A STUDY ON THE CORRELATION BETWEEN THE LEVELS OF SERUM URIC ACID AND THE PROGNOSIS OF ACUTE ISCHEMIC STROKE

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CERTIFICATE

This is to certify that this dissertation titled **"A STUDY ON THE CORRELATION BETWEEN THE LEVELS OF SERUM URIC ACID AND THE PROGNOSIS OF ACUTE ISCHEMIC STROKE"** submitted by submitted by **DR.A.PRABHAKAR** to the faculty of General Medicine, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree branch I General Medicine, is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I**, Dr.A.PRABHAKAR,** solemnly declare that the dissertation titled **"A STUDY ON THE CORRELATION BETWEEN THE LEVELS OF SERUM URIC ACID AND THE PROGNOSIS OF ACUTE ISCHEMIC STROKE"** has been prepared by me. This is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai,** in partial fulfillment of the regulations for the award of MD degree (branch I) General Medicine.

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CONTENTS

Abbreviations

BG	–	Blood Glucose
BMI	–	Body Mass Index
DM	-	Diabetes Mellitus
HT	-	Hypertension
DOS	-	Duration of stay
RFT	-	Renal function test
FO	-	Functional outcome
CT	-	Computerised Tomography

INTRODUCTION

Stroke is a major public health problem all over the world. It plays an important role in the morbidity and mortality in late middle age and in the elderly. Stroke is the third most common cause of death in the world after coronary artery disease and cancer. It is the single most important case of severe disability and also the most common life threatening neurological disease.

The burden of stroke is likely to increase substantially in the future because of the aging population. Apart from implementing effective stroke prevention programs, identification of factors associated with more severe stroke may help to ease the burden of this coming epidemic.

Stroke is a heterogenous disease. Ischaemic and haemorrhagic strokes are the 2 main types of stroke, with very different pathogenesis and outcome. For India, community surveys have shown, a crude prevalence rate for hemiplegia is in the range of 200 per 1,00,000 persons, nearly 1.5% of all urban hospital admission, 4.5% of all medical and around 20% of neurological cases.

Uric acid is the most abundant aqueous antioxidant in humans, and contributes as much as two-thirds of all free radical scavenging capacity in plasma. It is particularly effective in quenching hydroxyl, superoxide and peroxynitrite radicals, and may serve a protective physiological role by preventing lipid peroxidation. In a variety of organs and vascular beds, local Uric acid concentrations increase during acute oxidative stress and ischaemia, and the increased concentrations might be a compensatory mechanism that confers protection against increased free radical activity. In animal models, local Uric acid concentrations significantly increase in acute brain injury . For example, in the rat, middle cerebral artery occlusion causes a significant increase in cerebral Uric acid concentrations, which can persist for several days after the injury. These observations have prompted interest in the poten Cerebral infarction initiates a complex cascade of metabolic events in the surrounding tissue, and free-radical-mediated oxidative damage plays a key role in the pathogenesis of cerebral ischaemia. Free radicals are liberated from a variety of sources, including inflammatory cells, dysfunctional mitochondria and excitotoxic mechanisms stimulated by increased glutamate and aspartate concentrations. 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. Products of lipid peroxidation, for example malondialdehyde, irreversibly disrupt enzymes, receptors, and

membrane transport mechanisms. In acute ischaemic stroke**,** in *vivo* concentrations of lipid peroxidation products are significantly increased, arising from excess free radical activity. Plasma concentrations of cholesteryl ester hydroperoxides (CEOOH) are sensitive and specific markers of lipid peroxidation, and correlate positively with infarct volume, calculated by computed tomography, and clinical severity, determined by the National Institute of Health Stroke Scale. This emphasizes the role of oxidative stress in mediating cerebral ischaemic tissue damage, and is consistent with the observation that stroke volume is greater in patients with diminished antioxidant capacity. These observations have stimulated interest in the possibility that antioxidant treatments could offer benefits in acute ischaemic stroke**,** through their ability to defend against excess free radical activitytial impact of raised local Uric acid concentrations in the setting of acute ischaemic stroke.

Models of ischaemic neuronal injury have shown that the addition of physiological concentrations of Uric acid protects hippocampal neurons against excitotoxic and metabolic injury in vitro. The effects of raising circulating Uric acid concentrations, by direct administration, have also been studied in vivo in a rat model of acute ischaemic stroke**,** involving transient occlusion of one middle cerebral artery for 2 h. Administration of Uric acid, prior to ischaemia or during the subsequent reperfusion period, caused a

significant reduction in infarct volume, and led to improved behavioural outcome at 24 hours. These findings suggest that early elevation of Uric acid, during or shortly after acute ischaemic stroke**,** could confer significant protection against neurological deficit. This is consistent with the protective effects of Uric acid observed in other models of cerebral diseases mediated by free radicals.

A recent study lends support to this hypothesis in a clinical setting. Serum Uric acid concentrations measured in 881 consecutive ischaemic stroke patients at the onset of ischaemic symptoms were found to correlate inversely with early neurological impairment and final infarction size on computed tomography or magnetic resonance imaging. Additionally, serum Uric acid concentrations were positively associated with a good clinical outcome at hospital discharge (Matthew score of >75), where each mg/dl Uric acid increase (equivalent to 60 µmol/l; reference range 120–420 µmol/l) was associated with a 12% increase in the odds of a good outcome. Importantly, these relationships were independent of potential confounders, including age, diuretic use, renal function or the presence of major cardiovascular risk factors. This is the first study to characterize the relationship between serum UA concentration and neurological severity of acute ischaemic stroke in a large series of patients. A potential limitation of this observational data is that it does not directly address the potential mechanisms by which Uric acid could improve stroke outcome, for example measurements of antioxidant capacity or

oxidative stress. However, its findings support the potential benefits of raised Uric acid concentrations observed in vitro and in vivo experimental models.

Despite the widely held view that elevated serum Uric acid concentrations confer increased risk of atherosclerotic disease, there is no compelling biological evidence of a causal link. 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. In the context of acute ischaemic stroke, there is growing evidence to support a protective role for Uric acid. This underpins the importance of oxidative stress in the pathogenesis of acute stroke, and strengthens the rationale for further investigation of antioxidant treatments in this condition. The feasibility of Uric acid administration to temporarily increase circulating concentrations has recently been established, and might allow its potential therapeutic impact to be examined in a clinical setting. Ongoing basic research is likely to shed new light on the cardiovascular effects of Uric acid, and will hopefully allow the significance of serum concentrations to be interpreted more clearly.

This study is aimed at determining the correlation between the levels of serum uric acid and the prognosis of acute ischaemic stroke.

AIMS AND OBJECTIVES

1. To identify the role of serum uric acid in influencing the prognosis 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.

REVIEW OF LITERATURE

DEFINITION OF 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 cause other than that of vascular origin.

ANATOMY OF CEREBRAL CIRCULATION

ARTERIES OF THE BRAIN

Two intemal 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.

BRANCHES OF THE CEREBRAL PORTION

OPHTHALMIC ARTERY: The ophthalmic artery arises from the internal carotid artery. It 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: The posterior communicating artery is a small vessel that originates from the internal carotid artery close to its terminal bifurcation 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.

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.

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 intemal capsule.

VERTEBRAL ARTERY

The vertebral artery, a branch of the first part of subclavian artery, ascends in the neck by passing through the foramina in the transverse processes of the upper 6 cervical vertebrae. It enters the skull through the foramen magnum and pierces the duramater and arachnoid 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 aliery.

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

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.

CIRCLE OF WILLS

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

The burden of stroke on the community is best reflected by its incidence. Two incidence studies conducted in the late sixties and early seventies have been reported. The first population-based study was conducted in Vellore in two phases. In the first phase (1968 - 1969) a population of

2,58,576 in and around Vellore was surveyed to detect cases of hemiplegia. In the second phase (1969 - 197 I) the population was kept under surveillance for two years and attempts were made to record all cases of hemiplegia. An incidence of 13/1,00,000 population per year was observed. The second study was carried out as a part of WHO collaborative study in Rohtak. Halyana between 1971- 1974. An annual incidence of : 33/1,00,000 population was noted.

In India prevalence vary from region to region. Vellore, Gowribidanur, and Rohtak had a prevalence of 40-60/1,00,000 population, whereas the Eastern part of India showed a prevalence of 100-270/1,00,000.

Stroke incidence varies among different countries. In WHO Monica project has shown high prevalence and mortality among Finnish population. According to this study incidence of stroke varies from 100/1,00,000 in Germany to 290/1,00,000 population of men in Finland.

CLASSIFICATION OF STROKE

Stroke can be classified in various ways. Suggested classification of stroke

1. ANATOMICAL CLASSIFICATION.

A. By vascular supply

a. Carotid

b. Vertebrobasilar

B. By location

a. Supratentorial

i. Lobar

ii. Ganglionic /thalamic

b. lnfratentorial

i. Cerebel1ar

ii. Brain stern

2. ETIOLOGICAL CLASSIFICATION.

A. By result.

a. Cerebral infarct

b. Cerebral haemorrhage

i. Parenchyma

ii. Subarachnoid.

RISK FACTORS FOR STROKE

They can be grouped into modifiable and non-modifiable. Some of them are as follows.

- **Age**

The incidence of stroke increases dramatically with advancing age, and increasing age is an important risk factor for stroke.

- **Sex**

Male sex is associated with increased risk of stroke.

