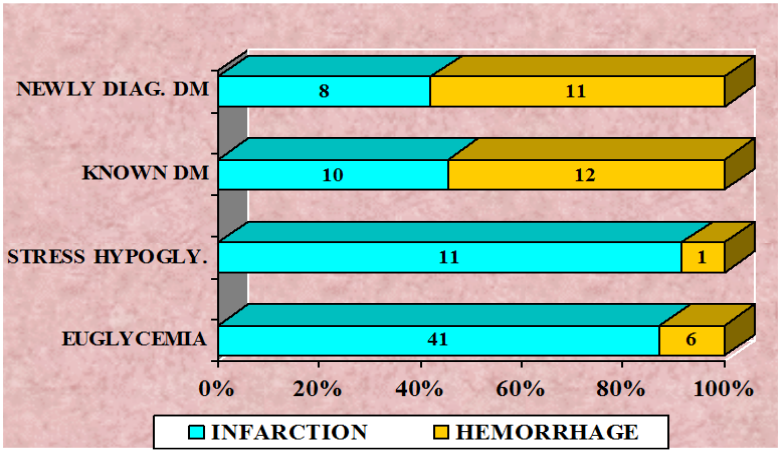
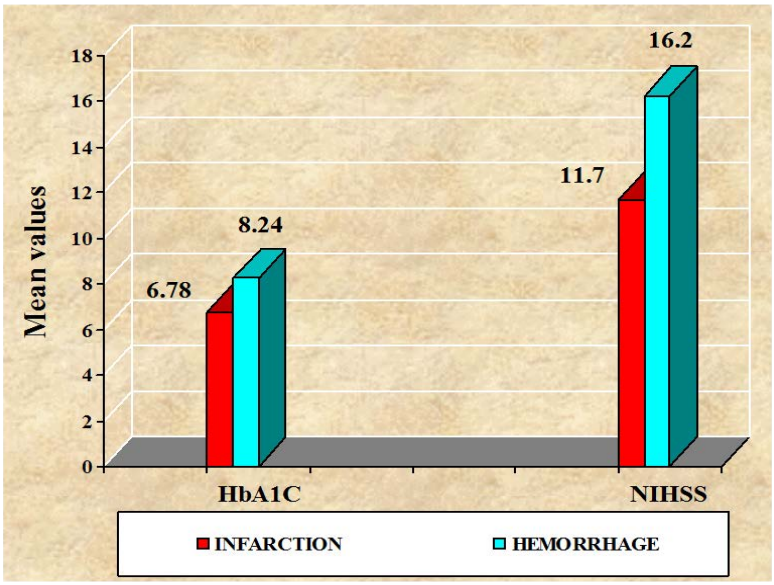


Table - 14

Type of stroke and other quantitative variables

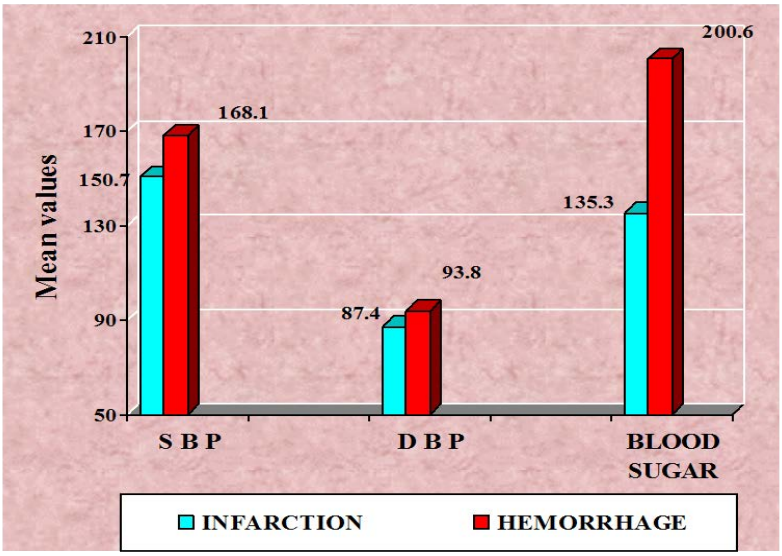
Variable	**Mean ± SD for**		**'p'**
	Infarction	**Hemorrhage**	
Blood sugar	135.3 ±61.8	200.6 ±61.7	**0.0001 Significant**
HbA1C	6.78 ±1.39	8.24 ±1.62	**0.0001 Significant**
NIHSS	11.7 ±6.4	16.2 ±6.8	**0.0008 Significant**

