A STUDY OF SERUM URIC ACID LEVELS IN A SETTING OF ACUTE ISCHEMIC STROKE IN GOVERNMENT VELLORE MEDICAL COLLEGE AND HOSPITAL, VELLORE

A DISSERTATION SUBMITTED TO

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

In partial fulfilment of the regulations for the award of the degree of

M.D. GENERAL MEDICINE – BRANCH I

DEPARTMENT OF GENERAL MEDICINE

GOVERNMENT VELLORE MEDICAL COLLEGE AND HOSPITAL

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI

MAY 2018

ETHICAL COMMITTEE CERTIFICATE

INSTITUTIONAL ETHICAL COMMITTEE

APPROVAL CERTIFICATE

GOVT. VELLORE MEDICAL COLLEGE, VELLORE-11

Title of the Study	–	A study of serum uric acid levels in a setting of acute ischemic stroke in G.V.M.C.H.
Principal Investigator	–	Dr.S.Nethaji.,
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The request for an approval from the Institutional Ethical committee (IEC) was considered on the IEC meeting held on 06.10.2016 at the Conference Hall, Govt. Vellore Medical College, Vellore-11.

The members of the committee, the secretary, the convenor and the president are pleased to approve the proposed work mentioned above submitted by the Principal Investigator.

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Intrkraniell blödning efter ischemisk stroke.docx (D12333520)
CNU-S-16-00112.pdf (D21591748)
https://link.springer.com/article/10.1186/s12872-016-0379-z
https://link.springer.com/article/10.1007/s11906-011-0242-7
http://www.who.int/whr/2002/en/
http://mbbsdost.com/Oxidative-stress-brain-ischemia-Brain-pathology-Zurich-Switzerland-Love-S--1999-Jan/pubmed/12878412
https://www.ncbi.nlm.nih.gov/books/NBK53302/
http://www.strokecenter.org/professionals/brain-anatomy/blood-vessels-of-the-brain/
http://www.who.int/healthinfo/statistics/bod_cerebrovasculardiseasestroke.pdf

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CERTIFICATE

This is to certify that the dissertation titled **"A STUDY OF SERUM URIC ACID LEVELS IN A SETTING OF ACUTE ISCHEMIC STROKE IN GVMCH" is** a bonafide work done by **Dr. S.NETHAJI,** Post Graduate student (2015 – 2018) in the Department of General Medicine, Government Vellore Medical College and Hospital, Vellore under the guidance of **Prof. Dr. D.ANBARASU, M.D.,**

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DECLARATION

I, **DR.S.NETHAJI** solemnly declare that this dissertation titled **"A STUDY OF SERUM URIC ACID LEVELS IN A SETTING OF ACUTE ISCHEMIC STROKE IN GVMCH"** is a bonafide work done by me in the Department of General Medicine, Government Vellore Medical College and Hospital, Vellore under the guidance and supervision of **Prof. Dr.D.ANBARSU, M.D.**, Guide and Chief, Medical Unit-IV.

This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfilment of the university regulations for the award of M.D., Degree (General Medicine) Branch – I.

Place : Vellore

Date: **Dr. S. NETHAJI.**

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ABBREVIATIONS

FBS – Fasting Blood Glucose

BMI – Body Mass Index

DM – Diabetes Mellitus

HT –Hypertension

DOS – Duration of stay

RFT – Renal function test

TIA – Transient ischemic attack

CT - Computerised Tomography

MRI – Magnetic Resonance Imaging

SUA – Serum uric acid

ROS – Reactive oxygen species

NOS – Nitric oxide synthase

CAD- Coronary Artery Disease

CVD – Cardiovascular Disease

CKD - Chronic kidney disease

ABSTRACT

BACKGROUND:

Stroke is socioeconomically a disabling disease with an enormous amount of loss to family and the country. The incidence and prevalence of stroke is on a rapid rise with number of risk factors emerging and is in the ascend with the modern living. Stroke is a disease of the elderly and people with risk factors like hypertension, diabetes, dyslipidaemia. The increased serum uric acid and cardiovascular risk factors has been debated for many years and there has been conflicting results over the study of clinical significance of increased serum uric acid in cardio and cerebrovascular diseases. Of it studies have concluded that increased SUA is an important risk factors for the development of CVD with strong association with diabetes mellitus, hypertension, dyslipidaemia, and BMI. Few study have shown that increased SUA has good prognosis with outcome of cerebrovascular disease due to its antioxidant property. Thus this study aims at study the levels of serum uric acid with other risk factors and its role in influencing the risk of incidence of acute ischemic stroke.

AIMS AND OBJECTIVES :

1. To identify the role of serum uric acid in influencing the risk of acute ischaemic stroke.

2. To identify whether any association exists between age, sex, hypertension, diabetes, dyslipidaemia, renal parameters and BMI and serum uric acid level.

METHODOLOGY:

The study was carried out in acute ischemic stroke patients admitted in medical wards under the department of general medicine in Government Vellore medical college and hospital (GVMCH), Vellore. A sample of 100 patients were include in the study after meticulously scrutinising the patients through a well prepared proforma over a period of one year starting from 01 September 2016 to 31 August 2017. After prior Institutional Ethical clearance and obtaining informed consent, the participants satisfying the inclusion criteria were asked detailed history and clinical examination was performed according to the well-designed proforma cited below.

RESULTS:

The mean age of the study subjects was 61.14 years. Most of the patients belonged to the age group 50 -70years. Out of 100 cases, there were 65 (65.0%) males and 35(35.0%) females. The Male to Female sex ratio was 1.85:1. Of the 100 patients 66 had normal BMI and 34 patients had abnormal BMI. Fasting blood sugar was elevated in 50 patients and 50 patients had normal fasting blood sugar. Of the 100 patients 68 patients had history of hypertension, 26 people were smokers.

Overall 69 patients had abnormal lipid profile of which 54 patients had elevated total cholesterol,60 patients had elevated LDL cholesterol,69 had hypertriglyceridemia and 30 had low HDL cholesterol. Clinically 81 patients had elevated systolic bp and 57 patients had elevated diastolic bp. Serum uric acid was elevated in 46 patients in our study with acute ischemic stroke.

CONCLUSION :

Serum Uric acid is an important risk factor for the onset of acute ischemic stroke independent of age, BMI, hypertension, diabetes, dyslipidemia. Of which most significant association was found with BMI, Total cholesterol, Serum triglycerides, LDL Cholesterol, Systolic and Diastolic Blood Pressure.

KEYWORDS:

Acute ischemic stroke, Serum uric acid, Diabetes mellitus, Hypertension, Dyslipidaemia, Antioxidants, Systolic and Diastolic Blood Pressure, BMI.

TABLE OF CONTENTS

INTRODUCTION

STROKE (cerebrovascular disease) is ranked the most common cause of death after ischemic heart disease and cancer consecutively. It is the most common cause of social and economic burden due to increased morbidity and mortality in middle aged and elderly. Stroke is the major cause of disability in India with more than million adults affecting yearly and has to adapt a life with disability and needing other people to assist their day to day activity .(1)

India has become a country with stroke epidemic like other developing countries in the recent years. The estimated adjusted prevalence rate of stroke range, 84-262/100,000 in rural and 334-424/100,000 in urban areas. The incidence rate is 119-145/100,000 based on the recent population based studies. There is a huge variation in the burden of stroke regionally .Stroke units, Thrombolysis, and Rehabilitation are predominantly available in urban areas, particularly in private sector hospitals. (2)

As a first step, the Government of India has started the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases & Stroke (NPCDCS). The government is focusing on early diagnosis, management, infrastructure, public awareness, and capacity building at different levels of health care for all the non-communicable diseases including stroke. An organised effort from both the government and the private sector is needed to tackle the rising stroke burden in India.(2)

In acute phase of stroke the mortality rate is as high as 20%, Thus it is vital on our part to establish the risk factors as early as possible to prevent the catastrophe.

Stroke due to cerebral ischemia initiates a complex cascade of metabolic events that leads to generating nitric oxide and free oxygen radicals. During ischemia, the activity

of NOS plays a vital role of which NOS1, NOS2 are harmful but NOS3 is helpful in vasodilatation of the cerebral vessels in the ischemic penumbra. These free radicals and reactive oxygen species (ROS) mediate a great part of injuries appearing after a transitory ischemic attack or during permanent ischemia, modifying macromolecules especially DNA, initiating apoptosis and necrosis. Free radicals are liberated from a variety of sources, including inflammatory cells, dysfunctional mitochondria and excitotoxic mechanisms stimulated by increased glutamate and aspartate concentrations.(3)

Hydroxyl radicals (formed from hydrogen peroxide) peroxynitrite and superoxide are powerful radicals that can cause lipid peroxidation, a self-propagating chain reaction, that irreversibly damages plasma and mitochondrial membranes. Oxyradical production and cellular calcium overload are believed to contribute to the damage and death of neurons that occurs following cerebral ischemia in victims of stroke. (3)

Thus, in acute ischemic stroke due to reduced or complete cut off of the blood supply to the brain cause the accumulation of reactive oxygen species (hydrogen peroxide and peroxynitrite), and lipid peroxidation associated with each insult. Mitochondrial function is also compromised by the excitotoxic and metabolic insults. This metabolic insult causes delayed elevations of intracellular free calcium levels induced by glutamate and cyanide is significantly essential for the cellular necrosis and damage in neurons. Some study data demonstrate a neuroprotective action of uric acid that involves suppression of oxyradical accumulation, stabilization of calcium homeostasis, and preservation of mitochondrial function, and was preserved in neurons treated with uric acid(4).Thus showing that a balance between oxidative free radicals and antioxidants play a vital role in the pathophysiology of stroke.

Uric acid is the end product of purine degradation. It is catalysed by the enzyme xanthine oxidase, which is responsible for the production of uric acid and damaging free radicals. In human beings serum uric acid is the most important aqueous antioxidant occupying more than two third of the free radical scavenging activity of the plasma.This is a central link in the association between serum uric acid and myocardial ischemia, myocardial dysfunction and non-cardiac function, which is determined primarily by impaired peripheral blood flow. Uric acid can serve as a marker of pathophysiological mechanisms in patients with cardiovascular disease, which may explain why serum uric acid contains prognostic information.

It was therefore considered than SUA to be neuroprotective(5) but a number of epidemiological studies has shown SUA as an risk factor for the occurrence of stroke.

Framingham study was the first epidemiological study to suggest that uric acid levels as a link between cardiovascular disease and other risk factors like hypertension ,CKD, dyslipidaemia ,and use of diuretics (6).There are a number of epidemiological studies have supporting evidence that serum uric acid is helpful in assessing the risk of cardiovascular events, hypertension, congestive heart failure and Type II diabetes mellitus and acute ischemic stroke and MI(7).

The Rotterdam study by Bos et al. did a study on 4385 participants to study the risk of stroke and MI even after adjusting with relevant confounders the study concluded that uric acid is a strong risk factor for the development of stroke (8).

Chen et al. conducted a large Chinese prospective cohort study with 41879 men and 48514 women participants aged equal or more than thirty five years of age to

compare the all-cause mortality and mortality from that of total CVD,ischemic stroke ,hypertension and CAD with uric acid and concluded that hyperuricemia was an independent risk factor of mortality from all causes, total cvd ,ischemic stroke ,and CAD(9) .Inhibition of xanthine oxidase with allopurinol may be used in future treatment of stroke and heart patients.(10)Thus our study aims at determining the role of serum uric acid in a setting of acute ischemic stroke.

AIMS AND OBJECTIVES

1. To identify the role of serum uric acid in influencing the risk of acute ischaemic stroke.

2. To identify whether any association exists between age, sex, hypertension, diabetes, dyslipidemia, renal parameters and BMI and serum uric acid level in patients with acute ischemic stroke.

REVIEW OF LITERATURE

DEFINITIONS

STROKE:

A stroke or cerebrovascular accident is a rapidly developing clinical symptoms and or signs of focal and at times global (applied to patients in deep coma and to those with subarachnoid haemorrhage) loss of cerebral function, with symptoms lasting for more than 24 hours or leading to death, with no apparent vascular cause (11)

TIA: (TRANSIENT ISCHEMIC ATTACK)

By applying this definition transient ischemic attack (TIA), which is defined to last less than 24 hours, and patients with stroke symptoms caused by subdural haemorrhage, tumours, poisoning, or trauma are excluded. (11)

ANATOMY OF CEREBRAL CIRCULATION ARTERIES OF THE BRAIN

Two internal carotid arteries and 2 vertebral arteries supply the brain. The 4 arteries lie within the substance of subarachnoid space and their branches anastamose on the inferior surface of the brain to form the circle of Willis.

INTERNAL CAROTID ARTERY:

The left common carotid artery arises directly from the aorta and the right common carotid from the innominate artery. The internal carotid artery begins at the bifurcation of the common carotid artery. This ascends the neck and perforates the base of the skull by passing through the carotid canal of the temporal bone. The artery then runs horizontally forward through the cavernous sinus and emerges on the medial side of the anterior clinoid process by perforating the duramater. It now enters the subarachnoid space by piercing the

arachnoid matter and turns posteriorly to the region of the medial end of the lateral cerebral sulcus. Here it divides into the anterior and middle cerebral arteries.

VERTEBRAL ARTERY

The vertebral artery is a branch of the first part of the subclavian artery, climbing up the neck passing through the foramina in the transverse process of the upper six cervical vertebrae entering the skull through the foramen magnum and piercing the both the dura and arachnoidmater to enter the subarachnoid space. It then passes upward, forward and medially on the medulla oblongata. At the lower border of the pons, it joins vessel of the opposite side to form the basilar artery.

BRANCHES OF THE CEREBRAL PORTION

OPHTHALMIC ARTERY:

The ophthalmic artery which is a branch of the internal carotid artery enters the orbit through the optic canal below and lateral to the optic nerve. It supplies the eye and other orbital structures and its terminal branches supply the frontal area of the scalp, the ethmoid and frontal sinuses and the dorsum of the nose.

POSTERIOR COMMUNICATING ARTERY:

This a small vessel originating near the terminal bifurcation of the internal carotid artery .The posterior communicating artery runs posteriorly above the oculomotor nerve to join the posterior cerebral artery to form part of the circle of Willis.

CHOROIDAL ARTERY:

The choroidal artery is a small branch that passes posteriorly, close to the optic tract, enters the inferior horn of lateral ventricle and ends in the choroids plexus. It gives off small branches to the crus cerebri, lateral geniculate body, optic tract and the internal capsule.

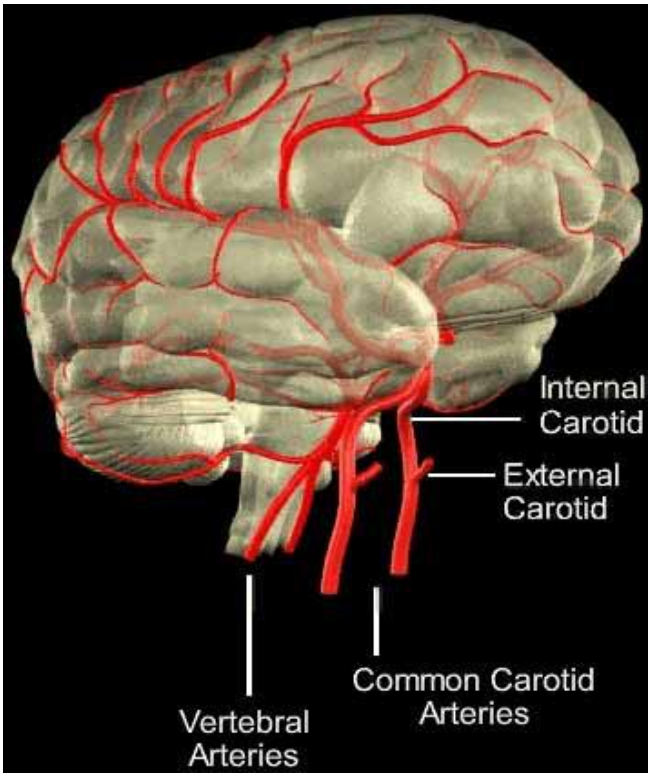


FIGURE 1: MAJOR ARTERIAL BLOOD SUPPLY TO THE BRAIN

(source of image:(12) http://www.strokecenter.org/professionals/brain-anatomy/blood-vessels-of-the-brain/)

ANTERIOR CEREBRAL ARTERY:

It runs forward and medially superior to the optic nerve and enters the longitudinal fissure of cerebrum. Here it joins with its fellow on the opposite side by means of the anterior communicating artery. It curves backward over the corpus callosum. The cortical

branches supply the whole of the surface of the cerebral cortex as far back as the parieto-occipital sulcus. They also supply a strip of cortex about 1 inch wide on the adjoining lateral side. The anterior cerebral artery thus supplies the leg area of the precentral gyrus. A group of central branches pierces the anterior perforated substance and helps to supply the parts of the lentiform and caudate nuclei and the internal capsule.

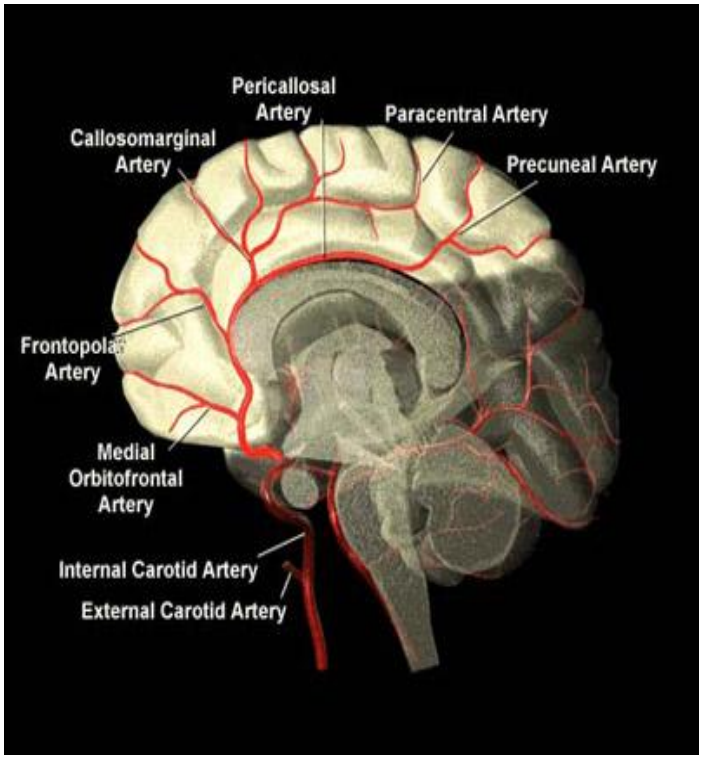


Figure 2: Anterior Cerebral Artery Blood Supply to the Brain.

(source of image:(12) http://www.strokecenter.org/professionals/brain-anatomy/blood-vessels-of-the-brain/)

MIDDLE CEREBRAL ARTERY:

It is the largest branch of the internal carotid artery, runs laterally in the lateral cerebral sulcus. Cortical branches supply the entire lateral surface of the hemisphere, except for the narrow strip supplied by the hemisphere, which are

supplied by the anterior cerebral artery, the occipital pole and the inferolateral surface of the posterior cerebral artery.

This artery thus supplies the whole motor cortex except the leg area. Central branches enter the anterior perforated substance and supply the lentiform and caudate nuclei and the internal capsule.

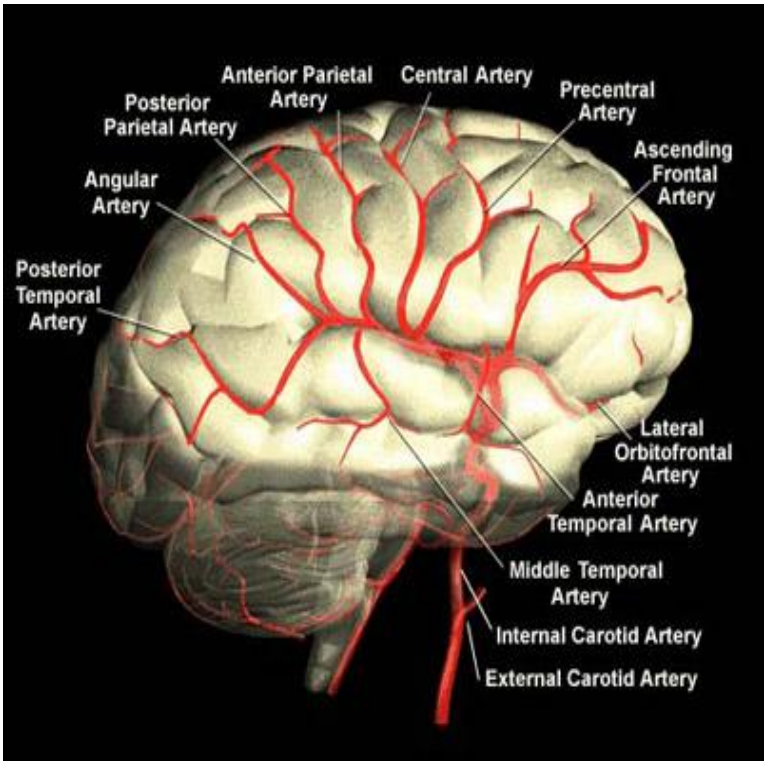


Figure 3: Middle Cerebral Artery Blood Supply to the Brain.