- **Race**

The rate of cerebral infraction is higher in blacks than in whites. This could be partially explained by the higher prevalence of diabetes and hypertension in them.

- **Blood pressure**

Hypertension is the single most dominant risk factor for both ischaemic and hemorrhagic stroke. Hypertension predisposes to ischaemic stroke by aggravating atherosclerosis. In India, one ICMR multicentric stroke

study on risk factors 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. Eastern stroke and coronary heart disease collaborative research found that blood pressure is an important risk factor in eastern Asian populations. They found that 3mm of Hg reduction in diastolic blood pressure should decrease the number of stroke by about a third. The SHEP study has shown a 36% reduction in non-fatal stroke events over 5 years in the age group 60 years and above with isolated systolic hypertension treated with active medication.

- **Diabetes Mellitus**

Diabetes mellitus increases the risk of cerebrovascular disease 2 – 4 fold compared with risk in nondiabetics. Stroke secondary to diabetes may be caused by cerebrovascular atherosclerosis, cardiac embolism, and rheological abnormalities. Diabetic patients with retinopathy and autonomic neuropathy are particularly at high risk for atherosclerosis.

- **Cardiovascular diseases**

Angina or myocardial infarction is clearly associated with stroke. ECG abnormalities reflecting hypertension and coronary artery disease are risk factors for stroke. Rheumatic heart disease and cardiac failure are other risk factors.

❖ **Claudication**

Claudication is a high risk factor for both myocardial infarction and stroke, presumably reflecting atheromatous disease in different parts of the circulation.

❖ **Cigarette smoking**

The relative risk is about 1.5. There is a dose dependent relationship between smoking and stroke. Cigarette smoking is a factor both in men and women. ICMR has shown that smoking is a risk factor both in the young and the elderly.

❖ **Atrial fibrillation**

Most frequent cardiac source of embolism to brain is atrial fibrillation either rheumatic or non rheumatic. Atrial fibrillation is associated with increased risk for stroke accounting for 6 -24 % of all ischaemic strokes.

❖ **Carotid artery disease**

Asymptomatic carotid artery disease less than 75% carries a stroke risk of 1.3% annually. With stenosis greater than 75% combined transient ischaemic attack and stroke rate is 10.5% per year. Carotid and

supraclavicular arterial bruit are strongly related to stenosis of underlying arteries.

❖ **Transient ischemic attacks**

A TIA patient has an excess risk of stroke by about 5 - 10 times greater than a non TIA patient.

❖ **Lipid abnormalities**

Increasing levels of total plasma cholesterol, LDL and decreased levels of HDL are strong risk factors for coronary artery disease than stroke. In a study conducted in NIMHANS they found that low HDL cholesterol is a risk factor in stroke group among various lipid fractions. Lipoprotein 'a' has been found to be an independent risk factor for stroke.

❖ **Other risk factors**

Abdominal obesity, plasma fibrinogen, homocysteine, dietary measures, snoring, cornel 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, hematocrit etc are some of the other risk factors.

PATHOPHYSIOLOGY OF ACUTE ISCHEMIC STROKE:

Cerebral infarction basically comprises two pathophysiological processes.

1. A loss of supply of oxygen and glucose secondary to vascular occlusion.
2. An array of changes in cellular metabolism consequent to the collapse of energy producing processes, with a disintegration of cell membranes.

Normal cerebral blood flow at rest in normal adult brain is 55ml/l00g/minute. When the blood flow decreases to 18ml/100g/mt brain reaches the threshold for electrical failure. When blood decreases to 8ml/100g/mt cell death can result. These thresholds mark the upper and lower limits for the ischaemic penumbra. Ischaemic penumbra is the condition of the ischaemic brain between these 2 flow threshold in which there are some neurons that are functionally silent but are structurally intact and potentially salvageable.

The recognition of penumbra has focused attention on the development of treatment to minimize or to even reverse the damage effects of the

ischaemic brain by drugs when started within a short period after the occlusion (therapeutic window).

PET studies have detected penumbral tissues lip to 72 hours post stroke. It may comprise up to 50% of final volume of infarction up to 17 hours after ischaemic insult and the out come of stroke patients depend upon this proportion.

Ischaemia impairs cellular energy production and depletion of ATP, which is followed by a failure of ATP dependent ion transport system leading to cellular efflux of potassium and influx of sodium and water. This ischaemic depolarization causes presynaptic voltage sensitive calcium channels to open and allow calcium to enter the cell. Intracellular calcium stimulates neural transmitters, most notably excitatory amino acid glutamate. Extra cellular glutamate then activates 2 postsynaptic receptors NMDA receptor and AMPA receptors. Massive release of glutamate causes depolarization of adjacent neurons, triggering further neurotransmitter release increasing their energy requirement and tripping them into energy failure. This is the basis for the so-called excitotoxic cell injury. Intracellular calcium triggers activation of enzymes, which affects the structure and function of cellular constituents. Stimulation of phospholipase leads to an inflammatory reaction through

leucotriene production and stimulation of NO synthase, which causes build up of nitric oxide and free radicals.

CLINICAL FEATURES OF STROKE.

It depends upon the site of lesion and type of stroke, ischaemic or hemorrhagic. Distinction between types of stroke is possible by history taking physical examination and investigation.

CLINICAL MAINFESTATIONS OF ISCHAEMIC STROKE

The typical ischaemic stroke presents with abrupt onset of focal neurological deficit and is characterized clinically by the mode of onset and subsequent course.

A transient ischaemic attack is arbitrarily defined as a neurological deficit lasting less than 24 hours (usually 5-20 minutes). It often portends an impending stroke. The pathophysiological mechanisms for TIA are a low flow in an artery due to a tight stenosis or occlusion or an embolism.

A completed stroke or cerebral infarction typically evolves into maximum deficit in a few hours. It is sometimes heralded by TIA's.

In stroke in evolution the focal ischaemia worsens from minute to minute or hour to hour. There are usually stepwise incremental increases in neurological deficit occuring over several hours.

The commonest sites of affection are

a. The origin of the ICA within its first 2cms

b. Siphon of ICA

c. Proximal segments of MCA and ACA

- ***Occlusion of ICA*** - Patient may have amaurosis fugax before the occurrence of contralateral hemiparesis.

- ***Occlusion of MCA stem*** - Resulting in contralateral hemiplegia, hemianaesthesia and global aphasia (dominant), apraxia and anosognosia (nondominant).

- ***Occlusion of inferior division MCA*** - Wernickes aphasia without weakness often with superior quadrantanopia. If nondominant hemisphere, hemi neglect and spatial agnosia.

- ***Occlusion of ACA***- Occlusion of Precommunal segment is well tolerated because of collateral flow. If both post communal segments arise from a single ACA patient suffers profound abulia (delayed motor and verbal response), bilateral pyramidal signs and paraplegia.

- ***Occlusion of PCA-*** Occlusion of PCA causes serious neurological deficits as important structure are involved (brain stem). Thalamic syndrome, Thalamoperforate syndrome, Weber's syndrome are some of the known syndromes.

- ***Vertebral artery and posterior inferior cerebellar artery lesions -*** This includes the well-known Lateral medullary syndrome. Medial medullary syndrome causes 12^{th} nerve lesion and contra lateral hemiplegia.

- ***Basilar artery***- Complete basilar syndrome results in bilateral long tract signs with variable cerebellar, cranial nerves and other segmental abnormalities of brain stem.

- ***Occlusion of Superior cerebellar artery -*** Ipsilateral cerebellar ataxia, contralateral hemianaesthesia, ipsilateral Horner's etc.

- ***Occlusion of Anterior inferior cerebellar artery -*** Ipsilateral cerebellar ataxia, Ipsilateral Horners syndrome, conjugate gaze palsy, contra lateral loss of pain temperature etc.

DIAGNOSIS OF STROKE SUBTYPE USING IMAGING

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.
- Hemorrhagic 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.

As mentioned above early finding on CT may be sudden loss of grey White matter contrast and effacement of adjacent subarachnoid spaces. However by 24 hours the abnormal low attenuating areas become obvious. Specifically insular ribbon sign has been defined as an early specific sign of MCA infarction. The early findings on noncontrast CT are the result of development of cytotoxic edema. Occasionally CT scan through the supra sellar cistern may show hyper dense MCA indicative of thrombus within the cytotoxic and vasogenic edema. Mass effect from cytotoxic edema is maximum between 3 - 10 days, and may lead to herniation. Mass effect I completely resolves by 3 weeks.

Lacunar infarction - These are secondary to arterial disease affecting the deep penetrating vessels of the brain. These arteries may demonstrate tiny foci of stenosis caused by micro atheroma or lipohyalinosis. Because of the small size CT may miss the infarct.

TREATMENT OF ACUTE ISCHAEMIC STROKE

a. Early evaluation and supportive treatment.

b. Reperfusion strategies directed at arterial decimalization.

c. Cytoprotective strategies aimed at cellular and metabolic targets.

Emergency care involves protection of the airway to avoid obstruction, hypoventilation and aspiration pneumonia. Care should be taken to prevent cerebral edema and those factors which exacerbate it like; hypoxia, hyperthermia, hypercarbia, hypovolemia, and hypertension. If the patient 33 develops cerebral edema it should be treated with mannitol (20%) solution Ig/kg over 30 min. bolus, followed by 0.25 - 0.5 gm/kg over 30 - 60 min every 4 - 6 hours, maintenance of euvolemia and avoidance of glucose containing solutions, endotracheal intubation and mechanical ventilation if Glasgow coma scale is <8, hyperventilating to a PCO_2 of 30 mm of Hg if the patient has herniation.

