# "MICROALBUMINURIA AS A PREDICTOR OF EARLY NEUROLOGICAL DETERIORATION IN ACUTE ISCHEMIC STROKE"

By

**Dr. PUJITHA S N** M.B.B.S

**DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, KOLAR, KARNATAKA**

***In partial fulfillment of the requirements for the degree of***

**DOCTOR OF MEDICINE**

**IN**

**GENERAL MEDICINE**

Under the Guidance of

Dr. **PRABHAKAR K** MD

Professor

**DEPARTMENT OF GENERAL MEDICINE,**

**SRI DEVARAJ URS MEDICAL COLLEGE,**

**TAMAKA, KOLAR-563101**

**APRIL/MAY 2020**

## SRI DEVARAJ URS MEDICAL COLLEGE,

## TAMAKA, KOLAR-563101

## DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation/thesis entitled "**MICROALBUMINURIA AS A PREDICTOR OF EARLY NEUROLOGICAL DETERIORATION IN ACUTE ISCHEMIC STROKE**" is a bonafide and genuine research work carried out by me under the guidance of **Dr.PRABHAKAR K**, Professor, Department of General Medicine, Sri Devaraj Urs Medical College, Tamaka, Kolar.

This work has not formed the basis for the award of any other degree or diploma to me previously by any other university.

Date: **DR PUJITHA S N**

Place: Kolar

## SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION, TAMAKA, KOLAR, KARNATAKA

## CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled "**MICROALBUMINURIA AS A PREDICTOR OF ON EARLY NEUROLOGICAL DETERIORATION IN ACUTE ISCHEMIC STROKE**" is a bonafide and genuine research work done by **Dr.PUJITHA S N** in partial fulfillment of the requirement for the degree of **M.D IN GENERAL MEDICINE.**

**Date :**

**Place** :

**Dr. PRABHAKAR K . MD**

Professor,

Department of General Medicine,

Sri Devaraj Urs Medical College,

Tamaka, Kolar.

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, TAMAKA, KOLAR, KARNATAKA**

## ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled "**MICROALBUMINURIA AS A PREDICTOR OF ON EARLY NEUROLOGICAL DETERIORATION IN ACUTE ISCHEMIC STROKE**" is a bonafide and genuine research work done by Dr. PUJITHA S N under the guidance of Dr. PRABHAKAR K. Professor, Department of General Medicine, Sri Devaraj Urs Medical College, Tamaka, Kolar.

**Dr. RAVEESHA A**

Professor & HOD

Department of General Medicine,

Sri Devaraj Urs Medical College,

Tamaka, Kolar

Date:

Place: Kolar

**Dr. SREERAMULU P. N.**

Principal,

Sri Devaraj Urs Medical College

Tamaka, Kolar

Date:

Place: Kolar

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, TAMAKA, KOLAR, KARNATAKA**

**ETHICAL COMMITTEE CERTIFICATE**

This is to certify that the Ethical committee of Sri Devaraj Urs Medical College & Research Center, Tamaka, Kolar has unanimously approved

**Dr.PUJITHA**

***Post-Graduate student in the subject of***

***GENERAL MEDICINE***

*at Sri Devaraj Urs Medical College, Kolar to take up the Dissertation work entitled*

"**MICROALBUMINURIA AS A PREDICTOR OF ON EARLY NEUROLOGICAL DETERIORATION IN ACUTE ISCHEMIC STROKE**"

*to be submitted to the*

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, TAMAKA, KOLAR, KARNATAKA,

Member Secretary

Sri Devaraj Urs Medical College,
& Research Center,Tamaka,
Kolar–563101

Date:

Place: Kolar

## SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION

## TAMAKA, KOLAR, KARNATAKA

## COPY RIGHT

## DECLARATION BY THE CANDIDATE

I hereby declare that the Sri Devaraj Urs Academy of Higher Education and Research Center, Kolar, Karnataka shall have the rights to preserve, use and disseminate this dissertation/thesis in print or electronic format for academic / research purpose.

Date:

Place: Kolar **DR PUJITHA S N**

SDUAHER

# Sri Devaraj Urs Academy of Higher Education and Research

## Certificate of Plagiarism Check for Thesis/Dissertation

| | |
|---|---|
| Author Name | Dr. Pujitha S N |
| Course of Study | M.D in General Medicine |
| Name of Supervisor | Dr. Prabhakar. K. |
| Department | General Medicine. |
| Acceptable Maximum Limit | – |
| Submitted By | librarian@sduu.ac.in |
| Paper Title | MICROALBUMINURIA AS A MARKER OF EARLY NEUROLOGICAL DETERIORATION IN PATIENTS WITH ACUTE ISCHEMIC STROKE |
| Similarity | 9 % |
| Paper ID | 191125121314 |
| Submission Date | 2019-11-25 12:13:14 |

* This report has been generated by DrillBit Anti-Plagiarism Software

| | |
|---|---|
| Signature of Student | Signature of Supervisor |
| Head of the Department | |
| University Librarian | Director Of Post Graduate Studies |

Dr. Pujitha S.N. Junior Resident Dept. of Medicine KMC NO-160358 Date 2/12/19 Time 10 a.m.

Prof & HOD of Medicine SDUMC, Tamaka, Kolar

Prof & HOD of Medicine SDUMC, Tamaka, Kolar

26/11/19

Senior Librarian, Library and Information Centre Sri Devaraj Urs Medical College Tamaka, KOLAR-563 101.

2/12/19

Director P.G. STUDIES Sri Devaraj Urs Medical College Tamaka, KOLAR-563 101

## ACKNOWLEDGEMENT

I would like to take this opportunity to thank all those who have been a part of this wonderful journey that has culminated in the completion of this thesis.

At the foremost I offer my gratitude and seek blessings from my parents, **Narayana Swamy C, Lalithamba N**, my brother **Deekshith Kumar S N** and my husband **Dr Phaneesh Bharadwaj B S** whose countless sacrifices and endless love has made me who I am today in life.

I offer my salutations and thank all my teachers who have not only guided me through the maze of new information and skills but also shaped my personality by chiseling out all the rough edges.

I am deeply indebted and grateful to my guide, **Dr.Prabhakar K**, Professor, Department of General Medicine, Sri Devaraj Urs Medical College, for his able guidance, support, timely advice and constant encouragement throughout the period of the study.

I would like to express my sincere gratitude to **Dr. Raveesha A**, Professor and Head of the department, Department of General Medicine, Sri Devaraj Urs Medical College, for his expert advice, help and support in preparation of this dissertation.

I convey my sincere thanks to **Dr. V.Lakshmaiah, Dr. B.N. Raghavendra Prasad, Dr.Vidya Sagar C R, Dr. Srinivasa S V, (major)Dr Jayaprasad V, Dr Mahesh K** for their advice and encouragement throughout the study.

If I have learnt to see far it is only by standing on the shoulders of my great teachers.

I am thankful to my postgraduate colleagues **Dr Jithendra Chaithanya Gubbala, Dr Parimi Samba Siva Rao, Dr Deepa S, Dr Rumaisa Ahmed, Dr Minni Meka, Dr Manoj A G and Dr Hamsa B T** for their motivation and for being a constant source of strength.

I am thankful to all my seniors especially **Dr Modugula S Naga Swetha, Dr Rakesh Garlapati, Dr Thanuj Reddy K V** and dear juniors for their love, motivation and help.

I am highly indebted to my patients for providing me an opportunity to carry out this study.

Last but not least, I am thankful to all Technical Staff and non-teaching staff for their invaluable help without which this study would not have been possible.

Date: **Dr PUJITHA S N**

Place:

# ABSTRACT

## MICROALBUMINURIA AS A PREDICTOR OF ON EARLY NEUROLOGICAL DETERIORATION IN ACUTE ISCHEMIC STROKE

**BACKGROUND**:

Stroke is a major cause of long-term disability among patients and has enormous emotional and socio-economic consequences. In 20-40 per cent of patients with acute ischemic stroke, neurological symptoms progress during the initial hours. Early Neurological Deterioration (END) has potentially serious consequences on the short term (morbidity and death) and long term (recovery from stroke) outcomes for the patients of acute ischemic stroke. Therefore, attempts to predict and prevent END should be made promptly and aggressively. The recent realization that atherosclerosis is disease of inflammation has led to a research for new stroke risk factors. Microalbuminuria is known to be associated with multiple risk factors for stroke such as obesity, aging, diabetes, hypertension, ischemic heart disease, smoking and left ventricular hypertrophy. Studies have shown a higher prevalance of microalbuminuria in those patients with acute ischemic stroke(1). However, there is very little information concerning microalbuminuria as an independent risk factor for stroke and as a prognostic indicator of stroke severity and outcome and hence the requirement for the study.

**OBJECTIVES:**

1. To measure microalbuminuria in acute ischemic stroke patients at the time of presentation by calculating urine albumin creatinine ratio (UACR).

2. To diagnose the Early Neurologic Deterioration among the patients with acute ischemic stroke by assessing NIHSS score on day 1 and day 3 of admission.

3. To correlate microalbuminuria at the time of presentation and development of early neurologic deterioration among the patients of acute ischemic stroke.

**MATERIALS AND METHODS** :

All patients with Acute ischemic stroke enrolling to General Medicine OPD and Emergency department at R L Jalappa hospital, Kolar satisfying the inclusion criteria were taken up for study.

**STUDY DESIGN:**

The study was conducted among acute ischemic stroke patients presented to the department of General medicine, RLJH. 73 atients with first episode of acute ischemic stroke presenting within first 24 hours after onset of symptoms were enrolled in the study. The neurological status of the patients and the severity of stroke were assessed by applying the NIHSS (National Institute of Health Stroke Scale) score on day 1 and day 3 on all the patients. Early Neurological Deterioration was diagnosed if there was an increase in the NIHSS score by 3 or more than 3 points from day 1 to day 3 of admission.

Presence of microalbuminuria in patients were assessed by calculating UACR. Microalbuminuria was then correlated with Early neurologic deterioration in patients with acute ischemic stroke.

**RESULTS:**

The presence of microalbuminuria is more among patients who developed Early neurologic deterioration than who did not develop Early neurologic deterioration. On comparing microalbuminuria status in groups of people with and without END, 80% of patients with END had microalbuminuria whereas in group without END, 18.86% had microalbuminuria.($p < 0.001$).

**CONCLUSION:**

Results of our study suggests that presence of microalbuminuria can predict development of early neurologic deterioration in acute ischemic stroke patients and hence to be treated aggressively.

**KEY WORDS**:

Acute ischemic stroke, Early Neurologic Deterioration,Microalbuminuira.

# ABBREVATIONS

| | |
|---|---|
| **UACR** | **URINE ALBUMIN CREATININE RATIO** |
| **CVA** | **CEREBROVASCULAR ACCIDENT** |
| **END** | **EARLY NEUROLOGICAL DETERIORATION** |
| **CT** | **COMPUTED TOMOGRAPHY** |
| **CVT** | **CORTICAL VEIN THROMBOSIS** |
| **IHD** | **ISCHAEMIC HEART DISEASE** |
| **RHD** | **RHEUMATIC HEART DISEASE.** |
| **AF** | **ATRIAL FIBRILLATION.** |
| **CAF** | **CHRONIC ATRIAL FIBRILLATION.** |
| **CHF** | **CONGESTIVE HEART FAILURE.** |
| **TIA** | **TRANSIENT ISCHAEMIC STROKE.** |
| **ICA** | **INTERNAL CAROTID ARTERY.** |
| **NIHSS STROKE SCALE** | **NATIONAL INSTITUTE OF HEALTH** |
| **TPA** | **TISSUE PLASMINOGEN ACTIVATOR.** |
| **WHO** | **WORLD HEALTH ORGANIZATION** |

# TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF FIGURES/CHARTS

# INTRODUCTION

# INTRODUCTION

Cerebrovascular accident is the third most leading cause of death worldwide after coronary heart disease and cancer, especially ischemic stroke(1). It is more often disabling than fatal and could be a major cause for long-term disability among patients and has vast emotional and socio-economic consequences. In 20-40% of patients with acute ischemic stroke, neurological symptoms progress especially during the first few hours(2), Early Neurological Deterioration (END) has potentially serious consequences on the short term (morbidity and death) and long term (recovery from stroke) outcomes for the patients of acute ischemic stroke. Therefore, attempts to predict and prevent END should be made promptly and aggressively.

Various studies have reported the following factors to be predictors of END, which include clinical variables like stroke severity at the time of presentation(3) ,history of diabetes mellitus(3), hypertension(3,4) and laboratory variables like elevated markers of coagulation (PT, aPTT) , markers of inflammation(ESR,CRP) and serum glucose levels at the time of admission(3,4) ,but most of these factors are either not reversible or difficult to be assessed.

The recent realization that atherosclerosis is disease of inflammation has led to a research for new stroke risk factors. Microalbuminuria is known to be associated with multiple risk factors for stroke such as obesity, aging, diabetes, hypertension, ischemic heart disease, smoking and left ventricular hypertrophy. Studies have shown a higher prevalance of microalbuminuria in those patients with acute ischemic

stroke(1). However, there is very little information concerning microalbuminuria as an independent risk factor for stroke and as a prognostic indicator of stroke severity and outcome and hence the requirement for the study.

# OBJECTIVES

# OBJECTIVES OF THE STUDY

1. To estimate microalbuminuria in patients with acute ischemic stroke patients at the time of presentation by calculating urine albumin creatinine ratio.
2. To diagnose the Early Neurologic Deterioration among the patients with acute ischemic stroke by assessing NIHSS score on day 1 and day 3 of admission.
3. To correlate the microalbuminuria at the time of presentation and development of Early Neurologic Deterioration among the patients of acute ischemic stroke.

# REVIEW OF LITERATURE

# REVIEW OF LITERATURE

Acute ischemic stroke is aninternationaldrawback that is related to significant mortality and morbidity. It is the third most common cause of death worldwide often disabling than fatal, stroke is the major cause of preventable disabilityworldwide(1). moreover, stroke causes major social and economic burden to society(2).

EPIDEMIOLOGY OF STROKE

The incidence of the first-onset stroke is 17 million per year worldwide(3). the risk of stroke in a person's lifetime after 55 years of age is 1 in 5 for women and 1 in 6 for men(3). one in eight people with stroke will succumb to death within the first 30 days. And 1 in 4 strokes are fatal within a year(3). Studies indicate that both the worldwide incidence and the associated mortality of stroke have plateaued over the last few decades(4).

But in contrast, the stroke incidence in India and other developing countries has been rising(5). More than four-fifth of all strokes are occurring in developing countries(5). Currently, the average incidence of stroke per annum in India is 145 per 100,000 population(6), which is more than the western countries. Socio-economic changes that are occurring rapidly are leading to change in people's lifestyles, work-connected stress, altered food habits and the risk of development of cardiovascular diseases, diabetes mellitus, and hyperlipidemia. These risk factors along with increased lifespan hasbeen the cause for an increase in the incidence of stroke worldwide.

**DEFINITION OF STROKE**

World health organization defines stroke as "rapidly developing clinical signs or symptoms of focal (at times global) disturbance of cerebral function with symptoms

lasting more than one-day (I.e., 24 hours) or leading to death with no apparent cause other than that of vascular origin(7).

**TYPES OF STROKE**

Stroke is of two categories – Ischemic and Hemorrhagic. Ischemic infarction is again classified into thrombotic and embolic. Ischemic stroke constitutes about 80% of the total stroke cases(7).

**ETIOLOGY OF ISCHEMIC STROKE :**

I.THROMBOSIS:

- Atherosclerosis
- Vasculitis — Collagen Vascular diseases, Syphilis. Meningitis etc.
- Arterial Dissection
- Hematological disorders -- Polycythemia, thrombocytosis, TTP, DIC, etc.

Miscellaneous — Binswanger's disease, MoyaMoya disease, fibromuscular dysplasia.

II.Embolism

- Cardiac sources
- Atherothrombotic arterial sources
- Unknown sources

**III. Vasoconstriction**

- Vasospasm

- Reversible cerebral vasoconstriction

IV. Venous

- Dehydration.
- Postpartum and post-op states,
- Systemic cancer etc.

**PATHOPHYSIOLOGY OF ISCHAEMIC STROKE**

Cerebral ischemia is due to a decrease in the blood flow that lasts longer than several seconds. Neurologic symptoms manifest within a few seconds of ischemia because neurons lack glycogen, so energy failure is rapid. If the cessation of flow lasts for more than a few minutes, infarction of brain tissue results(8).

**LACUNAR INFARCTS**

They are small infarcts in the deep white matter of the cerebral hemisphere or brainstem. They are usually due to hypertension-induced lipohyalinosis or arteriosclerosis of small penetrating arteries, rather than to large artery arteriosclerosis or cardioembolism(8).

- Patients presenting with acute ischemic stroke will have a neurological deficit that is maximum at the onset of stroke.
- 10-20% of thrombotic strokes may be associated with one or more episodes of transient ischemic attacks (TIAs)(8).

## ANATOMY OF CIRCULATION OF BRAIN:

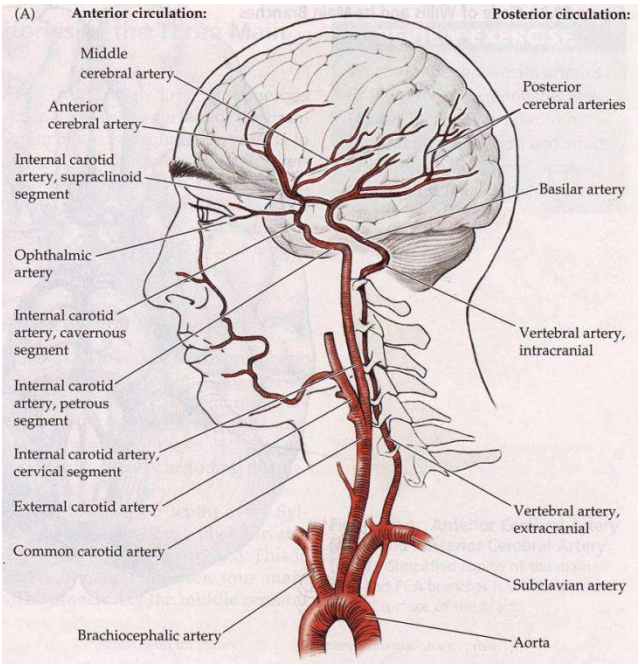



**Fig no.1 Anatomy of Blood supply of brain**

- At rest, the cardiac output is about 5 liters, of which 1 liter is retained by the brain9

Three types of vessels supply the brain(9):-

- Paramedian arteries: These vessels penetrate the brain on either side of the midline and supply the central nuclear areas near the midline.

