"PREVALANCE OF STRESS HYPERGLYCEMIA IN ACUTE CEREBROVASCULAR ACCIDENTS AND ITS IMPACT ON OUTCOME"

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MAY 2020

CERTIFICATE

This is to certify that this dissertation entitled "**PREVALANCE OF STRESS HYPERGLYCEMIA IN ACUTE CEREBROVASCULAR ACCIDENTS AND ITS IMPACT ON OUTCOME"** submitted **by Dr.B.SURESH** to the faculty of General Medicine, The Tamil Nadu Dr. M.G.R Medical University, Chennai, Tamilnadu, in partial fulfillment of the requirement for the award of **M.D DEGREE BRANCH-I (GENERAL MEDICINE)** is a bonafide research work carried out by him under my direct supervision and guidance.

Prof. Dr. C. HARIHARAN M.D.,
Head of the Department,
Department of Medicine,
Stanley Medical College and Hospital,
Chennai- 1.

Prof.Dr.R.SHANTHIMALAR, M.D., D.A.,
DEAN
Government Stanley Medical College and Hospital,
Chennai-1.

CERTIFICATE BY THE GUIDE

This is to certify that **Dr.SURESH B,** Post Graduate student (May 2017 to April 2020) in the Department of General Medicine, Government Stanley Medical College and Hospital,Chennai-1,has done this dissertation work titled "**PREVALANCE OF STRESS HYPERGLYCEMIA IN ACUTE CEREBROVASCULAR ACCIDENTS AND ITS IMPACT ON OUTCOME"** under my guidance and supervision in partial fulfillment of the regulations laid down by The Tamilnadu Dr.M.G.R.Medical University, Chennai for **M.D.,(General Medicine),** Degree examination to be held in May 2020**.**

Prof. Dr. A.RAVI M.D.,
Chief, Medical Unit-7,
Department of Medicine,
Stanley Medical College and Hospital,
Chennai - 1.

DECLARATION

I, **Dr.SURESH. B**, solemnly declare that the dissertation titled "**PREVALANCE OF STRESS HYPERGLYCEMIA IN ACUTE CEREBROVASCULAR ACCIDENTS AND ITS IMPACT ON OUTCOME"** is a bonafide work done by me at Government Stanley Hospital, Chennai during May 2018 to Oct 2018 under the guidance and supervision of Prof. Dr.A.Ravi M.D., Professor of Medicine, Government Stanley Hospital, Chennai. I also declare that this bonafide work or a part of this work was not submitted by me or any other for award degree or diploma to any other university, board either in India or abroad. This dissertation is submitted to the Tamilnadu Dr. M.G.R Medical University, towards the partial fulfillment of requirement for the award of M.D. Degree (Branch – I) in General Medicine.

Place: Chennai **Signature of the candidate**

Date: **(Dr .B. SURESH)**

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This is to certify that this dissertation work titled "**PREVALANCE OF STRESS HYPERGLYCEMIA IN ACUTE CEREBROVASCULAR ACCIDENTS AND ITS IMPACT ON OUTCOME"** of the candidate **Dr.B.SURESH** with Registration Number 201711071 for the award of **M.D., DEGREE** in the branch of **BRANCH-I (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 **ZERO** percentage of plagiarism in the dissertation.

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ABBREVIATIONS

ADC - apparent diffusion coefficient

AF - atrial fibrillation

AGE- advanced glycation end products

AHA - American Heart Association

AIDS - Acquired Immune Deficiency Syndrome

AIS - acute ischaemic stroke

AMP - adenosine monophosphate

AOL- Arterial Occlusive Lesion

ARR- Absolute Risk Reduction

ASA -American Stroke Association

ASL -arterial spin labeling

ATP -adenosine triphosphate

AVM- Arteriovenous Malformation

CBF -Cerebral Blood Flow

CBG- capillary blood glucose

CBV- Cerebral Blood Volume

CRP C-reactive protein

CT -Computerised Tomography

CU -cerebrovascular unit

EUSI- European Stroke Initiative

FBG- fasting blood glucose

FFA -free fatty acid

IDF -International Diabetes Federation

IFG Impaired Fasting Glucose

IGF -insulin-like growth factor

IGT- Impaired Glucose Tolerance

IIT -Intensive insulin therapy

IS- Ischaemic Stroke

IV- intravenous

LAC- lactate

LACS- lacunar syndrome

MI myocardial infarction

MR -magnetic resonance

MRA- Magnetic Resonance Angiography

MRI -Magnetic Resonance Imaging

MRS- magnetic resonance spectroscopy

mRS-Modified Ranskin scale

NADPH- nicotinamide adenine dinucleotide phosphate-oxidase

NIHSS -National Institute of Health Stroke Scale

NO- nitric oxide

NO MASS- North Manhattan Stroke Study

PSH-post-stroke hyperglycemia

PWI- Perfusion Weighted Imaging

ROS- reactive oxygen species

SAA- serum amyloid A

SAH- subarachnoid hemorrhage

SAINT Stroke-Acute Ischaemic NYX Treatment

SCMU- stroke care monitoring unit

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INTRODUCTION

Stroke is the third commonest cause of death and the leading cause of disability in the world wide. Recent national audit office figures estimate that in England there are 110,000 strokes and a further 20,000 transient ischaemic attacks each year. [1] In Scotland, there are an estimated 15,000 strokes annually. According, to the study carried out in Kolkata in 2007, incidence rate of stroke is approaching western figures of 145/1,00,000 population. Stroke is predominantly a condition affecting older people with 75% of strokes occurring in those greater than 65 years of age.

The estimated increase in the number of older people in society suggests that the cost of stroke will continue to rise.[2] A stroke is characterized by rapidly developing clinical signs of focal (or occasionally global) disturbance of cerebral function, lasting for more than 24 hours or leading to death with no apparent cause other than of vascular origin (World Health Organisation definition 1976).[3]

Stroke can be subdivided into the ischaemic stroke, accounting for 85% of all strokes and hemorrhagic stroke which accounts for the remaining 15%.5 Haemorrhagic strokes are then subdivided into primary intracerebral hemorrhages (PICH, 10%) or subarachnoid hemorrhages (SAH, 5%).[4] About 10% of all people with acute ischaemic stroke will die within 30 days of

stroke onset. Of those who survive, about 50% will experience some level of disability after six 26 months.[5] In contrast, 35% to 52% of patients with primary intracerebral hemorrhage will die within one month of symptom onset and only 20% are functionally independent at 6months.

Methodological factors within different populations have made comparison of stroke incidence difficult. Criteria have now been proposed for accurate case ascertainment. [6]The most common cardiac source in western societies is nonrheumatic atrial fibrillation, the prevalence of which increases with age. It is estimated that 30% of patients with stroke aged >80 years of age have atrial fibrillation compared to 5% of patients. [7]

Despite the proven benefit, recent figures taken from the national sentinel stroke audit estimate that as many as 38% of stroke patients in the United Kingdom are still not managed in stroke units during the period of their hospital stay. In addition, it has been shown that only 15% of patients are admitted to the stroke unit on the same day as their stroke.[8] Set standards defined by the sentinel stroke audit and the recently published stroke strategy should ensure optimal and continued improvements in patient management.

Recognition of stroke as a medical emergency with rapid hospital admission will allow many patients ineligible for lytic treatment to benefit from stroke unit care. A high proportion of patients suffering acute stress such as stroke or myocardial infarction may develop hyperglycemia, even in the absence of a preexisting diagnosis of diabetes. Both human and animal studies suggest that this is not a benign occurrence and that stress-induced hyperglycemia is associated with a high risk of mortality after both stroke and myocardial infarction. [9]

Moreover, recent evidence that glucose-lowering with insulin reduces ischemic brain damage in animal models of stroke suggests that stress-induced hyperglycemia may be a modifiable risk factor for brain damage. [10]We therefore systematically reviewed the published literature to summarize the available evidence and to estimate the strength of the association between admission hyperglycemia and both short-term mortality and functional recovery after stroke[11,12,13]

AIM AND OBJECTIVE OF THE STUDY

PRIMARY OBJECTIVE

1. The aim of the present study is to determine the prevalence of stress-induced hyperglycemia in patients with acute CVA
2. To study the blood sugar level and its correlation with the neurological outcome among the acute CVA patients on admission and discharge in Stanley Government Medical College Hospital.

SECONDARY OBJECTIVE:

1. To determine the frequency of stress-induced hyperglycemia in patients with acute CVA and to study the blood sugar level and its correlation with the neurological outcome among the acute CVA patients on admission and discharge

REVIEW OF LITERATURE

DEFINITION OF POST-STROKE HYPERGLYCAEMIA

Post-stroke hyperglycemia (PSH) is common and is recognized as a prognostic indicator of poor stroke outcomes. A proportion of patients with PSH will have underlying diabetes, already established from the clinical history or detected at the time of presentation.[14] The remainder of the patients with PSH is labeled as having "stress hyperglycemia", although a proportion has underlying impaired glucose tolerance when screened at later time points. Studies examining the influence of blood glucose on stroke outcomes have certain limitations. There remains no consensus definition for PSH and as such blood glucose levels and the timing and nature of the blood glucose sample vary among studies [15]

The definition for hyperglycemia has included both random and fasting blood glucose values greater than 6.1- 8.0mmol/l, at differing time points from stroke ictus. The time elapsed from stroke onset to blood glucose sampling in prospective trials has included patients presenting up to 72 hours from stroke onset.[16]

In view of this nonuniformity in PSH definition prevalence rates differ across studies. By combining studies from Chin SL et.al with documented numbers of patients with diabetes and stress hyperglycemia, the overall prevalence for each respective group (±SD) was (1) Diabetics 17.3% (±6.0%); (2) Stress Hyperglycaemia 20.3% (±14.2%) and (3) Normoglycaemia 62.4% (±18.0%). [17]

The chronological span of the studies cited date from 1976-2002 reflecting 46 both clinical practice and access to radiological imaging in improving the diagnostic classification. Earlier studies based on the stroke type on clinical scores and undoubtedly combined both ischaemic and hemorrhagic strokes in the analysis for the final outcome. [18,19]

In patients with primary intracerebral hemorrhage (PICH), admission hyperglycemia was not found to be associated with increased stroke mortality. Unfortunately, patient numbers with PICH included in the systematic review were small. [20,17,19]

Two larger studies have subsequently been published demonstrating that high admission blood glucose increases short-term mortality in both diabetic and non-diabetic patients with PICH. In no diabetic patients, admission blood glucose was associated with parameters of stroke severity: reduced

consciousness level, hematoma size, and intraventricular hemorrhage extension[22,23]

Hyperglycaemia and effect on stroke outcome

Despite the recognized association between hyperglycemia and poor stroke outcome, uncertainty remains as to whether blood glucose has a direct neurotoxic effect on the ischaemic brain or if it represents a pathophysiological response to increased stroke severity or unmasking of abnormal glucose metabolism.

A number of different hypotheses exist: (1) PSH is an epiphenomenon of stroke severity and plays no mechanistic role in poorer outcome; (2) PSH is an unmasking of previously undiagnosed diabetes or impaired glucose metabolism with its associated comorbidities that is relevant to long term outcome; (3) Hyperglycaemia is associated with infarction/injury within specific anatomical areas of the brain independent of stroke severity; (4) PSH regardless of the mechanism is harmful and needs to be treated and (5) PSH is irrelevant mechanistically in worsening of stroke and treatment is unnecessary or indeed harmful[24,25]

Diabetes prevalence is increasing worldwide. It is estimated that 28-44% of adults aged 45-74 have diabetes or impaired glucose tolerance, with an estimated 5.4 million Americans unaware of an underlying diagnosis of diabetes. Diabetes is an established risk factor for atherosclerosis. The prevalence of carotid artery disease in elderly diabetic patients is 20%.81 In any given stroke population the prevalence of diabetes is said to be of the order of 7-25%,50;61 with a further 6-32% having evidence of previously unrecognized diabetes prior to the acute event.55;56 Abnormalities in glucose metabolism insufficient to fulfill diabetic criteria are also known to increase cardiovascular risk.

In a meta-regression analysis of 18 studies involving 51 88,000 patients, cardiovascular disease increased continuously with glucose levels of greater than 4.2mmol/l.82 In patients with known coronary artery disease the relationship between fasting blood glucose and incident ischaemic stroke was J-Shaped, with stroke rate increasing with fasting glucose levels >5.6mmol/l.83 The metabolic syndrome characterized by high fasting glucose, high blood pressure, low high-density lipoprotein cholesterol, high triglycerides, and abdominal obesity84, is associated with an increased risk of morbidity and mortality from cardiovascular disease.85 In 14,000 patients with coronary artery disease followed prospectively for 4.8-8.1 years, patients with the metabolic syndrome had a 1.49 fold increased odds for ischaemic stroke or transient ischaemic attack (TIA) (95%CI, 1.20- 1.84).[26,27]

A total of 10,489 men and women followed for a mean of 8.5years had 164 incident strokes, with stroke ascertainment being defined on the basis of death certificate data and hospital record linkage. After adjustment for age, sex and cardiovascular factors the relative risk of stroke for participants with HbA1c (5-5.4%), (5.5- 6.9%) and (≥7%) were 0.78 (0.50 to 1,22), 0.83 (0.54 to 1.27) and 2.83 (1.40 to 5.74) respectively.87 Patients in the latter group who undoubtedly had undiagnosed diabetes had a significantly increased risk of stroke.[28,29]

The 52 methodologies of the study did not permit the breakdown of strokes into subtypes. Screening for abnormal glucose metabolism in patients manifesting "stress hyperglycemia" following stroke is not routinely performed. In a retrospective review of 90 acute stroke patients with no history of diabetes and a hyperglycemia prevalence of 31%, one patient had a management plan to screen for diabetes following discharge. A recent study using an oral glucose tolerance test after three months to screen 98 TIA/stroke patients with an initial fasting blood glucose [30,31]

TEMPORAL PROFILE OF GLUCOSE POST-STROKE

Elevated admission or fasting blood glucose at variable time points from stroke onset has been used to define post-stroke hyperglycemia (PSH). Blood glucose has been shown to increase in the first 12 hours after stroke with the

increase in blood glucose said to correlate with increased stroke severity. In an earlier publication of patients randomized to the placebo arm of the Glucose Insulin in Stroke Trial (GIST)-UK, blood glucose fell within the first eight hours of the infusion (median time to infusion 13 hours).[32,33]

Using a capillary glucose monitor to measure interstitial glucose over a 72-hour period, blood glucose was noted to decrease from a peak at eight hours following a stroke, reach its lowest level at 14 hours, plateau and then have a further peek at 66-88 hours.[35,36]

Recognition of the temporal profile of blood glucose in acute stroke is important for the management of PSH. In addition to 55 stroke severity, time to hospital presentation may be important in predicting hyperglycemia in the acute phase of the stroke. Additional factors often poorly described in the literature include the possible impact of feeding and fluid regimes. In determining the temporal profile it is important to have a consistent measure of determining blood glucose levels. Confusion remains surrounding the difference between capillary whole blood, venous whole blood and venous plasma in determining glucose levels. Following an OGTT in 75 healthy subjects, capillary blood glucose was significantly higher than venous blood. This has implications in determining profiles in patients during post-prandial monitoring phases.[37,38]

STROKE SEVERITY AND BLOOD GLUCOSE

Studies examining the interaction between stroke severity, blood glucose, counter-regulatory hormones, and catecholamines have reported conflicting results. Following an acute physiological illness, stress hyperglycemia is thought to develop through glucagon, adrenaline, and cortisol opposing the normal action of insulin. The more severe the stroke the more marked the stress response. Serum cortisol has been shown to correlate with stroke severity, blood glucose, and temperature and is an independent predictor of short-term outcome. However, plasma catecholamines associated with both stroke severity and hypertension were not found to correlate with glucose levels in a stroke population.[39,40]

In patients randomized to the NINDS rt-Pa trial, blood glucose within three hours of stroke onset was not associated with stroke severity measured 56 using the National Institute of Health Stroke Scale (NIHSS).[41,42]

100 Patients assessed using the Glasgow outcome scale within 24 hours of symptom onset had an association between hyperglycemia and stroke outcome but not between hyperglycemia and initial stroke severity. However, patients examined with two blood glucose tests within 12 hours of stroke onset had a strong association between blood glucose and stroke severity measured using the Scandinavian stroke scale[43,44]

Hyperglycaemia and Ischaemic Injury

Hyperglycaemia has been shown in experimental and clinical studies to act 57 on vascular and hemostatic function, altering local blood flow and platelet aggregation and influencing both vessel occlusion and recanalization. The “ischaemic penumbra” is also susceptible to the effects of hyperglycemia through its action on tissue cellular metabolism and has the potential to influence infarct progression and clinical outcome.[45,46]

Endothelial Abnormalities Epidemiological studies have consistently shown diabetes to be a major risk factor for atherosclerotic vascular disease. There is evidence that the primary initiating lesion in the pathogenesis of atherosclerosis is endothelial cell dysfunction. Hyperglycaemia has a direct effect on endothelial cell function and is known to induce a variety of biochemical changes.

It has been established that four independent biochemical abnormalities are involved - increased polyol pathway flux with increased consumption of NADPH (nicotinamide adenine dinucleotide phosphate-oxidase) and depletion of GSH (reduced Glutathione), increased formation of advanced glycation end products (AGE), activation of protein kinase C through increased flux of dihydroxyacetone phosphate to DAG (Diacylglycerol) and finally increased

hexosamine pathway flux with increase modification of proteins by O-linked N-acetylglucosamine (GLcNac)[47,48]

Ischaemic Penumbra

Controversy continues regarding the potential mechanism by which hyperglycemia causes neuronal injury. Experimental models demonstrate a consistent correlation between acidosis, hyperglycemia and brain injury.113 Anaerobic metabolism is less energy-efficient and produces lactate and unbuffered hydrogen ions. Experimental models have consistently shown that hyperglycemia prior to ischemia results in higher levels of lactate than euglycaemic controls.113;114 Hyperglycaemia may initially be neuroprotective, with increased glucose available for metabolism and ATP production. [50,51]

Persisting anaerobic metabolism results in the development of intracellular acidosis. It has been shown using both pH-sensitive microelectrodes and 31P nuclear magnetic resonance spectroscopy that the brain pH of animals pretreated with glucose is considerably more acidotic than saline-treated controls.115;116 The mechanism by which acidosis exaggerates neuronal injury is uncertain. Astrocytes were previously thought to be the target, with selective neuronal necrosis giving way to pan-necrosis through the failure of astroglial nutritional support and ion homeostasis. [49,53,54]

The pronounced acidosis seen with hyperglycemia provides an environment in which secondary mechanisms can act. Acidosis enhances free radical formation, activation of pH-dependent endonucleases and 62 glutamate release with subsequent alteration of intracellular Ca++ regulation and mitochondrial failure. 113;118-120 There is currently no direct proof that lactate is detrimental to the ischaemic brain. The “glucose paradox of cerebral ischemia” questions why glucose, the main energy substrate for the brain, causes the demise of brain tissue at the time of cerebral ischemia.[56,55]

Cellular injury hinges on the role of lactate in the brain. Recent in-vitro work using murine hippocampal slices has shown that glucose and acidosis are detrimental to cells whereas lactate is not.[56]

Work performed by Marquardt L, et al has continuously questioned the detrimental role of lactate and has proposed that the effect of hyperglycemia is related to the effect of corticosterone on the ischaemic brain, thus favoring a stress response.Support for this hypothesis comes from an animal model whereby blockade of corticosterone (the equivalent of human cortisol) with metyrapone attenuates the effect of pre-ischaemic hyperglycemia on the postischaemic outcome. It is postulated that lactate is a source of energy during cerebral ischemia. Using PET scanning it has been shown that lactate may be the preferred energy supply to the brain especially during times of stress.124 “The glucose paradox” remains unanswered.[57,58]

BLOOD GLUCOSE LOWERING THERAPIES

Controversy continues as to whether acute hyperglycemia is a cause of neurological deterioration or an epiphenomenon, a distinction pivotal in the management of stroke patients with hyperglycemia.

Post-stroke hyperglycemia is common and, at least in non-diabetic individuals, is associated with a poor stroke outcome. Control of hyperglycemia has generally been assumed to be beneficial but prospective trial data has been lacking. In the absence of such evidence, clinical practice has been guided by extrapolation of results from non-stroke populations that inform consensus guidelines. The absence of quality evidence in this area has been recognized and evidence derived from patients with acute stroke is becoming available.[59,60]

Insulin and stroke units: current practice American and European guidelines advise active treatment of hyperglycemia but the criteria for implementation of insulin treatment vary. European Stroke Initiative (EUSI) guidelines advise intervention if blood glucose exceeds 10mmol/l, whilst the American Stroke Association (ASA) guidelines have recently been updated to lower the threshold for intervention from 16.63mmol/l142 to 11.0mmol/l.46 [61,62]

McCowen KC et.al did not reveal the variation in practice among centers within individual countries, which we presume to be at least as great. The decision to intervene is made more complex by the risk of iatrogenic hypoglycemia during insulin treatment.

This needs to be considered when selecting the most appropriate glucose level, the method, and duration of insulin delivery, and the duration of glycaemic monitoring. A variety of methods of insulin administration exist, comprising continuous intravenous infusion, repeated subcutaneous dosing by sliding scale or 71 intravenous (IV) delivery of a reconstituted infusion containing insulin and dextrose with potassium supplementation (the GKI regime). [63,64]

Sliding scale regimens are largely reactive, correcting changes as and when they occur, whereas GKI regimens are largely proactive predicting insulin requirements and maintaining euglycemia within a therapeutic range. Concurrent administration of insulin, potassium, and glucose as a GKI infusion reduces the risk of hypoglycemia arising as a result of device or infusion failure.

Maintenance of euglycemia can prove difficult in patients who are eating and drinking normally, as such patients tend to develop post-prandial hyperglycemia before the insulin infusion rate is increased.The practical aspects and the safety profile of each method have been considered in different hospital settings including critical care, coronary care, general medical wards, and stroke units.

In the absence of trial data sufficiently powered to examine the effect of insulin on clinical outcomes in a stroke population, trials of insulin infusions in other contexts (such as coronary and intensive care units) need to be considered.[66]

Insulin use in brain-injured patients Limited evidence exists on the action of insulin in humans with CNS injury. Post hoc analysis of 63 patients with isolated brain injury from the larger Leuven cohort of 1,548 surgical ICU patients receiving intensive insulin 83 therapy examined the effect of insulin therapy on intracranial pressure, diabetes insipidus, seizures and long-term rehabilitation at 6 and 12 months follow-up. 57% of patients included had intracerebral or subarachnoid hemorrhage with 19% being classified as having brain ischemia.

When the conventional treatment population (n=30) was compared to the intensively treated population (n=33), patients receiving insulin had reduced mean and maximal intracranial pressure, fewer acute seizures and 12 months brain, injured survivors were more likely to be self-caring. [67]

Nonneurological morbidity was also reduced in the insulin group reflected by the reduced duration of mechanical ventilation, ICU stays, hospital stay and reduced incidence of systemic sepsis.

In a retrospective study of 960 patients with thromboembolic stroke, patients who had initial hyperglycemia (blood glucose >7.2mmol/l) that settled on repeated testing at 24 and 48hours had similar mortality rates to patients with persistent euglycemia.176 Insulin, oral hypoglycaemic agents or both were used in 63.7% of patients developing euglycemia after admission. These results although taken from a retrospective study suggest some benefit of blood glucose control, providing justification for prospective work in this area [68]

RECENT EVIDENCE IN STROKE PATIENTS

The GIST-UK study recruited patients with acute stroke and blood glucose between 6.1 and 17mmol/l, regardless of whether or not they were known to have diabetes, although insulin-requiring diabetic patients were excluded. 95 Patients were randomized to either placebo (normal saline) or a GKI infusion for 24 hours.

The objective of the GKI treatment was to maintain capillary blood glucose between 4 and 7mmol/l. The trial's primary end-point was mortality at day 90. The GKI regime in GIST-UK comprised 500mls of 10% dextrose, 20mmol KCL and 16 units (initial) of soluble recombinant human insulin. Since the GKI regime involved 100ml/h IV infusion, patients with renal or significant congestive cardiac failure were excluded. [67,69]

Whilst these volumes of fluid may present difficulties for older patients with co-morbidity there was only a 3% incidence of symptomatic heart failure reported. At infusion initiation blood glucose monitoring was undertaken hourly until euglycemia was reached and then changed to two-hourly.

Dosage escalations or reductions required bag disposal and adjustment due to the inflexibility of insulin titration independent of glucose, although the median number of bag changes over the 24 hours was two per patient. This regimen can prove difficult in patients who are eating or drinking normally,

requiring increased levels of insulin during the day and at times of meals with reduced requirements at night. This difficulty of dose titration is more relevant for 85 prolonged infusions and is relevant to infusion duration. The GKI regime is therefore very labor-intensive. [70,71]

One unexpected finding was an effect of GKI infusion upon blood pressure. Treatment with GKI was associated with significant decreases in blood pressure beyond that of medical therapy, with a mean fall in systolic blood pressure of 9.03 mmHg.

Although insulin is known to exert a vasodilatory effect upon resistance vessels, alternative explanations include the effect of potassium as part of the trial infusion or the pressor effect of saline. This observation requires further investigation. Despite the neutral result, the trial remains the first clinical trial of glucose modulation in acute stroke and subsequent trials will be informed through its results.

The trial recruited 933 patients of a proposed sample size of 2,355 patients and as such was underpowered to detect the pre-specified mortality difference between groups. As previously discussed, despite the glucose 86 enrolment range of 6.0-17mmol/l, the majority recruited had mild hyperglycemia; median blood glucose 7.8mmol/l (6.8-9.2) in the GKI group and 7.6mmol/l (6.7-8.8) in the placebo group. [72,73]

Over the course of the trial, one episode of transient hypoglycemia occurred, which responded well to oral glucose. In a separate study, a different method of IV insulin administration was used.181 24 patients (88% known diabetic) recruited within 12hours of an acute ischaemic stroke, with blood glucose in the range 9.4-22.2mmol/l, received insulin for a mean of 54 hours (range 17-72 hours).

The insulin protocol was adjusted after every patient to prevent hypoglycemia, with potential post-prandial hyperglycemia being covered with subcutaneous insulin 0.12 units/kg before each meal in those patients with 88 oral intakes.

The target glucose range was 3.9 - 7.2mmol/l. Hypoglycemia was defined as 6.1mmol/l) within 24 hours of symptom onset are randomized to tight glucose control (3.9-6.1mmol/l), loose glucose control (6.1-11.1mmol/l) or usual care. The infusion will be in the form of a GKI infusion and titrated to capillary glucose. The primary outcome is the rate of hypoglycaemic events (glucose < 3.05mmol/l).

This is a randomized, multi-center trial that recruited patients with acute ischemic stroke within 12 hours of symptom onset to usual treatment 89 (subcutaneous insulin four times daily) or aggressive treatment (continuous

intravenous insulin to a target glucose range 6.1- 7.2mmol/l). The experimental interventions continue for 72hours. [74,75]

The primary outcome measures were the modified Rankin scale, Barthel Index, NIH stroke scale and stroke-specific quality of life scale assessed at 90 days. Results are awaited. The study recruited 45 patients and as such, it seems unlikely that any significant clinical measure of the outcome will be discernible between groups[76,77]

MATERIALS AND METHODS

STUDY POPULATION: Emergency department Of Govt Stanley Hospital, Chennai.

STUDY AREA: General Medicine Department in Collaboration with Neurology

SAMPLE SIZE: 126 patients who are admitted in Emergency department for the incidence of stroke

SAMPLING METHOD: A prospective and comparative study

STUDY iDURATION: i6 imonths – May 2018 to October 2018

INCLUSION CRITERIA:

- All those patients presenting with acute CVA to the emergency department of general Medicine
- Adult patients with acute CVA of both the sexes

EXCLUSION CRITERIA:

- Patient already having CVA
- Stroke with related complication (aspiration pneumonia, septicemia)
- Patient already on steroids
- Acute CVA with alcohol intoxication

METHODOLOGY:

It is a perspective and comparative study done in a govt. Tertiary care hospital, medicine department, Chennai. All those patients fulfilling the inclusion criteria presenting with Acute Cerebrovascular accident (CVA) to emergency department or will be enrolled in the study. It includes 126 adult patients with acute Cerebrovascular accident (CVA) of both the sexes. All the participants will be evaluated by detailed history, clinical examination and severity assessment by the Modified Rankin Scale(mRS).

Adult patients (>18 years)presenting with acute CVA will be neurologically stratified based on the Modified Rankin Scale(mRS) and admission blood sugars will be noted. Hyperglycemia is defined as a blood sugar level of more than 140 mg/dl. Ischemic stroke was defined by CT brain (normal CT brain scan or recent infarct in the clinically relevant area on the scan is done within 72 hours of stroke).

The admission blood sugar was estimated in all patients and was later categorized into 3 groups. Hyperglycemia was defined as a blood sugar level of more than 140 mg/dl. The patients were subdivided into 3 groups based on RBS and HbA1c level.

They are subdivided into 3 groups

- Group 1 consisting of normoglycemic patients,
- Group 2 consisting of stress hyperglycemic patients,
- Group 3 consisting of known diabetes mellitus patients

All the patients were followed up with neurological assessment by mRS Score, FBS and PPBS till discharge.

INFORMED CONSENT: Consent form was written in both English and Tamil and also orally explained in their own language and consent was obtained from the participants, confidentiality was maintained.

STATISTICAL ANALYSIS

1. Descriptive and inferential statistical analysis has been carried out in the present study.

2. Results on continuous measurements are presented as mean ±SD (min-max) and results on categorical measurements are presented in numbers (%).

3. Data will be entered in the excel sheet and the analysis will be done using SPSS version 17. Chi-square test / Fischer exact test is used to compare between 3 groups

4. A p-value of < 0.05 was considered to be statistically significant.

RESULTS

TABLE: 1 AGE GROUP

AGE GROUP	FREQUENCY	PERCENT
40-50 Years	26	20.6
51-60 Years	47	37.3
61-70 Years	53	42.1
Total	126	100.0

GRAPH: 1 AGE GROUP

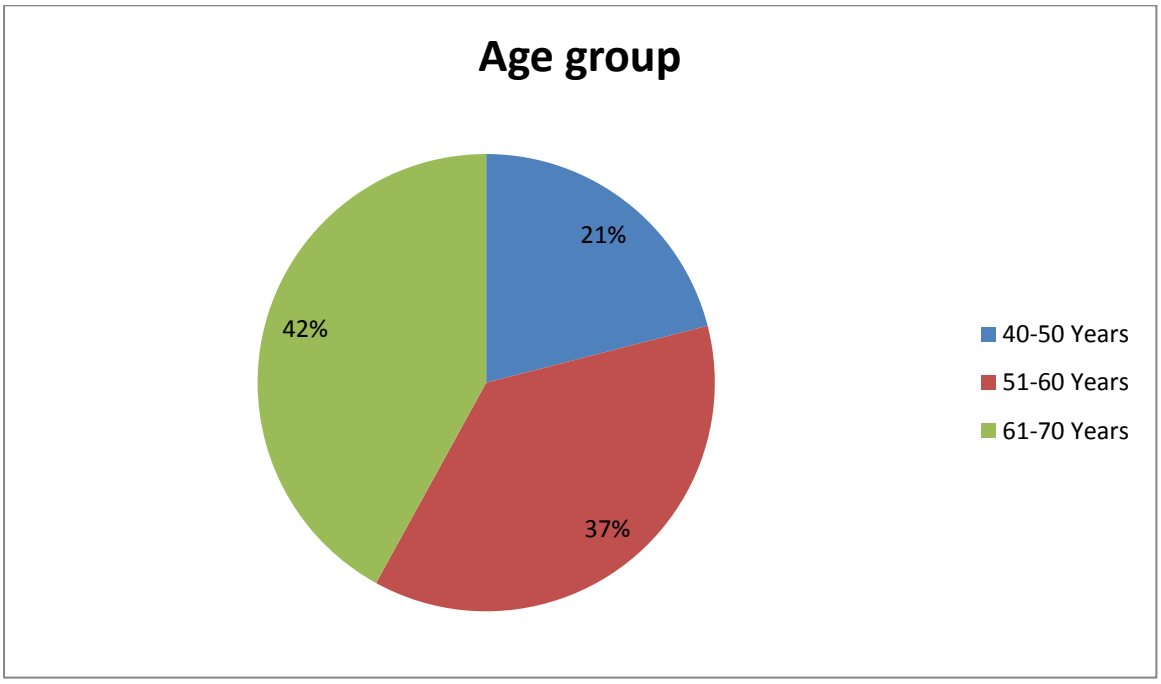


Table: 1 & graph: 1 shows Totally 126 cases were included in the study. Age group between 40-50 year were 26 cases, 51-60 years were 47, 61-70 years were 53 cases.

TABLE: 2 SEX DISTRIBUTION

SEX	Frequency	Percent
Male	73	57.9
Female	53	42.1
Total	126	100.0

GRAPH: 2 SEX DISTRIBUTION

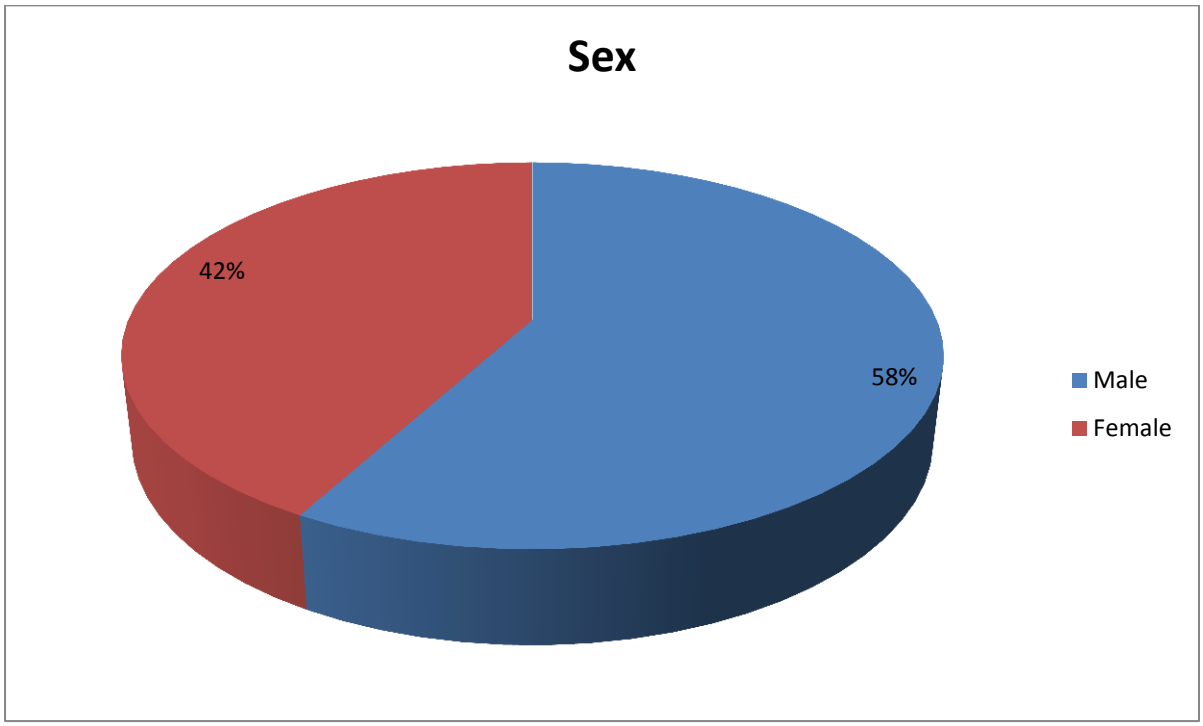


Table :2 & graph :2 shows In 126 cases 73 were male, female were 53 cases.

TABLE :3 DIABETIC STATUS

DM	Frequency	Percent
Yes	52	41.3
No	74	58.7
Total	126	100.0

GRAPH :3 DIABETIC STATUS

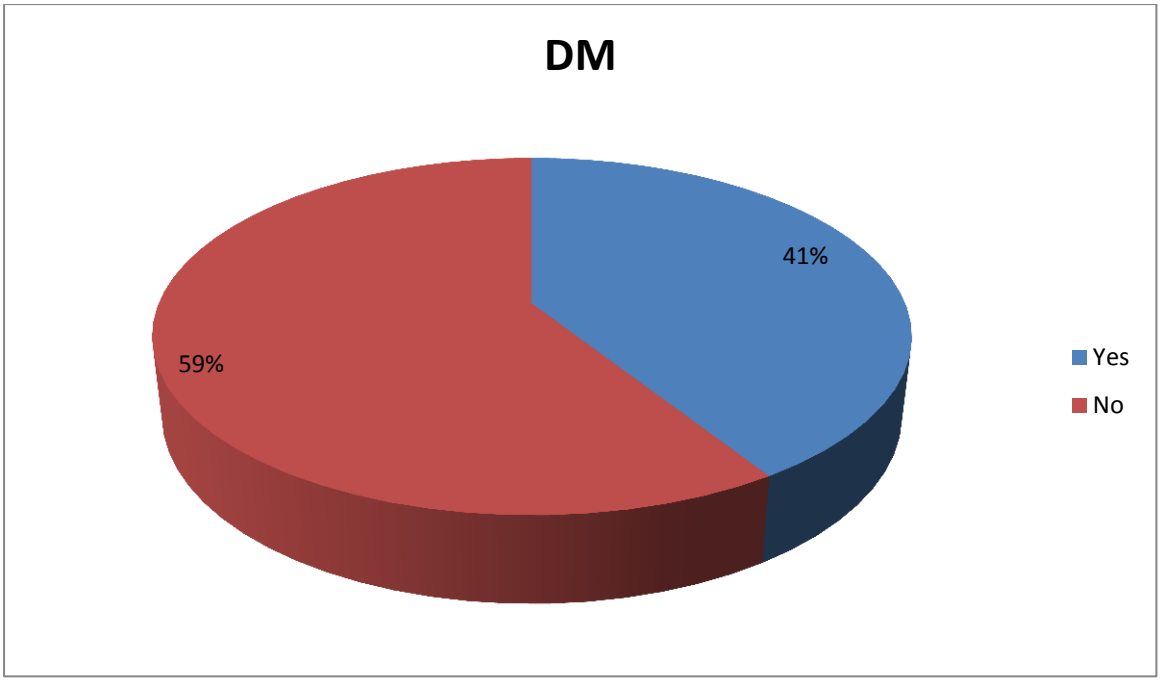


Table :3 & graph :3 shows 52 were diabetic, 74 were non –diabetic

TABLE: 4 PREVELANCE OF HYPERTENSION

SHT	Frequency	Percent
Yes	67	53.2
No	59	46.8
Total	126	100.0

GRAPH: 4 PREVELANCE OF HYPERTENSION

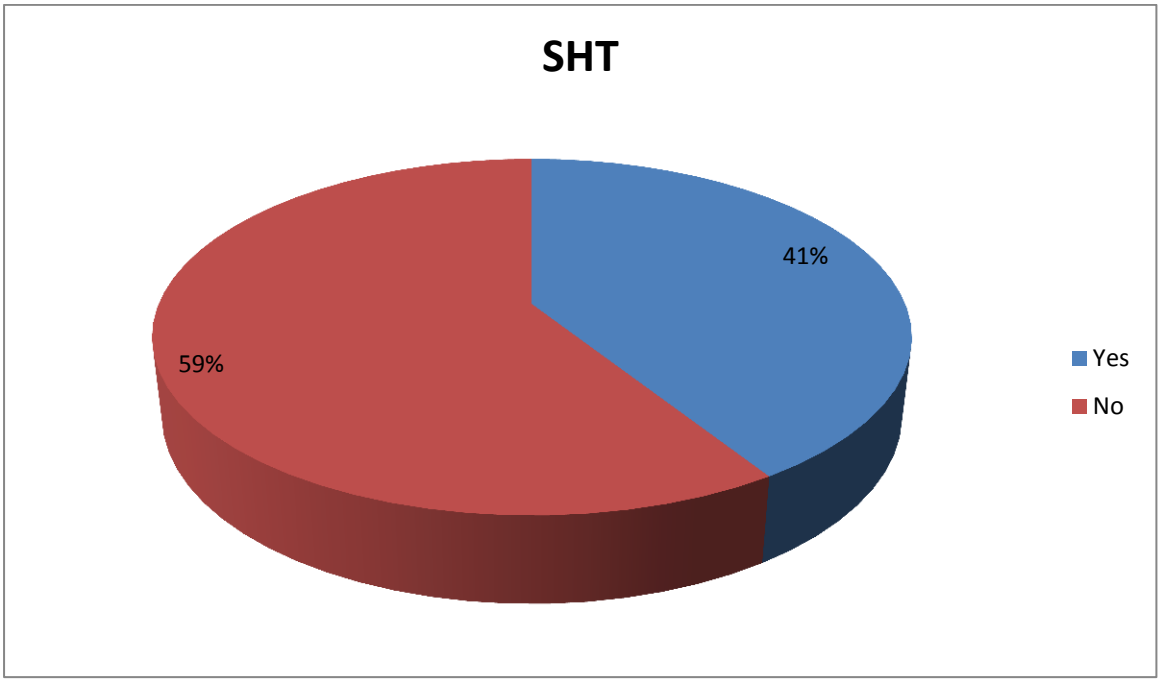


Table: 4 & Graph: 4 shows among 126 cases 67 were hypertensive, 59 were nonhypertensive

TABLE: 5 PREVELANCE OF CAD

CAD	Frequency	Percent
Yes	28	22.2
No	98	77.8
Total	126	100.0

GRAPH: 5 PREVELANCE OF CAD

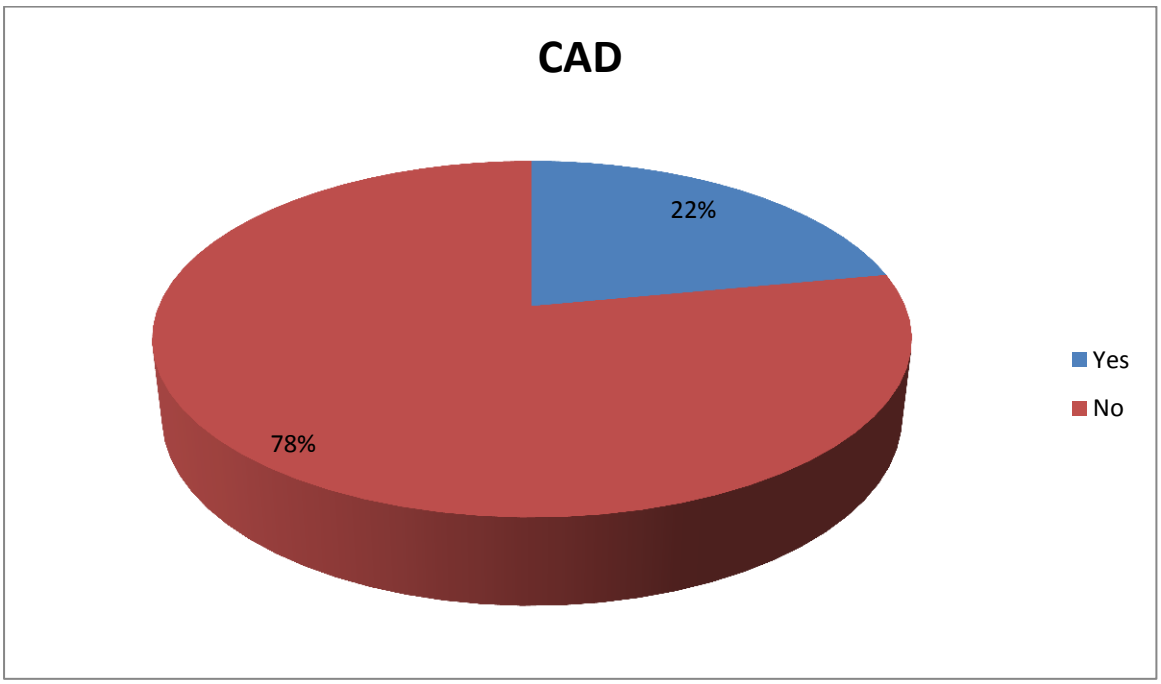


Table: 5 and graph: 5 shows 28 had CAD & 98 were free from CAD

TABLE: 6 SMOKING

SMOKING	Frequency	Percent
Yes	57	45.2
No	69	54.8
Total	126	100.0

GRAPH: 6 SMOKING

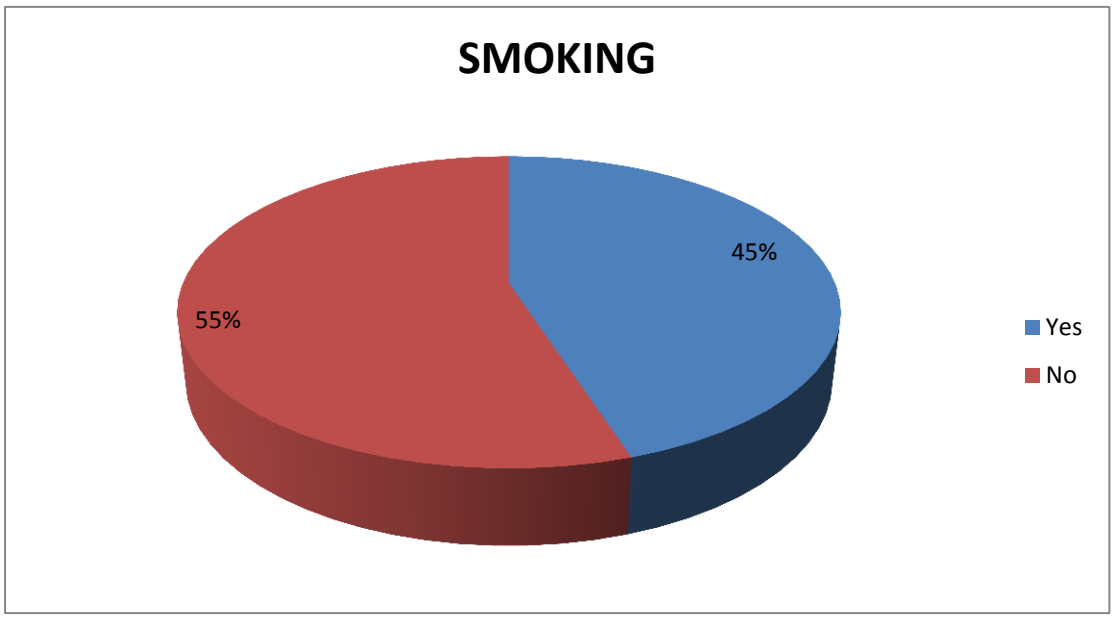


Table: 6, & Table: 6 57 patients had a history of smoking, 69 were non used smoking, forms of tobacco products

TABLE: 7 ALCOHOL

ALCOHOL	Frequency	Percent
Yes	66	52.4
No	60	47.6
Total	126	100.0

GRAPH: 7 ALCOHOL

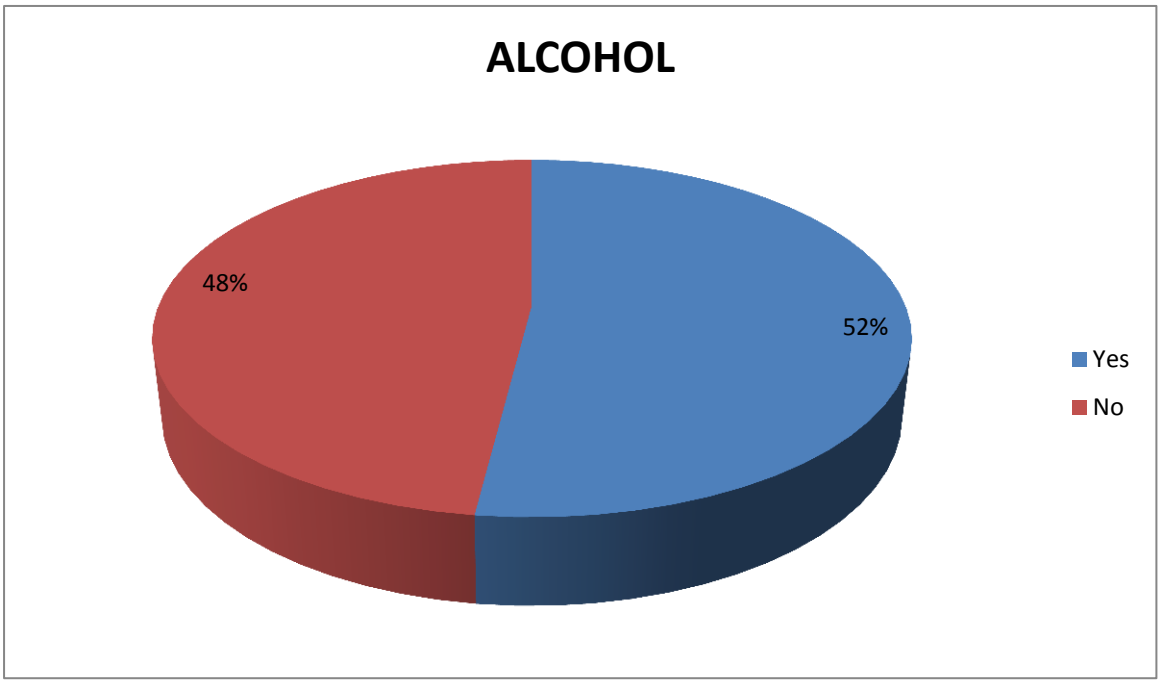


TABLE: 7 & GRAPH: 7 In 126 cases 66 were alcoholics & 60 were nonalcoholics

TABLE: 8 STROKE TYPE

STROKE TYPE	Frequency	Percent
ISCHEMIC	82	65.1
HEMORRHAGE	44	34.9
Total	126	100.0

TABLE: 8 TYPE OF STROKE

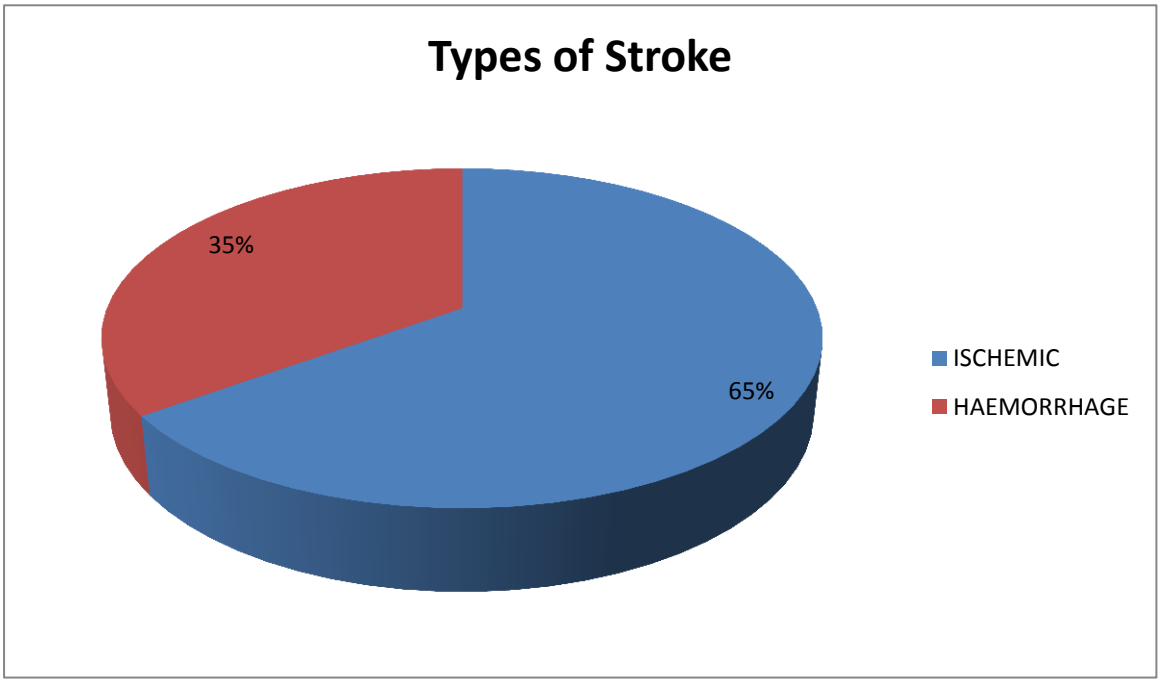


Table: 8 & Graph: 8 shows 44 patients were hemorrhage stroke, 82 were an ischemic stroke in our study

TABLE: 10 GLYCEMIC STATUS

GLYCEMIC STATUS	Frequency	Percent
Normoglycemia	35	27.8
Stress hyperglycemia	38	30.2
Diabetic	53	42.1
Total	126	100.0

GRAPH: 10 GLYCEMIC STATUS

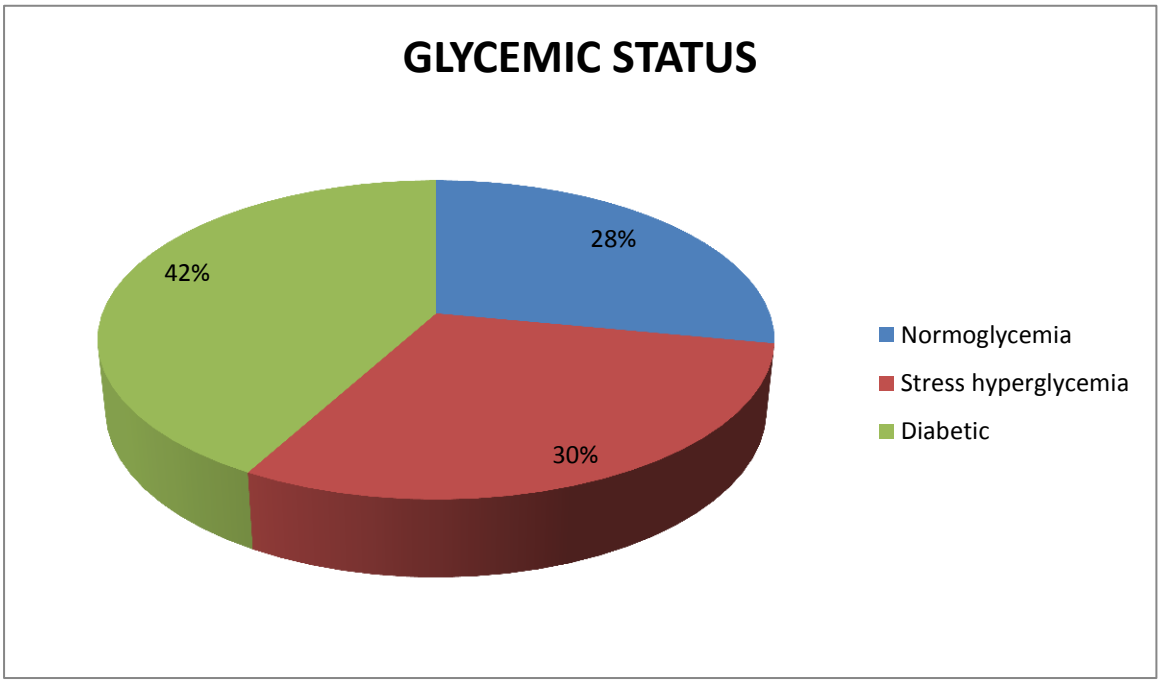
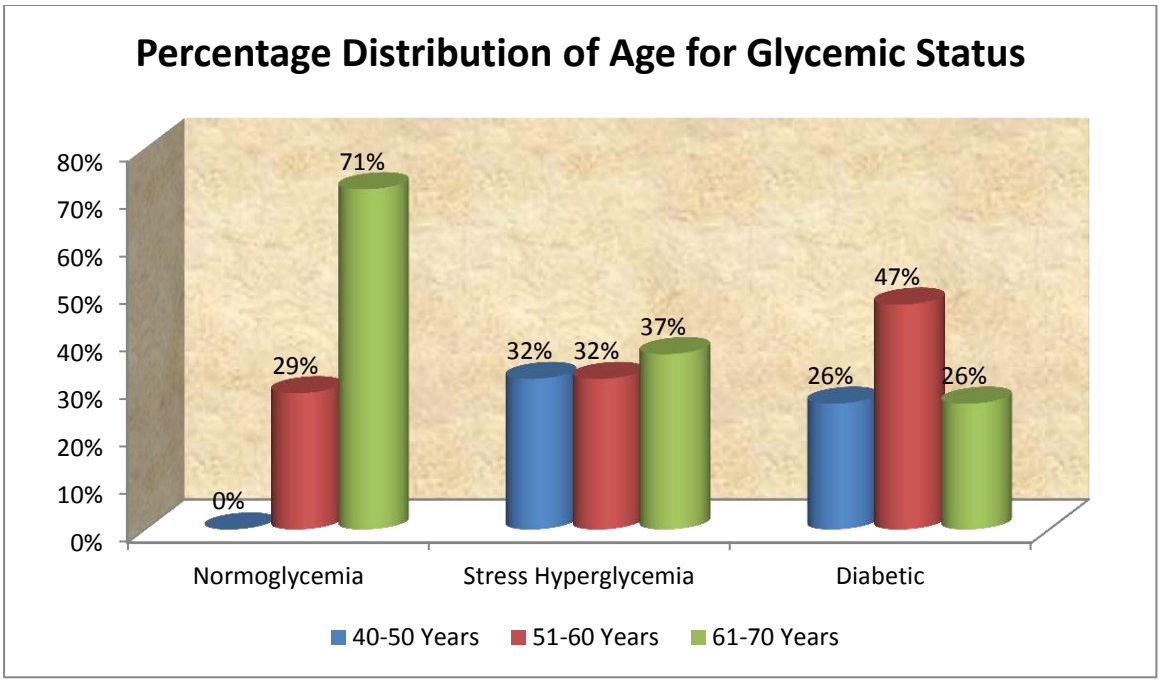


Table :10 & graph 10 shows normoglycemia was observed in 35 cases (27.8%) , stress induced hyperglycemia 38 patients (30.2) ,diabetic were (42.1%)

TABLE: 11 AGE GROUP CORRELATION WITH GLYCEMIC STATUS

			GLYCEMIC STATUS			Total
			Normoglycemia	Stress Hyperglycemia	Diabetic	
Age group	40-50 Years	Count	0	12	14	26
		%	0.0%	31.6%	26.4%	20.6%
	51-60 Years	Count	10	12	25	47
		%	28.6%	31.6%	47.2%	37.3%
	61-70 Years	Count	25	14	14	53
		%	71.4%	36.8%	26.4%	42.1%
Total		Count	35	38	53	126
		%	100.0%	100.0%	100.0%	100.0%

GRAPH: 11 AGE GROUP CORRELATION WITH GLYCEMIC STATUS

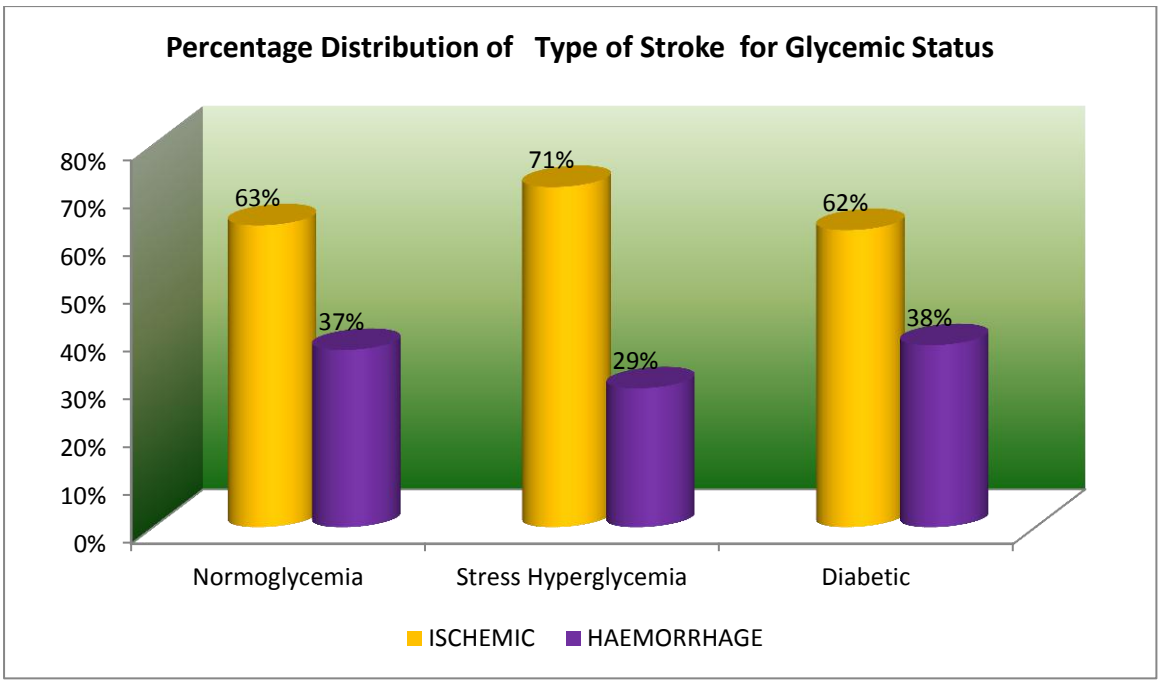


1.In 45-50 years,Normoglycemia-0,Stress Hyperglycemia,-12 (31.6%), Diabetic-14(26.4%) 2.In 51-60 years,Normoglycemia-10, (28.6%) Stress Hyperglycemia,-12 (31.6%),Diabetic-25(47.2%) 3.In age group -61-70 years,Normoglycemia-25,(71.4%) Stress Hyperglycemia-14,(36.8%0 Diabetic-14 (26.4%) Pearson Chi-Square=23.225** $p<0.001$

TABLE: 12 SHOWS TYPE OF STROKE AND GLYCEMIC STATUS

			GLYCEMIC STATUS			Total
			Normoglycemia	Stress Hyperglycemia	Diabetic	
STROKE TYPE	ISCHEMIC	Count	22	27	33	82
		%	62.9%	71.1%	62.3%	65.1%
	HAEMORRHAGE	Count	13	11	20	44
		%	37.1%	28.9%	37.7%	34.9%
Total		Count	35	38	53	126
		%	100.0%	100.0%	100.0%	100.0%

GRAPH : 12 SHOWS TYPE OF STROKE AND GLYCEMIC STATUS



In ischemic stroke Normoglycemia- 22(62.9%),Stress Hyperglycemia-27 (71.1%),Diabetic-33(62.3%).In haemorrhage stroke Normoglycemia-13 (37.1%),Stress Hyperglycemia-11(28.9%) 71.1%), Diabetic-20 (37.7 %) Pearson Chi-Square=0.857 p=0.651.which is statically significanct.

TABLE: 13 DISTRIBUTION OF GLYCEMIC STATUS AND mRS SCORE AT THE TIME OF ADMISSION

			mRS Admission				Total
			2.00	3.00	4.00	5.00	
GLYCEMIC STATUS	NORMOGLYCEMIA	Count	1	33	0	1	35
		%	100.0%	47.1%	0.0%	12.5%	27.8%
	STRESS HYPERGLYCEMIA	Count	0	2	33	3	38
		%	0.0%	2.9%	70.2%	37.5%	30.2%
	DIABETIC	Count	0	35	14	4	53
		%	0.0%	50.0%	29.8%	50.0%	42.1%
Total		Count	1	70	47	8	126
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=71.076** p<0.001

GRAPH : 13 DISTRIBUTION OF GLYCEMIC STATUS AND mRS SCORE AT THE TIME OF ADMISSION

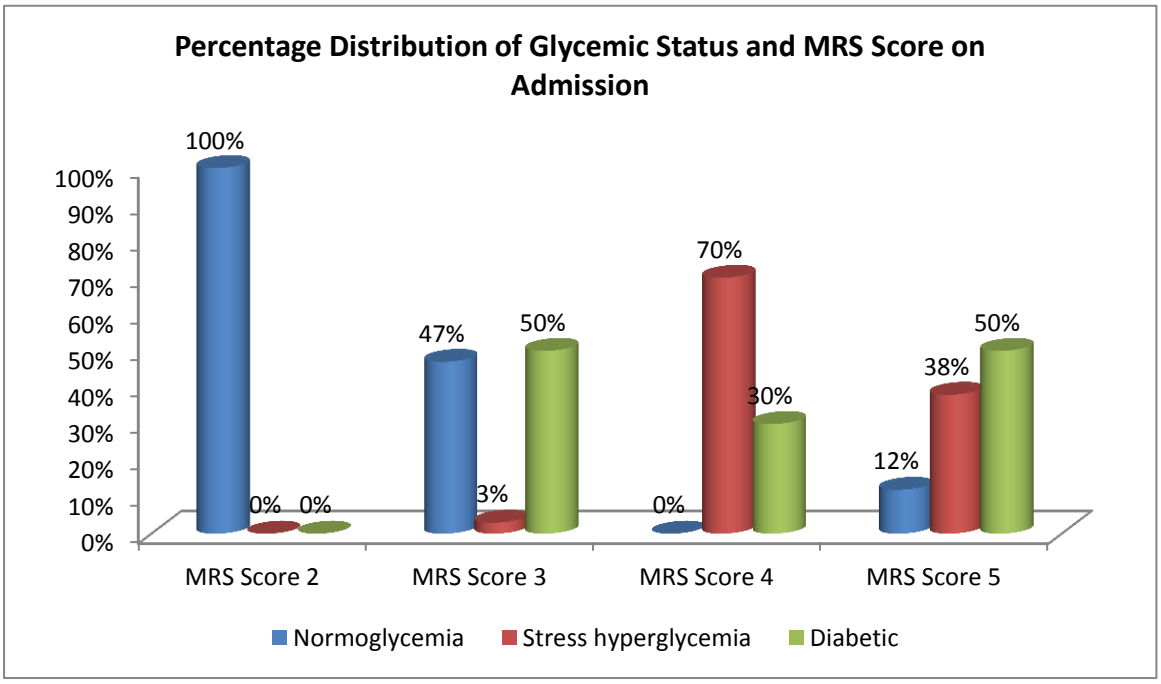
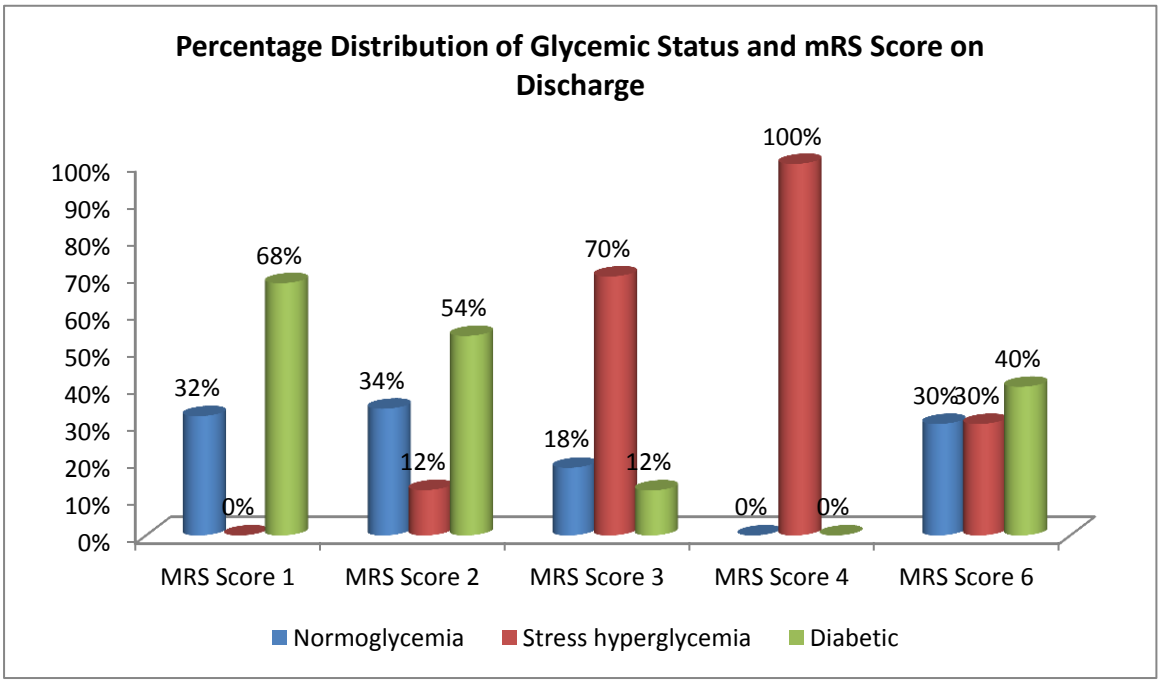


Table :13 & Graph 13 Shows 1.Normoglycemia- mRS SCORE -2 (1), mRS SCORE -3(33%) mRS SCORE -4(0) , mRS SCORE-5(1) 12.5% 2.Stress hyperglycemia- mRS SCORE – 2 (0) mRS SCORE -3(2.9%) mRS SCORE -4(37.5%) , mRS SCORE-5(3) 37.5% 3.Diabetic- mRS SCORE – 2 (1) mRS SCORE -3 (50%) mRS SCORE -4(29.8%) , mRS SCORE-5(4) 50.5 %

TABLE: 14 DISTRIBUTION OF GLYCEMIC STATUS AND mRS SCORE AT THE TIME OF DISCHARGE

			mRS Discharge					Total
			1.00	2.00	3.00	4.00	6.00	
GLYCEMIC STATUS	NORMOGLYCEMIA	Count	9	14	6	0	6	35
		%	32.1%	34.1%	18.2%	0.0%	30.0%	27.8%
	STRESS HYPERGLYCEMIA	Count	0	5	23	4	6	38
		%	0.0%	12.2%	69.7%	100.0%	30.0%	30.2%
	DIABETIC	Count	19	22	4	0	8	53
		%	67.9%	53.7%	12.1%	0.0%	40.0%	42.1%
Total		Count	28	41	33	4	20	126
		%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

GRAPH : 14 DISTRIBUTION OF GLYCEMIC STATUS AND mRS SCORE AT THE TIME OF DISCHARGE



Shows 1.Normoglycemia- mRS SCORE -1 (9) 32.1%, mRS SCORE -2(14) 34.1%, mRS SCORE -3(6) 18.2% , mRS SCORE-4(0) mRS SCORE-6(6) 30%.2. Stress hyperglycemia- mRS SCORE -1 (0), mRS SCORE -2(5%) 12.2%, mRS SCORE -3(23) 69.7%, mRS SCORE-4(4) 100% mRS SCORE-6(6) 30%.3. Diabetic- mRS SCORE -1 (19) 67.9% mRS SCORE -22 (53.7%) mRS SCORE -4(12.1%), mRS SCORE-4(0). mRS SCORE-6(8) 40%

Pearson Chi-Square=53.913** $p<0.001$ which is statically more significant.

TABLE: 15 COMPARISON OF mRS ON ADMISSION& mRS ON DISCHARGE

	mRS on Admission		mRS On Discharge	
	No	%	No	%
1.00	0	0.0	28	22.2
2.00	1	.8	41	32.5
3.00	70	55.6	33	26.2
4.00	47	37.3	4	3.2
5.00	8	6.3	0	0.0
6.00	0	0.0	20	15.9
Total	126	100.0	126	100.0

GRAPH : 15 COMPARISON OF mRS ON ADMISSION& mRS ON DISCHARGE

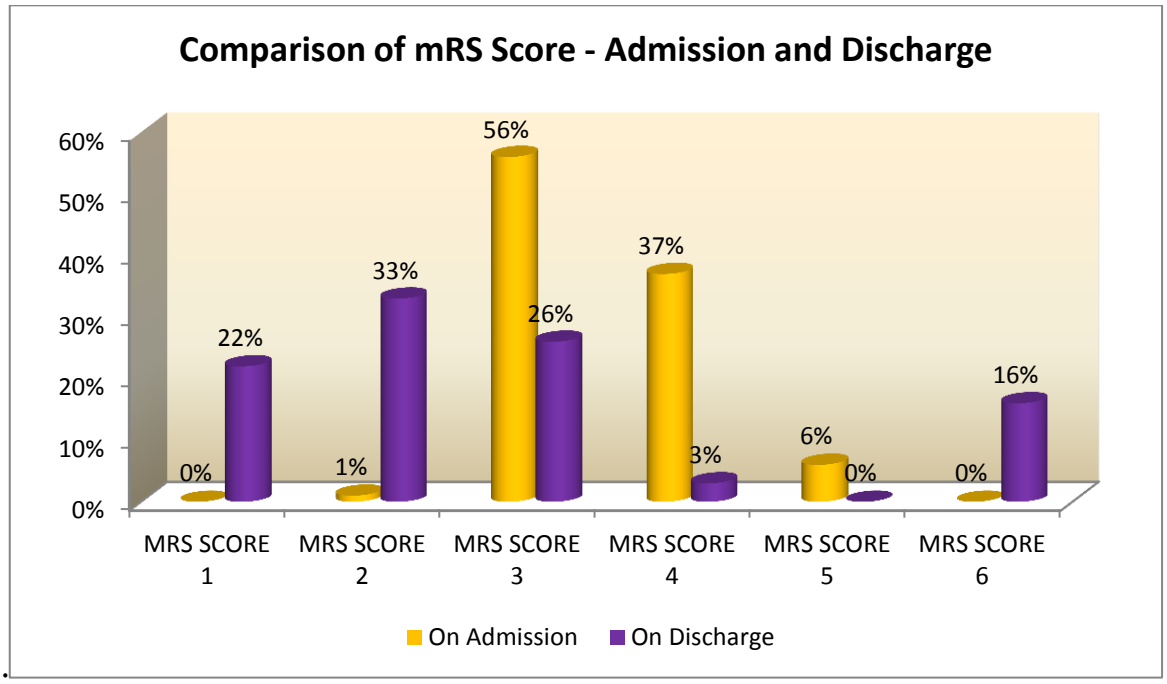


TABLE :15 & GRAPH 15 SHOWS

A. mRS SCORE 1 –(0%,) mRS SCORE 2 (8%,) mRS SCORE 3 (55.6%) mRS 4 (37.3%) mRS 5 (6.3%) mRS 6 (0%) at the time of admission.

B. mRS SCORE 1 – (22.2%,) mRS SCORE 2 (32.5%,) mRS SCORE 3 (26.2%) mRS 4 (3.2%) mRS 5 (0%) mRS 6 (15.9%) at the time of discharge .

TABLE: 16 OUTCOME

			Outcome		Total
			Alive	Death	
GLYCEMIC STATUS	NORMOGLYCEMIA	Count	33	2	35
		%	31.1%	10.0%	27.8%
	STRESS HYPERGLYCEMIA	Count	26	12	38
		%	24.5%	60.0%	30.2%
	DIABETIC	Count	47	6	53
		%	44.3%	30.0%	42.1%
Total		Count	106	20	126
		%	100.0%	100.0%	100.0%

Pearson Chi-Square=10.547** p=0.005

TABLE: 16 OUTCOME

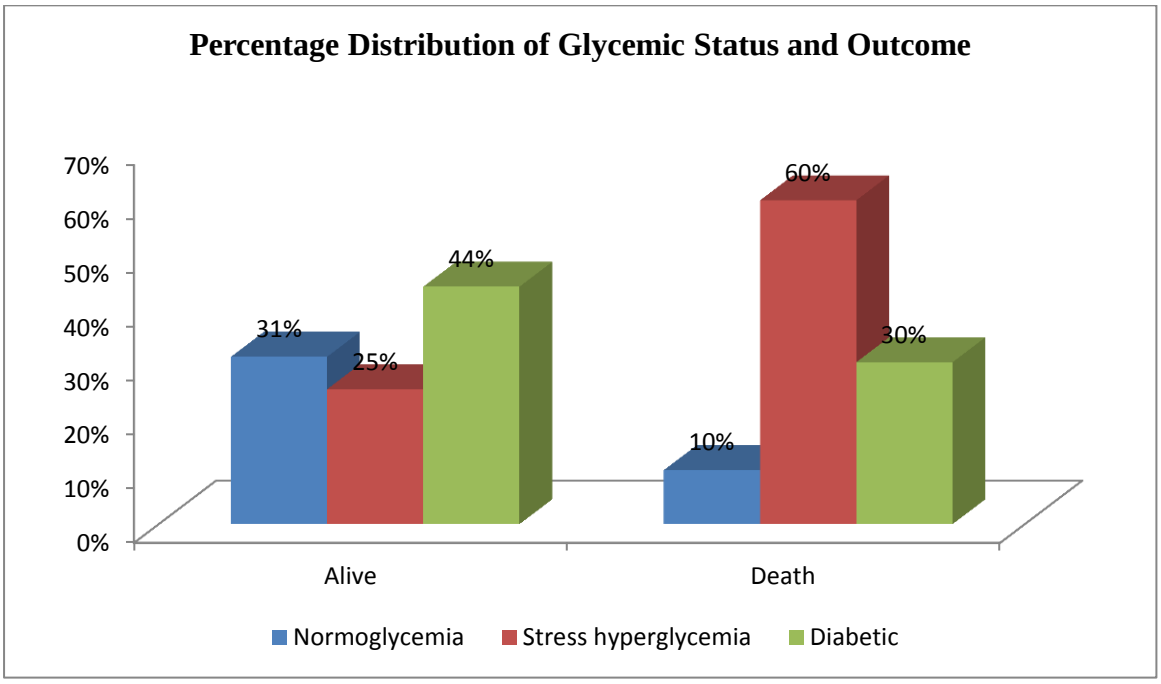


Table :16 & graph :16 shows Normoglycemia -33(31.1%) were alive, 2 were dead(10%) Stress Hyperglycemia -26(24.5%) were alive, 12 were dead (60%), Diabetic- 47(44.3%) 6 were dead (30%) Pearson Chi-Square=10.547** p=0.005 which is statistically significant

DISCUSSION

Diabetes mellitus is a highly prevalent and growing chronic disease affecting an estimated 415 million people globally in 2015 and is predicted to affect 642 million people by 2040. Given that diabetes is a well recognized risk factor for the neurovascular disease. it is postulated that a significant proportion of stroke inpatients will have comorbid diabetes mellitus. [1,2]

A large, international, multicenter case-control study across 32 countries (*n* = 26,919) showed that diabetes, defined using a threshold of glycated hemoglobin (HbA1c) of ≥6.5% (48 mmol/mol), was found in 26% of acute stroke inpatients compared with 22% of non stroke controls.

Additionally, studies have estimated that approximately 20–33% of acute stroke inpatients may have diabetes. A problem in the literature remains the lack of consistency in the definition of the diagnosis of diabetes.[3,4] A number of studies have shown an association between comorbid diabetes and increased mortality length of hospital stay, readmission rates, and poorer functional and rehabilitation outcomes after stroke. In contrast, other studies have reported no significant differences in post stroke outcomes between people with or without diabetes.[5,8]

The best measure of dysglycemia that predicts adverse stroke outcomes is unknown. Some researchers argue that it is the acute or ‘stress’ hyperglycemia; that is, peaks of blood glucose levels during an acute stroke admission, which confers poorer outcomes, whereas others propose that it is chronic dysglycemia that drives the pathological processes in stroke patients The uncertainty in the literature offers an opportunity for further research to inform best clinical practice.[24,25]

Compared with fasting blood glucose (FBG), testing of HbA1c has the advantage of providing an average measure of glycemia over the past 120 days, thereby reducing the potential for misdiagnosis as a result of stress hyperglycemia. Testing requires only one blood draw and does not require the patient to have fasted, and as such, has the potential to be utilized in the hospital setting for routine screening of diabetes mellitus A limitation of the use of HbA1c relates to conditions that affect red blood cell count and the survival time of red blood cells, such as anemia or other hemoglobinopathies. Previous studies have shown that HbA1c can predict the risk of incident stroke with the increasing burden of diabetes, there might be a role for routine HbA1c testing in all people admitted with stroke in order to identify and improve glycemic management[26,31,32]

The present meta analysis showed that the mean prevalence of diabetes was higher in stroke patients compared with the general inpatient population, which ranges between 20 and 33%and higher in ischemic compared with hemorrhagic stroke patients. The higher prevalence of diabetes in ischemic compared with hemorrhagic stroke is consistent with the findings of a recent systematic review and meta analysis of risk factors between ischemic and hemorrhagic stroke.[33,39,41]

An important observation in the present review of the literature is the heterogeneity in the method of diagnosing diabetes. The phenomenon of stress hyperglycemia is a significant confounder that might overestimate the prevalence of diabetes in studies using glucose based testing (i.e., FBG or OGTT). Despite this, studies using HbA1c alone still estimated the prevalence of known and undiagnosed diabetes to range between 16–56.2% and 5–30.9%, respectively.[43,44]

Stress hyperglycemia is a well recognized phenomenon that occurs after any acute illness and is usually detected during hospital admission. It is defined as ‘hyperglycemia resolving spontaneously after dissipation of an acute illness,’ which can also occur in people with pre existing diabetes.

Three prospective observational studies.showed that 50–70% of people with hyperglycemia on admission had a normal OGTT at 3 or 6 months post stroke, suggesting that stress hyperglycemia might be transient in many acute stroke inpatients. Post stroke hyperglycemia, defined as an elevated random or FBG, in people with and without diabetes, is common within hours of the stroke and has been independently associated with poorer outcomes after stroke, particularly in those without known diabetes.[45,46]

Identification and correct classification of post stroke hyperglycemia are clearly required to better clarify the pathophysiological relationships between glycemic control and stroke. Although FBG remains a commonly measured glycemic parameter to diagnose pre diabetes and diabetes its accuracy in acute stroke might be affected by stress hyperglycemia. In a majority of the studies included in the present review, an admission random glucose or an FBG was carried out and included in the analysis of the outcomes.[47,48]

Stress hyperglycemia has been associated with poorer functional outcomes and mortality. irrespective of diabetes status after an acute ischemic stroke. However, more studies have found that stress hyperglycemia has been associated with infarct volume growth, early neurological deterioration (an increase of ≥4 points on National Institute of Health Stroke Scale) poorer functional outcome higher mortality and a longer hospital stay in people

without a history of diabetes, including patients who underwent thrombolysis and mechanical thrombectomy.

This association remained even after adjusting for stroke severity and stroke subtype. The definition of diabetes in these studies was, however, heterogeneous.[52,53]

Acute hemorrhagic stroke, stress hyperglycemia has also been found to be associated with early mortality and worse functional outcome irrespective of prior diabetes status and after adjusting for stroke severity and subtype. In a study that included all stroke patients, Snarska *et al*. observed that hyperglycemia as a continuous variable on admission was associated with increased in hospital mortality, with a higher BGL threshold in those with diabetes (≥12.2 mmol/L) compared with those without diabetes (≥6.3 mmol/L).[54,55] This risk is likely to be an underestimate, given that diabetic status was recorded from medical records, therefore people with unrecognized diabetes were included in the 'non diabetic' group A separate study also found that every increase in 1.0 mmol/L in admission plasma glucose >5.0 mmol/L was associated with a 33% increased likelihood of 30 day mortality in people with hemorrhagic stroke, after adjusting for diabetic status.[56,57]

Overall, these studies highlight the importance of detecting hyperglycemia post stroke and recognizing the potential for poorer outcomes. However, the variability in the findings of stress hyperglycemia and stroke

outcomes between people with and without diabetes raises the question of whether chronic dysglycemia (i.e., existing diabetes) carries some degree of neuroprotection in the setting of post stroke stress hyperglycemia. The mechanisms are not clearly understood and warrant further research.[58,59]

Diabetes has been associated with an increased all cause in hospital mortality in general hospital inpatients, with a higher contribution from a cerebrovascular cause. Diabetes is associated with atherothrombotic strokes, whereas cardioembolic strokes are more common in patients without diabetes.[60,62]

Although there is some conflicting evidence in studies of people with ischemic and hemorrhagic stroke diabetes is typically associated with the poorer functional outcome especially in poorly controlled diabetes (HbA1c >7%).

Diabetes has also been associated with worse neurological deterioration (decrease of National Institute of Health Stroke Scale points <4 at 24 h, or <8 at day 7), poorer recovery (mRS >1 at 3 months) and increased risk of hemorrhagic development in people treated with thrombolysis for ischemic stroke.

An explanation for this might be incomplete recanalization after thrombolysis, as suggested in one study Diabetes has been associated with a reduced amount of recovery after rehabilitation, a higher risk of mortality in some but not all studies and a risk factor for recurrent ischemic stroke.

The effect of diabetes on length of hospital stay has been inconsistent. The relationship between diabetes and poorer stroke outcomes still remained after adjusting for stroke severity and subtypes.[68,69,70]

A larger study by Oddo M, *et al*. who followed 48,733 acute ischemic strokes found no significant difference in mortality between those with and without diabetes at 60 days and at 1 year.

A major limitation of that study was the confounding effect of having a strong male bias (98% men), limiting its generalizability, as women with diabetes might have a higher risk of cardiovascular mortality compared with men. Furthermore, the diagnosis of diabetes was based solely on discharge reports.[71,72]

Overall, diabetes has been associated with poorer clinical outcomes, except for mortality, after ischemic stroke, and there appears to be a relationship between increasing HbA1c and poorer clinical outcomes after stroke.

The lack of a strong association between diabetes and increased mortality after stroke is an interesting point and would warrant further larger, prospective studies using a combination of HbA1c as a measure of chronic glycemia and glucose based testing to evaluate this association.

The exact mechanism to explain the difference between the effects of acute vs chronic dysglycemia on poorer stroke outcomes remains unclear and could have implications in its management.[73,74,75]

In the present review, the evidence between diabetes and stroke outcomes in hemorrhagic stroke was heterogeneous. The fact that acute hyperglycemia was more strongly associated with poorer stroke outcomes compared with existing diabetes probably reflects the higher severity of stroke in patients with hyperglycemia rather than the effects of chronic dysglycemia.The studies in the present review varied in both the method and timing of diagnosing diabetes.

Studies using the OGTT might underestimate the prevalence of diabetes due to the inability to complete the test but might also overestimate the prevalence of diabetes as a result of stress hyperglycemia.[76]

In the present study, predominantly male patients were affected in all the 3 groups. Akbar DH et al showed predominance in males among the diabetic and nondiabetic stroke patients and female predominance among the new hyperglycemic stroke patients. Parsons M et al, on the other hand, showed a female predominance among all his groups. [77,]

In the present study, hypertension was the common comorbidity associated with stroke and the numbers were significantly higher in group 3 Piernik Yoder B et al in his study showed an equal number of hypertension between the diabetic and non-diabetic strokes group. In his study found that hypertension history was higher among the ischaemic stroke than the hemorrhagic stroke patients with a statistically significant p-value of 0.006.12 [78]

Poppe A et, al In the present study, smoking was observed in all the 3 groups, with group 3 having a higher number when compared to the other 2 groups.[79] Ribo M, et al observed a similar finding, where the number of smokers was high in diabetic group when compared to nondiabetic stroke group.

But on the contrary observed a higher number of smokers in non-diabetic group when compared to diabetic stroke group.6 In spite of knowing the fact that smoking is a risk factor for stroke, it could not be concluded that smoking influences the glycemic status of the patients[80]

Parsons M et al both used 2 values to define hyperglycemia, fasting blood glucose level of >126mg/dl and a random blood glucose level of >200mg/dl.6,10 Umpierrez et al in his study showed a mean RBG (mmol/l) of 6.3±0.4, 10.6±0.6 and 14.3±1.8 among the normoglycemic, new hyperglycemic and the diabetic group respectively, with a statistical significance.

Admission hyperglycemia is shown to have higher mortality and lower functional outcomes in the non-thrombolysis stroke patients and also a greater level of intracerebral hemorrhage in thrombolysed patients.[76,79]

In the present study, the mean FBS, PPBS was significantly higher in group 3 followed by group 2 and group 1 which was statistically significant. Ripley DL et al had a mean FBS and PPBS of 101.56±6.02 and 127.16±4.93 among the non-diabetic compared to 181.70±12.39 and 284.09±41.25 in the diabetic group. In his study, the mean FBS and PPBS of the normoglycemic stroke patient were similar to our observation, but the diabetic group had a much higher mean value.

There was no previous study showing the mean FBS and PPBS level in the stress hyperglycemic group. In the present study, the HbA1c was found to be significantly higher in the group.[80]

Dyslipidemia is a major risk for cardiovascular disease and cerebrovascular disease. A stroke patient with dyslipidemia has a higher risk of atherosclerosis of the carotid.

In the present study, the mean TC, TG, LDL-C, and VLDL-C were significantly higher in group 3 and group 2 when compared with group 1. But the level HDL-C was significantly lower in group 3 when compared to group 1 and 2. [81]

In several thrombolysis trials, hyperglycemia has been found to be associated with hemorrhagic events[16] and was reconfirmed recently as well as in a re-analysis of the NINDS rt-PA trial.[18]

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).

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 Liu A 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. [54,56]

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.

This study showed that lowering plasma glucose levels was safe without significant risk of hypoglycemia or 4-week excess mortality. However, until further results prove the effectiveness of this approach, it cannot be regarded as standard practice.

A reasonable target in most cases is to lower blood glucose levels between 100 and 200 mg/dL (5.5 and 11 mmol/L). The decision whether to treat the individual patient intensively with insulin, aiming at normalization of blood glucose levels, has also to take into account the clinical setting, ie, the ability of the medical staff to provide frequent glucose monitoring.[79,80]

CONCLUSION

1. Acute hyperglycemia predicts increased risk of in-hospital mortality after ischemic stroke in nondiabetic patients and increased risk of poor functional recovery in nondiabetic stroke survivors.

2. Stroke patients represent an enriched population for undiagnosed diabetes. We have observed 1 patient of newly diagnosed diabetes mellitus in every 5 ischaemic stroke patients.

3. Therefore, modification of these risk factors (diabetes, hypertension, hyperlipidemia, atrial fibrillation, myocardial ischemia, and smoking), if managed aggressively, can play a beneficial role in the secondary prevention of stroke

4. Stroke severity was not found to be a predictor of post-stroke hyperglycemia. Underlying dysglycaemia was common in non-diabetic patients manifesting hyperglycemia within 48hours of stroke ictus.

5. Screening of post-stroke patients with oral glucose tolerance testing is justified and provides a potential opportunity for secondary prevention.

6. Insular cortex involvement did not independently predict hyperglycemia in acute stroke.

7. our study revealed that persistent hyperglycemia after stroke was correlated with higher 30-day mortality. This suggests that high blood glucose during acute ischemic stroke should be carefully managed, especially during the first 24 h after stroke onset

8. Admission hyperglycemia in acute ischaemic stroke is a long time known factor and many studies about its significance and related impact on the short and long term outcome of the stroke are available.

9. Stress hyperglycemia in stroke was associated with a higher risk of poor functional outcomes in acute ischemic stroke. Hyperglycemia at stroke onset, without prior history of DM, have particularly poor prognosis than those with hyperglycemia in known diabetes.

10. Establishing its relation to the functional neurological outcome brings us to the awareness that the good achievement of blood glucose has a significant role in improving the neurological outcome and also the quality of life of the patient.

SUMMARY

1. A stroke is characterized by rapidly developing clinical signs of focal (or occasionally global) disturbance of cerebral function, lasting for more than 24 hours or leading to death with no apparent cause other than of vascular origin (World Health Organisation definition 1976).

2. The aim of the present study is to determine the prevalence of stress-induced hyperglycemia in patients with acute CVA.

3. To study the blood sugar level and its correlation with the neurological outcome among the acute CVA patients on admission and discharge in Stanley Government Medical College Hospital.

4. The admission blood sugar was estimated in all patients and was later categorized into 3 groups. Hyperglycemia was defined as a blood sugar level of more than 140 mg/dl. The patients were subdivided into 3 groups based on RBS and HbA1c level

5. **They are subdivided into 3 groups**

   Group 1 consisting of normoglycemic patients,

   Group 2 consisting of stress hyperglycemic patients,

   Group 3 consisting of known diabetes mellitus patients

6. All the patients were followed up with neurological assessment by mRS score, FBS, PPBS till discharge.

7. Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented as mean ±SD (min-max) and results on categorical measurements are presented in numbers (%). Data will be entered in the excel sheet and the analysis will be done using SPSS version 17. Chi-square test / Fischer exact test is used to compare between 3 groups. A p-value of < 0.05 was considered to be statistically significant.

8. Totally 126 cases were included in the study. Age group between 40-50 year were 26 cases, 51-60 years were 47, 61-70 years wee 53 cases.In 126 cases 73 were male, female were 53 cases.52 were diabetic, 74 was non –diabetic. In 126 cases 67 were hypertensive, 59 were nonhypertensive .8 had cases had showed CAD & 98 were free from CAD .57 patients had a history of smoking, 69 were non used

smoking, forms of tobacco products .In 126 cases 66 were alcoholics & 60 were nonalcoholics

9. 44 patients were hemorrhage stroke, 82 were an ischemic stroke in our study.Normoglycemia was observed in 35 cases (27.8%) , stress induced hyperglycemia 38 patients (30.2) ,diabetic were (42.1%) 1.In 45-50 years,Normoglycemia-0,Stress Hyperglycemia,-12(31.6%),Diabetic-14(26.4%) 2.In 51-60 years,Normoglycemia-10, (28.6%) Stress Hyperglycemia,-12 (31.6%),Diabetic-25(47.2%) 3.In age group -61-70 years,Normoglycemia-25,(71.4%) Stress Hyperglycemia-14,(36.8%0 Diabetic-14 (26.4%) Pearson Chi-Square=23.225** p<0.001

10. In ischemic stroke Normoglycemia-22(62.9%),Stress Hyperglycemia-27(71.1%),Diabetic-33(62.3%).In haemorrhage stroke Normoglycemia-13 (37.1%),Stress Hyperglycemia-11(28.9%) 71.1%), Diabetic-20 (37.7 %) Pearson Chi-Square=0.857 p=0.651.which is statically significanct

11. .Normoglycemia- mRS SCORE -2 (1), mRS SCORE -3(33%) mRS SCORE -4(0) , mRS SCORE-5 (1) 12.5% 2.Stress hyperglycemia-mRS SCORE – 2 (0) mRS SCORE -3(2.9%) mRS SCORE -4(37.5%) , mRS SCORE-5(3) 37.5% 3.Diabetic- mRS SCORE – 2 (1) mRS SCORE -3 (50%) mRS SCORE -4(29.8%) , mRS SCORE-5(4) 50.5 %.

12. 1.Normoglycemia- mRS SCORE -1 (9) 32.1%, mRS SCORE -2(14) 34.1%, mRS SCORE -3(6) 18.2% , mRS SCORE-4(0) mRS SCORE-6(6) 30%.2. Stress hyperglycemia- mRS SCORE -1 (0), mRS SCORE -2(5%) 12.2%, mRS SCORE -3(23) 69.7%, mRS SCORE-4 (4) 100% mRS SCORE-6(6) 30%.3.Diabetic- mRS SCORE -1 (19) 67.9% mRS SCORE -22 (53.7%) mRS SCORE -4(12.1%) , mRS SCORE-4(0). mRS SCORE-6(8) 40%. Pearson Chi-Square=53.913** $p<0.001$ which is statically more significant.

A. mRS SCORE 1 –(0%,) mRS SCORE 2 (8%,) mRS SCORE 3 (55.6%) mRS 4 (37.3%) mRS 5 (6.3%) mRS 6 (0%) at the time of admission.

B. mRS SCORE 1 – (22.2%,) mRS SCORE 2 (32.5%,) mRS SCORE 3 (26.2%) mRS 4 (3.2%) mRS 5 (0%) mRS 6 (15.9%) at the time of discharge .

13. Normoglycemia -33(31.1%) were alive, 2 were dead(10%) Stress Hyperglycemia -26(24.5%) were alive, 12 were dead (60%), Diabetic-47(44.3%) 6 were dead (30%) Pearson Chi-Square=10.547** p=0.005 which is statistically significant.

14. Stress hyperglycemia in stroke was associated with a higher risk of poor functional outcomes in acute ischemic stroke. Hyperglycemia at stroke onset, without prior history of DM, have particularly poor prognosis than those with hyperglycemia in known diabetes.

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PROFORMA

NAME

AGE SEX ADDRESS

CONTACT NUMBER

PRESENTING COMPLAINTS

Modified Rankin Scale (mRS)

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

PAST HISTORY

PERSONAL HISTORY

DRUG HISTORY

GENERAL EXAMINATION

SYSTEMIC EXAMINATION

- CVS
- RS
- ABDOMEN
- CNS

INVESTIGATIONS:

- RBS
- FBS
- PPBS
- HbA1C
- CT/MRI/MRA/MRV

ETHICAL COMMITTEE

GOVERNMENT STANLEY MEDICAL COLLEGE& HOSPITAL,CHENNAI -01
INSTITUTIONAL ETHICS COMMITTEE

Title of the Work : Prevalence of stress Hyperglycemia in acute CVA and impact on Its outcome.

Principal Investigator : DR. B. Suresh,

Designation : PG. MD General Medicine,
Department : Department of General Medicine,
Govt. Stanley Medical College.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 11.05.2018 at the Council Hall, Stanley Medical College, Chennai-1 at 10am.

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

MEMBER SECRETARY, 3115/11
IEC, SMC, CHENNAI

MEMBER SECRETARY
ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE
CHENNAI-600 001.

PLAGIARISM CERTIFICATE

URKUND

Urkund Analysis Result

Analysed Document:	THESIS.docx (D57315399)
Submitted:	10/20/2019 6:47:00 PM
Submitted By:	drsureshbalusamy@gmail.com
Significance:	0 %

Sources included in the report:

Instances where selected sources appear:

0

GOVT. STANLEY MEDICAL COLLEGE, CHENNAI – 600001

INFORMED CONSENT

PREVALANCE OF STRESS HYPERGLYCEMIA IN ACUTE CEREBROVASCULAR ACCIDENTS AND ITS IMPACT ON OUTCOME

Place of study: Govt. Stanley medical college, Chennai

I ……. have been informed about the details of the study in my own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I agree to collect samples of blood/saliva/urine/tissue if study needs.

I understand that I can withdraw from the study at any point of time and even then, I can receive

the medical treatment as usual.

I understand that I will not get any money for taking part in the study.

I will not object if the results of this study are getting published in any medical journal, provided

my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my

full cooperation for this study.

Volunteer:	Witness:
Name and address	Name and address
Signature/thumb impression:	Signature/thumb impression
Date:	Date:

Investigator Signature and date

GOVT. STANLEY MEDICAL COLLEGE, CHENNAI – 600001

INFORMED CONSENT

PREVALANCE OF STRESS HYPERGLYCEMIA IN ACUTE CEREBROVASCULAR ACCIDENTS AND ITS IMPACT ON OUTCOME IN GOVERNMENT STANLEY HOSPITAL, CHENNAI.

நான் இந்த ஆராய்ச்சியில் விவரங்களை முற்றிலும் புரிந்துகொண்டேன்.

ஆய்வில்பங்குஎடுத்துபோது,

சாத்தியமானஅபாயங்கள்மற்றும்பயன்களைபற்றிநான்அறிந்துள்ளேன்.

நான்எந்தவொருவேளையிலும்ஆய்வில்இருந்துதிரும்பமுடியும்,அதன்பின்னர்,

நான்வழக்கம்போல்மருத்துவசிகிச்சைபெறமுடியும்என்றுபுரிந்துகொள்கிறேன்

நான்ஆய்வில்பங்குஎடுத்துபணம்எதையும்பெறமுடியாதுஎன்றுஅறிந்துள்ளேன்.

இந்தஆய்வின்முடிவுகள்எந்தமெடிக்கல்ஜர்னலில்வெளியிடப்படஇருந்தால்நான்எதிர்க்கவில்லை, என்தனிப்பட்டஅடையாளத்தைவெளிப்படுத்தப்பட்டுஇருக்ககூடாது.

நான்இந்தஆய்வில்பங்கெடுப்பதன்மூலம்நான்என்னசெய்யபோகிறேன்என்றுதெரியும்

நான்இந்தஆய்வில்என்முழுஒத்துழைப்பையும்கொடுப்பேன்என்றுஉறுதியளிக்கிறேன்.

தன்னார்வளர் சாட்சி

பெயர்மற்றும்முகவரி பெயர்மற்றும்முகவரி

கையொப்பம் / விரல்ரேகை: கையொப்பம் / விரல்ரேகை:

ஆராய்ச்சியாளராக கையொப்பம்மற்றும்தேதி

NAME	AGE	SEX	DM	SHT	CAD	SMOKING	ALCOHOL	mRS adm	mRS dis	adm_Bld_sugar	HbA1C	GLYCEMIC_STATUS	STROKE_TYPE	Outcome
P1	40	Male	No	Yes	Yes	No	Yes	4	3	180	6.50	DIABETIC	ISCHEMIC	Alive
P2	52	Female	No	No	Yes	No	No	3	3	130	5.20	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P3	60	Male	No	No	Yes	No	Yes	4	6	160	5.00	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P4	64	Male	No	No	No	No	Yes	3	2	123	5.20	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P5	65	Male	No	Yes	No	No	Yes	3	3	137	5.30	NORMOGLYCEMIA	ISCHEMIC	Alive
P6	62	Male	No	No	Yes	Yes	Yes	2	1	132	5.30	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P7	49	Male	Yes	Yes	Yes	Yes	Yes	4	2	181	8.20	DIABETIC	ISCHEMIC	Alive
P8	43	Female	Yes	No	Yes	No	No	4	1	154	7.60	DIABETIC	HAEMORRHAGE	Alive
P9	63	Female	No	No	Yes	No	No	5	6	127	5.30	NORMOGLYCEMIA	ISCHEMIC	Alive
P10	53	Female	No	Yes	No	No	No	3	2	123	5.40	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P11	55	Female	Yes	No	Yes	No	No	5	6	162	8.10	DIABETIC	HAEMORRHAGE	Death
P12	62	Female	No	Yes	No	No	No	4	2	138	4.80	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P13	58	Male	Yes	No	No	No	Yes	4	1	148	8.00	DIABETIC	ISCHEMIC	Alive
P14	61	Male	No	Yes	No	No	Yes	4	4	118	5.20	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P15	63	Female	No	No	No	No	No	3	1	138	5.10	NORMOGLYCEMIA	ISCHEMIC	Alive
P16	42	Male	Yes	No	No	Yes	Yes	3	2	157	9.60	DIABETIC	HAEMORRHAGE	Alive
P17	58	Male	Yes	Yes	No	Yes	Yes	5	6	174	7.10	DIABETIC	ISCHEMIC	Death
P18	47	Female	No	Yes	No	No	No	4	3	119	4.90	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P19	55	Male	Yes	No	No	Yes	Yes	3	1	173	9.20	DIABETIC	ISCHEMIC	Alive
P20	51	Female	No	Yes	No	No	No	4	4	138	5.50	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P21	60	Male	No	No	No	Yes	Yes	5	6	121	5.30	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P22	62	Male	Yes	Yes	No	No	Yes	3	2	151	7.30	DIABETIC	ISCHEMIC	Alive
P23	60	Female	Yes	No	No	No	No	3	2	173	7.00	DIABETIC	ISCHEMIC	Alive
P24	58	Male	Yes	No	No	Yes	Yes	3	2	180	8.30	DIABETIC	ISCHEMIC	Alive
P25	63	Male	No	No	No	Yes	Yes	4	3	116	4.90	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P26	59	Male	Yes	Yes	No	Yes	Yes	3	2	182	9.30	DIABETIC	ISCHEMIC	Alive
P27	50	Female	No	Yes	No	No	No	4	6	137	5.60	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P28	55	Female	No	No	No	No	No	4	4	127	4.90	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P29	52	Male	No	Yes	No	No	Yes	3	6	110	5.30	NORMOGLYCEMIA	ISCHEMIC	Alive
P30	54	Female	Yes	Yes	No	No	No	4	2	180	10.00	DIABETIC	ISCHEMIC	Alive
P31	62	Female	No	No	No	No	No	3	2	119	5.30	NORMOGLYCEMIA	ISCHEMIC	Alive
P32	63	Female	No	No	No	No	No	3	2	129	4.80	NORMOGLYCEMIA	ISCHEMIC	Alive

P33	58	Male	No	No	No	Yes	Yes	3	2	128	4.80	NORMOGLYCEMIA	ISCHEMIC	Alive
P34	59	Female	No	Yes	No	No	No	3	1	116	5.40	NORMOGLYCEMIA	ISCHEMIC	Alive
P35	57	Male	Yes	No	No	No	Yes	3	2	152	8.10	DIABETIC	ISCHEMIC	Alive
P36	68	Female	No	No	No	No	No	3	1	117	5.40	NORMOGLYCEMIA	ISCHEMIC	Alive
P37	60	Male	Yes	Yes	No	No	Yes	3	2	164	9.20	DIABETIC	ISCHEMIC	Alive
P38	67	Male	Yes	Yes	No	No	Yes	3	1	171	7.40	DIABETIC	ISCHEMIC	Alive
P39	53	Male	Yes	Yes	No	No	Yes	3	1	145	9.10	DIABETIC	ISCHEMIC	Alive
P40	68	Male	No	No	No	Yes	Yes	3	3	111	4.90	NORMOGLYCEMIA	ISCHEMIC	Alive
P41	56	Female	No	Yes	No	No	No	4	3	117	5.60	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P42	55	Male	No	Yes	No	Yes	Yes	3	1	119	5.10	NORMOGLYCEMIA	ISCHEMIC	Alive
P43	66	Male	Yes	No	No	Yes	Yes	4	3	143	6.70	DIABETIC	ISCHEMIC	Alive
P44	69	Male	No	Yes	No	Yes	Yes	3	6	116	5.60	NORMOGLYCEMIA	ISCHEMIC	Alive
P45	61	Female	Yes	No	No	No	No	3	1	179	10.00	DIABETIC	HAEMORRHAGE	Alive
P46	71	Male	No	Yes	No	Yes	Yes	4	2	118	5.50	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P47	50	Male	Yes	Yes	No	Yes	Yes	4	2	181	7.60	DIABETIC	HAEMORRHAGE	Alive
P48	45	Male	No	No	No	Yes	Yes	4	3	119	5.00	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P49	58	Female	Yes	Yes	No	No	No	3	6	164	8.50	DIABETIC	HAEMORRHAGE	Death
P50	67	Female	Yes	No	Yes	No	No	3	2	162	9.50	DIABETIC	HAEMORRHAGE	Alive
P51	62	Female	Yes	Yes	Yes	No	No	3	6	147	7.10	DIABETIC	ISCHEMIC	Alive
P52	63	Female	No	Yes	No	No	No	4	4	111	5.00	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P53	49	Female	No	Yes	No	No	No	4	3	111	5.40	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P54	60	Female	Yes	Yes	No	No	No	3	2	170	7.80	DIABETIC	ISCHEMIC	Alive
P55	61	Male	No	No	No	Yes	Yes	4	3	117	5.30	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P56	68	Male	No	Yes	No	Yes	Yes	4	3	121	4.90	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P57	66	Female	Yes	Yes	No	No	No	3	1	149	10.00	DIABETIC	ISCHEMIC	Alive
P58	52	Male	Yes	No	Yes	Yes	Yes	3	1	185	10.00	DIABETIC	ISCHEMIC	Alive
P59	59	Male	Yes	No	No	Yes	Yes	3	1	155	9.70	DIABETIC	ISCHEMIC	Alive
P60	63	Male	No	Yes	No	Yes	Yes	3	2	133	5.40	NORMOGLYCEMIA	ISCHEMIC	Alive
P61	67	Male	No	No	No	Yes	Yes	3	2	119	5.20	NORMOGLYCEMIA	ISCHEMIC	Alive
P62	66	Male	No	Yes	No	Yes	Yes	4	3	127	5.20	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P63	66	Female	Yes	No	No	No	No	3	1	151	9.20	DIABETIC	ISCHEMIC	Alive
P64	60	Male	No	No	No	Yes	Yes	4	3	130	5.40	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P65	46	Female	Yes	No	No	No	No	3	2	186	10.10	DIABETIC	ISCHEMIC	Alive
P66	65	Male	No	No	No	Yes	Yes	3	6	128	5.20	NORMOGLYCEMIA	ISCHEMIC	Alive
P67	65	Male	No	No	No	Yes	Yes	3	1	120	5.30	NORMOGLYCEMIA	ISCHEMIC	Alive
P68	67	Male	No	Yes	No	Yes	Yes	4	3	127	4.80	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P69	57	Female	No	Yes	No	No	No	4	3	127	4.90	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive

P70	62	Male	Yes	Yes	No	Yes	Yes	3	2	157	6.90	DIABETIC	ISCHEMIC	Alive
P71	59	Male	No	No	No	Yes	Yes	4	3	131	5.20	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P72	56	Female	No	Yes	Yes	No	No	4	3	123	5.60	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P73	61	Female	No	Yes	No	No	No	4	3	120	5.30	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P74	61	Female	No	No	Yes	No	No	3	3	115	5.40	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P75	69	Male	No	Yes	Yes	Yes	Yes	4	3	129	5.40	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P76	55	Male	Yes	No	No	Yes	Yes	3	2	152	9.00	DIABETIC	ISCHEMIC	Alive
P77	45	Female	Yes	Yes	No	No	No	3	1	156	9.20	DIABETIC	ISCHEMIC	Alive
P78	59	Male	Yes	No	Yes	Yes	Yes	3	2	177	7.70	DIABETIC	ISCHEMIC	Alive
P79	48	Male	No	Yes	No	Yes	Yes	3	3	112	5.40	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P80	43	Female	Yes	Yes	No	No	No	3	6	175	9.70	DIABETIC	ISCHEMIC	Death
P81	66	Male	Yes	Yes	No	Yes	Yes	4	1	151	8.80	DIABETIC	ISCHEMIC	Alive
P82	58	Male	No	No	No	Yes	Yes	4	3	125	4.80	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P83	50	Female	Yes	Yes	Yes	No	No	4	1	174	8.90	DIABETIC	ISCHEMIC	Alive
P84	59	Male	Yes	Yes	Yes	Yes	Yes	3	2	162	6.90	DIABETIC	ISCHEMIC	Alive
P85	62	Male	Yes	Yes	No	Yes	Yes	3	1	164	10.20	DIABETIC	HAEMORRHAGE	Alive
P86	55	Male	Yes	Yes	Yes	Yes	Yes	4	2	176	8.90	DIABETIC	ISCHEMIC	Alive
P87	63	Female	Yes	No	Yes	No	No	3	1	165	8.10	DIABETIC	HAEMORRHAGE	Alive
P88	58	Male	Yes	No	No	No	Yes	3	1	168	8.60	DIABETIC	HAEMORRHAGE	Alive
P89	65	Male	Yes	No	No	Yes	Yes	3	6	156	7.20	DIABETIC	HAEMORRHAGE	Alive
P90	71	Female	No	No	No	No	No	3	3	114	5.20	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P91	50	Male	No	Yes	No	Yes	Yes	4	2	114	5.30	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P92	55	Female	Yes	Yes	No	No	No	3	1	145	9.20	DIABETIC	HAEMORRHAGE	Alive
P93	64	Female	No	No	No	No	No	3	6	113	5.10	NORMOGLYCEMIA	HAEMORRHAGE	Death
P94	48	Male	Yes	Yes	No	Yes	Yes	4	2	155	7.40	DIABETIC	ISCHEMIC	Alive
P95	63	Male	No	No	No	Yes	Yes	3	2	134	5.20	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P96	53	Female	No	Yes	No	No	No	3	2	119	5.40	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P97	61	Female	No	No	No	No	No	3	2	124	4.80	NORMOGLYCEMIA	ISCHEMIC	Alive
P98	47	Male	No	No	No	Yes	Yes	4	2	114	4.90	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P99	60	Male	No	Yes	No	Yes	Yes	5	6	128	5.00	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P100	54	Female	No	Yes	No	No	No	3	6	117	5.10	NORMOGLYCEMIA	HAEMORRHAGE	Death
P101	46	Male	Yes	Yes	No	Yes	Yes	4	1	164	8.30	DIABETIC	HAEMORRHAGE	Alive
P102	70	Male	No	Yes	No	Yes	Yes	3	1	131	5.60	NORMOGLYCEMIA	ISCHEMIC	Alive
P103	72	Male	No	Yes	No	No	Yes	3	1	136	5.30	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P104	44	Male	No	No	No	No	No	5	6	136	5.20	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P105	53	Female	Yes	No	No	No	No	3	2	145	10.20	DIABETIC	HAEMORRHAGE	Alive
P106	52	Male	No	Yes	No	Yes	No	3	2	125	5.10	NORMOGLYCEMIA	ISCHEMIC	Alive

P107	46	Female	No	Yes	No	No	No	4	3	120	5.60	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P108	65	Female	Yes	Yes	No	No	No	3	2	155	6.80	DIABETIC	HAEMORRHAGE	Alive
P109	63	Male	No	No	No	Yes	Yes	3	3	129	4.80	NORMOGLYCEMIA	ISCHEMIC	Alive
P110	52	Female	Yes	No	Yes	No	No	3	2	155	6.90	DIABETIC	HAEMORRHAGE	Alive
P111	56	Female	Yes	Yes	No	No	No	5	6	180	7.40	DIABETIC	HAEMORRHAGE	Death
P112	53	Female	Yes	Yes	Yes	No	No	4	1	149	10.20	DIABETIC	HAEMORRHAGE	Alive
P113	71	Male	No	No	No	Yes	No	3	2	135	5.20	NORMOGLYCEMIA	ISCHEMIC	Alive
P114	44	Male	No	Yes	No	Yes	Yes	4	3	117	4.90	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P115	47	Male	Yes	No	Yes	No	Yes	3	3	182	9.50	DIABETIC	ISCHEMIC	Alive
P116	61	Female	No	Yes	No	No	No	3	1	134	4.80	NORMOGLYCEMIA	ISCHEMIC	Alive
P117	47	Female	Yes	No	No	No	No	5	6	172	9.90	DIABETIC	HAEMORRHAGE	Death
P118	67	Male	No	Yes	Yes	Yes	No	3	2	114	4.80	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P119	70	Female	No	No	Yes	No	No	4	6	119	5.30	STRESS HYPERGLYCEMIA	ISCHEMIC	Death
P120	60	Female	No	Yes	Yes	No	No	3	2	134	5.00	NORMOGLYCEMIA	HAEMORRHAGE	Alive
P121	57	Male	No	Yes	No	Yes	No	4	3	118	5.50	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P122	48	Female	No	Yes	No	No	No	4	2	112	4.90	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P123	42	Male	Yes	No	Yes	Yes	Yes	4	3	185	8.10	DIABETIC	HAEMORRHAGE	Alive
P124	47	Male	No	Yes	No	Yes	Yes	4	3	129	4.90	STRESS HYPERGLYCEMIA	ISCHEMIC	Alive
P125	63	Male	No	No	Yes	Yes	Yes	4	3	130	4.80	STRESS HYPERGLYCEMIA	HAEMORRHAGE	Alive
P126	70	Male	No	No	Yes	Yes	No	3	3	134	4.80	NORMOGLYCEMIA	HAEMORRHAGE	Alive