During the first few hours after the onset of symptoms of stroke, treatment of severe hypertension is problematic, because, a precipitous decline in arterial pressure may cause harmful decrease in local perfusion. There is no evidence that antihypertensive therapy is beneficial in patients with stroke even above the Blood Pressure treatment thresholds recommended by various consensus panels – systolic > 200 to 220 mm of Hg, diastolic >

110 to 120 mm of Hg. Therapy is indicated in patients with stroke who have aortic dissection, acute myocardial infarction, heart failure, acute renal failure or hypertensive encephalopathy; and for patients receiving thromobolytic therapy in whom the systolic pressure is 180 mm of Hg higher or the diastolic pressure is 105 mm of Hg or higher. Precipitous decline in arterial perfusion may cause harmful decrease in local perfusion

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 6th 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 intraarterial thrombolysis for acute MCA infarct showed benefit.

ANTITHROMBOTIC AND ANTIPLATELET DRUGS,

- **Heparin** - in the international stroke trial 19,435 patients with ischaemic stroke were randomly assigned to receive subcutaneous herparin at a dose of 5,000 to 12,500 IU twice daily or no heparin, with or without 300mg of

aspirin per day, within 48 hours of onset of symptoms. There were no differences among the treatment groups in the primary outcome (death within 14 days or dependency at 6 months). Among the patients who received heparin, there was a significant reduction (0.9%) in the absolute risk of recurrent ischemic stroke during the first 14 days, an effect that was counter balanced by a significant increase (0.8%) in the absolute risk of hemorrhagic stroke.

Kay Richard et al used low molecular weight heparin within 48 hours of onset of symptoms and found that there was significant improvement in the outcome at 6 months though others do not share this thought. A meta analysis of data from trials of early treatment with anticoagulant drugs for patients with acute ischaemic stroke suggest no clinical benefit with such treatment.

- Aspirin - aspirin acts by irreversible inhibition of platelet function by inactivation of cyclo-oxygenase. International stroke trial and Chinese acute stroke trial showed that aspirin produces a small but real reduction of about 10 deaths or recurrent strokes per 1,000 during the first few weeks. Both trials suggest that aspirin should be started as soon as possible after the onset of ischaemic stroke.

In the international stroke trial, secondary analysis revealed a significant decrease in the rate of recurrence of ischaemic stroke at two weeks among the patients treated with aspirin (2.8 vs. 3.9%) among those not treated with aspirin. However, there were no differences among the groups, in the combined end point of severe disability and death. Combined analysis of the results of the lnternational stroke trial and the Chinese acute stroke trial suggest that early death, recurrent stroke or late death can be prevented in 1 patient with acute stroke by giving aspirin to 100 patients with acute stroke.

- **Cytoprotective drugs -** The recognition of penumbra has focused attention on the development of treatment to minimize or even reverse the damaging effects of ischaemic brain damage and such drugs are effective when they are started within a short period of time after the occlusion of the artery (therapeutic window).

Several groups of drugs have been tried. Calcium channel antagonists like nicardipine, nimodipine, NMDA receptor antagonists (Selfotel, Eliprodil), ICAM 1 antibodies (Enlimonab), glutamate antagonist (Lebeluzole), GABAergic antagonist (Diazepam, Clomethiozole), free radical scavengers (Tirilazed, dihydrolipoate), inhibitors of lipid peroxidation (Ebselen). Citicoline, intermediary in the biosynthesis of phosphatidyl choline

was found to improve functional outcome when started within 24 hours of onset of stroke.

Non-pharmacological therapy – Avoidance of atheroma risk factors as well as life style modification is important in primary and secondary stroke prevention.

Surgical therapy – Symptomatic carotid stenosis was studied in NASCET and ESCT. Both showed substantial benefit for surgery in patients with carotid stenosis of more than 70%. There was a 17% absolute reduction in the surgical group and 65% relative risk reduction favoring surgery.

RELATED STUDIES:

1. Uric acid: an important antioxidant in acute ischaemic stroke

W.S. WARING

*From the Clinical Pharmacology Unit and Research Centre, The University of Edinburgh, Western G e*Q J Med 2002;

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. In the context of

acute ischaemic stroke, there is growing evidence to support a protective role for Uric acid. This underpins the importance of oxidative stress in the pathogenesis of acute stroke, and strengthens the rationale for further investigation of antioxidant treatments in this condition. The feasibility of Uric acid administration to temporarily increase circulating concentrations has recently been established, and might allow its potential therapeutic impact to be examined in a clinical settingneral Hospital, Edinburgh, UK

2. **Prognostic Significance of Uric Acid Serum Concentration in Patients With Acute Ischemic Stroke**

Angel Chamorro, MD; Victor Obach, MD; Álvaro Cervera, MD; Marian Revilla, MD; Ramón Deulofeu, PhD John H. Aponte, MD

Increased uric acid values were found in men, hypertensives, alcohol drinkers, and patients with coronary, pulmonary, or renal diseases. Diabetic patients had lower uric acid levels on admission. In patients with acute ischemic stroke, there is a 12% increase in the odds of good clinical outcome for each milligram per deciliter increase of serum uric acid. This finding reinforces the relevance of oxidative damage in ischemic stroke.

3. **Prognostic Significance of Serum Uric Acid Concentration in Acute Stroke.Chakraborty D, Ghosh S, Guru S, Dash LK, Mohapatra MK, Barik BK**VSS Medical College, Burla, Orissa APICON 2009.

Diabetic patients had lower serum uric acid level on admission. Higher level of uric acid was found in patients with renal disease. Uric acid levels were directly associated with haematocrit, creatinine and triglyceride levels. Neurological impairment and the size of infarct on admission on CT scan was inversely associated. In patients with acute ischaemic stroke raised serum uric acid level was associated with good clinical outcome and reinforces the relevance of oxidative damage in stroke.

4.Serum uric acid and brain ischemia in normal elderly adults

D. J. Schretlen, PhD, A. B. Inscore, PsyD, T. D. Vannorsdall, PhD, M. Kraut, MD, PhD, G. D. Pearlson, MD, B. Gordon, MD, PhD and H. A. Jinnah, MD, PhD. 2007 American Academy of Neurology.

In this cross-sectional, observational study, we examined the relationship between serum Uric acid and aggregate volume of white matter hyperintense (WMH) signals observed on proton density and T2-weighted brain MR images in a community sample of 177 adults ages 20 to 92. Using logistic regression, we tested whether participants with Uric acid concentrations in the highest quartile of the sample—but still normal—would

have increased WMH volumes. These findings demonstrate that mildly elevated serum uric acid is associated with increased burden of cerebral ischemic pathology, particularly in older adults. We outline the potential pathogenesis of this association

5. Blood Markers for the Prognosis of Ischemic Stroke

William Whiteley, BM BCh, MRCP; Wei Li Chong, BM BCh; Anshuman Sengupta, BM BCh Peter Sandercock, MD, FRCP

We searched Medline and EMBASE from 1966 to January 2007 for studies of blood markers in patients with ischemic stroke and an assessment of outcome (death, disability, or handicap). We adopted several strategies to reduce bias.

6. Uric acid provides an antioxidant defense in humans against oxidant- and radical-caused aging. Bruce N. Ames, Richard Cathcart, Elizabeth Schwiers, and Paul Hochsteint

Urate is about as effective an antioxidant as ascorbate in these experiments. Urate is much more easily oxidized than deoxynucleosides by singlet oxygen and is destroyed by hydroxyl radicals at a comparable rate. The plasma urate levels in humans (about 300 microM) is considerably higher than the ascorbate level, making it one of the major antioxidants in human.

7. A Pilot Study of Dual Treatment With Recombinant Tissue Plasminogen Activator and Uric Acid in Acute Ischemic Stroke

Sergio Amaro, MD; Dolors Soy, PhD; Víctor Obach, MD; Álvaro Cervera, MD, PhD; Anna M. Planas, PhD Ángel Chamorro, MD, PhD

A very early assessment of the levels of Uric acid allowed the identification of a rapid reduction of Uric acid after stroke only in untreated patients, which was maximal 6 hours after the onset of symptoms. The study also showed lower lipid peroxidation at follow up in patients allocated the high-dose of Uric acid. These findings accord with acute stroke studies

describing a progressive decline of intracellular and extracellular antioxidants such as superoxide dismutase, carotenoids, or vitamin E. A fall of antioxidant vitamins in plasma has also been associated with increased oxidative stress and worse stroke outcome Yet, the early consumption of Uric acid observed in untreated patients, the effect on lipid peroxidation, and the lack of serious adverse effects support additional clinical assessment of Uric acid administration in acute stroke. The low cost of Uric acid is an additional bonus for a larger trial because even a mild clinical benefit would be cost-effective.

8.Antioxidant Profile and Early Outcome in Stroke Patients Antonio Cherubini, MD; Maria Cristina Polidori, MD; Mario Bregnocchi, MD; Salvatore Pezzuto, MD; Roberta Cecchetti, BS; 2000 American Heart Association

In conclusion, our longitudinal study of antioxidant levels during the first week after acute ischemic stroke reveals that almost all antioxidants are reduced immediately after a cerebrovascular accident and increase over the following days, suggesting the presence of a condition of oxidative stress in this setting. Furthermore, the finding of a relationship between antioxidant profile and early outcome of the cerebral infarct might provide new insights into the pathogenesis of ischemic stroke as well as open new therapeutic possibilities.