- Short circumferential arteries: These travel for some distance before supplying the brain.

- Long circumferential arteries: These travel on the surface of the brain for some distance and then anastomose with branches of other circumferential vessels.

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

The internal carotid artery (ICA) begins at the bifurcation of the common carotid artery. It ascends up the neck and perforates the base of the skull by passing through the carotid canal of the temporal bone. It enters the subarachnoid matter and turns posteriorly to a region of the anterior perforated substance of the brain at the medial end of the lateral cerebral sulcus. Here it divides into the anterior perforated substance of the brain at the medial end of the lateral cerebral sulcus. Here it divides into anterior and middle cerebral arteries. (10)

**ANTERIOR CIRCULATION**

**A) ANTERIOR CEREBRAL ARTERY**

It is a smaller terminal branch of the ICA. It runs forward and medially superior to the optic nerve and enters the longitudinal fissure of the cerebrum. Here it is joined by ACA of the opposite side by the anterior communicating artery. It curves backward over corpus callosum and finally anastomoses with posterior cerebral artery. (PCA) (10)the cortical branches supply whole of the medial surface of the cerebral cortex. They also supply a strip of cortex an inch wide on adjoining lateral surface. The ACA supplies the leg area of precentral gyrus10

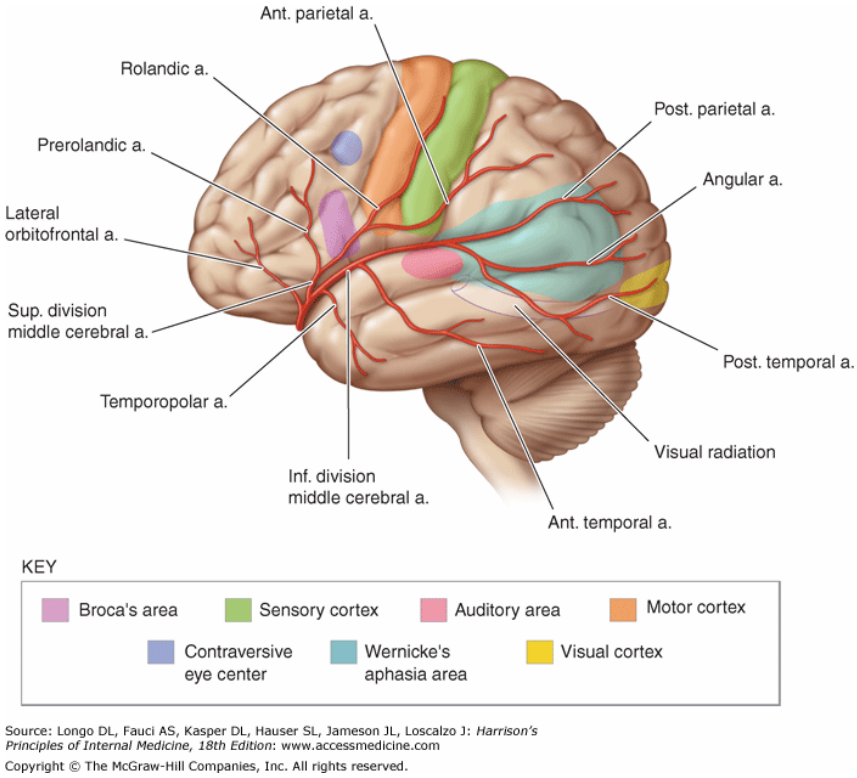




**FIG 2: Diagram of a cerebral hemisphere, lateral aspect, showing middle cerebral artery branches and distributionand the principal regions of cerebral localization. Note the division of the middle cerebral artery into superior and inferior division**

**B) MIDDLE CEREBRAL ARTERY (MCA)**

It is the largest branch of the internal carotid which runs laterally in the lateral cerebral sulcus. (10)

Cortical branches supply the entire lateral surface of the hemisphere except for the narrow strip supplied by the ACA, the occipital pole and the inferolateral surface of the hemisphere supplied by the Posterior Cerebral Arteries (PCA). The artery thus supplies all the motor area except the leg area(10). Cerebral branches enter the anterior perforated substance and supply the lentiform and caudate nuclei and the internal capsule(10).

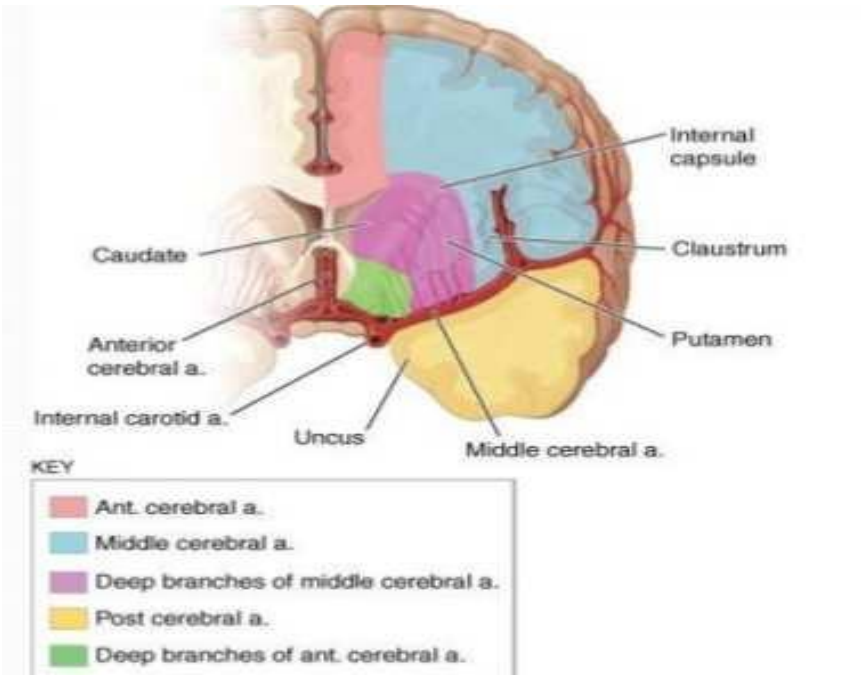



**Fig 3 : Diagram of a cerebral hemisphere in coronal section showing the major cerebral blood vessels territories that branch from the internal carotid arteries.**

## POSTERIOR CIRCULATION

### A) VERTEBRAL ARTERY

It is the branch of the first part of the subclavian artery which ascends the neck by passing through the foramina in the transverse processes of the upper six cervical vertebrae. It enters the skull through the foramen magnum and pierces the dura and arachnoid mater to enter the subarachnoid space, which then passes upward, forward and medially on the medulla. At the lower border of the pons, it joins the vessel on the opposite side to form the basilar artery. (10)

Branches of the cranial portion of the vertebral artery

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

**B) BASILAR ARTERY**

It is formed by the union of two vertebral arteries. It ascends in a groove on the anterior surface of the pons. At the upper border of the pons, it divides into two Posterior Cerebral Arteries (PCA)(10).

**BRANCHES**

Pontine arteries

- Labyrinthine artery-: This supplies the inner ear.
- Anterior Inferior Cerebellar Artery (AICA): This Supplies the anterior and inferior parts of the cerebellum.
- Superior Cerebellar Artery (SCA): This vessel arises close to the termination of the basilar artery, Supplies the superior surface of the cerebellum, pons, pineal gland, and superior medullary velum.
- PCA curves laterally and backward around the midbrain and is joined by the posterior communicating branch of the ICA.
- Cortical branches supply the inferolateral and medial surfaces of the temporal lobes and the lateral and medial surfaces of the occipital lobe. Thus PCA supplies the visual cortex. Cortical branches pierce the brain substance and supply parts of the thalamus. The lentiform nucleus, the midbrain, the pineal gland, and the medial geniculate bodies. Choroidal branches supply the choroid plexus.

**THE CIRCULUS ARTERIOSIS (CIRCLE OF WILLIS)**

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

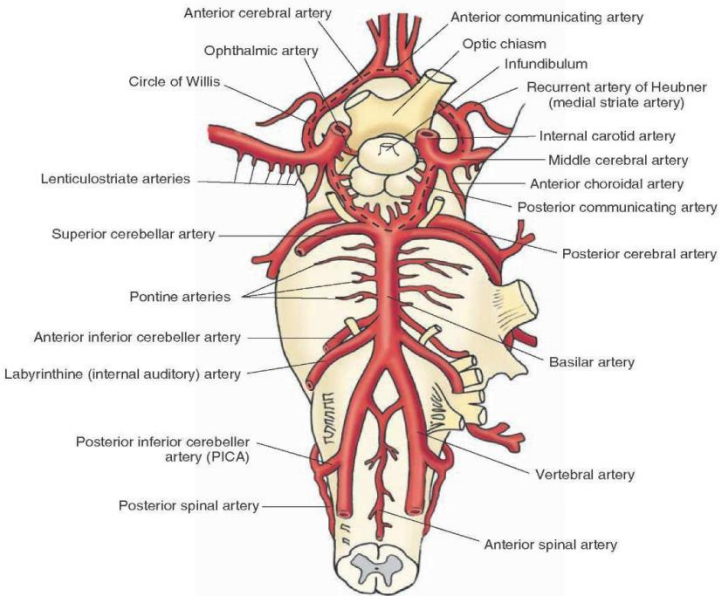



**FIGURE NO. 4 CIRCLE OF WILLIS**

RISK FACTORS IN CEREBROVASCULAR DISEASES

Risk factors were briefly classified as –

i. Non-modifiable

ii. Modifiable

NON MODIFIABLE RISK FACTORS INCLUDE:

Age – advanced age

Sex- male sex

Race/ ethnicity

Family history of stroke

Genetics

MODIFIABLE RISK FACTORS INCLUDE:

Hypertension (Diastolic, Systolic)

Diabetes mellitus

Heart Diseases

Transient Ischaemic Attacks

Obesity

Dyslipidemias

Alcoholism

Smoking

Hyperuricemia

Infections

Hematocrit (Increased, decreased)

Migraine

Usage of Oral contraceptives etc

Age:

People of age group between 5th to 8th decade are more prone to stroke(11,12). A study done by Nagaraja et al (13) found that the maximum incidence of stroke was in the sixth decade. The occurence of stroke continues to grow with advancing age due to decreased blood flow which occurs normally with age. According to studies from the UK, the risk of stroke in people aged between 75-84 years is 14.3/1000 / year i.e.25 times more compared to the risk in people of age between 45-54 years that is

0.57/1000/year(14). The joint committee for stroke facility estimated that the death rate was 1/1000 at age45-54 years and 9/1000 at age 65- 74 years(15).

**Sex:**

This change is more striking in women compared to men especially after 64 years of age(16). In Nagaraja et al's study13 men outnumbered women in both fatal and nonfatal stroke in the ratio of 1.3:1. In the Framingham cohort, stroke was responsible for 8% of all deaths in women and 5 % in men. The same study also implied that the incidence of stroke in the age group 65-74 years was 84/10,000 /year for men and 86/10,000 /year for women(17).

In Kamel Abdelaziz Mohamed's study in 2013, male patients were 61% and female patients were 39%(18).

In the Abdu Hameed AI Kassir study in 2012, male patients were 67.6% and female patients were 32.4%(19).

In Hala El Kawas study in 2006, male patients were 56.6% and female patients were

43.3%.(20)

**ARTERIAL HYPERTENSION**

Hypertension is one of the major risk factor for both ischemic and hemorrhagic stroke (21). Hypertension increases the stroke risk by increasing the extent and severity of atheroma(22) and the prevalence of the microvascular disease in the small penetrating arteries within the brain which are end arteries(23).

In a study done by A.G. Sharper et al Britain,60% of strokes were seen in men with systolic BP > 160 mmHg. It was also found that those patients with systolic BP

between 160 and 180 mm Hg had 4 times greater risk of stroke than in men with BP < 160 mm Hg. With systolic BP > 180 mm Hg, this risk increases to six-fold. They found a weaker relation of diastolic BP with a stroke which was lost on 4 regression analyses (24).

Stephen McMohan et al, In their study on hypertension as a risk factor found that disease rates were lowest among those individuals whose baseline diastolic BP was 65 mm Hg and whose usual diastolic BP was probably 73 mm Hg(25).

In Indian studies, it was found that 16-55 % to 23-47.4 % of the stroke patients were hypertensive. Nagaraja and Pratap Chand(13) found the incidence of hypertension to be 24 % in fatal and 16 % in nonfatal cases(17). In their study ,the relative risk for hypertension in ischaemic stroke was 3.6.

Isolated systolic hypertension was more frequent in fatal cases while isolated diastolic hypertension was seen mainly in the nonfatal cases(26).

**DIABETES MELLITUS (DM)**

WHO quotes diabetes mellitus to be a very important risk factor for CVD in the developed world .(27)

According to the WHO stroke report, Diabetes mellitus plays an important role as a risk factor in ischaemic strokes in large vessel diseases but is of questionable impact in small vessel disease. However, the role of its risk in hemorrhage stroke is yet to be clarified(27).

Control of hyperglycemia can decrease the severity of cerebral damage during the acute stroke period but there is no evidence that controlling diabetes decreases stroke incidence(28).

Some authors like Kier et al suggested that diabetics, as well as patients with stress hyperglycemia, have a severe stroke and these patients are associated with poor prognosis. (29)

Nagaraja and Pratap(13) from NIMHANS, Bangalore have found that DM was twice as common in fatal group as compared to the non -fatal group, possibly the mechanism suggested by Jorgensen.

**CARDIOVASCULAR DISEASES**

Rheumatic heart disease (RHD), coronary artery diseases with MI, cardiac arrhythmias, cardiac emboli are the most common risk factor for ischaemic stroke. (30)

Atrial fibrillation (AF) is one of the most important and frequent cardiac source of embolism to the brain. Peterson P et al in their study showed distinct clustering of emboli at the time of onset of paroxysmal atrial fibrillation(30). It is well established that chronic atrial fibrillation (CAF) leads to increased risk of strokes. In the Framingham study dealing only with CAF, an increased risk of stroke was found. AF in the absence of RHD was associated with more than a fivefold increase in stroke incidence, while AF with RHD had a 17 fold increase compared to the controls without AF(31).

Prevalence of AF was 17% for all stroke types and 18 % for infarction in the community stroke project in Oxfordshire. AF was not associated with a definite excess risk of recurrent strokes, either within 30 days or within the first few years. (32)

In Indian studies, cerebral emboli from cardiac pathology is a major detectable cause for stroke in the young. Sridharan noted that 36.5 % of non-hemorrhagic stroke patients had heart diseases, the relative risk being 2.250, Besides RHD with AF and ASD with a paradoxical embolus, MVP was also associated with increased risk of stroke. (33)

Patients with coronary artery disease were found to have a 3 times increased risk of stroke and those with CHF had almost fivefold increased risk. LVH in electrocardiography is associated with a 5 times increased risk of stroke. (32) Cardiac impairment which has been found to contribute independently to stroke includes LVH on ECG, cardiomegaly on CXR, coronary heart diseases, congestive heart failure and AF(24,25).

**TIAS AND COMPLETED STROKES**

TIAs and previously completed strokes are significant risk factors for all strokes more so for ischaemic strokes. Previous strokes are thegreatest risk factor for subsequent stroke than TIA alone (30).

From Indian studies, Agarwal et al(33) noted that the incidence of past history of TIA was 19.8 % in ischemic stroke and Sridharan noted 15 % TIAs in Ischaemic stroke (34).

In the Oxfordshire community stroke project, there was 12% risk of stroke in the first year after TIAs and approximately 6 % per year over the first 5 years. They found that patients who suffered a TIA had a 13 fold increased risk of stroke during the first year(35).

## THROMBOSIS OF EXTRACRANIAL VESSELS

Atherosclerosis in the extracranial cerebral vessels is an important risk factor for thrombotic stroke. The manifestations may be in the form of carotid bruit, occluded carotids and peripheral vascular diseases(27).

Sridharan noted carotid bruit in 6.8 % of ischemic stroke patients(34). carotid and a supraclavicular bruit are risk factors for subsequent stroke(36). The atherothrombotic disease of the large extracranial arteries including the carotids accounts for 34 % of strokes(37).

## DYSLIPEDMIA

Elevated levels ofLDL is a risk factor for atherosclerosis per se(38). Various lipid abnormalities have been studied and it has been proposed by Bansal et al that hyperlipidemia contributes to a large majority of non-embolic thrombotic strokes even in the young(39).

Agarwal et al had found elevated free fatty acids as significant in women with thrombotic strokes(33). Reed DM et al found that elevated blood LDL levels is correlated with extra and intracranial atheroma(22).

## ALCOHOLISM

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

## ORAL CONTRACEPTIVE PILLS

It is estimated that there isten-times increased risk of stroke in women taking OC pills when compared to women not taking them. In a study conducted among young women consuming OC pills, it was seen that the use of OC pills triples the risk of ischemic stroke in young women(34).

## OBESITY

Whether obesity is an independent risk factor for stroke or notis not yet established(30). the risk factor status of obesity in Indian studies is also not established(40).

## INFECTIONS

Infections commonly associated are tuberculosis, helminthic infestations, malaria, syphilis, and leptospirosis. Clinicians report that systemic viral and bacterial infectionsare risk factors for stroke but the data is inconclusive(30).

## HEMATOCRIT

Even though pathologically elevated hematocrit has long been recognized as a predisposing condition for stroke, the Framingham study showed that this was true even within the normal range of hematocrit (41).

In patients with hematocrit values between 36- 46 % ,cerebral blood flow has been found to be significantly low(42).

Dalal found that low hematocrit to be a significant risk factor in a case-control study of ischemic stroke in the young,(43). A study done by Chopra et al, it was found that 8% of patients with thrombotic stroke had low hematocritand in 61 % of patients with

puerperal intravenous occlusion(39). The mechanism by which a low hematocrit predisposes to cerebral Ischemia is uncertain.

Low normal hemoglobin percentagehas been reported as an important risk factor for stroke in young and elderly subjects in the ICMR stroke study (44).