(source of image:(12) http://www.strokecenter.org/professionals/brain-anatomy/blood-vessels-of-the-brain/)

BRANCHES OF THE CRANIAL PORTION MENINGIAL BRANCHES.

These are small branches and they supply the bone and dura and the posterior cranial fossa.

POSTERIOR SPINAL ARTERY

The posterior spinal artery may arise from the vertebral artery or the Posterior inferior cerebellar artery. It descends on the posterior surface of the spinal cord close to the posterior roots of the spinal nerves. Radicular arteries that enter the vertebral canal through the intervertebral foramina reinforce the branches.

ANTERIOR SPINAL ARTERY

It is formed from a contributory branch from each vertebral artery near its termination. The single artery descends on the anterior surface of the medulla oblongata and the spinal cord and is embedded in the piamater along the anterior median fissure. The radicular arteries that enter the vertebral canal through the vertebral foramen reinforce the artery.

POSTERIOR INFERIOR CEREBELLAR ARTERY

This largest branch of the vertebral artery passes on an irregular course between the medulla and cerebellum. It supplies the inferior surface of the vermis, central nuclei of cerebellum and the under surface of the cerebral hemisphere. It also supplies the medulla oblongata and the choroidal plexus of the fourth ventricle.

MEDULLARY ARTERIES

These are very small branches that are distributed to the medulla oblongata.

BASILAR ARTERY

The basilar artery, formed by the union of the 2 vertebral arteries, ascends in the groove on the anterior surface of the pons. At the upper border of the pons, it divides into 2 posterior cerebral arteries.

BRANCHES OF THE BASILAR ARTERY AND PONTINE ARTERIES.

These are numerous small arteries that enter the substance of the pons.

LABRINTHINE ARTERY

This is a long narrow artery that accompanies the facial and the Vestibulocochlear nerves into the internal acoustic meatus and supplies the internal ear. It often arises as a branch of the anterior inferior cerebellar artery.

ANTERIOR INFERIOR CEREBELLAR ARTERY

This artery passes posteriorly and laterally and supplies the anterior and inferior part of the cerebellum, a few branches pass to pons and upper part of the medulla.

SUPERIOR CEREBELLAR ARTERY

This arises close to the termination of the basilar artery. It winds around the cerebral peduncle and supplies the superior surface of the cerebellum. It also supplies the pons, the pineal gland and the superior medullary velum.

POSTERIOR CEREBRAL ARTERY

This curves laterally and backwards around the mid brain and is joined by the posterior communicating branch of the internal carotid artery. Cortical branches supply the inferolateral and medial surfaces of the temporal lobe and lateral and medial surfaces of the occipital lobe. Thus it supplies the occipital lobe.

Central branches pierce the brain substance and supply palis of the thalamus, the lentiform nucleus, the midbrain, the pineal gland and the medial geniculate body. A choroidal branch enters the inferior horn of the lateral ventricle and supplies the choroid plexus.

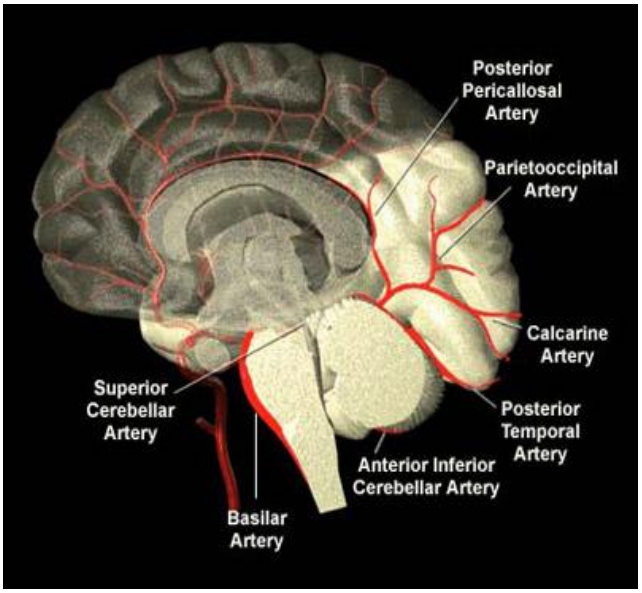


Figure 4: Posterior Cerebral Artery Blood Supply to the Brain

(source of image:(12) http://www.strokecenter.org/professionals/brain-anatomy/blood-vessels-of-the-brain/)

CIRCLE OF WILLIS :

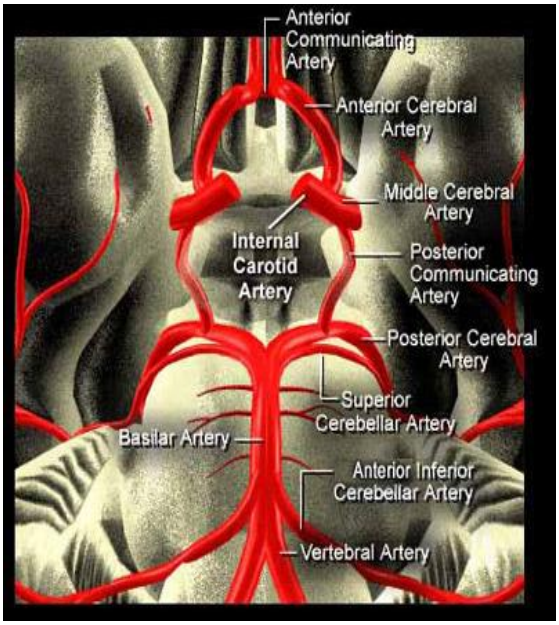


Figure 5: Circle of Willis

(source of image:(12) http://www.strokecenter.org/professionals/brain-anatomy/blood-vessels-of-the-brain/)

CIRCLE OF WILLIS:

The circle of Willis lies in the interpeduncular fossa at the base of the brain. It is formed by anastomosis between the two internal carotid arteries and the two vertebral arteries. The anterior communicating, the anterior cerebral, internal carotid, posterior communicating, posterior cerebral, and the basilar arteries all contribute to the circle. The circle of Willis allows blood that enters either by the internal carotid or the vertebral arteries to be distributed to any part of either cerebral hemisphere. The cortical and central branches arise from the circle and supply the brain substance.

ARTERIES TO SPECIFIC BRAIN AREAS

Mainly the medial and lateral striate central branches of the middle cerebral artery supply the corpus striatum and the internal capsule; the central branches of the anterior cerebral artery supply the remainder of the structures.

The posterior cerebral, posterior communicating and basilar arteries supply the thalamus.

The posterior cerebral, superior cerebellar, and basilar arteries supply the mid brain.

The basilar and anterior, inferior and superior cerebellar arteries supply the pons.

The vertebral, anterior and posterior spinal, posterior inferior cerebellar and basilar arteries supply the medulla oblongata.

VEINS OF THE BRAIN EXTERNAL CEREBRAL VEINS

The superior cerebral veins pass upward over the lateral surface of the cerebral hemisphere and empty into the superior sagittal sinus. The superficial middle cerebral veins drain the lateral surface of the cerebral hemisphere; it runs inferiorly in the lateral sulcus and empties into the cavernous sinus. The deep middle cerebral vein drains the insula and is joined by the anterior cerebral vein and striate veins to form the basilar vein. The basilar vein ultimately joins the great cerebral vein, which in turn drains into the straight sinus.

INTERNAL CEREBRAL VEINS

There are two internal veins, and the union of the thalamo-striate vein and the choroidal vein at the interventricular foramen forms them. These two veins form the great cerebral vein that drains into the straight sinus.

EPIDEMIOLOGY OF CEREBROVASCULAR DISEASES IN INDIA

Stroke is becoming an important cause of mortality and disability in India driven by various factors and demography. According to the India stroke factsheet updated in 2012, the estimated age-adjusted prevalence rate for stroke ranges between 84/100,000 and 262/100,000 in rural and between 334/100,000 and 424/100,000 in urban areas.(2) stroke fact sheet India. [Accessed 21 July 2013].
http://www.sancd.org/Updated%20Stroke%20Fact%20sheet%202012.pdf.

TYPES OF STROKE :

The pathological classification of stroke is based on the types of disturbance in the blood circulation of the brain.

ISCHEMIC STROKE (INFARCTION) :

Ischemic stroke occurs due to ischemia of the partial or all the territory of the occluded artery due to one of the several reasons, The major one being thrombotic cerebral infarct due atherosclerotic occlusion of the carotid and cerebral arteries. Secondly, embolic ischemic infarction from a clot in the cerebral arteries from other parts of the arterial system. Lacunar cerebral infarcts are minute infarcts due to chronic hypertension due to local pathology in the territory of small penetrating arteries.

HEMORRHAGIC STROKE

Intracerebral bleeding is other important cause of stroke which can be spontaneous or traumatic, There are a number of causes for spontaneous hemorrhage now the most important cause being hypertension, and in the older age the cause of hemmorrhage due to hypertension is cortical amyloid angiopathy. Other rare causes are Vascular malformations , Bleeding disorders, Rupture of aneurysms (13)

PATHOPHYSIOLOGY OF ISCHEMIC STROKE:

A Ischemic stroke happens when the blood flow to the brain is hindered, resulting in variable degree of neurological deficit depending on degree of occlusionof the involved blood vessel and area of involvement.

PATHOPHYSIOLOGY OF ISCHAEMIC STROKE:

Ischaemic strokes can be broadly subdivided into thrombotic and embolic strokes.

The most common cause of narrowing of the blood vessel is atherosclerosis, as the size of the fatty atherosclerotic plaque grows in size the luminal size reduces eventually leading to reduced blood supply to the brain.

THROMBOTIC STROKE

Occlusion of the blood vessel occurs due to blood clot formation of the damaged atherosclerotic plaque.

EMBOLIC STROKE

Occlusion of the blood vessels occur due to blood clot and debris from elsewhere in the body travelling the vessels and occluding narrower blood vessels.

Based on the aetiology of ischaemic stroke, a more accurate sub-classification is generally used:(14)

- **Large Artery Disease** – atherosclerosis of large vessels, including the internal carotid artery, vertebral artery, basilar artery, and other major branches of the Circle of Willis.

- **Small Vessel Disease** – changes due to chronic disease, such as diabetes, hypertension, hyperlipidaemia, and smoking, that lead decreased compliance of the arterial walls and/or narrowing and occlusion of the lumen of smaller vessels.

- **Embolic Stroke** – the most common cause of an embolic stroke is atrial fibrillation.

- **Stroke Of Determined Aetiology** – such as inherited diseases, metabolic disorders, and coagulopathies.

- **Stroke of Undetermined Aetiology** – after exclusion of all of the above.

ISCHAEMIC BRAIN OEDEMA:

Ischaemic brain oedema appears to involve two distinct processes, The first process occurs during the initial phase of infarction and before structural damage has occurred. Involves an increase in tissue Na^+ and water content accompanying increased pinocytosis and Na^+, K^+ ATPase activity across the endothelium. This phenomenon is augmented by reperfusion. A second process results after infarction of both the parenchyma and the vasculature after disruption of blood brain barrier with extravasation of serum proteases additionally apart from the major osmotic action of sodium. This results in cellular softening and swelling.

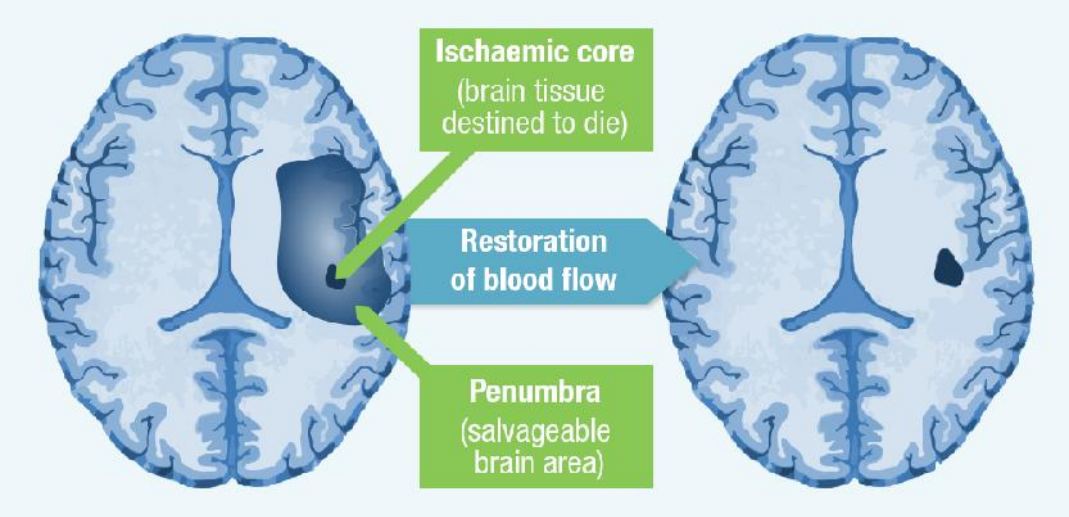


Figure 6: Ischemic Penumbra

SOURCE: (Source: http://neuro4students.wordpress.com/pathophysiology)

ISCHEMIC PENUMBRA:

The ischemic penumbra is defined as area surrounding the ischemic zone which is functionally silent due to reduced blood flow but metabolically active and hence they are salvageable if blood flow to the penumbra region is restored.

THE ISCHAEMIC CASCADE:

After seconds to minutes of cerebral ischaemia, the ischaemic cascade is initiated. This is a series of biochemical reactions in the brain and other aerobic tissues, which usually goes on for two to three hours, but can last for days, even after normal blood flow returns.

FLOW CHART OF ISCHEMIC CASCADE:

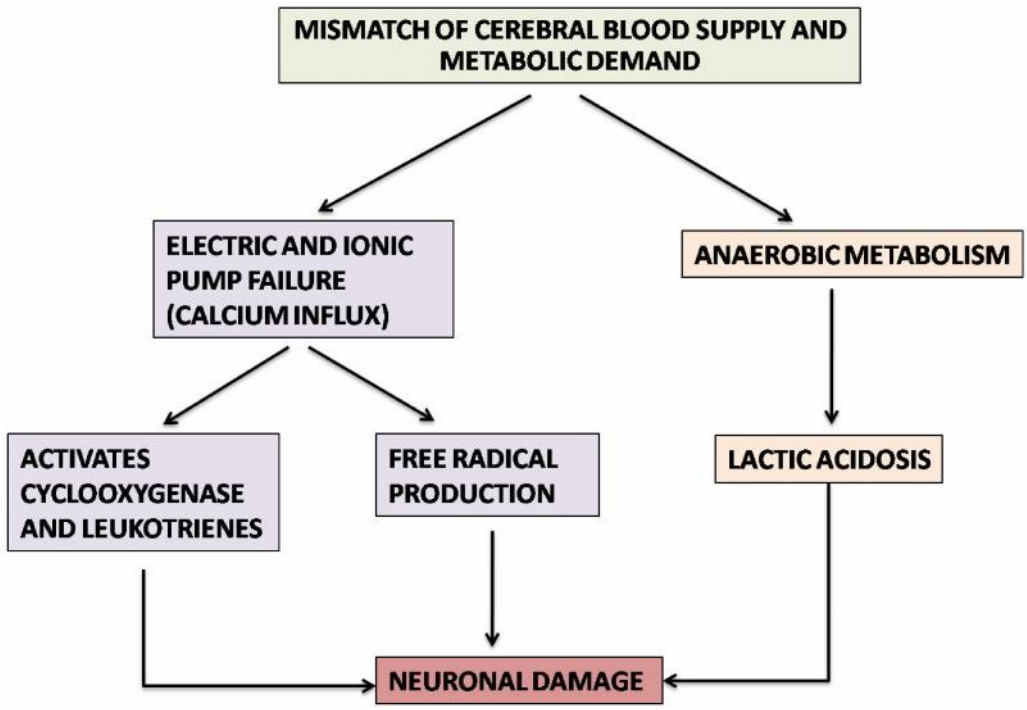


Figure 7: The ischaemic cascade

(Source: http://neuro4students.wordpress.com/pathophysiology)

IMPORTANT STEPS OF THE ISCHAEMIC CASCADE

1. Without adequate blood supply and thus lack of oxygen, brain cells lose their ability to produce energy - particularly adenosine triphosphate (ATP).

2. Cells in the affected area switch to anaerobic metabolism, which leads to a lesser production of ATP but releases a by-product called lactic acid.

3. Lactic acid is an irritant, which has the potential to destroy cells by disruption of the normal acid-base balance in the brain.

4. ATP-reliant ion transport pumps fail, causing the cell membrane to become depolarized; leading to a large influx of ions, including calcium (Ca^{++}), and an efflux of potassium.

5. Intracellular calcium levels become too high and trigger the release of the excitatory amino acid neurotransmitter glutamate.

6. Glutamate stimulates AMPA receptors and Ca^{++}-permeable NMDA receptors, which leads to even more calcium influx into cells.

7. Excess calcium entry overexcites cells and activates proteases (enzymes which digest cell proteins), lipases (enzymes which digest cell membranes) and free radicals formed as a result of the ischaemic cascade in a process called excitotoxicity.

8. As the cell's membrane is broken down by phospholipases, it becomes more permeable, and more ions and harmful chemicals enter the cell.

9. Mitochondria break down, releasing toxins and apoptotic factors into the cell.

10. Cells experience apoptosis.

11. If the cell dies through necrosis, it releases glutamate and toxic chemicals into the environment around it. Toxins poison nearby neurons, and glutamate can overexcite them.

12. The loss of vascular structural integrity results in a breakdown of the protective blood brain barrier and contributes to cerebral oedema, which can cause secondary progression of the brain injury.(15)(16)

RISK FACTORS OF STROKE:

AGE

Age is a non-modifiable risk factor. A large number of epidemiological studies have shown that the increase in age is associated with increased incidence of atherosclerosis and cardiovascular disease like myocardialinfarction, stroke. Although Age is not related to the severity and type of stroke, Age independently influences stroke outcome selectively in aspect of activity of daily living but not in terms of neurological aspect suggesting a poorer compensatory ability in elderly stroke patients. Therefore, rehabilitation of elderly stroke patients should be focused more on ADL and compensation rather than on the recovery of neurological status.(17)

SEX

Male are associated with increased risk of stroke(18) The association of hyperuricemia with hypertension was stronger in males than in females, and middle-aged men with hyperuricemia had greater association with hypertension.

RACE

Black race is associated with increased risk of stroke than the whites as the prevalence of hypertension and diabetes mellitus was more than whites.

HYPERTENSION:

Hypertension is one of the most important causative factor for stroke (ischemic and haemorrhagic). In India, ICMR multicentric study on risk factors for stroke found Hypertension, Smoking, Diabetes and Low haemoglobin as risk factors. According to them 40% of stroke can be attributed to systolic blood pressure more than 140 mm of mercury. A large Chinese study consisting of 2253 patients suggested that over 49.5 percent of patient with stroke had hypertension. Studies from this also shows the benefit of stroke in hypertensive patients treated with anti-hypertensive drugs.(19).

DIABETES MELLITUS:

Diabetes is a strong risk factor for stroke. Diabetes influences stroke in several aspects: in age, in subtype, in speed of recovery, and in mortality. Increased glucose levels on admission independently increase mortality from stroke(20). Insulin resistance plays a vital key role in the causal relationship between metabolic syndrome, Type 2 diabetes and hyperuricemia. Hyperuricemia and insulin resistance share a bidirectional causal effect

that should be evaluated further more. Diabetic patients with retinopathy and autonomic neuropathy are particularly at high risk for atherosclerosis.(21)

SMOKING:

The risk of stroke increased as the number of cigarettes smoked increased. The relative risk of stroke in heavy smokers (>40 cigarettes per day) was twice that of light smokers (fewer than ten cigarettes per day).

Lapsed smokers developed stroke at the same level as non-smokers soon after stopping. Stroke risk decreased significantly by two years and was at the level of non-smokers by five years after cessation of cigarette smoking. Cigarette Smoking is a Risk Factor for Stroke(22).

CLAUDICATION:

Claudication is a symptomatic clue for the increased risk of cardiovascular disease probably suggestive of atherosclerosis of the vessels. ARIC study suggest that uric acid well correlates with the accelerated atherosclerosis and hence increased risk of stroke.(23)

ATRIAL FIBRILLATION:

Framingham study examined the incidence of stroke in nonrheumatic atrial fibrillation, hypertension, coronary heart disease, and cardiac failure patients the Age-adjusted incidence of stroke was more than twice in the presence of coronary heart disease and thrice in the presence of hypertension. The risk quadrupled in subjects with cardiac failure and a near fivefold excess when atrial fibrillation was present. In persons with coronary heart disease or cardiac failure, atrial fibrillation doubled the stroke risk in men

and trebled the risk in women. Data also suggest that the elderly are more prone to stroke in the presence of atrial fibrillation .(24)

CAROTID ARTERY DISEASE:

Ischemic stroke is often a sequel of atherosclerotic risk factors(25). Carotid intima-media thickness (CIMT) is a surrogate marker of early atherosclerotic changes. Age-specific value of CIMT was significantly higher in stroke cases than in age-matched controls across all age groups. Right CIMT, along with the history of hypertension are important risk factors for ischemic stroke in the younger age group (20-40 years). With increasing age, along with the history of HTN and right CIMT, presence of plaque and daily smoking are also significant risk factors. CIMT is significantly related to the daily alcohol and smoking intake and the presence of plaques. Right CIMT is positively related to increasing age in normal population. Right CIMT and comorbid HTN are significant risk factors associated with the development of ischemic stroke across all adult age groups. Studies suggest that intima–media thickness of the common carotid artery and the internal carotid artery is strongly associated with the risk of myocardial infarction and stroke in asymptomatic older adults.(26)

TIA (TRANSIENT ISCHEMIC ATTACK)

Transient ischemic attacks (TIAs) have been found to be a strong predictor of subsequent stroke and death. Coull et al. found in their study the estimated stroke risks after a TIA were 8.0% at seven days, 11.5% at one month, and 17.3% at three months.(27).