9.**Fluorescent histochemical localization of lipid peroxidation during brain reperfusion following cardiac arrest.White BC**, **Daya A**, **DeGracia DJ**, **O'Neil BJ**, **Skjaerlund JM**, **Trumble S**, **Krause GS**, **Rafols JA**.

These observations indicate that neurons in the selectively vulnerable zones of the cortex and hippocampus are early and specific targets of lipid peroxidation during post-ischemic reperfusion.

10. Uric acid reduces exercise-induced oxidative stress in healthy adults

W. S. WARING, A. CONVERY, V. MISHRA, A. SHENKIN, D. J. WEBB* and S. R. J. MAXWELL

Uric acid administration abolished the exercise-induced elevation of plasma 8-iso-PGF_{2a} concentrations. High Uric acid concentrations are associated with increased serum antioxidant capacity and reduced oxidative stress during acute physical exercise in healthy subjects. These findings indicate that the antioxidant properties of Uric acid are of biological importance *in vivo*

11. **Antioxidant capacity after acute ischaemic stroke S.E. GARIBALLA, T.P. HUTCHIN[1] and A.J. SINCLAIR[1]© 2002 Association of Physicians**

Experimental studies have reported a rapid increase in the production of markers of oxidative damage following acute stroke due to the reperfusion event following ischaemia, and that endogenous antioxidant defences are rapidly depleted, permitting further tissue damage Ryan *et al*. have previously reported that in healthy subjects, TAC measured by ECL is almost completely accounted for by uric acid. Uric acid, which is the end product of purine metabolism, has long been regarded as a potent endogenous water-soluble antioxidant and radical scavenger in humans.However, its therapuetic benefit in diseases in which free radicals are thought to be involved is yet to be proven.

12. Uric acid administration for neuroprotection in patients with acute brain ischemia References and further reading may be available for this article. To view references and further reading you must this article.

Angel Chamorro, Anna M. Planas, Dolors Soy Muner and Ramon Deulofeu

Uric acid is the end product of purine metabolism and a powerful water-soluble antioxidant and radical scavenger in humans whose generation is increased in situations of oxidative stress, such as brain ischemia. Although hyperuricemia has been related to an increased risk of cardiovascular events,

the association was not found significant in many studies after adjustment for the effect of confonders. We hypothesize that the administration of uric acid could be beneficial and cost effective in patients sustaining acute oxidative stress, such as those with acute ischemic stroke. Uric acid could also extend to more than 3 h the therapeutic window of rt-PA after stroke.

13. The Continued Yin and Yang of Uric AcidJesse Dawson, MRCP; Terry Quinn, MRCP; Kennedy Lees, MD, FRCP Matthew Walters, MD, FRCP © 2008 American Heart Association,

The "positive" effect of Uric acid claimed by Amaro et al must be balanced against established data suggesting a link between increasing serum Uric acid and cardiovascular disease This relationship remains true for the acute infarct period We have previously shown that small increments in admission serum Uric acid are associated with significantly worse 90-day outcome. However, their group have previously suggested very different findings—that increasing serum Uric acid is associated with favorable outcome at 7 days.

MATERIALS AND METHODS

SETTING:

The study on "the correlation between the levels of serum uric acid and the prognosis of acute ischemic stroke" was carried out in the Department of Medicine, Madurai Medical College and Government Rajaji Hospital, Madurai

COLLABORATIVE DEPARTMENTS:

Department of Biochemistry, Neurology, Radiology, Madurai Medical College, Madurai

STUDY DESIGN: prospective study of consecutive patients with acute stroke admitted to Government Rajaji Hospital, Madurai.

PERIOD OF STUDY: OCTOBER 2008 TO SEPTEMBER 2009

SAMPLE SIZE:

Patients were classified into ischemic stroke or primary haemorrhage. CT 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. 50 Patients were included in this study.

DEFINITIONS:

Acute stroke is defined as “rapidly developing clinical signs of focal and global disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin” according to WHO criteria.

Hypertension was defined as a previous record of atleast 2 recordings above 140/90 mmHg or requirement of regular intake of antihypertensive drugs.

Diabetes was defined as having a fasting plasma glucose of >126 mg/dl, postprandial plasma glucose>200mg/dl or requirement of regular hypoglycemic drug intake.

Arm Impairment-inability to feed, dress without assistance of other person/mechanical device. Leg impairment-inability to walk without help from other person/mechanical device. Speech impairment-inability to communicate in unfamiliar situations

FUNCTIONAL OUTCOME:

Grade 1-neurosymptoms no signs or impairment

Grade 2-between 1 and 2

Grade 3-symptoms + signs without impairment

Grade 4-impairment of 1 limb or speech

Grade 5-between 4 and 6

Grade 6-impairment in 2 limbs and speech or death

DYSLIPIDEMIA:

Fasting lipid profile was done in all patients

The cut-off values of each class of lipids were taken as abnormal as follows:

Total cholesterol > 200mg/dl

HDL cholesterol < 40 mg/dl

LDL cholesterol >130 mg/dl

Triglyceride >150 mg/dl

INCLUSION CRITERIA:

1.All acute ischemic stroke within 24 hours of onset

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-SCAN

7.Subdural hematoma

ETHICAL CLEARANCE:

Necessary ethical clearance was obtained from ethical committee, Government Rajaji Hospital, Madurai.

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.

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-brain were done after admission.

The functional outcome at the time of discharge was noted. If the patient was discharged against medical advice in the terminal stage was recorded as a bad outcome. All relevant data were fed into a computer and results were calculated.

Statistical Tools (To be included at the end of Materials and Methods)

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2008).**

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

LIMITATIONS OF THE STUDY:

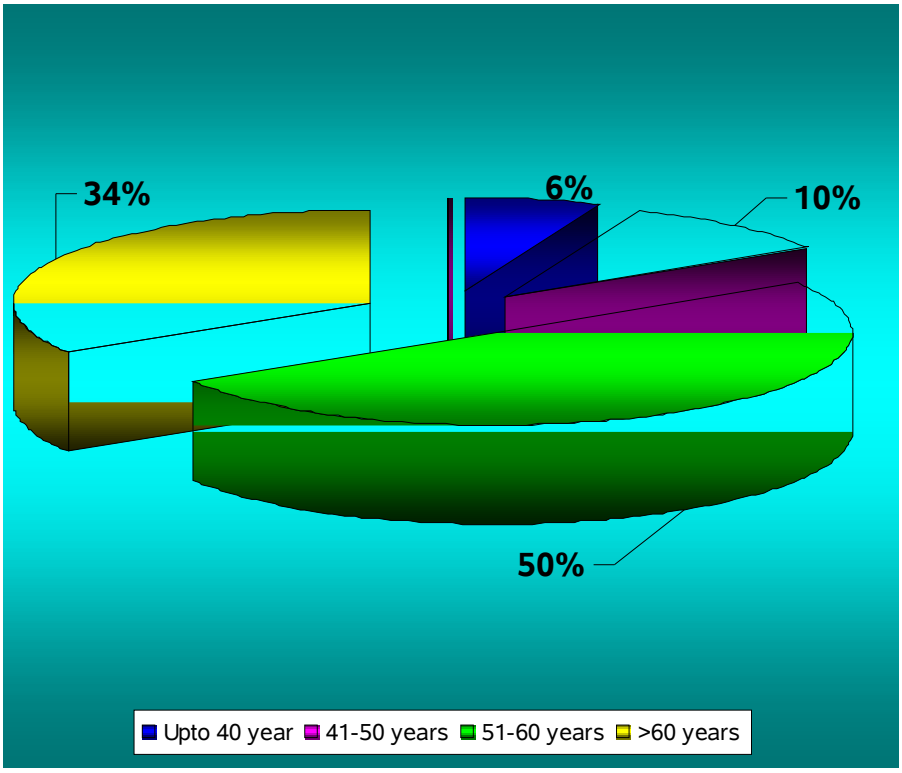
1. The number of patients evaluated had been small and this could have influenced the results of the study.

2.11 patients did not take CT scan due to various reasons among 61 patients studied and hence their data could not be entered into ischemic or haemorrhagic stroke category.