On the other hand, the EC / IC bypass study group concluded that the severity of strokes was not different in subjects with high hemoglobin concentration as against those with a lower value(45).

**SMOKING**

Cigarette smoking - An important risk factor for all strokes and also there is ample evidence that it can be eliminated as a risk factor once the patient stops smoking (15,30). Nicotine transiently elevates blood pressure and could increase the risk of stroke. It may also enhance platelet aggregation(21).

In earlier Indian studies, smoking cigarette was not found to be a risk factor for stroke(39,46) But the ICMR study confirms the relationship between cigarette smoking and stroke(44).

Sridharan in his study noted that the relative risk of 1.7 was seen in 33.5% of ischaemic stroke patients who were smokers (34).

**FACTORS AFFECTING OUTCOME OF STROKE:**

Many factors affect the outcome of ischemic stroke. Unlike the risk factors of the stroke, much is not known about the factors affecting the poor prognosis of stroke. Studies done suggest a diversity of factors are associated with an unfavorable outcome after acute IS.

Clinical characteristics such as –

1.Initial severity of stroke(47,48)

2. Older age at stroke onset(47,49) and

3. Existence of comorbid conditions like Type 2 diabetes and hypertension (50,51).

4. High blood sugar levels on presentation(51) are well-established factors.

**DIFFERENTIAL DIAGNOSIS OF ACUTE ISCHEMIC STROKE**

The hallmark of acute ischemic stroke is the sudden onset of a focal neurologic deficit, usually attributed to an area of brain supplied by a specific artery.

Other neurological conditions which present acutely can mimic stroke

1. Migraine with aura

   Patient can have focal neurologic deficits, including aphasia, visual changes, vertigo, weakness, numbness, and incoordination

2. Partial seizures

   Patient can have negative symptoms, including aphasia and paresis, and a patient with a postictal Todd paralysis may looks like hemiplegic patient.

   Also stroke itself can cause seizures complicating diagnosis.

3. First episode of multiple sclerosis
4. Mass lesion – Neoplasm and Brain abscess

   They usually have slowly worsening symptoms but can manifest acutely

5. Metabolic disorders like hypoglycemia or hyperglycemia
6. Toxin exposures and drug intoxications
7. Malingering or other psychiatric illness

## TREATMENT OF ACUTE ISCHEMIC STROKE

The main goal of treatment is to prevent further damage or reverse brain injury and improve clinical outcome. After diagnosis of acute ischemic stroke CT brain is done to rule out hemorrhage.

Treatment categories

1) Medical support
2) IV thrombolysis
3) Endovascular revascularization
4) Antithrombotic treatment
5) Neuroprotection
6) Stroke centers and rehabilitation.

### MEDICAL SUPPORT

The primary goal is to optimize cerebral perfusion in ischemic penumbra region.

A. Patient's airway, breathing and circulation (ABCs) are assessed and treated;

   Airway support and ventilator assistance are advised to patient who have low consciousness and bulbar stroke that compromises breathing.

   Saturation to be maintained > 94%

B. Care is taken to prevent complication of stroke like infections (pneumonia, skin or urine infections), deep vein thrombosis and pulmonary embolism.

   Infections are treated with antibiotics

   Subcutaneous heparin can be used as prophylaxis and pneumatic compressive stockings have proven benefit in preventing DVT

C. Collateral blood flow in brain may be dependent on blood pressure

a. Low Blood pressure and hypovolemia has to be corrected to maintain brain perfusion

b. If patient has high BP and is a candidate for thrombolysis BP should be carefully lowered to systolic BP < 185mmHg and diastolic < 110mmHg before treatment is initiated

Labetalol and Nicardapine are the drugs recommended to lower BP and BP to be maintained<180/105mmHg for first 24 hours after IV thrombolysis

c. If patient has elevated BP and is not a candidate for IV thrombolysis and BP <220/110mmHG there is no evidence that initaing treatment is of any mortality benigit and for those with pre existing HTN , antihypertensives has to be reinitiatied.

d. If patient has elevated BP and is not a candidate for IV thrombolysis and BP >220/110mmHG, BP has to be lowered by 15% in first 24 hours(112)

D. Fever is detrimental and should be treated with antipyretics and surface cooling, hypothermia is a good neuroprotective agent but its use in acute stroke is not proven and it may increase risk of infection like pneumonia.

E. Serum glucose should be maintained between 60 to 180 mg /dl by using insulin or glucose infusion whenever necessary.

F. IV Mannitol and fluid restriction therapy can be used if patient develops significant edema. Hemicraniectomy is a proven stratergy and reduces mortality by 50% and outcome is significantly improved in stroke survivors.

G. Extra care has to be taken in patients with cerebellar stroke as even small edema increases intracranial pressure by obstructing CSF and causing hydrocephalus and compressing brain stem which can cause coma and respiratory arrest which require decompression surgeries.(113,112).

H. Nutrition – enteral diet has to be begun within 1 week of stroke onset, ryles tube feeding in patients with dysphagia and percutaneous gastrostomy tubes for patients who fail to improve is adviced(112).

I. Depression screening with structured tool and treatment with antidepressant is recommended by AHA(112).

**INTRAVENOUS THROMBOLYSIS**

There is clear benefit of intravenous recombinant tissue plasminogen activator(rtPA) in acute ischemic stroke (114) . Administration of rtPA is approved between 3 – 4.5 hours in Europe and Canada where as in USA it is approved only for 0-3 hours.

**INDICATIONS**

1. Clinical diagnosis of stroke
2. Onset of symptoms to time of drug administration ≤4.5 Hours
3. CT scan showing no hemorrhage or edema of >1/3 of the MCA territory
4. Age 18 ≥ years

**CONTRAINDICATION**

1. Sustained BP >185/110 mmHg despite treatment
2. Bleeding diathesis
3. Recent head injury or intracerebral hemorrhage
4. Major surgery in preceding 14 days
5. Gastrointestinal bleeding in preceding 21 days
6. Recent myocardial infarction

**ADMINISTRATION OF rtPA**

1. IV access with two peripheral IV lines (avoid arterial or central line placement)
2. Review eligibility for rtPA

3. Administer 0.9 mg/kg IV (maximum 90 mg) of IV alteplase as 10% of total dose by bolus over 1 minute, followed by remainder of total dose over 60 minutes.
4. Frequent cuff blood pressure monitoring
5. No other antithrombotic treatment for 24 hours
6. For decline in neurologic status or uncontrolled blood pressure, stop infusion give cryoprecipitate, and reimage brain emergently
7. Avoid urethral catheterization for ≥2 hours

**ENDOVASCULAR REVASCULARIZATION**

Ischemic strokes which involve large vessels like Middle Cerbebral Artery, Internal Carotid and Basilar artery have poor prognosis and high risk of mortality and morbidity, they have high clot volume and IV rtPA alone fails to open up the occlusion so intraarterial thrombolytics were used to increase the chance of clot lysis and decrease systemic bleeding complication, PROCAT II trial found significant improvement in outcome for intraarterial prourokinase even upto 6 hours after onset in MCA strokes(115). Intraarteial thrombolysis is not approved by FDA many studies suggest it can be considered when mechanical thrombectomy fails (113)

In patients who have contraindication or failed IV thrombolysis, Endovascular mechanical thrombectomy has been tried as adjuvant or alternate treatment. The HERMES meta analysis study which included the 5 studies MR CLEAN, ESCAPE, REVASCAT, SWIFT PRME and EXTEND IA found that mechanical thrombectomy within 6 hours of stroke after large vessel occlusion improved the outcome and the number needed to treat to decrease disability by 1 point in modified rankin score was

2.6(116). The DAWN and DEFUSE 3 trials have reported good clinical outcome in patients undergoing mechanical thrombectomy with 24 and 12 hours of onset of stroke respectively (117,118). If the patient has good collaterals in CT or MRI perfusion imaging patient can be treated with mechanical thrombectomy for upto 24 hours(113,112).

Patient who meets following criteria should undergo mechanical thrombectomy with stent retriever(112).

1. Pre stoke mRS score 0-1
2. Internal carotid artery or Middle Cerebral artery (M1 Segment) occlusion
3. Age > 18 years
4. NIHSS score > 6
5. ASPECTS >6
6. Management can be started (groin puncture) within 6 hours of onset of symptoms

**ANTITHROMBOTIC TREATMENT**

Platelet Inhibition

Aspirin is the only drug proven to effective in treatment of acute ischemic stroke. The 2 trials IST and CAST where aspirin was given 300mg/ day and 160 mg/ day respectively reduced mortality and stroke recurrence(119,120). American heart association recommends initial Aspirin dose of 325mg (112).

## ANTICOAGULATION

There is no clear benefit of anticoagulation following acute ischemic stroke, routine use of heparin or other anticoagulants are not recommended and have shown high risk of hemorrhage(112).

## NEUROPROTECTION

Even though many drugs have shown positive results in animal studies in prolonging brain's tolerance to ischemia, no neuroprotectors have been approved by FDA in treatment of ischemic stroke. There is no benefit of either pharmacological or non pharmacological treatments according to AHA (112).

## STROKE CENTERS AND REHABILITATION

Many centres have a dedicated stroke team which provide emergency services round the clock like medical management, IV thrombolysis or thrombectomy in cases of acute ischemic stroke.

Rehabilitation of stroke patients includes early physical, occupational and speech therapies. Patient and family are educated about the neurological deficit and complications of stroke and its prevention are explained including prevention of DVT, back care to prevent bed sores, physiotherapy to prevent contractures, bowel and bladder care to prevent infections. The aim of rehabilitation is to increase recovery by giving a safe, progressive regimen(113)

## EARLY NEUROLOGICAL DETERIORATION (END)

Patients with acute ischemic stroke deteriorate clinically within the first few hours or days and is a serious complication which is associated with increasing rates of mortality and morbidity. The occurrence of deteriorating stroke varies from 13 to 37% among various published studies(52-59). The reasons for such wide variability in incidence may be due to differences in the study population, the difference in terminology and in the concept of progressive stroke.

The terms 'stroke-in-evolution','progressive stroke', 'worsening stroke' and 'deteriorating stroke' are used interchangeably regardless of whether the deterioration is caused by extension of the infarction or various other reasons(60). The terms 'stroke in- evolution' or progressive stroke' is used when the stroke progresses in a stepwise manner or smoothly over several hours. The term 'deteriorating stroke' includes not only 'stroke-in-evolution' but also other strokes that deteriorate as a result of either cerebral or systemic causes during the 1st week(61). Whereas 'progressive stroke' is used in those conditions in which neurological worsening parallels the progression of ischemia. (62)

END is defined as clinical worsening or recurrence within the first 72 h after ischaemic stroke. The consequences of this can be serious, with a poor short-term prognosis(63). Mechanisms of END include failure of development of collaterals for blood circulation in patients with critical stenosis or occlusion of a large vessel, either intra-cranial or extra-cranial(64); Increase in the size of thrombus leading to increase in the ischaemic area(65); early recurrence especially in atherothrombotic strokes (66); development of cerebral oedema in patients with large strokes(66) and last but

not the least haemorrhagic transformation in patients treated with fibrinolytic drugs(67).

Recent studies have shown that END is an independent predictor of poor outcomes in the setting of AIS. More specifically, the investigators of SORCan (Stroke Outcomes Research Canada) registry have reported that END (defined as 1-point decrease in NIHSS) was an independent predictor of 7-day, 30-day and 1-year case fatality rate in a cohort of 3631 patients(68) Similarly, END was associated with higher rates of death during hospitalization, longer duration of hospitalization and lower rates of functional independence in an Australian study (69) .

**MECHANISMS OF END**

Several mechanisms have been proposed to explain early neurological deterioration in AIS. Recent advancements in the brain and vascular imaging techniques have provided great insight into their role in END in AIS.

**Failure of collaterals**

The occlusion of major cerebral vessels is one of the most significant independent predictor of END. The occlusion of the vessel leads to a compromise of perfusion distal to it.

Unless effective collateral circulation develops, the region affected cannot be salvaged from being infarcted. The development of collaterals seems to be the mechanism underlying transient ischemic attacks(70).

Diabetic microangiopathy and chronic hypertension impair microvascular function and reduce the potential for collateral development. (71) This leads to reduced oxygen delivery and regional metabolic disturbances, which may aggravate cellular damage

by enhancing brain edema and free radical injury.( 71,72) Failure of development of collaterals appears to be the most common mechanism for END(73).

**Clot progression**

In the past, END in an acute ischaemic stroke had been attributed to clot progression, (74) though this concept is not proved. Recent studies of early MRI in acute stroke patients have shown that large vessel occlusion and failure of collaterals as the main mechanism of END rather than clot progression.(73,75,76) Hypoperfusion due to occluded vessels may impair washout of distal emboli. These two mechanisms can act together to cause the END. (70)

**Recurrent stroke**

There are high chances of recurrent stroke within the first week in patients with acute ischaemic stroke.(77,78)However, most of the recurrent strokes detected on diffusion-weighted MRI scans do not produce clinical deficits. (79) Transcranial Doppler can detect micro-embolic signals and may be useful for identifying patients at risk of early recurrent stroke. (80)

**Cerebral edema**

Raised intracranial pressure accounts for early deterioration in 19% of cases of acute ischemic stroke(81)

The risk of cerebral edema with anterior circulation stroke is low and is estimated to be 10–20%. (82)

Clinical features such as a decrease in the level of consciousness, bilateral ptosis, and the nondominant hemisphere involvement may suggest high risk of deterioration.

Lesion volume 145 ml on a diffusion-weighted imaging scan predicts evolution to fatal cerebral edema. (83)Cerebral edema in ischaemic stroke tends to be cytotoxic and does not respond to osmotic diuretics.

**Hemorrhagic transformation**

Hemorrhagic transformation in ischaemic stroke is common and ranges from small asymptomatic petechiae to a large hematoma with pressure effects. Symptomatic transformation occurs in only 0.6% of patients who are treated with supportive care, whereas the incidence is higher in those treated with intravenous recombinant tissue plasminogen activator (rt-PA) (6%),(84-86 )

Adverse outcomes are considered to be associated with only parenchymal hematoma type 2 (large hematoma - 30% volume of ischaemic lesion). (87)

**Seizures**

Seizures are common in large cortical ischaemic infarcts and may account for 5% of patients with ischaemic strokes developing END. (88) Seizures often cause only temporary worsening, though prolonged partial seizures can lead to persistent worsening. (89)

**High serum glucose values**

History of diabetes mellitus has been associated with END. (81) In a case-controlled study, the past history of diabetes along with elevated admission systolic blood pressure predicted END. (90) Persistent hyperglycemia in the first 24 h after stroke independently predicted the expansion of the volume of ischemic infarct and poor neurological outcomes. (91)

END has potentially serious consequences on the short term (morbidity and death) and long-run (recovery from a stroke) outcomes for the patient. Therefore, any number of attempts to prevent and treat END should be made promptly and aggressively. Recognition of the predictors of early worsening might help in choosing patients for admission to the high dependency units equipped with intensive monitoring and treatment of these ill patients and prompt initiation of appropriate therapy.

**MICROALBUMINURIA AS A PREDICTOR OF END**

Microalbuminuria (MA) indicates microvascular impairment of the blood–urine interface in renal glomeruli which reflects renal sign of global endothelial dysfunction.(92)It is well understood that MA is a marker of cardiovascular morbidity and mortality in both diabetic and non diabetic population.(93)A higher prevalence of MA in ischemic stroke patients was found in several studies in the early 21$^{st}$ century itself.(94,95,96)The relationship between microalbuminuria and endothelial dysfunction appears to be graded i.e, higher levels of MA is independently associated with a greater magnitude of vascular risk overtime. The presence of MA itself predicts poorer clinical outcomes following acute stroke.(92) Screening for MA is relatively easy and inexpensive and could be effective in identifying stroke patients at risk for unfavorable outcomes(92). It is gaining importance as anindependent indicator of symptomatic athero-sclerotic vascular disease(ASVD), is now being recognised as an aptitudeearly biomarker of vascular damage. An immensely compelling association between MA and carotid artery intima-media thickness was reported, which indicated MA to be the marker for atherosclerosis and points to a possible correlation between microalbuminuria and atherosclerotic stroke mechanism. From there on, most of the

research evaluating microalbuminuria in stroke has focused on its part as a risk factor for recurrent stroke and long term mortality. Various other vascular risk factors that are linked with microalbuminuria are increasing age, male gender, higher blood pressure, smoking, poor glycemic control, high sensitivity Creactive protein, ratio ofplasminogen activator inhibitor to tissue-type plasminogen activator, plasminogen activator inhibitor , insulin resistance, endothelial dysfunction, hyperhomocysteinaemia, and high-fibrinogen levels.(97-104) However the exact mechanisms ofhow these risk factors are linked to MA are not well understood. Postulated hypothesis is that people with increased urine albumin excretion have loss of glomerular charge and size selectivityand increased escape rate of albumin through capillaries. This increased albumin leakage in the glomerulus appears associated with greater capillary permeability for albumin in the systemic vasculature and leading to generalized hemodynamic strain and disequilibirum, and thenultimately initiating atherosclerosis with symptomatic vascular sequelae(105).level appears to be directly proportionate to the severity of many acute inflammatory processes including trauma, sepsis, surgery, muscle ischemia, and acute myocardial infarction .(106) MA is currently defined as urine albumin excretion of 30 to 300mg when measured in a 24hrs urine collection or urinary albumin-to-creatinine ratio(UACR) of 30 to 300 mg/g in a spot urine collection (107).

The samples used to determine the urine albumin creatinine ration can be collected at the time of admission; therefore, microalbuminuria can be assessed within 1 h of presentation to hospital.It remains unclear whether microalbuminuria influences mortality or functional recovery. To fill this gap in knowledge, this study was

conducted to determine if microalbuminuriais a risk factor for END in acute ischemic stroke patients.

## SCALES USED TO ASSESS STROKE SEVERITY AND OUTCOME

A variety of stroke scales are available to assess various aspects related to stroke. The ideal scale would be easy and quick to administer, acceptable to patients and researchers, valid for its chosen purpose, reliable, and responsive to meaningful clinical change. There is no ideal stroke measure that fulfills all these criteria.

Various scales(108) available are:

Scales used in pre hospital assessment:

1.cincinnati stroke scale

2.los angeles pre hospital stroke screen (LAPSS)

Scales used for acute assessment of neurological impairment in EMD:

1. Canadian Neurological Scale (CNS)

2. European Stroke scale

3. Glasgow Coma Scale

4. National Institute of Health Stroke Scale (NIHSS)

5. Scandinavian Stroke Scale (SSS)

Scales used to assess global disability and functional outcome:

1. Modified Rankin scale (mRS)

2. Stroke impact scale

3. Stroke specific quality of life scale (SS-QOL )

Scales used to assess global disability and functional outcome:

1. Modified Rankin scale (mRS)

2. Stroke impact scale

3. Stroke specific quality of life scale (SS-QOL )

Among these, three scales namely, NIHSS, mRS, BI are the most commonly used stroke scales worldwide(109,110). As we are assessing stroke severity on day 1 and day 3 if our study to detect early neurological deterioration, NIHSS was chosen in our study.

**National Institutes of Health Stroke Scale**

The NIHSS is a 15-item scale that incorporates assessment of language, motor function, sensory loss, consciousness, visual fields, extraocular movements, coordination, neglect, and speech.

It quantifies the neurological impairment, paying particular attention to those aspects most pertinent to stroke.

It assigns numerical values to various aspects of neurological function. It is scored from 0 (no impairment) to a maximum of 42.

Scores of 21 or greater are usually described as “severe.” It is a validated scale with proven utility and suited to different assessment scenarios.

The NIHSS has many advantages as a stroke outcome-assessment tool. It is relatively straightforward and takes around 6 minutes to perform, with no need for additional equipment.

NIHSS scores are reliable across observers, and this has been demonstrated both in cohorts of neurology-trained and non-neurologist raters(111). The availability of a reliable method for a neurological exam that is suitable for non-specialists is a particular strength of the NIHSS.

# METHODOLOGY

# METHODOLOGY

**SOURCE OF DATA:**

All the patients with Acute ischemic stroke enrolled in the General Medicine OPD and Emergency department at R L Jalappa hospital, Kolar satisfying the inclusion criteria were enrolled for the study.

**STUDY DESIGN:**

Observational prospective study

SAMPLE SIZE CALCULATION:

The sample size was estimated by using the proportion of patients with END among Acute Ischemic Stroke patients as 21.2% from a previous study(122)(SAMPLE – UMEMURA 2013) using the formula :

Sample size = Z1-alpha/22p(1-p)/d2

Here

Z = Standard normal variate [at 5% type 1 error ($p<0.05$), it is 1.96 and at 1% type 1 error ($p<0.01$), it is 2.58].

As in the majority of studies, p values are considered significant below 0.05, hence Z =1.96 is used in the formula.

p = Expected proportion in population-based on previous studies or pilot studies.

Here p = 21.2 or 0.212 and q,(1-p) = 78.9 or 0.789.

d = Absolute error or precision which is decided by researcher.

d = 10% or 0.1

Using the above values at 99% Confidence level, a sample size of 65 subjects with acute ischemic stroke should be included in the study. Considering 10% nonresponse, a sample size of 65+6.5 ~73 subjects were included in the study.

**INCLUSION CRITERIA:**

1. All the patients of acute ischemic stroke who are more than 18 years of age.
2. Patients with a first episode of acute ischemic stroke presenting within the first 24 hours after onset of symptoms.

**EXCLUSION CRITERIA:**

1. Patients with evidence of hemorrhagic stroke.
2. Patients with a transient ischemic attack.
3. Patients with co-morbid conditions like a congestive cardiac failure (CCF), renal failure and decompensated cirrhosis of the liver.

**METHOD OF STUDY:**

The study was conducted among acute ischemic stroke patients presenting to the department of General medicine, RLJH satisfying the inclusion criteria. Written informed consent was obtained from the patients or their relatives.

A detailed history was taken and a thorough general physical and systemic examination was performed. The following details were noted: age; sex; presenting complaints; a history of any comorbidities and signs on examination.

Urine albumin creatinine ratio of all the patients was estimated from the urine sample collected at the time of presentation.

The neurological status of the patients and the severity of stroke was assessed by using the NIHSS scoring system NIHSS (National Institute of Health Stroke Scale). NIHSS score was calculated immediately at the time of admission, then subsequently after 24 after the onset of symptoms and on day 3 of admission. Patients for whom the NIHSS score returned to zero within the initial 24 h will be classified as having a transient ischemic attack (TIA) and were excluded from the study. Early Neurological Deterioration was diagnosed if there was an increase in the NIHSS score by 3 or more than 3 points from day 1 to day 3 of admission.

At the end of the study, the study population was divided into two groups based on their neurologic outcome. One group included acute ischemic stroke patients who developed END and the second one included patients without END. In each group, the proportion of patients with microalbuminuria at the time of presentation was estimated. The correlation between dehydration at the time of presentation and development of END was assessed.

**STATISTICAL ANALYSIS**

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Data was also represented using appropriate diagrams like a bar diagram, pie diagram, and cluster bar.

The association between categorical explanatory variables and the quantitative outcome was assessed by comparing the mean values. The mean differences along with their 95% CI were presented. An independent sample t-test was used to assess

statistical significance. The association between explanatory variables and categorical outcomes was assessed by cross-tabulation and comparison of percentages. Univariate logistic regression was done to assess the factors associated with the occurrence of END. Unadjusted odds ratios along with their 95% CI were presented. Factors showing statistical significance in univariate analysis were included in the multivariate analysis. Adjusted odds ratios along with 95% CI and p-values were presented.

P-value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.(108)

# RESULTS

## OBSERVATIONS AND RESULTS

The present study was carried out over a month of 18 months from March 2018 to August 2019 in the Department of General Medicine, Sri Devraj Urs Medical College, Kolar, Karnataka. A total of 73 subjects were included in the study.

### DEMOGRAPHIC PROFILE:

### AGE DISTRIBUTION:

The mean age of the study population was 68.89 ± 8.92 years with the range 48 to 92 years. (Table 1)

**Table 1: Descriptive analysis for age in study population (N= 73)**

| PARAMETER | MEAN AGE +/- SD | MEDIAN | MIN | MAX | 95% C.I. EXP (B) | |
|---|---|---|---|---|---|---|
| | | | | | LOWER | UPPER |
| AGE | 68.89±8.924 | 70 | 48 | 92 | 51.05 | 86.73 |

Among the study population, 3 (4.1%) were in the age group of 41 to 50 years,16(21.91%) were in the age group of 51 to 60 and 27 (36.98%) were in the age group of 61 to 70 years and 18(24.65%) were in the age group of 71-80 years and 7(9.5%) were in the age group of 81-90 years and 2(2.7%) were in age group of 91-100 years(Table 2&figure5)

**Figure 5: Bar diagram showing study population in various age groups (N=73)**

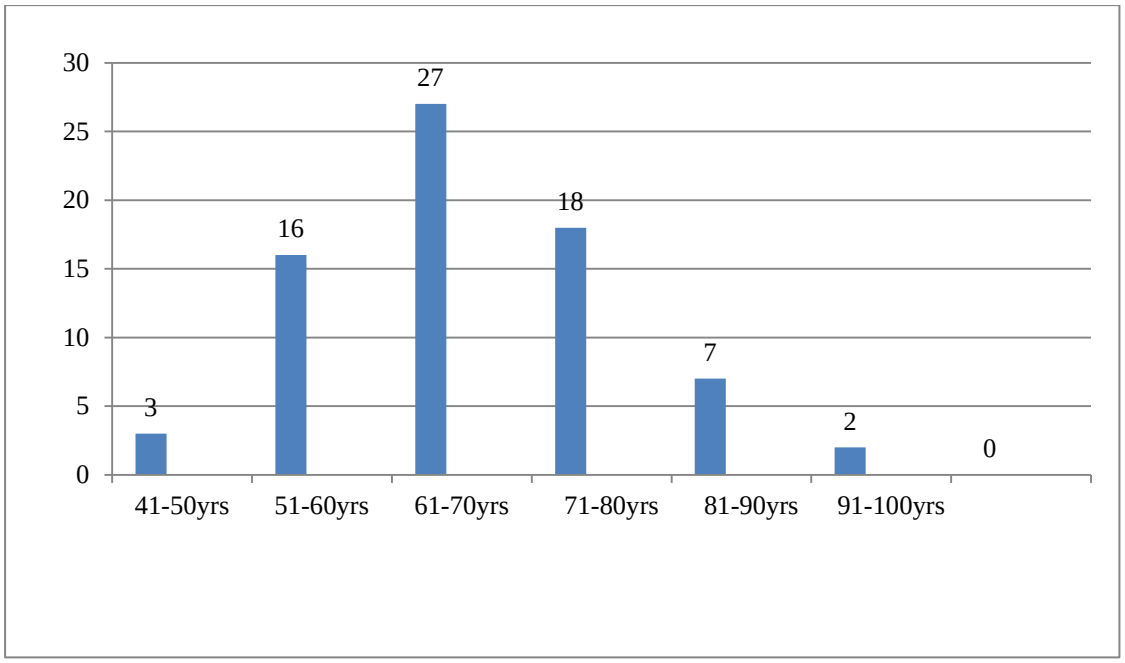



**Table 2: Descriptive analysis of age group in study population (N=73)**

| AGE | FREQUENCY | PERCENTAGE |
|---|---|---|
| 41-50 | 3 | 4.1% |
| 51-60 | 16 | 21.9% |
| 61-70 | 27 | 36.98% |
| 71-80 | 18 | 24.65% |
| 81-90 | 7 | 9.5% |

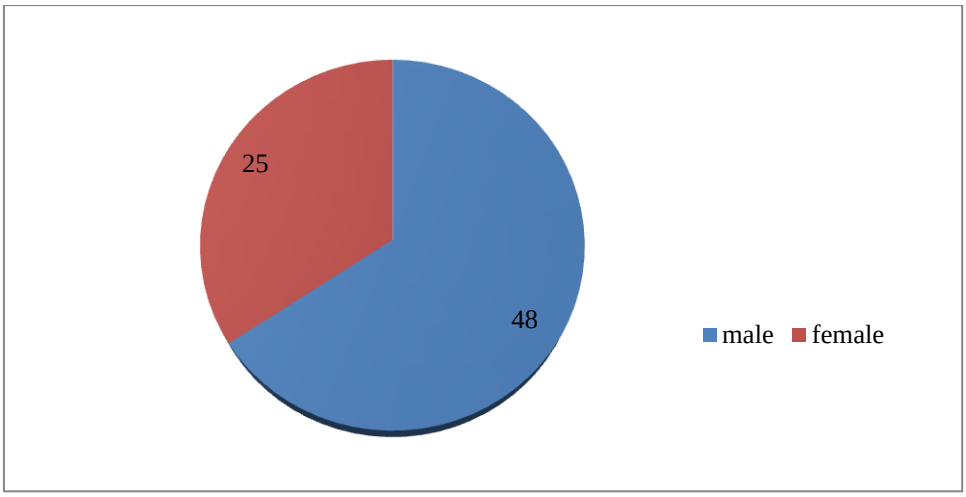
**GENDER DISTIBUTION:**

**Table 3: Descriptive analysis of gender in study population (N=73)**

| GENDER | FREQUENCY | PERCENTAGE |
|---|---|---|
| MALE | 48 | 65.75% |
| FEMALE | 25 | 34.24% |

Among the study population, 48(65.75%) were males and 25(34.24%) constitute females. (Table 3 & figure 6)

**FIGURE 6: PIE CHART OF GENDER IN THE POPULATION(N=73)**



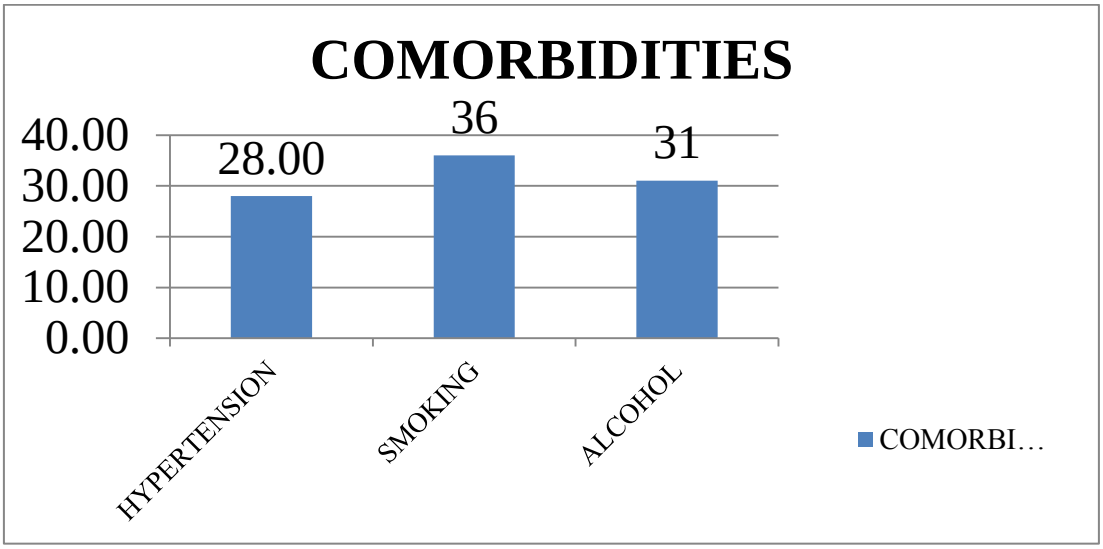

## COMORBIDITIES AMONG STUDY POPULATION

**Table 4: Descriptive analysis of comorbidities in study population (N=73)**

| COMORBIDITIES | FREQUENCY | PERCENTAGE |
|---|---|---|
| HYPERTENSION | 28 | 38.35% |
| SMOKING | 36 | 49.31% |
| ALCOHOL | 31 | 42.46% |

Among the study population, 28(38.35%) had hypertension, Smoking and alcohol consumption was present in 36(49.31%) and 31(42.26%) respectively. (Table 4 & figure 7)

**FIGURE 7: BAR CHART OF COMORBIDITIES IN THE POPULATION(N 73)**




**BLOOD PRESSURE VALUES AMONG STUDY POPULATION:**

**Table 5: Descriptive analysis for vital signs in study population (N=73)**

| BLOOD PRESSURE (mm Hg) | MEAN± STD | MEDIAN | MIN | MAX | 95% C.I. EXP (B) | |
|---|---|---|---|---|---|---|
| | | | | | LOWER | UPPER |
| SYSTOLIC BLOOD PRESSURE | 143.34±17.5 | 144 | 90 | 180 | 108.34 | 178.34 |
| DIASTOLIC BLOOD PRESSURE | 87.05±11.615 | 88 | 60 | 120 | 63.85 | 110.25 |

The mean Systolic and Diastolic blood pressures among study population was 143.34± 17.5 mm Hg and 87.05 ± 11.6 mm Hg.

**Table 6: Descriptive analysis for Random blood sugar in study population(N=73)**

| Random Blood Sugar (mg/dl) | MEAN± STD | MEDIAN | MIN | MAX | 95% C.I. EXP (B) | |
|---|---|---|---|---|---|---|
| | | | | | LOWER | UPPER |
| RBS | 135.86±36.99 | 126.00 | 90 | 383 | 129.31 | 142.40 |

The mean RBS value among study population was135.86 ± 36.99 mg/dl.

RENAL FUNCTION TESTS:

**Table 7: Descriptive analysis for renal function testst in study population(N=73)**

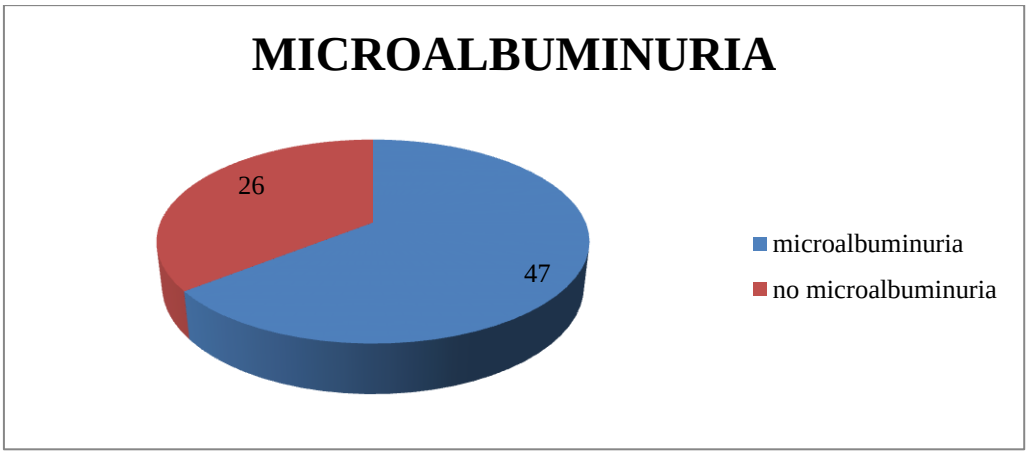
| PARAMETERS | MEAN±STD | MEDIAN | MIN | MAX | 95% C.I. EXP(B) | |
|---|---|---|---|---|---|---|
| | | | | | LOWER | UPPER |
| B UREA | 27±10.29 | 25 | 8 | 54 | 7.6 | 47.6 |
| S CREATININE | 0.94±0.25 | 0.95 | 0.5 | 1.6 | 0.69 | 1.19 |

The Mean blood urea was 27±10.29mg/dl and mean s creatinine was 0.94±0.25 mg/dl among the study population.

**Table 8: Descriptive analysis of microalbuminuria status in study population(N=73)**

| Microalbuminuria status | Frequency | Percentage |
|---|---|---|
| No. of patients had microalbuminuria at presentation | 26 | 35.61% |
| No. of patients did not have microalbuminuria at presentation | 47 | 64.38% |

**Figure 8: Pie chart of hydration status in study population (N=73)**




A total of 26(35.61%) patients had microalbuminuria at presentation out of total 73 patients and 47 (64.38%) did not have microalbuminuria at presentation.

**Table 9: Descriptive analysis for NIHSS Score on day 1 and 3 in study population (N=73):**

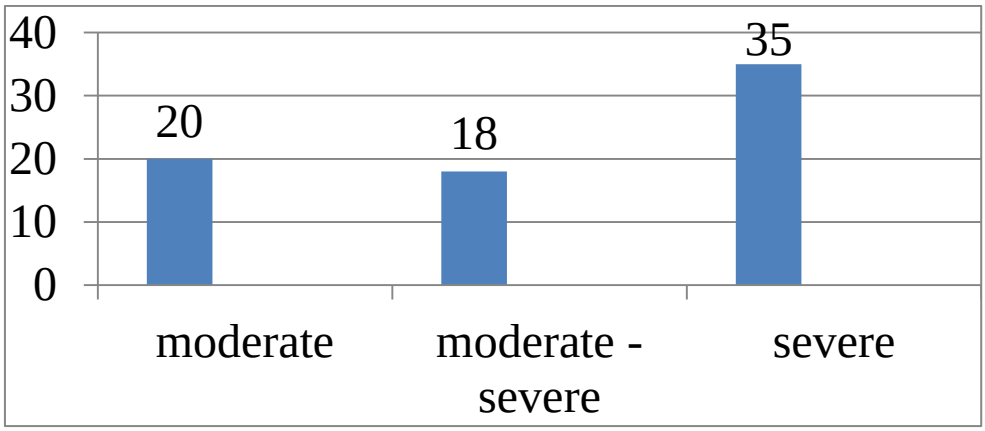
| PARAMETERS | MEAN±STD | MEDIAN | MIN | MAX | 95% C.I EXP(B) | |
|---|---|---|---|---|---|---|
| | | | | | lower | upper |
| NIH STROKE SCORE DAY 1 | 22.5±5.92 | 22 | 8 | 36 | 10.4 | 34.3 |
| NIH STROKE SCORE DAY 3 | 25.36±5.91 | 24 | 9 | 42 | 13.56 | 37.16 |

The mean NIHSS score on day 1 was 22.5± 5.92 and on day 3 was 25.36 ± 5.91.

**Table 10: Descriptive analysis of severity of stroke in study population(N=73)based on NIHSS score on day 1 :**

| NIHSS SCORE GROUP | FREQUENCY | PERCENTAGE |
|---|---|---|
| MILD STROKE | 20 | 27.39% |
| MODERATE-SEVERE | 18 | 24.65% |
| SEVERE STROKE | 35 | 47.94% |

**Figure 9 : Bar chart of stroke severity in study population (N=73)**

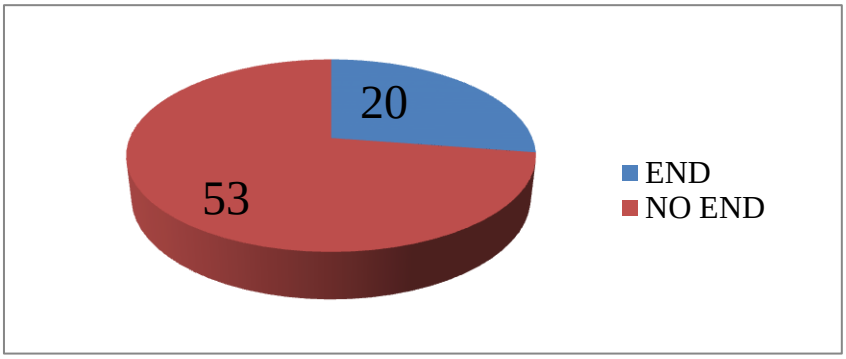



Based on NIHSS score on Day 1 of admission, majority of the patients had severe stroke-35(47.94%), 18 (24.65%) patients had moderate to severe stroke and 20(27.39%) had mild stroke.

**Table 11: Descriptive analysis of early neurologic deterioration in studypopulation (N=73)**

| EARLY NEUROLOGICAL DETERIORATION | FREQUENCY | PERCENTAGE |
|---|---|---|
| PRESENT | 20 | 27.39% |
| ABSENT | 53 | 72.6% |

**Figure 10: Pie chart of END in study population (N=73)**




Among the total study population, early neurologic deterioration was developed in 20(27.39%) patients and 53 (72.6%) patients did not develop early neurologic deterioration.

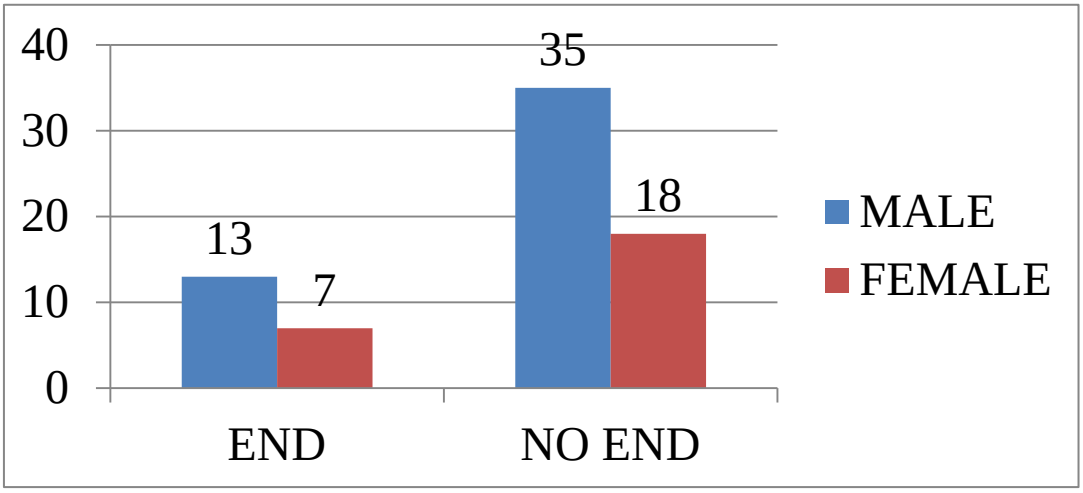
**Table 12: Comparison of mean age between 2 groups (with and without END)**

| EARLY NEUROLOGICAL DETERIORATION | MEAN AGE ± STD | MEAN DIFFERENCE | 95% C.I | | P VALUE |
|---|---|---|---|---|---|
| END | 72.3±8.405 | 6.81 | 2.01 | 11.60 | 0.006 |
| NO END | 65.49±9.43 | | | | |

**Table 13: Comparison of early neurologic deterioration with gender of study population (N=73)**

| GENDER | EARLY NEUROLOGICAL DETERIORATION | | CHI SQUARE | P VALUE |
|---|---|---|---|---|
| | END(N-20) | NO END(N=53) | | |
| MALE | 13(65%) | 35(66.03%) | 1.000 | 0.571 |
| FEMALE | 7(35%) | 18(33.97%) | | |

**Figure 11: Bar chart of early neurologic deterioration with gender in study population (N=125)**




The percentages of males and females in group with END were 65% and 35% with p value of 0.57, which was not significant.

**Table 14: Comparison of early neurologic deterioration with hypertension of study population (N=73)**

| HYPERTENSION | EARLY NEUROLOGICAL DETERIORATION | | CHI SQUARE | P VALUE |
|---|---|---|---|---|
| | YES | NO | | |
| YES(28) | 11 | 17 | 0.105 | 0.064 |
| NO(45) | 9 | 36 | | |

**Figure 12: Bar chart of early neurologic deterioration with hypertension in study population (N=73)**

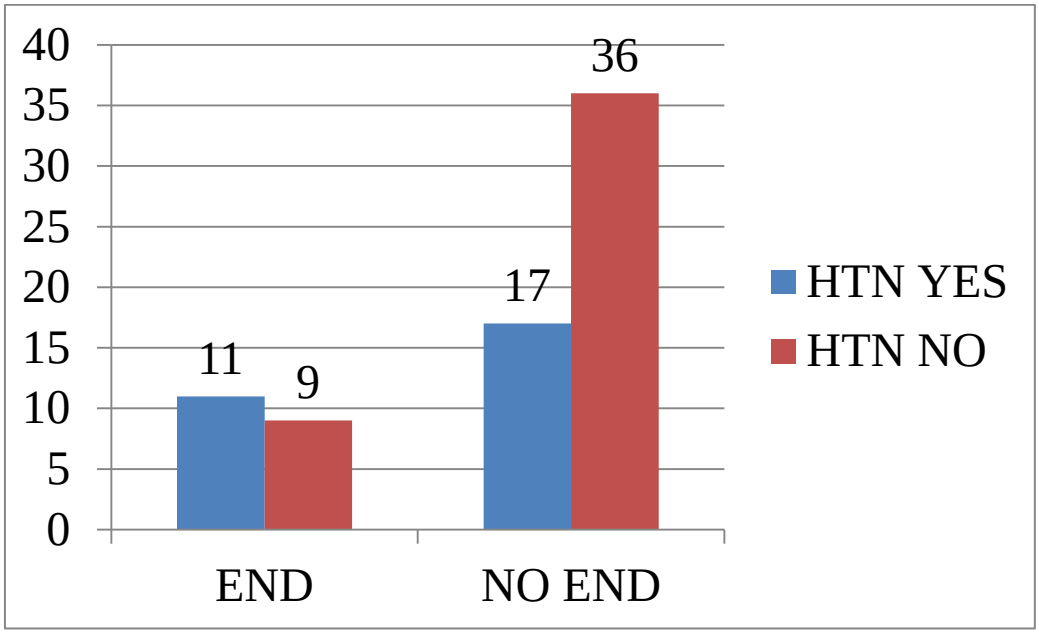
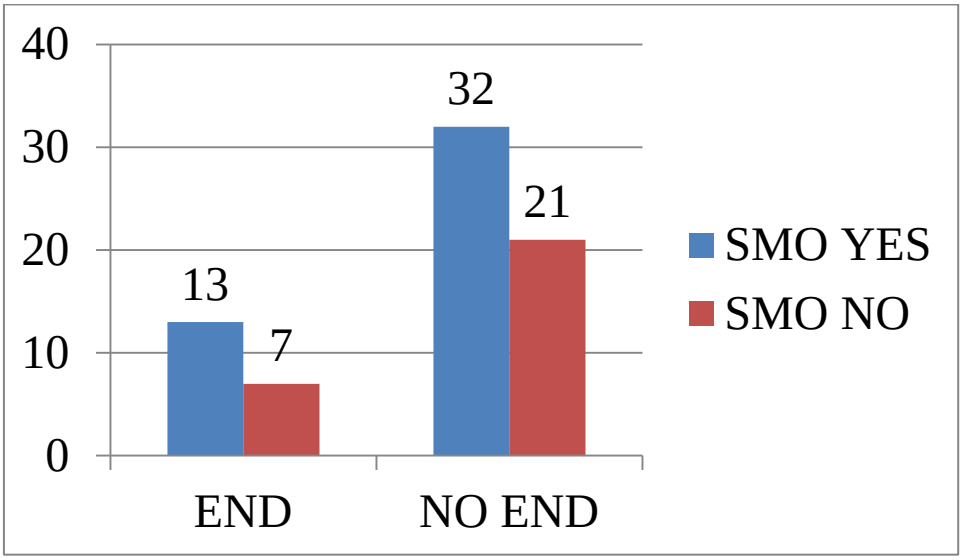



**Table 15: Comparison of early neurologic deterioration with smoking of study Population (N=73)**

| SMOKING | EARLY NEUROLOGICAL DETERIORATION | | CHI SQUARE | P VALUE |
|---|---|---|---|---|
| | YES(20) | NO(53) | | |
| YES(45) | 13(65%) | 32(60.37%) | 0.105 | 0.08 |
| NO(28) | 7(35%) | 21(37.63%) | | |

**Figure 13: Bar chart of early neurologic deterioration with smoking in study population (N=73)**




The percentages of patients with smoking history was 65 % and 60.37% among patients with and without END respectively with p value of 0.08, which was statistically insignificant.

**Table 16: Comparison of early neurologic deterioration with alcohol of study population (N=73)**

| ALCOHOL | EARLY NEUROLOGICAL DETERIORATION | | CHI SQUARE | P VALUE |
|---|---|---|---|---|
| | YES(20) | NO(53) | | |
| YES(36) | 7(35%) | 29(54.71%) | 5.673 | 3.24 |
| NO(37) | 13(65%) | 24(45.29%) | | |

The percentages of patients with history of alcohol consumption was 35.46% and 54.71% among patients with and without END respectively with p value of 0.23, which was not statistically significant.

**Figure 14: Bar chart of early neurologic deterioration with alcohol in study population (N=73)**

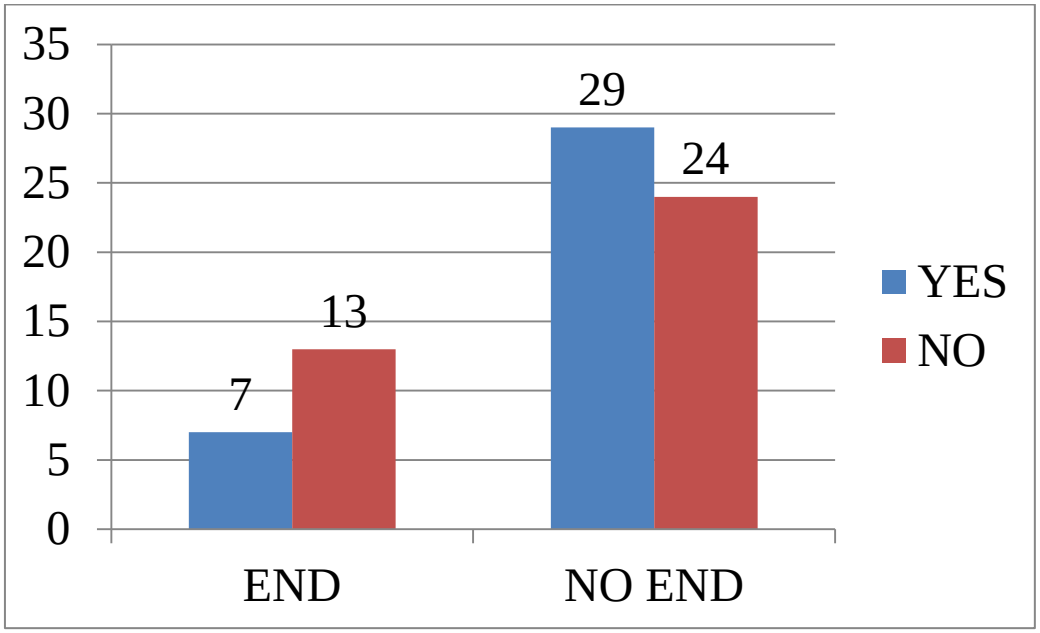



**Table 17: Comparison of mean systolic blood pressure between study groups (N=73)**

| EARLY NEUROLOGICAL DETERIORATION | MEAN SBP ± STD | MEAN DIFFERENCE | 95% C.I | | P VALUE |
|---|---|---|---|---|---|
| END | 150.5±23.610 | 14.31 | 6.1325 | 22.48 | 0.0008 |
| NO END | 136.19±11.410 | | | | |

**Table 18: Comparison of mean diastolic blood pressure between study groups**

**(N=73)**

| EARLY NEUROLOGICAL DETERIORATION | MEAN DBP ± STD | MEAN DIFFERENCE | 95% CI | | P VALUE |
|---|---|---|---|---|---|
| END | 92.45 ± 14.73 | 10.68 | 5.18 | 16.17 | 0.0002 |
| NO END | 81.77 ± 8.43 | | | | |

The difference in systolic and diastolic blood pressure was significant in patients with and without END (p vlue:0.02, p value:0.04).

**Table 19: Comparison of mean random blood sugar between study groups**

**(N=73)**

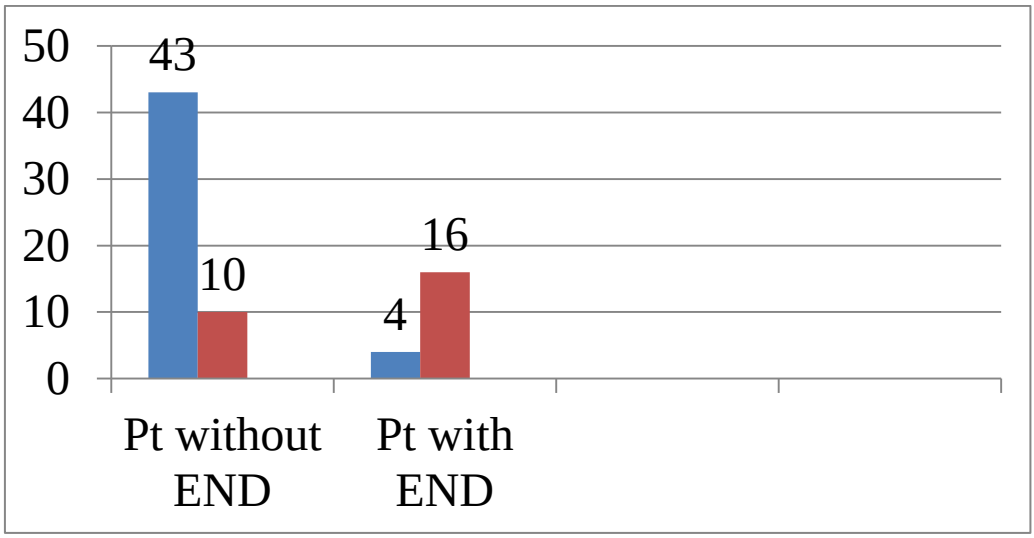
| EARLY NEUROLOGICAL DETERIORATION | RBS MEAN ± STD | MEAN DIFFERENCE | 95% C.I | | P VALUE |
|---|---|---|---|---|---|
| END | 150.72±49.77 | 21.60 | LOWER | UPPER | 0.002 |
| NO END | 129.12.77±27.22 | | 7.94 | 35.26 | |

And there was statistically significant difference between blood sugar levels on presentation between 2 groups with p value of 0.002.

**Table 20: Comparison of early neurologic deterioration with microalbuminuria of study population (N=73)**

| MICROALBUMINURIA | EARLY NEUROLOGICAL DETERIORATION | | CHI SQUARE | P VALUE |
|---|---|---|---|---|
| | YES(20) | NO(53) | | |
| YES(26) | 16(80%) | 10(18.86%) | 23.664 | <0.001 |
| NO(37) | 4(20%) | 43(81.14%) | | |

**Figure 15: Bar chart of early neurologic deterioration with microalbuminuria status in study population (N=73)**

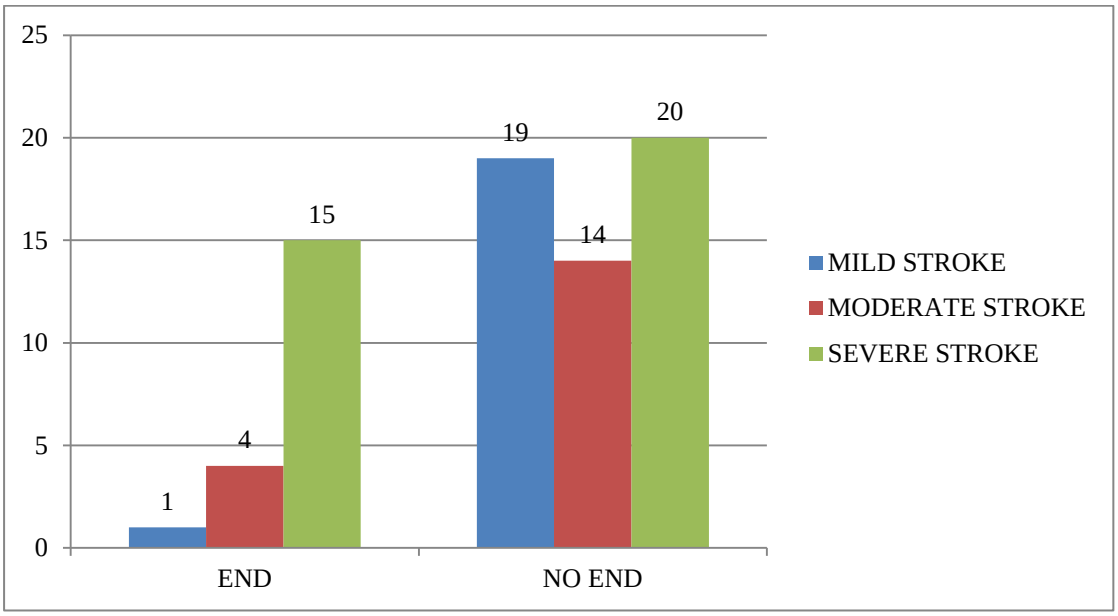



Among patients without END, 18.86% i.e, 10 had microalbuminuria on presentation whereas among patients who developed END, out of 20, 16 had microalbuminuria on presentation who constitute 80%. P value for microalbuminuria was <0.001which shows the difference as statistically significant.

**Table 21: Comparison of early neurologic deterioration with NIH stroke score group of study population (N=73)**

| NIHSS | EARLY NEUROLOGICAL DETERIORATION | | CHI SQUARE | P VALUE |
|---|---|---|---|---|
| | YES(20) | NO(53) | | |
| MILD(20) | 1(5)%) | 19(35.84%) | 15.155 | <0.001 |
| MODERATE(18) | 4(20%) | 14(26.41%) | | |
| SEVERE(35) | 15(75%) | 20(37.73%) | | |

**Figure 16: Bar chart of early neurologic deterioration with NIH stroke score in study population (N=73)**




Percentage of patients with moderate and severe stroke is more among patients with END whereas percentage of patients with mild stroke are more in patients without END with p value of <0.001, which was statistically significant.

Univariate logistic regression analysis was applied to age, gender, smoking history,hypertension Random blood sugar levels, dehydration status and stroke severity.

**Table22: Univariate logistic regression analysis of factors associated with END in study population(N=73)**

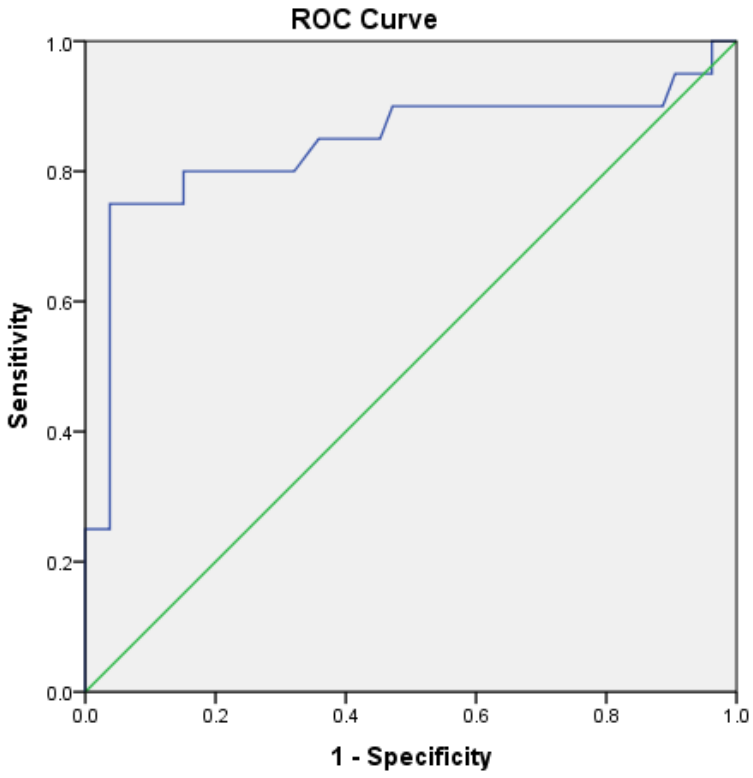
| FACTORS | Unadjusted odds ratio | 95% CI | | P value |
|---|---|---|---|---|
| | | Lower | Upper | |
| Age | 1.082 | 1.019 | 1.148 | 0.01 |
| Gender(baseline male) | 0.955 | 0.324 | 2.814 | 0.93 |
| Smoking(baseline=no) | 4.598 | 1.534 | 13.780 | 0.006 |
| Hypertension | 0.386 | 0.135 | 1.107 | 0.07 |
| Random blood sugar | 1.018 | 1.005 | 1.030 | 0.007 |
| Stroke severity(baseline mild) | 1 | - | - | - |
| Moderate | 0.047 | 0.006 | 0.394 | 0.05 |
| Severe | 1.156 | 0.038 | 0.640 | 0.01 |
| Microalbuminuria | 0.84 | 0.71 | 0.97 | <0.001 |

The factors which have shown statistically significant association with END in univariate analysis were presence of smoking history,hypertension, random blood sugar, microalbuminuria and stroke severity on presentation. Age and gender had no statistically significant association with END in the study.(Table 23)

After controlling for all the other factors in the univariate analysis, with each 1-yearincrease in age the odds of END have increased 1.082 times (95% CI 1.019 to

1.148 p value 0.01). The odds of END were 4.598 times more in people with presence of smoking ( 95% CI 1.534 to 13.78) Which was statistically significant. The odds of END are 1.018 times more with each 1unit Increase in random blood sugar (95% CI 1.005 to 1.030), which was not statistically significant. The odds of END were 0.84 times more in people with presence of microalbuminuria (95% CI 0.71 to 0.97), which was statistically significant. (Table 23)

ROC CURVE:



# DISCUSSION

# DISCUSSION

This study was aimed at evaluating the association of microalbuminuria with early neurological deterioration in acute ischemic stroke patients. Urine albumin creatinine ration of <30mg/g of creatinine was taken as surrogate marker for microalbuminuria. Stroke severity was determined based on clinical examination (NIHSS score).The primary outcome of interest was increase in NIHSS score by 3 or more than 3 from day 1 to day 3 of admission. .

In the study, the mean age of the study population was 68.89±8.924years with the range 48 to 92 years. Among the study population, 3 (4.1%) were in the age group of 41 to 50 years,16(21.91%) were in the age group of 51 to 60 and 27 (36.98%) were in the age group of 61 to 70 years and 18(24.65%) were in the age group of 71-80 years and 7(9.5%) were in the age group of 81-90 years and 2(2.7%) were in age group of 91-100 years. The maximum people are in the age group of 61-70years in our study.

Among the study population, both males and females are almost equal in number48(65.75%) were males and 25(34.24%) constitute females. Among the study population, 28(38.35%) had hypertension, Smoking and alcohol consumption was present in 36(49.31%) and 31(42.26%) respectively. A study done by Basu et al from India assessed various risk factors for stroke in 40 patients and found that 87.5% were hypertensives and 35% had diabetes(109). Study by Wu et al from China assessed various risk factors for stroke and found 66.3% were hypertensive, 31.5% were diabetic and 30.5% were smokers(110)

The mean Systolic and Diastolic blood pressures among study population was 143.34± 17.5 mm Hg and 87.05 ± 11.6 mm Hg.The mean blood sugar value among study population was135.86 ± 36.99 mg/dl.

The Mean blood urea was 27±10.29mg/dl and mean serum creatinine was 0.94±0.25 mg/dl among the study population. 35.61% of study population i.e., 26 patients had micro-albuminuria on presentation and 64.38%,47 patients did not have micro-albuminuriaon presentation to hospital.

The mean NIHSS score on day 1 was 22.5± 5.92 and on day 3 was 25.36 ± 5.91.

Based on NIHSS score on Day 1 of admission, majority of the patients had severe stroke-35(47.94%), 18 (24.65%) patients had moderate to severe stroke and 20(27.39%) had mild stroke.

Among the total study population, early neurologic deterioration was developed in 20(27.39%) patients and 53 (72.6%) patients did not develop early neurologic deterioration. This finding is similar to that of previously published studies(111-113 new references)

In the study done by Kunal Bhatia, out of the 114 stroke patients enrolled in the study, END was observed in 25 (21.9%) patients.(107)

The mean age of group with END was 72.3±8.40 years and that of group without END was 65.49±9.43 years with p value of 0.006, which is not significant.

The percentages of males and females in group with END were 65% and 35% with p value of 0.57, which was not significant.

The percentages of hypertensives is 39.28% and 60.71% among patients with and without END respectively with p value of 0.064, which was not significant.

The percentagesof patients with smoking history was 65 % and 60.37% among patients with and without END respectively with p value of 0.08, which was statistically insignificant.

The percentages of patients with history of alcohol consumption was 35.46% and 54.71% among patients with and without END respectively with p value of 0.23, which was not statistically significant.

The difference in systolic and diastolic blood pressure was significant in patients with and without END (p vlue:0.02, p value:0.04). And there was statistically significant difference between blood sugar levels on presentation between 2 groups with p value of 0.002.

These findings are similar to study done by Jorgensen HS et al. Their study showed statistically significant difference was present between blood sugar levels on presentation between group with and without END.(114)

The detrimental effects of hyperglycaemia have been attributed to tissue acidosis secondary to anaerobic glycolysis, lactic acidosis, free radical production, disruption of the blood–brain barrier, the development of brain oedema, and increased risk of hemorrhagic transformation.The independent role of hypertension as a predictor of END has not been established.

The current stroke guidelines, therefore, do not advise treatment of hypertension in acute stroke, except when thrombolysis is contemplated or in the presence of extremely severe hypertension.

Percentage of patients with moderate and severe stroke is more among patients with END whereas percentage of patients with mild stroke are more in patients without END with p value of <0.001, which was statistically significant. This finding is similar to other studies done on predictors of END.(115)

Among patients without END, 18.86% i.e., 10 had microalbuminuria on presentation whereas among patients who developed END, out of 20, 16 had microalbuminuria on presentation that constitutes 80%. P value for microalbuminuria was <0.001which

shows the difference as statistically significant.A recent study by Anumpa Thampy et al has also shown that microalbuminuria is a predictor of early neurological deficit in ischemic stroke even when adjusted for NIHSS score at admission.(123,124) A study done by Chen CH et al. also predicted that proteinuria independently predicts unfavorable outcome of ischaemic stroke patients receiving intravenous thrombolysis.(5) Study by Umemura T et al. implied that the lesion volume expansion was more in those patients with higher microalbuminuria and also correlated with early neurological deterioration.(122)

Univariate logistic regression analysis was applied to age, gender, smoking history, Random blood sugar levels, dehydration status and stroke severity.The factors which have shown statistically significant association with END in univariate analysis were presence of smoking history, random blood sugar,dehydration status and stroke severity on presentation. Age and gender had no statistically significant association with END in the study.

After controlling for all the other factors in the univariate analysis, with each 1-year increase in age the odds of END have increased 1.082 times (95% CI 1.019 to 1.148 p value 0.01). The odds of END were 4.598 times more in people with presence of smoking ( 95% CI 1.534 to 13.78)  Which was statistically significant. The odds of END are 1.018 times more with each 1unit Increase in random blood sugar (95% CI 1.005 to 1.030), which was not statistically significant. The odds of END were 0.84 times more in people with presence of microalbuminuria (95% CI 0.71 to 0.97), which was statistically significant.

## LIMITATIONS AND MERITS OF THE STUDY

One of the limitations of the study was a smaller sample size of 73 patients. The merit of this study is the clinical relevance of its results. Measurement of microalbuminuria is easy and inexpensive to measure and can be performed in any emergency department to assess the severity status of the patient.

# CONCLUSION

# CONCLUSION

In this study early neurological deterioration has occurred in more than one third of acute ischemic stroke patients presented to the hospital. Among patients who developed END, 80% had microalbuminuira. There was significant difference in the microalbuminuria status between patients with and without END. The patients who had microalbuminuria are 11.4 times at risk of developing early neurologic deterioration compared to who did not have.

Therefore, early detection of patients with microalbuminuria and aggressive treatment can prevent END and eventually improve their neurological status.

# SUMMARY

# SUMMARY


- Stroke is a major cause of long-term disability among patients and has enormous emotional and socio-economic consequences.
- Early Neurological Deterioration (END) has potentially serious consequences on the short term (morbidity and death) and long term (recovery from stroke) outcomes for the patients of acute ischemic stroke.
- Therefore, attempts to predict and prevent END should be made promptly and aggressively.
- The role of microalbuminuria in a patient at the time of presentation as a predictor for END is not yet proved and studies on the effect of microalbuminuria on stroke outcome are limited.
- So the present study was designed to evaluate microalbuminuria as a predictor of early neurological deterioration in patients of acute ischemic stroke.
- A total of 73 patients with Acute ischemic stroke presenting to General Medicine OPD and Emergency department at R L Jalappa hospital, Kolar were enrolled in the study.
- The neurological status of the patients and the severity of stroke were assessed by applying the NIHSS (National Institute of Health Stroke Scale) score on day 1 and day 3 on all the patients.
- Early Neurological Deterioration was diagnosed if there was an increase in the NIHSS score by 3 or more than 3 points from day 1 to day 3 of admission.
- Microalbuminuria was assessed using urine albumin creatinine ratio, 30-300mg/g of creatinine is considered as microalbuminuira.
- Microalbuminuria was then correlated with Early neurologic deterioration.

- In our study, the mean age of the study population was 68.89±8.924 years. The maximum people are in the age group of 61-70years in our study.
- Among the study population, both males and females are almost equal in number48(65.75%) were males and 25(34.24%) constitute females.
- Among the study population, 28(38.35%) had hypertension, Smoking and alcohol consumption was present in 36(49.31%) and 31(42.26%) respectively.
- The mean Systolic and Diastolic blood pressures among study population was 143.34± 17.5 mm Hg and 87.05 ± 11.6 mm Hg. The mean blood sugar value among study population was135.86 ± 36.99 mg/dl.
- The Mean blood urea was 27±10.29mg/dl and mean serum creatinine was 0.94±0.25 mg/dl among the study population.
- 35.61% of study population i.e., 26 patients had micro-albuminuria on presentation and 64.38%,47 patients did not have micro-albuminuria on presentation to hospital.
- The mean NIHSS score on day 1 was 22.5± 5.92 and on day 3 was 25.36 ± 5.91.
- Based on NIHSS score on Day 1 of admission, majority of the patients had severe stroke-35(47.94%), 18 (24.65%) patients had moderate to severe stroke and 20(27.39%) had mild stroke.
- Among the total study population, early neurologic deterioration was developed in 20(27.39%) patients and 53 (72.6%) patients did not develop early neurologic deterioration.
- The mean age of group with END was 72.3±8.40 years and that of group without END was 65.49±9.43 years with p value of 0.006, which is not significant.
- The percentages of males and females in group with END were 65% and 35% with p value of 0.57, which was not significant.

- The percentage of hypertensives is 39.28% and 60.71% among patients with and without END respectively with p value of 0.064, which was not significant.
- The percentagesof patients with smoking history was 65 % and 60.37% among patients with and without END respectively with p value of 0.08, which was statistically insignificant.
- The percentages of patients with history of alcohol consumption was 35.46% and 54.71% among patients with and without END respectively with p value of 0.23, which was not statistically significant.
- The difference in systolic and diastolic blood pressure was significant in patients with and without END (p vlue:0.02, p value:0.04). And there was statistically significant difference between blood sugar levels on presentation between 2 groups with p value of 0.002.
- Among patients without END, 18.86% i.e., 10 had microalbuminuria on presentation whereas among patients who developed END, out of 20, 16 had microalbuminuria on presentation that constitutes 80%. P value for microalbuminuria was <0.001which shows the difference as statistically significant.
- After controlling for all the other factors in the univariate analysis, with each 1-year increase in age the odds of END have increased 1.082 times (95% CI 1.019 to 1.148 p value 0.01).
- The odds of END were 4.598 times more in people with presence of smoking ( 95% CI 1.534 to 13.78) Which was statistically significant.
- The odds of END are 1.018 times more with each 1unit Increase in random blood sugar (95% CI 1.005 to 1.030), which was not statistically significant.

- The odds of END were 11.4 times more in people with presence of microalbuminuria (95% CI 0.71 to 0.97), which was statistically significant.
- Our study suggests that presence of microalbuminuria can predict development of END and hence the need for aggressive management.

# BIBLIOGRAPHY

# BIBLIOGRAPHY


1. Heart Disease and Stroke Statistics-2017 Update: A Report from the American Heart Asociation.Shah B, Mathur P.
2. Stroke surveillance in India. Indian Council of Medical Research (ICMR) Workshop2.2006 Nov 13-15.
3. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990–2010: Findings from the global burden of disease study 2010. Lancet. 2014;383(9913):245–254.
4. Valery L. Feigin, Bo Norrving, George A. Mensah Global Burden of Stroke Circulation Research. 2017;120:439-448
5. Banerjee TK, Das SK. Fifty years of stroke researches in India. Annals of IndianAcademy of Neurology. 2016;19(1):1-8. doi:10.4103/0972-2327.168631.
6. Kaul S1, Bandaru VC, Suvarna A, Boddu DB. Stroke burden and risk factors indeveloping countries with special reference to India.J Indian Med Assoc. 2009 Jun;107(6):358, 367-70.
7. Mitchell SV, Elkind, Ralph LS.Pathogenesis, classification and epidemiology of cerebrovascular disease.Merritt's Neurology, 12th edition, Lippincott Williams &Wilkins 2010; 253-265.
8. Smith-WS, Claiborne JS. Donald JE. Cerebrovascular diseases . In: Anthony SF,Eugene B Eds Harrison's principles of internal medicine. 16th Ed 2005.McGraw Hill publication2373 -2393.
9. Allen HR. Cerebrovascular diseases In: Raymond DA, Maurice V Eds. Principles of neurology. 6th Ed 1997. McGraw Hill Publications: 777 — 873.

10. Snell RS. Blood supply of the brain In: Clinical neuranatomy for medical students 2ndEd, Little Brown Publication: 507 – 530
11. Dalai. Current concepts in stroke 2015.Association of physicians of India.
12. Jain S, maheshwari MC cerebrovascular diseases- A review of the Indian experience in the last 35 years .Neuroepidemology 1986:5;1-16
13. Nagaraja P pratap CR prognostic factors in cerebral infarction .NIMHANS journal july 1983;1(2);141-144
14. Bamford J. Sandercock P. A prospective study of acute cerebrovascular disease in community - The Oxfordshire community stroke project 1981-1986 J of neurol Neurosurg and Psych 1990;53:
15. Jorgen M. Natural history and prognosis ©f cerebrovascuiar diseases. Churchill Livingstone, Edinburgh; 1983 : 25.
16. Araki N, Greenberg' J11. The effect of hyperglycemia on intracellular calcium in stroke. I. of CBF metabolism 1992; 12 (3):472-476.
17. Kamel Abdelaziz Mohameda, Ahmad Saadb Outcome of critically ill hyperglycemic stroke patients admitted to the intensive care unit. J Internal Medicine, Faculty of Medicine;2013,23(3): 604
18. Abdul- Hameed Al-Kassir1 FICMS, Zaid Tarik2 MBChB.The incidence of stress hyperglycemia in acute ischemic stroke patients. J of neuropathology andexperimental neurology.1968; 11: 82 – 86
19. Hala El-Khawas, Ayman Nasef, Ahmed Gaber and Hany Zaki. Admission Hyperglycemia in Acute Ischemic Stroke: Effects on Short Term Prognosis J. Neurol. Psychiat. Neurosurg., 2006, 43(1): 603-613)
20. Epidemiology of stroke. Advances in neurology; 19: 299 - 310.

21. Nagaraja P pratap CR prognostic factors in cerebral infarction .NIMHANS journaljuly 1983;1(2);141-144
22. Ashok.Cerebrovascular disease in the community. Results of a WHO collaborative study Bulletin of WHO 1980; 58(1): 113-130.
23. Fisher M, Adams RD. Observation on brain embolism with special reference to mechanism of hemorrhagic infarction. J of neuropathology and experimental neurology.1951; 10: 92 - 94.
24. Colandrea MA, Friedman GP. Systolic hypertension in the elderly.An epidemiology assessment. Circulation 1970; 41: 239.
25. Tharakar J, Ahuja GK. Mitral valve prolapse and cerebrovascular accidents in the young.Acta neuro Scandinavia 1982; 66: 295 – 30.
26. Sridharan R. Risk Factors for Ischeinic Stroke. A Case Control Analysis. Neuroepidemiology 1992;11:24-30.
27. Denis M, Bamford J, Sandercock P. Prognosis of TIAs in Oxfordshire community stroke project. Stroke 1990; 21 (6): 848 - 53.
28. Wiebers DO, Whishnant JP. Prospective comparison of a cohort with symptomatic carotid bruit population based cohort withcarotid bruit. Stroke 1990; 21: 984.
29. Mohr JP, Caplan CR. The Harward cooperative stroke registry.A prospective registry neurology 1978; 28: 754.
30. Chopra J S, Prabhakar S .Clinical features and risk factors in stroke in young. ACTA,Neur. 1979 ; 60 : 289 – 300.
31. Agarwal JK, Sornani PN. A study of risk factors in non embolic cerebrovascular disease.Neurology 1976; 24: 125 - 133.

32. Kannel Wi3 Gordon T. Hemoglobin and risk of cerebral infarction. framingham study1972; 3: 409
33. Thomas D j, Marshall J. Effect of hematocrit on cerebral blood flow in man. Lancet 1977; 2: 941 .
34. Dalai PM. Low hemoglobin level as a risk factor in cerebral infarction. Stroke 1989: 20.
35. Wade JPH. Hemoglobin concentration and prognosis in symptomatic obstructive C Stroke 1987; 18: 68-71
36. Gorelick PB, Rodin MB, Langenberg P.Weekly alcohol consumption, cigarette smoking and the risk of ischaemic stroke. Neurology 1989; 39: 339.
37. Kagan A, Popper JS. Rhoads GC. Factors related to stroke incidence in Hawaii Japanese men: The Honolulu heart study. Stroke 1980; 11: 14.
38. Kozararevic DJ, MeGee D, Vojvodic N. Frequency of alcohol consumption and morbidity and mortality: The Yugoslavia cardiovascular disease study. Lancet 1980;1: 613.
39. Siesjo BK. Cerebral circulation and metabolism. .J of neurosurgery 1984 ; 60:883-90840.
40. Els T. Hyperglycemia delays terminal depolarization and enhances repolarisation after peri_infarct spreading depression as measured by serial diffusion MR imaging.Cerebral bloodflow and metabolism 1997;17:591- 5.
41. wagner KR. Hyperglycemia versus norrnoglycemic stroke. Topography of brain .metabolites, intracellular pH and infarct size. J cerebral blood flow metab 1992; 12:213-22
42. Siesjo BK et al. Acid - base changes in complete brain ischaemia. Stroke 1990;21:194-8

43. Jose B, Love BB. Diabetes & stroke MCNA Jan 1993; 77: 95-111

44. Fothergroval J. Focal and perifocal changes in tissue energy state during MCA occlusion in normo and hyperglycemic rats. CBF and metabolism 1992; 12:25-33.

45. Siesjo K Kastura KI T. Kristian T. Acidosis related damage. Advances in neurologyVol:71:1111-6.

46. Orgogozo JM, Asplund K, Boysen J: A unifi ed form for neurological scoring ofhemispheric stroke with motor impairment. Stroke 1992; 23: 1678–1679.

47. Macciocchi SN, Diamond PT, Alves WM, Mertz T. Ischemic stroke: relation of age,lesion location, and initial neurologic deficit to functional outcome. Arch Phys Med Rehabil.1998;79(10):1255–1257. doi: 10.1016/S0003-9993(98)90271-4.[PubMed] [Cross Ref]

48. Ayala C, Croft JB, Greenlund KJ, Keenan NL, Donehoo RS, Malarcher AM, et al.Sex differences in US mortality rates for stroke and stroke subtypes by race/ethnicity and age, 1995–1998. Stroke. 2002;33(5):1197–1201. doi: 10.1161/01.STR.0000015028. 52771.D1. [PubMed] [Cross Ref]

49. Kelly-Hayes M, Beiser A, Kase CS, Scaramucci A, D'Agostino RB, Wolf PA. The influence of gender and age on disability following ischemic stroke: the Framingham study. J Stroke Cerebrovasc Dis. 2003;12(3):119–126. doi: 10.1016/S1052-3057(03)00042-9. [PubMed] [Cross Ref]

50. Strazzullo P, D'Elia L, Cairella G, Garbagnati F, Cappuccio FP, Scalfi L. Excess bodyweight and incidence of stroke: meta-analysis of prospective studies with 2 million participants. Stroke 2010;41(5):e418–e426. doi: 10.1161/STROKEAHA. 109.576967. [PubMed] [Cross Ref]

51. Williams LS, Rotich J, Qi R, Fineberg N, Espay A, Bruno A, et al. Effects ofadmission hyperglycemia on mortality and costs in acute ischemic stroke. Neurology. 2002;59(1):67–71. doi: 10.1212/WNL.59.1.67.[PubMed] [Cross Ref]

52. Castillo J: Deteriorating stroke: diagnostic criteria, predictors, mechanisms and treatment.Cerebrovasc Dis 1999; 9(suppl 3):1–8.

53. Britton M, Roden A: Progression of stroke after arrival at hospital. Stroke 1985; 16:629–632.

54. Davalos A, Cendra E, Teruel J, Martinez M,Genis D: Deteriorating ischemic stroke:risk factors and prognosis. Neurology 1990; 40:1865–1869.

55. Jorgensen HS, Nakayama H, Raaschou HO, Olsen TS: Effect of blood pressure and diabetes on stroke in progression. Lancet 1994; 344:156–159.

56. Toni D, Fioreli M, Gentile M, Bastianello S,Sacchetti ML, Argentino C, Pozzilli C, Fieschi C: Progressing in neurological defi cit secondary to acute ischemic stroke. Arch Neurol 1995; 52: 670–675.

57. Castillo J, Davalos A, Noya M: Progression of ischaemic stroke and excitotoxicamino acids. Lancet 1997; 349: 79–83.

58. Davalos A, Castillo J, Pumar JM, Noya M: Body temperature and fibrinogen arerelated to early neurological deterioration in acute ischemic stroke . Cerebrovasc Dis1997; 7: 64–69

59. Yamamoto H, Bogousslavsky J, van Melle G: Different predictors of neurologicalworsening in different causes of stroke. Arch Neurol 1998;55: 481–486.

60. Roberts JK, Mohr JP: Stroke-in-evolution; in Welch KMA, Caplan LR, Reis DJ, Siesjo, Weir B (eds): Primer on cerebrovascular disease. San Diego, Academic Press, 1997, pp 765–767.
61. Hachinski V, Norris JW: The Acute Stroke. Philadelphia, Davis, 1985, pp 123–140.
62. Davalos A, Castillo J: Progressing stroke; in Fisher M, Bogousslavsky J (eds):Current Review of Cerebrovascular Disease, ed 3. Philadelphia,Current Medicine,1999, pp 149–160.
63. Britton M, Roden A. Progression of stroke after arrival at hospital. Stroke 1985;16:629–32.
64. Castillo J. Deteriorating stroke: diagnostic criteria, predictors,mechanisms and treatment. Cerebrovasc Dis 1999; 9:1–8.
65. Mayer SA, Brun NC, Begtrup K, Broderick J, Davis S, Diringer MN, Skolnick BE,Steiner T. The recombinant activated factor VII intracerebral hemorrhage trial investigators. Recombinant activated factor VII for acute intracerebral hemorrhage. N Engl J Med 2005; 352:777–85.
66. Castillo J, Davalos A, Noya M. Progression of ischaemic stroke and excitotoxicaminoacids. Lancet 1997; 349:79–83.
67. Jorgensen HS, Reith J, Nakayama H, Kammersgaard LP, Houth JG, Raaschou HO,Olsen TS. Potentially reversible factors during the very acute phase of stroke and their impact on the prognosis: is there a large therapeutic potential to be explored? Cerebrovasc Dis 2001; 11:207–11.
68. Kwan J, Hand P. Early neurological deterioration in acute stroke: clinicalcharacteristics and impact on outcome. QJM 2006;99:625—33.

69. Saposnik G, Hill MD, O'Donnell M, Fang J, Hachinski V, Kapral MK, et al.Variables associated with 7-day, 30-day, and 1-year fatality after ischemic stroke.Stroke 2008;39:2318—24.

70. Caplan LR. Worsening in ischemic stroke patients: is it time for a new strategy? Stroke 2002;33:1443–5.

71. Pulsinelli W. Pathophysiology of acute ischaemic stroke. Lancet 1992;339:533–6.

72. Toni D, De Michele M, Fiorelli M, et al. Influence of hyperglycaemia on infarct sizeand clinical outcome of acute ischemic stroke patients with intracranial arterial occlusion. J Neurol Sci 1994;123:129–33.

73. Ali LK, Saver JL. The ischemic stroke patient who worsens: new assessment and management approaches. Rev Neurol Dis 2007;4:85–91

74. Fisher CM. The use of anticoagulants in cerebral thrombosis. Neurology 1958;8:311–32.

75. chellinger PD, Fiebach JB, Jansen O, et al. Stroke magnetic resonance imaging within 6 hours after onset of hyperacute cerebral ischemia. Ann Neurol 2001;49:460–9.

76. Rajajee V, Kidwell C, Starkman S, et al. Early MRI and outcomes of untreated patients with mild or improving ischemic stroke. Neurology 2006;67:980–4.

77. Rothwell PM, Giles MF, Chandratheva A, et al for the Early use of Existing Preventive Strategies for Stroke (EXPRESS) Study. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. Lancet 2007;370:1432–42.

78. Kang DW, Latour LL, Chalela JA, et al. Early ischemic lesion recurrence within a week after acute ischemic stroke. Ann Neurol 2003;54:66–74.

79. Kang DW, Chu K, Ko SB, et al. Lesion patterns and mechanism of ischemia in internal carotid artery disease: a diffusion-weighted imaging study. Arch Neurol 2002;59:1577–82.

80. Valton L, Larrue V, le Traon AP, et al. Microembolic signals and risk of earlyrecurrence in patients with stroke or transient ischemic attack. Stroke 1998;29:2125–8.

81. Weimar C, Mieck T, Buchthal J, et al for the German Stroke Study Collaboration.Neurologic worsening during the acute phase of ischemic stroke. Arch Neurol 2005;62:393–7.

82. lexandrov AV, Grotta JC. Arterial reocclusion in stroke patients treated withintravenous tissue plasminogen activator. Neurology 2002;59:862–7.

83. Oppenheim C, Samson Y, Manai R, et al. Prediction of malignant middle cerebral artery infarction by diffusion-weighted imaging. Stroke 2000;31:2175–81.

84. Furlan A, Higashida R, Wechsler L, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. Prolyse in Acute Cerebral Thromboembolism. JAMA 1999;282:2003–11.

85. National Institute of Neurological Disorders, Stroke rt-PA Stroke Study Group. Tissueplasminogen activator for acute ischemic stroke.The National Institute ofNeurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med1995;333:1581–7.

86. Smith WS, Sung G, Starkman S, et al for the MERCI Trial Investigators. Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the MERCI trial. Stroke. 2005;36:1432–8.

87. Berger C, Fiorelli M, Steiner T, et al. Hemorrhagic transformation of ischemic braintissue:asymptomatic or symptomatic? Stroke 2001;32:1330–5.

88. Johnston KC, Li JY, Lyden PD, et al. Medical and neurological complications ofischemic stroke: experience from the RANTTAS trial. RANTTAS Investigators.Stroke 1998;29:447–53.

89. Bogousslavsky J, Martin R, Regli F, et al. Persistent worsening of stroke sequelaeafter delayed seizures. Arch Neurol 1992;49:385–8.

90. Barber M, Wright F, Stott DJ, et al. Predictors of early neurological deterioration afterischaemic stroke: a case-control study. Gerontology 2004;50:102–9.

91. Dysphagia. 2013 Mar;28(1):69-76. doi: 10.1007/s00455-012-9414-0. Epub 2012 Jun 9. Dysphagia, nutrition, and hydration in ischemic stroke patients at admission and discharge from acute care.

92. B. ovbiagele.Microalbuminuria: Risk factor and potential therapeutic target for stroke?. Journal of neurological sciences 271 (2008) 21-28

93. De Zeeuw D, Parving H-H, Henning RH. Microalbuminuria as an early marker for cardiovascular disease.J Am Soc Nephrol. 2006;17(8):2100–05.

94. Muralidhara N, Rajanna R, Varakanahalli S, Goyal VK.Prevalence of microalbuminuria in patients with non diabetic acute ischemic stroke.Int J Res Med Sci. 2015 Apr;3(4):954-957.

95. Nakayama T, Date C, Yokoyama T, Yoshiike N, Yamaguchi M, Tanaka H.A 15.5-year follow up study of stroke in a Japanese provincial city: The Shibata Study. Stroke. 1997;28:45-52

96. Beamer NB, Coull BM, Clark WM,Wynn M.Microalbuminuria in aschemic stroke.ARCH NEUROL/VOL 36,JUNE 1999.

97. Bennett PH, Lee ET, Lu M, Keen H, Fuller JH. Increased urinary albumin excretion and its associations in the WHO Multinational Study of Vascular Disease in Diabetes. Diabetologia 2001;44(Suppl 2):S37–45.

98. Rudy A, Kowalska I, Straczkowski M, Kinalska I. Homocysteine concentrations and vascular complications in patients with type 2 diabetes. Diabetes Metab 2005;31:112–7.

99. Nakamura M, Onoda T, Itai K, Ohsawa M, Satou K, Sakai T, et al.Association between serum C-reactive protein levels and microalbuminuria:a population-based cross-sectional study in northern Iwate,Japan. Intern Med 2004;43: 919–25.

100. Pannacciulli N, Cantatore FP, Minenna A, Bellacicco M, Giorgino R,De Pergola G. Urinary albumin excretion is independently associated with C-reactive protein levels in overweight and obese nondiabetic premenopausal women. J Intern Med 2001;250:502–7.

101. Yu Y, Suo L, Yu H, Wang C, Tang H. Insulin resistance and endothelial dysfunction in type 2 diabetes patients with or without microalbuminuria. Diabetes Res Clin Pract 2004;65:95–104.

102. Barzilay JI, Peterson D, Cushman M, Heckbert SR, Cao JJ, Blaum C, et al. The relationship of cardiovascular risk factors to microalbuminuria in older

adults with or without diabetes mellitus or hypertension:the cardiovascular health study. Am J Kidney Dis 2004;44:25–34.