OTHER RISK FACTORS :

Abdominal obesity, plasmafibrinogen, homocysteine, dietary measures, snoring, corneal arcus, psychological factors, diagonal ear lobe crease, physical inactivity, maternal history of stroke, left ventricular hypertrophy, peripheral vascular disease, alcohol consumption, oral contraceptives, plasma factor seven factor coagulant activity.

DIAGNOSIS OF STROKE SUBTYPE USING IMAGING (28)(29)

The basic aims of imaging, in patients who have symptoms of stroke are

- To document the presence or absence of haemorrhage. This information is critical as the treatment of the two vary.
- To determine the location and extend of brain damage.
- To assess the current and impending herniation.
- To exclude other entities, which may mimic stroke syndrome.
- To find out the cause of stroke.

Acute infarcts are more frequently visible on MRl than on CT scans. On admission, approximately 90% of the MRI are positive compared to 60% in CT scans in acute infarcts.

COMPUTERISED TOMOGRAPHY OF ISCHAEMIC STROKE

The CT appearance of cerebral infarction is time dependent. Although the findings may be detected within 6 -8 hours of onset, CT may be normal up to 24 hours.

- **HYPER ACUTE INFARCT (LESS THAN 12 HOURS)**

Normal 50 -60%

Hyper dense artery 25 -50%

Obscuration of lentiform nuclei.

- **ACUTE (12 - 24 HOURS)**

Loss of grey white interfaces (insular ribbon sign, obscuration of cortex medullary white matter border)

Low density basal ganglia.

Sulcal effacement 1 – 3 days

Increasing mass effect.

Wedge shaped low-density area that involves both grey and white matter.

Haemorrhagic transformation may occur.

- **4-7 DAYS**

Gyral enhancement

Mass effect, edema persist.

- **1-8 WEEKS**

Contrast enhancement persists.

Mass effect resolves

- **MONTHS TO YEARS**

Encephalomalacic change

Volume loss and

Rarely calcification.

MULTIMODAL MAGNETIC RESONANCE IMAGING OF ISCHEMIC STROKE :

The multimodal MRI approach for acute stroke evaluation includes

A. Diffusion-weighted imaging (DWI)
B. Perfusion weightedimaging (PWI)
C. MR angiography
D. Gradient echo
E. Fluid-attenuated inversion recovery
F. T2-weighted sequences.

Standard MRI sequences (T1 weighted, T2 weighted, and proton density) are relatively insensitive to the changes of acute ischemia.

DWI SEQUENCE (diffusion-weighted imaging)

DWI allows visualization of ischemic regions within minutes of symptom onset and early identification of the lesion size, site, and age.DWI also provides information about the involved vascular territory and has a high sensitivity (88% to 100%) and specificity (95% to 100%) for detecting ischemic lesions, even at very early time points.

PWI (PERFUSION WEIGHTED IMAGING)

PWI analytical method focus on identifying the highest correlation of ischemic volume with acute clinical deficits (symptomatic hypoperfusion) or with volume of chronic infarct (tissue at risk).

GRADIENT ECHO SEQUENCE:

Gradient echo sequences also have the ability to detect clinically silent prior micro bleeds not visualized on CT scan

MR ANGIOGRAPHY:

MR angiography is increasingly used for non-invasive screening of the extracranial and intracranial circulation

TREATMENT OF ACUTE ISCHEMIC STROKE(28)(30)

- Early evaluation of diagnosis and supportive treatment
- Reperfusionstrategies
- Neuroprotective agents
- Supportive care

Emergency care for acute complications is of utmost importance as if unattended can be fatal in most cases of stroke. It includes protection of airway to avoid obstruction, hypoventilation and aspiration pneumonitis. Care should be taken to prevent cerebral edema and the factors that exacerbate cerebral edema like Hypoxia, hyperthermia, hyperventilation, hypovolemia, arterial hypertension, cardiac arrhythmias.

If the patient develops Acute cerebral oedema it should be treated with mannitol (20%) solution 1g/kg over 30 min. bolus, followed by 0.25 - 0.5 gm/kg over 30 - 60 min every 4 - 6 hours. The usual maximal dose is 2 g/kg.

Holter monitoring is recommended atleast for 24 hours to screen for atrial fibrillation and other potentially serious cardiac arrhythmias that would necessitate emergency cardiac interventions.

Patients in whom are eligible to be treated with intravenous rtPA and has elevated blood pressure should their blood pressure carefully lowered so that their systolic blood pressure is <185 mmHg and their diastolic blood pressure is <110 mmHg before fibrinolytic therapy is initiated. If medications are given to lower blood pressure the blood pressure should be stabilized at the lower level before beginning treatment with intravenous rtPA and maintained below 180/105 mmHg for at least the first 24 hours after intravenous rtPA treatment. No definitive guidelines are there for definitive treatment of hypertension but consensus to reduce the blood pressure if systolic pressure >200 to 220 mmHg,diastolic pressure >110 to 120 mmHg with caution that precipitous decrease in blood pressure decreases local perfusion.

Airway support and ventilator assistance are rec- commended for the treatment of patients with acute stroke who have decreased consciousness or who have bulbar dysfunction that causes compromise of the airway Supplemental oxygen should be provided to maintain oxygen saturation >94%

As hyperthermia (temperature >38°C) has poor outcome source of hyperthermia should be diagnosed and treatment should be and treated promptly.

Hypovolemia should be corrected with intravenous normal saline, and cardiac arrhythmias that might be reducing cardiac output should be corrected

Strict sugar levels are to be maintained for good outcome in stroke patients. Hypoglycaemia (blood glucose <60 mg/dL) should be treated in patients with acute ischemic stroke with glucose containing solutions. The goal is to achieve normoglycemia. Evidence indicates that persistent in-hospital hyperglycaemia has worst outcomes in the first 24 hours of the stroke episode treatment should be targeted to achieve blood glucose levels in a range of 140 to 180 mg/dL and to closely monitor to prevent hypoglycaemia in patients with acute ischemic stroke.

THROMBOLYSIS

The use of thrombolytic agents in acute cerebral infarction has been studied extensively. Three early intravenous streptokinase trials were stopped because of higher death rate mainly due to intracerebral bleedings.

The European Co-operative Acute Stroke Study (ECASS) tested recombinant tissue plasminogen activator (rtPA - 1 mg/kg to 100mg max, 10% as a bolus, then remainder over 60 min. IV) versus placebo in patients with ischaemic stroke within 6 hours of onset of symptoms. Overall thrombolysis was not beneficial because of excess of cerebral haemorrhage. However, in those patients who had no signs of major infarction on initial CT scan, the functional outcome was improved.

The National Institute of Neurological Disorder and Stroke (NINDS) rtPA stroke study showed a clear benefit for rtPA in selected patients with acute stroke. The NlNDS study used rtPA versus placebo in patients with acute ischaemic stroke within 3 hours of

onset. Symptomatic intracerebral haemorrhage occurred in 6.4% patients on rtPA and 0.6% on placebo. There was a nonsignificant reduction in mortality and a significant absolute increase in number of patients with only minimal disability (32% placebo vs. 44% on rtPA). Thus despite increase in rate of ICH, treatment with IV rtPA within 3 hours of onset of ischaemic stroke improved clinical outcome.

Finally, ECASS II tested the NINDS dose of rtPA (0.9 mg/kg, max dose of 90 m) but allowed patients to receive drug up to 6^{th} hour as in ECASS I. No significant benefit was found.

Many hospitals have developed expert stroke teams to facilitate this treatment. The drug is now approved in the USA and Canada for acute stroke within 3 hours of onset of symptoms. Two recent trials (PROACT and PROACT II) using intra-arterial thrombolysis for acute MCA infarct showed benefit.

ENDOVASCULAR INTERVENTIONS

The number of options for endovascular treatment of ischemic stroke has increased substantially over the past decade to include intra-arterial fibrinolysis, mechanical clot retrieval with the Mechanical Embolus Removal in Cerebral Ischemia (Merci) Retrieval System (Concentric Medical)Inc., Mountain View, CA), mechanical clot aspiration with the Penumbra System (Penumbra, Inc. Alameda, CA), and acute angioplasty and stenting.

ANTITHROMBOTIC AND ANTIPLATELET DRUGS

HEPARIN: Both unfractionated heparin and low molecular weight heparin has not shown any benefit in the outcome and neurological worsening of acute ischemic stroke .It was further associated with increased risk of bleeding complications with early administration of UFH and LMWH.

ASPIRIN: Aspirin acts by irreversible inhibition of platelet function by inactivation of cyclooxygenase. Oral administration of aspirin (initial dose is 325 mg) within 24 to 48 hours after stroke onset is recommended for treatment of most patients.

OTHER ANTIPLATELET AGENCES:

The role of use of Clopidogrel, intravenous tirofiban and eptifibatide**,** inhibitors of glycoprotein IIb/IIIa receptor are not recommended in the use of acute ischemic stroke**.**

NEUROPROTECTIVE AGENTS:

Neuroprotection refers interventional therapy that is directed to delay the infarction or salvage the brain tissue of the still viable ischemic penumbra of the ischemic zone.

SEVERAL GROUP OF DRUGS TRIED ARE:

a.) Calcium channel blockers (nicardipine, nimodipine)

b.) NMDA receptor antagonists (Selfotel, Eliprodil),

c.) ICAM 1 antibodies (Enlimonab),

d.) Glutamate antagonist (Lebeluzole),

e.) GABAergic antagonist (Diazepam, Clomethiozole),

f.) Free radical scavengers (Tirilazed, dihydrolipoate),

g.) Inhibitors of lipid peroxidation (Ebselen).

h.) Citicoline, intermediary in the biosynthesis of phosphatidyl choline.

SURGICAL THERAPY:

Carotid Endarterectomy:

Symptomatic carotid artery stenosis with intraluminal mobile or sessile thrombus associated with an atherosclerotic plaque at the carotid bifurcation. The indication for this is controversial. The morbidity associated with surgery appears to be high among patients who already have intraluminal thrombus demonstrated by cerebral angiography.

SUPPORTIVE CARE:

a.) Nutrition and hydration

b.) Infections

c.) DVT and PE prevention.

d.) Physiotherapy

MATERIALS AND METHODS

STUDY DESIGN:

Cross sectional study.

SETTING:

The study on "A Study Of serum uric acid levels in setting of acute ischemic stroke in GVMCH" was carried out in the Department of Medicine, Government Vellore medical college and hospital, Vellore.

COLLABORATIVE DEPARTMENTS:

Department of Biochemistry, Neurology, Radiology, Government Vellore Medical College and Hospital, Vellore.

STUDY DESIGN:

The study will be done in acute ischemic stroke patients admitted as In-patient in department of General medicine of Government Vellore Medical College and Hospital. Necessary ethical clearance was obtained from ethical committee, Government Vellore medical college and hospital, Vellore.

PERIOD OF STUDY: 12 months (01-September- 2016 to 31-August- 2017)**.**

SAMPLE SIZE:

A total sample of 100 patients will be studied using carefully prepared proforma. Information will be collected through a preformed and pre-tested proforma from each patient. Fasting blood samples were drawn within 24h of admission, and examined for uric

acid and a standard battery of biochemical and haematological tests. Qualifying patients will be undergoing detailed history, clinical, biochemical and radiological examination. CT/MRI scan of brain was required for the diagnosis of ischemic stroke. Patients without neuroimaging were classified as having as uncertain stroke type were excluded in statistical analysis.

INCLUSION CRITERIA:

1.All acute ischemic stroke patients presenting within 24 hours of onset and acute ischemic stroke confirmed by CT/MRI scan.

EXCLUSION CRITERIA

1. Haemorrhagic stroke
2. Ischaemic stroke >24 hours from onset
3. CNS tumours
4. Vasculitic stroke
5. CNS infections
6. Patients who did not do CT/MRI SCAN
7. Subdural hematoma
8. Past history of PVD
9. Drugs causing hyperuricemia
10. Elevated RFT OR LFT
11. Thyroid disorder
12. COPD (Chronic obstructive pulmonary disease)
13. Chronic inflammatory bowel disease;
14. Excessive alcohol consumption

ETHICAL CLEARANCE:

This study was approved by the ethical committee of Govt. Vellore Medical College and Hospital, Vellore-11.

METHODS

After obtaining the verbal consent either from the patient or the relatives, all patients were evaluated by complete medical history, full neurological examination, standardized blood tests imaging studies and data was recorded in a standardized sheet

Clinical history was obtained from the patient, his/her relatives or past records. History regarding diabetic status, hypertension, TIA, smoking, alcoholism, chronic kidney diseases, COPD, Thyroid disorder was obtained Clinical examination was done to assess the side of the stroke, Glasgow coma scale on admission, presence of gaze palsy, papillary abnormality, plantar reflex facial palsy, speech difficulty, admission blood pressure.

Electrocardiography, blood sugar, urea, creatinine, lipid profile, serum uric acid and CT/MRI-brain were done after admission.

All relevant data were fed into a computer and results were calculated.

DEFINITIONS:

HYPERTENSION :

Hypertension was diagnosed as present if the patients exhibited a systolic blood pressure 140 mm Hg or a diastolic blood pressure 90 mm Hg, or had a history of diagnosis of hypertension and anti-hypertensive medications.

DIABETES:

Diabetes was defined if patients exhibited a fasting glucose level 7.0 mmol/L (126 mg/dL) or had a history of diabetes diagnosis and anti-diabetic medications.

DYSLIPIDEMIA :

A diagnosis of hypercholesterolemia was made for patients with a history of using cholesterol-lowering agents or who had a cut off of fasting serum total cholesterol level (200 mg/dL) on admission and LDL cholesterol >130 mg/dl. Hypertriglyceridemia when the level of Triglycerides ≥ 150 mg/dl, Low HDL cholesterol: <40 mg/dl.

URIC ACID ESTIMATION:

Uric acid level was measured by uric acid oxidase reagent on a Dax analyser (Bayer-Technicon). The definition of high uric acid level was when patients had more than 7 mg/dl in both men and women.

SMOKING:

A patient was labelled smoker when he had smoked atleast 10 cigarettes per day for more six month / more or if he had smoked daily for more than a year regardless of the number [5].

OBESITY:

A patient was defined as obese when his or her BMI was more than or equal to 24.9 kg/m2.

STATISTICAL ANALYSIS:

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using SPSS v16 software. Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. PEARSON chi- square test was used to test the significance of difference between quantitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

DEMOGRAPHIC DETAILS OF THE STUDY POPULATION:

TABLE 1: Baseline Characteristics Of Cases.

BASELINE PARAMETERS	MEAN± SD
AGE(YEARS)	61.14±12.67
BMI	23.19±3.01
FASTING BLOOD SUGAR (mg/dl)	174.46±74.59
TOTAL CHOLESTROL(mg/dl)	222.13±54.96
TRIGLYCERIDES (mg/dl)	172.85±38.83
LDL (mg/dl)	149.60±42.44
HDL(mg/dl)	43.62±5.70
SYTOLIC BP (mm hg)	165.84±25.09
DIASTOLIC BP (mm hg)	92.11±12.50
URIC ACID(mg/dl)	6.97±1.26

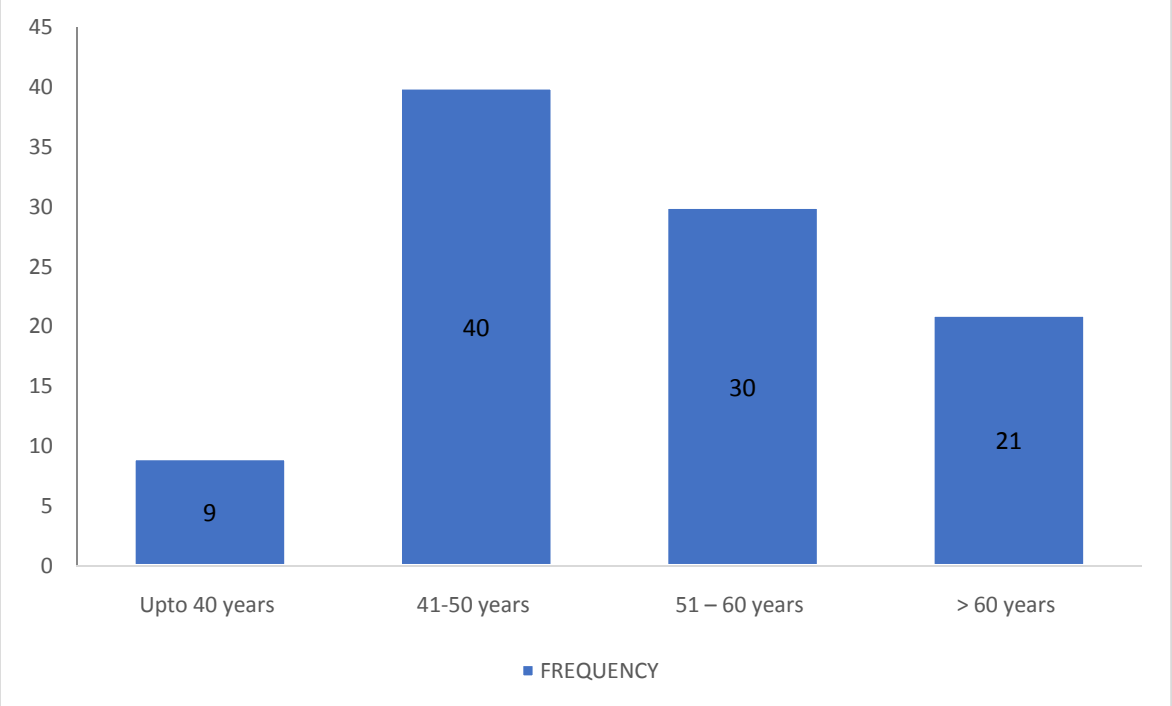
DEMOGRAPHIC DETAILS OF THE STUDY POPULATION:

AGE AND SEX:

Table 2: Frequency distribution of age of the study population

Age group	Frequency (n=100)	Percentage %
≤ 40 years	9	9
41-50 years	40	40
51 – 60 years	30	30
> 60 years	21	21

Graph 1: Frequency Distribution Of Age Of The Study Population

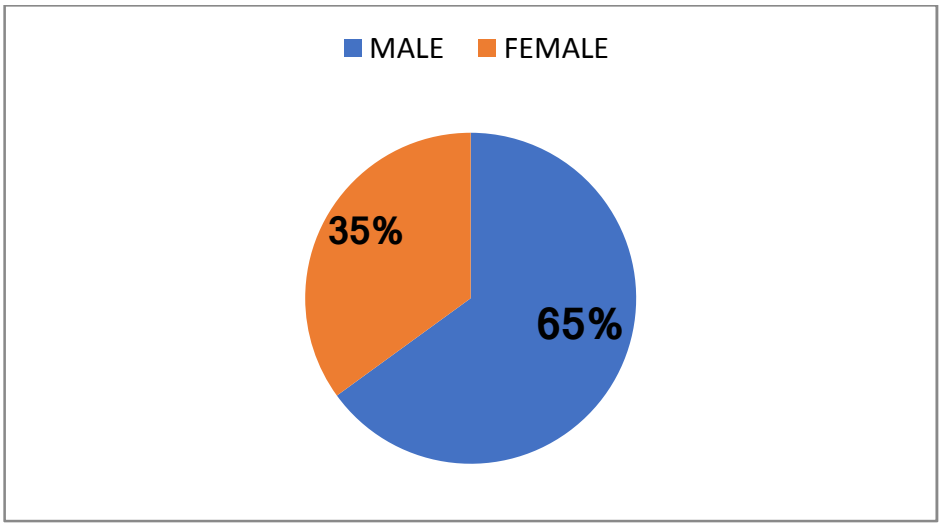


The present study included 100 patients with acute stroke with age ranging from 29 to 95 years. The mean age of the study group was 61.1± 12.6 years. The age was stratified and their frequency distribution was shown in table 1. The majority of the patients are within the age group of50 -70 years (40%). The Mean age of males in the study is 64.69±12.89 years and that of females is 63.68±11.23 yrs.

Table 3: Frequency distribution of sex of the study population

Sex	Frequency (n = 100)	Percentage (%)
Male	65	65
Female	35	35
Total	100	100

Graph 2: Frequency distribution of sex of the study population



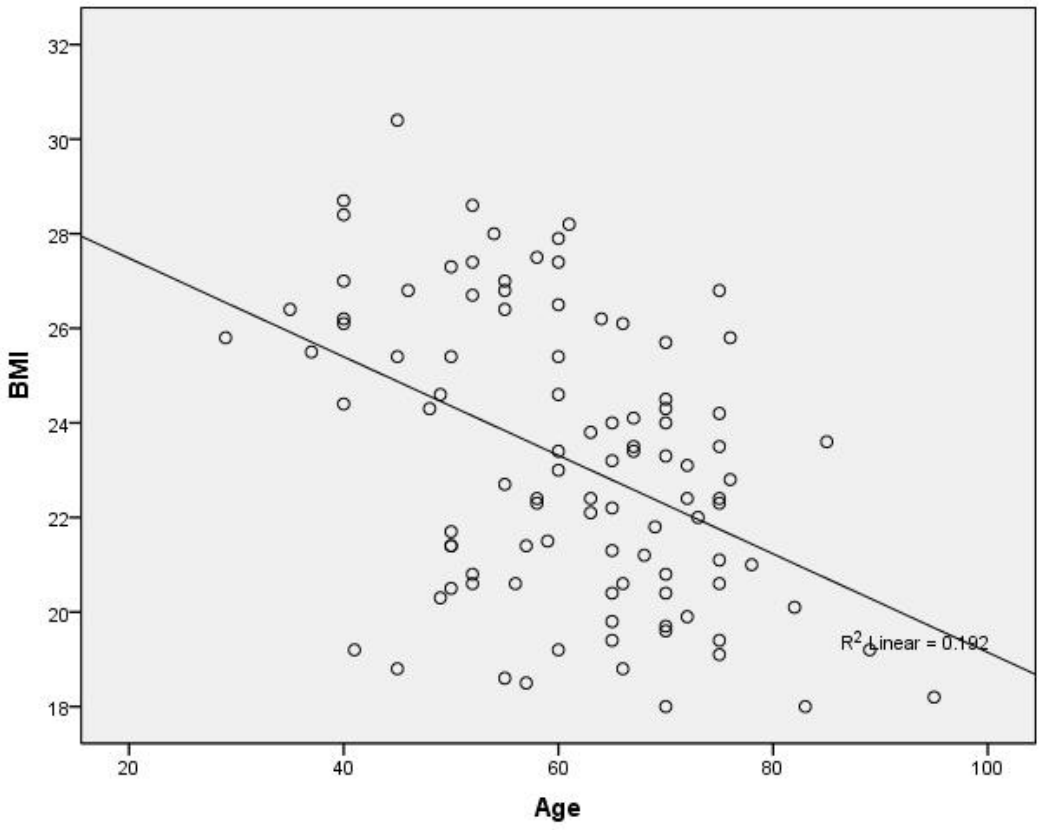
Of the 100 patients studied, 65 are males and 35 are females (Table 2)

RISK FACTORS:

AGE WITH BMI:

The BMI was found to be inversely correlated with age by Pearson's correlation analysis. On regression analysis, for every one year increase in age, BMI decreases by a factor of 0.44.

Graph 3: Distribution of age (years) with BMI (BODY MASS INDEX) kg/m^2 in study population:

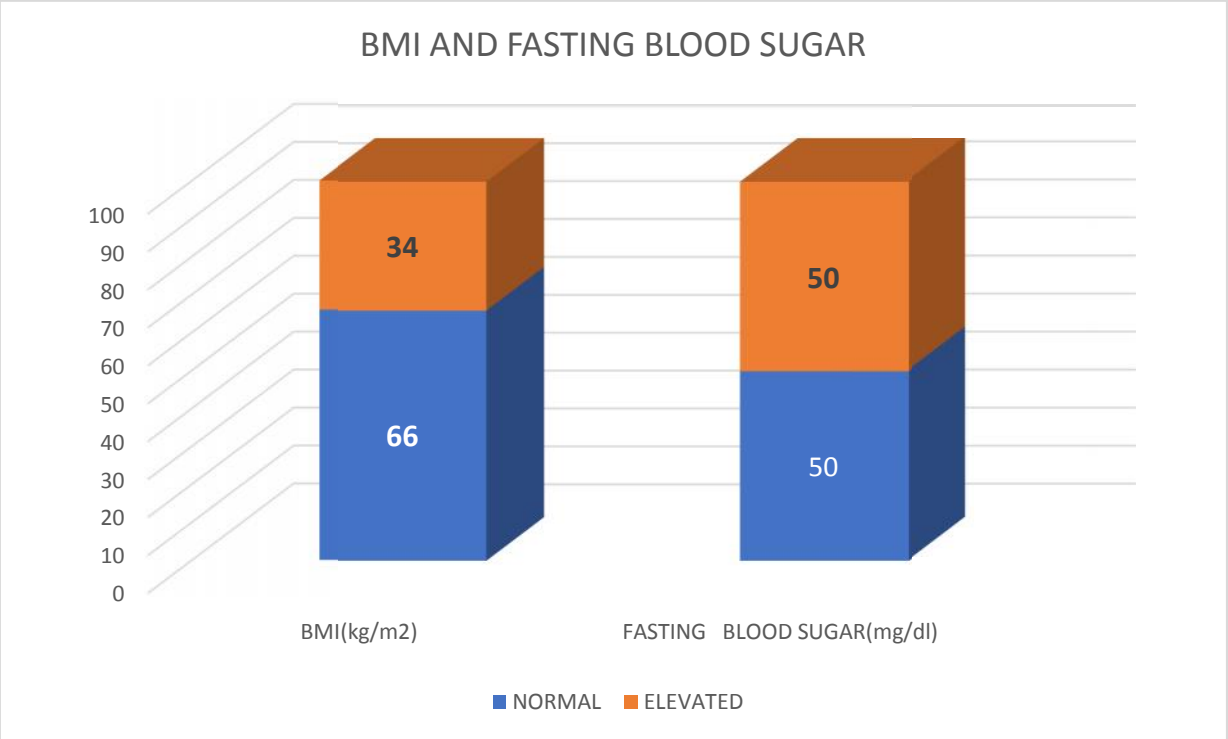


BMI AND FASTING BLOOD GLUCOSE:

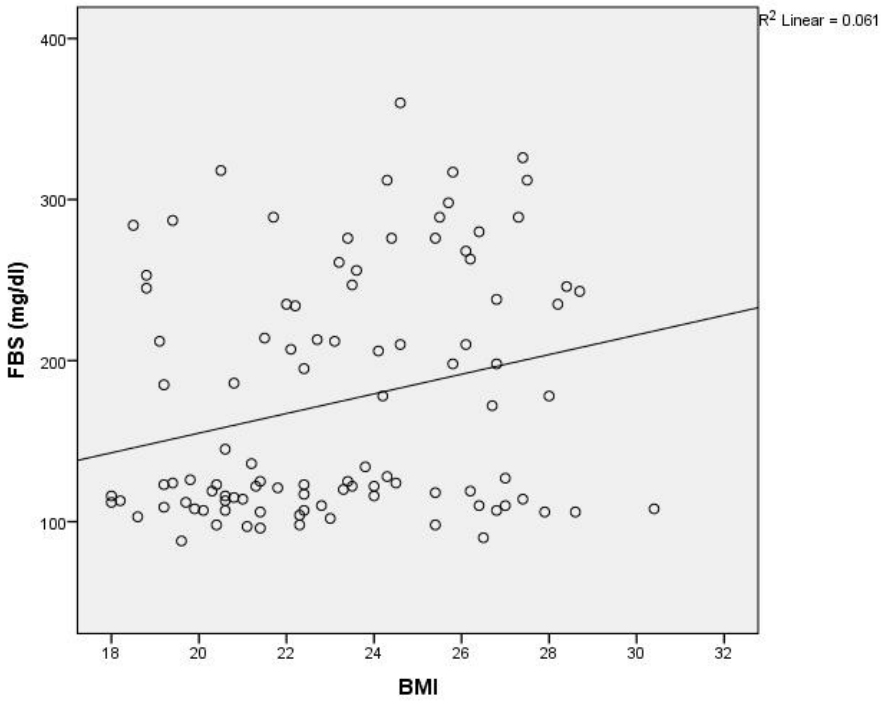
Table 4: Descriptive statistics of elevated BMI and fasting blood sugar in the study population

Parameters	Range	Mean	Standard deviation
BMI(kg/m^2)	18 - 30.4	23.1	3.01
Fasting Blood sugar (mg/dl)	88 - 360	174	74.5

Graph 3: Distribution of elevated BMI and fasting blood sugar in the study population



Graph 4: Pearson correlation between BMI and Fasting blood sugar in patients with acute ischaemic stroke.



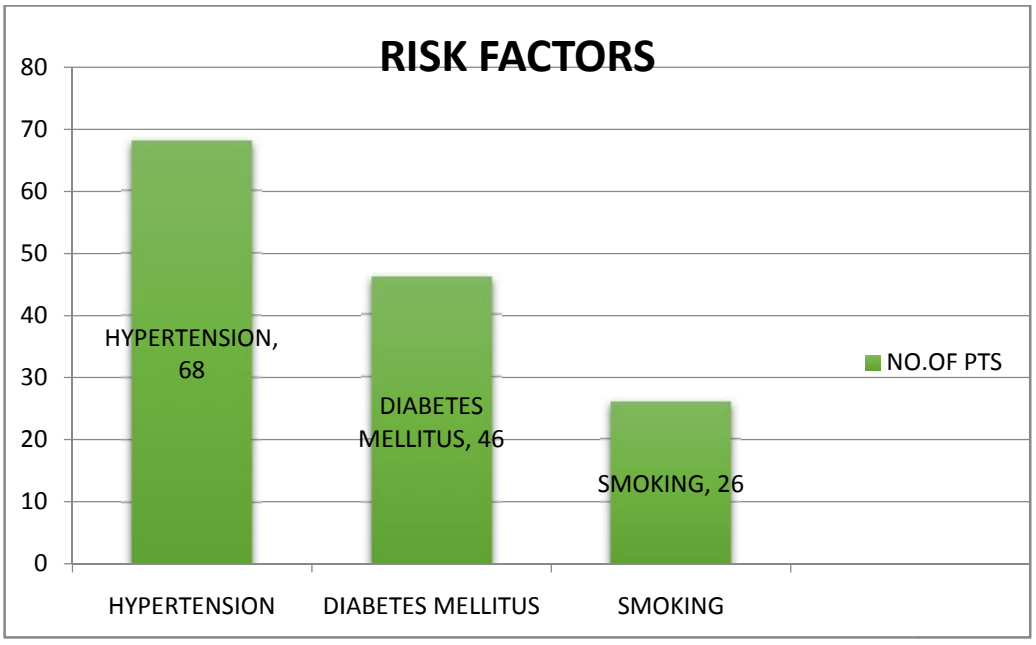
In our study majority 2/3 rd (n=66) of the patients had normal BMI and 1/3rd (n=34) of patients are obese, as their BMI was more than or equal to 24.9. Most of the patients fell into normal BMI. BMI of the study population ranges from 18 to 13.4 with a mean of 23.1 ± 3.01. The fasting blood sugar was elevated in 50 patients and rest of the 50 had normal fasting sugar values. Fasting sugar value ranges from 88 to 360 mg/dl with a mean of 174 ± 74.5 mg/dl. Pearson correlation showed that fasting blood sugar increased with increase in BMI ($p<0.01$). On doing simple linear regression analysis, For every single unit rise in BMI the fasting blood sugar will increase by a factor of 6.09. For every one unit rise in cholesterol levels, FBS rises by a factor 0.25.

HYPERTENSION, DIABETES MELLITUS AND SMOKING:

Table 5 : Distribution of hypertension, diabetes mellitus and smoking in the study population

Parameters	Yes	No
Smoking (n=100)	26	74
Diabetes mellitus (n=100)	46	54
Hypertension (n=100)	68	32

Graph 5: Distribution of hypertension, diabetes mellitus and smoking in the study population



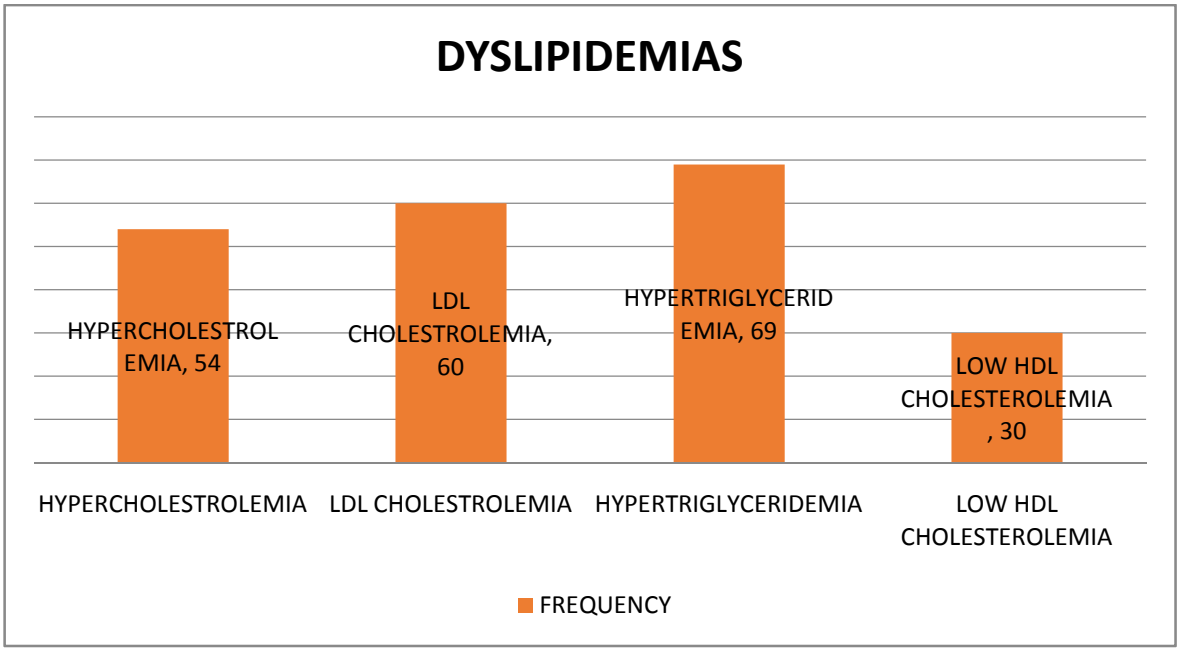
Of the risk factors focussed in the study population of acute ischemic stroke patients namely hypertension, smoking and diabetes mellitus, Hypertension was the most commonly found to be associated with acute stoke with 68 % (n=68), followed by diabetes mellitus in 46% (n=46) of patients. Smoking was associated with 26% (n=26) of which, all of them were males.

DYSLIPIDEMIA:

Table 6: Distribution of dyslipidaemias in the study population with their descriptive statistics

Dyslipidemias	YES	NO	Mean ± SD (mg/dl)
Hypercholesterolemia	54	46	222.1 ±55.0
Elevated LDL Cholesterol	60	40	149.6 ±42.4
Hypertriglyceridemia	69	31	172.8 ±38.8
Lowered HDL Cholesterol	30	70	43.6±5.7

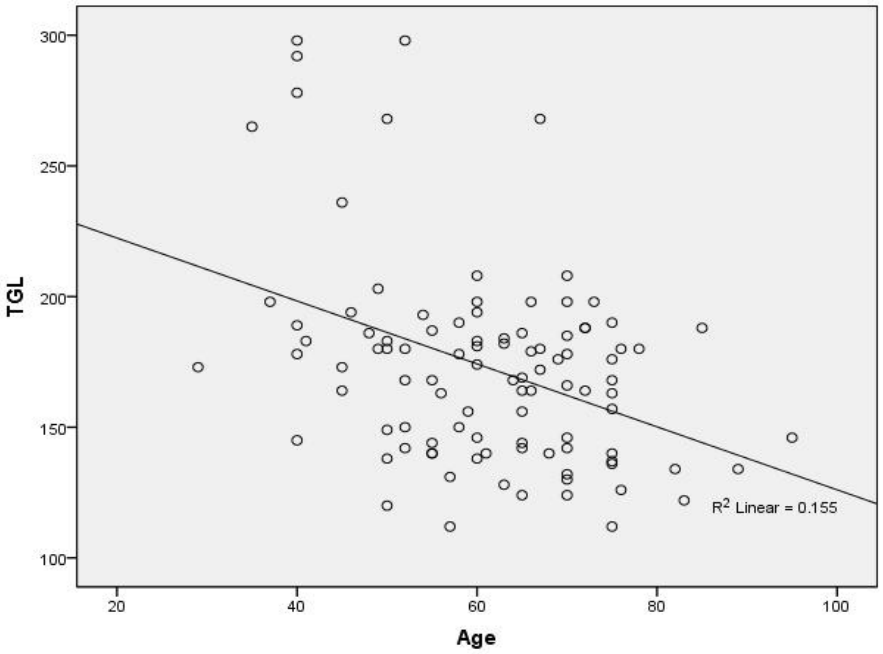
Graph 6: Distribution of dyslipidaemias in the study population



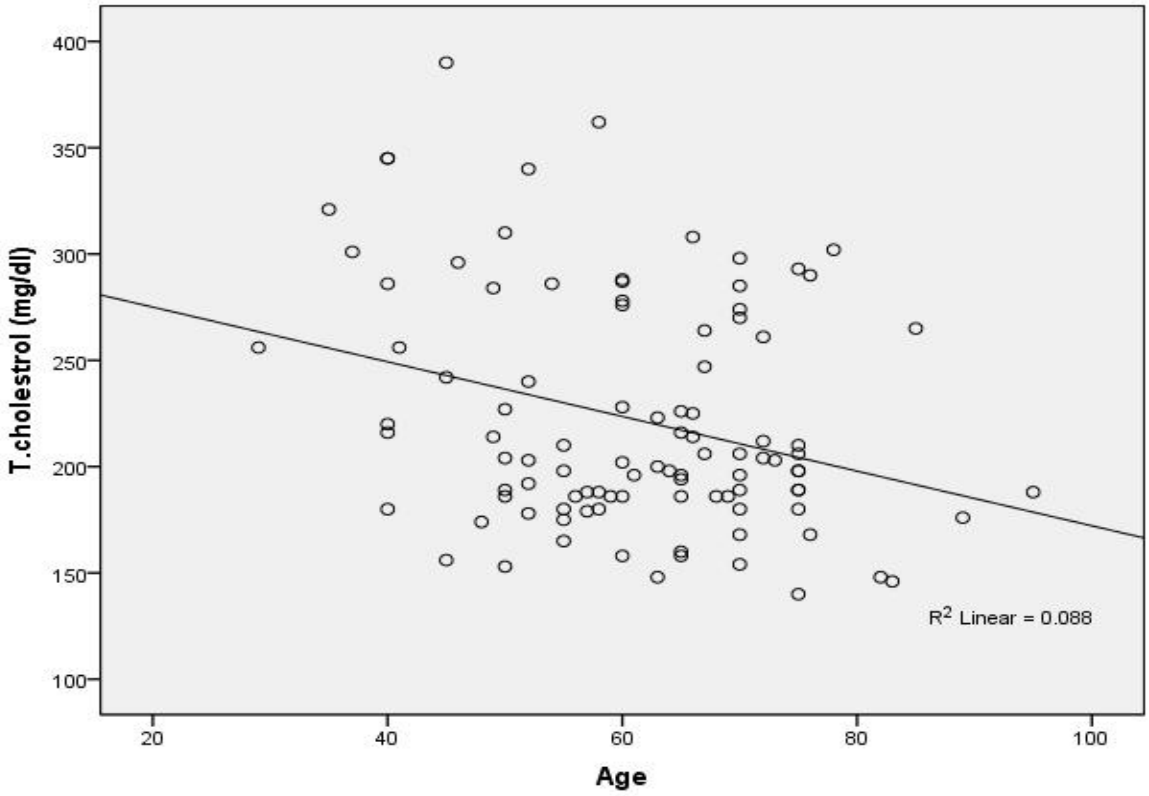
Most of the patients with acute stroke were found to have dyslipidemia in one or the other form of abnormal lipid profile. Hypercholesterolemia (total cholesterol >200 mg /dl) was found in 54% of patients (n=54).Patients with hypertriglyceridemia (triglycerides >150 mg/dl)was found to be69% (n=69). HDL cholesterol which was considered to be beneficial was low (<40 mg/dl) in 30% of cases (n = 30).

The data on subjecting to Pearson correlation it was found that, As age increase, total cholesterol and triglycerides levels decreases. Regression analysis showed that for every unit rise in age the total cholesterol and TGL decreased by a factor of 0.30 ($p< 0.05$) and 0.39 ($p<0.05$) respectively.

Graph 7: Distribution of triglycerides in the study population with their age :



Graph 8 : Distribution of total cholesterol to their ages in study patients:

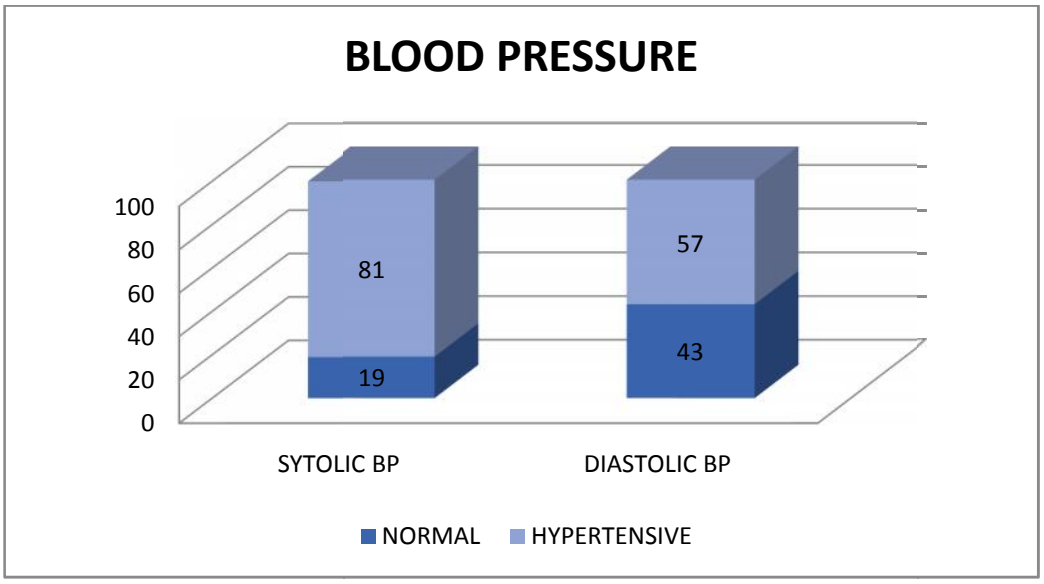


BLOOD PRESSURE:

Table 7: Distribution of Blood Pressure in the study population with their discriptive statistics

Blood pressure	Normotensive	Hypertensive	Mean ± SD
Systolic BP (mm of Hg)	19	81	165.84±25.09
Diastolic BP (mm of Hg)	43	57	92.11±12.50

Graph 9: Distribution of Blood Pressure in the study population



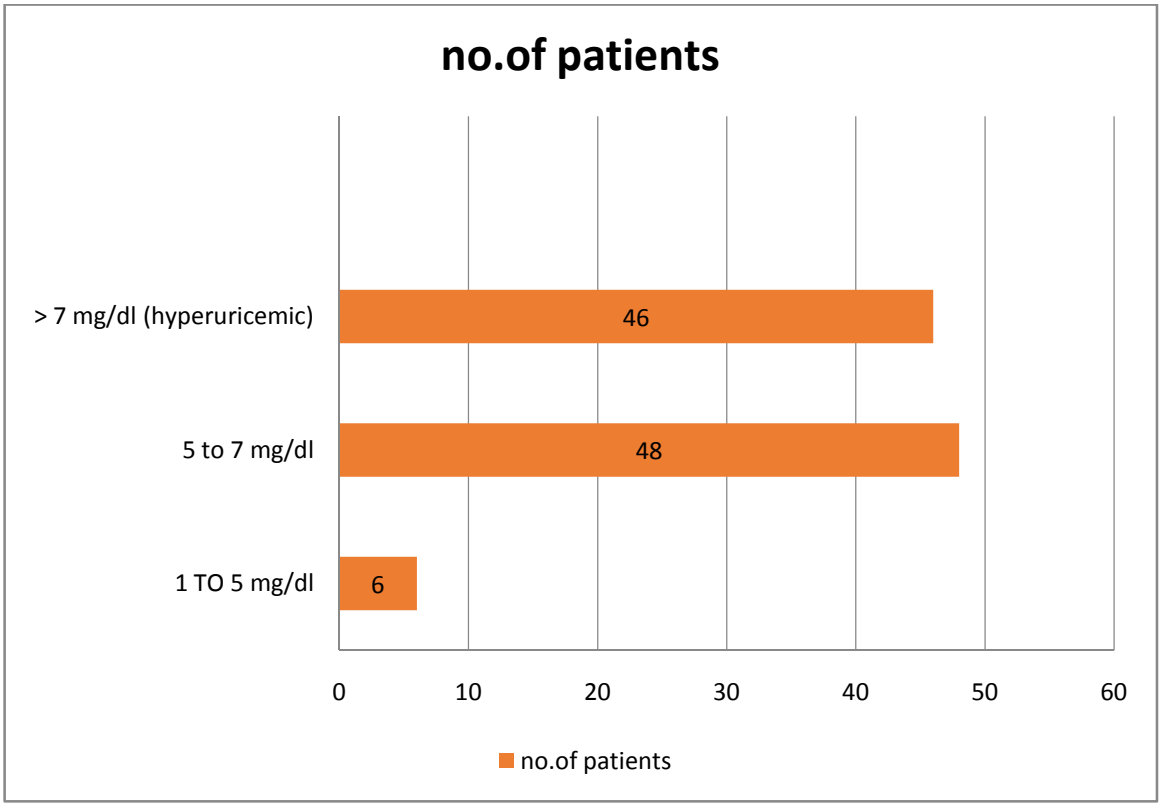
In our study, as already learnt from the history most of the patients had elevated blood pressure on measuring the blood pressure it was found that most of patients had elevated Systolic blood pressure (>140 mm of Hg) in 91% (n=91). Diastolic blood pressure was elevated (>90 mmhg) in 43% of patients.

URIC ACID LEVELS

Table 8: Distribution of serum uric acid levels in the patients with acute ischemic stroke.

Uric acid mg/dl	Frequency (n=100)
1 to 5	6
5 to 7	48
>7(hyperuricemia)	46

Graph 10 : Distribution of serum uric acid levels in the patients with acute ischemic stroke.



In the present study, the mean serum uric acid level was 7 mg/dl with a standard deviation of 1.2 mg/dl. The minimum value noted was 4.5 mg/dl and the maximum serum uric acid levels was 10.1 mg/dl. Hyperuricemia (elevated serum uric acid levels> 7mg/dl) was noted in 46% of cases (n=46) and the other 54 % had uric acid levels below 7 mg/dl of which 6% (n=6)had uric acid levels below 5mg/dl and 48% (n=48) had serum uric acid levels within 5 to 7 mg/dl.

RELATIONSHIP BETWEEN URIC ACID AND OTHER PARAMETERS:

- **AGE AND URIC ACID:**

Table 9: Distribution of age with serum uric acid levels in study population:

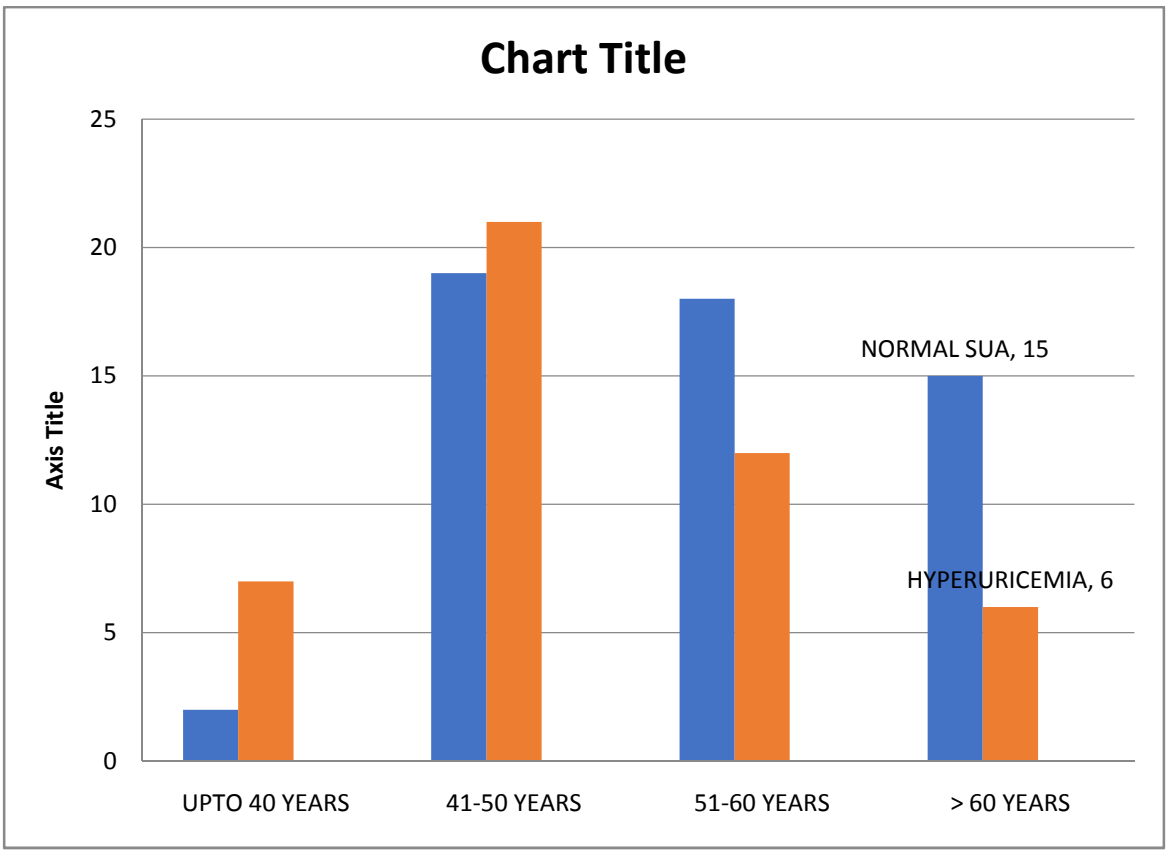
Age Group	Serum Uric Acid Levels		Total
	Normal	Hyperuricemic	
Upto 40 years	2	7	9
41 to 50 years	19	21	40
51 to 60 years	18	12	30
>60 years	15	06	21

Table 10: Stratified age group in the study patients with uric acid levels:

AGE STRATIFIED	NORMAL	HYPERURICEMIA	TOTAL
< 60 YEARS	21	28	49
> 60 YEARS	33	18	51

p value was significant in Pearson chi square test($p < 0.05$)

Graph 11: Distribution of serum uric acid with different age groups:



In present study correlation between age and serum uric acid was done using bivariate analysis which showed no correlation between the various age group and serum uric acid levels in acute ischemic stroke. But interestingly when another bivariate analysis was done with stratifying the patients into two group, first group as age less than 60years(n=49) and other second group with age more than 60 years of age(n=51),a statistically ignificant correlation (p value <0.05) between the age group and SUA was found.

TABLE 11 : SEX AND URIC ACID LEVELS

SEX	**SERUM URIC ACID LEVELS**		
	NORMAL	**HYPERURICEMIC**	**TOTAL**
MALE	35	30	65
FEMALE	19	16	35
			100

In current study, no significant correlation between the sex (gender) distribution and SUA in patients with ischemic stroke was found.

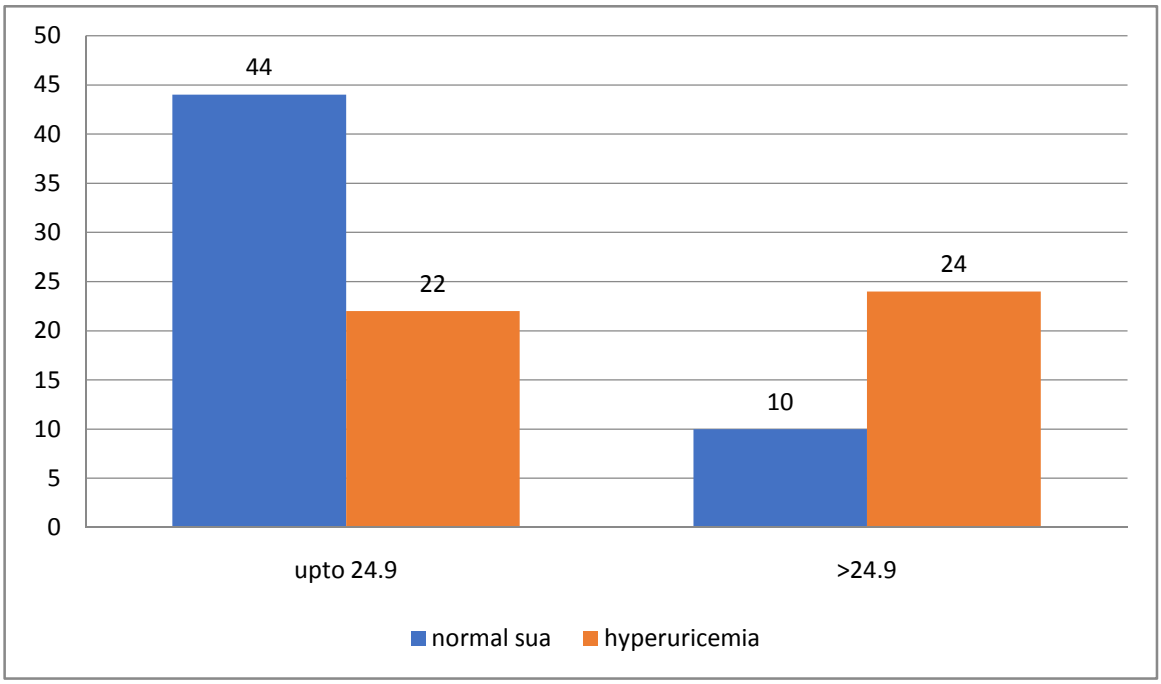
- **BODY MASS INDEX AND URIC ACID:**

TABLE 12: BMI AND URIC ACID LEVELS

BMI	Uric acid		TOTAL
	NORMAL	HYPER	
UPTO 24.9	44	22	66
>25	10	24	34
			100

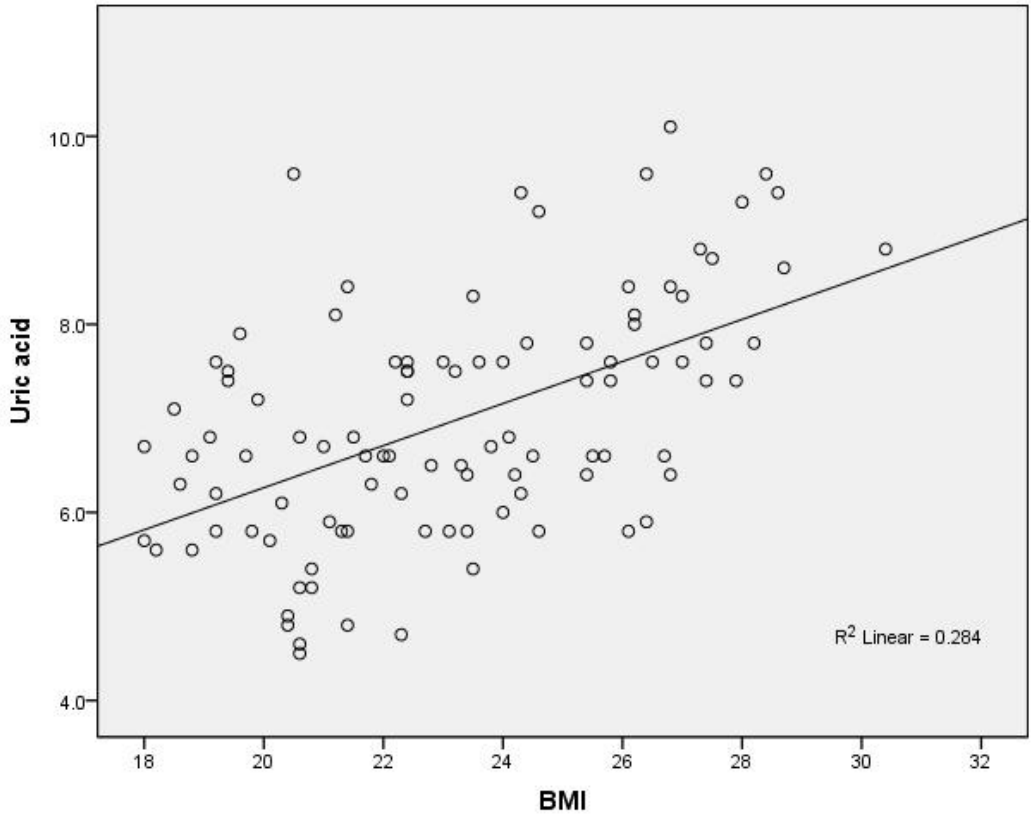
p value was significant in Pearson chi square test(p <0.01)

Graph 12: Distribution of serum uric acid with BMI of the study population:



In our study, we have (n=34) thirty-four patients with BMI in the range of obesity, other 66 patients had BMI within normal range. Using bivariate analysis, with Pearson chi square test in the present study we found a statistically significant correlation between BMI and serum uric acid($p<0.01$). On simple linear regression analysis, for every one unit rise in serum uric acid, BMI(body mass index) increases by a factor of 1.3.

- **Graph 13: Distribution of serum uric acid with BMI in study population;**

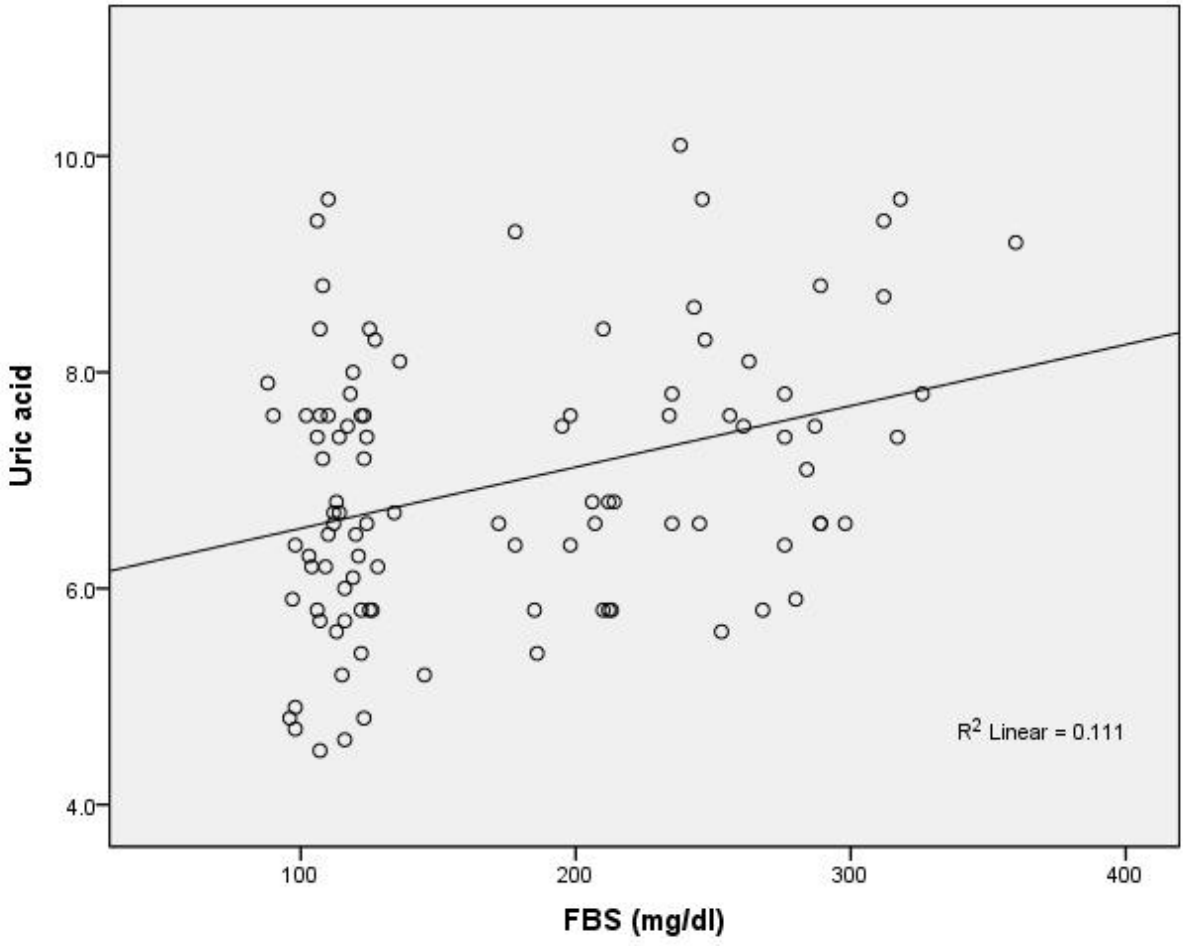


- **DIABETES MELLITUS AND URIC ACID:**

TABLE13:Distribution of diabetes mellitus and SUA levels in our study:

	SERUM URIC ACID LEVELS		
	NORMAL	**HYPERURICEMIC**	**TOTAL**
DIABETES	21	25	46
NON-DIABETIC	33	21	54

Graph 14: Distribution of serum uric acid levels with FBS Fasting blood glucose levels in our study population:



In our current study, there was a statistically significant positive correlation between fasting blood sugar and serum uric acid level ($p < 0.05$). On simple linear regression analysis, For every single unit rise in BMI there was an increase in fasting blood glucose by factor of 6.09. For every one unit rise in serum uric acid, FBS increases by a factor of 19.67.

LIPID PROFILE AND URIC ACIDTABLE

Table 14: Distribution of Total Cholesterol and uric acid.

	NORMAL	HYPERURICEMIA	TOTAL
NORMAL	34	12	46
HYPERCHOLESTROLEMIA	20	34	54

p value was significant in Pearson chi square test ($p < 0.01$)

A statistically significant correlation was foundusing bivariate analysis using Pearson chi square test(p value < 0.01) between hypercholesterolemia (n=54) patients with elevated serum uric acid with acute ischemic stroke. on simple linear regression analysis, for every one unit rise in serum uric acid T. Cholesterol increases by a factor of 21.21.

Graph 15: Distribution of Total Cholesterol and uric acid in our patients:

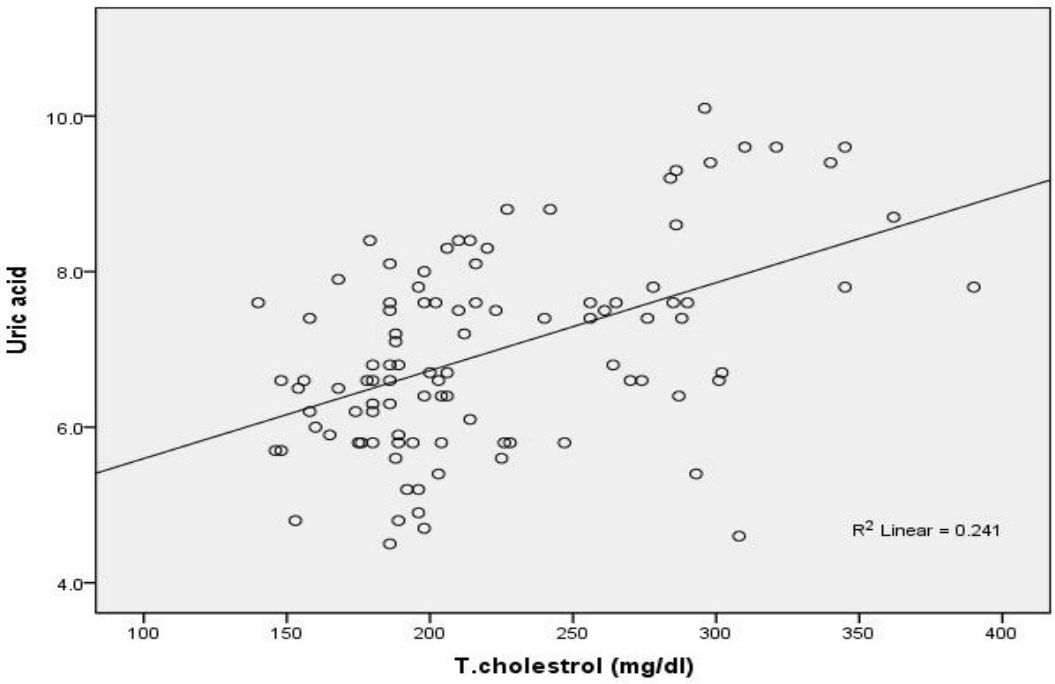


Table 15: Distribution of TGL with serum uric acid in our study population:

	NORMAL	HYPERURICEMIA	TOTAL
NORMAL	22	09	31
HYPER TGL	32	37	69

p value was significant in Pearson chi square test (p <0.01)

In our current study around sixty nine patients (n=69) had hypertriglyceridemia and a statistically significant correlation was found in between patients with hypertriglyceridemia and elevated SUA using bivariate analysis and pearson chi square test with a p value(p value <0.01). on simple linear regression analysis, for every one unit rise in serum uric acid TGL increases by a factor of 15.1

Graph 16: Distribution of TGL with serum uric acid in our study population:

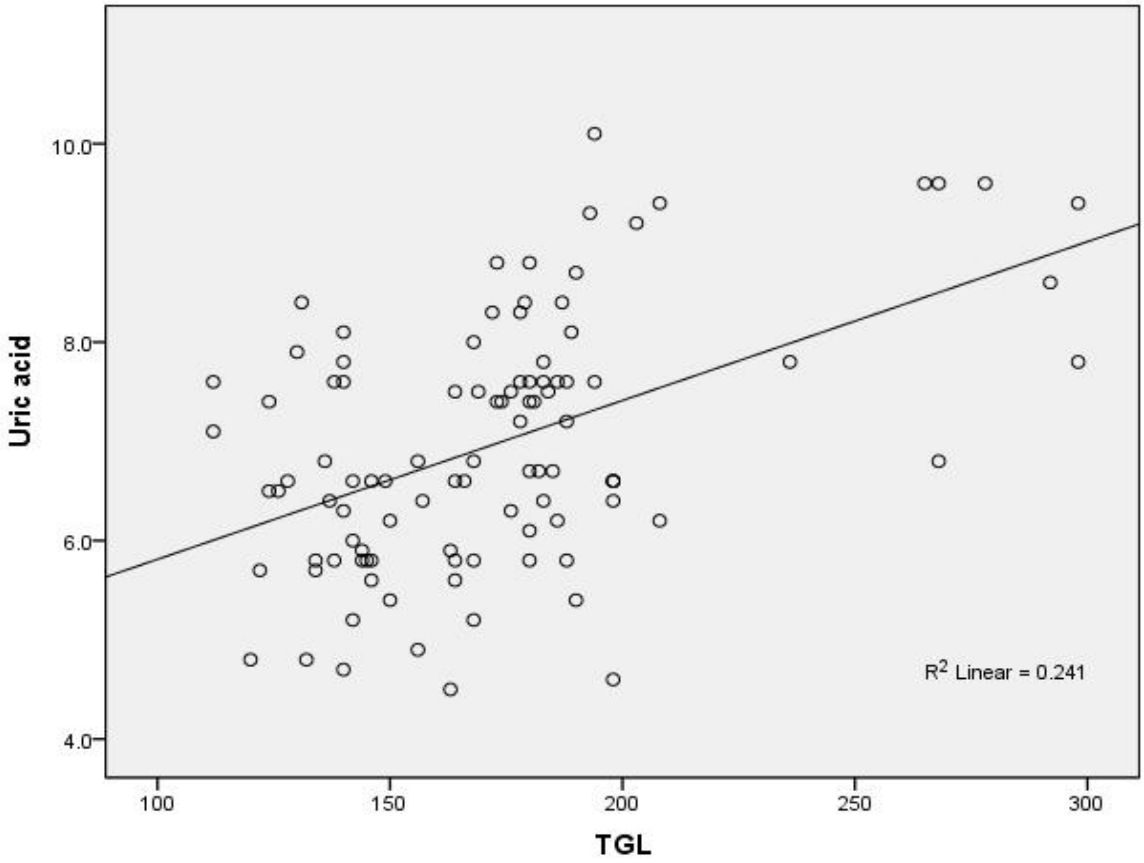


Table 16: Distribution of LDL Cholesterol and uric acid in our study population

	NORMAL	HYPERURICEMIA	TOTAL
NORMAL	29	11	40
HYPERCHOLESTROLEMIA	25	35	60

p value was significant in Pearson chi square test ($p < 0.01$)

In the present study, a statistically significant correlation was found using bivariate analysis using Pearson chi square with p value significant (pvalue<0.01) between patients with elevated LDL cholesterol (n=60) and serum uric acid in stroke patients.on simple linear regression analysis, for every one unit rise in serum uric acid LDL increases by a factor of 15.38

Graph 17:Distribution of LDL Cholesterol and uric acid in our study population

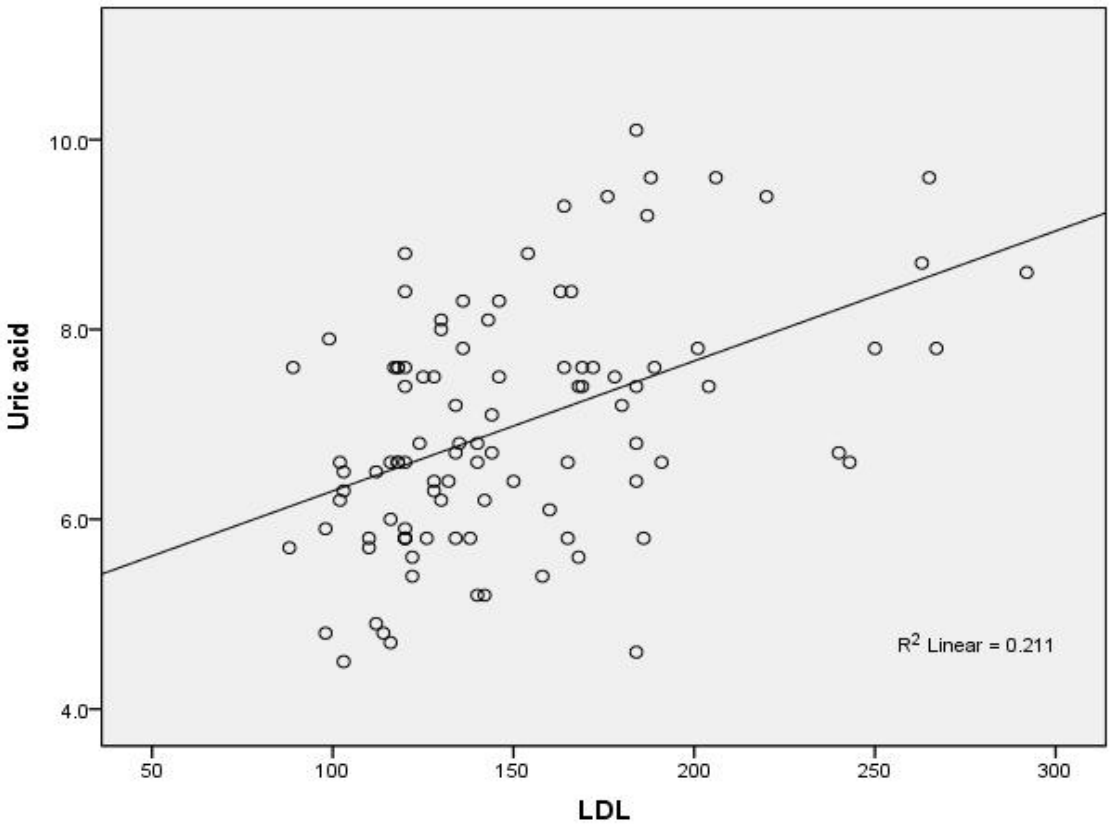


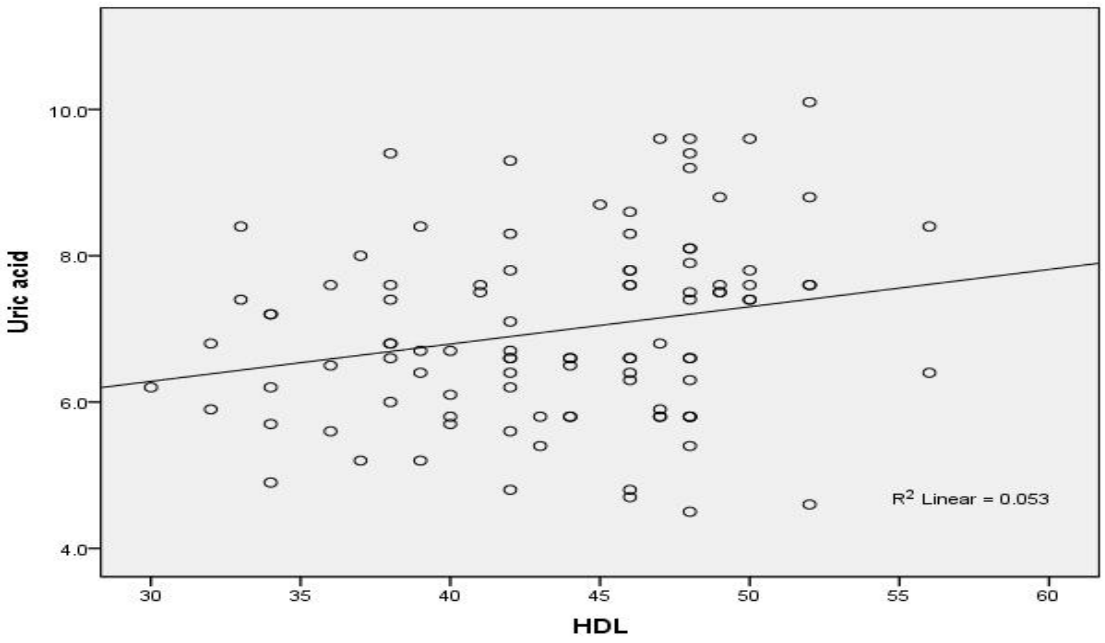
Table17: Distribution of HDLCholesterol and uric acid in our study population:

	NORMAL	HYPERURICEMIA	TOTAL
NORMAL	20	10	30
HYPERCHOLESTROLEMIA	34	36	70

p value is statistically significant with (p value <0.05)

In our present study, significant positive correlation was found between HDL cholesterol and serum uric acid levels (p<0.05). on simple linear regression analysis, for every one unit rise in serum uric acid HDL increases by a factor of 1.03.

Graph 18 :: Distribution of HDL Cholesterol and uric acid in our study population



BLOOD PRESSURE AND URIC ACID LEVELS:

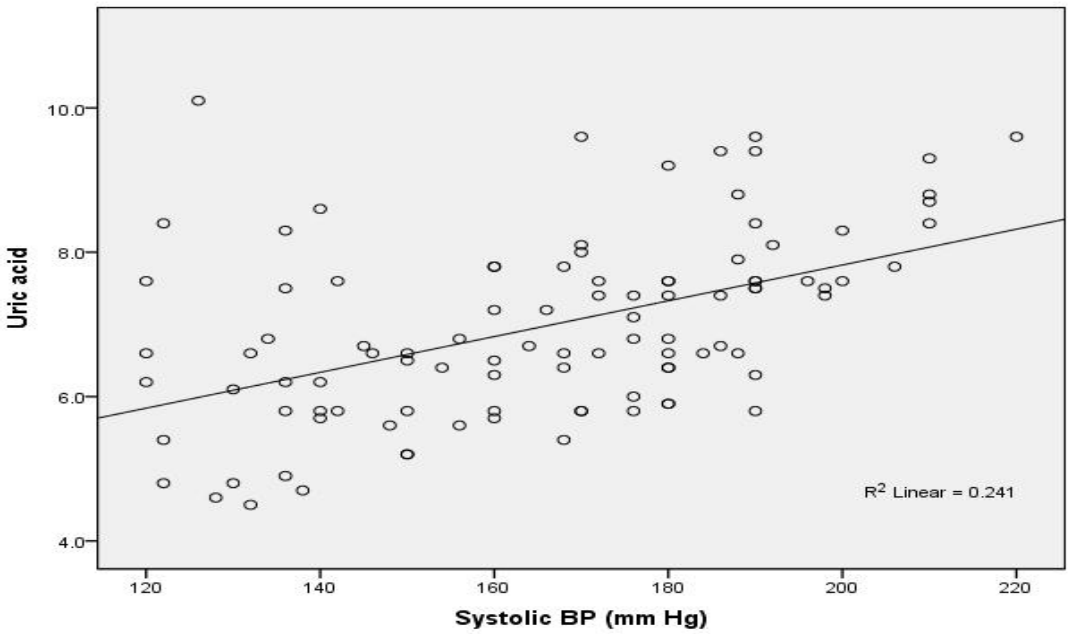
SYSTOLIC BP WITH SERUM URIC ACID :

Table 18: Distribution of serum uric acid with systolic bp in our study population:

SYSTOLIC BP	NORMAL	HYPERURICEMIA	TOTAL
NORMAL	14	5	19
SYSTOLIC HYPERTENSION	40	41	81

p value was significant in Pearson chi square test (p <0.01)

Graph 19: Distribution of serum uric acid with systolic bp in our study population:



In the present study a statistically significant correlation was found between SUA and Systolic BP, using bivariate analysis using pearson chi square with p value significant (pvalue<0.01).on simple linear regression analysis, for every one unit rise in serum uric acid Sys. BP increases by a factor of 9.7

DIASTOLIC BP WITH SERUM URC ACID :

Table19 : Distribution of serum uric acid with Diastolic BP in our study population:

	NORMAL	HYPERURICEMIA	TOTAL
NORMAL	30	13	43
DIASTOLIC BP	24	33	57

p value was significant in Pearson chi square test (p <0.01)

In our current study, we found there was significant correlation between hypertension and elevated serum uric acid levels using Pearson chi square test with p value(p=<0.01). Interestingly our study showed a significant correlation between diastolic more than systolic blood pressure with elevated serum uric acid as an important risk factor for the development of acute ischemic stroke.

On simple linear regression analysis, for every one unit rise in serum uric acid Diastolic. BP increased by a factor of 3.8.

Graph 20 : Distribution of serum uric acid with Diastolic BP in our study population:

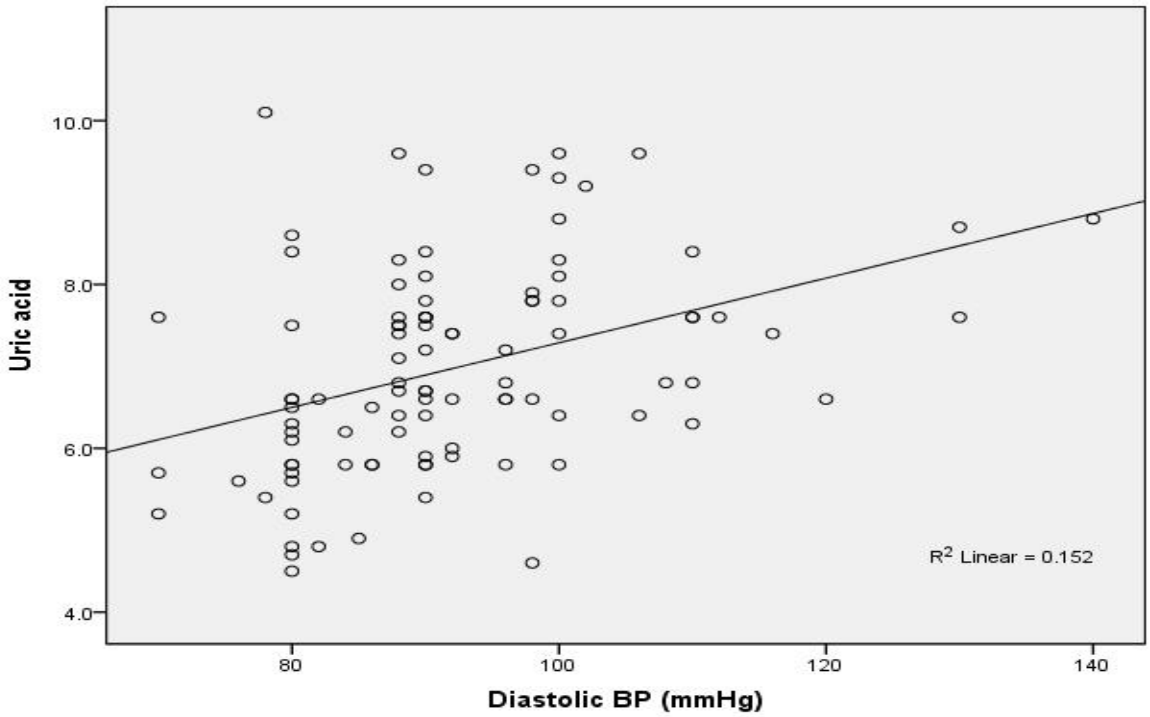


TABLE 20 : Distribution of Smokers and uric acid levels in acute ischemic stroke patients:

HISTORY SMOKING	NORMAL	HYPERURICEMIA	TOTAL
YES	12	14	26
NO	42	32	74

In our study, no statistical significance was found in patients with history of smoking and elevated serum uric acid in acute ischemic stroke patients.

MULTIPLE LOGISTIC REGRESSION:

In our study Multiple, logistic regression analysis was done between multiple parameters that were significant in bivariate analysis like BMI (Body mass index), Blood pressure (systolic and diastolic blood pressure), Total cholesterol, Triglycerides. Of those BMI (body mass index), Diastolic blood pressure, Total cholesterol were the ones that was statistically significant (p value< 0.05). whereas systolic blood pressure, triglycerides, and LDL cholesterol that was significant in bivariate analysis was not statistically significant.

DISCUSSION

100 cases of acute ischemic stroke within 24 hours of onset were admitted in the department of General Medicine, Government Vellore Medical College and hospital during the period of October 2016 to May 2017.

Among total number stroke patients 100 patients who underwent CT/MRI scan, and diagnosed to have acute ischemic stroke only then they were included in the statistical analysis.

AGE DISTRIBUTION:

Age is a non-modifiable risk factor which has a significant correlation between with increased incidence of stroke. Copenhagen stroke study(17) by Nakayama et al. suggest stroke is a disease of elderly and age plays a major role in the prognosis and recovery of the patients.

Our study correlates well with the finding of Kuzuya et al. that as age increases there is an significant increase in SUA which independent of other factors, which further increases the risk of stroke(31). Our study also has shown a similar result ,As age increased (> 60 years of age) there was as statistically significant increase in SUA in our acute ischemic stroke patients.

SEX DISTRIBUTION:

In Journal of American heart association, Zhong et al. published that there was no significant sex difference was found with hyperuricemia in males and females but a significant relation with modest increase in the risk of stroke was associated with both male and female with elevated serum uric acid(32),In our study also there was no significant correlation between sex difference and serum uric acid.

RISK FACTORS IN STROKE:

HYPERTENSION:

In the present study, 68 percentage of cases were hypertensives. Hypertension is an important risk factor for stroke(33).There are number of novel studies that show significant correlation between hypertension and hyperuricemia(34)(35) . Hyperuricemia is an independent predictor of hypertension and is present in 25% of patients with new-onset primary hypertension who were not treated previously(36)· This hyperuricemia in hypertensives can be explained due to reduced renal perfusion which stimulates urate reabsorption due to decrease in renal blood flow(37)Experimentally-induced hyperuricemia also increased the blood pressure in rats by a renal mechanism linked to inhibition of nitric oxide (NO), activation of the renin–angiotensin system, and development of renal arteriosclerosis(38)·

Once renal arteriosclerosis develops, the kidney plays a major role in the maintenance of hyper- tension(39)Prolonged elevated serum uric acid in rats also caused progressive kidney injury via a crystalline-independent mechanism(38)and accelerated established renal disease(40)· Finally, UA stimulated synthesis of monocyte chemoattractant protein-1 by the rat vascular smooth muscle cells(41)and this is known to stimulate macrophage infiltration of atherosclerotic vessels (42)

Thus, we know atherosclerotic vessels is an important source of thrombus increasing the risk of stroke(43).Thereby suggesting that elevated SUA in hypertensives is an important atherogenic risk factor that increases the occurrence of acute ischemic stroke(44).

As various studies suggest, In our study there was very high statitcallly significant correlation (pvalue<0.01) between both systolic blood pressure(mean 165.84±25.09 mmhg) as well as diastolic blood pressure (mean 92.11±12.50mmhg) andelevated serum uric acid levels in acute ischemic stroke patients. Thus,helping us suggest that hypertensive patients with elevated serum uric acid are at risk for acute ischemic stroke.

4.DIABETES:

In our study 50 % of patients were diabetics. Diabetes is an important cause of cardiovascular risk factors like stroke and myocardial infarction. Dehgan et al. found that hyperuricemia is a strong and independent risk factor for diabetes(45). Hyperuricemia is an important risk factor and strong predictor of stroke due to diabetes independently of other risk factors (46).Hyperuricemia is an important risk

factor for the development of diabetes and diabetic nephropathy(47).Emerging studies are also suggestive that hyperuricemia as an important risk factor for insulin resistance(48). In turn insulin resistance has shown to increases purine biosynthesis and turnover, with its attendant increase in SUA levels. In contrast to the popular belief our study showed that there was no significance between diabetes and serum uric acid levels this result could be due to small sample size.

BMI :

Body mass index has a significant correlation with hyperuricemia and risk of stroke. Bonoro et al. data states that elevated uric acid is associated with multiple components of metabolic /insulin resistance syndrome In addition, these data suggest that obesity and central body fat distribution, and not hyperinsulinemia & insulin resistance, that plays a major role in linking hyperuricemia with CVD risk factors. Dyslipidaemia is related to hyperuricemia independently of obesity and central body fat distribution.(49) Oyama et al shows clearly that serum uric acid levels are significantly increased with increased BMI and could be used as one of indicators for risk factors stratification even in early adolescence.(50)

DYSLIPIDEMIA:

In a large meta-analysis of 90,000 patients showed that administration of statins reduces the risk of stroke among patients with coronary heart disease and those at increased risk for cerebrovascular disease and that this risk reduction is primarily related to the extent to which LDL-C levels are lowered. (51) Dyslipidaemia is a risk factor for cerebrovascular accident ,its relation with serum

uric acid is as SUA concentration is positively correlated with Triglycerides, Total Cholesterol, LDL-Cholesterol, and negatively correlated with HDL-C.

However, in the acute stroke setting, several studies have shown the opposite; that is, low cholesterol levels are associated with short-term mortality or worse functional outcome in patients with ischemic stroke, particularly in those who are older(52).On the contrary, in patients with prior cerebrovascular disease, high levels of total cholesterol increase the risk of myocardial infarction，whereas treatment with a statin reduces the incidence of major cardiovascular events in this population.(53)(54) . Studies also suggest that administration of statins reduces the serum uric acid levels and also improve renal functions thus thereby reducing the additional risk of hyperuricemia for cerebrovascular stroke.(55)(56)

In our study, we also observed that SUA levels were associated with TG and non-HDL-C(51) that suggesting that serum uric acid as an additional risk factor for the incidence of acute stroke in already high risk patients.

SMOKING:

Currently there are no study relating uric acid with smoking in stroke patients. In our study also there was no statistically significant correlation between smoking and uric acid in acute ischemic stroke patients.

URIC ACID :

Free radical activity is characteristically increased in patients with any one of several major cardiovascular risk factors, and is thought to play a key role in the early development of atherosclerosis. As an antioxidant, Uric acid could be expected to confer protection against free radicals. There are accumulating evidences suggesting that uric acid as a causal factor for number of cardiovascular complications. Thus abnormally high level of serum uric acid in blood suggest that there is increased oxidative stress which induces endothelial dysfunction thereby cerebrovascular slow blood flow(57).

There are different mechanism in which UA may directly affect atherogenesis or the clinical course of cerebrovascular disease. Cerebral ischemia is a result of free radical mediated oxidative damage and complex cascade of metabolic events. powerful oxidative radicals that are generated during the process causes lipid peroxidation that irreversibly damages plasma and mitochondrial membranes (58).thus the importance of local antioxidants is clearly understood from the above explanations. Stroke is associated with rapid reduction in serum antioxidants(59).Uric acid is the most abundant aqueous antioxidant in humans and contributes to the major junk of the antioxidant capacity of plasma. It is particularly effective in quenching superoxide radicals and peroxynitrite radical and may protect the neuronal cells from lipid peroxidative damage.(60) It might therefore be expected that having an elevated SUA level during an acute stroke would be beneficial.

But contrary to the traditional belief of anti-oxidant properties of uric acid large series of study has shown the opposite that uric acid acts as pro oxidant and accentuates the inflammatory cascade and therefore causing damage and poor outcome (61)

One hypothesis would be that UA can become a pro-oxidant under certain circumstances, particularly if other antioxidants such as ascorbate are lowThus, in patients with acute stroke the fall in ascorbate levels could predispose the SUA to take on pro-oxidant properties.(62) Consistent with this hypothesis is the observation that in acute stroke, those with high SUA and low ascorbate levels have the worst outcome.(63)

Other hypothesis, uric acid causes vascular disease by causing vascular endothelial dysfunction. Uric acid stimulates LDL cholesterol oxidation and granulocyte adherence to the endothelium thus favouring endothelial injury(64).uric acid also has the tendency to form crystals in atherosclerotic plaque.(65)

Uric acid also increases its cerebrovascular risk with its association with metabolic syndrome through its relation with insulin resistance(66) .as insulin resistance is directly related to the level of serum uric acid .serum uric acid induces insulin resistance by its ability to induce endothelial dysfunction through nitric oxide bioavailability inhibition (67), Because insulin requires NO to stimulate glucose uptake, it has been hypothesized that hyperuricemia may have a key role in

the pathogenesis of IR(68).In our study, we found that hyperuricemia independent of the other risk factors of metabolic syndrome like blood pressure, cholesterol, triglyceride levels hasbeen an important accentuating factor to other risk factor of acute ischemic stroke.

In our study, also we have found a negative correlation with age and body mass index along with low cholesterol associated with elderly population. Hypercholesterolemia and triglyceridemia are an important risk factor of ischemic stroke as shown by numbers of studies on its risk and administration of statins and fenofibrate has reduced the risk of acute stroke in patients with CAD and increased risk of cardiovascular diseases(69). But several studies have shown that low cholesterol levels are associated which poor prognosis in an setting of acute ischemic stroke particularly elderly people(70)(71). This paradox might be explained by the fact that these patients might had poor nutritional status or severe disease (71).

Thus more importantly this finding should not be misinterpreted as elevated cholesterol levels might be considered as a good prognostic factor in acute ischemic stroke as we have a number of study suggestive that elevated cholesterol levels are risk factor for acute ischemic stroke which doesn’t confer protection to these study population against stroke.

Thus, we had concluded in our study that SUA (serum uric acid) is an important risk factor for the development of acute ischemic stroke. Eventhough the traditional risk factors of stroke like hypertension, diabetes mellitus, dyslipidaemia

is being treated aggressively for reducing the incidence of stroke there is a need for identifying other modifiable risk factors for the associated with mortality and morbidity of stroke.

Therefore, it would be prudent for us to use allopurinol and other uricosuric drug other drug like losartan and fenofibrate (72).Statins also has shown to reduce SUA(73) and preserve renal function (74)which can help prevents vascular catastrophe in people with high risk factors(75).Thus, these treatment with drugs lowering serum uric acid might be helpful in reducing the risk of acute ischemic stroke. However, further prospective studies are needed to assess the precise role of elevated serum uric acid in these high-risk patients and the use of drugs to treat them before the onset of acute ischemic stroke has to be studied to be recommended for routine use in detail.

LIMITATIONS OF THE STUDY:

1. The number of patients evaluated had been small and this could have influenced the results of the study.

2. Large samples could not be entered into the study because most of the patients admitted after 24 hours of onset of stroke.

CONCLUSION

The following conclusions were derived from the study.

1. The serum Uric acid is an important risk factor for the onset of acute ischemic stroke of independent of age, BMI, hypertension, diabetes, dyslipidaemia.
2. For every one unit rise in serum uric acid, we found a significant rise of risk factors i.e. BMI rise by factor of 1.3, fasting blood sugar rise by factor of 19.67.
3. For every one unit rise in serum uric acid, total cholesterol rises by 21.21, triglycerides by 15.1, LDL cholesterol by 5.28.
4. For every one unit rise in serum uric acid, systolic blood pressure rises by factor of 9.7, diastolic blood pressure rises by factor of 3.8.
5. Our study showed a significant association between serum uric acid and acute ischemic stroke. This brings new insight into uric acid being used in day to day practice and a trigger for physician to screen patients with risk factors and hyperuricemia for acute ischemic stroke.
6. Eventhough traditional risk factors of stroke like hypertension, diabetes, hyperlipidaemia is treated aggressively, our study opens up the possible suggestion of additional therapeutic administration of drugs that reduce serum uric acid to patients with high risk factors associated with hyperuricemia to decline the incidence of acute ischemic stroke.

BIBLIOGRAPHY:

1. WHO | The world health report 2002 - Reducing Risks, Promoting Healthy Life [Internet]. WHO. [cited 2017 Sep 6]. Available from: http://www.who.int/whr/2002/en/
2. Pandian JD, Sudhan P. Stroke Epidemiology and Stroke Care Services in India. J Stroke. 2013 Sep;15(3):128–34.
3. NEET Mbbs. Oxidative stress in brain ischemia. Love S, Brain pathology (Zurich, Switzerland) 1999-Jan;9()119-31 DOI: full article [Internet]. MBBSdost NEET. [cited 2017 Sep 6]. Available from: http://mbbsdost.com/Oxidative-stress-brain-ischemia-Brain-pathology-Zurich-Switzerland-Love-S--1999-Jan/pubmed/12878412
4. Yu ZF, Bruce-Keller AJ, Goodman Y, Mattson MP. Uric acid protects neurons against excitotoxic and metabolic insults in cell culture, and against focal ischemic brain injury in vivo. J Neurosci Res. 1998 Sep 1;53(5):613–25.
5. Chamorro A, Obach V, Cervera A, Revilla M, Deulofeu R, Aponte JH. Prognostic significance of uric acid serum concentration in patients with acute ischemic stroke. Stroke. 2002 Apr;33(4):1048–52.
6. Abbott RD, Brand FN, Kannel WB, Castelli WP. Gout and coronary heart disease: the Framingham Study. J Clin Epidemiol. 1988;41(3):237–42.
7. Lehto S, Niskanen L, Rönnemaa T, Laakso M. Serum uric acid is a strong predictor of stroke in patients with non-insulin-dependent diabetes mellitus. Stroke. 1998 Mar;29(3):635–9.
8. Bos MJ, Koudstaal PJ, Hofman A, Witteman JCM, Breteler MMB. Uric Acid Is a Risk Factor for Myocardial Infarction and Stroke: The Rotterdam Study. Stroke. 2006 Jun 1;37(6):1503–7.

9. Chen J-H, Chuang S-Y, Chen H-J, Yeh W-T, Pan W-H. Serum uric acid level as an independent risk factor for all-cause, cardiovascular, and ischemic stroke mortality: A chinese cohort study. Arthritis Care Res. 2009 Feb 15;61(2):225–32.
10. Calberg MJ, Kjøller E. [Uric acid as a marker of pathophysiological mechanisms in patients with cardiovascular disease]. Ugeskr Laeger. 2005 Oct 3;167(40):3771–4.
11. Conditions (UK) NCC for C. Introduction [Internet]. Royal College of Physicians (UK); 2008 [cited 2017 Sep 6]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK53302/
12. Blood Vessels of the Brain | Internet Stroke Center [Internet]. [cited 2017 Sep 18]. Available from: http://www.strokecenter.org/professionals/brain-anatomy/blood-vessels-of-the-brain/
13. bod_cerebrovasculardiseasestroke.pdf [Internet]. [cited 2017 Sep 9]. Available from: http://www.who.int/healthinfo/statistics/bod_cerebrovasculardiseasestroke.pdf
14. Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993 Jan 1;24(1):35–41.
15. Dirnagl U, Iadecola C, Moskowitz MA. Pathobiology of ischaemic stroke: an integrated view. Trends Neurosci. 1999 Sep;22(9):391–7.
16. Doyle KP, Simon RP, Stenzel-Poore MP. Neuropharmacology – Special Issue on Cerebral Ischemia Mechanisms of Ischemic Brain Damage – Review Article. Neuropharmacology. 2008 Sep;55(3):310–8.
17. Nakayama H, Jørgensen HS, Raaschou HO, Olsen TS. The influence of age on stroke outcome. The Copenhagen Stroke Study. Stroke. 1994 Apr;25(4):808–13.

18. Wang S-F, Shu L, Wang S, Wang X-Q, Mu M, Hu C-Q, et al. Gender difference in the association of hyperuricemia with hypertension in a middle-aged Chinese population. Blood Press. 2014 Dec;23(6):339–44.
19. Li J, Jiang S, Zhang Y, Tang G, Wang Y, Mao G, et al. H-type hypertension and risk of stroke in chinese adults: A prospective, nested case–control study. J Transl Intern Med. 2015;3(4):171–8.
20. Jørgensen H, Nakayama H, Raaschou HO, Olsen TS. Stroke in patients with diabetes. The Copenhagen Stroke Study. Stroke. 1994 Oct;25(10):1977–84.
21. Li C, Hsieh M-C, Chang S-J. Metabolic syndrome, diabetes, and hyperuricemia. Curr Opin Rheumatol. 2013 Mar;25(2):210–6.
22. Wolf PA, D'Agostino RB, Kannel WB, Bonita R, Belanger AJ. Cigarette Smoking as a Risk Factor for Stroke: The Framingham Study. JAMA. 1988 Feb 19;259(7):1025–9.
23. Iribarren C, Folsom AR, Eckfeldt JH, McGovern PG, Nieto FJ. Correlates of uric acid and its association with asymptomatic carotid atherosclerosis: The ARIC study. Ann Epidemiol. 1996 Jul 1;6(4):331–40.
24. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991 Aug 1;22(8):983–8.
25. Saxena Y, Saxena V, Mittal M, Srivastava M, Raghuvanshi S. Age-Wise Association of Carotid Intima Media Thickness in Ischemic Stroke. Ann Neurosci. 2017 May;24(1):5–11.
26. Carotid-Artery Intima and Media Thickness as a Risk Factor for Myocardial Infarction and Stroke in Older Adults — NEJM [Internet]. [cited 2017 Sep 10]. Available from: http://www.nejm.org/doi/full/10.1056/NEJM199901073400103#t=article

27. Coull AJ, Lovett JK, Rothwell PM, Oxford Vascular Study. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. BMJ. 2004 Feb 7;328(7435):326.
28. Adams HP, Zoppo G del, Alberts MJ, Bhatt DL, Brass L, Furlan A, et al. Guidelines for the Early Management of Adults With Ischemic Stroke: A Guideline From the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Circulation. 2007 May 22;115(20):e478–534.
29. Neuroimaging of Ischemic Stroke With CT and MRI [Internet]. Medscape. [cited 2017 Sep 11]. Available from: http://www.medscape.com/viewarticle/587073
30. Jauch EC, Saver JL, Adams HP, Bruno A, Connors JJ (Buddy), Demaerschalk BM, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2013 Mar 1;44(3):870–947.
31. Kuzuya M, Ando F, Iguchi A, Shimokata H. Effect of aging on serum uric acid levels: longitudinal changes in a large Japanese population group. J Gerontol A Biol Sci Med Sci. 2002 Oct;57(10):M660-664.
32. Zhong C, Zhong X, Xu T, Xu T, Zhang Y. Sex-Specific Relationship Between Serum Uric Acid and Risk of Stroke: A Dose-Response Meta-Analysis of Prospective Studies. J Am Heart Assoc. 2017 Mar 29;6(4).
33. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R, Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a

meta-analysis of individual data for one million adults in 61 prospective studies. Lancet Lond Engl. 2002 Dec 14;360(9349):1903–13.

34. Sundström J, Sullivan L, D'Agostino RB, Levy D, Kannel WB, Vasan RS. Relations of serum uric acid to longitudinal blood pressure tracking and hypertension incidence. Hypertens Dallas Tex 1979. 2005 Jan;45(1):28–33.
35. Masuo K, Kawaguchi H, Mikami H, Ogihara T, Tuck ML. Serum uric acid and plasma norepinephrine concentrations predict subsequent weight gain and blood pressure elevation. Hypertens Dallas Tex 1979. 2003 Oct;42(4):474–80.
36. Cannon PJ, Stason WB, Demartini FE, Sommers SC, Laragh JH. Hyperuricemia in primary and renal hypertension. N Engl J Med. 1966 Sep 1;275(9):457–64.
37. Messerli FH, Frohlich ED, Dreslinski GR, Suarez DH, Aristimuno GG. Serum uric acid in essential hypertension: an indicator of renal vascular involvement. Ann Intern Med. 1980 Dec;93(6):817–21.
38. Mazzali M, Hughes J, Kim YG, Jefferson JA, Kang DH, Gordon KL, et al. Elevated uric acid increases blood pressure in the rat by a novel crystal-independent mechanism. Hypertens Dallas Tex 1979. 2001 Nov;38(5):1101–6.
39. Watanabe S, Kang D-H, Feng L, Nakagawa T, Kanellis J, Lan H, et al. Uric acid, hominoid evolution, and the pathogenesis of salt-sensitivity. Hypertens Dallas Tex 1979. 2002 Sep;40(3):355–60.
40. Kang D-H, Nakagawa T, Feng L, Watanabe S, Han L, Mazzali M, et al. A role for uric acid in the progression of renal disease. J Am Soc Nephrol JASN. 2002 Dec;13(12):2888–97.
41. Kanellis J, Watanabe S, Li JH, Kang DH, Li P, Nakagawa T, et al. Uric acid stimulates monocyte chemoattractant protein-1 production in vascular smooth muscle

cells via mitogen-activated protein kinase and cyclooxygenase-2. Hypertens Dallas Tex 1979. 2003 Jun;41(6):1287–93.

42. Gu L, Okada Y, Clinton SK, Gerard C, Sukhova GK, Libby P, et al. Absence of monocyte chemoattractant protein-1 reduces atherosclerosis in low density lipoprotein receptor-deficient mice. Mol Cell. 1998 Aug;2(2):275–81.
43. Atherosclerosis and Stroke [Internet]. [cited 2017 Sep 26]. Available from: http://www.strokeassociation.org/STROKEORG/LifeAfterStroke/HealthyLivingAfterStroke/UnderstandingRiskyConditions/Atherosclerosis-and-Stroke_UCM_310426_Article.jsp#.WcqhYdMjFE4
44. Mutluay R, Deger SM, Bahadir E, Durmaz AO, Çitil R, Sindel S. Uric Acid is an Important Predictor for Hypertensive Early Atherosclerosis. Adv Ther. 2012 Mar 1;29(3):276–86.
45. Dehghan A, Hoek M van, Sijbrands EJG, Hofman A, Witteman JCM. High Serum Uric Acid as a Novel Risk Factor for Type 2 Diabetes. Diabetes Care. 2008 Feb 1;31(2):361–2.
46. Lehto S, Niskanen L, Rönnemaa T, Laakso M. Serum Uric Acid Is a Strong Predictor of Stroke in Patients With Non–Insulin-Dependent Diabetes Mellitus. Stroke. 1998 Mar 1;29(3):635–9.
47. Shah P, Bjornstad P, Johnson RJ. Hyperuricemia as a potential risk factor for type 2 diabetes and diabetic nephropathy. J Bras Nefrol Orgao Of Soc Bras E Lat-Am Nefrol. 2016 Dec;38(4):386–7.
48. Yoo TW, Sung KC, Shin HS, Kim BJ, Kim BS, Kang JH, et al. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. Circ J Off J Jpn Circ Soc. 2005 Aug;69(8):928–33.

49. Bonora E, Targher G, Zenere MB, Saggiani F, Cacciatori V, Tosi F, et al. Relationship of uric acid concentration to cardiovascular risk factors in young men. Role of obesity and central fat distribution. The Verona Young Men Atherosclerosis Risk Factors Study. Int J Obes Relat Metab Disord J Int Assoc Study Obes. 1996 Nov;20(11):975–80.
50. Oyama C, Takahashi T, Oyamada M, Oyamada T, Ohno T, Miyashita M, et al. Serum Uric Acid as an Obesity-Related Indicator in Early Adolescence. Tohoku J Exp Med. 2006;209(3):257–62.
51. Amarenco P, Labreuche J, Lavallée P, Touboul P-J. Statins in stroke prevention and carotid atherosclerosis: systematic review and up-to-date meta-analysis. Stroke. 2004 Dec;35(12):2902–9.
52. Zuliani G, Cherubini A, Atti AR, Blè A, Vavalle C, Di Todaro F, et al. Low cholesterol levels are associated with short-term mortality in older patients with ischemic stroke. J Gerontol A Biol Sci Med Sci. 2004 Mar;59(3):293–7.
53. Amarenco P, Bogousslavsky J, Callahan A, Goldstein LB, Hennerici M, Rudolph AE, et al. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med. 2006 Aug 10;355(6):549–59.
54. Collins R, Armitage J, Parish S, Sleight P, Peto R, Heart Protection Study Collaborative Group. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20536 people with cerebrovascular disease or other high-risk conditions. Lancet Lond Engl. 2004 Mar 6;363(9411):757–67.
55. Athyros VG, Elisaf M, Papageorgiou AA, Symeonidis AN, Pehlivanidis AN, Bouloukos VI, et al. Effect of statins versus untreated dyslipidemia on serum uric acid levels in patients with coronary heart disease: a subgroup analysis of the GREek

Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study. Am J Kidney Dis Off J Natl Kidney Found. 2004 Apr;43(4):589–99.

56. Athyros VG, Elisaf M, Papageorgiou AA, Symeonidis AN, Pehlivanidis AN, Bouloukos VI, et al. Effect of statins versus untreated dyslipidemia on serum uric acid levels in patients with coronary heart disease: a subgroup analysis of the GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study. Am J Kidney Dis Off J Natl Kidney Found. 2004 Apr;43(4):589–99.
57. Gagliardi ACM, Miname MH, Santos RD. Uric acid: A marker of increased cardiovascular risk. Atherosclerosis. 2009 Jan;202(1):11–7.
58. Radak D, Resanovic I, Isenovic ER. Link Between Oxidative Stress and Acute Brain Ischemia. Angiology. 2014 Sep 1;65(8):667–76.
59. Gariballa SE, Hutchin TP, Sinclair AJ. Antioxidant capacity after acute ischaemic stroke. QJM Int J Med. 2002 Oct 1;95(10):685–90.
60. Squadrito GL, Cueto R, Splenser AE, Valavanidis A, Zhang H, Uppu RM, et al. Reaction of uric acid with peroxynitrite and implications for the mechanism of neuroprotection by uric acid. Arch Biochem Biophys. 2000 Apr 15;376(2):333–7.
61. Weir CJ, Muir SW, Walters MR, Lees KR. Serum urate as an independent predictor of poor outcome and future vascular events after acute stroke. Stroke. 2003 Aug;34(8):1951–6.
62. Abuja PM. Ascorbate prevents prooxidant effects of urate in oxidation of human low density lipoprotein. FEBS Lett. 1999 Mar 12;446(2):305–8.
63. Cherubini A, Polidori MC, Bregnocchi M, Pezzuto S, Cecchetti R, Ingegni T, et al. Antioxidant profile and early outcome in stroke patients. Stroke. 2000;31(10):2295–300.

64. Boogaerts MA, Hammerschmidt DE, Roelant C, Verwilghen RL, Jacob HS. Mechanisms of vascular damage in gout and oxalosis: Crystal induced, granulocyte mediated, endothelial injury. Thromb Haemost. 1983;50(2):576–80.
65. Patetsios P, Song M, Shutze WP, Pappas C, Rodino W, Ramirez JA, et al. Identification of uric acid and xanthine oxidase in atherosclerotic plaque1. Am J Cardiol. 2001 Jul 15;88(2):188–91.
66. Tsouli SG, Liberopoulos EN, Mikhailidis DP, Athyros VG, Elisaf MS. Elevated serum uric acid levels in metabolic syndrome: an active component or an innocent bystander? Metab - Clin Exp. 2006 Oct 1;55(10):1293–301.
67. Waring WS, Webb DJ, Maxwell SRJ. Uric acid as a risk factor for cardiovascular disease. QJM Int J Med. 2000 Nov 1;93(11):707–13.
68. Nakagawa T, Hu H, Zharikov S, Tuttle KR, Short RA, Glushakova O, et al. A causal role for uric acid in fructose-induced metabolic syndrome. Am J Physiol Renal Physiol. 2006 Mar;290(3):F625-631.
69. Amarenco P, Labreuche J, Lavallée P, Touboul P-J. Statins in stroke prevention and carotid atherosclerosis: systematic review and up-to-date meta-analysis. Stroke. 2004 Dec;35(12):2902–9.
70. Brescianini S, Maggi S, Farchi G, Mariotti S, Di Carlo A, Baldereschi M, et al. Low total cholesterol and increased risk of dying: are low levels clinical warning signs in the elderly? Results from the Italian Longitudinal Study on Aging. J Am Geriatr Soc. 2003 Jul;51(7):991–6.
71. Zuliani G, Cherubini A, Atti AR, Blè A, Vavalle C, Di Todaro F, et al. Low cholesterol levels are associated with short-term mortality in older patients with ischemic stroke. J Gerontol A Biol Sci Med Sci. 2004 Mar;59(3):293–7.

72. Daskalopoulou SS, Tzovaras V, Mikhailidis DP, Elisaf M. Effect on serum uric acid levels of drugs prescribed for indications other than treating hyperuricaemia. Curr Pharm Des. 2005;11(32):4161–75.

73. Athyros VG, Elisaf M, Papageorgiou AA, Symeonidis AN, Pehlivanidis AN, Bouloukos VI, et al. Effect of statins versus untreated dyslipidemia on serum uric acid levels in patients with coronary heart disease: a subgroup analysis of the GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study. Am J Kidney Dis Off J Natl Kidney Found. 2004 Apr;43(4):589–99.

74. Athyros VG, Mikhailidis DP, Papageorgiou AA, Symeonidis AN, Pehlivanidis AN, Bouloukos VI, et al. The effect of statins versus untreated dyslipidaemia on renal function in patients with coronary heart disease. A subgroup analysis of the Greek atorvastatin and coronary heart disease evaluation (GREACE) study. J Clin Pathol. 2004 Jul;57(7):728–34.

75. Amarenco P, Bogousslavsky J, Callahan A, Goldstein LB, Hennerici M, Rudolph AE, et al. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med. 2006 Aug 10;355(6):549–59.

PROFORMA

NAME :

AGE/SEX :

IP NO :

OCCUPATION :

ADDRESS :

FAMILY INCOME :

PRESENTING COMPLAINTS : YES NO

- WEAKNESS
- HEADACHE
- VOMITING
- LOSS OF CONSCIOUS
- SEIZURES
- UNSTEADY GAIT
- SPEECH DISTURBANCES

ONSET OF SYMPTOMS : SUDDEN GRADUAL

PAST HISTORY: YES NO

1. SYSTEMIC HYPERTENSION
2. DIABETES MELLITUS
3. PREVIOUS HISTORY OF STROKE OR TIA
4. RHEUMATIC HEART DISEASE
5. CORONARY ARTERY DISEASE
6. ATRIAL FIBRILLATION
7. SMOKING
8. ALCOHOLISM

FAMILY HISTORY:

CLINICAL EXAMINATION:

- HEIGHT
- WEIGHT
- BMI
- BP
- TEMPERATURE
- CARDIOVASCULAR SYSTEM
- RESPIRATORY SYSTEM
- ABDOMEN
- CNS

LAB INVESTIGATIONS

CBC

RFT

FBS / PPBS (IF NEEDED)

URINE SUGAR

LIPID PROFILE

ECG

ECHOCARDIOGRAM

(CT / MRI BRAIN) INFRACTION VESSEL INVOLVEMENT

MCA

ACA

PCA

PATIENT CONSENT FORM

STUDY DETAIL :

STUDY CENTRE :

PATIENT'S NAME :

PATIENT'S AGE :

IDENTIFICATION NUMBER:

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

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

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

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests.

Signature/thumb impression:

Patient’s name and address: Place:

Date:

Signature of the investigator:

Name of the investigator: Place:

Date:

ஒப்புதல்படிவ

ஆராய்ச்சிதலை : **A STUDY OF SERUM URIC ACID LEVELS IN A SETTING OF ACUTE ISCHEMIC STROKE IN GVMCH VELLORE**

முழுபெய :
தந்தை / தாயார்பெயர் :
பிறந்ததே / வய :

I. நான் மேலே குறிப்பிட்டுள் ஆராய்ச் குறித் விளக உரையய் படித்துபுரிந் கொண்டேன் என்று , எனக் கேள்விகேட்க வாய்ப் அளிக்கப்பட்ட என்று உ செய்கிறேன்.

II. நான் இந்த ஆராய்ச்சியி பங்குபெறுவ; தன்னிச்சையாகத் தான் என்று , நான் எப்பொழுதுவேண்டுமானாலு , காரணம் ஏது தெரிவிக்காம இந்த ஆராஃய்ச்சியிலிரு வில முற்ட எனக் அதிகார உண் என்று , அப்ப செய்வதனால் என் சட்ட ரீதியா மற்று சிகிச்சைச பந்தபட்ட உரிமைகள் பாதிக்கப்படமாட்ட என்று நான் அறிகிறே .

III. இந்த ஆராய்ச்சியி புரவல மற்று அவர்கள் சார்பாக பணிபுரிபவர்க நெறிமுறைக குழு மற்று கட்டுபாட் குழுவி ஆகியோ , இந்த ஆராய்ச்சியி போதும் , பின்ன இதன்சம் பந்தமாக வே ஆராய்ச் செய்யும்போதும் , என் சம்பந்தப்பட்ட சிகிச்ச விவரங்கள மேலு என அனும இன் காண அனும அளிக்கிறேன் . மூன்றா நபர்களுக இந்த ஆராய் சிசிக பற் விளக்கு போதும் , இந்த ஆராய்சியி முடிவுகள பிரசுரிக்கு போதும் என அடையாளம் வெளியிடப்படமாட்ட என்று நான் அறிகிறே .

IV. இந்த ஆராய்ச்சியி மூல அறியப்படு விஷயங்க மற்று முடிவுக அறிவிய சார்ந்த காரணங்களுக்க வெளியிட படுவத நான் எப்போதும் தடுக்கமாட்டே என் உ அளிக்கிறேன் .

V. நான் இந்த ஆராய்சிசிய பங் பெறசம்மதம் தெரிவிக்கிறே .

1) ஆராய்சிசிய பங் பெறும்நப / சட்டப் ர்வ பிரதினிதி கையெழு / ஆள்காட் வி பதிட்

பெயர் / உறவுமு

2) ஆராய்சியாள சாட் கையெழுத்; , தே

KEY TO MASTER CHART :

1. Age in years

2. Sex; 1=male, 2=female

3. Systolic BP in mmhg.

4. Diastolic BP in mmhg

5. Body mass index in kg/m^2

6. Fasting blood glucose in mg/dl

7. Serum Urea in mg/dl

8. Serum creatinine in mg/dl

9. Total Cholesterol in mg/dl

10. Triglycerides (TGL) in mg/dl

11. Low density lipoprotein cholesterol in mg/dl

12. High density lipoprotein cholesterol in mg/dl

13. Serum uric acid in mg/dl

14. Smoking; 1= yes , 2 = no

15. Diabetes mellitus; 1= yes, 2= no

MASTER CHART

S.No.	AGE	SEX	Systolic BP	Diastolic	BMI	FASTING GLUCOSE	UREA	CREAT ININE	Total Cholestrol	TGL	LDL	HDL	URIC ACID	SMO KING	DM
1	61	1	160	100	28.2	235	35	1.1	196	140	136	46	6.8	2	1
2	63	1	136	88	22.4	187	42	0.8	223	184	128	49	7.5	2	2
3	67	1	200	100	23.5	247	21	0.5	206	172	136	46	8.3	2	1
4	45	2	168	96	18.8	245	32	0.8	156	164	118	42	6.6	2	1
5	59	1	156	108	21.5	244	39	0.9	186	156	124	38	6.8	2	1
6	60	1	196	110	23	142	33	1.3	202	194	118	36	7.6	2	2
7	35	2	220	106	26.4	110	26	0.5	221	165	122	44	9.6	2	2
8	40	1	136	88	21.1	167	19	0.6	220	178	146	42	4.3	1	2
9	55	1	142	90	22.7	213	38	0.9	175	168	120	47	4.8	2	1
10	41	1	172	90	19.2	173	23	0.7	256	183	172	46	5.6	1	2
11	45	1	188	100	28.5	108	28	0.5	202	173	154	52	4.8	1	2
12	50	2	120	82	19.7	289	45	0.7	186	149	118	44	6.2	2	1
13	63	1	146	96	22.1	207	31	0.8	148	128	102	40	6.6	2	1
14	52	1	172	88	27.4	154	22	0.4	240	180	148	38	7	2	2
15	54	1	210	100	28	278	41	0.6	286	193	164	42	9.3	2	1
16	50	1	154	88	25.4	98	39	0.7	204	183	150	46	6.4	1	2
17	75	2	168	90	23.5	165	39	0.9	293	190	158	48	5.4	2	2

18	66	2	128	98	20.6	116	42	1.4	308	198	168	52	4.6	2	2
19	70	1	200	88	19.6	122	36	0.5	285	178	164	49	7.6	2	2
20	49	1	l	80	20.3	119	46	1.2	214	180	160	40	6.1	1	2
21	50	2	170	96	21.4	188	23	0.6	169	138	126	48	5.8	2	2
22	70	2	186	90	24.3	312	28	0.7	198	140	116	38	6.8	2	1
23	50	1	210	140	27.3	289	33	0.7	227	180	120	49	8..8	2	1
24	75	1	180	106	24.3	178	38	0.8	198	138	128	39	6.4	2	2
25	29	2	176	92	25.8	317	27	0.9	256	173	104	48	7.4	2	1
26	60	1	206	98	27.4	326	18	0.5	278	183	122	46	7.8	2	1
27	55	1	160	80	18.4	103	39	0.6	180	140	103	48	6.3	1	2
28	66	1	156	76	18.7	253	33	0.7	225	164	128	36	5.6	2	2
29	70	2	172	90	25.7	298	26	0.8	274	166	131	46	6.3	2	1
30	60	1	186	92	25.4	276	36	0.9	288	174	127	50	7.4	1	1
31	50	1	122	82	21.4	96	24	0.6	153	120	98	48	4.8	1	2
32	60	2	190	86	24.6	210	35	0.9	228	146	134	47	5.8	2	1
33	60	1	210	98	26.5	90	28	0.7	186	138	118	52	7	2	2
34	57	1	176	88	18.5	184	29	0.7	188	112	144	42	6.1	1	2
35	95	2	148	80	16.8	113	39	0.8	188	146	102	42	5.6	2	2
36	65	1	150	86	18.8	176	25	0.6	226	164	112	48	5.8	2	2
37	60	2	168	78	23.4	276	37	0.8	287	198	184	42	6.2	2	1
38	65	1	136	85	18.7	198	22	0.7	196	136	98	46	4.6	1	2

39	72	2	198	88	20.4	195	34	1.1	261	164	139	49	7.5	2	2
40	52	1	150	80	20.6	145	18	1.3	192	168	140	39	5.2	2	2
41	85	1	142	70	21.6	256	26	0.7	265	188	169	52	7.6	2	1
42	76	2	150	86	22.8	110	48	0.8	168	126	112	48	6.5	2	2
43	72	1	176	84	23.1	212	25	0.9	204	188	165	44	5.8	2	1
44	60	1	120	84	19.2	162	34	0.8	158	148	132	34	5.2	1	2
45	40	1	192	88	26.2	263	23	1.2	216	189	143	48	8.1	1	1
46	65	1	180	100	19.4	174	28	0.7	158	124	120	42	7.4	2	2
47	66	2	122	80	24.1	210	39	0.6	214	179	163	56	8.1	2	1
48	70	1	164	88	18	112	27	0.6	206	185	114	42	6.7	2	2
49	56	1	132	80	20.6	167	36	0.8	186	163	103	48	4.2	1	2
50	52	2	188	98	26.7	172	35	0.9	178	142	116	48	6.6	2	2
51	55	2	190	90	19.7	110	29	1	198	140	98	50	7.6	2	2
52	67	1	140	90	23.4	135	56	0.9	247	180	143	43	5.8	2	2
53	50	2	170	88	20.5	318	38	0.8	210	168	120	47	9.6	1	1
54	46	1	126	78	24.8	238	46	0.5	242	148	110	52	10.1	1	1
55	75	2	190	110	18.5	107	27	1.2	140	112	89	50	7.6	2	2
56	70	1	132	60	24.5	146	48	0.6	270	198	165	44	5.5	1	2
57	67	1	170	90	21.2	176	38	1	186	140	130	48	6.1	2	2
58	89	2	160	80	19.2	185	28	0.8	176	134	110	40	5.8	2	2
59	70	2	150	70	19.8	115	37	1.1	196	142	142	37	4.7	2	2

60	76	1	180	88	25.8	198	43	1	290	180	189	38	6.4	2	2
61	52	1	122	78	20.3	186	39	0.9	203	150	122	49	5.4	1	2
62	60	1	198	116	27.9	146	45	0.6	276	181	169	50	7.4	2	2
63	70	2	180	120	19.7	152	29	0.7	180	146	120	46	6.6	2	2
64	52	2	190	98	18.9	106	26	0.5	169	132	110	45	6.4	2	2
65	58	1	160	80	22.4	143	34	0.6	188	178	141	34	6.2	1	2
66	63	1	186	90	23.8	174	33	0.8	200	182	134	40	6.7	2	2
67	40	2	140	80	23.7	185	30	1.3	186	43	120	46	5.1	2	2
68	75	1	180	100	20.1	198	32	1.2	206	157	132	56	6.4	2	2
69	65	2	190	90	23.2	201	45	0.9	190	169	156	48	7.4	2	1
70	55	2	210	110	21.8	107	44	1	210	187	140	41	8.4	2	2
71	65	1	176	92	24	176	31	1.1	180	143	116	48	6	Y	2
72	65	1	180	130	22.2	234	48	0.7	216	186	170	41	7.6	2	1
73	40	2	136	80	21.1	168	34	0.8	180	145	108	44	5.8	2	2
74	75	1	138	80	22.3	157	28	0.8	198	140	116	46	4.7	1	2
75	45	2	160	98	24.4	118	33	1.2	196	136	117	42	5	2	2
76	57	2	190	90	21.4	146	25	1	179	131	120	38	8.4	2	2
77	70	1	130	80	20.4	183	30	1.2	189	132	114	46	4.2	2	2
78	75	1	176	110	19.1	212	36	0.9	189	136	135	47	6.8	2	1
79	73	1	150	80	22	235	45	0.6	203	198	140	42	6.6	2	1
80	49	1	180	102	24.6	360	44	1	184	203	187	48	9.2	1	1

81	37	1	184	92	25.5	289	40	1	301	198	188	48	6.6	1	1
82	78	1	145	90	21	114	38	0.6	302	131	188	39	6.7	2	2
83	48	2	136	80	22.3	178	27	0.7	174	186	142	40	5.4	2	2
84	75	1	180	92	21.1	97	34	0.8	189	163	98	47	5.9	2	2
85	75	1	190	78	19.4	287	48	0.9	210	176	125	41	7.5	1	1
86	58	2	210	130	24.5	312	46	1.2	362	190	163	45	8.7	2	1
87	70	2	188	98	19.6	88	37	0.7	168	130	99	48	7.9	2	2
88	83	1	140	70	18	116	22	0.6	146	122	188	40	5.7	2	2
89	70	2	160	80	23.3	120	39	0.8	154	124	103	44	6.5	2	2
90	67	2	134	88	24.1	206	36	1	264	268	164	38	6.8	2	1
91	52	1	168	80	24	234	39	1.3	218	175	140	47	7.6	1	1
92	60	1	180	120	27.9	146	45	1	280	194	168	48	8.6	2	2
93	70	2	180	120	19.7	152	29	0.7	180	146	120	46	6.6	2	2
94	52	2	190	86	20.4	106	26	0.5	169	146	110	45	6.4	2	2
95	58	1	160	80	22.4	143	34	0.6	188	150	141	34	7.6	1	2
96	63	1	186	90	23.8	174	33	0.8	200	180	131	40	6.7	2	2
97	40	2	140	80	18.6	185	30	1.3	186	146	120	46	5.1	2	2
98	75	2	180	100	20.1	198	32	1.2	206	157	132	56	6.4	2	2
99	65	2	190	90	23.2	201	45	0.9	190	169	156	48	7.4	2	1
100	55	2	210	110	21.8	107	44	1	210	187	140	41	8.4	2	2