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

RESULTS AND ANALYSIS

AGE DISTRIBUTION



RESULTS AND OBSERVATIONS

A : CHARACTERISTICS OF CASES STUDIED

Table 1 : Age distribution

AGE GROUP	CASES	
	No.	%
Upto 40 years	3	6
41-50 years	5	10
51 – 60 years	25	50
> 60 years	17	34
Total	50	100
Range	32 – 72 years	
Mean	57.6 years	
S.D.	9.0 years	

SEX

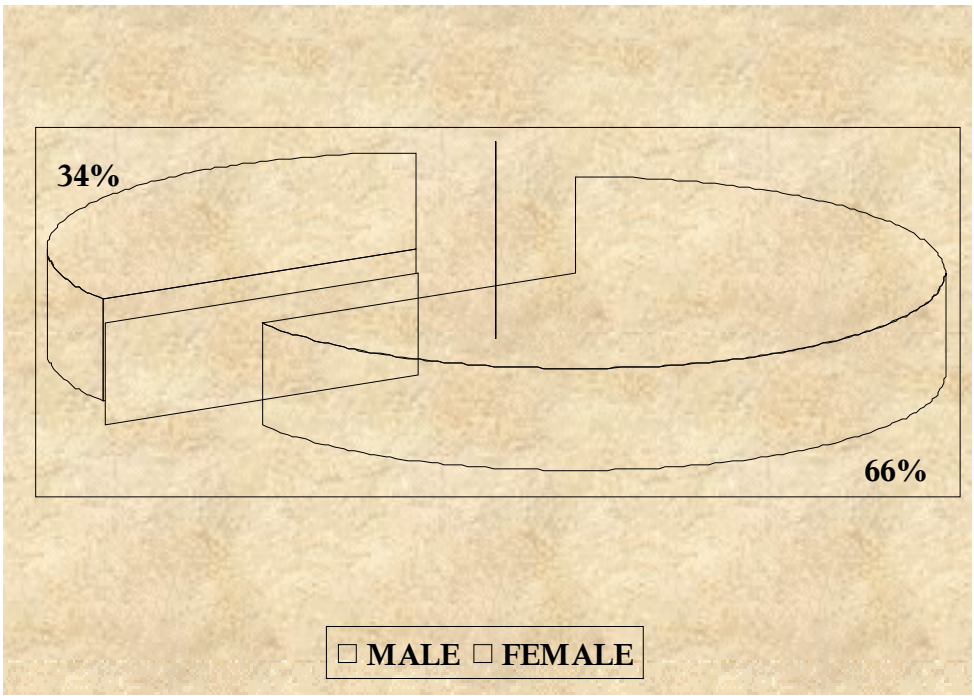


Table 2

Sex

Sex	CASES	
	No.	%
Male	33	66
Female	17	34
Total	50	100

BMI & BLOOD SUGAR VALUES

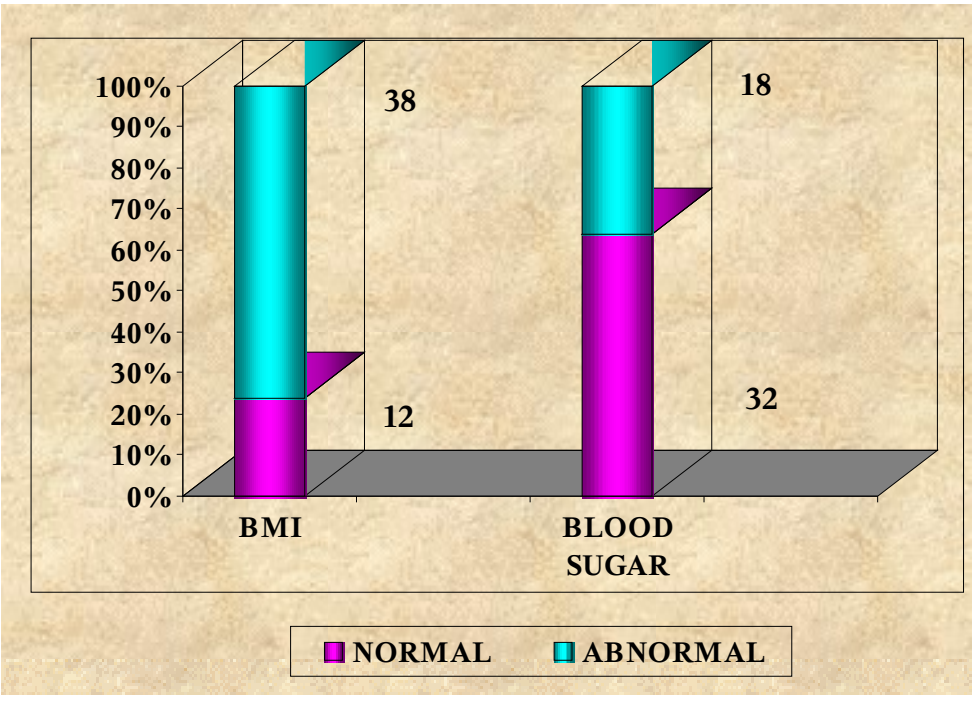


Table 3

Quantitative parameters

Parameter	Normal cases		Abnormal cases		Range	Mean	S.D.
	No.	%	No.	%			
B.M.I	12	24	38	76	20.6-29.2	25.6	1.6
Blood Sugar	32	64	18	36	60-260	134.1	57

HISTORY

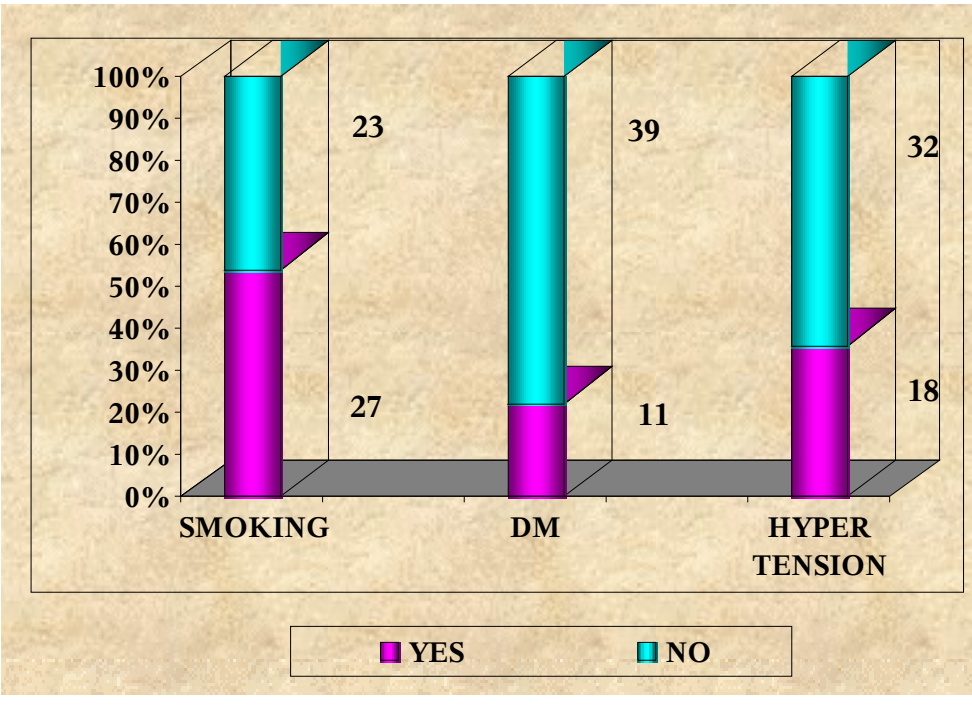


Table 4

Duration of Stay

Parameter	Range	Mean	S.D.
Duration of Stay	4.8-13.2	9.96	1.81

Table 5

History

Parameter	Yes		No	
	No.	%	No.	%
Smoking	27	54	23	46
D.M.	11	22	39	78
Hyper Tension	18	36	32	64

INVESTIGATIONS

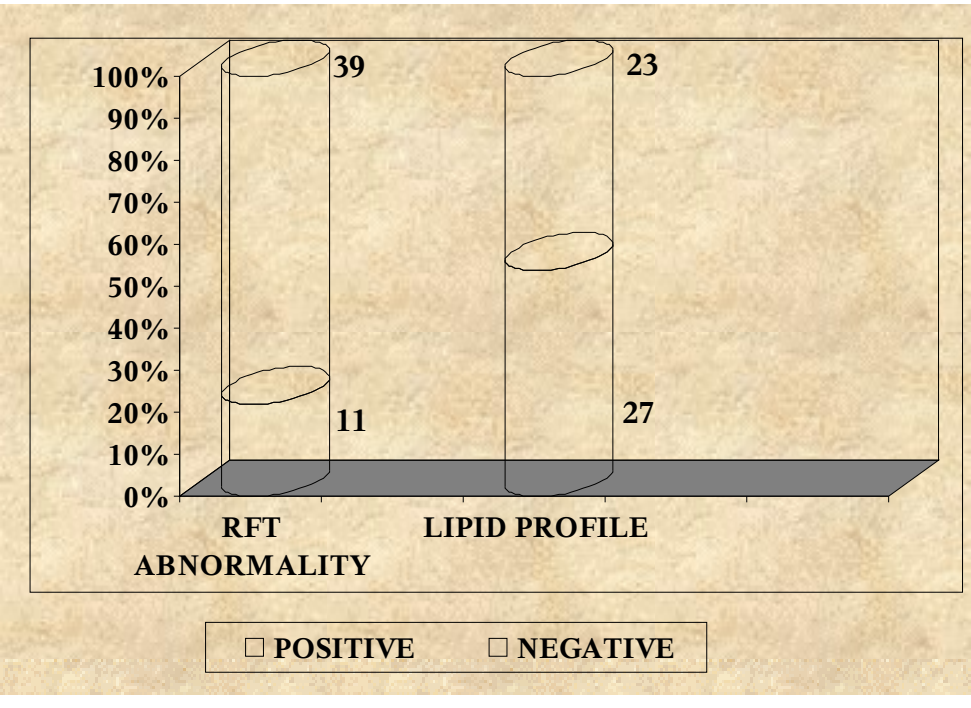


Table 6

Investigations

Investigations	Positive		Negative	
	No.	**%**	**No.**	**%**
Renal Function Test Abnormality	11	22	39	78
Dyslipidemia	27	54	23	46

