"STRESS HYPERGLYCEMIA AS A PROGNOSTIC MARKER IN ACUTE ISCHAEMIC STROKE "

By

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IN

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Under the Guidance of

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ABSTRACT

STRESS HYPERGLYCEMIA AS A PROGNOSTIC MARKER IN ACUTE ISCHAEMIC STROKE

OBJECTIVES:

To evaluate the outcome in acute ischemic stroke patients with stress hyperglycemia in terms of mortality and functional recovery based on National Institute of Health Stroke Scale (NIHSS)

MATERIALS AND METHODS:

This is a case control study. 100 patients with CT evidence of acute ischaemic stroke meeting the inclusion and exclusion criteria's admitted to R.L.Jalappa Hospital and Research center attached to Sri Devaraj Urs Medical college, Tamaka, Kolar during may2014 to September 2015 were included in the study. The data was collected based on detailed history and clinical examination done as per the proforma along with few investigations like CT brain, RBG levels at admission,FBS,PPBS,HbA1c and RBG at discharge. Neurological status was assessed using NIHSS scale. Functional recovery was assessed based on the difference between NIHSS score on day of admission and 7^{th} day.

RESULTS:

The maximum number of patients in our study were in the age group between 71 and 80 years. The mean age in both sexes was 62.71±14.09years.male is to female ratio M:F is 1.38:1. Of the total100 patients 53 patients had stress hyperglycemia

(RBG>140mg/dl) and 47 were normoglycemic (RBG<140).mean RBG value in stress hyperglycemic patients on admission was 183.06 ± 35.99 and mean RBG value in normoglycemic patients was 121.55 ± 14.03. Functional recovery which was better in normoglycemia patients compared to stress hyperglycemia patients. There was mortality in 5 patients with stress hyperglycemia.

CONCLUSION:

Functional recovery was better in the patients with normal RBG on admission than in patients having stress hyperglycemia. This suggests a possible association between stress hyperglycemia and poor outcome with stroke.

Key words: stress hyperglycemia, Acute ischaemic stroke

ABBREVATIONS

CVD	Cerebrovascular Disease
WHO	World Health Organization.
CT	Computed Tomography
CVT	Cortical Vein Thrombosis
LVH	Left Ventricular Hypertrophy.
IHD	Ischaemic Heart Disease
RHD	Rheumatic Heart Disease.
AF	Atrial Fibrillation.
CAF	Chronic Atrial Fibrillation.
ASD	Atrial Septal Defect.
MVP	Mitral Valve Prolapse
CHF	Congestive Heart Failure.
TIA	Transient Ischaemic Stroke.
ICA	Internal Carotid Artery.
LDL	Low Density Lipoprotein.
ICMR	Indian council of Medical Council of Medical Research.
HDL	High Density Lipoprotein.
TPA	Tissue Plasminogen Activator.
ADP	Adenosine Di Phosphate.
ATP	Adenosine Tri-Phosphate.
FFA	Free Fatty Acids.
NADH	Dihydro Nicotinamide Adenine Dinucleotide.
NMDA	N Methyl D Aspartate.
HBA1C	Glycated Haemoglobin. RBG- Random Blood Glucose.
PPBS	Post Prandial Blood Sugar.
FBS	Fasting Blood Sugar.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES/GRAPHS

INTRODUCTION

Stroke is the third most leading cause of death worldwide after coronary heart disease and cancer especially ischemic infarcts ,comprise one of the most common devastating disorders[1]. They cause about 200,000 deaths each year in the united states and are a major cause of disability .The incidence of these cerebrovascular events increases with age, and the number of strokes is projected to increase as the elderly population grows, with a doubling in stoke deaths in the united states by 2030.Most cerebrovascular diseases manifest by the abrupt onset of a neurologic deficit, as if the patient was ‘’struck by the hand of God’’ [2].

Hyperglycemia and Diabetes mellitus are more common in the hospital setting .In the 1989 National Health Survey,it was found that 24% of adults with diabetes and hyperglycemia are being hospitalized atleast once in the year[3].

Of all acute ischemic stroke patients 20% to 50% have stress hyperglycemia at presentation[4].Admission hyperglycemia in acute ischaemic stroke patients have been associated with longer in-hospital stay, increased cost ,and mortality[5] .

Large number of patient’s suffering from acute stress conditions like stroke may develop stress hyperglycemia, even in the absence of a preexisting diabetes[6].Both human and animal studies suggest that stress hyperglycemia is associated with a high risk of mortality after stroke[7].

Hyperglycemia is common in the early phase of stroke .The prevalence of stress hyperglycemia has been observed in two thirds of all ischemic stroke sub types on admission including lacunar strokes[8]. Hyperglycemia is not only common in the hospitalized patient, but is also being recognized as a marker for in-hospital mortality.

Factors contributing to stress hyperglycemia in the hospital setting are stroke, myocardial infarction,infections,corticosteroid therapy, medication or insulin omission,insulin errors[9] .

Identifying hyperglycemia as a marker for poor functional recovery and inhospitalmortalityhas provided a rationale for the pursuit of tight glucose control.Benefits of tight glucose control include reduced mortality and decreased infection rates.Stroke patients who have stress hyperglycemia at admission have been associated with three fold higher risk of poor functional recovery and death[10].Mortality risk was greater in patients who had hyperglycemia without a diabetes(representing stress hyperglycemia)than in those with diabetes[11].

In our study we systemically reviewed the literature to summarize and assess the strength of the association between stress hyperglycemia and both short-term mortality and functional recovery in acute ischemic stroke patients.

OBJECTIVES

To evaluate the outcome in acute ischemic stroke patients with stress hyperglycemia in terms of mortality and functional recovery based on National Institute of Health Stroke Scale (NIHSS)[12]

REVIEW OF LITERATURE

Cerebrovascular disease (CVD) is defined as abnormality of brain resulting from a pathologic process of the blood vessels[13]

Definition of Stroke

World health organization defines the clinical syndrome of 'Stroke' as rapidly developing clinical signs or symptoms of focal (or global) disturbance of cerebral function with symptoms lasting more than 24 hours or leading to death with no apparent cause other than vascular origin [14]

Cerebrovascular disease is of two categories – Ischaemic and Haemorrhagic.Ischaemic infarction is again classified in to thrombotic and embolic and constitutesn86-90% of the total deaths due to CVD in western countries . The term atherothrombotic or atheroemboic stroke is used when Ischemia occurs in elderly patients especially those with other manifestations of atherosclerosis .10-20% of thrombotic strokes may be associated with one or more transient ischeamic attacks(TIAs)[15].

INCIDENCE AND PREVALENCE

In General:

Cerebro vascular disease accounts for 50% of neurological admissions in USA. It is commonly seen in between the 5^{th} to 8^{th} decade of life. They cause approximately 200000 deaths in the USA [16].

The incidence of stroke varies among countries and increases exponentially with age. About 80% of strokes are caused by focal cerebral ischaemia due to arterial occlusion, and remaining 20% are caused by hemorrhages in western countries[17].

Thirty- day case fatality rates for ischemic stroke in western societies range between 10 and 17% [17].The incidence of a poor outcome after stroke increases with coexistence of diseases such as ischaemic heart disease and diabetes mellitus , with increasing age and with increasing size of the infarct.Mortalityhas been reported to range from 2.5% in patients with lacunar infarcts[18] to 75% in patients with space-occupying hemispheric infarction in first month after stroke [19].

A global stroke registry and a collaborative study of stroke in the community coordinated by WHO was carried out between 1971 and 1974 .In this study it was found that the incidence of stroke was 2.55 in Denmark ;1.17 in Osaka,Japan;1.51 in Ireland; 0.33 in Rohtak, india and 0.28 in Colombo , srilanka [14]. The higher incidence in the west probably reflects the much larger elderly population in these countries.

As age advances the incidence of atherothrombotic infarction also increase .This is due to decreased blood flow which occurs normally with age.Obirst demonstrated 25% reduction in cerebral blood flow by age 80[13].This change is more striking in women than in men with a sharp increase being noted after 64 yeras. Based on the Framingham data, the chances of atherothrombotic brain infarction before 70 years is 1 in 20.One fifth of the strokes occur in persons under 65 years [20].

IN OUR COUNTRY

Cerebrovascular disease constitutes 9.2-30% of total neurological admissions and 0.9 to 4.5% of total medical admissions [21].

In south India in 1970 , Abhraham Daniel and sunder rao found that the prevalence varies with age markedly . Between 40-49yrs, the prevalence in males was 94.8/100,000 and in females 100.2/100,000. Between 50-59yrs in males, the prevalence was 184.4 and in females 86.1 with a total of 650.7/100,000. Above 70

years the prevalence in males was 813.3/100,000 and in females it was 476.2 / 100,000 and a mean of 650.7 /100,0.

The prevalence when all age groups were put together was 68.5/100000 in males,44.8/100000 in female with a total prevalence of 56.9/100000.In an extension of the study in 1971 the 2 year prevalence was 84 /100000 population and the annul incidence was 13/100000. In a study (1980) conducted in Rohtak as a part of WHO collaborative study,the figures reported were lower.The prevalence in the urban population was 44.28/100000 and in the rural population it was 44.28 /100000.The total prevalence was calculated as 44.54/100000[19 16].

Bansal et al between 1967 and 1971 noted that 2.24% of all medical admissions and 10.99% of all neurological admissions were due to CVD.Venkatraman et al between 1973 and 1975 found that 18.8% of all neurological admissions were due to CVD[21].

In another stroke prevalence study conducted in different regions in rural India. Dhamija in 1997 showed that prevalence ranged from 40-270/100000 population[22] .The prevalence in urban population is higher .In the study conducted by Abraham and Daniel ,the 2year prevalence in urban population was 94.1/100,000 and in rural population it was 76.5/100,000.The annual incidence was 19.4/100,000 in urban population and 8.3/100000 in rural population[21]. This highlights the higher incidence and prevalence rates in urban population. In the study carried out in Rohtak,Haryana between 1971 and 1974, the annual incidence was 33/100000 with an incidence of 27/1000000 for first ever strokes.

MORTALITY TRENDS IN STROKE

Stroke is the third leading cause of death in the world[23,24] with highest mortality in low- and middle- income countries. According to the World Health Organization (WHO), about 5.71 million people died from stroke in 2004[25] and it is estimated that this number will climb to 6.3 million in2015 and 7.8 million in 2030.[26]

In 2001, 85.5% of the world's stroke deaths occurred in developing countries, where loss of disability-adjusted life years (DALYs) was seven times higher than in developed countries.[27] In the past 20 years, in developed countries, there has been a 29% decline in the incidence of all types of stroke, especially in women, and a 25% reduction in mortality, except for hemorrhagic stroke[24,27].

WHO estimated that in 1990 the stroke mortality rate was 73 /100,000 [15] .A country wise and ethnic variation in mortality from CVD has been found Fratiglioni et al in their study found that Japan had the highest CVD mortality rate with Phillipines and Mexico recording the lowest mortality rate. USA, England and Wales had intermediate rates [28].

Kagan et al. in their study found a worldwide decline in stroke mortality. This decline has been particularly striking in Japan where stroke has until recently been the leading cause of death. They found that 11 % of infarcts, 63 % of hemorrhages and 68 % of strokes of unknown type were fatal [29].

Balarajan R in 1991 stated that mortality from CVD differed significantly in different ethnic groups in England and Wales. The age adjusted morality among men was highest in the Caribbean (SMR 176) and Africans (SMR 163), followed by men from the Indian sub continent *(153)* and Ireland (123). Women also showed a similar pattern. Western European immigrants had greatly lowered mortality from CVD [30].

In England and Wales mortality from CVD fell by 28 % from 1970-71 to 1970- 83, a rate of decline showed by most groups. The decline among Caribbean and African immigrants exceeded that observed for England and Wales, but Indian men showed comparatively little improvement with a fall of only 3% [30].

While mortality rate is declining steadily since 1940s in the US and other Western countries, it is likely to increase in India. The various reasons quoted for this expected rising trend are [31]

- Increase in Life expectancy
- Urbanization with changing lifestyle. This being an important determinants of

PATHOPHYSIOLOGY OF ISCHAEMIC STROKE

Cerebral ischemia is caused by a reduction in blood flow that lasts longer than several seconds . Neurologic symptoms manifests with in seconds because neurons lack glycogen, so energy failure is rapid .If the cessation of flow lasts for more than a few minutes, infarction of brain tissue results [15].

LACUNAR INFARCTS

They are small infarcts in the deep white matter of the cerebral hemisphere or brainstem. They are usually due to hypertension induced lipohyalinosis or arteriosclerosis of small penetrating arteries, rather than to large artery arteriosclerosis or cardio embolism[15] .

STROKE SUBTYPES

Stroke can be classified according to

1. Anatomic location
2. Etiology [14]

ANATOMIC CLASSIFICATION :The most important is according to the vascular supply.

a. Carotid

b. Vertebrobasilar

ETIOLOGIC:

1. By Result

a. CEREBRAL INFARCT :	Arterial
	Arteriolar
	Venous
2. CEREBRAL HEMORRAGHE:	Parenchymal
	Subarachnoid

By Cause

a) ISCHEMIA :	Embolism
	Extra cranial vascular diseases
b) HEMORRAGHE :	Hypertension
	Amyloid angiopathy
	Vascular malformation
	Aneurysm

ISCHAEMIC STROKE

These patients presentwith a neurological deficit that is maximum at onset.

The thrombus may be either in the anterior circulation (MCA and ACA territory) or in the posterior circulation (PCA territory)".

It is classified as **:-**

A) Thrombosis

- Atherosclerosis
- Vasculitis — Collagen Vascular diseases, Syphilis. Meningitis etc.
- Arterial Dissection
- Hematological disorders -- Polycythemia, thrombocytosis, TTP, DIC etc.
- Miscellaneous — Binswanger's disease,MoyaMoya disease,fibromuscular dysplasia.

B) Embolism

- Cardiac sources
- Atherothrombotic arterial sources
- Unknown sources

C) Vasoconstriction

- Vasospasm
- Reversible cerebral vasoconstriction

D Venous

- Dehydration, postpartum and post- op states, systemic cancer etc. Intracerebral Haemorrhage.

This can occur in the brain parenchyma, the subarachnoid space or the subdural or epidural space.

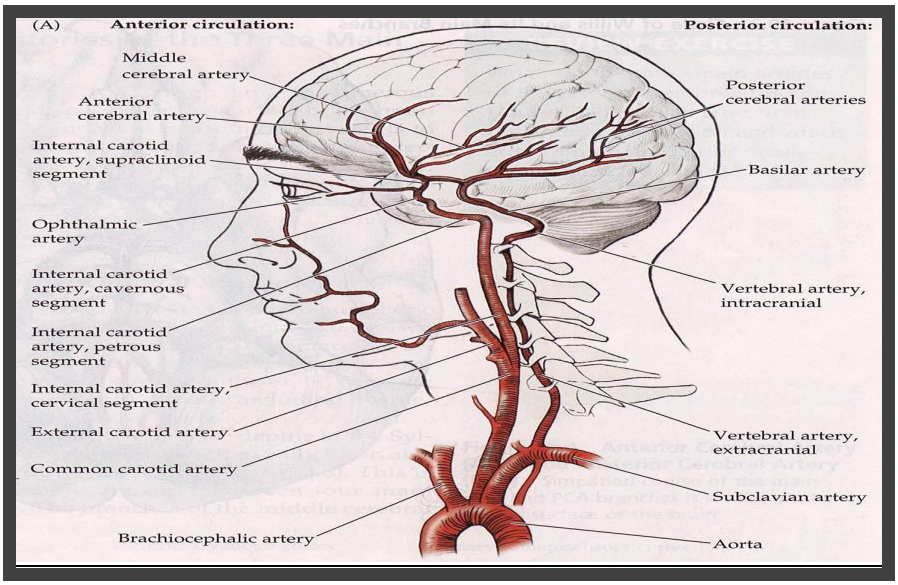

Fig no.1 Anatomy of Blood supply of brain

At rest the cardiac output is about 5 litres, of which 1 liter is retained by the brain[13]

Three types of vessels supply the brain 15 [13]:-

- **Paramedian arteries**: These vessels penetrate the brain on either side of the midline and supply the central nuclear areas near the midline.
- Short circumferential arteries: These travel for some distance before supplying the brain.
- Long circumferential arteries : These travel on the surface of the brain for some distance and then anastomoses with branches of other circumferential vessels.

The brain is supplied by two internal carotids and two vertebral arteries .the carotid circulation is designated as anterior circulation and vertebra basilar circulation as posterior circulation.

The internal carotid artery (ICA) begins at the bifurcation of the common carotid artery. It ascends the neck and perforates the base of the skull by passing

through the carotid canal of the temporal bone. It enters the subarachnoid matter and turns posteriorly to region of anterior perforated substance of brain at medial end of lateral cerebral sulcus .Here it divides into anterior perforated substance of the brain at the medial end of lateral cerebral sulcus. Here it divides into anterior and middle cerebral arteries.[32]

ANTERIOR CIRCULATION

A) ANTERIOR CEREBRAL ARTERY

It is smaller terminal branch of the ICA. It runs forward and medially superior to the optic nerve and enters the longitudinal fissure of cerebrum. Here it is joined by ACA of opposite side by anterior communicating artery .It curves backwards over corpus callosum and finally anastomoses with posterior cerebral artery.(PCA)[32]

The cortical branches supply all of medial surface of cerebral cortex. They also supply a strip of cortex an inch wide on adjoining lateral surface. The ACA supplies the leg area of pre central gyrus[32].

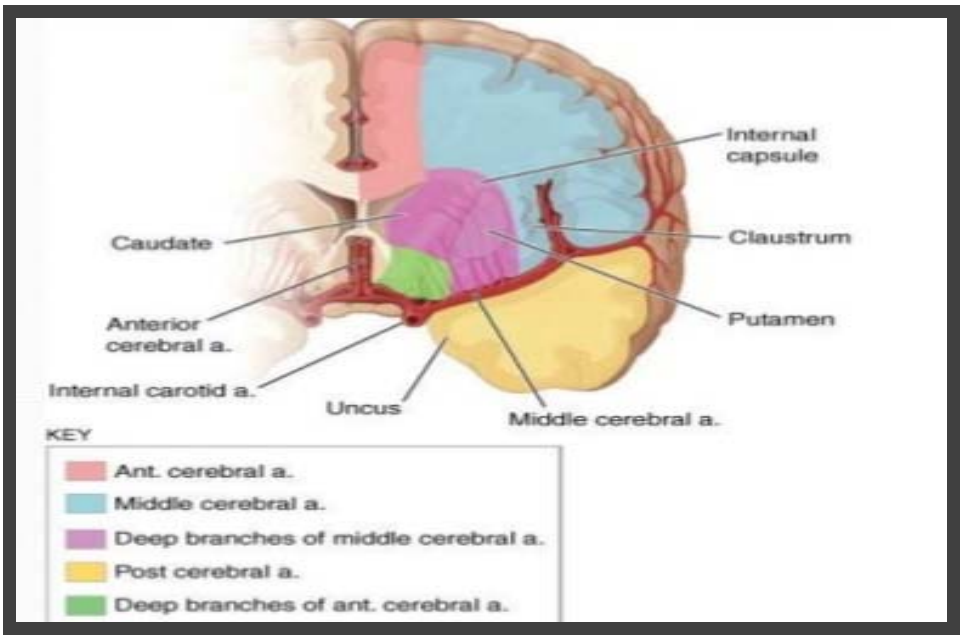

Fig 2: Diagram of a cerebral hemisphere in coronal section showing the territories of the major cerebral vessels that branch from the internal carotid arteries.

B) MIDDLE CEREBRAL ARTERY

It is the largest branch of the internal carotid which runs laterally in the lateral cerebral sulcus[32].

Cortical branches supply the entire lateral surface of the hemisphere except for the narrow strip supplied by the ACA, the occipital pole and the inferolateral surface of the hemisphere supplied by the Posterior Cerebral Arteries (PCA). The artery thus, supplies all the motor area except the leg area [32]

Cerebral branches enter the anterior perforated substance and supply the lentiform and caudate nuclei and the internal capsule[32].

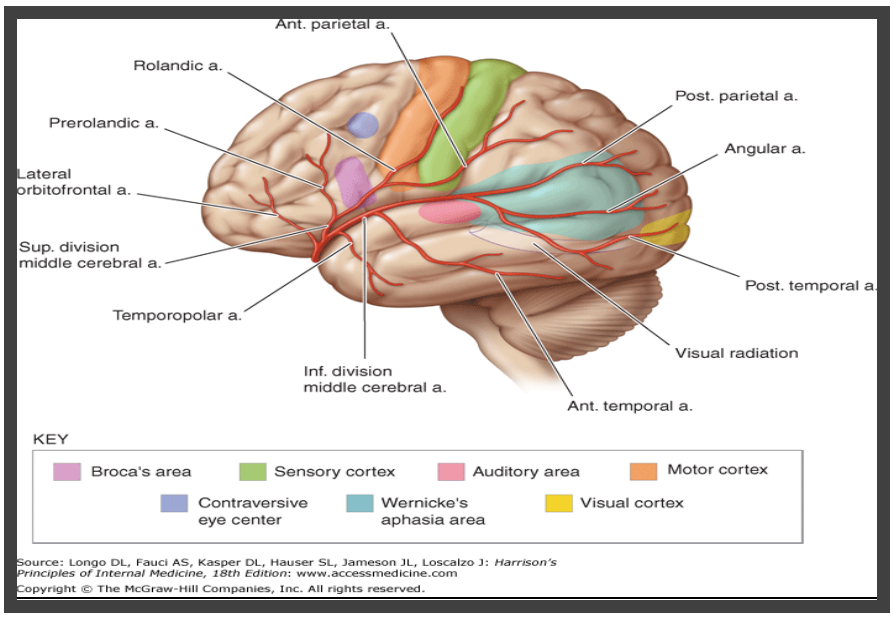

FIG 3: Diagram of a cerebral hemisphere , lateral aspect , showing the branches and distribution of the middle cerebral artery and the principal regions of cerebral localization.Note the bifurcation of middle cerebral artery in to suoerior and inferior division

POSTERIOR CIRCULATION

A) VERTEBRAL ARTERY

It is the branch of the first part of the subclavian artery which ascends the neck by passing through the foramina in the transverse processes of the upper six cervical vertebra. It enters the skull through foramen magnum and pierces the Jura and arachnoid mater to enter the sub arachnoid space. It then passes upward, forward and medially on the medulla. At the lower border of the pons it joins the vessel on the opposite side to form the basilar artery[32].

Branches of the cranial portion of the vertebral artery

- Meningeal branches : They supply the bone and the dura in the posterior cranial fossa.
- Posterior spinal artery : This vessel arises from the vertebral artery or the Posterior Inferior Cerebellar Artery (PICA). It descends as two branches, one anterior and one posterior, to the posterior roots of the spinal nerves. The branches are reinforced by radicular arteries that enter the vertebral canal through the intervertebral foramina
- Anterior spinal artery : This is formed from a contributory branch from each vertebral artery near its termination. The spinal artery descends on the anterior surface of the medulla and spinal cord and is embedded in the piamater along the anterior median fissure.
- Posterior Inferior Cerebellar Artery(PICA) : This is the largest branch of the vertebral artery which passes on an irregular course between the medulla and the cerebellum.It supplies the anterior surface of the vermis, Central nuclei of the cerebellum, the under surface of the cerebral hemisphere. It also supplies the medulla oblongata and the choroid plexus of the fourth ventricle.

- The medullary arteries: They are very small branches that are distributed to the medulla.

B) BASILAR ARTERY

It is formed by the union of two vertebral arteries. It ascends in a groove on the anterior surface of the pons. At the upper border of the pons it divides into two Posterior Cerebral Arteries (PCA)[32].

BRANCHES

- Pontine arteries
- Labryinthine artery- :This supplies the inner ear.
- Anterior Inferior Cerebellar Artery (AICA) : This Supplies the anterior and inferior parts of the cerebellum.
- Superior Cerebellar Artery (SCA) : This vessel arises close to the termination of the basillar artery, Supplies the superior surface of the cerebellum, pons, pineal gland and superior medullary velum.

PCA curves laterally and backward around the mid brain and is joined by the posterior communicating branch of the ICA.

Cortical branches supply the inferolateral and medial surfaces of the temporal lobes and the lateral and medial surfaces of the occipital lobe. Thus PCA supplies the visual cortex. Cortical branches pierce the brain substance and supplies parts of the thalamus. The lentiform nucleus, the mid brain, the pineal gland and the medial geniculate bodies. Choroidal branches supplies the choroid plexus.

THE CIRCULUS ARTERIOSIS (CIRCLE OF WILLIS)

This lies in the interpeduncular fossa at the base of the brain. It is formed by the anastamoses between the two ICAs and two vertebral arteries, Cortical and central branches arise from the circle and supply the brain substance.

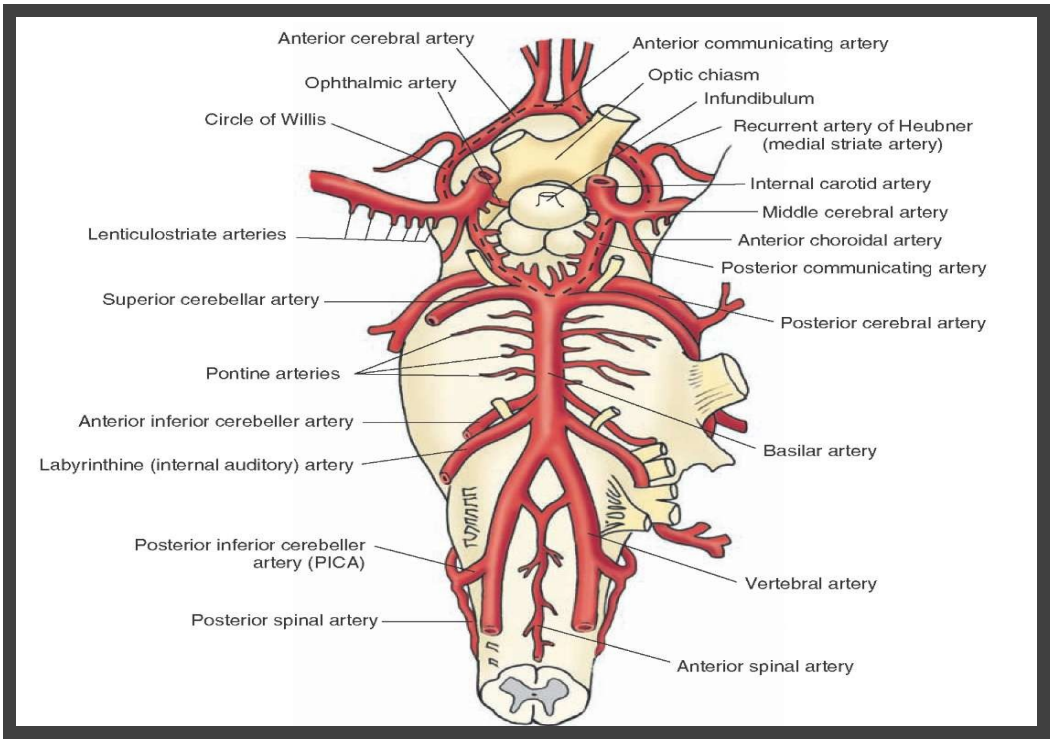

FIGURE NO. 4: CIRCLE OF WILLIS

RISK FACTORS IN CEREBROVASCULAR DISEASES

After studies done in Europe, North America and Japan with contribution from China,India, few Africans and Latin American countries WHO has strarified these risk factors[33].

Risk factors were briefly classified as genetic or non modifiable (e.g: age, sex), environmental factors that are preventable (e.g., infections), functions of lifestyle which are controllable (e.g: smoking), and some being a combination of the above and often manageable (e.g.. hypertension)

The various risks factors are mainly

- Age & Sex
- Hypertension (Diastolic, Systolic)
- Diabetics mellitus
- Heart Diseases
- Transient Ischaemic Attacks
- Obesity
- Platelet Hyperaggregability
- Alcoholism
- Smoking
- Blood lipids
- Hyperuricemia
- Infections
- Hematocrit (Increased, decreased)
- Migraine
- Increased fibrinogen

- Oral contraceptives
- Others — cold temperature, socio-economic status ,proteinuria, sodium intake.
- Genetic or non-modifiable risk factors.

Age & Sex

People of age group between 5th to 8th decade are more prone for CVDs[14 21].

Nagaraja and Pratap (Thailand) found that the peak incidence of stroke was in the 6th decade [37 34]. The incidence of stroke continues to increase with advancing age. This is due to decreased blood flow which occurs normally with age. The change more striking in women than in men especially after the age of 64 years[14] .

In Nagaraja et al's study men outnumbered women in both fatal and non fatal stroke in the ratio of 1.3:1 .

In the Framingham cohort, 8% of all deaths in women and 5 % inmen were due to stroke. This study also showed that the incidence of stroke in the age group 65-74 years was 84/10,000 /year for men and 86/10,000 /year for women [16].Studies from UK have shown that the risk of stroke in people aged between 75-84 years is 14.3/1000 / year i.e.25 times the risk in people aged between 45-54 years which is 0.57/1000/year[35] .

The joint committee for stroke facility in 1972 estimated that the death rate was 1/1000 at age 45-54 years and 9/1000 at age 65- 74 years [36].

In Kamel Abdelaziz mohamed study in 2013 male patients were 61% and female patients were 39%.[37]

In Abdu Hameed AI Kassir study in 2012 male patients were 67.6% and female patients were 32.4% [38]

In Hala El Kawas study in 2006 male patients were 56.6% and female patients were 43.3%. [39]

Stroke in young is defined as stroke in patients < 40 years is commoner in India and the other underdeveloped countries than in the West. Nayak et al claimed that stroke in young constitutes 15-30 % of all strokes [40].

In the west the incidence is 3 -8.5 %. This disparity is partly due to a large population of younger subjects in India. It is also contributed to by the higher incidence of post partum CVT and stroke[40].

In a study by Srinivasan found that 15-20 % of all young strokes is due to CVT . The male to female ratio of young strokes in 1.1:1. This greater incidence in females as compared to the Western figures is attributed to stroke related to pregnancy and puerperium[21].

ARTERIAL HYPERTENSION

Hypertension is a major risk factor for both ischaemic and haemorrhagic stroke [41]. Hypertension increases the stroke risk by increasing the extent and severity of atheroma [42] and the prevalence of microvascular disease in the small penetrating arteries within the brain which are endarteries[43].

60 % of strokes occurred in men with systolic BP > 160 mm Hg ,ina study done by A.G. Sharper et al Britain . They also found that patients with systolic BP between 160and 180 mm Hg had a 4 times higher risk of stroke than in men with BP < 160 mm Hg. With the systolic > 180 mm Hg, this risk increases to six fold. They found a weaker relation of diastolic BP with stroke which was lost on 4 regression analysis [44].

Individuals who have other clinical manifestations of hypertension such as LVH, proteinuria or retinopathy[41] the risk of stroke will be more. Sharper and colleagues found LVH as a contributory factor in patients with Ischaemic Heart Disease (IHD) [44].

Stephen McMohan et al in their study on hypertension as a risk factor found that diseases rates were lowest among those individuals whose baseline diastolic BP was 65 mm Hg and whose usual diastolic BP was probably 73 mm Hg[45].

In Indian studies It was found that the incidence of hypertension in stroke patients varied from 16-55 % to 23-47.4% . Nagaraja and Pratap Chand found the incidence of hypertension to be 24 % in fatal and 16 % in non fatal cases 17. The relative risk for hypertension is ischaemic stroke was 3.6 in the study by Sridharan.

Isolated systolic hypertension was more frequent in fatal cases while isolated diastolic hypertension was seen mainly in the non fatal cases [46].

DIABETES MELLITUS (DM)

Diabetes mellitus is quoted as an important risk factor for CVD in the developed world by WHO [47].

According to WHO stroke report, DM forms a risk factor in ischaemic strokes in large vessel diseases but is of questionable impact in small vessel diseases. The role of their risk in hemorrhage stroke is yet to be clarified[47].

Control of hyperglycemia can diminish the severity of cerebral damage during the acute stroke period but there is no evidence that controlling diabetes decreases stroke incidence [48].

Some author like Kier et al suggest that diabetics as well as patients with stress hyperglycemia have severe stroke and these patients are associated with poor prognosis. [49]

Nagaraja and Pratap ,from NIMHANS, Bangalore have found that DM was twice as common in fatal as compared to the non -fatal group[34], possibly the mechanism suggested by Jorgensen.

CARDIOVASCULAR DISEASES

Rheumatic heart disease (RHD), coronary artery diseases with MI,. cardiac arrhythmia ,cardiac emboli are themost common risk factor for ischaemic stroke [33].

Atrial fibrillation (AF) isthe most important and frequent cardiac source of embolism to the brain . Peterson P et al in their study showed a distinct clustering 16 of emboli at the time of onset of paroxysmal atrial fibrillation [33]. It is well established that chronic atrial fibrillation (CAF) carries an increased risk of strokes. In the Framingham study dealing only with CAF, an increased risk of stroke was found. AF in the absence of RHD was associated with more than a five fold increase in stroke incidence, while AF with RHD had a 17 fold increase compared to the controls without AF[50].

Prevalence of AF was 17% for all strokes types and 18 % for infarction in the community stroke project in Oxfordshire. AF was not associated with a definite excess risk of recurrent strokes, either within 30 days or within the first few years[51].

In Indian studies cerebral emboli from cardiac sources is a major detectable cause of stroke in the young. Sridharan noted that 36.5 % of ischaemic stroke patients had heart diseases, the relative risk being 2.250, Besides RHD with AF and ASD with paradoxical embolus. MVP was also associated with increased[52]

Incidence of strokes

Patients with coronary heart disease were found to have three fold increase risk of stroke. Those with CHF had almost five fold increased risk. ECG- LVH is associated with five fold increased risk of stroke[51] Cardiac impairment which have been found to contribute independently to stroke include LVH on ECG. cardiomegaly on CXR, coronary heat diseases, congestive heart failure and AF[45 44].

TIAS AND COMPLETED STROKES

TIAs and previous completed strokes are important risk factors for all strokes more so for ischaemic strokes. Previous strokes is a greater risk factor for subsequent stroke than TIA alone [33].

From Indian studies Agarwal et al noted an incidence of 19.8 % TIM in lschemic stroke and Sridharan noted 15 % TIAs in Ischaemic stroke [53].

In Oxfordshire community stroke project, the risk of stroke in the first year after TIAs was 12 % and approximately 6 % per year over the first 5 years. They found that patients who suffered a TIA had a 13 fold excess risk of stroke during the first year[54].

ATHEROSCLEROSIS

Atherosclerosis in extra cranial cerebral vessel is a risk factor forthrombotic stroke. The manifestations may be in the form of carotid bruit, occluded carotids and peripheral vascular diseases [47].

Sridharan noted carotid bruit in 6.8 % of lschemic stroke patients[53]. Carotid and supraclavicular bruit is a risk factor for subsequent stroke[55]. Atherothrombotic

disease of the large extracranial arteries including the carotids accounts for 34 % of strokes[56].

ELEVATED LIPID LEVELS

Elevated levels of LDL is an important risk factor for atherosclerosis per se[20]. Various lipid abnormalities have been studied and it has been proposed by Bansal et al, Vijayan and Chopra that hyperlipidemia contributes to a large majority of non embolic thrombotic strokes even in the young [57].

Agarwal et al had found elevated free fatty acids as significant in women with thrombotic strokes [58]. Reed DM et al found that elevated blood lipid levels is associated with extra and intracranial atheroma[42].

HEMATOCRIT

Eventhough pathologically elevated hematocrit has long been recognised as a predisposing condition for stroke, the Framingham study showed that this was true even within the normal range of hematocrit[59].

Cerebral blood flow has been found to be significantly lower in patients with hemotocrit values between 36- 46 % [60].

In a case control study of ischaemic stroke in the young, Dalal found a low hematocrit to be a significant risk factor70. Chopra et al found a low hematocrit in 8% Patient with thrombotic stroke and in 61 % of patients with puerperal intravenous occlusion[57]. The mechanism by which a low hematocrit predisposes to cerebral Ischemia is uncertain.

In the ICMR stoke study, low normal haemoglobin % has been reported as an important risk factor in young and elderly subjects[61].

On the other hand, the EC / IC bypass study group concluded that severity of strokes was not different in subjects with high hemoglobin concentration as against those with lower values[72]

SMOKING

Cigarette smoking is an important risk factor for all strokes. There is also ample evidence that cessation of cigarette smoking will eliminate it as a risk factor [36 33].

Nicotine transiently elevates denotes blood pressure and could enhance the risk of stroke this way. It may also enhance platelet aggregation [41].

In earlier Indian studies cigarette smoking was not found to be a significant risk factor for stroke[27 57]. But the ICMR study confirms the relationship between cigarette smoking and stroke.

Sridharan in his study noted 33.5% smoking in ischaemic stroke patients with a relative risk of I .7 [50 53].

ALCOHOLISM

Heavy drinking may be an independent risk factor ,moderate drinking can be protective[77 63] . the Hisagama study and the Honolulu studies have shown increased risks of hemorrhagic stroke in alcoholics [64]. There is evidence that an acute alcoholic episode or chronic alcoholism are each important risk factors for all strokes and for ischeamic stroke[65].

ORAL CONTRACEPTIVE PILLS

It is estimated that there is tenfold increased risk of stroke in women taking OC pills when compared to women not taking them. The use of OC pills triples the risk of stroke in young women [53].

OBESITY

Whether obesity is an independent risk factor for stroke is not known[33]. The risk factor status of obesity in Indian studies is also not established[58]

INFECTIONS

Infections commonly associated are tuberculosis, helminthic infestations, malaria, syphilis and leptospirosis. Clinicians report that systemic viral and bacterial infection is a risk factor for stroke but the data is inconclusive[33].

PIATELETS AND ENHANCED THROMBOGENESIS

Enhanced thrombosis may he major factors in the development of atherosclerotic plaque[41].

DIABETES AS A RISK FACTOR FOR STROKE

Diabetics are known to have an increased susceptibility to coronary, femoral and cerebral atherosclerosis. For atherothrombotic brain infarction,glycosuria or a blood sugar greater than 150 mg % is greater in women than in men[14].

Pathogenesis of CVD in Diabetes Mellitus

Atherosclerosis is more extensive and occurs earlier in diabetics than in the normal population. The cause of this could be non enzymatic glycation of lipoproteins. The atherosclerotic lesion appears to be initiated by oxidized LDL in a complicated cascade that operates through the acetyl LDL or scavenger receptor. Both HDL and antioxidants have the capacity to impair LDL oxidation thereby exerting an antiatherogenic action. A low HDL : LDL ratio favours atherosclerosis presumably because reverse cholesterol transport out of arteries is impaired and because diminished antioxidant activity by the HDL associated enzyme paraoxonase accelerates foam cell and plaque formation[13 15].

Other factors of potential importance are, increased platelet adhesiveness possibly due to enhanced thromboxane A2 synthesis, and decreased prostacyclin synthesis.

Hyperglycemia has been reported to increase secretion of endothelin in vitro, and production of nitric oxide (NO) is diminished in the coronary microvasculature. Diabetes appears to be a procoagulant State with increased levels of tissue factor and deficiency of tissue factor pathway inhibitor type I playing major roles.

Fibrinolysis is impaired, probably due to elevated leads to Tpa. inhibitor type I. The combination of hyperglycemia, hypertriglyceridemia and hyperinsulinemia increases the concentration of PAI.

GLUCOSE METABOLISM IN BRAIN

AEROBIC CELL METABOLISM

It is a balance between utilisation of ATP during the performance of work, and its resynthesis in anabolic sequences which provide the energy required to re-phosphorylate ADP. In the absence of ketosis, brain utilizes glucose as its sole substrate. This can he oxidized to CO2, and water. The energy yielded following oxidative metabolism is much higher than that following anaerobic glycolysis. Hence the brain relies on oxidative metabolism for its continuing functions [66] .

ANAEROBIC CELL METABOLISM

When energy production by oxidative metabolism is impeded by 0xygenlack, anaerobic metabolism takes over and some ATP can be produced by shifts in the creatinine kinase and adenylate kinase equilibrium. This is the glycolytic pathway where energy production is much less when compared to the oxidative metabolism. Anaerobic metabolism produces lactic acid which increases the intracellular pH and hence can accelerate cell damages[66]. The energy thus produced is used for various activities at the cellular and sub- cellular level.

ION TRANSPORT

The influx of Na and efflux of K. activates membrane bound Na - K dependent ATPase at the expense of ATP which is hydrolyzed to ADP and inorganic phosphate . Energy failure will lead to influx of Na and Cl in excess of any K lost. This leads to cellular edemas [66].

Another condition where cellular concentration is important is Calcium. Influx of Calcium into presynaptic terminals is a presumptive site for transmitter release.

METABOLIC EVENTS IN ISCIAEMIC STROKE

Metabolic changes during ischemia constitutes grossly exaggerated responses to physiologic stimuli. Three major metabolic changes occur during complete or near complete ischemia mainly those affecting cellular energy state, acid- base metabolism and Free Fatty Acids (FFAs). Following complete interruption of oxygen supply, tissue ATP content decreases to zero within 5- 7 minutes.[66]

Lactic acid production is limited by the pre ischaemic stores of glucose and glycogen. The lactic acid concentration reaches a maximum value within 2-3 minutes and the pH has been estimated to fall to about 6.5. By contrast, the FFA content does not attain a plateau value. In fact, FFA concentration continues to rise even if the ischemia is prolonged beyond the 15 minute point[66].

All the metabolic reactions in ischemia are initiated by ATP shortage which allows —

1. Release of K from cells which in turn leads to influx of Ca into neurons and
2. Uptake of Na and Cl by glial cells.

This leads to cellular edema[66].

Two primary events- ATP shortage and Ca2+ influx, probably act in conjunction to initiate and sustain release of FFAs from phospholipids. Ca2+ influx can accelerate proteolysis and degrade structural proteins, including those constituting the cytoskeleton. It also seems likely that accelerated lipolysis can cause damage to membrane bound enzymes for maintenance of membrane integrity. Thus aberrations of protein metabolism and inactivation of enzymes may well constitute yet another cascade triggered by ATP shortage and Ca2+ influx [66].

It is thought that initially hyperglycemia is neuroprotective by reducing ischaemic depolarization through delayed breakdown of transmembrane anion gradients with extended anaerobic glycolysis[67].

With persistent ischemia however, hyperglycemia produces a profound cellular acidosis due to excessive substrate for the predominant anaerobic glycolysis leading to local lactic acid production[84 68]. Once a critical threshold of acidosis is reached, hyperglycemia becomes detrimental[69].

Numerous studies have unequivocally established that hyperglycemia augments the extent of ischaemic brain damage. High serum glucose results in increased anaerobic metabolism, raised lactic acid production and cellular acidosis in the ischaemic brain tissue. The presence of diabetes or hyperglycemia may affect the degree of recovery, the severity of acute ischaemic stroke and the risk of early stroke recurrence. In addition, hyperglycemia intensifies the risk of cerebral edema and mortality after stroke [70].

It has been observed that these adverse effects occur when hyperglycemia is induced before, and not after ischemia. This is presumably because excessive acidosis during the period of energy depletion triggers additional adverse reactions whose effects become manifest later [71].

Both ischemia and hypoxemia retard or block electron transport and thereby also the activity of mitochondrial dehydrogenases. Lack of oxygen at the cytochrome a-a leads to an upstream accumulation of reduced compounds with arise in NADH / NAD ratio. This leads to increased lactate formation. This reaction consumes H+ ions. However when glucose is anaerobically converted to two molecules of lactate and the ATP formed in the process is hydrolyzed again. 2H+ ions are released. When pre-

existing ATP is hydrolyzed more H^* ions are released. This leads to intracellular and extracellular decrease in pH[73].

Calcium plays an important role in an irreversible cell damage during cerebral ischemia and reperfusion in relation to glucose levels. Primarily, influx of Ca2+ into presynaptic terminals is a presumptive site for transmitter release. Increased influx activates ornithine decarboxylase leading to the formation of intermediates which act on NMDA receptors and release more calcium [14].

Acidosis can release calcium from intra cellular binding sites leading to a reduction in the capacity of the cell to buffer calcium loads[73].

Even in the absence of diabetes, hyperglycemia can result from a stress response after stroke. This response leads to increased release of catecholamines, increased lipolysis, elevation of free fatty acids and blunting of insulin activity. Elevated catecholamine output is associated with marked increase in mortality after stroke[70] .studies have shown that the mortality of stroke is actually highest in non-diabetics with the reactive hyperglycemia (54 % -78%). intermediate in diabetics (35 % - 45 %) and least in non-diabetics without reactive hyperglycemia (17 % - 29 %) [74].These results indicate that the Stress response is a marker of poor prognosis after stroke. The cause of poor prognosis maybe related to a greater tendency towards production of cerebral edema.

Although previous studies have shown elevated plasma catecholamine's in the acute phase of stroke, only one study has addressed the relation between these stress parameters and the blood glucose levels. O'Neill et al found no significant relation between catecholamine's and blood glucose levels[75].

Van Kooten et al found that a significant proportion of stroke patients have latent diabetes[76]. This is in agreement with Oppenheimer et al who found a significant correlation between HbA1C and the non-fasting blood glucose in the acute phase.

These authors suggest that the poor prognosis of hyperglycemic patients found in earlier reports is probably caused by the underlying disease i.e.. diabetes, and that the concept of stress hyperglycemia has outlived its usefulness. Van Kooten et al's findings support that view and in addition show that it may be more relevant to identify other causes of hyperglycemia[76].

STRESS HYPERGLYCEMIA IN STROKE

Diabetes and hyperglycemia are common in the hospital setting. In the 1989 National Health Interview Survey, 24% of adults with diabetes reported being hospitalized at least once in the previous year [77].

In 1997, diabetes was the fourth most common comorbid condition in hospital discharges, and the prevalence of diabetes was 29% among cardiac surgery patients in 2001[78].

From 1980 to 2003, the number of hospital discharges with diabetes as any-listed diagnosis more than doubled (from 2.2 to 5.1 million discharges)-an increase of 234[79].

Hyperglycemia was present in 38% of adult noncritically-ill medical and surgical patients admitted to one community teaching hospital, of whom 26% had a known history of diabetes and 12% were without prior diagnosis or recognition of diabetes[80].

Stress hyperglycemia (also called stress diabetes or diabetes of injury) is transient elevation of the blood glucose due to the stress of illness. It usually resolves spontaneously, but must be distinguished from various forms of diabetes mellitus[81]. A high proportion of patients suffering an acute stress such as stroke or myocardial infarction [82]may develop hyperglycemia, even in the absence of a preexisting diagnosis of diabetes.

The definition of stress hyperglycemia also varied among studies. Most studies did not specify whether whole blood or plasma glucose was measured.

A random glucose level drawn on admission was used to define stress hyperglycemia in 10 of the 32 studies (with cutoffs ranging from 6 to 10 mmol/L [108 to 180 nwidL]). Another 9 studies based the definition of stress hyperglycemia on fasting glucose level the morning after admission (ranging from 6.1 to 7.8 mmol/L (110 to 141 mg/Dl).

In present study stress hyperglycemia was defined as random blood glucose levels >140mg/dl.Recognition of hyperglycemia as a marker for in-hospital mortality has provided a rationale for the pursuit of tight glucose control.

The American Association of Clinical Endocrinologists (AACE) Consensus Conference recommended blood glucose be maintained below 110 mg/dL in intensive care unit (ICU) patients, preprandial levels be maintained below 110 mg/dL, and peak postprandial levels be maintained below 180 mg/dL in noncritically ill patients 128.Similarly, the American Diabetes Association (ADA) has proposed target blood glucose of about 110 mg/dl, 90-130mg/(11 and <180mg/dI for these three categories of hospitalized patients[83].

Hyperglycemia is a common and costly health care problem in hospitalized patients. In hospital hyperglycemia is defined as any glucose value >7.8 mmol/l (140mg/dl). The American Diabetes Association and American Association of Clinical Endocrinologists consensus on inpatient hyperglycemia defined stress hyperglycemia or hospital-related hyperglycemia as any blood glucose concentration > 7.8 mmol/l (140 mg/dl).[84]

In multivariate analysis, as admission blood glucose increased, the odds for neurologic improvement decreased with an OR of 0.76 per 100mg/dl increase in admission glucose (95% CI 0.61-0.95, P = 0.01 [85]

Pulsinelli et al. 60 reported worse outcomes for both patients with diabetes and hyperglycemic patients without an established diagnosis of diabetes compared with those who were normoglycemic. Stroke-related deficits were more severe when admission glucose values were >120 mg/dl (6.7 mmo1/1).

Demchuk et al. [86] studied the effect of admission glucose level and risk for intracerebral hemorrhage or infarct when treatment with recombinant tissue plasminogen activator. The authors reported admission blood glucose and/or history of diabetes as the only independent predictors of hemorrhage.

Kiers et al. [87] prospectively studied acute stroke patients and threshold blood glucose for euglycemia was defined as fasting blood glucose <140 mg/di (7.8 mmo1/1). Patients were divided into four groups: euglycemia with no history of diabetes, patients with "stress hyperglycemia" (blood glucose >140 mg/dl, 7.8 mmo1/1, and HbA lc <8%), newly diagnosed diabetes (blood glucose >140 mg/dl, 7.8 mmol/l, and HbA lc >8%), and known diabetes. No difference was found in the type or site of stroke among the four groups. Compared with the euglycemic, nondiabetic patients, mortality was increased in all three groups of hyperglycemic patients.

Williams et al. [88] reported on the association of hyperglycemia and outcomes in a group of 656 acute stroke patients. 52% percent of the cohort had a known history of diabetes. Hlyperglycemia, defined as a random blood glucose >=130 mg/dl (7.22 mmol/l), was present in 40% of patients at the time of admission.

Hyperglycemia was an independent predictor of death at 30 day (RR 1.87) and at 1 year (RR 1.75) (both P <= 0.01). Other outcomes that were significantly correlated with hyperglycemia, when compared with normal blood glucose, were length of stay (7 vs. 6 days, P = 0.015) and charges ($6,611 vs. $5,262, P < 0.001)

Parsons et al[88]reported a study of magnetic resonance imaging (MR1) and MRS in acute stroke. Median acute blood glucose was 133.2 mg/di (7.4 mmo1/1), range 104.4-172.8 mg/dl (5.8-9.6 mmo1/1). A doubling of b71-eod glucose from 90 to 180 mg/dl (5-10 mmo1/1) led to a 60% reduction in penumbral salvage and a 56 cm3 increase in final infarct size.

Hala El Kawas study found that Acute hyperglycemia predicts increased risk of poor neurological and functional outcome. Measures to normalize blood glucose level in the setting of acute stroke could be of value in improving stroke outcome [89].

Sagarbasu study suggests that stroke severity is the most important predictor of stroke outcome, with high sugar level as a marker of stroke severity [90].

Bogdan timar study in 2013 concluded that: T2DM is a major risk factor for stroke. Plasma glucose level at admission was correlated positively with stroke mortality, both in patients with T2DM and in those without previously diagnosed T2DM, independently of other related factors.[91]

STRESS HYPERGLYCEMIA

DEFINITION

Stress hyperglycemia has been defined as hyperglycemia in previously euglycemic patients that corrects once the acute process resolves. Hyperglycemia occurs in 60% of the cases with acute stroke and in 12- 53% cases without the prior diagnosis of diabetes.

It imposes a range of adverse effects like abnormal immune function[92], hemodynamic and electromyocardial disturbances and increased infection rate[93]. Various studies have shown a direct relationship between the extent of stress hyperglycemia and severity and outcome of stroke, including mortality. Hyperglycemia in both diabetic and non- diabetic (i.e., stress hyperglycemia) patients is associated with poor prognosis both in terms of mortality and functional recovery, irrespective of patient's age, severity of condition or stroke sub- type[94]

The WHO criteria of blood glucose for diagnosis of diabetes mellitus are used to define the minimum cut- off point for hyperglycemia as RPG ≥ 140 mg/dl. HbA1c cut point of 6.5% is used according to the recommendation of International Expert Committee in 2009.[95]

Hyperglycemia is a common and costly health care problem in hospitalized patients. In hospital hyperglycemia is defined as any glucose value >7.8 mmol/l (140mg/dl). The American Diabetes Association and American Association of Clinical Endocrinologists consensus on inpatient hyperglycemia defined stress hyperglycemia or hospital-related hyperglycemia as any blood glucose concentration > 7.8 mmol/l (140 mg/dl).[96]

PATHOPHYSIOLOGY

Hyperglycemia may be directly toxic to the ischemic brain. Accumulation of lactate and intracellular acidosis in the ischemic brain (produced through anaerobic cerebral glucose metabolism)[97]. promotes and accelerates ischemic injury by enhancing lipid peroxidation and free radical formation[98], and impairing mitochondrial function[99]. These neurotoxic effects may be particularly important in the ischemic penumbra where neurons are injured but still viable[100].

Hyperglycemia facilitates the development of cellular acidosis in the ischemic penumbra and results in a greater infarct volume, thus promoting the recruitment of potentially salvageable neurons into the infarction.

Hyperglycemic patients are relatively deficient in insulin. This leads to both reduced peripheral uptake of glucose (increasing the amount of glucose available to diffuse into brain) and increased circulating free fatty acids. Free fatty acids may impair endothelium-dependent vasodilation[101].

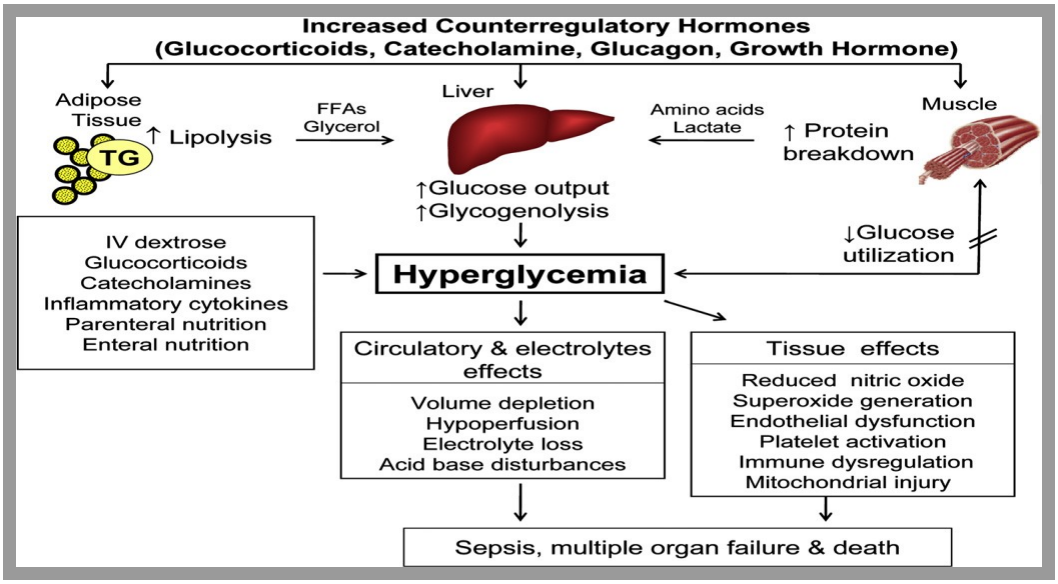

Fig 5. Showing pathogenesis of stress hyperglycemia

Pathogenesis of stress hyperglycemia Stress hyperglycemia results from increased hepatic glucose production and impaired glucose utilization in peripheral tissues. Excess counterregulatory hormones (glucagon, cortisol, catecholamines, and growth hormone) increases lipolysis and protein breakdown (proteolysis), and impaired glucose utilization by peripheral tissues. Hyperglycemia causes osmotic diuresis that leads to hypovolemia decreased glomerular filtration rate and worsening hyperglycemia. At the cellular level increased blood glucose levels results in mitochondrial injury by generating reaction oxygen species and endothelial dysfunction by inhibiting nitric oxide production.

Hyperglycemia increases levels of pro-inflammatory cytokine such as TNFa, and IL-6 leading to immune system dysfunction, also increases plasminogen activator inhibitor-1 and fibrinogen causing platelet aggregation and hypercoagulable state. These changes can eventually lead to increased risk of infection, impaired wound healing, multiple organ failure, prolonged hospital stay .

Stress hyperglycemia patients are likely to have dysglycemia (ie, blood glucose level above the normal range but below the threshold for diabetes or undiagnosed diabetes [103]when not stressed. These patients have a higher risk of vascular disease than patients with normal blood glucose level[104]. These patients could sustain more ischemic damage at the time of infarction as a result of more extensive underlying cerebral vasculopathy compared with those who do not develop stress hyperglycemia. Hyperglycemia is an important determinant of the widespread changes in both small cerebral blood vessels[105]and large extracranial vesselsseen in diabetic patients[106]..

Hyperglycemia may disrupt the blood-brain barrier[107] and promote hemorrhagic infarct conversion. Higher admission serum glucose level is associated

with a higher risk of hemorrhagic conversion of the infarct, with a substantial rise in risk with levels >8.4 mmol/L[108.]

Stress hyperglycemia may be a marker of the extent of ischemic damage in patients with stroke19.[109]

Hyperglycemia-Associated Reduction in Perfusion

Hyperglycemia causes 24% reduction in regional blood flow, reduction in blood circulation to the marginal ischemic areas and converts ischemic penumbra to infarct[110]. CO2-induced increase in cerebral blood flow is decreased in diabetics[111]. CO2-induced cerebral vasodilatation is mediated through NO, and diabetics are known to have decreased endothelial NO production[92].

Hyperglycemia and Thrombosis

Multiple studies have identified a variety of hyperglycemia-related abnormalities in hemostasis, favoring thrombosis[112]. Human studies in patients with type 2 diabetes have shown platelet hyperactivity indicated by increasedthromboxane biosynthesis Hyperglycemia-induced elevations of interleukin (IL)-6 levels have been linked to elevated plasma fibrinogen concentrations and fibrinogen mRNA[113].

Increased platelet activation as shown by shear-induced platelet adhesion and aggregation on extracellular matrix has been demonstrated in patients with diabetes[114]

In the healthy state, the vascular endothelium maintains the vasculature in a quiescent, relaxant, antithrombotic, antioxidant, and antiadhesive state. Acute hyperglycemia may directly alter endothelial cell function by promoting chemical inactivation of nitric oxide, triggering production of reactive oxygen species (ROS) or activating other pathways[102].

MANAGEMENT OF STRESS HYPERGLYCEMIA IN ACUTE ISCHEMIC STROKE

It is reasonable to treat patients with acute ischemic stroke according to American Diabetes Association inpatient glycemic control guidelines,initiating therapyto achieve glucose targets of 140to 180mg/dl if fasting glucose is greater than 140mg/dl or random glucose is constantly higher than 180mg/dl.

Lower glucose targets (<140mg/dl) may be appropriate for patients with well controlled diabetes and those with stress hyperglycemia. Lowering glucose levels less than 80mg/dl should be avoided[115].

Patients who present with extreme or persistent hyperglycemia,are critically ill and should be started on intravenous insulin to improve blood glucose control for atleast 24 to 48hrsof hospitalization .They should then be transitioned to a subcutaneous insulin regimen that incudes basal long acting insulin and short acting insulin[115].

MATERIALS AND METHODS

SOURCE OF DATA

- Hundred patients satisfying inclusion criteria presenting to RLJHRC are included in the study.
- Sample size is calculated with 80 % power , 95% confidence interval, α error of 0.05, according to the formula

$$n = \frac{2\,S^2\,(Z\alpha/2 + Z\beta)^2}{(d)^2}$$

METHOD OF COLLECTION OF DATA:

- Informed consent has been obtained from all subjects.
- Baseline clinical data includes clinical history, examination. Data from those patients satisfying inclusion and exclusion criteria are collected.
- Patient status was evaluated by NIHS Scale on the day of admission and 7th day of admission and functional recovery was assessed based on difference of score.

INCLUSION CRITERIA FOR CASES:

- Age> 18 yrs.
- Patients with CT evidence of acute ischemic stroke or progressive stroke < 24 hrs of onset.
- RBS >140 mg/dl at the time of admission.

INCLUSION CRITERIA FOR CONTROLS :

- Age > 18 yrs.
- Patients with CT evidence of acute ischemic stroke or progressive stroke < 24 hrs of onset.

.EXCLUSION CRITERIA FOR CASES:

- Previously treated outside.
- Head injury, CT showing any space occupying lesion, bleed.

EXCLUSION CRITERIA FOR CONTROLS:

- Previously treated outside.
- Head injury, CT showing any space occupying lesion, bleed.

INVESTIGATIONS DONE

- CT brain in 24hrs of admission
- Glycated Haemoglobin levels.
- RBS at the time of presentation and on 7th day of admission.
- FBS, PPBS in next 24 hrs.

Fig no.6 Instrument used to calculate blood sugars

CT IMAGES

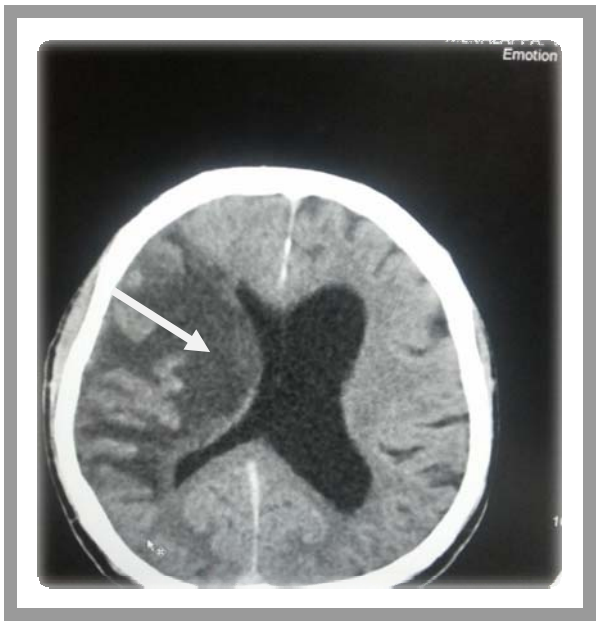

Fig no.7 showing acute infarct in the right parietal region compressing the ventricle

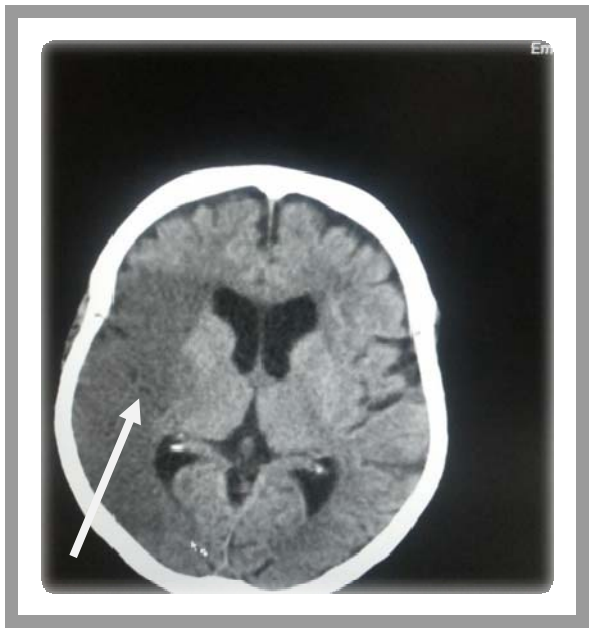

Fig no.8 showing acute infarct in the Right Parietal region involving whole MCA territory

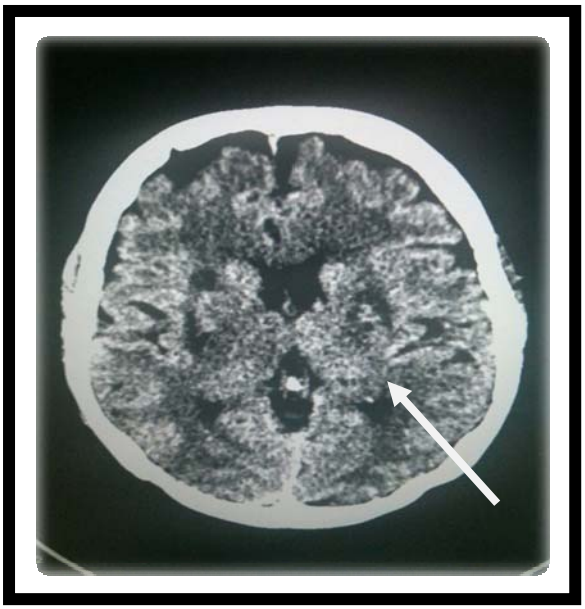

Fig no. 9 acute infarct in left parietal lobe

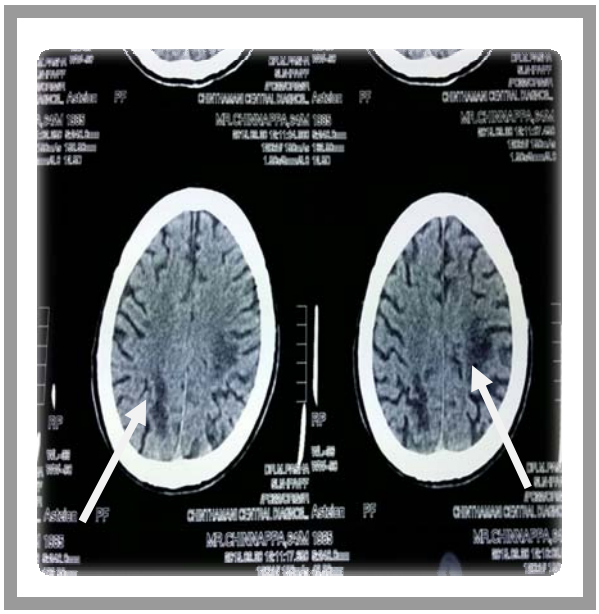

fig no.10 acute infarct in left parietal and right parieto-occipital region

Statistical Methods:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two groups. Paired t test was used to find the mean difference on day 1 and day 7 values. p value <0.05 was considered as statistically significant.

RESULTS

Table 1: Age distribution of subjects

		Frequency	Percent
Age	**< 40 years**	7	7.0
	41 to 50 years	16	16.0
	51 to 60 years	22	22.0
	61 to 70 years	26	26.0
	> 70 years	29	29.0
	Total	**100**	**100.0**

Majority of subjects were in the age group > 70 yrs (29%), 26% were in age group 61 to 70 yrs, 22% were in age group 51 to 60 yrs and 7% were aged < 40 years. Mean age of subjects was 62.71 ± 14.09 yrs.

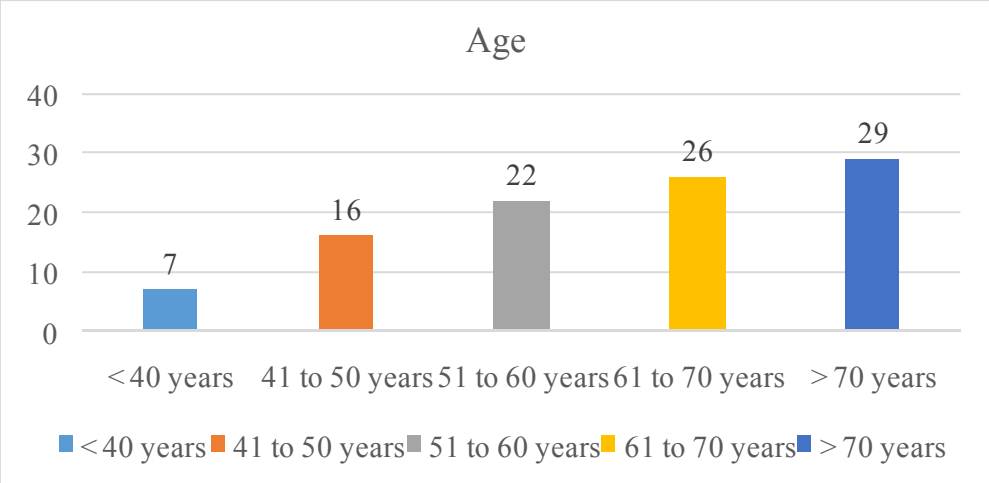

Figure 11: Bar diagram showing Age distribution

Table 2: Gender distribution of subjects

		Frequency	Percent
Gender	**Female**	42	42.0
	Male	58	58.0
	Total	**100**	**100.0**

58% of subjects were males and 42% were females.

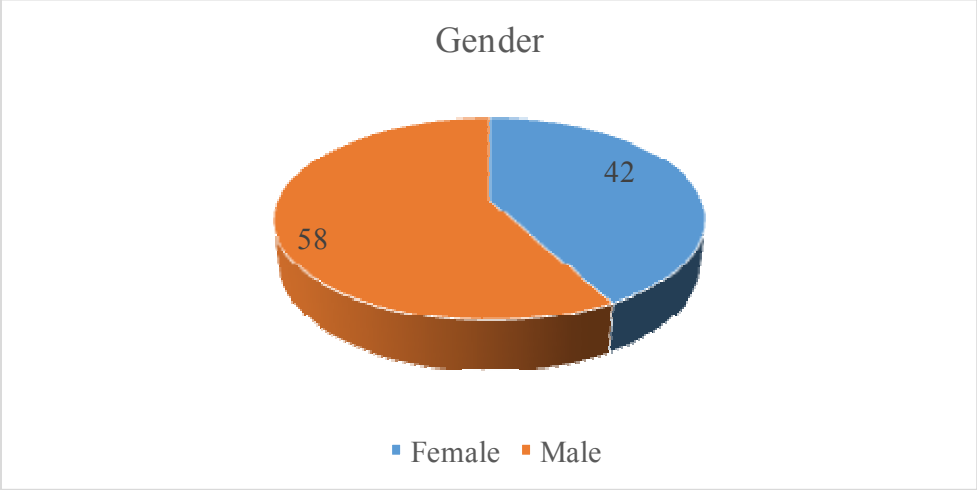

Figure 12: Pie diagram showing Gender distribution

Table 3: Distribution of subjects according to groups (Cases & Controls)

		Frequency	Percent
Groups	**Cases**	53	53.0
	Controls	47	47.0
	Total	**100**	**100.0**

53% of them were cases and 47% controls were selected based on RBS. In Cases RBS was > 140 (Stress Hyperglycemia) and in controls RBS was < 140.

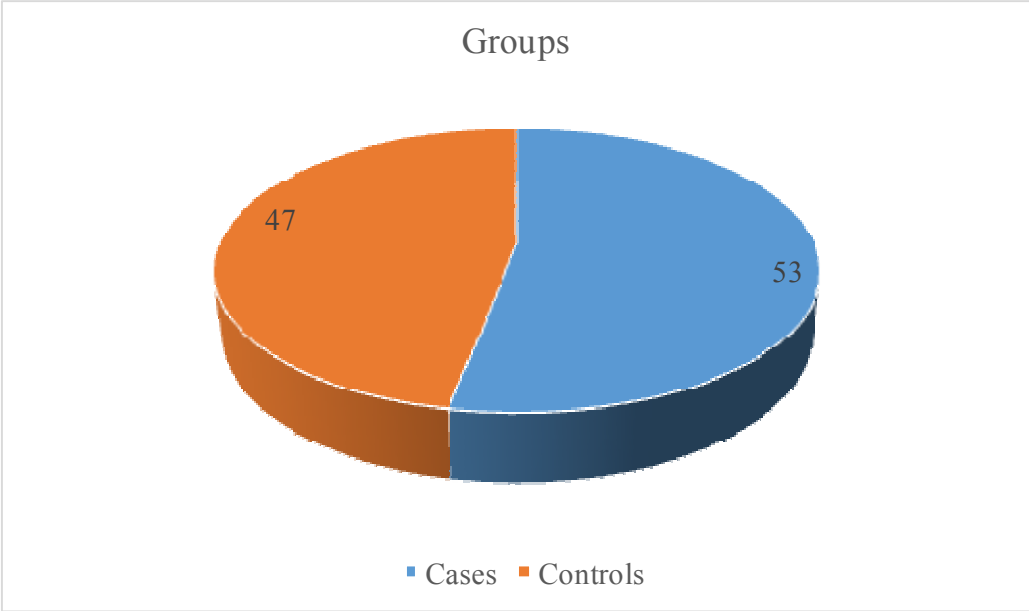

Figure 13: Pie diagram showing distribution of cases and controls

Table 4: Association between Groups and Age

		Groups				P value
		Cases		Controls		
		Count	%	Count	%	
Age	< 40 years	2	3.8%	5	10.6%	0.145
	41 to 50 years	6	11.3%	10	21.3%	
	51 to 60 years	10	18.9%	12	25.5%	
	61 to 70 years	18	34.0%	8	17.0%	
	> 70 years	17	32.1%	12	25.5%	

In cases majority of subjects were in the age group 61 to 70 years (34%), followed by > 70 years. In controls Majority were in age group 51 to 60 yrs and 70 years respectively (25.5%). There was no significant association between age and groups. Age matching was achieved.

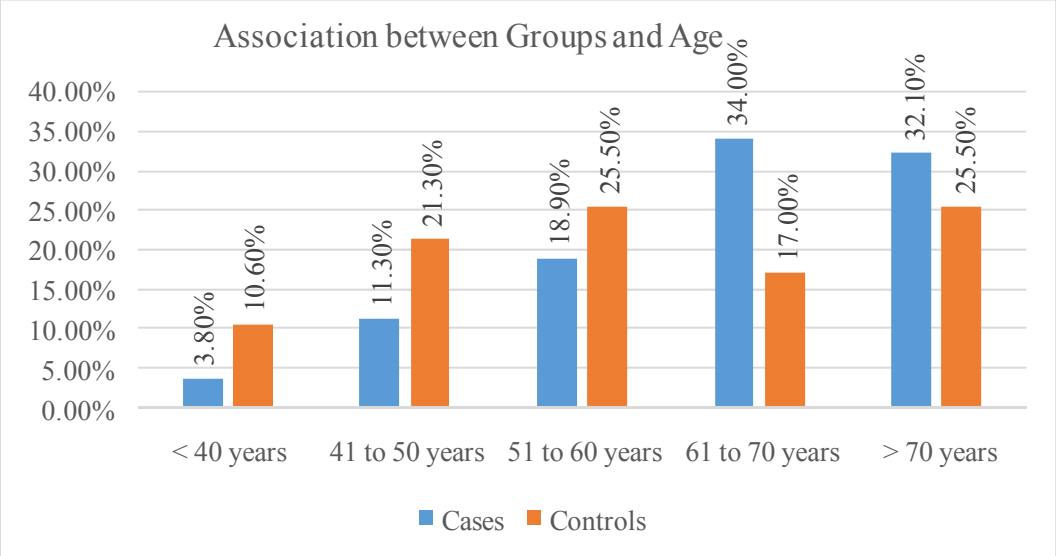

Figure 14: Bar diagram showing Association between Groups and Age

Table 5: Association between Groups and Gender

		Groups				P value
		Cases		Controls		
		Count	%	Count	%	
Sex	Female	21	39.6%	21	44.7%	0.609
	Male	32	60.4%	26	55.3%	

In cases and controls majority of subjects were males (60.4% & 55.3% respectively), followed. There was no significant association between gender and groups. Gender matching was achieved.

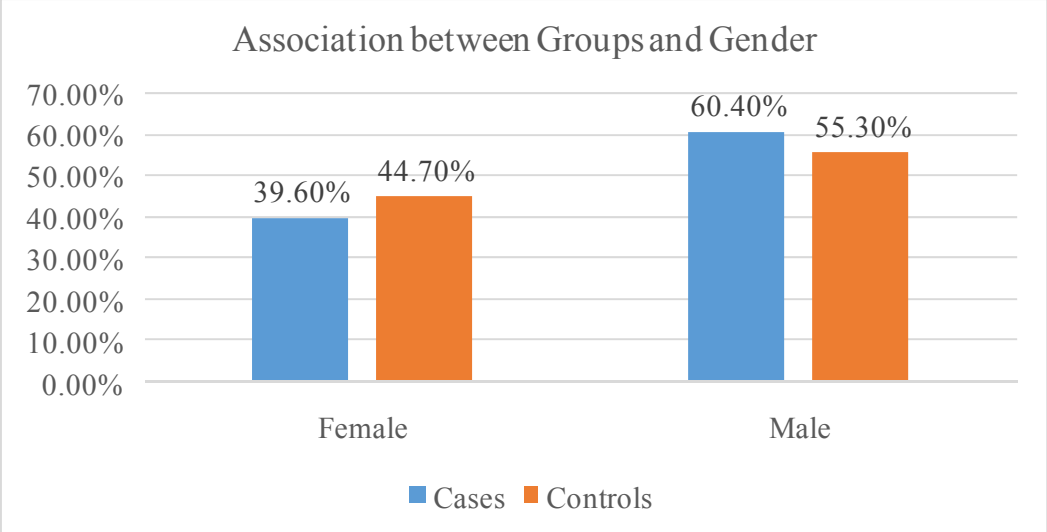

Figure 15: Bar diagram showing Association between Groups and Gender

Table 6: Comparison of Glycemic Parameters with cases and controls

	Groups				P value
	Cases		**Controls**		
	Mean	**SD**	**Mean**	**SD**	
RBS on day of admission	183.06	35.99	121.55	14.03	<0.001*
FBS in next 24 hrs	134.58	14.66	115.91	7.18	<0.001*
PPBS	170.62	20.58	140.96	10.09	<0.001*
Glycated Hb%	5.59	0.34	5.20	0.29	<0.001*

Mean RBS on day of admission was 183.06 ± 35.99 in cases and 121.55 ± 14.03 mg/dl in controls. This difference in mean was statistically significant. i.e. Higher RBS values were seen in Cases than controls.

Mean FBS was 134.58 ± 14.66 in cases and 115.91 ± 7.18 mg/dl in controls. This difference in mean was statistically significant. I.e. Higher FBS values were seen in Cases than controls.

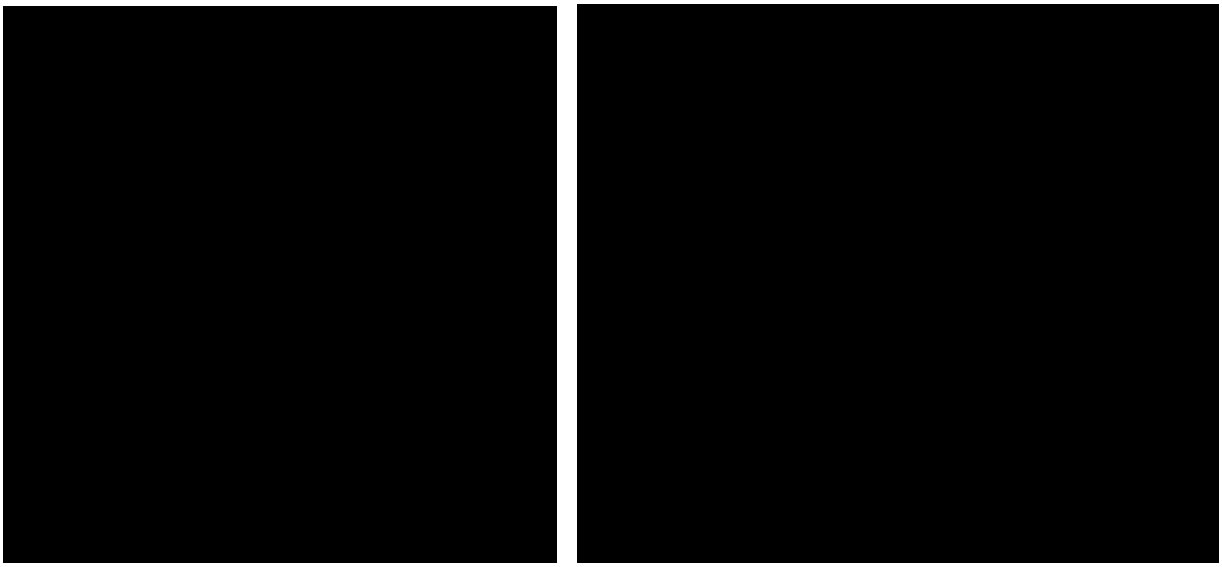

Figure 17: FBS between cases and controls

Mean PPBS was 170.62 ± 20.58 in cases and 140.96 ± 10.09mg/dl in controls. This difference in mean was statistically significant. i.e. Higher PPBS values were seen in Cases than controls.

Mean HbA1c was 5.59 ± 0.34 in cases and 5.20 ± 0.29 mg/dl in controls. This difference in mean was statistically significant. I.e. Higher HbA1c values were seen in Cases than controls.

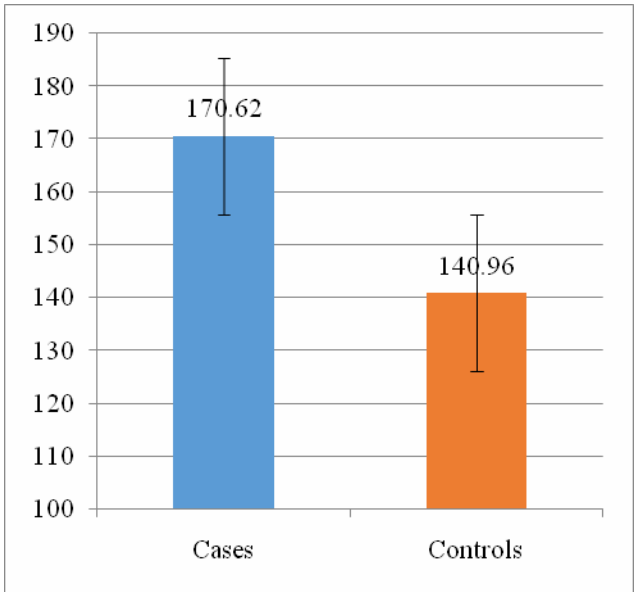

Figure 18: PPBS between cases and controls

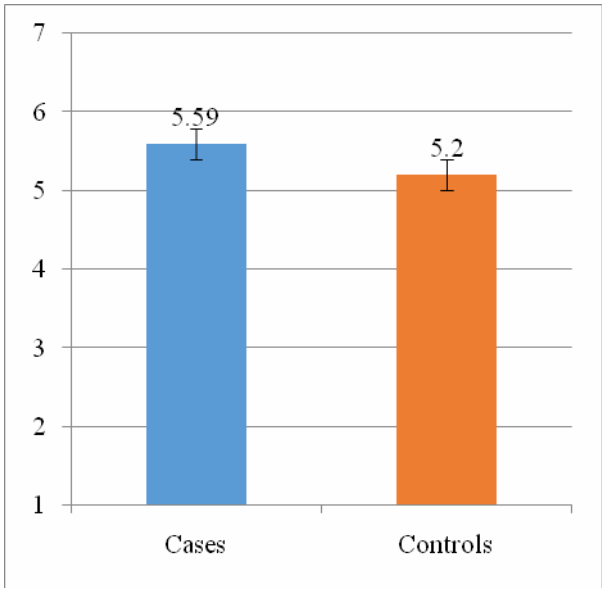

Figure 19: HbA1c between cases and controls

Table 7: Comparison of RBS at admission and on 7th day in cases and controls

	Cases		Controls	
	Mean	**SD**	**Mean**	**SD**
RBS on day of admission	181.588	35.5624	121.553	14.031
RBS on 7th day	151.31	14.747	124.36	10.182
P value	**<0.001***		**0.018***	

When RBS values were measured on day 7 it was observed that mean RBS was 151.31 ± 14.747 in cases and 124.36 ± 10.182 in controls. There was significant reduction in RBS at 7th day when compared to 1st day RBS in both cases and controls.

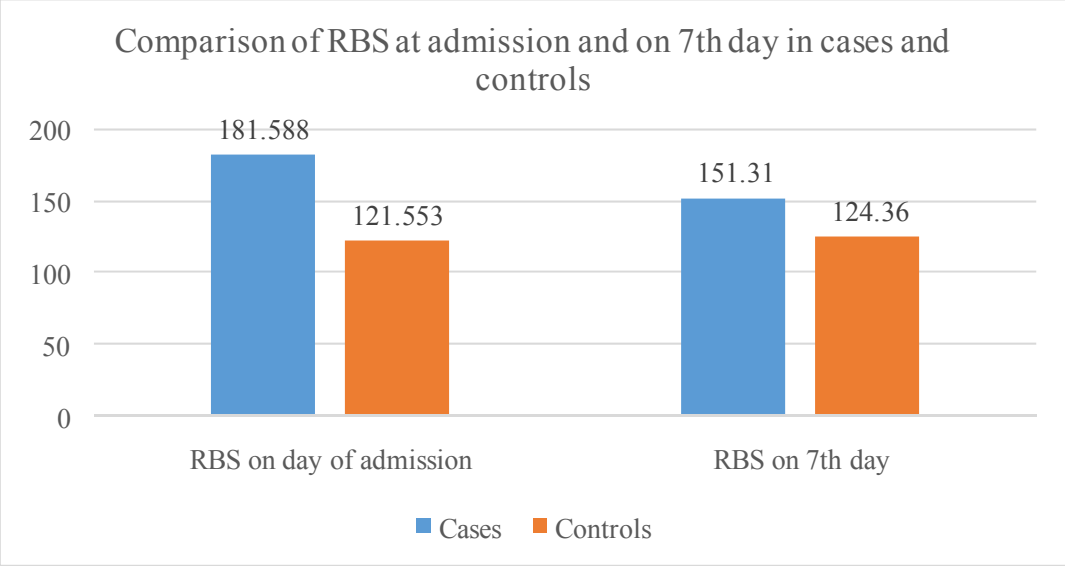

Figure 20: Bar diagram showing Comparison of RBS at admission and on 7th day in cases and controls

Table 8: Comparison of NIHSS score at Day 1 and on 7th day in cases and controls

	Cases		Controls		P value
	Mean	**SD**	**Mean**	**SD**	
NIHS scale on day 1	12.208	2.34	9.404	1.59	<0.001*
NIHS scale on day 7	8.98	2.177	4.62	1.636	<0.001*
P value	**<0.001***		**<0.001***		

Mean NIHSS score on day 1 in cases was 12.208 ± 2.34 and in controls was 9.404 ± 1.59. This difference was statistically significant. I.e. cases had higher scores of NIHSS than controls.

Mean NIHSS score on day 7 in cases was 8.98 ± 2.17 and in controls was 4.62 ± 1.63. This difference was statistically significant. I.e. cases had higher scores of NIHSS than controls.

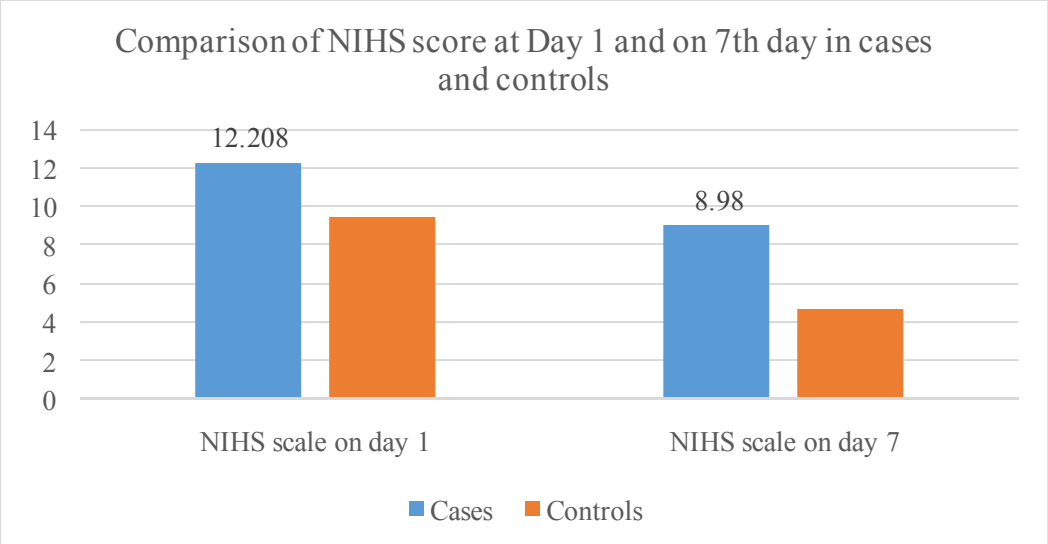

Figure 21: Bar diagram showing Comparison of NIHSS score at Day 1 and on 7th day in cases and controls

Table 9: Comparison of Difference in NIHSS score between cases and controls

		Groups				P value
		Cases		Controls		
		Count	%	Count	%	
Difference in score	2	10	18.9%	0	0.0%	<0.001*
	3	27	50.9%	1	2.1%	
	4	11	20.8%	15	31.9%	
	5	2	3.8%	24	51.1%	
	6	1	1.9%	7	14.9%	

In cases difference in score of NIHS from day 1 to day 7 was 2 in 18.9%, 3 in 50.9%, 4 in 20.8%, 5 in 3.8% and 6 in 1.9%. Lower difference was observed in cases than in controls. This observation was statistically significant.

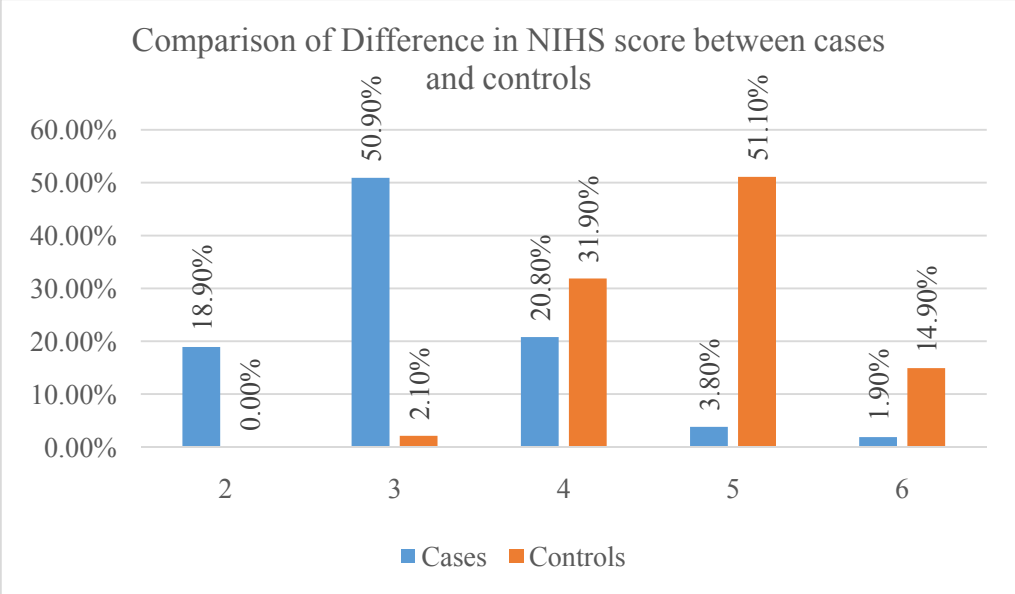

Figure 22: Bar diagram showing Comparison of Difference in NIHS score between cases and controls

Table 10 : Mean Functional Score difference in cases & controls

	Groups	N	Mean	SD	P value
Functional Score	Cases	51	3.16	0.857	**<0.0001****
	Controls	47	4.79	0.720	

In the study mean functional score was higher for controls than cases and this difference was statistically significant.

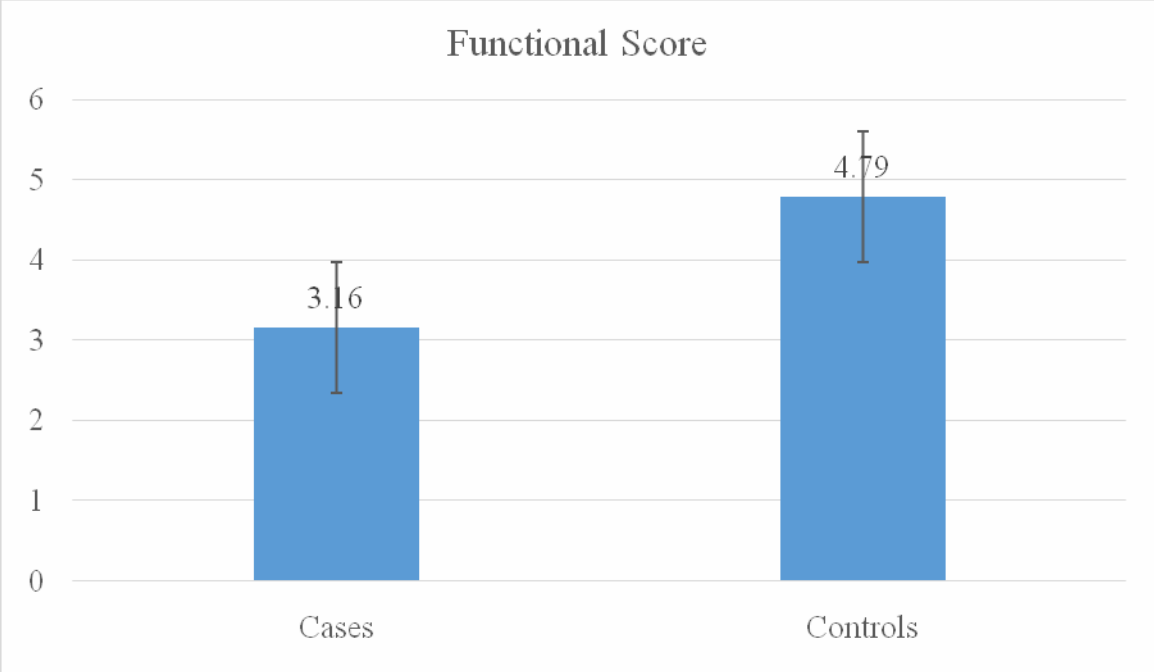

Figure:23 Bar diagram showing Functional Score difference in cases & controls

Table 11: Comparison of Outcome between cases and controls

		Groups				P value
		Cases		Controls		
		Count	%	Count	%	
Outcome	Death	5	9.4%	0	0.0%	0.179
	Improved	48	90.5%	47	100.0%	

In the study 5 cases (9.4%) had mortality and none of the controls had mortality. There was no significant association between outcome in cases and controls.

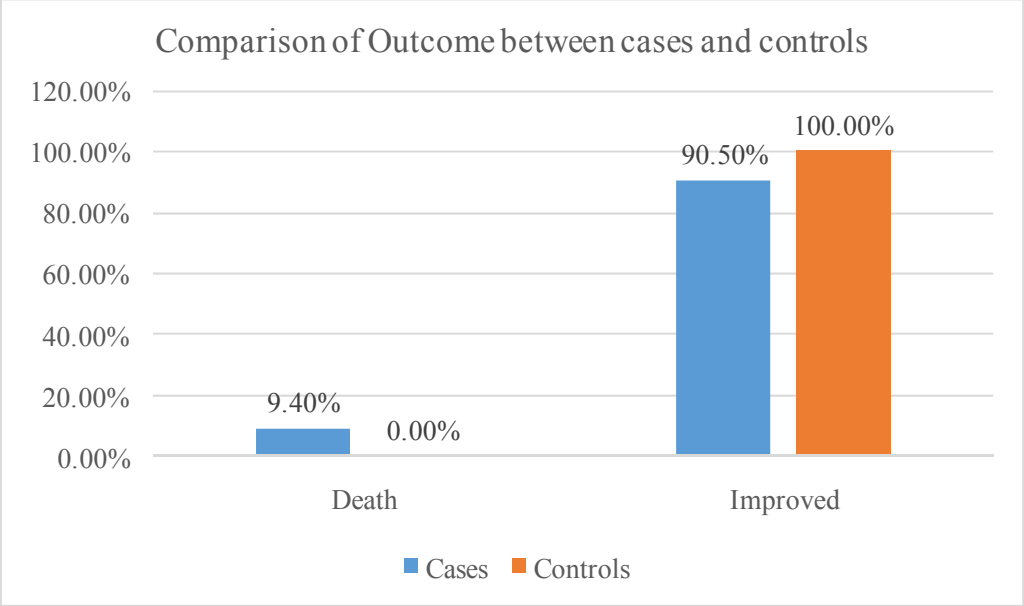

Figure 24: Bar diagram showing Comparison of Outcome between cases and controls

Table 12: Comparison of RBS on admission with outcome

	Outcome	N	Mean	SD	P value
RBS on day of admission	**Recovered**	95	148.842	33.5582	**<0.001***
	Death	5	255.000	53.0141	

In the study mean RBS values was higher for patients who had mortality (255.0 ± 53.01) than recovered patients (148.84 ± 33.55). This difference was statistically significant.

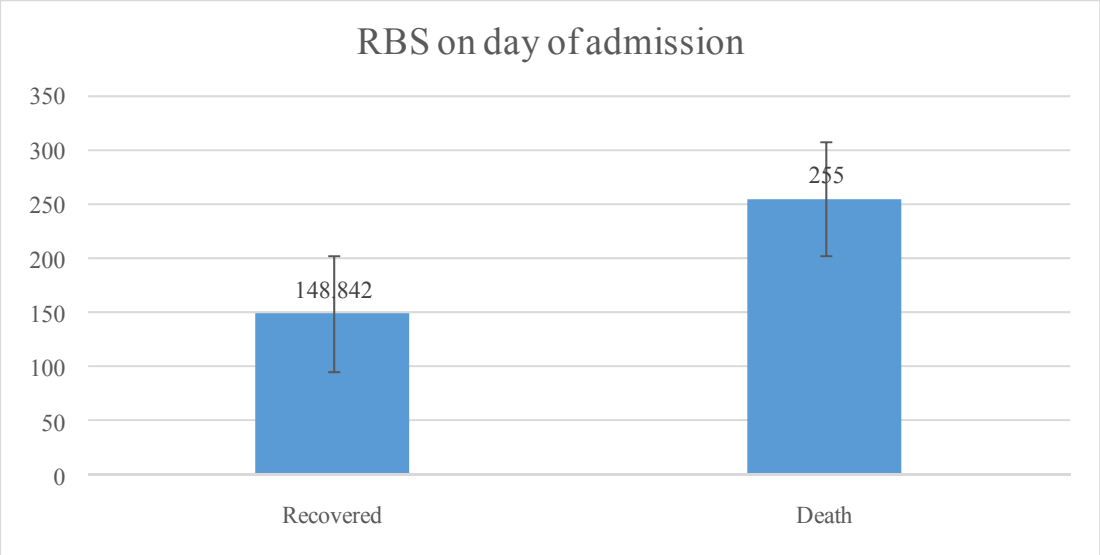

Figure: 25 Bar diagram showing Comparison of RBS on admission with outcome

Table 13: Comparison of FBS with outcome

	Outcome	N	Mean	SD	P value
FBS at 24 hrs	**Recovered**	95	124.147	12.4490	**0.0001***
	Death	5	157.400	24.5622	

In the study mean FBS values was higher for patients who had mortality (157.4 ± 24.56) than recovered patients (124.14 ± 12.44). This difference was statistically significant.

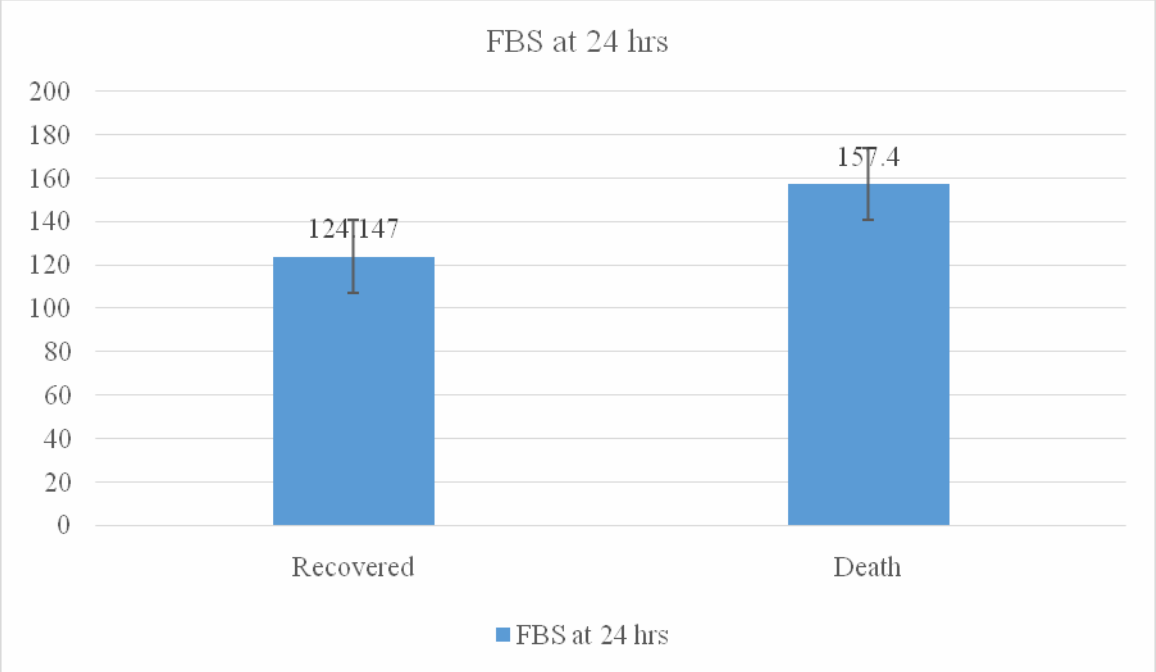

Figure: 26 Bar diagram showing Mean FBS with outcome

Table 14 : Comparison of PPBS with outcome

	Outcome	N	Mean	SD	P value
PPBS	**Recovered**	95	154.884	20.6536	**0.0001***
	Death	5	190.800	24.4990	

In the study mean PPBS values was higher for patients who had mortality (190.8 ± 24.49) than recovered patients (154.88 ± 20.65). This difference was statistically significant.

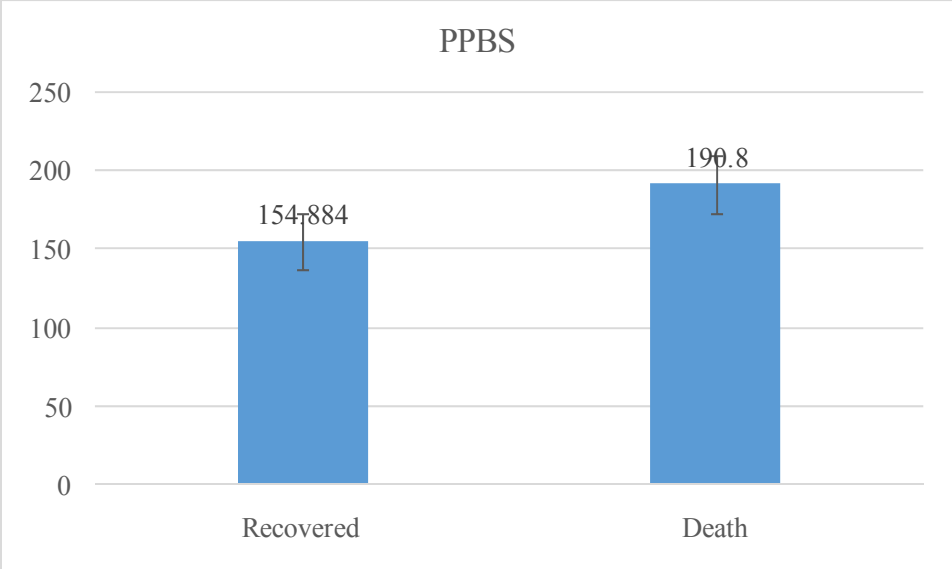

Figure:27 Bar diagram showing Mean PPBS with outcome

DISCUSSION

This study was aimed at evaluating the outcome in acute ischemic stroke patients with stress hyperglycemia in terms of mortality and functional recovery based on National Institute of Health Stroke s Scale [NIH SS][12] .100 patients were included in the study . These subjects were non diabetic patients.

CASE CHARACTERISTICS

AGE DISTRIBUTION OF SUBJECTS

The age of patients in this study ranged between 20 and 99 years . The maximum number of patients in this study were in the age group between 71 and 80 years. The mean age of both sexes was 62.71 + 14.09 .this correlates with the findings of other authors .

STUDIES	**PRESENT STUDY**	**FRAMINGHAM STUDY**	**SRIDHARAN STUDY**
AGE in years	62.71 + 14.09	65 - 74	**60 - 70**

AII studies have shown that the rate of stroke increases with age. The Framingham study showed that only 1/5th of atherothrombotic strokes occurs below 65 years. The study also demonstrated a sharp increase of stroke after 65 years and a peak incidence of stoke between 65 – 74 years of age[20]

Among the Indian studies, Sridharan[53] found a peak incidence of stroke between 60 – 70 years and Agarwal et al[58]showed a peak age incidence in the 6th decade. Abraham, Daniel and sunder Rao[116]study on South Indian subjects described

a sharp increase in the prevalence of stroke after 60 years in both sexes with a peak prevalence above 70 years in males.

Nagaraja and Pratap chand[45] in their study from NIMHANS found that the peak incidence of stroke was in the 6th decade.

The WHO collaborative stroke study group from Rohtak, Haryana in 1974 reported that the prevalence of stroke increases from 86.96 /100,000 below 60 years to 622.22/100,000 above the age of 60[14].

SEX DISTRIBUTION

In the present study male subjects were 58% and female subjects were of 42%.

In Kamel Abdelaziz mohamed study in 2013 male patients were 61% and female patients were (39%. [37]

In Abdu Hameed AI Kassir study in 2012 male patients were 67.6% and female patients were 32.4% [38]

In Hala El Kawas study in 2006 male patients were 56.6% and female patients were 43.3%[39].

PERCENTAGE	**PRESENT STUDY**	**KAMEL ABDELAZIZ MOHAMED STUDY 2013**	**ABDUL HAMEED AI KASSIR STUDY 2012**	**HALA EL KAWAS STUDY 2006**
MALES	**58%**	61%	67.6%	56.6%
FEMALES	**42%**	39%	32.4%	43.3%

MALE: FEMALE RATIO

The male: female ratio (M:F) is 1.38: 1 in the present study. As in the other studies, there is male excess of strokes[107].

	PRESENT STUDY	**AGARWAL STUDY**	**SRIDHARAN STUDY**
M : F RATIO	**1.38 : 1**	5.8 : 1	2.3 : 1

In India a wide variation in male sex prominence is seen . Agarwal noted a male : female ratio of 5.8 : 1 and Sridharan[50].

.**PR0P0RTIONS OF STRESS HYPERGLYCEMIA**

In our study we have total of 100 patients of which 53 patients had **stress hyperglycemia** with RBS> 140 mg/dl at admission who were included as cases. Remaining 47 patients who had RBS < 140 mg/dl at admission were included as controls.

So in our study proportion of stress hyperglycemia was 53%

In Kamel Abdelaziz mohamed study in 2013 proportion of stress hyperglycemia was 31%[37].

In Abdul Hameed AI Kassir study in 2012 proportion of stress hyperglycemia was 36.8%[38]

In Hala El Kawas study in 2006 proportion of stress hyperglycemia was 24%[39]

PROPORTION OF STRESS HYPERGLYCEMIA	**PRESENT STUDY 2015**	**KAMEL ABDELAZIZ MOHAMED STUDY 2013**	**ABDUL HAMEED AI KASSIR STUDY 2012**	**HALA EL KAWAS STUDY 2006**
PERCENTAGE	**53%**	31%	36.8%	24%

We, can see that there is an increase in proportion of stress hyperglycemia, may be due to the modern life style changes.

ODDS RATIO

	PRESENT STUDY	BOGDAN TIMAR STUDY 2013	ALVAREZ – SABIN et al study
Odds ratio (OR)	**1.979**	3.63	8.4

The odds ratio for the present study was 1.979 less compared to the other studies.

MEAN RANDOM BLOOD GLUCOSE LEVELS AT ADMISSION

	PRESENT STUDY	**ABDUL HAMEED AI KASSIR STUDY 2012**	**ACUTE STROKE TREATMENT TRIAL**
MEAN RANDOM BLOOD GLUCOSE LEVELS AT ADMISSION	**183.06 + 35.99**	163 +40.3	144 + 68

The mean RBG on admission in the present study is higher compared to that of other studies.

NIHS SCORE:

NIHS score was more in stress hyperglycemia patients (cases) than normoglycemia Patients (control).

Mean NIHSS score on day 1 in cases was 12.208 ± 2.34 and in controls was 9.404 ± 1.59.

	STRESS HYPERGLYCEMIA	**NORMOGLYCEMIA**
MEAN NIHSS SCORE ON ADMISSION	12.208 ± 2.34	9.404 ± 1.59.

NIHSS Score on 7th day of admission was also high in stress hyperglycemic patients compared to normoglycemic patients.

	STRESS HYPERGLYCEMIA	**NORMOGLYCEMIA**
MEAN NIHS SCORE on 7th day	8.98 ± 2.17	4.62 ± 1.63

Mean NIHSS score on day 7 in cases was 8.98 ± 2.17 and in controls was 4.62 ± 1.63. This difference was statistically significant. I.e. cases had higher scores of NIHSS than controls.

FUNCTIONAL RECOVERY BASED ON DIFFERENCE IN NIHSS SCORE

Mean Difference in NIHSS score was 4.79 in Normoglycemic patients .

Mean difference in NIHSS score was 3.16 in stress hyperglycemic patients.

	STRESS HYPERGLYCEMIA	**NORMOGLYCEMIA**
MEAN DIFFERENCE IN SCORE	3.16	4.79

More the difference in NIHS score, better is the functional recovery. So, if we see difference in the NIHS score was more in normoglycemic patients (controls) when compared to that of stress hyperglycemic patients.

Hence functional recovery was more in normoglycemic patients than stress hyperglycemic patients.

	MEAN RBG ON ADMISSION	**NIHS SCORE ON DAY 1**	**NIHSS SCORE ON DAY 7**	**FUNCTIONAL RECOVERY(Difference between the score)**
STRESS HYPERGLYCEMIA	183.06 + 35.99	12.208 ± 2.34	8.98 ± 2.17	3.16
NORMOGLYCEMIA	121.55 ± 14.03	9.404 ± 1.59.	4.62 ± 1.63	4.79

OUTCOME

In 53 patients of stress hyperglycemia 5 patients had mortality.

Percentage of mortality was 9.4%.

There was no mortality in normoglycemic patients.

	PRESENT STUDY	KAMEL ABDELAZIZ MOHAMED STUDY 2013	SAGAR BABU STUDY 2006
MORTALITY RATE IN STRESS HYPERGLYCEMIA PATIENTS	9.4%	25.8%	89%

Mortality was less in our study because of adequate treatment of stress hyperglycemia with insulin since the time of admission.

NUMBER OF DEATHS	MEAN RBS ON ADMISSION IN THESE PATIENTS	MEAN FBS IN NEXT 24HRS IN THESE PATIENTS	MEAN PPBS IN NEXT 24 HRS IN THESE PATIENTS	MEAN GLYCATED HAEMOGLOBIN
5	255	157.4	190.8	5.02

All these 5 patients had high RBG, FBS and PPBS values

HbA1C was normal in these patients. Hence, this shows that stress hyperglycemia is associated with poor out come in terms of mortality compared to normoglycemic patients. Hence stress hyperglycemia has an impact on acute ischemic stroke patients and helps in accessing the prognosis in terms of functional recovery and outcome in terms of mortality.

It has been postulated that in cerebrovascular accidents an elevated blood glucose concentration is directly harmful to the ischemic brain.numerous studies have demonstrated that stress hyperglycemia augments extent of ischemic brain damage [74]

.mediated by anaerobic metabolism and consequent acidosis.hyperglycemia intensifies the risk of cerebral edema and mortality after stroke [71].this has given rise to the association between serum glucose concentration immediatedly after stroke and subsequent morbidity and mortality [71]

Williams et al 66 0ld stress hyperglycemia was present in 40% of patients at the time of admission ,hyperglycemia was an independent predictor of death at 30 days.

Hala El Kawas study found that Acute hyperglycemia predicts increased risk of poor neurological and functional outcome. Measures to normalize blood glucose level in the setting of acute stroke could be of value in improving stroke outcome [39].

Sagarbasu study suggested with high sugar level as marker stroke severity [90].

Bogdan timar study in 2013 concluded thatType2DM is a major risk factor for stroke. Plasma glucose level at admission was correlated positively with stroke mortality, both in patients with T2DM and in those without previously diagnosed Type2DM.[91]

CONCLUSION

The maximum number of patients in the present study were in the age group between 71 to 80 years. Male patients were of 58% and female patients were of 42%. The male: female ratio (M:F ratio) is 1.38: 1. Stress hyperglycemia was noted in 53 patients and 47 patients were normoglycemics. Functional recovery (based on difference in then NIHSS score on day one and 7^{th} day) was more in the normoglycemia patients compared to the stress hyperglycemic patients.

There was mortality in 5 patients (9.4%) with stress hyperglycemia patients.There was no mortality in normoglycemic patients. This suggest a possible association between stress hyperglycemia and bad outcome with stroke. Functional recovery and Outcome was better in our study compared to other study because of adequate treatment of stress hyperglycemia with insulin.

SUMMARY

100 Patients with CT evidence of acute ischaemic stroke meeting the inclusion and exclusion criteria's admitted to R.L, JALAPPA Hospital and Research center attached to Sri Devaraj Urs Medical college,Tamaka,Kolar during may 2014 to September 2015 were included in the study .The data was collected based on detailed history and clinical examination .

The condition of the patient was assessed on admission and 7^{th} day using NIHS scale (National Institute Of Health Stroke scale) . Functional recovery was assessed based on the difference between the score on admission and discharge. Functional recovery of the patient was correlated with random blood glucose levels.

In our study male subjects were more (58%) compared to female subjects (42%).Male is to female ratio is M:F-1.38:1.Mean difference in NIHSS score was 3.16 in stress hyperglycemia patients and 4.79 in normoglycemia patients. This shows that functional recovery which is assessed based on the difference between the NIHSS scores was better in normoglycemia patients than compared to stress hyperglycemia patients. The mean RBG levels in patients who had mortality was 255mg/dl. So outcome was also better in normoglycemia patients compared to stress hyperglycemia patients.

Hence Stress hyperglycemia has a positive impact on functional recovery and outcome in acute ischemic stroke patients.

BIBILOGRAPHY

1. Kannel WB, McGee DL. Diabetes and cardiovascular disease- The Framingham study.J.Aim. Med.Assn .1979 ; 241: 2035-2038
2. Allen HR. cerebrovascular diseases . In :Raymond DA , Maurice v Eds.PRINCIPLES OF Neurology. 6th Ed 1997 McGraw Hill publications: 777-873
3. Umpierrez GE, Issac SD , Bazargan n, You X ,Thaler LM, kitabchi AE. Hperglycemia : An independent marker of in hos[ital mortality in patients with undiagnosed diabetes J clin Endocrinal Metab 2002; 87(3) : 978-982
4. Toni D,Sacchetti ML, Argentino C,Gentile M,cavalleti c, Frontoni m et al. does hyperglycemia play a role in outcome of acute ishemic stroke patients? J neural 1992; 239:382-386
5. Bruno A , Levine SR, Frankel MR, Brott TG ,lin Y, Tilley BC , Lyden PD et al . Admission glucose level and clinical outcomes in NINDS rt-PA stoke Trial. NEUROLOGY 2002;59:669-674
6. Melamed E. Reactive hyperglycemia in patients with acute stroke j Neurol Sci 1976 ; 29 : 267-275
7. Mankovsky BN, Metzger BE, Molitch ME, Biller J. Cerebrovascular disorders in patients with diabetes milletus . • J Diabetes Complications 1996; 10: 228-242.
8. Scott JF, Robinson GM, Fre neh JM, O'Connell JE, Alberti KGMM, GRAY CS. Prevalence of admission hyperglycemia across clinical su types of acute stroke. Lancet. 1999; 353:376-377
9. Kitabchi AE, Umpierrez GE, Murphy MB. Management of hyperglycemic crises in patients with diabetes. Diabetes Care 2001; 24(1): 131-153.

10. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. Stroke 2001; 32(10): 2426-2432.
11. Falciglia M, D'Alessio DA, Almenoff PL, Freyberg RW, Diab D, Render ML. Hyperglycemia and mortality in 252,000 critically ill patients In: abstract 3-LBCS. 66th Annual Scientific Sessions. Washington, DC: June 9-13, 2006.
12. The NIH stroke scale: a window into neurological status. Nurse.Com Nursing Spectrum (Greater Chicago) [serial online]. September 12, 2011;24.
13. Allen HR. Cerebrovascular diseases In: Raymond DA, Maurice V Eds. Principles of neurology. 6th Ed 1997. McGraw Hill Publications: 777 — 873.
14. Dalai. Current concepts in stroke 2015.Association of physicians of India.
15. Smith-WS, Claiborne JS. Donald JE. Cerebrovascular diseases . In: Anthony SF, Eugene B Eds Harrison's principles of internal medicine. 16th Ed 2005. McGraw Hill publication2373 -2393.
16. Donald JE. Cerebrovascular diseases . In: Anthony SF, Eugene B Eds Harrison's principles of internal medicine. 19th Ed 2015. McGraw Hill Publications : 2373 - 2393.
17. Feigin VL, Lawes CM, Bennett DA, Anderson CS. Stroke epidemiology: a review of population based studies of incidence , prevalence, and case-fatality in the late 20th century. Lancet Neurol 2003; 2: 43-53.
18. Norrving B. Long term prognosis lacunar infarction.Lancet Neurol 2003:2;238-45
19. Hacks w, Schwab S, Horn M, Spranger M, De Georgia M, v on Kummer R. 'Malignant' middle cerebral artery infarction: clinical course and prognostic signs. Arch Neurol 1996 ;53: 309-15.

20. Kannel WB. Epidemiology of Cerebrovascular diseases. Churchill Livingstone. Edinburgh 1983:1
21. Jain S, maheshwari MC cerebrovascular diseases- A review of the Indian experience in the last 35 years.Neuroepidemology 1986:5;1-16
22. Dhamija. Prevalence of stroke in rural India, JAPI 1997 45(11): 902.
23. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol. 2007 Feb;6(2):182–7.
24. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 populationbased studies: a systematic review. Lancet Neurol. 2009 Apr;8(4):355–69.
25. Bonita R, Beaglehole R. Stroke prevention in poor countries. Time for action. Stroke. 2007 Nov;38(11):2871–2.
26. Mackay J, Mensah G. The Atlas of Heart Disease and Stroke. Geneva: World Health Organization; 2004.
27. Mathers CD, Loncar D. Projections of Global Mortality and Burden of Disease from 2002 to 2030. PLoS Med [Internet]. 2006 Nov 28 [cited 2010 Jan 22];3(11)
28. Fratiglioni. Mortality from cerebrovascular disease. Neuroepidemiology 1983; 2: 101¬116.
29. Kagan. Dietary and other risk factors for stroke in Hawaiian Japanese men. Stroke 1985; 16(3): 390-396.
30. Balarajan R. Ethnic differences in mortality from ischaemic heart disease and cerebrovasular disease in England & Wales. BMJ 1991; 302 : 560 - 4.
31. Abraham J. An epidemiological study of hemiplegia due to stroke in South India. Stroke 1970; 1: 477 – 81

32. Snell RS. Blood supply of the brain In: Clinical neuranatomy for medical students 2nd Ed, Little Brown Publication: 507 – 530
33. Recommendation on stroke prevention, diagnosis and therapy. Special report from WHO stroke 1989;1407-1431.
34. Nagaraja P pratap CR prognostic factors in cerebral infarction .NIMHANS journal july 1983;1(2);141-144
35. Bamford J. Sandercock P. A prospective study of acute cerebrovascular disease in community - The Oxfordshire community stroke project 1981-1986 J of neurol Neurosurg and Psych 1990;53: 16 - 22.
36. Jorgen M. Natural history and prognosis ©f cerebrovascuiar diseases. Churchill Livingstone, Edinburgh; 1983 : 25.
37. Outcome of critically ill hyperglycemic stroke patients admitted to the intensive care unit Kamel Abdelaziz Mohameda, Ahmad Saadb Departments of Critical Care, bInternal Medicine, Faculty of Medicine, Cairo University, Cairo, Egypt 2013
38. The incidence of stress hyperglycemia in acute ischemic stroke patients (in Al-Yarmouk teaching hospital) Abdul- Hameed Al-Kassir1 FICMS, Zaid Tarik2 MBChB, MD Department of Internal Medicine, College of Medicine, Al-Mustansiriya University, Baghdad, Iraq2Department of Internal Medicine, Al-Yarmouk Teaching Hospital, Baghdad, Iraq 2011
39. Admission Hyperglycemia in Acute Ischemic Stroke: Effects on Short Term Prognosis Hala El-Khawas, Ayman Nasef, Ahmed Gaber and Hany Zaki Department of Neurology, Ain Shams University (Egypt J. Neurol. Psychiat. Neurosurg., 2006, 43(1): 603-613)
40. Nayak DS, Nair M,Radhakrishnan K, Sarma P S . Ischaemic stroke in the young adult clinuical features, risk factors and outcome. NMJ1 1997 10 (3): 107-111.

41. Epidemiology of stroke. Advances in neurology; 19: 299 - 310.
42. Reed DM, Resch JA, Hayashi T. A prospective study of cerebral artery atherosclerosis. stroke 1988; 19: 820
43. .RusselRWR. Observation in intracerebral aneurysms. Brain 1963; 86: 425.
44. sharper AG, Philips AN , Pocock SE Risk factor for stroke in middle aged British men BMJ, 1991; 302: 1 1 1 1 - 1 1 15.
45. Stephen MM. Prolonged diff in blood press-prospective observational studies corrected for regressiom dilution bias.lancet 1990,325;765-974
46. Nagaraja P pratap CR prognostic factors in cerebral infarction .NIMHANS journal july 1983;1(2);141-144
47. Cerebrovascular diseases prevention, treatment and rehabilitation. WHO technical report series;469.
48. Ashok Cerebrovascular disease in the community. Results of a WHO collaborative study Bulletin of WHO 1980; 58(1): 113-130.
49. Gray CS, Taylor R. The prognostic value of stress hyperglycemia and previous unrecognised diabetes in acute stroke. Diabetic medicine 1987; 4: 237-40.
50. Fisher M, Adams RD. Observation on brain embolism with special reference to mechanism of hemorrhagic infarction. J of neuropathology and experimental neurology.1951; 10: 92 - 94.
51. Colandrea MA, Friedman GP. Systolic hypertension in the elderly. An epidemiology assessment. Circulation 1970; 41: 239.
52. Tharakar J, Ahuja GK. Mitral valve prolapse and cerebrovascular accidents in the young. Acta neuro Scandinavia 1982; 66: 295 – 30.
53. Sridharan R. Risk Factors for Ischeinic Stroke. A Case Control Analysis. ,Neuroepidemiology 1992;11:24-30.

54. Denis M, Bamford J, Sandercock P. Prognosis of TIAs in Oxfordshire community stroke project. Stroke 1990; 21 (6): 848 - 53.

55. Wiebers DO, Whishnant JP. Prospective comparison of a cohort with symptomatic carotid bruit population based cohort withcarotid bruit. Stroke 1990; 21: 984.

56. Mohr JP, Caplan CR. The Harward cooperative stroke registry. A prospective registry neurology 1978; 28: 754.

57. Chopra J S, Prabhakar S . Clinical features and risk factors in stroke in young. ACTA, Neur. 1979 ;60 : 289 – 300.

58. Agarwal JK, Sornani PN. A study of risk factors in non embolic cerebrovascular disease. Neurology 1976; 24: 125 - 133.

59. Kannel Wi3 Gordon T. Hemoglobin and risk of cerebral infarction. frarningham study 1972; 3: 409

60. Thomas D j, Marshall J. Effect of hematocrit on cerebral blood flow in man. Lancet 1977; 2: 941 .

61. Dalai PM. Low hemoglobin level as a risk factor in cerebral infarction. Stroke 1989: - 20,

62. Wade JPH. Hemoglobin concentration and prognosis in symptomatic obstructive C Stroke 1987; 18: 68-71

63. Gorelick PB, Rodin MB, Langenberg P.Weekly alcohol consumption, cigarette smoking and the risk of ischaemic stroke. Neurology 1989; 39: 339.

64. Kagan A, Popper JS. Rhoads GC. Factors related to stroke incidence in Hawaii Japanese men: The Honolulu heart study. Stroke 1980; 11: 14.

65. Kozararevic DJ, MeGee D, Vojvodic N. Frequency of alcohol consumption and morbidity and mortality: The Yugoslavia cardiovascular disease study. Lancet 1980; 1: 613.

66. Siesjo BK. Cerebral circulation and metabolism. .J of neurosurgery 1984 ; 60:883-908
67. Els T. Hyperglycemia delays terminal depolarization and enhances repolartsation after peri_infarct spreading depression as measured by serial diffusion MR imaging.! Cerebral bloodflow and metabolism 1997;17:591- 5.
68. Wagner KR. Hyperglycemia versus norrnoglycemic stroke. Topography of brain .metabolites, intracellular pH and infarct size. J cerebral blood flow metab 1992; 12: 213-22
69. Siesjo BK et al. Acid - base changes in complete brain ischaemia. Stroke 1990; 21:194-8
70. Jose B, Love BB. Diabetes & stroke MCNA Jan 1993; 77: 95-111
71. Fothergroval J. Focal and perifocal changes in tissue energy state during MCA occlusion in normo and hyperglycemic rats. CBF and metabolism 1992; 12:25-33.
72. Siesjo K Kastura KI T. Kristian T. Acidosis related damage. Advances in neurology Vol:71:1111-6.
73. Araki N, Greenberg' J11. The effect of hyperglycemia on intracellular calcium in stroke. I. of CBF metabolism 1992; 12 (3):472-476.
74. Candelise L. Landi G. Prognostic significance of hyperglycemia in acute stroke. Archives of neurology 1985 ; 42: 661 - 663.
75. O'Neill PA, Davies I. Stress hormones and bloodglucose response following acute stroke in the elderly. Stroke 1991; 22: 842 – 847.
76. Kooten FV, Hoogerbrugge N. Hyperglycemia in acute phase of stroke is not caused by stress. Stroke 1993; 24{8): 412-417.
77. Aubert RE, Geiss LS, Ballard DJ, Cocanougher B, Herman WH. Diabetes-relate - hospitalization and hospital utilization. In: Diabetes in America. 2nd ed. Bethesda, M 'Cational Diabetes Information Clearinghouse; 1995:553-570.

78. Garber AJ, Moghissi ES, Bransome ED Jr, et al. American College of Endocrinology position statement on inpatient diabetes and metabolic control. Endocr Pr-act 2004;10(1);77-82

79. National Diabetes Surveillance System. Centers for Disease Control and Prevention. www.cdc. go v/di abetes/statistics/dmany/figl.htm

80. umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitahchi Hyperglycemia: an independent .marker of in-hospital mortality in patients with undiagnosed diabetes. J Clin Endocrinol Metab. 2002; 87(3): 978-982.

81. Melamed E. Reactive hyperglycaemia in patients with acute stroke. J Neurol Sci 1976;

82. Peterson P and Godtfredson J. Embolic complications in paroxysmal atrial fibrillation stroke 1986;17;622.

83. American Diabetes Association. Standards of medical care in diabetes-2006. Diabetes care 2006;29(supp 1);S4-S42.gty.

84. Greci LS, Kailasam M, Malkani S . Utility of HbA(1c) levels for diabetes case finding in hospitalized patients with hyperglycemia. Diabetes Care 2003; 26(4).

85. Bruno A, Biller J, Adams HP, Clarke WR, Woolson RF, Williams LS et al. Acute bloo, glucose level and outcome from ischaemic stroke: Trial of ORG 10172 in Acute Strok Treatment (TOAST) Investigators. Neurology 1999; 52: 280-284.

86. Demchuk AM, Morgenstern LB, Krieger DW, Linda Chi T, Hu W, Wein TH. Serum glucose level and diabetes predict tissue plasminogen activator-related intracerebral hemorrhage in acute ischaemic stroke. Stroke 1999; 30: 34-39.

87. Kiers L, Davis SM, Larkins R, Hopper J, Tress B, Rossiter SC. Stroke topography an outcome in relation to hyperglycaemia and diabetes. J Neurol Neurosurg Psychiatry 1992: 55: 263-270.

88. Parsons M, Barber P, Desmond P, Baird T, Darby D, Byrnes G et al. Acute hyperglycemia adversely affects stroke outcome: a magnetic resonance imaging an(spectroscopy study. Ann Neurol 2002; 52: 20-28.
89. Admission Hyperglycemia in Acute Ischemic Stroke: Effects on Short Term Prognosis Hala El-Khawas, Ayman Nasef, Ahmed Gaber and Hany Zaki Department of Neurology, Ain Shams University (Egypt J. Neurol. Psychiat. Neurosurg., 2006, 43(1): 603-613
90. Is post-stroke hyperglycemia a marker of stroke severity and prognosis: A pilot study Sagar BASU, *Debashish SANYAL *K ROY KB BHATTACHARYA MD, DMBangur Institute of Neurology, Kolkata; *Calcutta National Medical College & Hospitals, Kolkata, India Neurology Asia 2007; 12 : 13 – 19
91. RELATIONSHIP BETWEEN BASAL PLASMA GLUCOSE LEVELS AND RECOVERING PROSPECTIVE OF PATIENTS WITH ACUTE STROKE Simona Popescu ,Bogdan Timar, Corresponding author Mihaela Simu Romulus Timar Victor Babeș University of Medicine and Pharmacy, Timișoara, Emergency Clinical Hospital Timisoara 2013
92. Perner A, Nielsen SE, Rask-Madsen J. High glucose impairs superoxide production from isolated blood neutrophils. Intensive Care Med.2003; 29:642-5
93. Khaodhiar L, McCowen K, Bistrian B. Perioperative hyperglycemia, infection or risk. Curr Opin Clin Nutr Metab Care. 1999;2:79-82.
94. Sarkar RN, Banerjee S, Basu A. Comparative evaluation of diabetic and non-diabetic stroke –Effect of glycemia on outcome. J Indian Med Assoc 2004;102(10): 551-3.
95. Mostafa SA, Davies MJ, Srinivasan BT, Carey ME, Webb D, Khunti K. Should glycated haemoglobin (HbA1c) be used to detect people with type 2 diabetes mellitus and impaired glucose regulation?. Postgrad Med J 2010;86:656-62.

96. Greci LS, Kailasam M, Malkani S . Utility of HbA(1c) levels for diabetes case finding in hospitalized patients with hyperglycemia. Diabetes Care 2003; 26(4).

97. Levine SR, Welch KM, Helpern JA, Chopp M, Bruce R, Selwa J, et al. Prolonged deterioration of ischemic brain energy metabolism and acidosis associated with hyperglycemia: human cerebral infarction studied by serial 31P NMR spectroscopy. Ann Neurol.1988; 23: 416–8.

98. Siesjö BK, Bendek G, Koide T, Westerberg E, Wieloch T. Influence of acidosis on lipid peroxidation in brain tissues in vitro. J Cereb Blood Flow Metab.1985; 5: 253–8

99. Anderson RE, Tan WK, Martin HS, Meyer FB. Effects of glucose and PaO2 modulation on cortical intracellular acidosis, NADH redox state, and infarction in the ischemic penumbra. Stroke 1999; 30: 160–70.

100. Olsen TS, Larsen B, Herning M, Skriver EB, Lassen NA. Blood flow and vascular reactivity in collaterally perfused brain tissue: evidence of an ischemic penumbra in patients with acute stroke. Stroke. 1983; 14: 332–41.

101. Steinberg HO, Tarshoby M, Monestel R, Hook G, Cronin J, Johnson A, et al. Elevated circulating free fatty acid levels impair endothelium-dependent vasodilation. J Clin Invest.1997; 100: 1230

102. Glycemic control in non-diabetic critically ill patientsFarnoosh Farrokhi, MD, Fellow of Endocrinology 1, Dawn Smiley, MD, Assistant Professor of Medicine 2, Guillermo E. Umpierrez, MD, Professor of Medicine *Department of Medicine, Division of Endocrinology, Emory University School of Medicine, 49 Jesse Hill Jr Dr. Atlanta, GA 30303, USA

103. Gerstein HC, Yusuf S. Dysglycaemia and risk of cardiovascular disease. Lancet. . 1996; 347: 949–50.

104. Coutinho M, Gerstein HC, Wang Y, Yusuf S. The relationship between glucose and incident cardiovascular events: a metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. Diabetes Care.1999; 22: 233–40.

105. Alex M, Baron EK, Goldenberg S, Blumenthal HT. An autopsy study of cerebrovascular accident in diabetes mellitus. Circulation.1962; 25: 663–73.

106. Salonen R, Salonen JT. Determinants of carotid intima media thickness: a population based ultrasonography study in eastern Finnish men. J Intern Med.1991; 229: 225–31

107. Dietrich WD, Alonso O, Busto R. Moderate hyperglycemia worsens acute blood-brain barrier injury after forebrain ischemia in rats. Stroke.1993; 24: 111–6.

108. DeCourten-Myers GM, Kleinholz M, Holm P, DeVoe G, Schmitt G, et al. Hemorrhagic infarct conversion in experimental stroke. Ann Emerg Med.1992; 21: 121–6.

109. Demchuk AM, Morgenstern LB, Krieger DW, Chi TL, Hu W, Wein TH, et al. Serum glucose level and diabetes predict tissue plasminogen activator–related intracerebral hemorrhage in acute ischemic stroke. Stroke.1999; 30: 34–9.

110. Czlonkowska A, Ryglewicz D, Lechowicz W. Basic analytical parameters as the predictive factors for 30-day case fatality rate in stroke. Acta Neurol Scand.1997; 95: 121–4.

111. Knobler H, Savion N, Shenkman B, Kotev-Emeth S, Varon D: Shear-induced platelet adhesion and aggregation on subendothelium are increased in diabetic patients. Thromb Res 1998; 90:181–90.

112. Kado S, Nagase T, Nagata N: Circulating levels of interleukin-6, its soluble receptor and interleukin-6 /interleukin-6 receptor complexes in patients with type 2 diabetes mellitus. Acta Diabetol 1999; 36:67–72.

113. Brodsky SV, Morrishow AM, Dharia N, Gross SS, Goligorsky MS: Glucose scavenging of nitric oxide. Am J Physiol Renal Physiol 2001; 280:480–6.

114. Managementof hyperglycemia in acute ischemic stroke.Baker L,Juneja R,BronoA 2011 Dec;13(6) : 616-28.

115. Abraham. Prevalence studies in stroke.Stroke 1970; 1:477.

ANNEXURES

STRESS HYPERGLYCEMIA AS A PROGNOSTIC MARKER IN ACUTE ISCHAEMIC STROKE .

PROFORMA

Name of the patient:

Age:

Occupation:

Address:

HOSPITAL NO.:

Sex:

Socio economic status**:**

History of presenting illness:

Past history:

History of diabetes mellitus:

History of hypertension:

History of TIA:

Family history:

Personal history:

Treatment history:

General physical examination:

Vitals:

Neurological status assessment using National institute of health stroke scale:

NIHSS Score on day 1:

NIHSS Score on day 7:

Other systemic examination:

Investigations:

Ct scan of brain:

RBG on admission:

FBS in 24hrs:

PPBS in 24hrs:

HbA1c:

RBG on day 7^{th}/discharge:

ANNEXURE 1

NATIONAL INSTITUTE OF HEALTH STROKE SCALE [NIHSS] :

- The NIHSS is composed of 11 items, each of which scores a specific ability between a 0 and 4. For each item, a score of 0 typically indicates normal function in that specific ability, while a higher score is indicative of some level of impairment.
- The individual scores from each item are summed in order to calculate a patient's total NIHSS score. The maximum possible score is 42, with the minimum score being a 0.
- It includes the following :

1. Level of Consciousness

A) LOC Responsiveness:

Score	Test Results
0	Alert; Responsive
1	Not alert; Verbally arousable or aroused by minor stimulation to obey, answer, or respond.
2	Not alert; Only responsive to repeated or strong and painful stimuli
3	Totally unresponsive; Responds only with reflexes or is areflexic

B) LOC Questions:

Score	Test Results
0	Correctly answers both questions
1	Correctly answers one question
2	Does not correctly answer either question

C) LOC Commands

Score	Test Results
0	Correctly performs both tasks
1	Correctly performs 1 task
2	Does not correctly perform either task

2. Horizontal Eye Movement

Score	Test Results
0	Normal; Able to follow pen or finger to both sides
1	Partial gaze palsy; gaze is abnormal in one or both eyes, but gaze is not totally paralyzed. Patient can gaze towards hemisphere of infarct, but can't go past midline
2	Total gaze paresis; gaze is fixed to one side

3. Visual field test :

Score	Test Results
0	No vision loss
1	Partial hemianopia or complete quadrantanopia; patient recognizes no visual stimulus in one specific quadrant
2	Complete hemianopia; patient recognizes no visual stimulus in one half of the visual field
3	Bilateral Blindness, including blindness from any cause

4. Facial Palsy

Score	Test Results
0	Normal and symmetrical movement
1	Minor paralysis; function is less than clearly normal, such as flattened nasolabialfold or minor asymmetry in smile
2	Partial paralysis; particularly paralysis in lower face
3	Complete facial Hemiparesis, total paralysis in upper and lower portions of one face side

5. Motor Arm

Score	Test Results
0	No arm drift; the arm remains in the initial position for the full 10 seconds
1	Drift; the arm drifts to an intermediate position prior to the end of the full 10 seconds, but not at any point relies on a support
2	Limited effort against gravity; the arm is able to obtain the starting position, but drifts down from the initial position to a physical support prior to the end of the 10 seconds
3	No effort against gravity; the arm falls immediately after being helped to the initial position, however the patient is able to move the arm in some form (e.g. shoulder shrug)
4	No movement; patient has no ability to enact voluntary movement

6. motor Leg :

Score	Test Results
0	No leg drift; the leg remains in the initial position for the full 5 seconds
1	Drift; the leg drifts to an intermediate position prior to the end of the full 5 seconds, but at no point touches the bed for support
2	Limited effort against gravity; the leg is able to obtain the starting position, but drifts down from the initial position to a physical support prior to the end of the 5 seconds
3	No effort against gravity; the leg falls immediately after being helped to the initial position, however the patient is able to move the leg in some form (e.g. hip flex)
4	No movement; patient has no ability to enact voluntary movement in this leg

7. Limb Ataxia:

Score	Test Results
0	Normal coordination; smooth and accurate movement
1	Ataxia present in 1 limb; rigid and inaccurate movement in one limb
2	Ataxia present in 2 or more limbs: rigid and inaccurate movement in both limbs on one side

8. Sensory:

Score	Test Results
0	No evidence of sensory loss
1	Mild-to-Moderate sensory loss; patient feels the pinprick, however he or she feels as if it is duller on one side
2	Severe to total sensory loss on one side; patient is not aware he or she is being touched in all unilateral extremities

9. Language:

Score	Test Results
0	Normal; no obvious speech deficit
1	Mild-to-moderate aphasia; detectable loss in fluency, however, the examiner should still be able to extract information from patient's speech
2	Severe aphasia; all speech is fragmented, and examiner is unable to extract the figure's content from the patients speech.
3	Unable to speak or understand speech

10. SPEECH

:Score	Test Results
0	Normal; clear and smooth speech
1	Mild-to-moderate dysarthria; some slurring of speech, however the patient can be understood
2	Severedysarthria; speech is so slurred that he or she cannot be understood, or patients that cannot produce any speech

11. Extinction and Inattention:

Score	Test Results
0	Normal; patient correctly answers all questions
1	Inattention on one side in one modality; visual, tactile, auditory, or spatial
2	Hemi-inattention; does not recognize stimuli in more than one modality on the same side

INFORMED CONSENT FORM

Name of the investigator: Dr. Sandeep Reddy Adam

Name of the organization: R L Jalappa Hospital and Research centre

attached to Sri Devaraj Urs Medical College

Name of the participant: Sl no:

Stress hyperglycemia as a prognostic marker in acute ischemic stroke :

I/we the patients attenders have been invited to take part in this research study. The information in this document is meant to help me to decide whether or not to take part.

I / we have clarified my doubts regarding this study with the principal investigator.

I /we the patients attenders have been asked to participate in this study because I satisfy the eligibility criteria

I/we the patients attenders request and authorize Dr. Sandeep Reddy Adam to perform the designated tests for my blood sample. My signature below constitutes my acknowledgment that the benefits, risks and limitations of this testing have been explained to my satisfaction by a qualified health professional.

Participation is totally voluntary and there would be no payment for sample collection. All test results are treated with medical confidentiality and will not be disclosed to any outsider except if it is required by the law.

I/we the patients attenders give consent to allow my sample to be used for medical research, test validation or education as long as my privacy is maintained

I/we the patients attenders understand that I remain free to withdraw from this study at any time and this will not change my future care.

I/we the patients attenders have read and understand the information provided in this document.

I /we the patients attenders have had the opportunity to ask questions I might have about the testing, the procedure, the associated risk and alternatives.

Subject name and signature/ Thumb impression DATE:

Parents/Guardian's name and signature/thumb impression DATE:

Signature of the person taking the consent DATE:

MASTER CHART

Sl no.	Hospital no.	Age in years	sex	RBS on day of admission	FBS in next 24 hrs	PPBS	Glycated Hb%	RBS on 7th day	NIHS scale on day 1	NIHS scale on day 7	Difference of score
1	1020810	46 yrs	Female	130	110	132	5.4	128	9	4	5
2	104419	70 yrs	Male	150	136	160	5	145	15	11	4
3	129313	43 yrs	Female	147	135	150	5.8	145	14	12	2
4	130346	65 yrs	Female	170	140	156	5.5	170	12	10	2
5	107476	70 yrs	Male	170	155	176	5.9	165	13	9	4
6	130622	75 yrs	Female	145	130	140	4.9	139	10	6	4
7	109965	29 yrs	Male	135	115	130	5.6	130	9	4	5
8	133152	60 yrs	Female	169	140	180	6	170	10	7	3
9	135162	76 yrs	Male	199	130	150	5.9	170	9	7	2
10	137050	70 yrs	Female	127	116	145	5.3	130	8	3	5
11	144467	70 yrs	Female	129	105	136	5.5	125	8	4	4
12	110405	67 yrs	Male	159	135	160	5.7	162	10	7	3
13	111329	75 yrs	Male	144	129	140	5	135	9	5	4
14	146826	48 yrs	Female	137	110	139	4.9	132	9	3	6
15	146866	62 yrs	Female	150	130	152	5.4	146	14	9	5
16	148153	80 yrs	Female	133	110	140	5.5	126	9	3	6
17	1021426	73 yrs	Female	198	140	200	5.7	170	13	10	3
18	113804	60 yrs	Female	136	122	145	5.6	130	10	6	4
19	114244	65 yrs	Male	170	140	167	5.7	166	16	12	4
20	115594	76 yrs	Male	186	130	175	5	160	10	8	2
21	117400	60 yrs	Male	129	116	130	4.9	120	11	6	5
22	148691	50 yrs	Female	135	120	139	5	130	10	5	5
23	149030	82 yrs	Female	201	118	165	5.5	170	13	10	3
24	159838	70 yrs	Female	220	130	190	5.8	186	15	12	3
25	119933	78 yrs	Male	156	120	165	5.6	140	16	13	3
26	10887	52 yrs	Male	133	110	140	5	137	9	6	3
27	125296	88 yrs	Male	122	116	139	5.2	130	9	5	4
28	129212	50 yrs	Male	169	140	165	5.8	160	6	3	3
29	130703	20 yrs	Male	110	110	125	5	108	12	6	6
30	130779	52 yrs	Male	190	135	189	5.5	144	10	7	3
31	166245	99 yrs	Female	157	129	140	5.7	132	13	10	3
32	168033	47 yrs	Female	160	127	165	5	130	10	8	2
33	171241	45 yrs	Female	133	126	135	5.3	120	6	2	4
34	132579	94 yrs	Male	130	117	132	5.3	131	15	11	4
35	131317	52 yrs	Male	198	130	201	5.6	160	13	10	3
36	133396	89 yrs	Male	155	120	149	5.2	130	14	9	5
37	133851	60 yrs	Male	132	120	140	5.1	126	10	5	5
38	17349	65 yrs	Female	187	125	156	5.2	145	10	8	2
39	131791	63 yrs	Male	149	129	152	5.5	138	8	6	2
40	137321	68 yrs	Male	160	130	154	5	140	15	11	4
41	174643	35 yrs	Female	130	122	136	5	130	8	3	5
42	186574	68 yrs	Female	109	115	129	4.5	110	9	5	4
43	140343	50 yrs	Male	194	130	152	6.1	154	12	10	2
44	141863	72 yrs	Male	111	118	130	5.4	120	10	5	5
45	146291	58 yrs	Male	201	126	159	5.9	166	10	7	3
46	191515	80 yrs	Female	149	116	135	5	130	16	10	6
47	146767	57 yrs	Male	190	130	189	5.8	146	9	6	3
48	197644	63 yrs	Female	126	120	146	5.2	130	8	3	5
49	150510	60 yrs	Male	159	126	145	5.4	139	12	9	3

MASTER CHART

50	153548	65 yrs	Male	126	110	140	5.1	130	8	4	4
51	199991	75 yrs	Female	134	126	149	5.25	130	10	6	4
52	56227	65 yrs	Male	199	130	186	5.59	168	16	12	4
53	158042	65 yrs	Male	201	132	190	5.12	152	12	9	3
54	1021622	59 yrs	Male	106	110	149	4.92	110	8	3	5
55	159884	48 yrs	Male	123	115	137	5.04	122	10	5	5
56	166782	60 yrs	Male	127	120	144	5.75	135	12	8	4
57	141648	38 yrs	Female	196	150	198	5.9	D	14	D	D
58	113433	62 yrs	Female	117	120	135	5.6	126	11	5	6
59	83140	73 yrs	Female	144	126	159	5.72	139	10	7	3
60	98855	60 yrs	Male	151	130	169	6.1	142	11	7	4
61	106296	60 yrs	Female	89	90	120	5	90	8	3	5
62	91471	80 yrs	Female	162	130	190	6.2	143	11	8	3
63	81674	38 yrs	Female	225	150	184	6.2	170	14	11	3
64	167181	43 yrs	Male	197	134	186	5.35	162	12	9	3
65	171627	75 yrs	Male	245	137	165	5.45	D	14	D	D
66	180403	49 yrs	Male	129	119	147	5.12	130	10	5	5
67	65739	60 yrs	Female	142	120	167	5.75	139	12	9	3
68	17236	70 yrs	Male	335	153	169	5.3	D	15	D	D
69	36248	58 yrs	Male	131	112	140	4.98	126	10	5	5
70	41519	60 yrs	Male	216	135	160	5.4	170	12	8	4
71	23165	75 yrs	Male	87	109	120	5.1	100	9	4	5
72	34071	60 yrs	Female	79	100	120	5	100	10	6	4
73	38382	80 yrs	Female	142	122	145	5.9	130	13	9	4
74	29785	79 yrs	Female	121	109	154	5.8	135	12	6	6
75	55176	65 yrs	Female	135	129	145	5.3	134	12	8	4
76	50072	45 yrs	Male	130	120	159	5.12	140	10	5	5
77	29464	65 yrs	Male	204	181	207	5.9	170	15	12	3
78	68974	55 yrs	Female	112	114	145	5.7	120	8	3	5
79	48605	75 yrs	Male	274	200	225	5.75	D	14	D	D
80	53415	64 yrs	Male	171	120	170	5.65	145	12	8	4
81	51391	72 yrs	Male	137	124	165	5.2	129	10	5	5
82	84366	32 yrs	Male	96	110	144	4.98	110	12	6	6
83	181915	75 yrs	Male	170	130	196	5.52	162	10	7	3
84	182909	75 yrs	Male	126	113	154	5.7	130	8	4	4
85	183843	75 yrs	Female	130	129	148	4.75	127	8	3	5
86	186187	75 yrs	Male	179	124	187	5.32	150	10	7	3
87	187076	60 yrs	Female	109	122	147	5.42	126	9	5	4
88	189027	45 yrs	Male	121	118	139	5	127	8	4	4
89	195734	65 yrs	Male	155	116	147	5.7	130	12	9	3
90	197110	35 yrs	Male	112	120	144	5.2	124	10	4	6
91	199589	60 yrs	Female	199	140	187	5.75	135	10	8	2
92	206631	75 yrs	Male	101	120	146	5	120	9	4	5
93	209161	85 yrs	Male	120	117	136	5.4	129	8	3	5
94	206841	65 yrs	Female	235	145	184	5.7	D	13	D	D
95	197170	45 yrs	Male	134	115	149	5.2	129	9	4	5
96	187176	54 yrs	Male	122	119	147	4.8	130	8	4	4
97	181413	50 yrs	Female	213	150	198	5.9	160	15	12	3
98	181995	70 yrs	Female	122	120	159	5	128	8	3	5
99	186584	65 yrs	Male	225	147	197	5.95	150	12	9	3
100	209853	50 yrs	Male	110	120	155	5.5	115	8	3	5