103. Stehouwer CD, Gall MA, Twisk JW, Knudsen E, Emeis JJ, Parving HH. Increased urinary albumin excretion, endothelial dysfunction, and chronic low-grade inflammation in type 2 diabetes: progressive, interrelated, and independently associated with risk of death. Diabetes 2002;51:1157–65.
104. Gruden G, Cavallo-Perin P, Bazzan M, Stella S, Vuolo A, Pagano G. PAI-1 and factor VII activity are higher in IDDM patients with microalbuminuria. Diabetes 1994;43:426–9.
105. Deckert T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen T, KofoedEnevoldsen A. Albuminuria reflects widespread vascular damage. The Steno hypothesis. Diabetologia 1989;32:219–26.
106. Sarafidis PA, Bakris GL. Microalbuminuria and chronic kidney disease as risk factors for cardiovascular disease. Nephrol Dial Transplant 2006;21:2366–74.
107. Donnelly R, Yeung JM, Manning G. Microalbuminuria: a common, independent cardiovascular risk factor, especially but not exclusively in type 2 diabetes. J Hypertens Suppl 2003;21:S7–S12.
108. The internet stroke centre[internet]. Texas:Stroke assessment scales;2012[cited 2012 Nov 26].Available from : http://www.strokecentre.org/professionals/stroke diagnosis/stroke-assesment - scales.
109. Harrison JK, McArthur KS, Quinn TJ. Assessment scales in stroke: clinimetric and clinical considerations. Clinical Interventions in Aging. 2013;8:201-211. doi:10.2147/CIA.S32405.

110. Jennifer K Harrison,1 Katherine S McArthur,2 and Terence J Quinn2 Assessmentscales in stroke: clinimetric and clinical considerations Clinical Interventions in Aging. 2014;8:20-21
111. Adams HP, Davis PH, Leira EC, et al. Baseline NIH stroke scale strongly predictsoutcome after stroke: a report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST) Neurology. 1999;53:126–131
112. Powers William J., Rabinstein Alejandro A., Ackerson Teri, Adeoye Opeolu M., Bambakidis Nicholas C., Becker Kyra, et al. 2018 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. 2018 Mar 1;49(3):e46–99.
113. Smith WS, Johnston SC, Hemphill III JC. ISCHEMIC STROKE. In: HARRISON'S PRINCIPLES OF INTERNAL MEDICINE. 20th ed. Mc Graw Hill education; 2018. p. 3079–91.
114. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995 14;333(24):1581–7.
115. Furlan A, Higashida R, Wechsler L, Gent M, Rowley H, Kase C, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. Prolyse in Acute Cerebral Thromboembolism.JAMA. 1999 Dec 1;282(21):2003–11.
116. Goyal M, Menon BK, van Zwam WH, Dippel DWJ, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet Lond Engl. 2016 Apr 23;387(10029):1723–31.

117. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. N Engl J Med. 2018 Jan 4;378(1):11–21.
118. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging. N Engl J Med. 2018 Feb 22;378(8):708–18.
119. CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. CAST (Chinese Acute Stroke Trial) Collaborative Group. Lancet Lond Engl. 1997 Jun 7;349(9066):1641–9.
120. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. International Stroke Trial Collaborative Group. Lancet Lond Engl. 1997 May 31;349(9065):1569–81.
121. Biller jose, Ruland S, J. Schneck M. ISCHEMIC CEREBROVASCULAR DISEASE. In: Bradley's Neurology in Clinical Practice. 7th ed. ELSEVIER; 2016. p. 920–67.
122. Umemura T, Senda J, Fukami Y, Mashita S, Kawamura T, Sakakibara T, et al. Impact of albuminuria on early neurological deterioration and lesion volume expansion in lenticulostriate small infarcts. Stroke. 2014;45(2):587-90.
123. Thampy A, Pais CC.Early clinical implications of microalbuminuria in patients with acute ischemic stroke. Journal of Clinical and Diagnostic Research. 2016 Sep, Vol-10(9): OC29-OC31
124. Takuya Kanamaru, Satoshi Suda, Kanako Muraga, Seiji Okubo, Yoko Watanabe, Syuichi Tsuruoka, Kazumi Kimura, Albuminuria predicts early

neurological deterioration in patients with acute ischemic stroke, Journal of the Neurological Sciences.2016

# ANNEXURES

# ANNEXURE

# PROFORMA

Sl. No: Date:

OP/ IP No:

Name:

Age:

Occupation:

Address:

CHIEF COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

PAST MEDICAL HISTORY:

FAMILY HISTORY :

PERSONAL HISTORY :

DRUG HISTORY :

PHYSICAL EXAMINATION :

GENERAL PHYSICAL EXAMINATION:

VITAL DATA :

SYSTEMIC EXAMINATION:

• CENTRAL NERVOUS SYSTEM :

Level of consciousness:

Cranial Nerves examination:

Motor system examination:

Sensory system examination:

NIHSS SCORE:

On day 1:

After 24 hrs of onset of Symptoms:

On day 3:

Is there decrease in NIHSS score from day 1 to day 3 ?

Yes No

If yes, by how much the score decreased?

• CARDIOVASCULAR SYSTEM:

• RESPIRATORY SYSTEM:

• GASTROINTESTINAL SYSTEM:

INVESTIGATIONS:

1. NCCT Brain Report :

2. Blood urea :

3. Serum creatinine :

4. Urine albumin creatinine ratio:

PROVISIONAL DIAGNOSIS:

# PATIENT INFORMATION SHEET

**Study Title**:Microalbuminuria as a predictor of early neurological deterioration in patients with acute ischemic stroke.

**Study site**: R.L Jalappa hospital, Tamaka, Kolar.

**Aim**: To determine the association of microalbuminuria and early neurological deterioration in patients with acute ischemic stroke.5 ml of venous blood will be taken from the median cubital vein and sent for CBC,RFT, S ELECTROLYES,RBS and other investigations, 5ml of mid stream urine sample is colllected and sent for urine albumin creatinine ratio. This information is intended to give you the general background of the study. Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

**For any further clarification you can contact the study investigator:**

Dr. PUJITHA S N
Mobile no: 9741120512
E-mail id: poojitha.sn03@yahoo.in

# CONSENT FORM

I ---------- participant, hereby give consent to participate in the study entitled "Microalbuminuria as a predictor of early neurological deterioration in patients with acute ischemic stroke"

I have been explained that;

1. I would have to provide a blood sample for the study purpose.
2. I have to answer the questionnaires related to project.
3. I do not have to incur any additional expenditure on my inclusion into the study.
4. The data generated from my clinical examination and laboratory tests and other reports will be used in the study (which may be subsequently published) without revealing my identity in any manner.

I affirm that I have been given full information about the purpose of the study and the procedures involved and have been given ample opportunity to clarify my doubts in my mother tongue. In giving my consent, I have not faced any coercion. I have been informed that, notwithstanding this consent given, I can withdraw from the study at any stage.

**For any further clarification you can contact the study investigator:**

Dr. PUJITHA S N

Mobile no: 9741120512

E-mail id: poojitha.sn03@yahoo.in

Signature of participant: Place:

Name of participant: Date:

# KEY TO MASTER CHART

| | |
|---|---|
| IP. NO. | Inpatient number |
| HTN | Hypertension |
| SBP | Systolic Blood Pressure |
| DBP | Diastolic Blood Pressure |
| RBS | Random Blood Sugar |
| UACR | Urine Albumin Creatinine Ratio |
| S.Creat | Serum Creatinine |
| NIHSS | National Institute of Health Stroke Severity |
| END | Early Neurological Deterioration |

| SERIAL NO. | IP NO | AGE | GENDER | HTN | T2DM | SBP | DBP | UACR | BD UREA | S CREAT | 2D ECHO | NIHSS 1 | NIHSS 3 | END | SMOKING | ALCOHOL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 213568 | 63 | M | N | N | 138 | 86 | 9 | 37 | 1.1 | N | 22 | 24 | N | Y | Y |
| 2 | 215763 | 74 | M | N | N | 126 | 80 | 45.6 | 25 | 1 | N | 30 | 35 | Y | N | Y |
| 3 | 215583 | 56 | M | Y | N | 144 | 94 | 72 | 45 | 0.9 | LVH,EF 55% | 14 | 15 | N | Y | N |
| 4 | 216782 | 58 | M | N | N | 160 | 100 | 76.4 | 31 | 0.7 | N | 34 | 37 | Y | Y | N |
| 5 | 220127 | 61 | F | N | N | 132 | 80 | 4 | 26 | 1.2 | N | 23 | 24 | N | N | N |
| 6 | 256348 | 62 | M | N | N | 130 | 82 | 12 | 54 | 1 | N | 15 | 15 | N | N | N |
| 7 | 296549 | 66 | M | Y | N | 176 | 110 | 56.1 | 17 | 1.6 | LVH,EF 55% | 30 | 35 | Y | N | Y |
| 8 | 304569 | 59 | F | Y | N | 154 | 96 | 23.7 | 30 | 0.7 | N | 16 | 18 | N | Y | Y |
| 9 | 304876 | 57 | F | N | N | 140 | 90 | 26 | 26 | 0.9 | N | 12 | 12 | N | N | N |
| 10 | 316543 | 49 | M | N | N | 134 | 86 | 42 | 28 | 1 | LVH,EF 55% | 17 | 18 | N | N | N |
| 11 | 347562 | 51 | F | N | N | 130 | 80 | 28.4 | 45 | 1.1 | N | 12 | 13 | N | Y | N |
| 12 | 345987 | 63 | F | N | N | 128 | 70 | 20 | 40 | 1.2 | N | 16 | 18 | N | N | N |
| 13 | 398610 | 64 | F | Y | N | 162 | 90 | 66.7 | 43 | 0.8 | LVH,EF 55% | 30 | 34 | Y | Y | Y |
| 14 | 405621 | 57 | M | N | N | 120 | 70 | 29 | 21 | 0.6 | N | 26 | 28 | N | N | N |
| 15 | 412341 | 58 | M | N | N | 110 | 60 | 34.6 | 16 | 0.9 | N | 14 | 15 | N | Y | N |
| 16 | 419569 | 66 | M | N | N | 126 | 80 | 22 | 32 | 1.1 | N | 18 | 20 | N | N | N |
| 17 | 453126 | 78 | M | Y | N | 144 | 90 | 78.5 | 35 | 1 | LVH, EF 55% | 26 | 30 | Y | N | N |
| 18 | 459871 | 92 | F | Y | N | 154 | 94 | 26 | 26 | 1.4 | LVH,EF 55% | 27 | 31 | Y | Y | Y |
| 19 | 487513 | 87 | F | Y | N | 150 | 90 | 12 | 14 | 1 | N | 28 | 29 | N | Y | Y |
| 20 | 488562 | 76 | M | Y | N | 180 | 120 | 121.4 | 15 | 0.8 | LVH,EF 55% | 34 | 37 | Y | Y | Y |
| 21 | 501023 | 77 | F | N | N | 126 | 80 | 27 | 27 | 0.9 | N | 14 | 15 | N | N | N |
| 22 | 512342 | 71 | F | N | N | 114 | 70 | 26 | 31 | 1.2 | N | 11 | 12 | N | N | N |
| 23 | 524986 | 58 | M | N | N | 90 | 60 | 45.8 | 28 | 1.4 | N | 24 | 28 | Y | N | N |
| 24 | 541267 | 63 | M | N | N | 106 | 70 | 42.1 | 30 | 1.1 | N | 34 | 34 | N | Y | N |
| 25 | 543764 | 54 | M | Y | N | 148 | 96 | 24.6 | 53 | 1 | N | 11 | 13 | N | Y | Y |
| 26 | 578672 | 57 | M | Y | N | 136 | 80 | 40 | 26 | 0.6 | LVH,EF 55% | 12 | 14 | N | Y | Y |
| 27 | 576953 | 70 | F | Y | N | 174 | 96 | 52.6 | 20 | 0.9 | LVH, EF 55% | 32 | 35 | Y | Y | Y |
| 28 | 574398 | 67 | M | N | N | 126 | 70 | 21 | 16 | 0.6 | N | 16 | 18 | N | N | N |
| 29 | 564982 | 60 | M | Y | N | 132 | 80 | 15 | 40 | 1.2 | N | 24 | 26 | N | N | N |
| 30 | 598675 | 62 | F | N | N | 142 | 86 | 18 | 10 | 0.5 | N | 26 | 28 | N | N | Y |
| 31 | 586741 | 59 | M | N | N | 130 | 70 | 24.4 | 8 | 0.8 | N | 14 | 15 | N | N | N |
| 32 | 599466 | 64 | M | N | N | 146 | 90 | 32.1 | 54 | 1.5 | N | 19 | 21 | N | Y | Y |
| 33 | 604452 | 76 | F | N | N | 136 | 86 | 23 | 18 | 0.6 | N | 21 | 22 | N | N | N |
| 34 | 610988 | 80 | M | N | N | 142 | 80 | 26.5 | 19 | 0.9 | N | 10 | 12 | N | Y | Y |
| 35 | 615349 | 82 | M | Y | N | 156 | 96 | 156.4 | 43 | 1.1 | N | 36 | 42 | Y | N | Y |
| 36 | 624351 | 65 | F | Y | N | 154 | 90 | 40.1 | 18 | 0.7 | N | 24 | 25 | N | Y | N |
| 37 | 655432 | 74 | M | Y | N | 146 | 86 | 27 | 23 | 0.5 | N | 12 | 12 | N | N | N |
| 38 | 654986 | 82 | M | N | N | 172 | 96 | 56.4 | 35 | 1 | LVH,EF 55% | 28 | 35 | Y | Y | N |
| 39 | 665409 | 61 | M | N | N | 130 | 80 | 12.6 | 31 | 1 | N | 31 | 32 | N | N | N |
| 40 | 673897 | 92 | F | Y | N | 126 | 76 | 16 | 27 | 0.9 | N | 18 | 20 | N | Y | Y |
| 41 | 659734 | 64 | M | N | N | 130 | 80 | 18 | 30 | 1.1 | N | 13 | 14 | N | Y | Y |
| 42 | 687512 | 70 | F | N | N | 110 | 60 | 12.6 | 25 | 0.7 | N | 14 | 21 | Y | N | N |
| 43 | 654352 | 59 | M | Y | N | 154 | 96 | 25.5 | 16 | 0.8 | LVH EF 55% | 27 | 28 | N | Y | N |
| 44 | 765453 | 62 | M | N | N | 144 | 88 | 40.2 | 24 | 0.6 | N | 20 | 22 | N | N | N |
| 45 | 786540 | 66 | F | N | N | 136 | 86 | 12 | 19 | 0.6 | N | 13 | 14 | N | Y | Y |
| 46 | 769562 | 73 | M | Y | N | 140 | 94 | 65.9 | 34 | 1.2 | LVH,EF 55% | 24 | 28 | Y | N | Y |
| 47 | 865409 | 75 | F | N | N | 120 | 70 | 18 | 36 | 1.1 | N | 26 | 28 | N | Y | Y |
| 48 | 875215 | 80 | F | N | N | 144 | 86 | 22.3 | 14 | 0.7 | N | 19 | 21 | N | Y | Y |
| 49 | 835492 | 87 | M | N | N | 130 | 70 | 24 | 26 | 0.9 | N | 16 | 16 | N | N | N |
| 50 | 898784 | 67 | M | Y | N | 126 | 68 | 28 | 18 | 0.7 | LVH,EF 55% | 18 | 19 | N | N | N |
| 51 | 986452 | 75 | F | N | N | 142 | 92 | 24.6 | 20 | 0.6 | N | 30 | 34 | Y | N | Y |
| 52 | 967459 | 58 | F | N | N | 156 | 96 | 17.6 | 40 | 1.2 | N | 12 | 13 | N | Y | N |
| 53 | 154768 | 74 | M | Y | N | 152 | 84 | 23.8 | 35 | 0.9 | LVH EF 55% | 21 | 23 | N | Y | Y |
| 54 | 254234 | 70 | M | Y | N | 166 | 98 | 43.6 | 27 | 1.1 | LVH,EF 55% | 25 | 30 | Y | N | N |
| 55 | 312654 | 68 | M | N | N | 124 | 74 | 21.6 | 46 | 0.8 | N | 14 | 15 | N | N | Y |
| 56 | 435652 | 72 | F | Y | N | 144 | 84 | 24.7 | 17 | 1.4 | N | 16 | 16 | N | N | N |
| 57 | 514328 | 64 | M | N | N | 146 | 86 | 25.5 | 39 | 1 | N | 18 | 20 | N | Y | Y |
| 58 | 553476 | 71 | M | Y | N | 134 | 86 | 28.1 | 45 | 1.1 | N | 15 | 15 | N | Y | N |
| 59 | 564872 | 66 | F | N | N | 126 | 76 | 10.8 | 10 | 0.6 | N | 25 | 30 | Y | Y | N |
| 60 | 587634 | 68 | M | N | N | 142 | 80 | 70.5 | 19 | 0.9 | N | 8 | 9 | N | N | N |
| 61 | 593158 | 48 | M | N | N | 156 | 90 | 23.7 | 17 | 0.6 | N | 12 | 14 | N | N | N |
| 62 | 590846 | 69 | M | N | N | 140 | 90 | 25.7 | 30 | 1.2 | N | 23 | 25 | N | N | Y |
| 63 | 599632 | 72 | M | Y | N | 140 | 80 | 32.1 | 26 | 1 | LVH,EF 55% | 31 | 32 | N | Y | Y |
| 64 | 623870 | 66 | M | N | N | 136 | 76 | 17 | 19 | 0.7 | N | 17 | 18 | N | Y | N |
| 65 | 637516 | 73 | M | N | N | 142 | 90 | 32.7 | 18 | 0.8 | N | 20 | 25 | Y | N | N |
| 66 | 614329 | 65 | F | Y | N | 136 | 80 | 14.7 | 16 | 0.6 | N | 26 | 27 | N | N | N |
| 67 | 614985 | 67 | M | Y | N | 146 | 90 | 17 | 20 | 1.1 | N | 16 | 18 | N | N | Y |
| 68 | 634187 | 71 | M | N | N | 154 | 96 | 67.9 | 17 | 0.8 | N | 16 | 20 | Y | Y | Y |
| 69 | 628749 | 70 | M | N | N | 136 | 70 | 14 | 27 | 1 | N | 30 | 30 | N | Y | N |
| 70 | 687153 | 82 | F | Y | N | 160 | 100 | 55.4 | 30 | 1.1 | LVH EF % | 22 | 25 | Y | Y | N |
| 71 | 645286 | 59 | M | N | N | 130 | 80 | 19 | 37 | 0.9 | N | 23 | 24 | N | N | N |
| 72 | 627509 | 49 | M | N | N | 140 | 90 | 25 | 10 | 0.5 | N | 14 | 16 | N | N | N |
| 73 | 760562 | 66 | M | Y | N | 176 | 110 | 162.2 | 26 | 1 | LVH,EF 55% | 24 | 28 | Y | Y | Y |