URIC ACID LEVELS

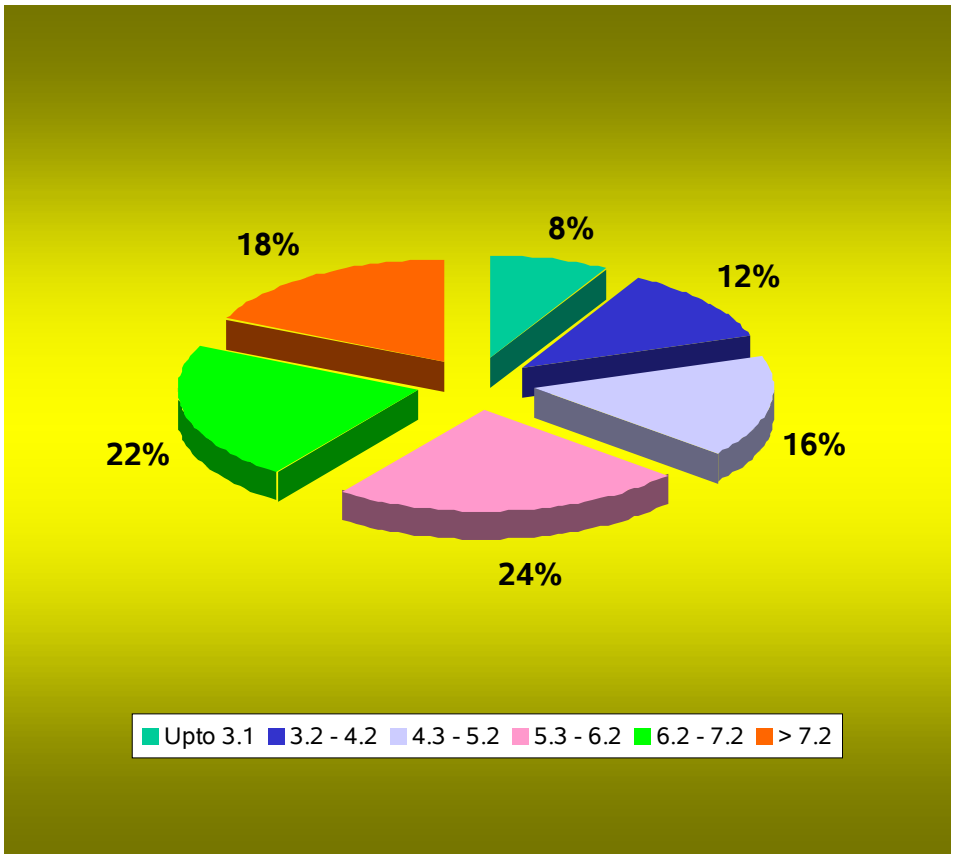


Table 7

Uric Acid

Uric Acid	CASES	
	No.	%
Upto 3.1	4	8
3.2 – 4.2	6	12
4.3-5.2	8	16
5.3-6.2	12	24
6.3-7.2	11	22
> 7.2	9	18
Total	50	100
Range	2.3-11.3	
Mean	5.9	
S.D.	2.0	

C T FINDINGS

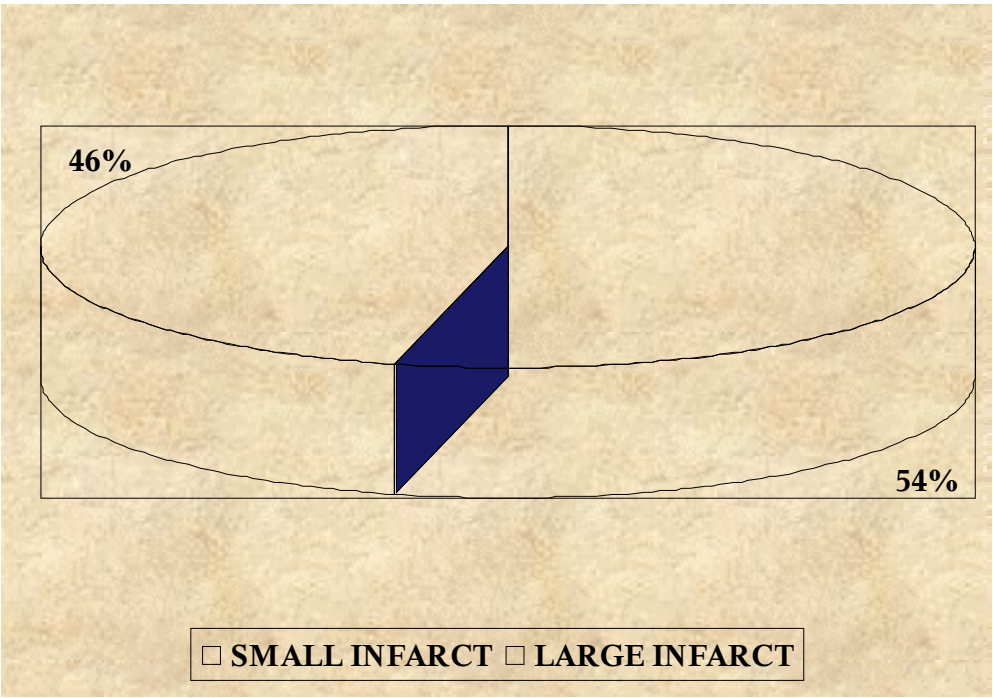


Table 8

C.T.Findings

C.T. Findings	Cases	
	No.	%
< 6 = Small infarct	27	54
> 6 Large infarct	23	46
Total	50	100

FINAL OUTCOME

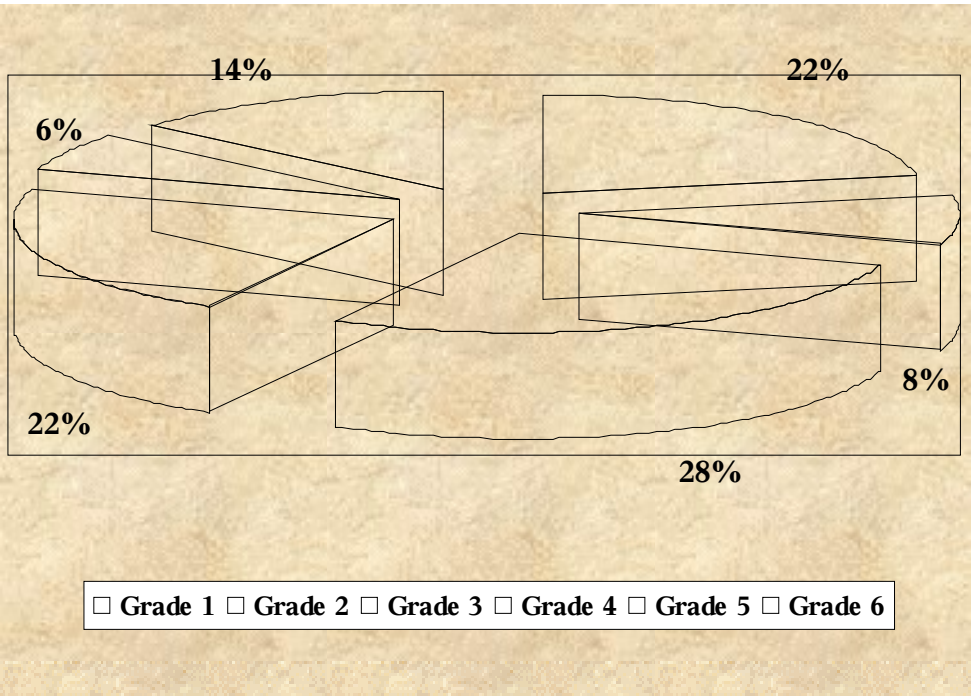
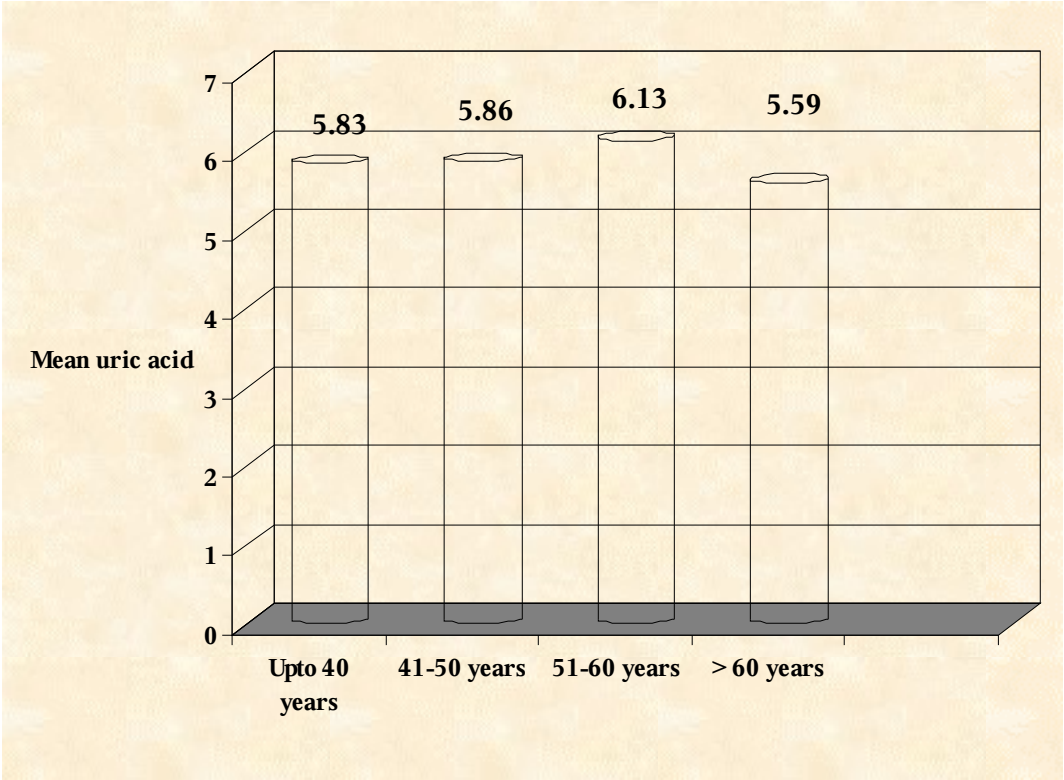