Hba1C & NIHSS & TYPE OF STROKE



BLOOD PRESSURE & SUGAR &

TYPE OF STROKE



6. DISCUSSION

Age sex and risk factors

Our study of hundred patient showed a male preponderance which is commonly seen with most other studies. Majority of patients, (36%) were between 60-69 years. Among our study group 63% of males and 53% of the females had a favourable prognosis. More than half of the patients were smokers and one third had history of alcohol intake.

Glycemic status

In our study group, 53 patients had elevated admission day blood sugar level out of which 19% were newly diagnosed diabetics, 12% were stress hyperglycemics, 47% were euglycemics, 22% were known diabetics. Nearly 90% of the euglycemic and stress hyperglycaemic patients had infarction where as less than 50% of known diabetics and newly diagnosed patients had infarction.

Severity of stroke

Severity of stroke was assessed with NIH Stroke scaling system. Admission day hyperglycaemic patients had a higher score when compared to Euglycemic patients (17.89 vs. 9.11 respectively), which was statistically significant ($p = 0.0001$). Among the admission day hyperglycaemic patients

newly detected diabetes had the higher mean NIHSS values than euglycemic patients. Hence elevated blood sugar level at the time of admission was found to correlate with increasing severity of stroke.

SIZE OF LESION

The size of the lesion was analyzed with the help of CT brain. Most of the euglycemic patients had small sized infarcts and hemorrhage whereas majority of the admission day hyperglycemic patients had a larger sized lesion with edema and midline shift which was found to be statistically significant ($p = 0.0001$). 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 increased changes for hemorrhage and hemorrhagic transformation of infarcts

TYPE OF STROKE:

Among the euglycemic group eighty seven percent of the patients had Ischemic stroke and thirteen percent had hemorrhagic stroke. Among patients with admission day hyperglycemia, in the newly detected patients 57.9% had hemorrhagic stroke followed by 54.5% in known diabetes patients and 8.3% in stress hyperglycemics and half of them had hemorrhagic stroke. Our study shows an increasing incidence of hemorrhagic stroke among diabetic patients.

OUTCOME OF STROKE:

In this study euglycemic patients had a better outcome when compared to admission day hyperglycemic patients. Sixty eight percent of euglycemic patients had a good functional recovery. On the contrary only 16.7% of admission day stress hyperglycemic patients had good functional recovery at the end of thirty day follow up.

The mortality rate was 6% among euglycemic patients which was much less when compared to those of hyperglycemic patients (>50%). Among euglycemic patients 21.3% had moderate prognosis and which was 58.3% of stress hyperglycemic patients. Poor outcome was noticed in 4% of euglycemic patients where as 26% of hyperglycemic patients had poor prognosis. Hence there was an increased risk of early mortality in admission day hyperglycemic patients when compared to euglycemics.

In the ischemic stroke group early mortality was noticed in 11.5% of euglycemic patients and 78% of hyperglycaemic patients. 88% of euglycemic patients and 22% of hyperglycaemic patients had good prognosis. Hence hyperglycemia was associated with an increased early mortality rate and poor functional outcome in ischemic stroke group which was also statistically significant (P : 0.0001).

In hemorrhagic stroke group early mortality was noticed in 28% of euglycemic patients and 78% of hyperglycaemic patients which is statistically significant (P 0.0256).

In nondiabetic ischemic group stress hyperglycemia had poor outcome when compared with euglycemic group. Poor outcome was 23% in stress hyperglycemic group where as 4.3% in euglycemic group.

HbA1C was found to be low in euglycemic group and elevated in hyperglycemic group which is also statistically significant (P.0001).

Patients with associated with additional risk factors like hypertension coronary artery disease had high mortality rate than normal patients which was also statistically significant. ($P < 0.05$)

In our study the HbA1C was 6.78 among ischemic stroke patients where as 8.24% among hemorrhagic stroke patients. Our study clearly shows a positive correlation 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 hyperglycemia was noted in two third (66%) of all ischemic stroke patients(40).

In our study hyperglycemia was noticed in 53% of patients. In their study known diabetes and newly diagnosed diabetes contributed one third of cases (33%). In our study the same group contributed to 41%.

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(41). The mean NIHSS was 9.11 in euglycemics and 17.89 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 (42). Our study in hundred acute stroke patients had similar results.

In hemorrhagic stroke patients, admission hyperglycemia was associated with higher mortality in both diabetic and non diabetics patients. In our study, in ischemic patients, who had elevated admission day glucose level experienced a six and half fold increased early mortality than euglycemics(43). In hemorrhagic stroke group there was a two and half risk of increased mortality in hyperglycemics when compared with euglycemics. Non diabetic stress hyperglycemic patients with ischemic stroke had five 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. Hence there is an urgent need to confirm the improvement in these patients by normalizing blood sugar. Several trials are now under way to improve the outcome of stroke by normalizing the blood glucose with human recombinant insulin.

7. CONCLUSION

There is a linear correlation between admission day hyperglycemia and 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 though conclusive evidences are lacking. 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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9. PROFORMA

NAME OF THE PATIENT : **IP NO :**

AGE : **SEX :**

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

Glycosylated Hemoglobin when required

FINAL DIAGNOSIS

PROGNOSIS (30 DAY FOLLOW UP) :

Good / Moderate / Poor / Death

MASTER CHART

S.No.	Name	Age	Sex	Past History	BP	NIHss	Sugar	HBA1c	CT Brain	Prognosis
1	Chandran	80	M	HT/DM	170/100	15	180	8	LFP	Moderate
2	Rajan	65	M	HT	170/90	7	112	6.1	LF/VS	Good
3	Padma	54	F	DM	130/80	8	220	9.4	LPH	Poor
4	Ranjanbeevi	60	F	HT/DM	150/100	16	300	10.2	RCH	Death
5	Muniammal	60	F	DM/HT	120/80	20	270	9	RFP/MLS	Death
6	Raman	80	M	HT	170/100	9	113	6	LPT/VS	Moderate
7	Antony	50	M	-	130/80	20	284	11	LPT	Moderate
8	Arokyam	65	M	S/A/HCH	130/80	7	96	6.1	RF	Good
9	Sakthi	68	F	HT	170/86	23	101	6	LCG	Good
10	Paramasivam	52	M	DM/S	130/80	23	270	10.2	LFP	Death
11	Mohamed	70	M	HT	160/90	4	90	6.1	LF	Good
12	Santhiya	70	F	-	130/80	10	116	6.1	LCG	Good
13	Kanthan	50	M	-	130/80	15	215	10	LPH	Poor
14	Chitra	60	F	HCH	140/80	8	88	6	RF	Good
15	Papathi	75	F	-	130/80	10	116	6.1	RPT	Moderate
16	Saleema	75	F	HT	200/110	12	198	7	LFP/MLS	Death
17	Ravi	55	M	HT/S/A	170/100	8	92	7.1	RCH	Moderate
18	Narayanan	80	M	HT	180/110	12	98	6.5	LF	Poor
19	Narasimman	60	M	DM/S	130/80	8	260	9	LFP	Death
20	Arunachalam	60	M	HT/CAD	160/90	8	90	6.1	RCH	Moderate
21	Manohar	48	M	S/A	120/84	7	98	6	LCG	Good
22	Arumugam	70	M	HT	170/100	10	118	6.1	LPT	Moderate
23	Murthy	58	M	HT/DM	180/90	23	280	10.6	PRT	Death
24	Leelavathy	55	F	-	200/110	25	236	8	LFPH	Death
25	Vadiyu	70	F	HT	170/110	16	210	9.6	LFPH	Poor
26	Muniyandi	75	M	-	120/80	7	90	6	LLCG	Good

27	Prema	48	F	HCH	130/80	7	88	6	LF	Good
28	Palani	47	M	DM/CAD	140/80	16	200	8	LTH	Poor
29	Arumugan	70	M	HT	170/104	12	118	6.1	LPT	Moderate
30	Kanaga	70	F	HT	200/110	25	212	8	RFP/MLS	Death
31	Ramalingam	55	M	S/A/HCH	120/80	9	120	6.2	RFT	Moderate
32	Ponniammal	70	F	HT/HCH	170/110	16	124	6	LFP/MLS	Poor
33	Abdul Kadhar	50	M	HT/DM/S	200/110	24	220	6.9	LFP/MLS	Death
34	Murugan	47	M	DM/CAD	130/80	16	230	8	LFH	Poor
35	Manohar	48	M	S/A	130/70	7	98	6	LCG	Good
36	Munusamy	60	M	-	130/80	4	88	6.1	LF	Good
37	Sonali	75	F	HT	200/100	23	140	6.4	LPH/MLS	Death
38	Manikandan	63	M	DM	140/70	7	170	7.4	RCG	Moderate
39	Narayanan	60	M	DM/OCM	120/80	10	220	8.4	LPH	Poor
40	Mani	55	M	DM/S	130/70	24	276	9.8	RFP/MLS	Death
41	Boopalan	48	M	S/A/HCH	130/84	5	90	6.1	LCG	Moderate
42	Annammal	74	F	HT	140/90	7	80	6	RCG	Good
43	Indirani	60	F	DM/HCH	130/80	7	120	6.2	LCG	Good
44	Panchacharam	53	M	HT/S/A	200/110	23	188	6.8	RFP/MLS	Death
45	Parvathy	55	F	-	130/80	10	108	6	RCG	Moderate
46	Rajendran	49	M	HIS	180/100	10	194	10	LPH	Moderate
47	Munusamy	60	M	-	130/80	4	88	6.2	LF	Good
48	Dasanathan	80	M	-	120/80	8	115	6.1	LPT	Moderate
49	Santhanam	55	M	S/A	130/80	5	90	6	LCG	Good
50	Gajendran	55	M	-	140/80	20	232	8	LFP/MLS	Death
51	Ranganayagi	64	F	HT	200/110	25	246	7.8	RPH/MLS	Death
52	Cinnathai	68	F	DM	140/70	15	121	6.1	LPT	Moderate
53	Amir	60	M	CAD/DM	140/88	8	198	7.4	RCH	Poor
54	Krishnan	55	M	HT/S/A	176/96	5	84	6	LCH	Good
55	Ramu	50	M	HCH/DM	170/100	16	216	8	RFP/MLS	Death
56	Akthar	50	M	HT	170/90	10	121	6.1	RFP	Moderate

57	Andal	60	M	RHD/AF	104/80	7	86	6	LF	Good
58	Raja	65	M	HT/CAD	176/100	14	198	10.4	RPH	Moderate
59	Pitchai	65	M	S/A	130/82	14	120	6.1	LPT/MLS	Poor
60	Ramayee	52	F	HT	170/90	17	124	6	LPT	Poor
61	Muthu	60	M	HT	130/100	7	89	6.2	LCG	Good
62	Narayanan	50	M	HT/S/HCH	172/100	25	284	10.4	RFP/MLS	Death
63	Raghu	54	M	HT/DM	180/90	7	90	6	LPT	Good
64	Balan	60	M	HT/S/A	200/11	10	100	6	LCH	Moderate
65	Doss	70	M	HT	200/110	25	101	6	RPT/MLS	Death
66	Sethu	54	M	S	120/70	10	110	6	LF	Moderate
67	Guru	65	M	DM/S/HCH	130/70	25	204	8	LFPH	Poor
68	Santhy	60	F	HT	190/110	7	100	6	RCG	Good
69	Naren	50	M	HT/S/HCH	172/100	25	200	8	RPH	Moderate
70	Ramasamy	60	M	HT/DM	190/90	10	188	-	RPH	Moderate
71	Ismail	57	M	-	120/80	7	90	6.2	RCG	Good
72	Fathima	60	F	HT	170/90	17	120	6.1	RCG	Good
73	Sankar	48	M	HT	180/90	7	96	6	LF	Good
74	Arul	50	M	HT/DM	190/100	10	200	9	RPH	Poor
75	Solai	56	M	HT	190/80	12	100	6.2	LCG	Good
76	Gowri	60	F	HT	190/100	18	125	6.1	RPH/MLS	Poor
77	Narmatha	62	F	-	120/80	16	104	6	LCG	Good
78	Lakshmi	70	F	HT/CAD	170/90	16	220	10	RPT	Poor
79	Natraj	45	M	S/A	130/70	10	121	6	PFP	Moderate
80	Balamurali	49	M	HT/DM	190/90	24	280	11	LPH/MLS	Death
81	Chokki	50	F	DM	170/80	5	206	8	LCG	Moderate
82	Kuppusamy	60	M	HT/S/A	180/110	7	90	6.2	LTHA	Good
83	Sundar	60	M	-	130/80	24	280	9	RPH/MLS	Death
84	Alagammal	65	F	HT/DM	180/90	14	192	6.9	RPH	Moderate
85	Balu	50	M	HT/DM	190/80	24	287	11	LPH/MLS	Death
86	Ramani	60	M	DM	120/80	7	89	6	LF	Good

87	Nallan	58	M	HT	210/120	23	240	7.2	LFPH/MLS	Death
88	Rahimbai	65	M	S/A/HCH	120/80	7	80	6	LFP	Moderate
89	Malar	67	F	HT	160/90	8	118	6	RFH	Moderate
90	Alagu	52	F	-	130/80	7	100	6.2	RCG	Good
91	Raman	60	M	S/HCH	120/80	7	97	6.1	LF	Good
92	Nelakandan	58	M	HT/S	210/110	23	240	7.4	LFPH/MLS	Death
93	Raghu	54	M	HT/S/A	180/90	7	89	6	LPT	Good
94	Anthony	60	M	HT	210/90	25	101	6.4	RPT/MLS	Death
95	Laxmanan	52	M	S/A	120/70	6	92	6	LCG	Good
96	Andal	47	M	HT	180/110	6	89	6.1	LTHA	Good
97	Lashmi	65	F	CAD/HT	180/90	16	222	10.4	LPT	Poor
98	Kuppam	56	M	-	130/80	8	108	6	LCG	Good
99	Sundarambal	56	F	-	130/80	24	290	10.6	RPH/MLS	Death
100	Mangalam	40	F	RHD/MS	130/80	7	89	6.2	RF	Good

MASTER CHART ABBREVIATIONS

HT	–	Hypertension
DM	–	Diabetes
S	–	Smoker
A	–	Alcohol
CAD	–	Coronary Artery Disease
Hb A1c	–	Glycosylated haemoglobin
L	–	Left
R	–	Right
FI	–	Frontal infarct
FPI	–	Fronto parietal infarct
FH	–	Frontal Haemorrhage
FPH	–	Fronto parietal haemorrhage
PH	–	Parietal haemorrhage
MLS	–	Midline shift
PTH	–	Parito temporal haemorrhage
CH	–	Capsulo ganglion haemorrhage
CG	–	Capsule ganglion infarct
PT	–	Parieto temporal infarct
THA	–	Thalamic infarct
AF	–	Atrial Fibrillation
HCh	–	Hyper Cholesterolemia
SUGAR	–	Admission day blood glucose level
RHD	–	Rheumatic heart disease
DCM	–	Dilated cardio myopathy