Table 9

Final Outcome

Final Outcome	Cases	
	No.	**%**
Grade 1	11	22
Grade 2	4	8
Grade 3	14	28
Good Prognosis Total	29	58
Grade 4	11	22
Grade 5	3	6
Grade 6	7	14
Bad Prognosis Total	21	42
Total	50	100

AGE AND URIC ACID



B : RELATIONSHIP BETWEEN URIC ACID LEVELS & OTHER PARAMETERS

Table 10

Age and Uric Acid levels

Age Group	Uric Acid	
	Mean	**S.D.**
Upto 40 years	5.83	1.73
41-50	5.86	2.12
51-60	6.13	2.16
> 60 years	5.59	1.83
'p'	0.8393 Not Significant	

The age of this study group was not significantly correlated with serum uric acid level

Table 11

Sex and Uric Acid levels

Sex	Uric Acid	
	Mean	**S.D.**
Male	6.04	2.24
Female	5.65	1.39
'p'	0.6873 Not Significant	

The sex of this study group was not significantly correlated with serum uric acid.

Table 12

B.M.I. and Uric Acid levels

B.M.I.	Uric Acid	
	Mean	**S.D.**
Upto 25	5.64	2.01
> 25	5.79	2.0
'p'	0.5318 Not Significant	

The BMI of this study group was not significantly correlated with serum uric acid.

Table 13

Blood Sugar and Uric Acid levels

Blood Sugar	Uric Acid	
	Mean	**S.D.**
Normal (Upto 140)	6.1	2.09
Abnormal (Above 140)	5.56	1.8
'p'	0.3315 Not Significant	

The Blood sugar of this study group was not significantly correlated with serum uric acid level.

Table 14

Past History and Uric Acid levels

History of	Uric acid level of cases				'p'
	Yes		No		
	Mean	**S.D.**	**Mean**	**S.D.**	
Smoking	6.06	2.39	5.7	1.4	0.9612 Not Significant
D.M.	4.61	1.19	6.37	2.03	**0.0065** **Significant**
H.T.	6.2	2.44	5.74	1.71	0.6332 Not Significant

The history of smoking and alcohol of this study group was not significantly correlated with serum uric acid level. But the history of diabetes was significantly associated with serum uric acid level.

Table 15

Other Investigation results and Uric Acid levels

Investigations	Uric acid level of cases				'p'
	Positive		Negative		
	Mean	S.D.	Mean	S.D.	
Renal Function Test	5.93	2.28	5.9	1.93	0.8789 Not Significant
Lipid Profile	5.41	1.43	6.49	2.4	0.07 Not Significant

The renal function test and lipid profile abnormality of this study group was not significant correlated with serum uric acid level.

C T FINDINGS AND URIC ACID

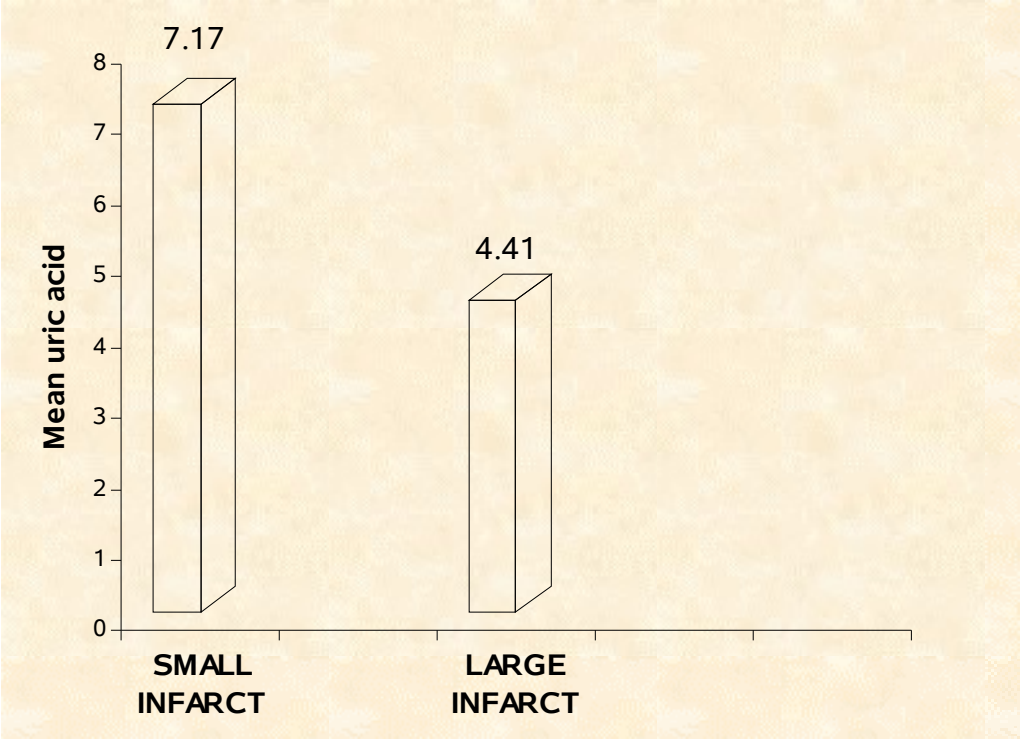


Table 16

C.T. Findings and Uric Acid levels

C.T. Findings	Uric Acid	
	Mean	**S.D.**
Good Prognosis- < 6	7.17	1.64
Bad Prognosis - > 6	4.41	1.14
'p'	**0.0001** **Significant**	

The CT Brain finding in this study group was significantly correlated with serum uric acid level in the form of small sized infarcts in patients with raised serum uric acid.

FINAL OUTCOME AND URIC ACID

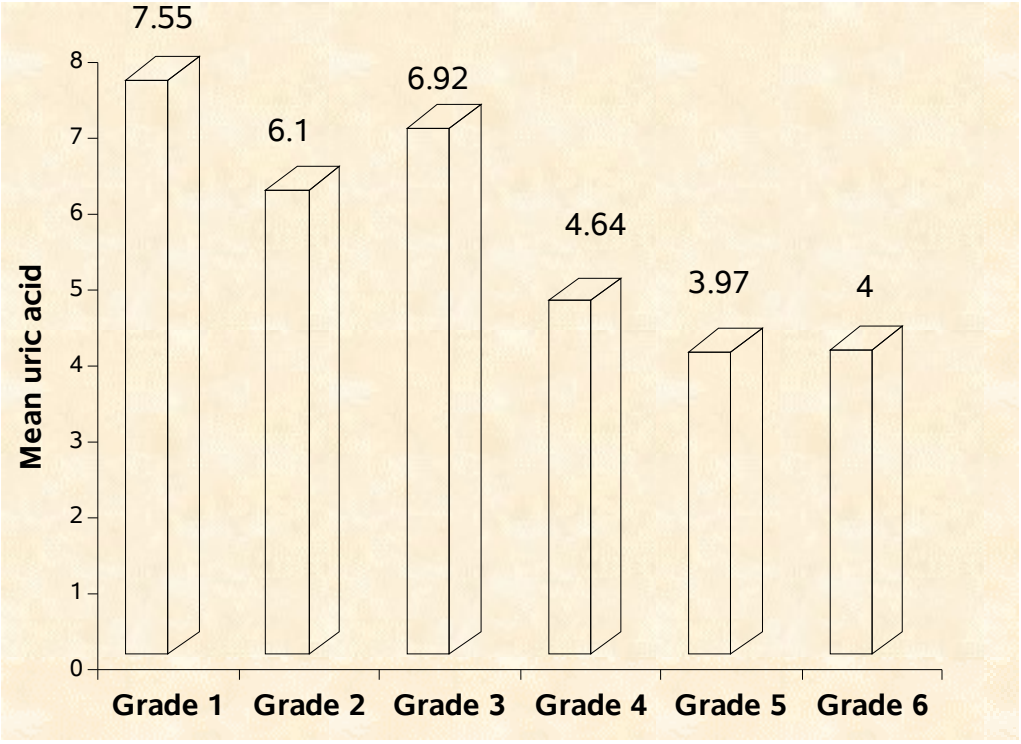


Table 17

Uric Acid levels and Final Outcome

Final Outcome	**Uric Acid**	
	Mean	**S.D.**
Grade 1	7.55	1.71
Grade 2	6.1	0.86
Grade 3	6.92	1.71
Grade 4	4.64	1.29
Grade 5	3.97	1.18
Grade 6	4.0	1.04
'p'	**0.0001** **Significant**	

The functional outcome of this study group was significantly correlated with serum uric acid level in the form of better immediate outcome in patients with raised serum uric acid.

DISCUSSION

50 cases of acute ischemic stroke within 24 hours of onset were admitted in the department of Medicine, Madurai Medical College and Government Rajaji Hospital during the period of October 2008 to May 2009.

Among total number stroke patients 50 patients who underwent CT scan, and they were included in the statistical analysis. All the 50 patients were found to have ischemic stroke.

1. AGE DISTRIBUTION:

The total number of cases were 50. Maximum number of cases were seen in the age group between 51-70 years. The youngest patient was 34 years and the oldest patient was 72 years. This correlates with study by Daga et al[32]. There was no significant correlation between the age of onset of stroke and serum uric acid levels.

2. SEX DISTRIBUTION:

There were 33 male patients and 17 female patients. This observation correlates with Daga et al[32]. There is no significant difference in uric acid level with regard to sex.

3. RISK FACTORS IN STROKE:

In the present study,

36% of cases were hypertensives. There was no significant correlation between Hypertension and serum uric acid level even though following study shows significant correlation.

Strong epidemiological data have linked uric acid to hypertension in humans (cannon et al, 1966, Kinsey et al, 1961; and Klien et al, 1973)[17] experimental animal data suggests hyperuricemia causes hypertension (Mazzali et al,2001: Sanchez et al, 2002; and Watanabe, 2002)[33]. Olivetti heart study (Jossa et al, 1994)[21] had shown an independent positive association between serum uric acid and the development of hypertension.

In the present study there is no significant correlation between uric acid level and hypertension.

DIABETES MELLITUS:

In our study 22% of patients had diabetes.

In this study, Prognostic Significance of Uric acid Serum Concentration in Patients With Acute Ischemic Stroke by Angel Chamorro, MD; Victor Obach, MD; Alvaro Cervera, MD; Marian Revilla, MD; Ramón Deulofeu, PhD John H. Aponte, MD, shows that increased Uric acid values were found in men, hypertensives, alcohol drinkers, and patients with coronary, pulmonary, or renal diseases. Diabetic patients had lower uric acid levels on admission. Uric acid was directly associated with hematocrit (P=0.001), sodium (P=0.001), creatinine (P=0.001), and triglycerides (P=0.001) and inversely related with nonfasting glucose (P=0.001) levels. Neurological impairment on admission (P=0.001) and final infarction size on CT/MRI (P=0.01) were also inversely associated with uric acid. A logistic regression adjusted for confounders confirmed the following independent (odds ratio, 95% CI) good outcome predictors: age (0.97, 0.96 to 0.99), Mathew score on admission (1.14, 1.12 to 1.17), erythrocyte sedimentation rate (0.98, 0.97 to 0.99), infarction volume (0.98, 0.98 to 0.99), and uric acid (1.12, 1.00 to 1.25) Di Yi Jun Yi Da Xue Xue Bao. 2002 Jan;22(1):70-1.

Even though Canon et al[17] showed a prevalence of hyperuricemia in 25% of long standing uncontrolled diabetes mellitus. Our study did not show correlation between serum uric acid level and diabetes was not significant.

BMI:

A large body of evidence links uric acid with metabolic syndrome of insulin resistance, obesity, hypertension, and dyslipidemia. In this study relationship between obesity, hypertension, dyslipidemia, and hyperuricemia was statistically not significant.

Cappcio et al (1998) reported an association of hyperuricemia with increased tubular reabsorption of sodium, thus providing a link with hyperuricemia, hypertension and hyperinsulinemia.

The mean uric acid in those subjects with BMI>25 were higher than those with BMI< 25 and the difference was statistically significant. Shoba kelker et al, Healey et al, (1973)[34] observed a significant correlation between serum uric acid and obesity.

But in contrast to the above mentioned studies our study did not show any correlation between various components of metabolic syndrome and serum uric acid.

DYSLIPIDEMIA:

Elevated triglycerides is the most important risk factor in acceleration of atherosclerosis according to vnitr lek (1990).

According to Cadeddu et al, (1983) in their study of hyperuricemia and cardiac risk factors there was strict correlation of hyperuricemia and dyslipidemia.

Bouvenot G et at (1986)[16] also showed the relationship between serum uric acid and dyslipidemia. In the present study the relationship between serum uric acid and dyslipidemia was not significant.

SMOKING:

There were no current studies regarding the correlation between smoking and serum uric acid in stroke patients.

URIC ACID:

Despite the widely held view that elevated serum Uric acid concentrations confer increased risk of atherosclerotic disease, there is no compelling biological evidence of a causal link. 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. In the context of acute ischaemic stroke[1], there is growing evidence to support a protective role for Uric acid. This underpins the importance of oxidative stress in the

pathogenesis of acute stroke, and strengthens the rationale for further investigation of antioxidant treatments in this condition. The feasibility of Uric acid administration to temporarily increase circulating concentrations has recently been established,[15] and might allow its potential therapeutic impact to be examined in a clinical setting. Ongoing basic research is likely to shed new light on the cardiovascular effects of Uric acid, and will hopefully allow the significance of serum concentrations to be interpreted more clearly

In this study 80% of the patients had elevated uric acid level. In this study we found that significant association of serum uric acid with functional outcome.(those who had high uric acid level at the time of admission had good final outcome).

In this study we found significant association between the level of serum uric acid and infarct size in CT brain (those who had high serum uric acid at the time of admission had small infarct in CT-brain).

A recent study[2] lends support to this hypothesis in a clinical setting. Serum Uric acid concentrations measured in 881 consecutive ischaemic stroke patients at the onset of ischaemic symptoms were found to correlate inversely with early neurological impairment and final infarction size on computed tomography or magnetic resonance imaging. Additionally, serum Uric acid

concentrations were positively associated with a good clinical outcome at hospital discharge (Matthew score of >75), where each mg/dl Uric acid increase (equivalent to 60 µmol/l; reference range 120–420 µmol/l) was associated with a 12% increase in the odds of a good outcome. Importantly, these relationships were independent of potential confounders, including age, diuretic use, renal function or the presence of major cardiovascular risk factors. This is the first study to characterize the relationship between serum Uric acid concentration and neurological severity of acute ischemic stroke in a large series of patients

In the study by Chakraborty D, Ghosh S, Guru S, Dash LK, Mohapatra MK, Barik BK VSS Medical College, Burla, Orissa APICON 2009 [3]. Uric acid levels were directly associated with haematocrit, creatinine and triglyceride levels. Neurological impairment and the size of infarct on admission on CT scan was inversely associated with serum uric acid levels. In patients with acute ischemic stroke raised serum uric acid level was associated with good clinical outcome and reinforces the relevance of oxidative damage in stroke.

CONCLUSION

The following conclusions were derived from the study.

1. The serum Uric acid was independent of age, sex, BMI, hypertension, diabetes, smoking, dyslipidemia and renal parameters.

2. Outcome in patients with acute ischemic stroke was better in patients with high serum uric acid level in terms of higher function recovery, motor activity, self – care, small size infart etc.

3. Every 1mg increase in Uric acid above 4.2mg /dl was associated with better outcome.

4. The antioxidant capacity of serum Uric acid is a favourable independent factor that improves the clinical prognosis of patients with acute ischemic stroke.

5. This study opens up the possibility of therapeutic administration of Intravenous infusion of uric acid along with rtPA to improve the immediate prognosis of acute ischemic stroke.

SUMMARY

This study "CORRELATION BETWEEN SERUM URIC ACID LEVEL AND THE PROGNOSIS OF ACUTE ISCHEMIC STROKE" was carried out in Govt.Rajaji Hospital, Madurai Medical college, Madurai from October 2008 to September 2009.

50 cases of acute ischemic stroke within 24 hours of onset were admitted in this period. Male out numbered stroke. Males - 66%, females-34%.

The risk factors in this study group were increasing age, hypertension, smoking, diabetes, dyslipidemia.

Raised serum uric acid associated with small size infarct and good functional outcome at the time of discharge.

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PROFORMA

NAME: AGE: SEX:

I.P.NO:

OCCUPATION: WARD:

BMI:

HISTORY:

1.HYPERTENSION: YES/NO

REGULAR TREATMENT: YES/NO

2.DIABETES : YES/NO

REGULAR TREATMENT: YES/NO

3.SMOKING : YES/NO

4.DURATION OF STAY :

VITAL SIGNS:

PR- BP-

EXAMINATION

1.TIME OF PRESENTATION AFTER STROKE:

2.CVA : RIGHT/LEFT

3.HANDEDNESS : RIGHT/LEFT

4.LEVEL OF CONSCIOUSNESS :

5.LANGUAGE :

6.CRANIAL NERVES :

7.MOTOR SYSTEM :

8.SENSORY SYSTEM :

9.CEREBELLUM :

10.AUTONOMOUS NERVOUS SYSTEM :

11.FINAL OUTCOME ON DISCHARGE :

INVESTIGATIONS :

BLOOD SUGAR :

NORMAL RENAL PARAMETERS : YES/NO

URIC ACID :

DYSLIPIDEMIA :YES/NO

CT-BRAIN : INFARCT SIZE: