SERUM FERRITIN LEVEL AS A SEVERITY MARKAR IN PATIENTS STROKE USING MODIFIED RANKING SCALE(mRS)

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Dissertation submitted to

BLDE (Deemed to be University) Vijayapur, Karnataka

In partial fulfillment of the requirements for the degree of

DOCTOROFMEDICINE

IN

GENERAL MEDICNE

Under the guidance of

Dr. ANAND.P.A

PROFESSOR

DEPARTMENTOFGENERAL MEDICNE

BLDE (Deemed to be University)

SHRIB.M.PATILMEDICALCOLLEGE

HOSPITAL & RESEARCH CENTRE, VIJAYAPUR

KARNATAKA

2020

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DOCTOR OF MEDICINE
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ABBREVIATIONS

ICA - INTERNAL CAROTID ARTERY

ACA - ANTERIOR CEREBRAL ARTERY

MCA - MIDDLE CEREBRAL ARTERY

POCA - POSTERIOR COMMUNICATING ARTERY

AOCA - ANTERIOR COMMUNICATING ARTERY

PCA - POSTERIOR CEREBRAL ARTERY

BBB - BLOOD BRAIN BARRIER

BP - BLOOD PRESSURE

SBP -SYSTOLIC BLOOD PRESSURE

DBP - DIASTOLIC PRESSURE

DM - DIABETES MELLITUS

ICP - INTRA CRANIAL PRESSURE

IHD -ISCHEMIC HEART DISEASE

ICA -INTERNAL CAROTID ARTERY

SAH -SUB ARACHNOID HEMORRHAGE

TIA -TRANSIENT ISCHEMIC ATTACK

CT - COMPUTER TOMOGRAPHY

MRI – MAGNETIC RESSONANCE IMAGING

FES - FUNCTIONAL ELECTROSTIMULATION

VKAS - VITAMIN K ANTAGONISTS

NOACS - NOVEL ORAL ANTICOAGULANTS

ABC'S - AIRWAY, BREATHING, CARDIAC STATUS.

ACA - ANTERIOR CEREBRAL ARTERY

AOCA-ANTERIOR COMMUNICATING ARTERY

ADL -ACTIVITIES OF DAILY LIVING

AF - ATRIAL FIBRILLATION

CCA- COMMON CAROTID ARTERY

CVA - CEREBRO VASCULAR ACCIDENT

DSY-DYSLIPEDEMIA

GCS - GLASGOW COMA SCALE

HDL - HIGH DENSITY LIPOPROTEINS

ICH -INTRA CEREBRAL HEMORRHAGE

LDL -LOW DENSITY LIPOPROTEINS

MCA -MIDDLE CEREBRAL ARTERY

MI- MYOCARDIAL INFARCTION

NINDS -NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

OCP -ORAL CONTRACEPTIVE PILLS

PACS -PARTIAL ANTERIOR CIRCULATION STROKE

PCA -POSTERIOR CEREBRAL ARTERY

POCA-POSTERIOR COMMUNICATING ARTERY

POCS -POSTERIOR CIRCULATION STROKE

RTPA -RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR

RHD -RHEUMATIC HEART DISEASE

RIND- REVERSIBLE ISCHEMIC NEUROLOGIC DEFICIT

SHT -SYSTEMIC HYPERTENSION

TACS -TOTAL ANTERIOR CIRCULATION STROKE

TG- TRIGLYCERIDES

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ABSTRACT

NEED FOR THE STUDY:

According to the World Health Organization (WHO), Stroke is defined as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting for more than 24 hours, or leading to death, with no apparent cause, other than that of vascular origin."

Stroke is considered as an important health issue for every individual and society. Ischemic stroke is the third leading cause of death after Acute Myocardial Infarction and malignancy, and it is also one of the leading causes of disability.

A recent study was published in 2021 in India, which stated that 30 days case fatality rate of stroke varied from 41.08% to 42.06% in the urban population and 18% to 46.3%.in the rural population.

Iron overload in stroke is poorly documented. However, high serum ferritin on the admission of acute stroke patients (within 24 to 48 h after stroke onset) was reported to predict a bad prognosis suggesting that increased body iron stores before stroke onset can aggravate the cytotoxicity of brain ischemia. Initially, serum ferritin is considered only as a stress response to stroke, but now serum ferritin is under research as a prognostic indicator in stroke.

Serum ferritin can be used to assess iron overload in the absence of inflammation, cancer, and infectious diseases as serum ferritin is directly proportional to cellular iron stores.

Serum ferritin is, consequently, might be related to the availability of iron in the infarcted area, In brain tissue, most of the non-heme iron is in the form of ferritin, which is localized in astrocytes and microglia.

During cerebral ischemia, ferritin will be released from the cell, which is free iron, which will catalyze the preformed radicals like hydrogen peroxide (H_2O_2) and superoxide ($O_2^{\bullet -}$) into highly

reactive toxic hydroxyl radical (•OH) Few experimental data showed that iron being a cause for endothelial damage and ischemia brain.

Recent research has revealed that ferroptosis plays a significant regulatory function in the onset and development of many illnesses, and it has become a focus and hotspot of study for the treatment and improvement of prognosis in related diseases.

The **modified Rankin Scale** (**mRS**) is the most commonly used scale for measuring dependence in the daily activities of people or the degree of disability who have suffered neurological deficit due to stroke or any other causes. It's been widely accepted and used for measuring clinical outcomes in stroke.

Hence, our study intends to know the association between a Serum Ferritin level and severity of the ischemic stroke using the modified Rankin Scale (mRS).

Materials and method

Our study was a hospital-based cross-sectional study conducted on 68 patients admitted to the wards with a history of clinical findings and radiological evidence for ischemic stroke in BLDEDU Shri B M Patil Medical College and Research Centre, Vijayapura, after getting approval from the institutional ethical committee.

RESULTS

The study conducted to evaluate the serum ferritin as severity maker in ischemic stroke using modified Rankin Scale (mRS) in a total 68 patients and the results are as follows,

Serum ferritin and modified Rankin Scale

In our study, mRS scale was applied in all the patients presented within 24hr of onset of weakness and correlated with serum ferritin level. We graded mRS from 1 to 5 and we found 8 (11.7%) patients were under mRS-1 and 22 in mRS-2, 20 in mRS-3, 7 in mRS-4, and 11 in mRS-5. Average

serum ferritin found in patients under mRS-1 was 90.9(±77.5), mRS-2 112.3(±107.1), mRS-3 173.1 (±114.2), mRS-4 292.9 (±133.9), mRS-5 595.3 (±392.2).

Results were plotted using a scatter diagram which showed ferritin was in an increasing trend as the mRS grading was increasing which signifies higher the ferritin, more the severity of stroke.

The correlation between serum ferritin and mRS had a P-value < 0.0001 which is statically significant and SPERSON'S CORRELATION COEFFICIENT was **r=0.609** which signifies the moderate correlation.

Conclusion:

The present study conducted to evaluate Serum ferritin level as a severity marker in patients with ischemic stroke using modified Rankin Scale (mRS) revealed a significant correlation of serum ferritin with severity of the ischemic stroke, illustrating higher the level of serum ferritin, more the severe stroke. Patients with higher levels of serum ferritin at admission tend to deteriorate more as compared to those with lower serum ferritin levels. Thus, serum ferritin can be used as a severity marker in patients with acute ischemic stroke and iron chelation therapy can be considered for a better outcome but still many studies have to be conducted in a large-scale using iron chelator in a stroke patient. And we conclude serum ferritin is to be evaluated in ischemic stroke patients at admission as a routine investigation.

INTRODUCTION

According to the World Health Organization (WHO), Stroke is defined as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting for more than 24 hours or leading to death, with no apparent cause, other than that of vascular origin."[1]

Stroke is considered as an important health issue for every individual and society. Ischemic stroke is the third leading cause of death after Acute Myocardial Infarction and malignancy, and it is also one of the leading causes of disability.

A recent study was published in 2021 in India, which showed the data from different parts of India, Prevalence rate of stroke for the total population inclusive of the urban and rural population, varied from 44.54 to 150/100000. For the urban population prevalence rate was 45 to 487/100000 and the for rural population 55 to 388.4/100000. The incidence rate in the urban population varied from 33 to 123/100000 and in the rural population, it was estimated to be 123.57/100000. The 30 days case fatality rate of stroke varied from 41.08% to 42.06% in the urban population and 18% to 46.3%.in the rural population.[2]

Because of better cardiovascular disease prevention, and improvements in the acute stroke setting, such as specialized facilities like stroke units and the development of recanalizing therapies, such as thrombolysis and thrombectomy, both age-standardized mortality and stroke prevalence rates have decreased significantly over the last three decades. Despite this, the absolute number of stroke fatalities and disability-adjusted life years (DALY) continues to rise in most nations due to longer life expectancies and population growth [3]. These figures are expected to rise dramatically over the next 30 years.[4]

Cerebrovascular disorders are due to either ischemia or haemorrhage within the central nervous system. The site and size of the lesion depict the neurological deficit.

Ischemic stroke is more commonly secondary to cerebral artery occlusion due to thrombosis or embolism. Atherosclerotic or thromboembolic arterial occlusions account for around 80- 85% of all stroke cases. Cerebral atherothromboembolism involves predominantly the middle cerebral artery, followed by the posterior cerebral artery, anterior cerebral artery and basilar artery, which are involved less commonly.

Iron overload load in stroke is poorly documented. However, high serum ferritin on the admission of acute stroke patients (within 24 to 48 h after stroke onset) was reported to predict a bad prognosis [5] suggesting that increased body iron stores before stroke onset can aggravate the cytotoxicity of brain ischemia. Initially, serum ferritin is considered only as a stress response to stroke, but now serum ferritin is under research as a prognostic indicator in stroke, the possible mechanisms of ferritin are discussed below

Serum ferritin can be used to assess the iron overload in the absence of inflammation, cancer, and infectious diseases as serum ferritin is directly proportional to cellular iron stores.[6]

Serum ferritin is, consequently, might be related to the availability of iron in the infarcted area,[7] In brain tissue, most of the non-heme iron is in the form of ferritin, which is localized in astrocytes and microglia.[8]

In response to hypoxic acidosis or oxidative stress, the synthesis of ferritin will be induced in brain cells to reduce the accumulation of reactive oxygen species (ROS). [9]

During cerebral ischemia, ferritin will be released from the cell, which is free iron, which will catalyze the preformed radicals like hydrogen peroxide (H_2O_2) and superoxide ($O_2^{\bullet-}$) into highly reactive toxic hydroxyl radical ($^{\bullet}OH$) [10,] Few experimental data showed that iron being cause for endothelial damage and ischemia brain.

In 2012, Dixon suggested the concept of ferroptosis, a non-apoptotic, iron-dependent form of cell death characterized by the accumulation of lipid (ROS) reactive oxygen species. Ferroptosis is

clearly distinct from necrosis, apoptosis, and autophagy in cell morphology and function. ferroptosis lacks the morphological hallmarks of conventional necrosis, such as swelling of the cytoplasm and organelles and cell membrane rupture, as well as classic cell apoptosis, such as cell shrinkage, chromatin condensation, production of apoptotic bodies, and cytoskeleton breakdown. Ferroptosis, unlike autophagy, does not produce closed bilayer membrane structures (autophagic vacuoles). Ferroptosis is distinguished from other types of cell death by visible shrinking of mitochondria, increased membrane density, and a reduction in or disappearance of mitochondrial cristae.[11]

Recent research has revealed that ferroptosis plays a significant regulatory function in the onset and development of many illnesses, and it has become a focus and hotspot of study for the treatment and improvement of prognosis in stroke related diseases.

The **modified Rankin Scale** (**mRS**) have become most commonly used scale for measuring dependence in the daily activities of people or the degree of disability who have suffered neurological deficit due to stroke or any other causes. It's been widely accepted and used for measuring clinical outcomes in stroke [12]

Hence, our study intends to know the association between a Serum Ferritin level on the severity of the ischemic stroke using the modified Rankin Scale (mRS).

AIM OF THE STUDY

To study the association between a Serum Ferritin level on the severity of the ischemic stroke using the modified Rankin Scale (mRS).

REVIEW OF LITERATURE

According to the World Health Organization (WHO), Stroke is defined as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting for more than 24 hours or leading to death, with no apparent cause, other than that of vascular origin."[1]

History

It took about 2,500 years assembling numerous pieces of information to achieve a reasonably well-defined picture of Stroke. The term "stroke", which signifies an acute event leading to the clinical symptoms of neural dysfunction, is evolved from the ancient word "apoplexy", which refers to a clinical concept characterized by the rapid loss of various manifestations of brain dysfunction and consciousness.

Hippocrates was the first person who is responsible for the recording the term "apoplexy". The concept of apoplexy was mentioned in his many of the extensive works which described the clinical picture with some variations[13]. He defined apoplexy as "Suddenly a healthy person is seized with head pain, immediately the voice fails, he snores, and the mouth is open (gapes), and if someone calls or moves, he only groans, nothing with meaning, gives (releases) copious urine, and does not perceive. If the fever does not seize (appears), he dies in seven days. Because it seize (comes), the health is generally spared"

After Hippocratic age modification of term was followed by many of personalities, such as Celsus (25 BC-50 AD), Aretaeus (I^{st} century AD), Archigenes(I^{st}-II^{nd} century AD), Galen (129 to 210 AD), Caelius Aurelianus (IV^{th}-V^{th} century AD), among many others. The term kept having modifications over the medieval era, renaissance and modern era.

Essential milestones in Modern era journey were as follows.

1. Jacob Werter(1620-95), a Swiss physician, suggested that apoplexy was caused by a disease of the blood vessel in the brain.
2. In 1664, Thomas Willis described about the circle of wills.
3. In 1689, William Cole (1635-1716) first to use the term "stroke" to denote "apoplexy" in English medical writing.[14]
4. In 1814, Jean André Rochoux (1787-1852), Defined "hemorrhagic apoplexy" [cerebral hemorrhage], and introduced the term ramollissement du cerveau [softening of the brain] [infarction]
5. In 1813, Seddicot described about spontaneous intracerebral haemorrhage.
6. Johan Friedrichcrell emphasized the pultaceous or atheromatous elements in some arterial lesions although he did not use the term atheroma.
7. Von Haller made similar observations and applying the term "atheroma" to the arterial lesions.
8. In 1852, Virchow created the terms "thrombosis" and "embolism", and revived the notion of "arteriosclerosis"[15]
9. In 1927, the term cerebrovascular accident was introduced.
10. In 1971, WHO defined Stroke as "A sudden onset of disturbance of focal bran function due to the blockage or rupture of blood vessels."
11. In 1980, WHO modified stroke definition as "Rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin."
12. IN 2013, AHA-ASA (American Heart Association-American Stroke Association) defined stroke as "An episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage, persisting ≥ 24 hours or until death, but without sufficient evidence to be classified as one of the above."[16]

EPIDEMIOLOGY

Every year in the US, more than 7,00,000 people have a stroke, which constitutes roughly 3% of the adult population and the incidence increase along with age; among the population who were aged 35-44, the incidence rate (IR) was 30-120 for 1lakh and for the population aged 65-74 incidence rate increase to 670-970 for 1lakh population which is very significant. There was about a 6.2million stroke death in 2015, making it the second leading cause of death worldwide. [17]

A recent study was published in 2021 in India, which showed the data from different parts of India, Prevalence rate of stroke for total population inclusive of urban and rural population, varied from 44.54 to 150/100000. For the urban population prevalence rate was 45 to 487/100000 and for rural population 55 to 388.4/100000. The incidence rate in the urban population varied from 33 to 123/100000 and in the rural population it was estimated to be 123.57/100000. The 30 days case fatality rate of stroke varied from 41.08% to 42.06% in urban population and 18% to 46.3%.in the rural population.[2]

IMPACT OF STROKE

Because of better cardiovascular disease prevention in general, and improvements in the acute stroke setting, such as specialized facilities like stroke units and the development of recanalizing therapies, such as thrombolysis and thrombectomy, both age-standardized mortality and stroke prevalence rates have decreased significantly over the last three decades. Despite this, the absolute number of stroke fatalities and disability-adjusted life years (DALY) continues to rise in most nations due to longer life expectancies and population growth[18.] These figures are expected to rise dramatically over the next 30 years.[4]

As per a conventional rule of thumb in stroke recovery, those with minor deficits are more capable of attaining a good recovery than patients with initially relatively severe deficits. The 'proportional

recovery rule' suggests that within 3-6 months following a stroke, individuals can regain roughly 70% (+/-15%) of their lost function.[19]

On average, in developing countries like India, the incidence of stroke has considerably increased; in comparison with high-income countries, stroke occurs 15 years earlier and causes more deaths in low and middle economic countries. This rise in incidence reflects increased life span, sedentary lifestyle, a high-fat diet,smoking, alcohol, increasing prevalence of central obesity, diabetes mellitus and hypertension. But the chances in the adult population can be controlled by early detection and controlling of the above risk factors.

We must give a lot of importance to prevention because if a stroke occurs at a younger age whole family will suffer if he is the only earner in the family. If it is the older people, they become bedridden and may be neglected by family members, making older people depressed and develop bedsores which eventually lead to sepsis and ultimately death.

Out of many severity indicators, in recent days, serum ferritin has got its own importance in predicting the severity of the stroke and hence can enhance the treatment protocol to give better care to the patient.

BRAIN CIRCULATION

The paired carotid and vertebral arteries provide vascular flow to the brain. The carotid arteries and their branches carry roughly 600-700 ml of blood each minute, while the vertebral-basilar system carries about 100-200 ml.

Extracranially, the carotid and vertebral arteries branch out and travel through the neck and base of the skull to reach the cranial cavity. The anterior 2/3 of the cerebral hemispheres, comprising the deep white matter and basal ganglia, are supplied by the internal carotid arteries and their branches. The remaining posterior and medial areas of the hemispheres, most of the diencephalon, the

brainstem, cerebellum, and cervical spinal cord, are supplied by the vertebral arteries and basilar artery, as well as their branches.

Through the circle of Willis (FIGURE 1), the carotid and vertebral-basilar circulations are physically related to each other and to their counterparts in the opposite hemisphere.

The brain, which accounts for 2% of total body weight, gets 20% of cardiac output and requires 20% of total inspired oxygen when at rest.

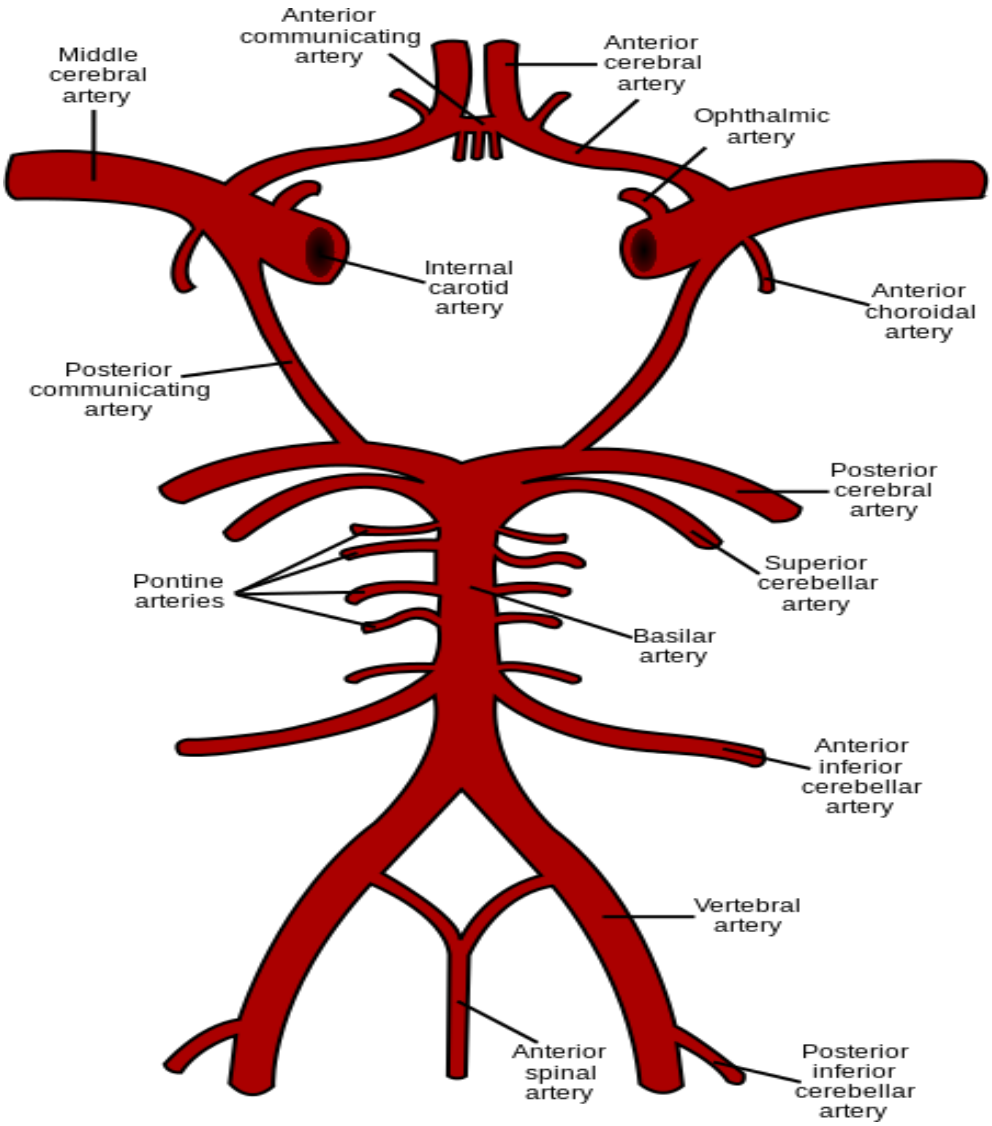
The internal carotid artery (ICA) starts at the level of thyroid cartilage at the carotid sinus at the bifurcation of the common carotid artery. It gives no branches in the neck, it runs in the neck till the skull base and then passes through the foramen lacerum and enter the carotid canal then runs through the cavernous sinus and finally divides into middle and anterior cerebral artery.

Anterior Cerebral artery (ACA) and the larger Middle cerebral artery (MCA).

The first branch of the ICA is Ophthalmic artery which feeds the eye and other orbital tissues. Next artery from the ICA is the Posterior communicating artery (PoCA). It joins Posterior Cerebral Artery (PCA) at its first division. The anterior choroidal artery emerges from the ICA's final section.

The ACA goes horizontally and enters the interhemispheric fissure medially, anastomoses with the opposite side through the anterior communicating artery (AoCA), bends along the genu of the corpus callosum, and supplies blood to the cerebral hemisphere medially and anteriorly.

FIGURE 1: CIRCLE OF WILLIS



The MCA enters the sylvian fissure and separates into 2-4 branches that feed the lateral portions of the cerebral hemisphere. The lenticulostriate arteries extend from the proximal MCA (M1 segment) and serve the caudate nucleus, internal capsule posterior limb, neighboring corona radiata, outer globus pallidus, and putamen. In the sylvian fissure, MCA is divided into superior and inferior divisions, with the superior division supplying the frontal and parietal cortex and the inferior division supplying the temporal cortex and the parietal lobe.

In the transverse foramina of the sixth to second vertebrae, the vertebral artery, a branch of the subclavian artery, go upwards. It joins the opposing vertebral artery at the pontomedullary junction to produce the basilar artery. The posterior and anterior spinal arteries, the posterior inferior cerebellar artery, and minor penetrating arteries to the medulla all originate from the vertebral artery. The brainstem, cerebellar hemisphere posterior and inferior surface, and inferior vermis all get supplied from branches of the posterior inferior cerebellar artery.

In the interpeduncular cistern, the basilar artery ascends and separates into two PCA at the Ponto-midbrain junction. The basilar artery branches off into the anterior inferior cerebellar artery, which supplies blood to the brainstem, rostral cerebellum, cochlea, and vestibule. The superior cerebellar artery branches out to the upper part of the cerebellar hemisphere, the dentate nucleus, and the vermis. Near the third cranial nerve The PCA wraps around the midbrain and serves the temporal and occipital lobes' inferior regions. Many tiny perforating arteries nourish the midbrain, thalamus, hypothalamus, and geniculate bodies from the proximal section of the PCA.

Sometimes PoCA is direct continuation of PCA in around 15% of people, and its major blood supply is from the ICA rather than the basilar artery.

Collateral blood supply to the brain

Collateral circulation is crucial in acute ischemic stroke because it keeps blood flowing to the tissue that is at threat of becoming ischemia and hence increases the rate of successful recanalization without haemorrhagic change. Well-developed collateral circulation has been linked to a lower infarct volume and a better long-term neurological result, and it goes away quickly if successful recanalization is established. Higher recanalization rates, lower infarction volumes, and better neurological outcomes are associated with good collateral status.[20]

ICA normally supplies the anterior 2/3rd of the same side cerebral hemisphere. Because there is little blood mixing via the PoCA, the PCA, basilar, and vertebral arteries supply the posterior course. However, distal to obstruction of main arteries in the neck and head, collateral blood flow to the brain can form in a variety of ways. The actual pattern of collateral blood flow is determined by where the primary blood vessels are obstructed, as well as which collateral channels are anatomically available and disease-free in an individual.[21]

Collateral blood flow development

When the main conduits fail, the cerebral collateral circulation is the alternative network of vascular channels that sustains cerebral blood flow. Extracranial and intracranial blood vessels make up collateral blood vessels, which include the facial, maxillary, middle meningeal, and occipital arteries. The primary pathway comprises the Willis circle, whereas secondary pathways are pre-existing collateral channels that do not ordinarily feed the area but arise in the situation of altered cerebral hemodynamic following an ischemic stroke. The ocular artery and leptomeningeal anastomoses with Dural arterioles and Parenchymal anastomoses are examples of secondary routes.[22]

The circle of Willis is formed by the proximal parts of the two ACAs, which are connected by the ACoA, and the proximal parts of the two PCAs, which are connected by PoCA to the distal ICAs.

Several pathways are involved in revascularization following a vascular blockage. Hypoxia causes 'angiogenesis,' or the sprouting of endothelial cells to form capillary networks: hypoxia activates hypoxia-inducible factor 1 and downstream transcription factors like vascular endothelial growth factor, which bind to endothelial cells and signal them to proliferate, migrate, and eventually form new vessels. Endothelial cells are active during post-stroke angiogenesis, and they collaborate with smooth muscle cells and pericytes to generate functional and mature arteries. Arteriogenesis, the induced formation of new vasculature induced by fluid shear stress after vascular stenosis or occlusion, is another revascularization pathway in ischemic stroke. Due to the proliferation of endothelial and smooth muscle cells, increasing shear stress causes the creation of extensive collateral arteries. Pre-existing arterioles redistribute blood flow by interconnecting high-perfusion and low-perfusion locations after the hemodynamically important stenosis or occlusion occurs, raising shear stress in pre-existing arterioles and contributing to the creation of collateral arteries. The collateral circulation's strength deteriorates with age and other vascular comorbidities, such as hypertension and diabetes, making it more common in people with these illnesses.[20] (FIGURE 2)

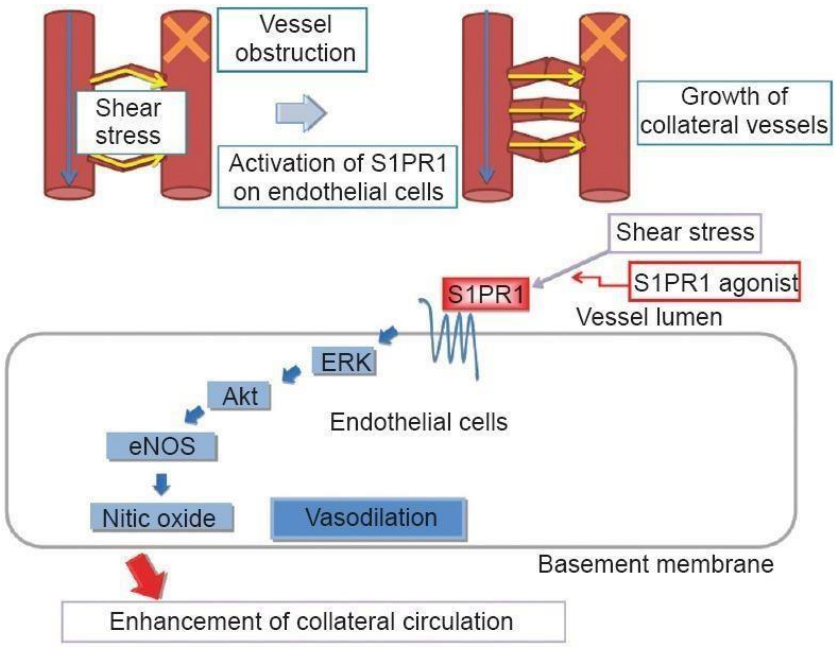


FIGURE 2: MECHANISM OF FORMATION OF COLLATERAL CIRCULATION

Vessel occlusion increases fluid shear stress, consequently up regulating and activating sphingosine-1-phosphate receptor 1 (S1PR1) and leading to the growth of collateral vessels presumably through the phosphorylation of extracellular signal-regulated kinases (ERK), protein kinase B (Akt), and endothelial nitric oxide synthase (eNOS) activation.[20]

Venous drainage

Inside the cranial cavity, the venous compartment includes around 70% to 80% of the circulatory volume. The cerebral venous system is separated into two parts: superficial and deep venous system.

The superficial vein system drains both cerebral hemispheres' cortical surfaces. According to their region, superficial veins are divided into four groups: superior sagittal sinus, sphenoparietal sinus, and cavernous sinus, inferior sagittal sinus, and Galen vein, as well as sinus tributaries. The deep system includes the deep cortical draining veins, the lateral sinus, straight sinus, and sigmoid sinus, which are responsible for the drainage of the hemispheres' core structures, basal ganglia, corpus callosum, limbic system, and thalamus.

Both systems drain into the internal jugular veins.

The cerebral venous system differs significantly from the cerebral artery system in terms of structure. To begin with, tiny veins and venules lack encircling smooth muscle cells. As a result, they are unable to constrict as strongly as arteries. The venule plays an important role in cerebrovascular resistance. The veins can be readily squeezed and flattened by high ICP under pathological circumstances. Increases in central venous pressure or intracranial venous pressure can cause the hydrostatic pressure of upstream cerebral veins to rise, reducing blood outflow. The blood flow via cerebral veins is frequently in the same direction as the blood flow through nearby arteries.

Second, unlike arteries, brain veins have weak walls and no valves to prevent venous blood from flowing backwards. Because arteries have higher blood pressure and faster blood flow than veins, the risk of thrombosis in veins is substantially higher.

For brain homeostasis, there must be a balance between arterial blood influx and venous outflow.

Brain ischemia events, infarction, and venous bleeding, all of which are endpoints of increased cerebral venous pressure and have adverse consequences on the homeostatic environment, occur in roughly 10% to 75% of individuals with cerebral venous hypertension.

When venous flow is reduced while arterial flow is increased, venous congestion can develop, leading to catastrophic consequences such as capillary blockage, collapse, or bleeding.[23]

RISK FACTORS FOR STROKE

I. Unmodifiable riskfactors

- Age
- Sex
- Race
- Family history
- Previousstroke

II. Majormodifiableriskfactors

- Atrialfibrillation
- Hypertension
- Isolated systolic hypertension
- Diabetes mellitus

- Transient ischemicattacks
- Smoking
- Blood lipids
- Alcohol
- Obesity
- Oral contraceptives
- Cardiovascular heart disease
- Socioeconomic status

I. Unmodifiable risk factors

a. Age

Ageisthesinglemostpowerfulriskfactorforcerebralinfarction.Sincetheincreasewithageisexponential, Aging is the most robust non-modifiable risk factor for incident stroke, which doubles every 10 years after age 55 years. Approximately three-quarters of all strokes occur in persons aged ≥65 years. As the number of people aged ≥ 65 years is projected to grow, the number of incident strokes in older adults is expected to rise.[24]

b. Sex

Males suffer from stroke 1.25 times more commonly than females, who have greater mortality than men for stroke each year.[25]

c. Race

There is generally a higher incidence of all stroke types and cerebral infarction in blacks. [25]

d. Heredity

Increased incidence of stroke is noted in families. [25]

e. Previousstroke

The recurrence rate of cerebral infarction is 10-30%. The first 6 months is theperiod of highest risk. Hypertension, Diabetes and Smoking increase the risk, while aninfarctionofundeterminedcauseisassociatedwithdiminished risk. [25]

II. Modifiableriskfactors

a. Hypertension

After age, hypertension is the most powerful risk factor for cerebral infarction.Bothsystolicanddiastolicpressuresareimportant.Sexdifferencesarenotprominent in analyses of the effects of hypertension on stroke. Prolonged treatment of diastolic BP toproduce a fall of 6mm Hg decrease the stroke risk by 40% and the benefits occur within 3years [26]

b. DiabetesMellitus

Though variable, the evidence now supports diabetes as a risk factor for stroke.Impaired glucose tolerance may be a risk factor and an elevated glycosylated hemoglobinmay be found in upto 42% patients with cerebral infarcts not previously known to havediabetes.[27]

c. Smoking

The risk of stroke increased as the number of cigarettes smoked increased. The relative risk of stroke in heavy smokers (>40 cigarettes per day) was twice that of light smokers (fewer than ten cigarettes per day). Lapsed smokers developed stroke at the same level as nonsmokers soon after stopping. Stroke risk decreased significantly by two years and was at the level of nonsmokers by five years after cessation of cigarette

smoking. [28]

d. Alcohol

The effect of alcohol on cerebral infarction has two aspects. These are suddenheavy (binge) drinking and chronic consumption. There is evidence for an associationbetween sudden heavy drinking and the onset of cerebral infarction in young adults[29].

e. Blood lipids

Dyslipidemias increase the risk of stroke by 1-2 times. There is a higher incidence in patients with low level of high density lipoproteins (HDL) and high levels of low density lipoproteins(LDL) and triglycerides(TG).[30] The 20-30% relative risk reduction in stroke that occurs within 1-2 years aft institution of statins is due to its pleotropic effect which improves the endothelial function, Plaque stabilization, anti-thrombotic properties, diminished inflammation and improved hemorheological environment.

f. Cardiovascular diseases

According to Framingham study, ―ECG changes of LVH increases the risk of ischemic stroke by tenfold; nonspecific ST and T changes by four-fold and congestive cardiac failure by nine-fold. [31] Mitral valve prolapse, prosthetic valves, endocarditis, peripheral vascular disease, MI, cardiac arrhythmias are the risk factors for embolic stroke. [32]

g. Oral contraceptives

The higher estrogen dosage significantly increased the risks of total stroke[33]

h. Obesity-

In the study by Whitehall et al showed that ―body mass index (BMI) was predictive of stroke in both smokers and non-smokers. It was estimated that having a BMI above 25kg/m2 and

smoking accounts for 60% strokes in up to 65years [34]

The Framingham Stroke Risk Profile, a continuously updated, well-known, and widely used score, combines stroke predictors such as age, systolic blood pressure, antihypertensive therapy, diabetes mellitus, cigarette smoking, left ventricular hypertrophy by ECG, and the presence of cardiovascular disease (coronary heart disease, peripheral vascular disease, and congestive heart failure), and can be used to estimate 10-year stroke risk stratified by sex.[35]

CLASSIFICATION OF STROKE

1) According to the pathogenesis

A. Ischemic strokes

1. With cerebral infarction

1.1. Cerebral thrombosis with or without atherosclerosis

1.2. Cerebral embolism

1.3. Cerebral venous thrombosis

1.4. Arteritis

1.5. Coagulopathy disorders

1.6. Cerebral anoxia

1.7. Dissecting aneurysm of brachiocephalic vessels

1.8. Angiographic complications

2. With cerebral ischemia

2.1. Transient ischemic attacks

2.2. Local embolism from proximal atheromatous plaques

2.3. With cardiac arrhythmias

2.4. Arterial hypotension

2.5. Vasospasm with migraine

2.6. Idiopathic types (drugs and oral contraceptives)

B. Haemorrhagic stroke

1. Hypertensive cerebral haemorrhage
2. Ruptured aneurysm
3. Ruptured angioma
4. Trauma
5. Complications of anticoagulant therapy

C. Stroke of undetermined origin

1. Multi infarct dementia in lacunar syndrome
2. Fibro muscular disease
3. Buerger disease
4. Aortic arch syndrome

2) Etiological classification

1. Atherosclerotic thrombosis
2. Transient ischemic attacks
3. Embolism
4. Ruptured or unruptured saccular aneurysm
5. Arteritis
6. Cerebral thrombophlebitis
7. Amyloid angiopathy
8. Dissecting aortic aneurysm

3) Clinical classification

I. Arterial territories (Oxfordshire stroke subtype classification)

i. Anterior circulation syndrome

1. Anterior cerebral artery syndrome (ACA)
2. Middle cerebral artery syndrome (MCA)

ii. Posterior circulation syndrome

1. Vertebrobasilar artery syndrome
2. Posterior cerebral artery syndrome [36]

II. Clinical manifestations

1. TIA: Focal neurological deficit with complete recovery within 24 hrs.
2. Reversible ischemic neurological deficit (RIND): Neurological deficit with complete recovery within a period of one week.
3. Evolving stroke: Gradual stepwise development of neurological deficit.
4. Complete stroke: sudden onset persisting neurological deficit not progressing beyond 96hrs. [37]

1) According to the pathogenesis

A. Ischemic strokes

1. ATHEROTHROMBOSIS CAUSING CEREBRAL INFARCTION

Minor symptoms or one or more transitory episodes of focal neurologic impairment can occur before a stroke. There are various ways that thrombotic stroke syndrome arises. Although there may be a single incident, the entire stroke usually happens in a matter of minutes or hours. Atheromatous plaques occur more frequently near the cerebral arteries' branching points and curvatures. A "stuttering" or intermittent progression of neurological impairments is the distinctive characteristic.

It's possible that the deficits are episodic and develop over time in a slow stroke.

The most frequent areas are:

1. In the internal carotid artery where it origin from the common carotid.
2. At the confluence of the vertebral arteries in the cervical region where basilar artery is formed.
3. Primary bifurcations or at the stem of middle cerebral arteries.
4. At the proximal posterior cerebral arteries as they loop around the midbrain.
5. As proximal anterior cerebral arteries proceed anteriorly and curve across the corpus callosum.

The endothelial plaque or thrombus blocks the lumen of a large intracerebral vessel, such as the MCA, and prevents blood flow to the regions served by the artery.

Atherosclerosis occlusion of a more proximal vessel, such as the distal carotid artery, causes infarction in the zone between the main branches of the internal carotid circulation, which is the most vulnerable to diminished blood flow leading to watershed infarct.

Atherothrombosis in a proximal artery that acts as a nidus for an embolus- artery to artery embolism

2. CEREBRAL EMBOLISM:

Cerebral embolism is the most common cause of ischemic strokes, and of all the forms of stroke, it develops the fastest, "like a bolt from the blue."

Within seconds, the full-fledged image emerges. The rapid onset of the stroke and the absence of prodromal symptoms strongly suggest embolism.

The embolic can be a component of a thrombus within the heart that has broken away - "cardio-embolic."

A source of the clot can originate from,

1. Any clots which are formed in the Systemic venous system like in deep vein thrombosis (DVT) can dislodge and they pass through an aperture in the heart walls,
2. The distal end of a thrombus within the lumen of an occluded or severely stenotic carotid or vertebral artery,
3. An embolus that originates from large atheromatous plaques in the aorta.

Thrombotic or infected material (endocarditis) which are attached to mitral and aortic valves detached from the aortic or mitral heart valves, as well as clots developing on prosthetic heart valves, are further causes of embolism.

Only in rare circumstances can embolism produced by fat, tumour cells (atrial myxoma), fibrocartilage, amniotic fluid, or air enter makes the differential diagnosis of stroke.

The embolus is generally stopped at a bifurcation or other natural constriction of an intracranial vessel's lumen.

The middle cerebral artery's areas, notably the superior division, are the most affected.

Because embolic blockage develops quickly, there is no time for helpful collateral inflow to form which is opposite to thrombotic stroke.

3. <u>CEREBRAL VENOUS THROMBOSIS:</u>

A venous infarct stroke is caused by the occlusion of cortical veins that are tributaries of the dural sinuses.

Taking birth control pills, as well as postpartum and postoperative conditions, which are commonly characterized by thrombocytosis and hyperfibrinogenemia, are risk factors for venous thrombosis.

Cancer (especially pancreatic and colon cancers, as well as other adenocarcinomas), cyanotic congenital heart disease, sickle cell disease, antiphospholipid antibody syndrome, protein S or C deficiency, and primary or secondary polycythemia are all examples of hypercoagulable disorders.

A stroke in a patient with any of these systemic diseases should raise suspicions of venous thrombosis.

Multiple haemorrhagic infarctions in one hemisphere without a cause of embolism or atherothrombosis should be suspected of cortical vein thrombosis.

4. ARTERITIS:

Immunologic analyses demonstrated that an inappropriate deposit of complement-fixing immune-complex on the endothelium occurs in the majority of these events, resulting in inflammation, vascular blockage, or rupture with minor haemorrhage.

5. HYPERCOAGULABLE STATES

Fibrin and platelets make up nonbacterial thrombotic endocarditis, and they're loosely linked to the mitral and aortic valves, as well as the surrounding endocardium. Cerebral embolism is frequently caused by them.

There are numerous minor infractions in the brain as a result of extensive fibrin thrombi in tiny arteries seen in DIC. Cerebral bleeding can be fairly substantial in some situations, similar to a primary hypertensive haemorrhage.

Antiphospholipid Antibody Syndrome, Thrombotic Thrombocytopenic Purpura, Polycythaemia Vera, Thrombocytosis, and Thrombocythemia are some of the other diseases.

6. CEREBRAL ANOXIA:

This infarction occurs after cardiac arrest or other persistent hypotension or hypoxia.

The deep nuclei, or the most metabolically active parts of the cerebral hemispheres, are similarly affected by widespread cortical infarction.

When blood supply to the cerebral hemispheres is diminished, regional infarctions, also known as watershed infarctions, are more likely to develop in the areas with the lowest blood flow, which are located between the major surface arteries.

Pure hypoxia-anoxia without hypotension causes a different form of damage in places that are vulnerable to low oxygen levels, primarily the hippocampi.

The most frequent neurologic consequences in Sickle Cell Disease are large and small ischemia lesions of the brain.

7. DISSECTION OF THE CERVICAL AND INTRACRANIAL ARTERIES:

Internal Carotid Artery Dissection: The ischemic manifestations consist of transient attacks in the territory of the internal carotid, followed frequently by the signs of hemispheral stroke, which can be sudden or progress slowly over minutes to hours or days in a fluctuating or stepwise pattern.

Patients with intracranial arterial dissection have experienced abrupt strokes that indicate embolic infarction, while a small percentage had subarachnoid haemorrhage.

8. ANGIOGRAPHIC COMPLICATIONS:

During cerebral arteriography, emboli may form at the catheter's tip, or movement of the catheter may displace atheromatous material from the aorta, carotid, or vertebral arteries, causing some of the strokes.

B. CEREBRAL ISCHEMIA:

TRANSIENT ISCHEMIC ATTACKS:

'A brief episode of neurological dysfunction caused by focal brain or retinal ischaemia, with clinical symptoms typically lasting less than 1 hour, and without evidence of acute infarction'[38]. 20 percent

of infarcts that follow TIAs occur within a month after the first attack, and approximately 50 percent within a year [39].

Most cases are intimately related to vascular stenosis and, usually, to ulceration as a result of atherosclerosis and thrombus formation

TABLE 1: DIFFERENCES BETWEEN VARIOUS TYPES OF STROKE

Type	**Thrombosis**	**Embolism**	**Haemorrhage**
Incidence		Most Common cause of ischemic stroke	Least common than thrombotic and embolic
Age	Usually Old age	Usually Young	Usually young
Causes	Thrombus superimposed on atherosclerotic plaques.	Cardio-embolic atrial fibrillation, Cardiac mural thrombi, Myocardial dysfunction, valvular disease, atheromatous plaques in the aorta, tumour cells in atrial myxoma	Spontaneous, Uncontrolled and chronic hypertension, Ruptured aneurysms and vascular malformations
Common sites	1. ICA at the origin of CCA 2.Cervical part of vertebral arteries and at their junction to form	The territory of MCA, a direct extension of the internal carotid artery Particularly the superior division of MCA.	Intraparenchymalhaemorrhage d/t HTN-basal ganglia, thalamus, pons, cerebellum SAH-saccular/berry aneurysms.

	basilar artery 3. Stem/bifurcation of MCA. 4. In the proximal PCA and ACA.		
Clinical presentation	Varied Stuttering/Intermittent progression. Step like fashion. stroke is preceded by minor signs or TIA Watershed infarcts.	Rapid progression "Like a bolt out of the blue" Lack of prodromal symptoms. No Collateral circulation is formed. Seizures	Apoplexy a/w vomiting, headaches, seizures, decreased level of consciousness.
Time of onset	Subacute, began during sleep or within1 hour of awakening suggested thrombosis with atherosclerosis	Hyperacute rapid onset of symptoms and a lack of warning symptoms	Hyperacute Occurs at the height of emotion/excitement.
Weakness	Slow stroke Intermittent progression of	Full at onset, Rapid progression.	Progressing over hours with increasing size of the hematoma.

	neurological deficits over several hours or a day. Episodic deficits.	Full blown picture evolves within seconds.	
Headache	+/-	-	+++
Seizures	+/-	+	++
Progression	Can progress over 72hours	High at onset	Upto 6 hours

PATHOGENESIS OF STROKE

Cerebrovascular disorders are due to either ischemia or haemorrhage within the central nervous system. The site and size of the lesion depict the neurological deficit.

Ischemic stroke is more commonly secondary to cerebral artery occlusion due to thrombosis or embolism. Atherosclerotic or thromboembolic arterial occlusions account for around 80- 85% of all stroke cases. Cerebral atherothromboembolism involves predominantly the middle cerebral artery, followed by the posterior cerebral artery, anterior cerebral artery and basilar artery, which are involved less commonly.

Haemorrhage may be epidural, subdural, subarachnoid, intraparenchymal or intraventricular in location. Haemorrhage could result from arterial hypertension, saccular aneurysm, arteriovenous malformations, blood dyscrasias, vasculitis, sympathomimetic drugs, cerebral amyloid angiopathy, trauma and neoplasms. [40]

Pathophysiology of cerebral infarction

The pathogenesis of cerebral infarction can be separated into two sequential processes.

1. Vascular and haematological events that causes reduction of local cerebral blood flow leading to loss of supply of oxygen and glucose.
2. Ischemia induced alteration of cellular chemistry and metabolism leading to necrosis of neurons, glia and supportive brain cells.

The molecular outcome of brain ischemia is changing in cell signalling (neurotransmitters, neuromodulators) in signal transduction, in metabolism and in gene regulation/expression

Cerebral blood flow at rest in the adult is approximately 50-55ml/100gm/min. The cerebral microcirculation distributes blood to the brain. Any decrease in blood supply to the microcirculation leads to cerebral ischemia. The magnitude of flow reduction is a function of collateral blood flow that depends on individual vascular anatomy and the site of occlusion.

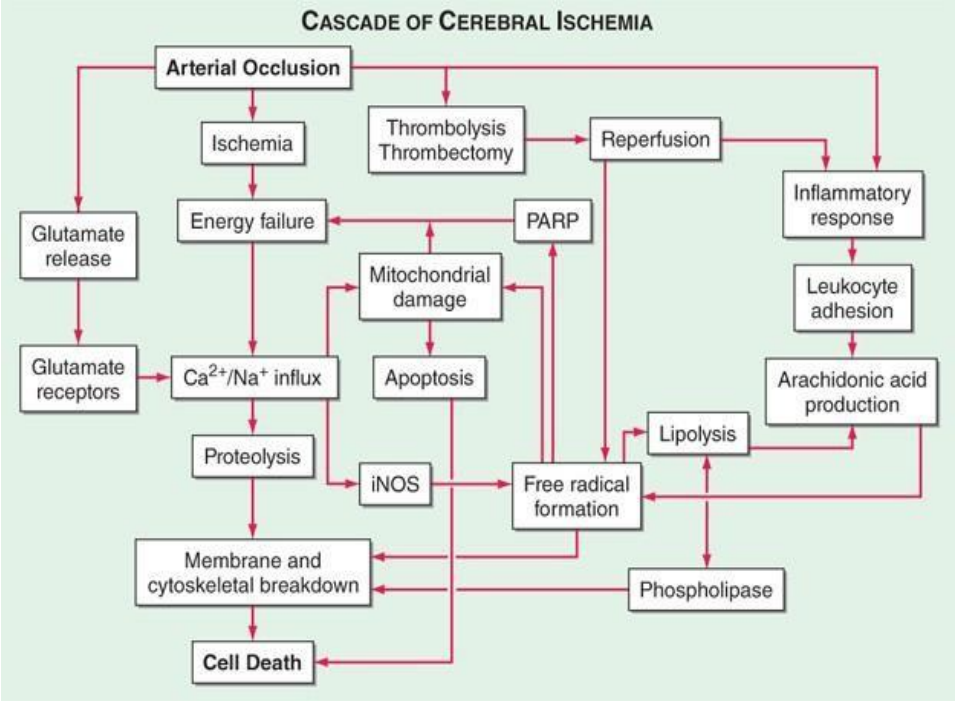
Complete interruption of cerebral blood flow suppresses electrical activity within 12-15 seconds, inhibits synaptic excitability of cortical neurons after 2-4 minutes and inhibits electrical excitability after 4-6 minutes. As the blood flow reduces to 18ml/100gm per minute, the brain reaches a threshold for electrical failure. The neurons still have the capacity for recovering though they are not functioning normally. When the blood flow reduces to 8ml/100gm per minute, membrane failure occurs. This can result in cell death. Fall in cerebral flow to zero causes death of brain tissue within 4-10 minutes.

The upper threshold of blood flow, i.e., 18ml/100gm per minute and lower threshold of blood flow, i.e., 8ml/100gm per minute mark the limits of the ischemic penumbra. The area of misery perfusion or the ischemic penumbra is the area of the ischemic brain between these two flow thresholds in which there are some neurons that are functionally silent but structurally intact and potentially salvageable. This ischemic penumbra will eventually infarct if blood flow is not restored. Thus, saving the penumbra is the goal of thrombolytic therapy and newer therapies under investigation.

Cellular death via two distinct mechanisms:

1. A necrotic pathway: cellular cytoskeletal breakdown is rapid, principally because of failure of energy of the cell.
2. An apoptotic pathway: where programmed cell death occurs.
3. Ferroptosis: A newly discovered iron-dependent regulated cell death [41]

FIGURE 3: CASCADE OF CEREBRAL ISCHEMIA



CARDIOEMBOLIC STROKE

Out of all ischemic strokes, Cardio embolism is responsible for 20%, mainly because of dislodgement of thrombus formed on the wall of the atrium or ventricle or mitral or aortic valves. Embolic strokes occur during exertional activity and are sudden in onset, having maximum

neurologic deficit at the onset. The fragmentation of thrombus or quick lysis produces only transient ischemic attack (TIA).

Embolism usually occurs in PCA territory and middle cerebral artery; less commonly, it involves the anterior cerebral artery (ACA) territory.

The stem of the MCA can be blocked by large emboli of 3-4mm. A tiny embolus can obstruct the passage of penetrating arterial branches. The collateral circulation inside the vascular territory indicates the intensity of an infarct. The important causes of cardioembolic stroke are atrial fibrillation, ischemic cardiomyopathy, MI, prosthetic valves, and RHD.

Artery to artery embolism appears to be the dominant vascular mechanism causing ischemia. It is secondary to distal embolization to intracranial arteries from thrombus on atherosclerotic plaques. Atherosclerosis of Carotid bifurcation is the most common source of artery-to-artery embolus. Arch of aorta, common and internal carotid arteries are other sources.

An estimated 5% of ischemic stroke are due to carotid atherosclerosis and the risk of stroke increases with the increase in carotid narrowing.

It is estimated that the risk of a recurrence is about 15% per year following stroke or TIA from intracranial atherosclerosis.

Internal carotid dissection, vertebral artery dissection, and even dissection of vessels beyond the circle of Willis are also prevalent causes of embolic stroke in patients under 45 years old. It is usually painful and occurs in several hours or days before the stroke. [17,42]

Cerebral infarction is not a single disease, and distinguishing between many clinical, pathophysiologic, and etiologic subgroups may be necessary for proper patient management.

The most prevalent cause of ischemic stroke is embolism, which can result from either an atheromatous arterial lesion (artery to artery thromboembolism), Cardio embolism condition like

atrial fibrillation, valvular heart disease and prosthetic valve replacements. Out of all atrial fibrillation is still a major cause for embolic stroke.

In the absence of embolism, in situ obstruction of an extracranial or cerebral artery may be implicated.

1. When the occluded artery is a small perforating branch with no collateral supply, seen in a lacunar infarct.
2. When a large-artery blockage causes hemodynamic failure in the corresponding territory due to the absence of functional anastomoses (Hemodynamic infarction).
3. Finally, blood abnormalities (such as coagulation disorders) might cause ischemic stroke. Anemia, hyper viscosity, anemia, leukemia, and related disorders. [43]

Intracranial atherosclerosis plays a major role in Asians and to a lesser extent in blacks. In whites, extracranial atherosclerosis causes artery to artery embolism. However, this distinction is valid mainly for anterior circulation. Recent research has revealed that atherosclerosis of the intracranial vertebral or basilar arteries is a major source of posterior circulation infarcts. [44]

CLINICAL FEATURES OF ISCHEMIC STROKES

Anterior Circulation Stroke: Internal carotid artery and its branches supplies the anterior part of brain.

A. MIDDLE CEREBRAL ARTERY:

The MCA territory is the arterial territory most frequently affected by ischaemic stroke. MCA infarcts can be divided into

1. Superficial (involving underlying white matter and the cortex)
2. Deep (involving the internal capsule, the basal ganglia and the deep white matter)
3. Combined MCA infarcts are mainly caused by cardio embolism, internal carotid artery (ICA) thrombosis, dissection, or embolism.

Whether the left (dominant for language) or right (non-dominant) hemisphere is involved influences the clinical presentation. In left hemispheric stroke oral and written language disturbances dominate, in right-sided strokes neglect is almost always present.

The lateral surface of the hemisphere is supplied by the cortical branches except for

1) The lower temporal and occipital pole convolutions which is supplied by the PCA.
2) ACA supplies the frontal pole and strip of the superomedial border of the parietal and frontal lobes.

FIGURE 4: DIAGRAM SHOWING LATERAL ASPECT OF CEREBRAL HEMISPHERE SHOWING DISTRIBUTION AND BRANCHES OF MIDDLE CEREBRAL ARTERY

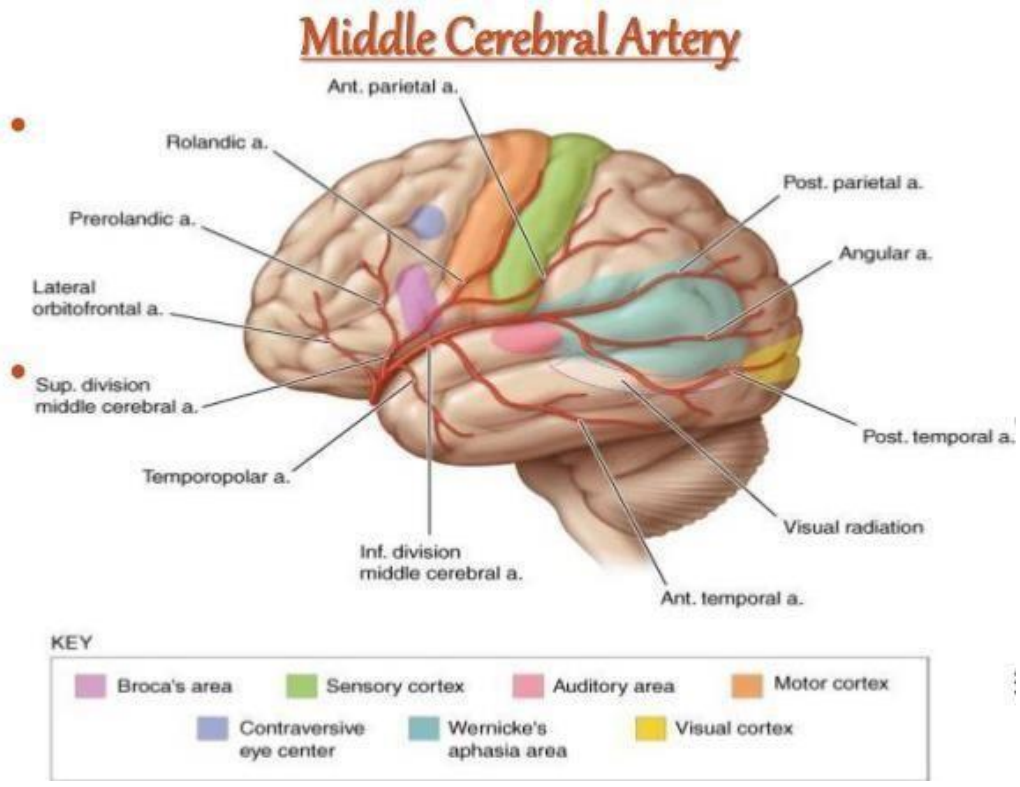
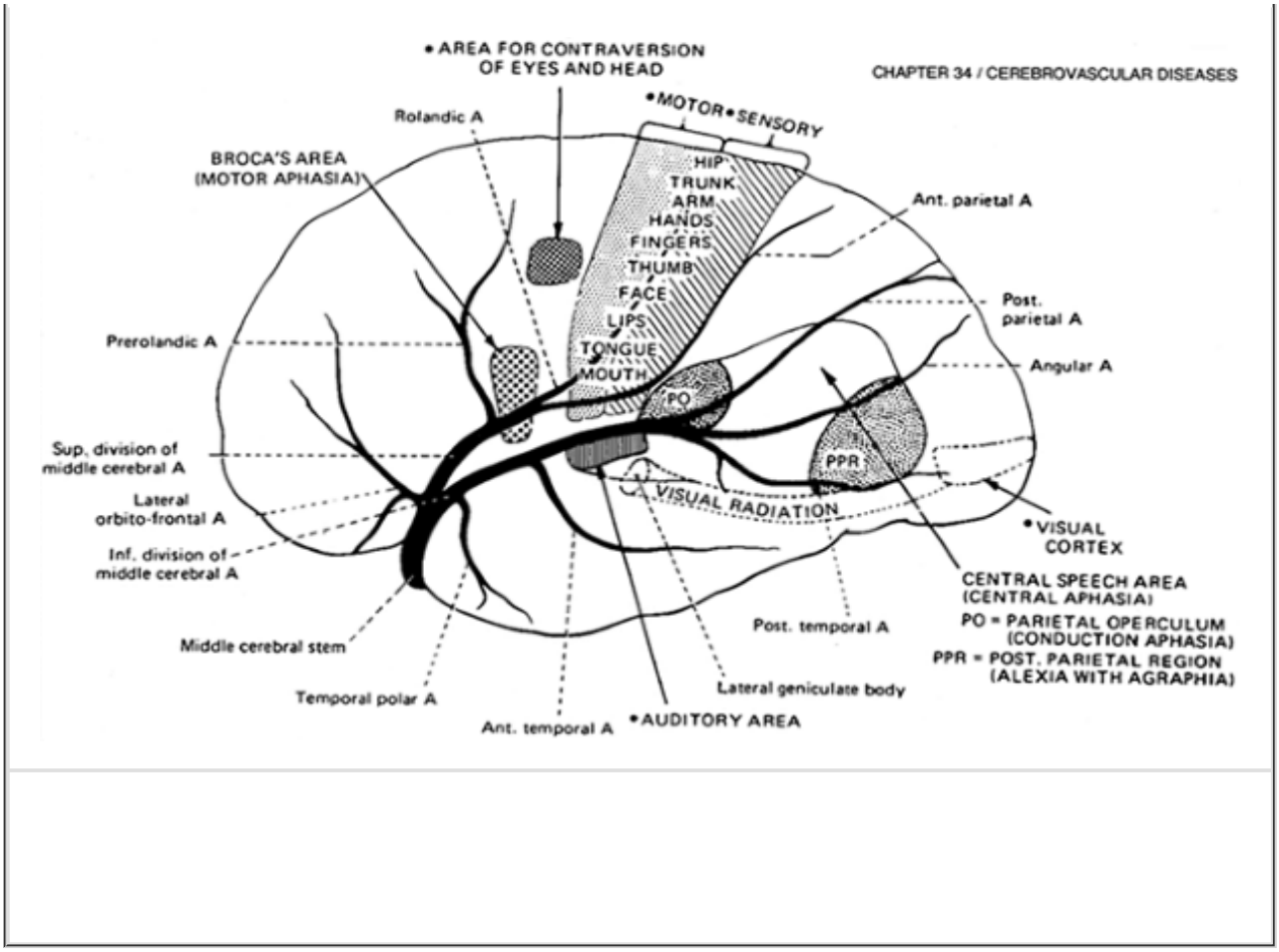


FIGURE 5: MCA DIVISIONS



Signs and symptoms of MCA territory involvement:

FUNCTIONAL DEFICITS:

1. **Large middle cerebral artery infarcts:** large infarcts cover at least two sub territories of the MCA (deep or superficial, posterior or inferior and anterior or superior)

They are usually caused by cardio embolism, ICA occlusion or dissection

They have an unfavourable prognosis and produce a severe neurological deficit:

- gaze deviation
- contralateral hemiplegia
- global aphasia
- neglect with anosognosia

- hemianopia
- Reduced consciousness.

a) Middle cerebral artery anterior or superior division infarcts:

- contralateral hemiparesis with predominant faciobrachial deficit,
- hemisensory loss
- gaze deviation towards the lesion
- Decreased visual exploration toward the opposite side.
- Left -sided infarcts also produce a non-fluent aphasia, ranging from mutism to typical Broca's aphasia and to articulatory syntactical and naming difficulties.
- Bucco-facial apraxia

b) Middle cerebral artery posterior or inferior division infarcts

- Hemisensory loss is common and visual field defects (homonymous hemianopia or upper quadrantanopia) are usually present.
- Motor deficits are absent or mild.
- In left -sided strokes, fluent aphasia predominates.
- The most severe form is Wernicke's aphasia with anosognosia and behavioral disturbances including persecutory delusions. In right hemispheric stroke, neglect, anosognosia, and
- An agitated confusional state usually occurs.
- Constructional apraxia can be present.

c) Anterior choroidal artery infarcts

- Pure motor deficit followed by motor and sensory dysfunction.
- The classical '3H' syndrome composed by hemiparesis, hemihypesthesia, hemianopia
- Isolated hemianopia
- pseudobulbar palsy.

TABLE 2: clinicalmanifestationsproducedbyinfarctioninmiddle cerebral arteryterritoryandthecorrespondingregionsofdamage [49]

Signsandsymptoms	Structuresinvolved
contralateral Paralysisoftheface,armandleg	Somatic motor area in precentral gyrus for faceand arm and the fibersdescending from the leg area which enterthecoronaradiata.
the contralateral Sensoryimpairment over the face,arm and leg (crude/fine touch, vibration, proprioception, two-pointdiscrimination, stereognosis, tactile localization,graphasthesia)	Face and arm area in somatosensory region, and thalamoparietal extension
1. motor/Brocaspeech	Broca areaandadjacentmotorarea of the dominanthemisphere
2. "Central"aphasia,worddeafness,anomia,jargonspeech ,alexia, agraphia, acalculia, finger agnosia, right-leftconfusion (the last four comprise the Gerstmannsyndrome)	Central language area andparieto-occipital cortex of thedominant hemisphere
3. Apractagnosia (amorphosynthesis), anosognosia, hemiasomatognosia, unilateral neglect, visual	nondominant hemisphere

coordination problem, imprecise localization in the half of the body field, impaired ability to judge distance, upside-down reading, visual illusions, agnosia for the left half(non-dominant) of external space, “dressing apraxia,” “constructional apraxia,”	of parietal lobe. Loss of topographic memory is usually dueto a nondominant lesion, occasionally to a dominant hemisphere side.
4. Homonymoushemianopia(oftensuperiorto homonymousquadrantanopia)	Optic radiation deep to secondtemporalconvol ution
5. Paralysisofconjugategazetotheoppositeside	Frontalcontraversivefieldor fibersprojectingtherefrom
6. Avoidancereactionofoppositelimbs	Parietallobe
7. Puremotor typehemiplegia	the upper section of the internal capsule's posterior limb and the adjacent corona radiata

MIDDLE CEREBRAL ARTERY – SUPERFICIAL TERRITORY INFARCTS

The Superficial branches of the middle cerebral artery (MCA) originate distal to the origin of lenticulostriate arteries. As they course in the subarachnoid space, they are called pial branches. They supply the cortical, subcortical territory of the MCA after the MCA trunk divide into two

(upper and lower) or three (upper, middle and lower) divisions which in their turn divide into several branches.

When only a distal branch is blocked, MCA pial region infarcts can be small, or they can be rather extensive when the blockage is more proximal at the level of the MCA bifurcation or trifurcation and the collateral system is inadequate. Multiple distal emboli are required since the pial artery network is characterized by extensive anastomoses.

In fact, at least half of patients with MCA pial territory infarct may have angiographic evidence of distal occlusion, indicating embolism, and the majority of angiography normal cases may be attributable to delayed angiography since these occlusions tend to dissipate quickly.

Large-artery disease (>50%), internal carotid artery (ICA) or MCA stenosis or blockage in one-third of the patients, and cardiac disease in one-quarter of the patients are thought to be the causes of embolism. Interestingly, infarcts in the upper division region are more likely to have possible cardiac origins of embolism.

THE DEEP PERFORATORS OF CAROTID SYSTEM TERRITORY INFARCTS:

The deep perforators from the distal ICA or MCA trunk are terminal branches that perforate the basal portion of the cerebral hemispheres, in contrast to the pial artery network. As a result, obstruction of one or more perforators is usually followed by a mild infarct in the corresponding territory. These small deep infarcts are often called 'Lacunar'. However, it should be remembered that lacunar may be caused by non-ischaemic processes such as small haemorrhage or non-ischaemic dilatation of periarteriolar space.

Lacunar infarcts are believed to be caused by occluding the corresponding tiny perforator in situ by micro atheromatous or lipohyalinotic processes associated with persistent arterial hypertension. This assumption appears correct for very small lacunar infarcts (<0.3-0.5 cm) associated with occlusion of one single perforator, but these infarcts are usually asymptomatic[43].

Although small artery disease probably remains a leading etiology, in larger (0.5-1.5 cm or larger) and symptomatic small deep infarcts, other potential causes may have a potential cardiac source of embolism or large artery disease (>50%) ICA stenosis or occlusion, often in the absence of concomitant hypertension.[45]

Embolism to the MCA trunk is a prevalent cause of complete lenticulostriate territory infarction (known as large striata capsular infarcts or extended infarcts of the lentiform nucleus) by occluding the lenticulostriate arteries at their origin while collateral circulation explains sparing of the superficial pial territory.[46]

While it is unclear whether large-artery or cardiac disease is simply coincidental in many patients with small deep infarcts, atherosclerosis of the MCA trunks (or the basilar artery for small paramedian infarcts in the brain stem), which can occlude the origin of deep perforators, has largely been overlooked as a potential etiology of small deep infarcts.

The size of the infarct has a significant impact on the clinical symptoms. Large infarcts may develop impairment that is similar to that seen in superficial MCA territory infarcts.[47] Smaller infarcts are frequently associated with localized contralateral motor or sensory problems (lacunar syndrome). The term lacunar infarction refers to infarction due to occlusion of a small artery (30- 300µm) in the brain, now termed as small vessel stroke. The arteries forming circle of Willis gives rise to 30 to 300 micrometre branches that penetrate the deep gray and white matter of the cerebrum or brainstem. These small arteries can obliterate either by atherothrombotic disease or by lipolinotic thickening. The infarct formed by Thrombosis of these vessels known as lacunes. The size may vary from 3 mm to 2 cm. Hypertension and age are the major risk factors.

The classic lacunar syndromes are:

1. The face, arm, and leg are nearly invariably involved in pure motor hemiparesis caused by an infarct in basis pontis or the posterior limb of the internal capsule.

2. Pure sensory stroke – from an infarct in the ventrolateral thalamus.
3. Ataxic hemiparesis – from an infarct in the basis pontis.
4. Dysarthria and clumsy hand/arm due to infarction in the genu of the internal capsule in the base of the pons.
5. A thrombotic occlusion of a lenticulostriate branch serving the genu and anterior limb of the internal capsule, as well as surrounding white matter of the corona radiata, produces pure motor hemiparesis with motor or Brocas aphasia.

The artery of Heubner from the anterior cerebral artery (ACA) and the anterior choroidal artery from the carotid siphon are not only perforators, but they also supply cortical territories. Thus, the arterial system can compare with that of the MCA, and their etiologic spectrum of infarction is similar.[17]

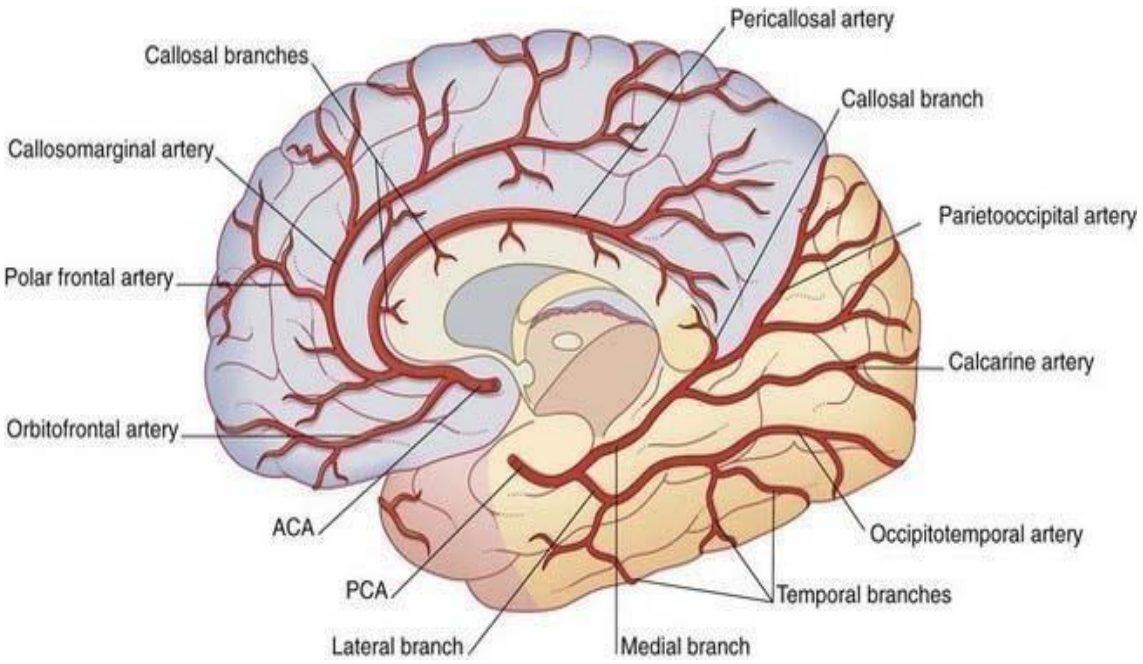
B. <u>Anterior Cerebral Artery (ACA) territory involvement:</u>

Strokes in the anterior cerebral artery (ACA) territory are uncommon (<2% in stroke registries).

The ACA it categorized into two parts:

- Pre-communal (A1) segment; connecting the internal carotid artery to the anterior communicating artery.
- Post-communal (A2) segment; distal to the anterior communicating artery.

FIGURE 6: DIAGRAM SHOWING MEDIAL ASPECT OF CEREBRAL HEMISPHERE SHOWING DISTRIBUTION AND BRANCHES OF ANTERIOR CEREBRAL ARTERY



Signs and symptoms of ACA territory involvement

FUNCTIONAL DEFICITS:

- Left -sided infarcts cause mutism,
- Transcortical motor aphasia,
- Hemiparesis
- Occasionally left –arm apraxia.
- Right-sided infarcts cause acute confusion state, hemiparesis, and motor neglect
- When the precentral gyrus is affected, hemiparesis is more common in the lower limb.
- When the recurrent artery of Heubner, which feeds the internal capsule, is occluded, proportional hemiparesis develops.
- Bilateral infarcts may produce akinetic mutism

- Gait apraxia
- Paraparesis
- Sphincter dysfunction.
- Basal ganglia symptoms, including parkinsonian gait, tremor, and facial dystonia, can be observed in bilateral ACA infarcts

NEUROLOGICAL DEFICITS:

TABLE 3: clinicalmanifestationsproducedbyinfarctioninAnterior Cerebral Arteryterritoryandthecorrespondingregionsofdamage.[49]

Signs and symptoms	Structures involved
1. Paralysis of contralateral foot and leg	Motor leg area in precentral primary motor cortex
2. A paresis of contralateral arm	Motor arm area in precentral primary motor cortex or fibers coming to corona radiata from cortex
3. loss of sensation over toes, foot and leg	Areas for foot and leg in postcentral sensory cortex
4. Urinary incontinency	bilateral Posteromedial part of superior frontal gyrus
5. Contralateral sucking reflex, grasp reflex,"frontal tremor" and paratonic rigidity,	The posterior frontal lobe's medial surface.
6. absence of spontaneity, akinetic mutism (Abulia), slowness, delay,	Uncertain localization—probably superomedial lesion near sub-callosum

whispering, motor inaction, reflex distraction to sounds and sights	
7. Impairment of gait and stance (gait "apraxia")	Inferomedial frontal-striatal
8. Mental impairment (perseveration and amnesia)	Localization unknown
9. Miscellaneous: dyspraxia of left limbs	Corpus callosum
10. Tactile aphasia in left limbs	Corpus callosum
11. Cerebral paraplegia	Motor leg area bilaterally (due to bilateral occlusion of anterior cerebral arteries

Internal Carotid Artery Territory Involvement:

Occlusion of ICA often goes unnoticed because of the competent circle of willis. If the thrombus progresses up the internal carotid artery into the MCA or embolizes it, the symptoms are similar to those of proximal MCA occlusion.[48]

Repeated amaurosisfugax is seen in about 25% of internal carotid artery disease.

Stroke within The Posterior Circulation

PCA infarcts are due to cardio embolism in one-third of cases. Significant vertebrobasilar atheroma with occlusion or artery-to-artery embolism accounts for another one-quarter.

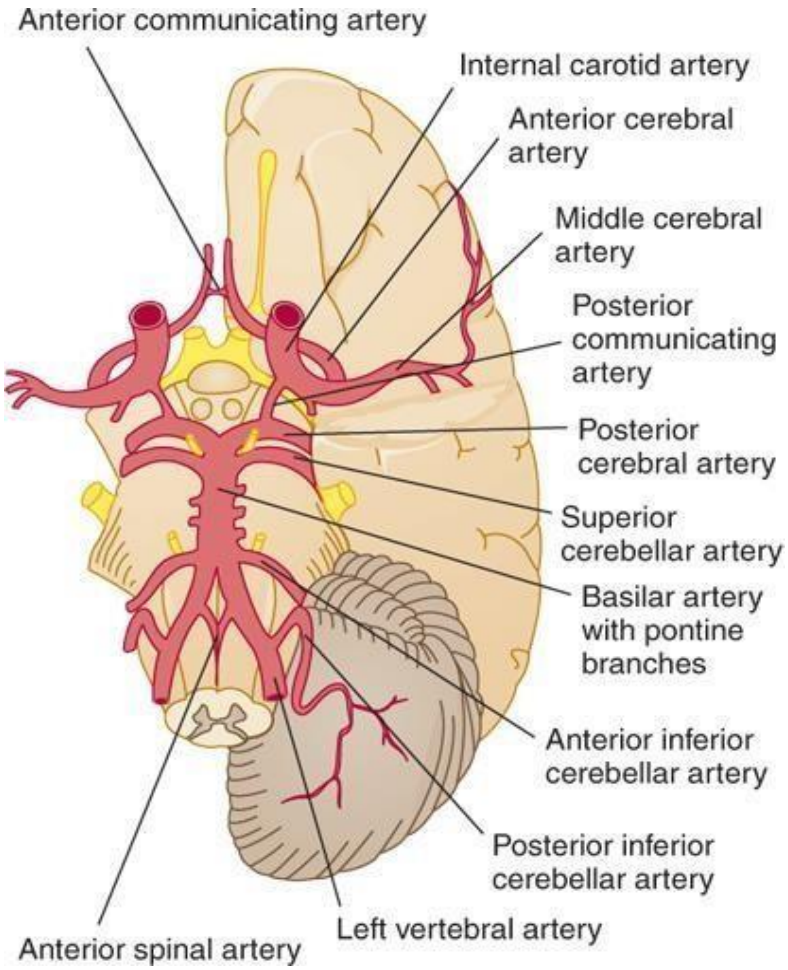
Local PCA stenosis or occlusions are much less frequent.

The occlusion of the posterior cerebral artery involvement leads to two syndromes.

P1 syndrome: Thalamic, midbrain and subthalamic signs.

P2 syndrome: occipital lobe signs, cortical signs, and temporal lobe signs.

FIGURE 7: DIAGRAM SHOWING INFERIOR ASPECT OF THE BRAIN WITH THE DISTRIBUTION AND BRANCHES OF POSTERIOR CEREBRAL ARTERY



Signs and symptoms of PCA territory involvement

FUNCTIONAL DEFICITS:

- Visual field defects
- Hemianopia
- Severe unilateral headache

- ataxia or involuntary movements.
- Transient paresis.
- Hemiparesis in PCA infarcts can be due to infarction of the cerebral peduncle or less frequently to infarction of the anterior segment of the posterior limb of the internal capsule
- Superior quadrantanopia is more common than inferior because the inferior striate cortex is more susceptible to ischaemia due to poor collateral circulation.
- Neuropsychological manifestations: transcortical sensory aphasia or anomic aphasia, alexia with or without agraphia, visual or color agnosia

TABLE4 : clinicalmanifestationsproducedbyinfarctioninposterior cerebral arteryterritoryandthecorrespondingregionsofdamage [49]

Signs and symptoms	**Structures involved**
Central territory	
1. Thalamic syndrome: all modalities of sensory loss, spontaneous pain, dysesthesias, choreoathetosis, intentional tremor, mild hemiparesis, and spasms of hand	Ventroposterolateral nucleus of the thalamusthe in territory of thalamogeniculate artery. Involvement of the adjacent subthalamic nucleus or its pallidal connections results in hemiballismus and choreoathetosis.
2. Thalamoperforate syndrome: • superior branch - crossed cerebellar ataxia. • inferior branch - Claude syndrome crossed cerebellar ataxia with ipsilateral third nerve palsy	dentatorubrothalamic tractand third cranial nerve
3. Weber syndrome— contralateral hemiplegia	oculomotor fascicles in the interpeduncular

and third nerve palsy	cisterns and cerebral peduncle
4. Hemiplegia of contralateral side	involvement of Cerebral peduncle
5. vertical eye movement Paralysis or paresis, skew deviation, slight miosis and ptosis and sluggish pupillary responses to light.	High midbrain tegmentum ventral to superior colliculus (nucleus of Cajal, nucleus of Darkschevich, rostral interstitial nucleus of the MLF, and posterior commissure) and Supranuclearfibers to third cranial nerve
6. Contralateralataxicorposturaltremor	Dentatothalamic track after
7. Decerebrate attacks	decussation. Precise site of lesionunknown.
Peripheralterritory	
8. Homonymoushemianopia	Calcarine cortex or optic radiation; hemi achromatopsia may be present.Macular or central vision is preserved ifposteriorstriateareaisspared.
9. Bilateral homonymous hemianopia, cortical blindness, unawareness, or denial ofblindness;achromatopsia, failure to see to-and-fromovements, inability to perceive objects not centrally located, apraxia of ocular movements, inability to count or enumerateobjects	Bilateral occipital lobe, possibly withinvolvementofparieto-occipitalregion
10. Dyslexiawithoutagraphia, color anomia	Dominantcalcarinelesionandposterior partofcorpuscallosum

11. Memorydefect	Lesion of inferomedial portions oftemporal lobe bilaterally; occasionally ofthedominantsideonly
12. Topographicdisorientationandprosopagnosia	Nondominantcalcarineandlingualgyri,usuallybilateral
13. Simultagnosia	Dominant visual cortex,sometimesbilateral
14. Unformed visual hallucinations,metamorphopsia,teleopsia,illusoryvisualspread, palinopsia, distortion of outlines,photophobia.	Calcarinecortex

INTRODUCTION OF FERRITIN

In recent years, inflammatory process plays an important role in pathophysiology of stroke. When an individual is exposed to any insult in terms of infection and injury, there is a production of proteins called Acute Phase Proteins. This Acute phase protein participates in all inflammatory process and plays a major role in both acute and chronic inflammatory states. The Acute phase reactants are 10 fibrinogen, ferritin, haptoglobin, highly sensitive C – reactive protein, Complements (C3), Complements (C4), Tumour necrosis factor. For a long time, serum ferritin was measured only to know the stored iron status. Now it has been suggested that it influences the prognosis of ischemic stroke1 and acts as a risk factor for ischemic episodes by enhancing atherogenesis. [50 51]

Although controversial, elevated body iron stores as evidenced by classical markers including serum Ferritin, serum total iron, transferrin saturation, or iron binding capacity were associated with increased risk of ischemic events [52,53]. Carriers of the hemochromatosis gene appear to be at increased risk of myocardial infarction and cardiovascular death [54]. Recent animal experiments have

suggested that iron overload contributes to the development of vascular diseases by promoting thrombosis after arterial injury [55]. The role of iron overload in stroke is poorly documented. However, high serum ferritin on admission of acute stroke patients (within 24 to 48 h after stroke onset) was reported to predict a bad prognosis [5,56] suggesting that increased body iron stores before stroke onset can aggravate the cytotoxicity of brain ischemia. Initially, serum ferritin is considered only as a stress response to stroke, but now serum ferritin is under research as a prognostic indicator in stroke, the possible mechanisms of ferritin are discussed below

Serum ferritin can be used to assess the iron overload in the absence of inflammation, cancer, and infectious diseases as serum ferritin is directly proportional to cellular iron stores.[7 6]

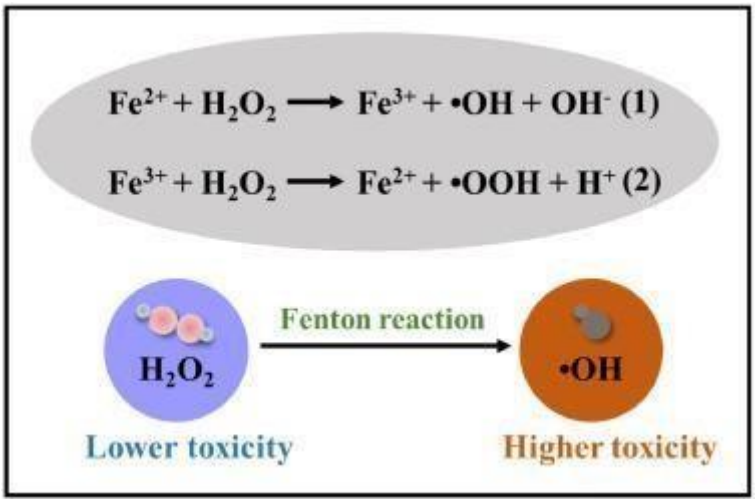
Serum ferritin consequently might be related to the availability of iron in the infarcted area,[57] In brain tissue, most of the non-heme iron is in the form of ferritin, which is localized in astrocytes and microglia.[8]

In response to hypoxic acidosis or oxidative stress, the synthesis of ferritin will be induced in brain cells to reduce the accumulation of reactive oxygen species (ROS). [58,9]

Therefore, in the Neuroprotective mechanism processes, increased ferritin could help in sequestering the toxic-free iron in the ischemic brain released due to stroke.

During cerebral ischemia, ferritin will be released from the cell, which is free iron, will catalyse the preformed radicals like hydrogen peroxide (H_2O_2) and superoxide ($O_2^{\bullet-}$) into highly reactive toxic hydroxyl radical ($^{\bullet}OH$) [10]**FIGURE 8.** Few experimental data showed that iron being cause for endothelial damage and ischemia brain.

Figure 8: FENTON REACTION



The study on rats showed that iron intake had been associated with larger infarct volumes, glutamate release, inflammatory response and higher oxidative stress after permanent middle cerebral artery occlusion [59]. Whereas iron depletion or chelation reduces brain edema, infarct size, and metabolic failure in ischemia/reperfusion experimental stroke models.[60]

Another proposed mechanism where iron may play a role in ischemic vascular disease is in ischemia/reperfusion injury which might be more relevant to the stroke risk. After the infarction of brain tissue, there will be the formation of reactive oxygen radicals and the release of iron ions, once reperfusion takes place, there will be an enhancement of the formation of reactive oxygen radicals leading to rapid cellular death.[61,62,63]

In addition, there is a study in which high Ferritin levels on admission were not associated with deteriorating stroke [64]. Ferritin is a positive acute phase protein and stroke is associated with systemic inflammation [65]. Hence conditions like acute infections, malignancies, myocardial infarction, recently received iron injection, renal cell carcinoma, chronic liver disease etc., can have a falsely high value of ferritin. For these reasons, the hypothesis that high ferritin levels on admission were secondary to stroke and ferritin levels increased during the interval between stroke onset and blood sampling as a reflection of stroke severity cannot be excluded.

FERROPTOSIS

Cell death is an unavoidable and essential link in the process of life that signals the end of a cell's life, whether under physiological or pathological settings. Apoptosis and necrosis have traditionally been used to classify cell death. Recent research has revealed that, in addition to necrosis and apoptosis, several novel programmed death mechanisms, such as autophagy, necrosis, and necrotic apoptosis, occur, where each of them has its biological processes and pathological properties. In 2012, Dixon suggested the concept of ferroptosis, a non-apoptotic, iron-dependent form of cell death characterised by the accumulation of lipid (ROS) reactive oxygen species. Ferroptosis is clearly distinct from necrosis, apoptosis, and autophagy in cell morphology and function. **TABLE 5**[11,41]

Ferroptosis lacks the morphological hallmarks of conventional necrosis, such as swelling of the cytoplasm and organelles and cell membrane rupture, as well as classic cell apoptosis, such as cell shrinkage, chromatin condensation, production of apoptotic bodies, and cytoskeleton breakdown. Ferroptosis, unlike autophagy, does not produce closed bilayer membrane structures (autophagic vacuoles). Ferroptosis is distinguished from other types of cell death by visible shrinking of mitochondria, increased membrane density, and a reduction in or disappearance of mitochondrial cristae. [41]

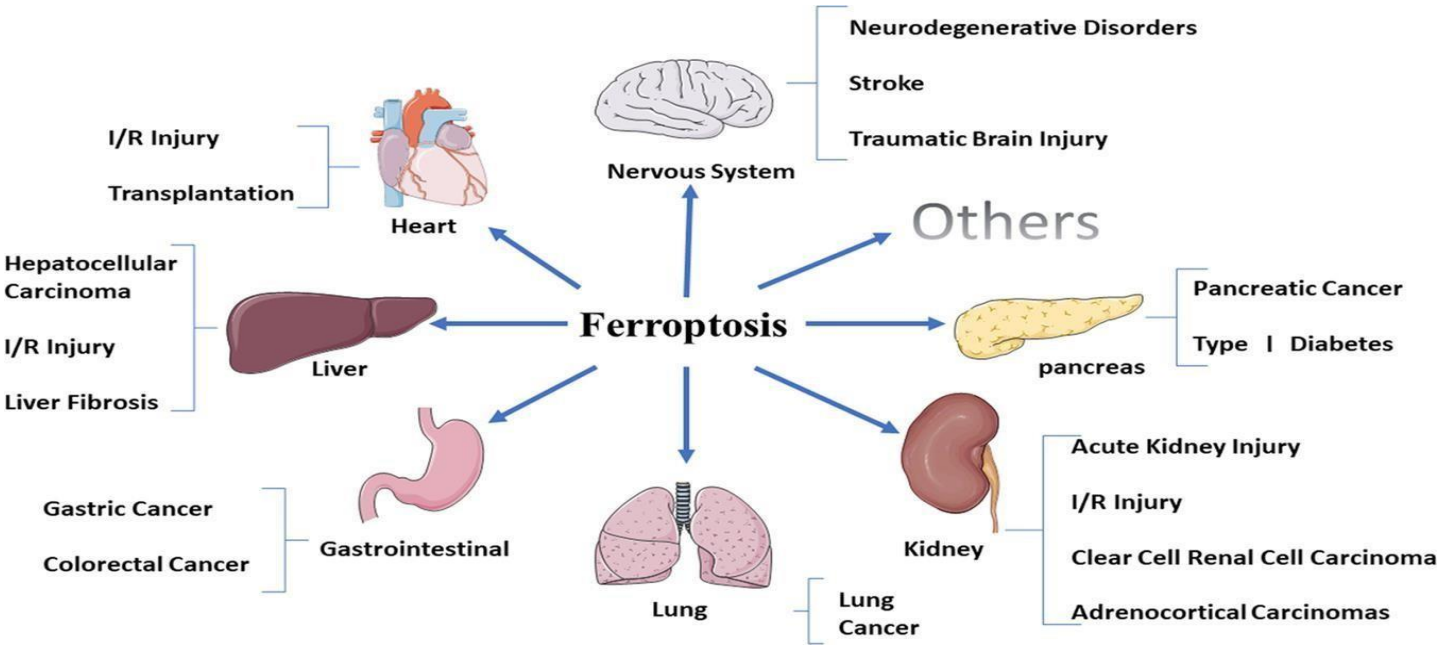
Recent research has revealed that ferroptosis plays a significant regulatory function in the onset and development of many illnesses, and it has become a focus and hotspot of study for the treatment and improvement of prognosis in related diseases. **FIGURE 9**

TABLE 5 :DIFFERENCE BETWEEN FERROPTOSIS APOPTOSIS AUTOPHAGY AND NECROPTOSIS.

	Ferroptosis	**Apoptosis**	**Autophagy**	**Necroptosis**
Morphological Features	Small mitochondria with increased mitochondrial membrane densities, reduction or vanishing of mitochondria Crista, normal nucleus, and outer mitochondrial membrane Rupture	Cellular and nuclear volume reduction, formation of apoptotic bodies and cytoskeletal disintegration, chromatin agglutination, nuclear fragmentation, no significant changes in mitochondrial structure	Formation of double-membraned autolysosomes, including micro-autophagy, chaperone-mediated autophagy and macro-autophagy.	Plasma membrane breakdown, moderate chromatin condensation, generalized swelling of the cytoplasm and organelles, spillage of cellular constituents into the microenvironment.
Biochemical Features	lipid peroxidation and Iron accumulation.	DNA fragmentation	Increased lysosomal activity	Decrease in ATP levels
Regulatory Pathways	Xc- /GPX4, MVA, sulfur transfer pathway, ATG5-ATG7-NCOA4 pathway, P62-Keap1-NRF2 pathway, P53/SLC7A11, FSP1-COQ10-NAD(P)H pathway P53-SAT1-ALOX15 pathway, HSPB1-TRF1.	Death receptor pathway, P53, Bcl-2 mediated signalling pathway mitochondrion pathway and endoplasmic reticulum pathway, Caspase.	mTOR, Beclin-1, P53 signalling pathway	TNF-R1 and RIP1/RIP3-MLKL related signalling pathways; ROS-related metabolic regulation pathway PKC-MAPK-AP-1 related signalling pathway.
Key genes	GPX4, TFR1, ACSL4, FSP1, SLC7A11, NRF2, NCOA4, P53, HSPB1.	Caspase, Bax, P53, Fas, Bcl-2.	ATG5, ATG7, LC3, DRAM3, TFEB, Beclin-1.	RIP1, RIP3

ACSL4 acyl-CoA synthetase long-chain family member 4, MLKL mixed lineage kinase domain-like protein, MVA mevalonate, LC3 microtubule-associated protein 1 light chain3, NCOA4 nuclear receptor coactivator 4, ATG5 autophagy-related 5, ATG7 autophagy-related 7, ALOX-15 arachidonate lipoxygenase 15, SLC7A11 solute carrier family seven-member 11, system Xc- cysteine/glutamate transporter receptor, mTOR mammalian target of rapamycin, AP-1 activator protein-1, TFEB transcription factor EB, TFR1 transferrin receptor 1, TNF-R1 tumor necrosis factor R1, COQ10 coenzyme Q10, DRAM3 damage-regulated autophagy modulator 3, FSP1 ferroptosis suppressor protein 1, GPX4 - glutathione peroxidase 4, HSPB1 heat shock protein beta-1, Keap1 Keleh-like ECH-associated protein 1, MAPK mitogen-activated protein kinase, NRF-2 nuclear factor erythroid 2-related factor 2, PKC protein kinase C, RIP receptor-interacting serine/threonine kinase, ROS reactive oxygen species, SAT1 spermidine/spermine N1-acetyltransferase 1. [11]

FIGURE 9: FERROPTOSIS ON DIFFERENT ORGANS [11]



Ferroptosis in stroke

Ischemic stroke is responsible for around 80% of all strokes. Iron deposition rises in the basal ganglia, thalami, periventricular, and subcortical white matter regions after severe ischemia and hypoxic brain damage. The amount of Glutathione in neurons is dramatically reduced in a mouse model of ischemic stroke, the degree of lipid peroxidation is increased, and the activity of Glutathione peroxidase is diminished, according to few studies[66]. Furthermore, the use of ferroptosis inhibitors like Deferoxamine improves the prognosis of ischemic stroke patients dramatically.[67]

EVALUATION OF SEVERITY OF STROKE

The modified Rankin Scale (mRS):

History of Rankin Scale: Introduced by one of the great physician John Rankin who was born in Glasgow in 1923. After completion of medical schooling, he started working in Stobhill which was a general hospital providing a range of medical and surgical services. During Rankin's time at Stobhill these John Rankin circa 1961 beds mostly comprised patients with rheumatic heart disease or stroke. The combination of a young

physician with innovative research ideas and an active academic department, made Rankin work on stroke where he collected lot of observational data on cerebrovascular diseases. As stroke had a very few active interventions in those periods, stroke contributed to high mortality, Rankin's optimistic attitude to stroke was highly unusual. He argued that positive results could be achieved through rehabilitation by early mobilization. In contemporary stroke care, it is certainly true that Rankin's ideals of early rehabilitation and multidisciplinary working remain core principles. Despite his many great achievements, it is for his early stroke work that Rankin is best remembered in the UK - in particular his tool for describing post-stroke disability. Rankin had submitted many series of papers regarding stroke care. It was in this work that Rankin described his eponymous stroke scale, a tool that became instrumental in future stroke studies. Rankin described good outcomes in the majority of patients cared for using his unorthodox methods of holistic stroke care. To aid his descriptive work he formulated a novel outcome scale[68]. **Table 6**.

Table 6: The Rankin Scale

Grade I	No significant disability, able to carry out all usual duties
Grade II	Slight disability, unable to carry out some of previous activities but able to look after own affairs without assistance
Grade III	Moderate disability, requiring some help but able to walk without assistance
Grade IV	Moderately severe disability, unable to walk without assistance and unable to attend to own bodily needs without assistance
Grade V	Severe disability, bedridden, incontinent, and requiring constant nursing care and attention

In 1980s The United Kingdom Transient Ischaemic Attack (UK TIA) study[69], the first multi-centre trial in neurology - they needed an easily administered measure of stroke outcomes. Rather than developing new instrument they turned to Rankin's eponymous scale. Following initial pilot work, for better reliability the UK

TIA team revised the wording of Rankin's original gradings – Charles warlow named it as the modified Rankin scale (mRs) **Table 7**. In 1988 van Swieten et al[70], first examined its reproducibilitySubsequently the mRS was used in the first International Stroke Trial[71]. The success of these trials alerted the stroke community to the utility of Rankin's scale.

Table 7: The modified Rankin Scale(mRS)

Grade 0	No symptom at all
Grade I	No significant disability, able to carry out all usual duties
Grade II	Slight disability, unable to carry out some of previous activities but able to look after own affairs without assistance
Grade III	Moderate disability, requiring some help but able to walk without assistance
Grade IV	Moderately severe disability, unable to walk without assistance and unable to attend to own bodily needs without assistance
Grade V	Severe disability, bedridden, incontinent, and requiring constant nursing care and attention
Grade VI	Dead

The **modified Rankin Scale** (**mRS**) have become most commonly used scale for measuring dependence in the daily activities of people or the degree of disability who have suffered neurological deficit due to stroke or any other causes. It's been widely accepted and used for measuring clinical outcomes in stroke [12]

INVESTIGATIONS

Neuroimaging became one of the most effective tools in cerebrovascular disease therapy in the decade since thrombolytic treatment of acute ischemic stroke innovated it. It can provide health care professionals with critical information for proper management of acute stroke patients, such as:

1. Accurate identification of ischemic stroke (exclusion of hemorrhage and conditions which mimic stroke).
2. Identification of individual arterial stenosis and occlusions.
3. Prediction of stroke severity, i.e., differentiating large infarcts in eloquent regions from smaller infarcts in "silent" brain regions.
4. Identification of patients with vascular lesions which are eligible for surgical treatments.
5. Assessment of recanalization after thrombolysis therapy, and visualization of the collateral arterial blood flow formed secondary to occlusion.
6. To look for possible mechanisms of stroke, directing long-term preventive strategies.[72]

COMPUTER TOMOGRAPHY (CT)

Computer Tomography has a well-established role in the diagnosis of cerebral infarction. CT can tell the difference between a non-haemorrhagic ischemic stroke, a haemorrhagic infarction, and a primary intracerebral haemorrhage.

A CT scan generally shows no significant changes in the clinical context of a transient ischemic attack (TIA). White matter or capsular hypodensity (chronic ischemic alteration) which indicates the existence of underlying vascular pathology.

The CT scan accurately reflects the typical neuropathologic processes that occur throughout the progression of cerebral infarction.

The goals of CT in the acute setting are to exclude

1. intracranial haemorrhage, which would allow to make decision for thrombolysis.
2. other intracranial pathologies that may mimic a stroke, such as a tumour.

The radiologic imaging characteristics are divided into four stages and are dependent on the time from the onset of ictus. Thesestages are divided into

1. Hyperacute for less than 24 hrs

2. Acute 24 hrs – 7 days

3. Subacute 8-21 days

4. Chronic more than 21 days [73]

Images showing infarcts in CT

FIGURE 10: CT SHOWING LEFT BASAL GANGLIA INFARCTION

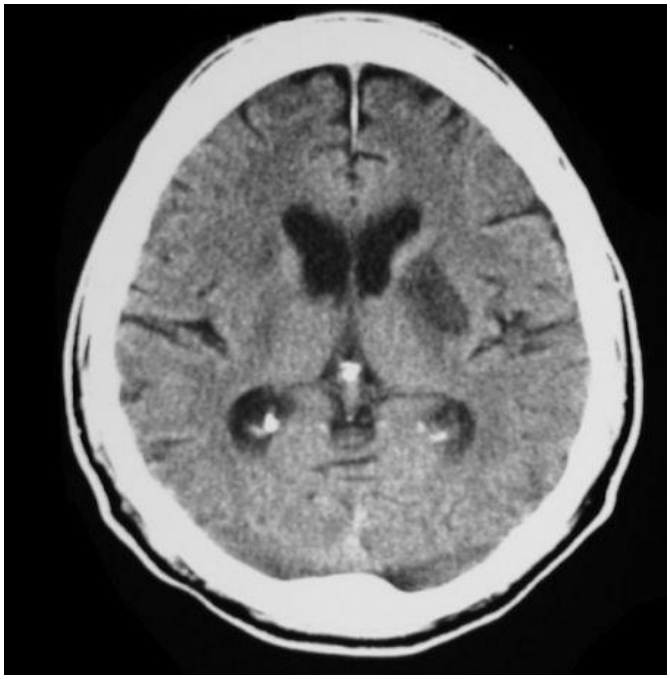


FIGURE 11: CT SHOWING MCA TERRITORY INFRACTION WITH MIDLINE SHIFT

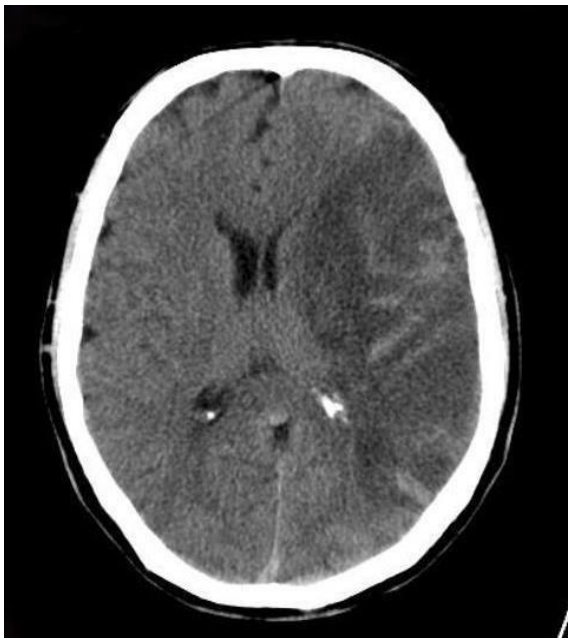
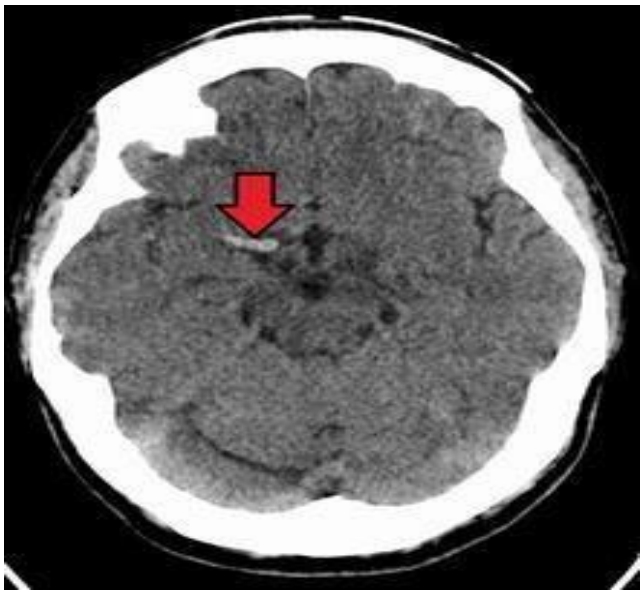


FIGURE 12: CT SHOWING HYPER DENSE MCA SIGN(ARROW) CONSISTENT WITH AN ACUTE THROMBUS

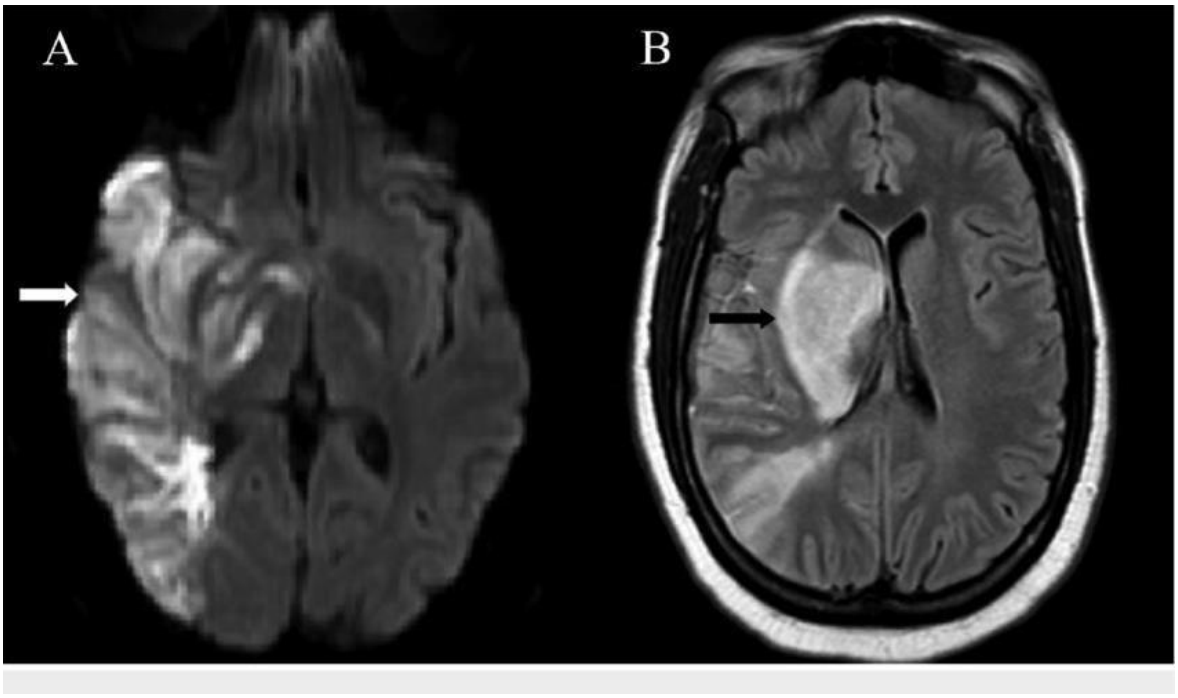


MAGNETICRESONANCEIMAGING(MRI)

Image contrast with magnetic resonance imaging is dependent on three tissuevariables.T_1 Relaxationtime,T_2–RelaxationtimeandProtondensity.

Ischaemia one hour after the event can be detected by MR imaging. MRI reliably documents the extent and location of infarction in all areas of the brain, including the posterior fossa and cortical surface. Diffusion weighted imaging (DWI) is more sensitive forearlybraininfarction.MagneticResonanceangiographyishighlysensitiveforextracranial internal carotid plaque as well as intracranial stenosis of large vessels. MRIprovessuperiorinformationcomparedwithCTinnearlyeverycaseof stroke.

Figure13: MRI showing right MCA territory acute infarcts



CEREBRALANGIOGRAPHY

The "gold standard" for finding and measuring atherosclerotic stenosis of the cerebral arteries and other diseases is conventional X-ray cerebral angiography. Recent research has shown that thrombolytic agents delivered intra arterially to individuals with acute MCA infarction can efficiently recanalize arteries and improve clinical outcomes.

ELECTROCARDIOGRAM

ECG is done to evaluate any cardiac aetiology which might have led to cause of embolic events, like arrhythmias like atrial fibrillation or any old ischemic changes.

In a study, the most common ECG abnormalities associated with stroke were T-wave abnormalities 39.9%, prolonged QTc interval 32.4%, and arrhythmias 27.1%, found in stroke patients and 28.9%, 30.7%, and 16.2 respectively of the patients with no primary cardiac disease. [74]

LIPID PROFIE

Circulating lipid and lipoprotein biomarkers have consistently been associated with cardiovascular diseases as myocardial infarction and stroke. Many studies have concluded that lowering the level of cholesterol also reduce risk of stroke.[75]

Total cholesterol:<200 mg/dL.

LDL cholesterol: <70 mg/dL.

HDL cholesterol: <40 mg/dL in men AND <50 mg/dl in women.

Triglycerides: <150 mg/dL.

2D ECHOCARDIOGRAPHY

2D-ECHO will be help full in looking for cardio aetiology of stroke like clots in heart which might lead to embolic events causing stroke.

RANDOM BLOOD SUGAR

Hyperglycaemia detected in the acute stroke phase—regardless of the presence of diabetes mellitus—reflects physiological stress and manifests relative insulin deficiency, which is related to increased lipolysis. In addition, hyperglycaemia in stroke patients may result from an interaction between several hormones, including glucagon, cortisol, cytokines, and growth hormone, which play a crucial role in blood glucose regulation.

Several mechanisms have been identified by which hyperglycaemia could increase brain damage in ischemic stroke and result in unfavourable outcomes. These include endothelial dysfunction, impaired fibrinolysis, and increased tendency of red blood cells to form micro aggregates. Moreover, hyperglycaemia might result in several cellular derangements, including loss of the blood-brain barrier integrity, increased excitatory neurotransmitters production, enhancement of anaerobic glycolysis, and induction of oxidative stress. Persistent or poorly controlled hyperglycaemia has been shown to reduce cerebral blood flow, increase intracranial pressure, and cause cerebral oedema and neuronal death[76].A blood sugar level less than 140 mg/dL (7.8 mmol/L) is normal.

CAROTID DOPPLER ULTRASOUND

Carotid pathology is known to be associated with strokes, and Carotid Doppler ultrasonography (CDU) is a powerful tool for use in evaluating atherosclerosis of the carotid artery. This will help preventing further episodes of stroke by carotid artery stentings.

SERUM FERRITIN

Serum ferritin can be used as severity marker as increased iron overload causes increased severity by forming hydroxyl radical from hydrogen peroxide radical in ischemic condition. Normal value considered was Male: 16 – 243 ng/mL and Female: 10 – 158 ng/mL

TREATMENT OF ACUTE ISCHEMIC STROKE:

(A) General supportive care

1. OXYGENATION:
2. AIRWAY:
3. BREATHING:
4. CIRCULATION:
5. HEAD POSITION:
6. MAINTENANCE OF OPTIMAL BODY TEMPERATURE:
7. MAINTENANCE OF GLYCAEMIA CONTROL:

(B) Measures to Restore or Improve Perfusion

1. **Thrombolytic therapy:**

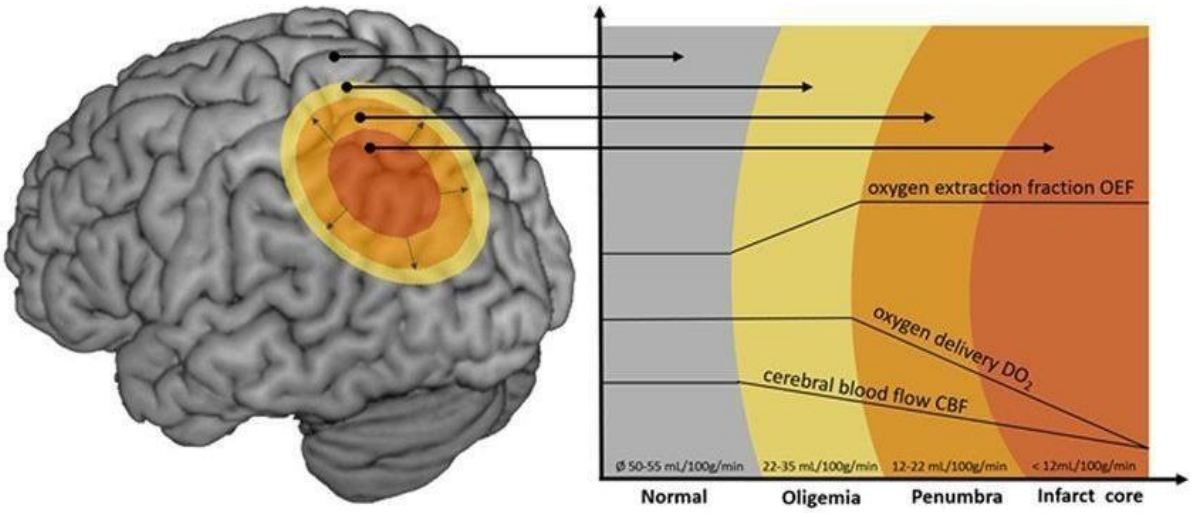
The goal of the thrombolytic therapy is to clear the blockage and restore blood flow to the brain tissue that has been hypoperfused. The hypoperfused region is usually made up of permanently

injured brain tissue (infarct core) surrounded by possibly salvageable brain parenchyma (ischaemic penumbra). A early vascular recanalization can save the ischemic penumbra. **FIGURE 14**

Intra-arterial thrombolysis can be used in selected patients with severe stroke of time <6 hours due to occlusion of large artery.

Agents used are tissue plassiminogen activator (tPA) like alteplase, reteplase and tenecteplase.

FIGURE 14: PENUMBRA



Indications:

- Age >18 years
- Time window <4.5 hours
- Symptoms persisting for ≥30 minutes without significant improvement
- National Institutes of Health Stroke Study (NIHSS) score: 4–25 points

Absolute contraindications

- History or evidence of Intracranial hemmorahage within 3months
- Clinical presentation suggestive of sun arachnoid hemmorhage

- Known arteriovenous malformation
- Systolic BP >185 mm Hg or diastolic BP >110 mm Hg despite repeated measurements and treatment
- Seizure with postictal residual neurologic impairment
- Platelet count < 100,000/µL
- Prothrombin time (PT) >15 or INR > 1.7
- Active internal bleeding or acute trauma
- Head trauma or stroke in the previous 3 months

Relative contraindications

- Pregnancy
- Rapidly improving stroke symptoms
- Myocardial infarction (MI) in the previous 3 months
- Glucose level <50 mg/dL or > 400 mg/dL

2. **Anticoagulants**
3. **Antiplatelet Aggregation Agents**
    - Aspirin
    - Ticlopidine
    - Clopidogrel
4. **Treatment of Acute Neurological Complications**
    - Brain oedema and increased intracranial pressure-
    - Seizures

- Haemorrhagic Transformation

Motor recovery from stroke

The first two to three months are crucial for stroke recovery. Within 2-3 years, more than 90% of the damage was repaired. At one year after a stroke, 75-85% of patients are ambulatory, 48-58% regain independence in daily activities, and 10-29% require nursing home care.

Arm motor recovery in hemiplegic stroke patients has a poor prognosis, with just 5–20% of patients achieving good functional outcomes.

The outcome is not as bad if any arm grip is present within the first weeks, but the absence of a handgrip within a month indicates a very poor motor outcome.

Recovery of leg movements is at a greater extent compared to arm.

The absence of return of motor function in the leg within two weeks is associated with poor functional arm outcome.

Conditions contributing to the lack of good outcomes are: Raised blood glucose levels, cardiac manifestations, ECG irregularity, history of stroke, functional dependence, and lack of sensory, visual and cognitive activities.

Language does not improve evenly across all components. Recovery from aphasia and hemiparesis appears to occur independently.

Neurophysiologic mechanism for recovery from stroke

Reduce in the amount of oedema and repair of ischemic shade from the dissemination. The above procedures are analysed and reported by Brodal that these procedures will not help for rehabilitation after 4-6 weeks of stroke.

Increased glutamatergic activity, inhibition removal, loss of perilesional GABA-ergic inhibition, enhanced synaptic transmission, and changes in neuronal membrane excitability are all factors that contribute to brain reorganisation following stroke.

Specific clinical observations show the bilateral representation of the brain.

Stroke recovery may be assisted by cortical remodelling, which involves the development of new synapses and the removal of inhibition.

Cortical reorganisation through the formation of new synapsis and freeing from inhibition may lead to stroke recovery.

The development of denervation hypersensitivity occurs when dormant synapses are activated, and rearrangement might take the form of axonal or dendritic sprouting in the later phase.

Spasticity and seizures are caused by the inappropriate creation of new synapses and neural development. Physiotherapy is beneficial in the early stages of dendritic progression.

The restoration of inhabitation after a stroke might be crucial to rehabilitation. The lack of inhibition is manifested by a loss of fine movements and increased reflexes. The reappearance of inhibitory mechanisms might be responsible for the return of fine coordinated movements.

Treatment in high iron load

Deferoxamine, Deferiprone and Deferasirox are the most important specific US FDA-approved iron chelators.

The FDA has approved the iron chelator DEFEROXAMINE for the treatment of acute iron overload and chronic iron intoxication caused over by transfusion-dependent anaemia. Following systemic injection, it can quickly cross the BBB and build up in the brain tissue. Deferoxamine chelates iron by establishing a stable complex that bars iron from participating in more chemical reactions. Deferoxamine reduces hematoma and hemoglobin-induced edema in vivo. According to several research, deferoxamine lessens the neurological impairments, brain atrophy, and neuronal death brought on by ICH. By inhibiting the Fenton/Haber-Weiss reaction, deferoxamine prevents the production of hydroxyl radicals by binding ferric iron. In numerous ischemia models, the benefits of iron chelator therapy have been documented. Deferoxamine can cause ischemia tolerance in the brain by acting as a free radical scavenger.[77]

REHABILITATION

A goal of stroke rehabilitation should be to facilitate relearning of skills that were possible before the stroke, however, in some circumstances, adaptation and deficit-compensation must be the main goals of rehabilitation. This procedure, which starts while the patient is in the hospital, involves training adaptive techniques, retraining motor skills and preventing complications using comprehensive approach.

Physical therapy, speech & language therapy, occupational therapy and other specialised fields are frequently used in the rehabilitation process. The team's responsibilities include creating goals, periodically reviewing these goals, and modifying the rehabilitation strategy as necessary. Training caregivers is a crucial component of rehabilitation in addition to helping the patient function better. Speech and language pathologists (i.e., speech therapists) help stroke survivors learn strategies to overcome swallowing and language deficits.[78]

Quality of life of stroke patients can be increased by using aids like walkers, using wall mount grab rails at house and toilets, slip-resistant mats, shower chairs etc,.

Functional electrostimulation (FES) is another technique than can be used to enhance motor recovery in patients with stroke. Another method that can help stroke patients with their motor rehabilitation is functional electrostimulation (FES). This method includes stimulating specific muscles using electrical stimulation. Commercially available functional electrostimulation devices may be improved, and this is a topic of active research. An example of a functional electrostimulation device is shown in **Figure 15** [79]

FES seems to be a promising tool for improving UL function in post-stroke patients.

Figure 15. Representation of two tasks of different levels of motor control complexity assisted by multifield FES, drinking task (on the **left**) and turn on the light tasks (on the **right**).[79]

PREVENTION

After a stroke, patients are more likely to have recurrent stroke, a myocardial infarction, and vascular death. Because many recurrent events happen early, prevention of these events should begin as soon as possible after stroke and should be targeted to the particular cause of stroke, which may need specific therapy. For all stroke patients, lifestyle recommendations include quitting smoking, engaging in regular exercise, eating a Mediterranean-style diet, and limiting salt and alcohol intake. Controlling risk factors, such as bringing blood pressure under 140/90 mmHg and LDL cholesterol below 1 g/L, as well as administering antiplatelet or oral anticoagulant therapy, depending on the cause of the stroke, has been shown to reduce the risk of subsequent strokes and cardiovascular events for the majorly to patients with ischemic stroke or

TIA.Forsecondary prevention in individuals with ischemic stroke or transient ischemic attack (TIA) of arterial origin,dual-anti platelet like aspirin + clopidogrel, or the combination of aspirin and dipyridamole are all appropriate alternatives. After a TIA or minor ischemic stroke, dual treatment with aspirin and clopidogrel may be suggested for 3 weeks, and for 3 months in individuals whose stroke was caused by significant intracranial stenosis. Cardioembolic stroke can be prevented very effectively with oral anticoagulants.

In patients with a recent (within six months) non-disabling ischemic stroke or transient ischemic attack (TIA) in the territory and significant carotid artery stenosis, carotid endarterectomy reduces risk of an ipsilateral stroke. In individuals under the age of 70 or those who are at higher surgical risk due to anatomical or physiological issues or unique situations like radiation-induced stenosis or restenosis following surgery, carotid stenting may be an option instead of surgery.

Preventing all modifiable risk factors which mentioned previously reduces the stroke incidences.

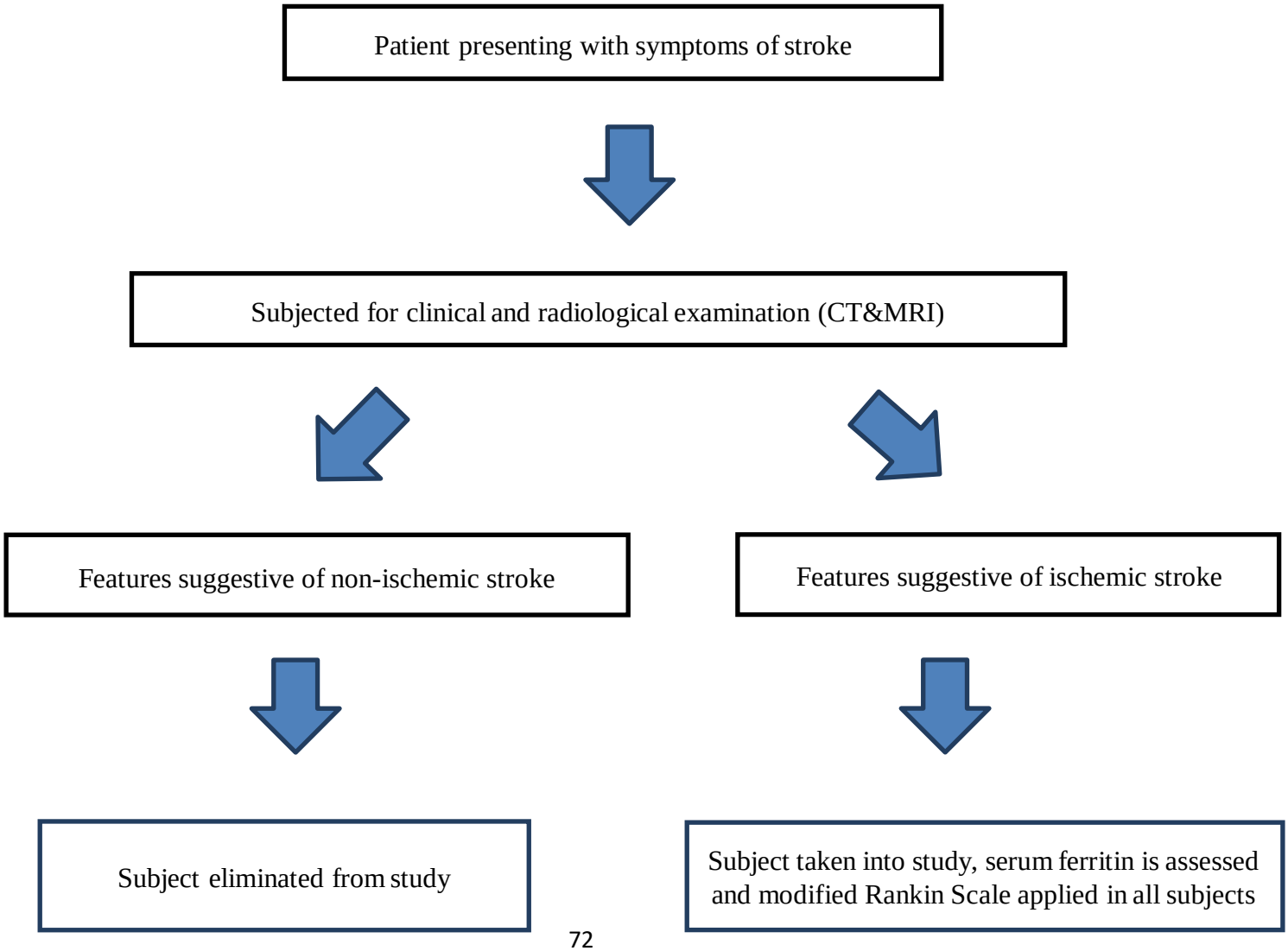
In conclusion, over the past 50 years, advances in understanding of stroke pathophysiology have led to development of therapies with proven efficacy, including antihypertensive therapy, antiplatelet therapy, vitamin K antagonists (VKAs) and novel oral anticoagulants (NOACs), statins, carotid endarterectomy, and carotid stenting.[80]

MATERIALS AND METHOD

Our study was hospital based cross-sectional study conducted on 68 patients admitted in the wards with history of clinical findings and radiological evidence for ischemic stroke in BLDEDU Shri B M Patil Medical College and Research Centre, Vijayapura, after getting approval from the institutional ethical committee.

METHOD OF COLLECTION OF DATA:

The data is collected according to Pro-forma in terms of detailed history, clinical examination and necessary investigations of the patients who fulfil the inclusion criteria.



STUDY DESIGN:

HOSPITAL BASED CROSS-SECTIONAL STUDY.

PERIOD OF STUDY: From January 2021 to June 2022.

Sample size

With the anticipated proportion of abnormal Serum ferritin level among Ischemic stroke cases 34.5%[86], the study would require a sample size of **68 subjects** with 95**%** level of confidence and 10% absolute precision**.**

Formula used

- $\mathbf{n=\frac{z^2\ p*q}{d^2}}$

Where Z= Z statistic at α level of significance

d^2= Absolute error

P= Proportion rate

q= 100-p

Statistical Analysis

- The data obtained will be entered in a Microsoft Excel sheet, and statistical analysis will be performed using statistical package for the social sciences (Version 20).
- Results will be presented as Mean (Median) ±SD, counts and percentages and diagrams.

- For normally distributed continuous variables will be compared using independent t-test. For not normally distributed variables Mann Whitney U test will be used. using the Chi-square test categorical variables will be compared.
- Correlation between variables will be found by Pearson's/Spearman's correlation.
- P<0.05 will be considered statistically significant. All statistical tests will perform two-tailed.

Inclusion criteria:

1. All the patients above 18 years irrespective of sex who admitted in the medicine ward due to newly diagnosed ischemic stroke confirmed by clinical findings and CT&MRI admitted within 24hrs of onset of symptoms.

Exclusion criteria:

1. Patient with a history of recent infection like pneumonia, UTI in the previous month.
2. Patient with a history of malignancy.
3. Patient with anemia.
4. Recent Parenteral iron supplementation in past one month.
5. Cerebrovascular accidents more than once.

RESULTS

The study results conducted to evaluate the serum ferritin as severity maker in ischemic strokeusing modified Rankin Scale (mRS) in a total 68 patients are as follows,

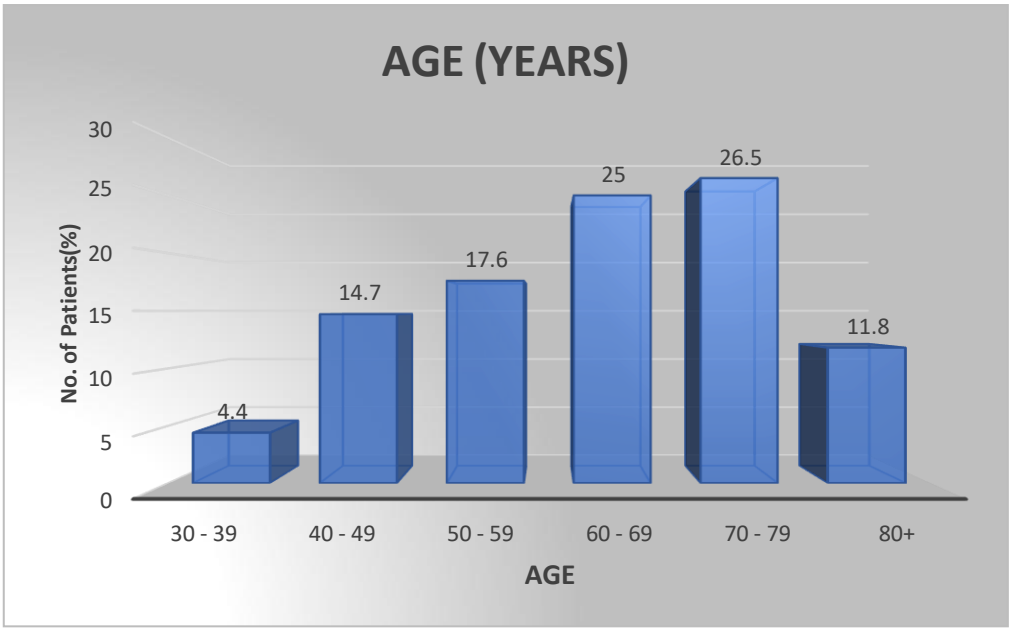
AGE DISTRIBUTION

In our study mean age observed was 62.82 ±15.07 SD. We categorized age in to 30 – 39 years, 40 – 49 years, 50 – 59 years, 60 – 69 years, 70 – 79 years and 80+ years which constituted 3 (4.4%), 10 (14.7%), 12(17.6%), 17 (25.0%), 18(26.5%) and 8 (11.8%) respectively. Majority were between 70 -79 years which was 26.5% **TABLE –8&FIGURE16.**oldest patient was 97-year-old male.

TABLE 8: AGE DISTRIBUTION

AGE (YEARS)	NO. OF PATIENTS	PERCENTAGE %
30 - 39	03	4.4
40 - 49	10	14.7
50 - 59	12	17.6
60 - 69	17	25.0
70 - 79	18	26.5
80+	08	11.8
TOTAL	68	100.0

FIGURE **16: AGE DISTRIBUTION**



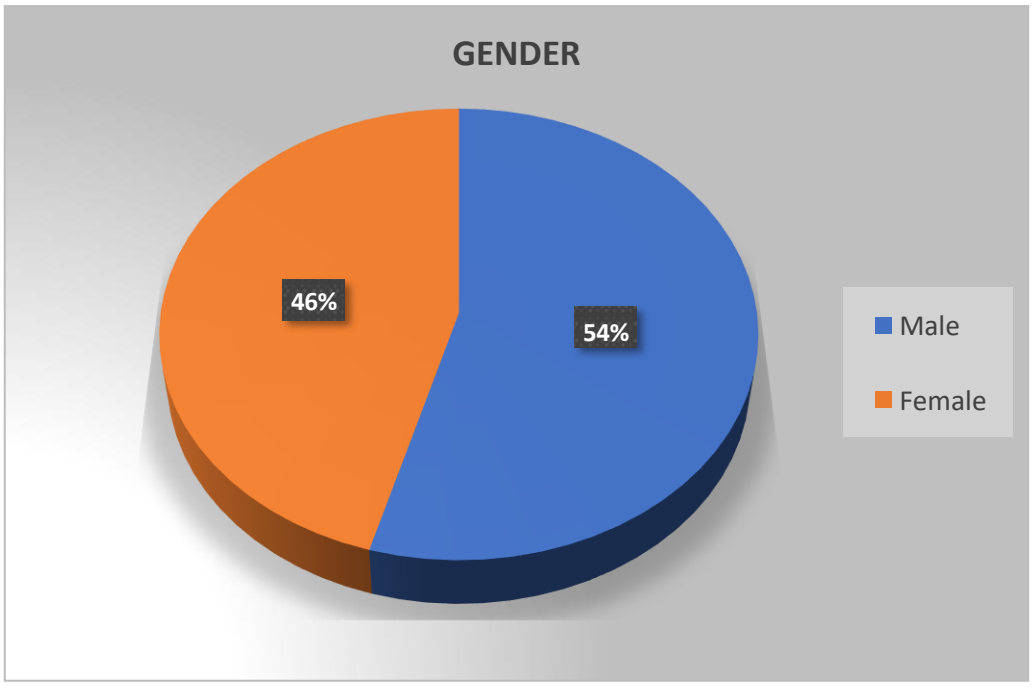
SEX DISTRIBUTION

In our study population of 68 patients, most of the patients were male 37 (54.4%)and female constituted 31 (45.6%)**TABLE –9&FIGURE 17**.

TABLE 9: **SEX DISTRIBUTION**

SEX	NO. OF PATIENTS	PERCENTAGE %
Male	37	54.4
Female	31	45.6
TOTAL	68	100.0

FIGURE 17: **SEX DISTRIBUTION**



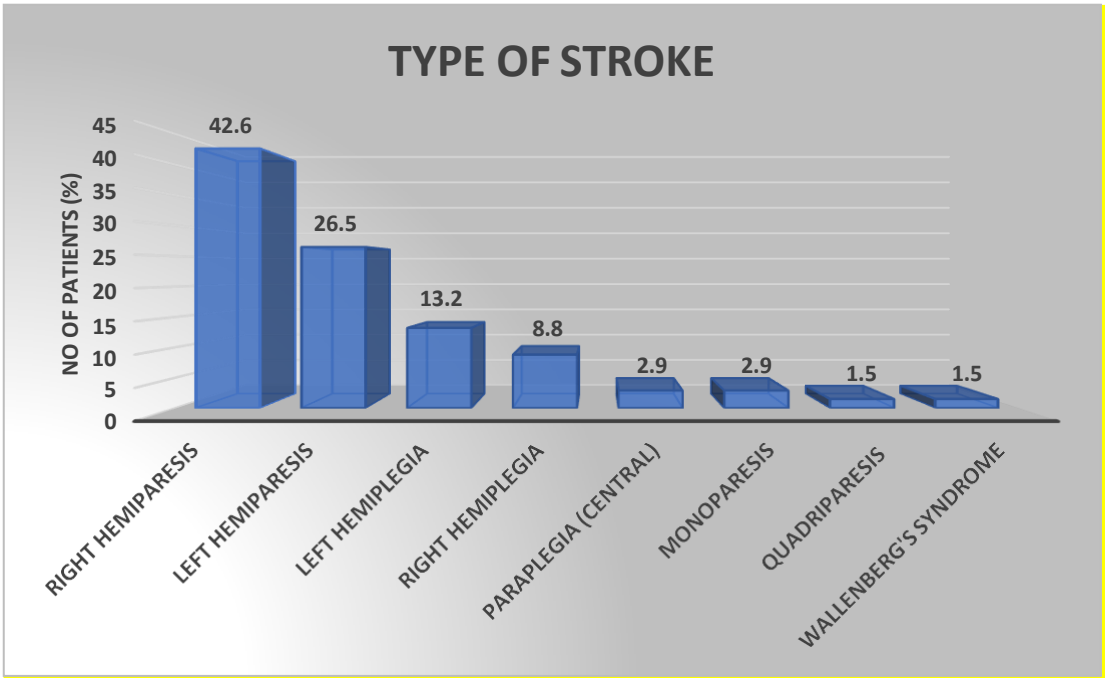
TYPE OF STROKE:

In our study, out of 68 Patients we found that most common type of stroke being right hemiparesis 29 (42.6%) followed by left hemiparesis 18 (26.5%), left hemiplegia in nine (13.2%), right hemiplegia in six (8.8%),paraplegia(central cause) was seen in two (2.9%), monoparesiswas seen in two (2.9%), quadriparesis was seen in one (1.5%),and Wallenberg's syndrome was seen in one (1.5%). **TABLE –10& FIGURE 18**

TABLE 10: TYPE OF STROKE

TYPE	NO. OF PATIENTS	PERCENTAGE %
RIGHT HEMIPARESIS	29	42.6
LEFT HEMIPARESIS	18	26.5
LEFT HEMIPLEGIA	9	13.2
RIGHT HEMIPLEGIA	6	8.8
PARAPLEGIA(CENTRAL)	2	2.9
MONOPARESIS	2	2.9
QUADRIPARESIS	1	1.5
WALLENBERG'S SYNDROME	1	1.5
TOTAL	68	100.0

FIGURE 18: TYPE OF STROKE



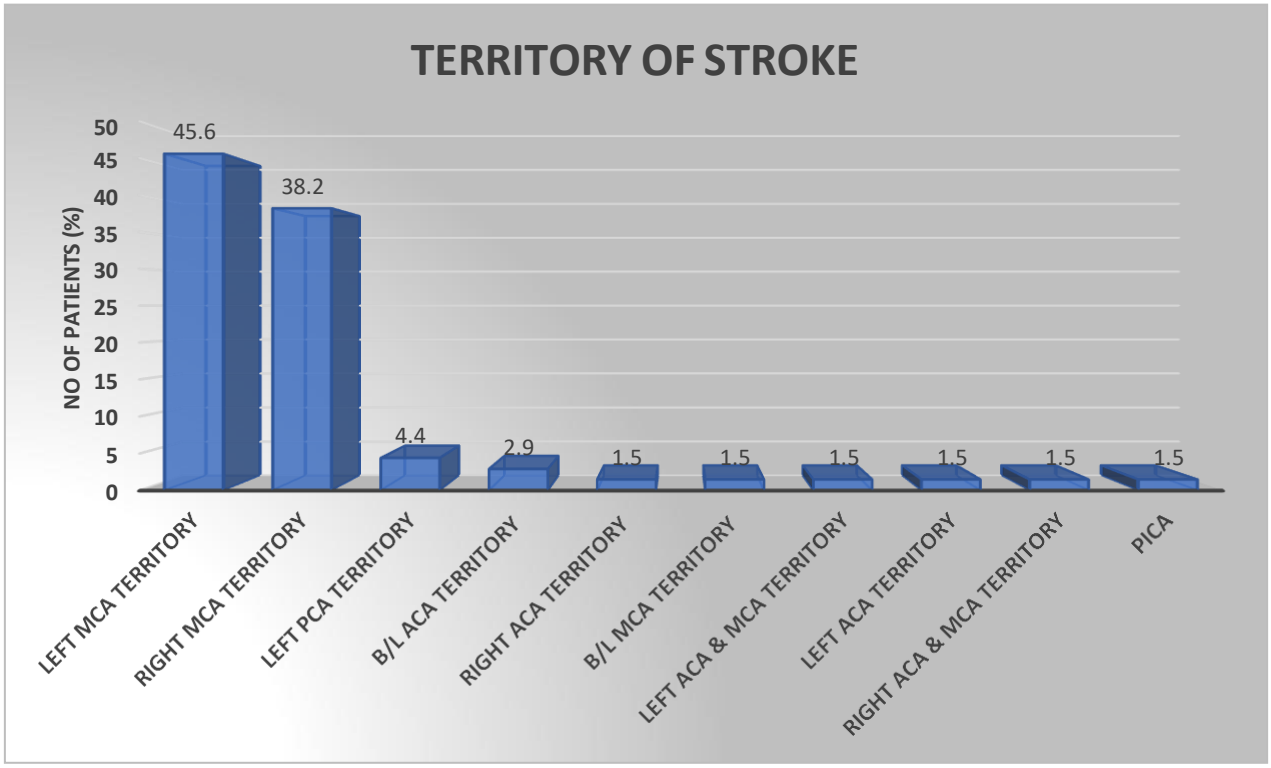
TERRITORY OF STROKE:

In our study, out of 68 Patients we found that the most common territory of stroke was most common in left MCA territory 31 (45.6%), right MCA territory 26 (38.2%), left PCA territory three (4.4%),B/L ACA territory was in two (2.9%), right ACA territory was in one (1.5%), B/L MCA territory was in one (1.5%), Left ACA & MCA territory was in one (1.5%), Left ACA territory constituted one (1.5%), right ACA & MCA territory was in one (1.5%)and posteroinferior cerebellar artery (PICA) was in one (1.5%).**TABLE 11&FIGURE 19**

TABLE 11: TERRITORY OF STROKE

TYPE	NO. OF PATIENTS	PERCENTAGE %
LEFT MCA TERRITORY	31	45.6
RIGHT MCA TERRITORY	26	38.2
LEFT PCA TERRITORY	3	4.4
B/L ACA TERRITORY	2	2.9
RIGHT ACA TERRITORY	1	1.5
B/L MCA TERRITORY	1	1.5
LEFT ACA & MCA TERRITORY	1	1.5
LEFT ACA TERRITORY	1	1.5
RIGHT ACA & MCA TERRITORY	1	1.5
PICA	1	1.5
TOTAL	68	100.0

FIGURE 19: TERRITORY OF STROKE

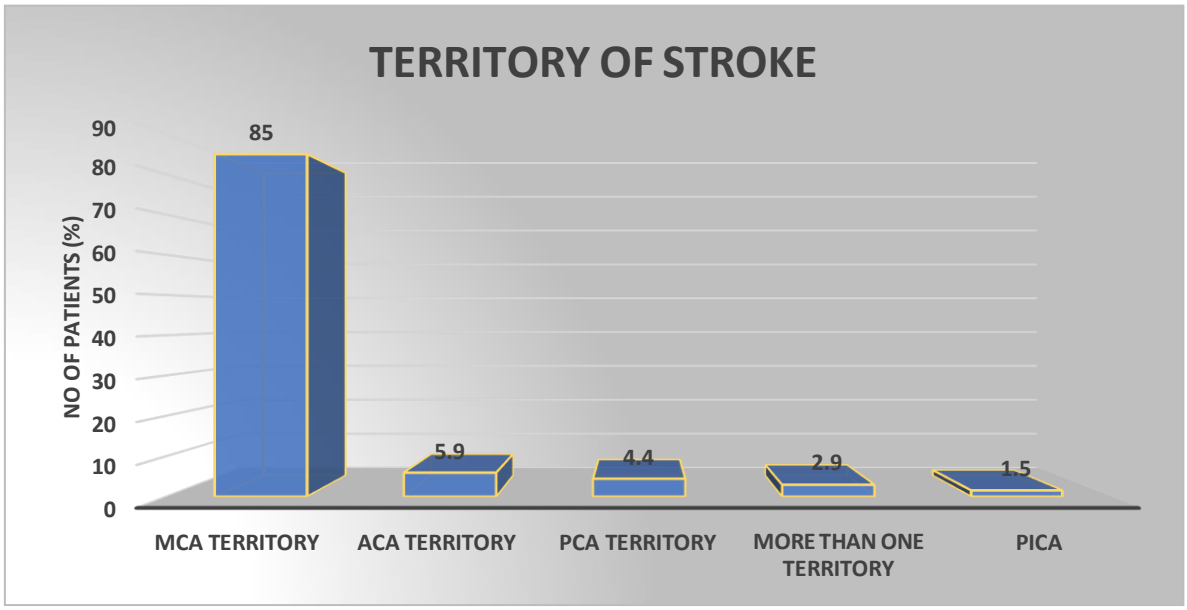


In our study, out of 68 Patients we found that the most common territory of stroke was most common in MCA territory 58 (58%), ACA territory seen in four (5.9%), PCA territory three (4.4%), more than one territory in 2 (1.5%) and PICA in one (1.5%). TABLE-5 FIGURE 5

TABLE 12:MAJOR TERRITORY OF STROKE

TYPE	NO. OF PATIENTS	PERCENTAGE %
MCA TERRITORY	58	85
ACA TERRITORY	4	5.9
PCA TERRITORY	3	4.4
MORE THAN ONE TERRITORY	2	2.9
PICA	1	1.5

FIGURE 20: MAJOR TERRITORY OF STROKE



Comorbidities:

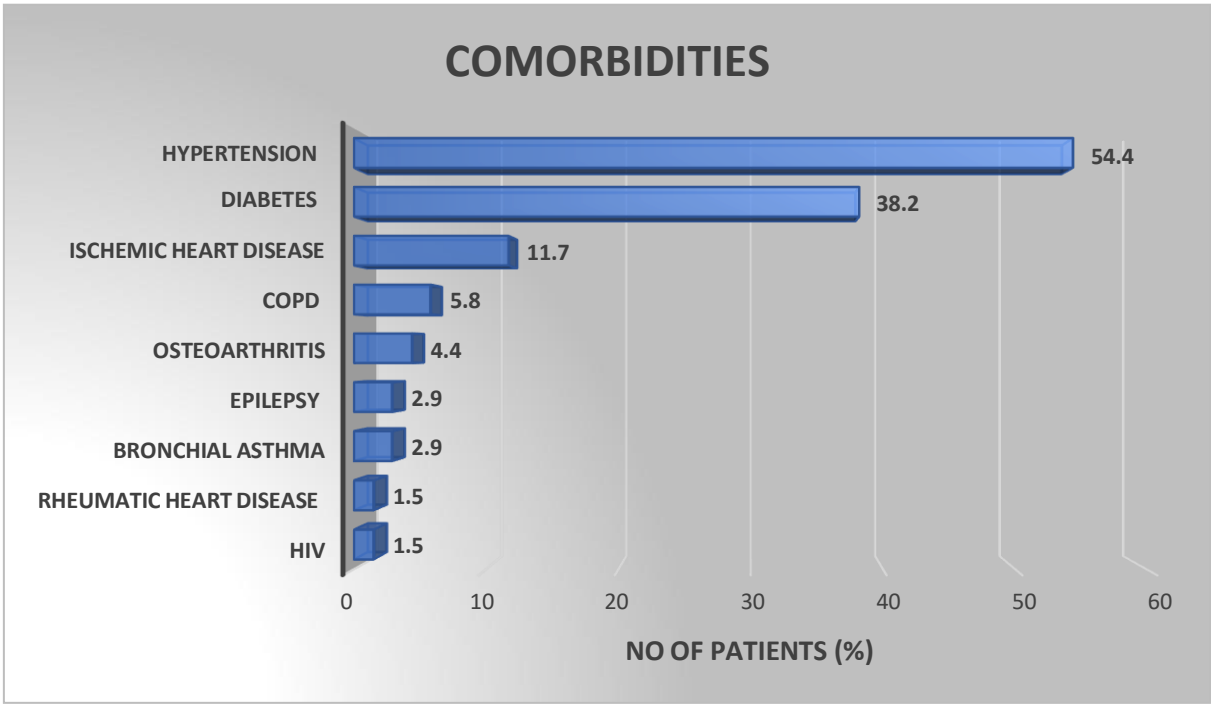
In our study the comorbidities in single or combinations of two or more was observed and commonest comorbidity was found to be hypertension 54.4% (37) followed by diabetes 38.2% (26), ischemic heart disease 11.7% (8), chronic obstructive pulmonary disease COPD 5.8% (4), osteoarthritis 4.4% (3), bronchial asthma & epilepsy constituted 2.9% (2) each, and human immune deficiencyvirus HIV & rheumatic heart disease constituted 1.5 % (1) each. **TABLE –13& FIGURE 21**

TABLE 13: COMORBIDITIES

TYPE	NO. OF PATIENTS	PERCENTAGE %
HYPERTENSION	37	54.4
DIABETES	26	38.2
ISCHEMIC HEART DISEASE	8	11.7
COPD	4	5.8
OSTEOARTHRITIS	3	4.4
BRONCHIAL ASTHMA	2	2.9
EPILEPSY	2	2.9

HIV	1	1.5
RHEUMATIC HEART DISEASE	1	1.5

FIGURE 21: COMORBIDITIES



ALCOHOL

In our study, it was found that out of 68 patients, 14 (20.5%) patients were alcoholics and 54 (79.5%) patients were non alcoholics, this was compared with mRS severity scale results were as under mRS-1 two were alcoholics and 6 were non alcoholics, mRS-2 two were alcoholics and 20 were non alcoholics, mRS-3 four were alcoholics and 16 were non alcoholics, mRS-4 threewere alcoholics and 4 were non alcoholicsand mRS-5 three were alcoholics and 8 were non alcoholics.

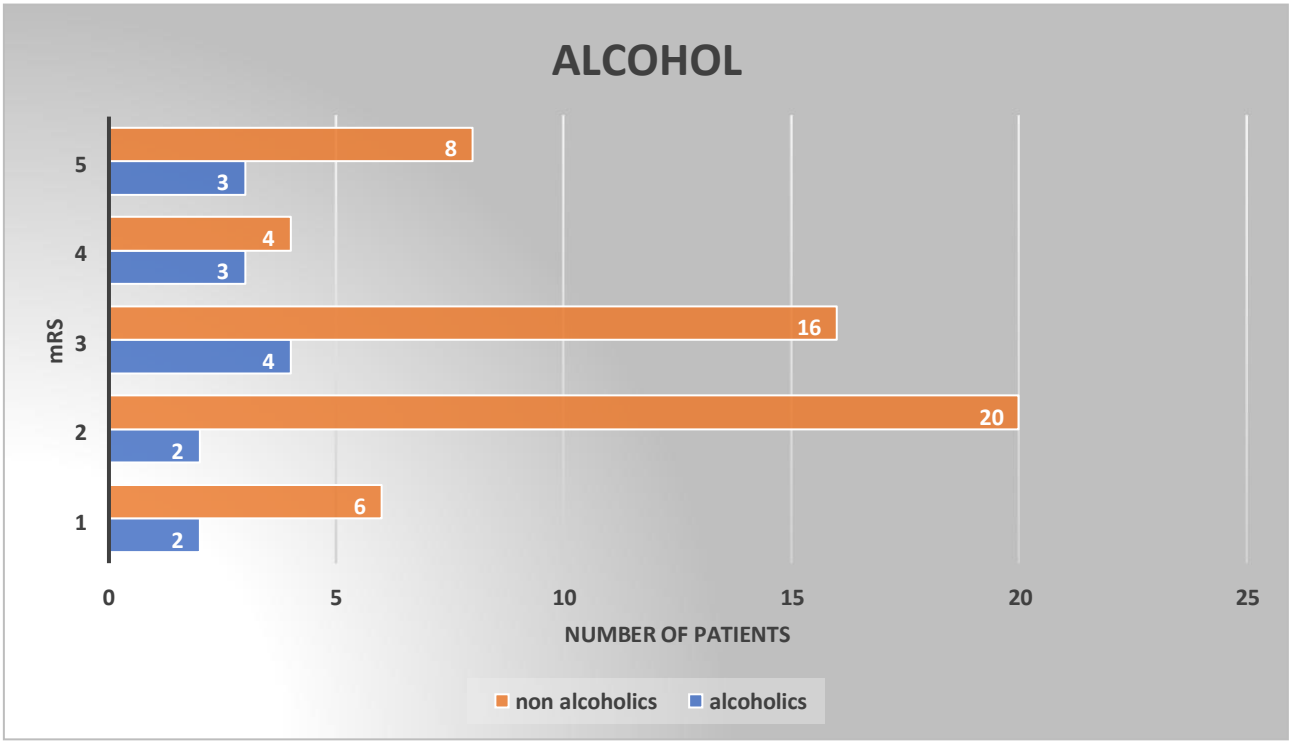
TABLE 14& FIGURE 22

TABLE 14: ALCOHOLICS

mRS	Alcoholics	Non Alochlics
1	2	6
2	2	20

3	4	16
4	3	4
5	3	8
Total	14	54

FIGURE 22: ALCOHOLICS



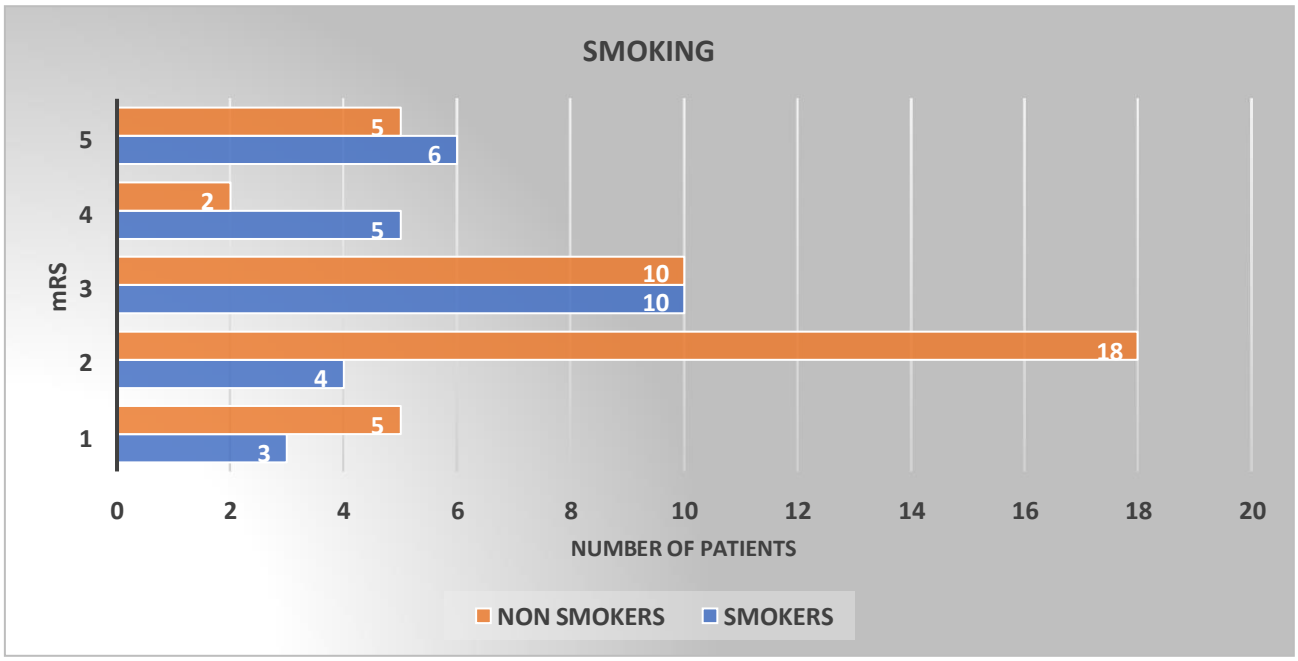
SMOKING

In our study, it was found that out of 68 patients, 28 (41.1%) patients were smokers and 40 (58.8%) patients were non-smokers, this was compared with mRS severity scale results were as under mRS-1 three were smokers and 5 were non-smokers, mRS-2 four were smokers and 18 were non-smokers, mRS-3 10 were smokers and 10 were non-smokers, mRS-4 five were smokers and two were non-smokers and mRS-5 6 were smokers and five were non-smokers. **TABLE 15 & FIGURE 23.**

TABLE 15: SMOKERS

mRS	SMOKERS	NON-SMOKERS
1	3	5
2	4	18
3	10	10
4	5	2
5	6	5
Total	28	40

FIGURE 23: SMOKERS



OUTCOME

In our study, we categorized outcomes into improved and bedridden. mRS 1, mRS 2, mRS 3 were categorised improved and mRS 4 and Mrs 5 were categorised bedridden. No mortality was observed within 24hrs of admission.

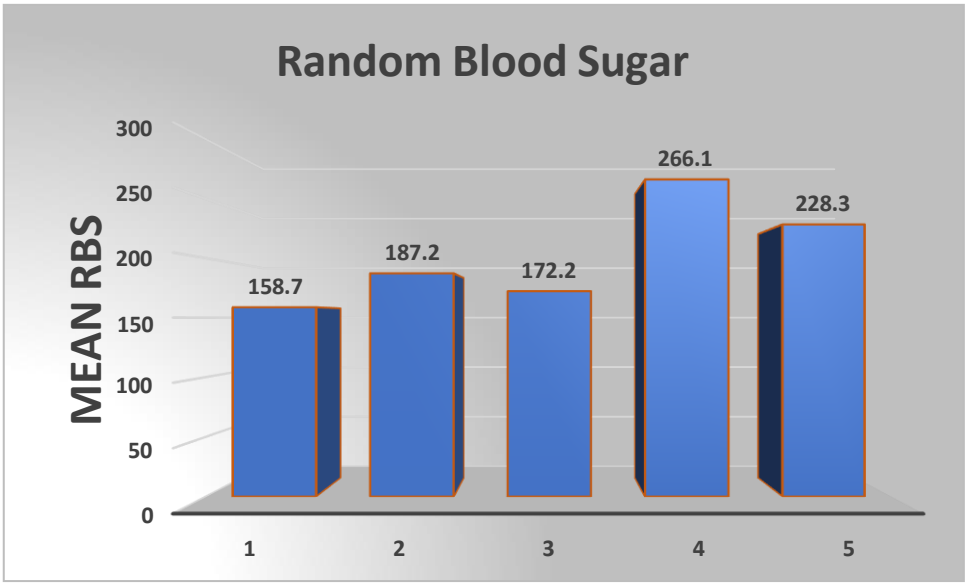
Random blood sugar and modified Rankin Scale

In our study we evaluated the RBS at presentation in casualty and compared with mRS severity scale. We graded mRS from 1 to 5 and we found 8 (11.7%) patients were under mRS-1 and mRS-2 were 22 (32.4%), mRS-3 were 20 (29.4%), mRS-4 were 7 (10.3%), and mRS-5 were 11 (16.2%). Average random blood glucose level found in patients mRS-1 was 158.7(±76), under mRS-2 187.2(±121.2), mRS-3 172.2 (±67.5), mRS-4 266.1 (±137.7), mRS-5 228.3 (±99.3). Hence higher the blood sugar level more the severity. **TABLE 16 & FIGURE 24**

TABLE 16: CORRELATION OF RANDOM BLOOD SUGAR WITH mRS

mRS	N	Percentage %	RBSmg/dl	
			MEAN	±SD
1	8	11.7	158.7	76.0
2	22	32.4	187.2	121.2
3	20	29.4	172.2	67.5
4	7	10.3	266.1	137.7
5	11	16.2	228.3	99.3

FIGURE 24: CORRELATION OF RANDOM BLOOD SUGAR WITH mRS



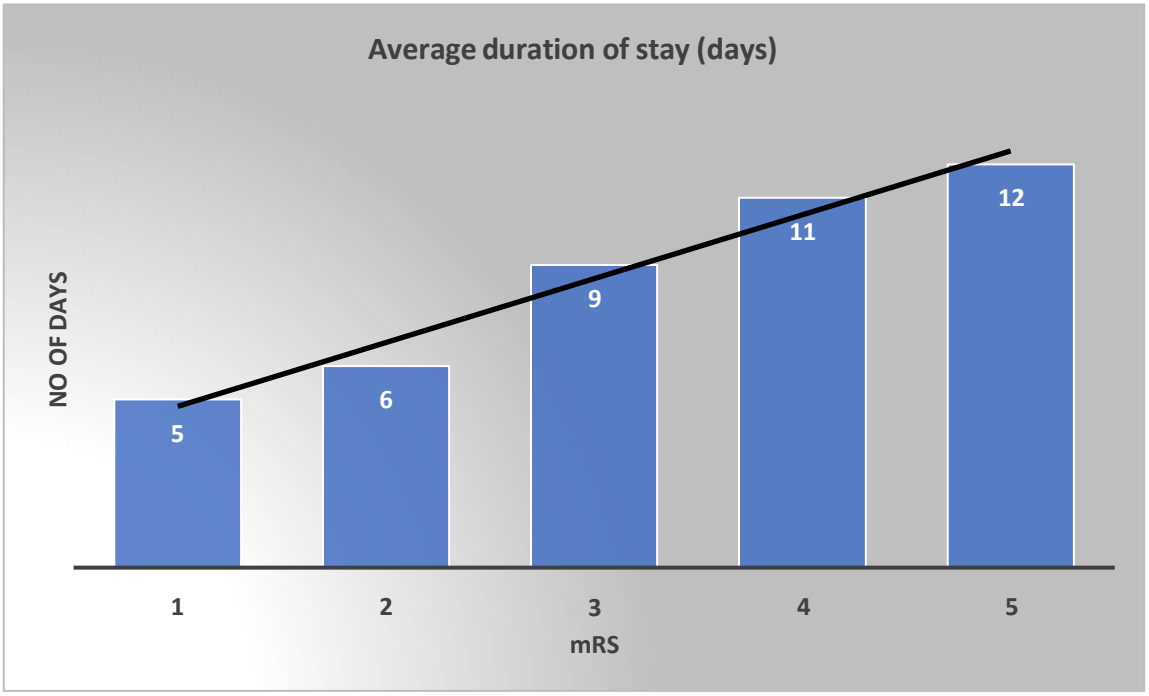
DURATION OF STAY IN HOSPITAL

Average duration of stay of the patients was calculated and compared with modified Rankin Scale and graph was plotted which showed patients with higher severity grade had stayed higher number of days stay in hospital.**TABLE 17 & FIGURE 25**

TABLE 17 : CORRELATION OF DURATION OF STAY WITH mRS

mRS	Average duration of stay (days)
1	5
2	6
3	9
4	11
5	12

FIGURE 25: CORRELATION OF DURATION OF STAY WITH mRS



Serum ferritin and modified Rankin Scale

In our study,mRS scale was applied in all the patient presented within 24hr of onset of weakness and correlated with serum ferritin level. we graded mRS from 1 to 5 and we found 8 (11.7%) patients were under mRS-1 and mRS-2 were 22 (32.4%), mRS-3 were 20 (29.4%), mRS-4 were 7 (10.3%), and mRS-5 were 11 (16.2%). Average serum ferritin found in patients under mRS-1 was 90.9(±77.5), mRS-2 112.3(±107.1), mRS-3 173.1 (±114.2), mRS-4 292.9 (±133.9), mRS-5 595.3 (±392.2). **TABLE – 18**

Results were plotted using scatter diagram which showed ferritin was in increasing trend as the mRS grading was increasing which signifies higher the ferritin, more the severity of stroke. **FIGURE - 26**

The correlation between serum ferritin and mRS had a P-value < 0.0001 which is statically significant and SPERSON'S CORRELATION COEFFIENT was **r=0.609**which signifies the moderate correlation. **TABLE - 19**

TABLE –18: CORRELATION OF SERUM FERRITIN WITH mRS

mRS	N	Percentage %	FERRITIN ng/dl		KRUSKAL-WALLIS TEST	P VALUE
			MEAN	±SD		
1	8	11.7	90.9	77.5	26.627	P=0.0001*
2	22	32.4	112.3	107.1		
3	20	29.4	173.1	114.2		
4	7	10.3	292.9	133.9		
5	11	16.2	595.3	392.2		
		* STATISTICALLY SIGNIFICANT				

FIGURE -26: CORRELATION OF DURATION OF STAY WITH mRS

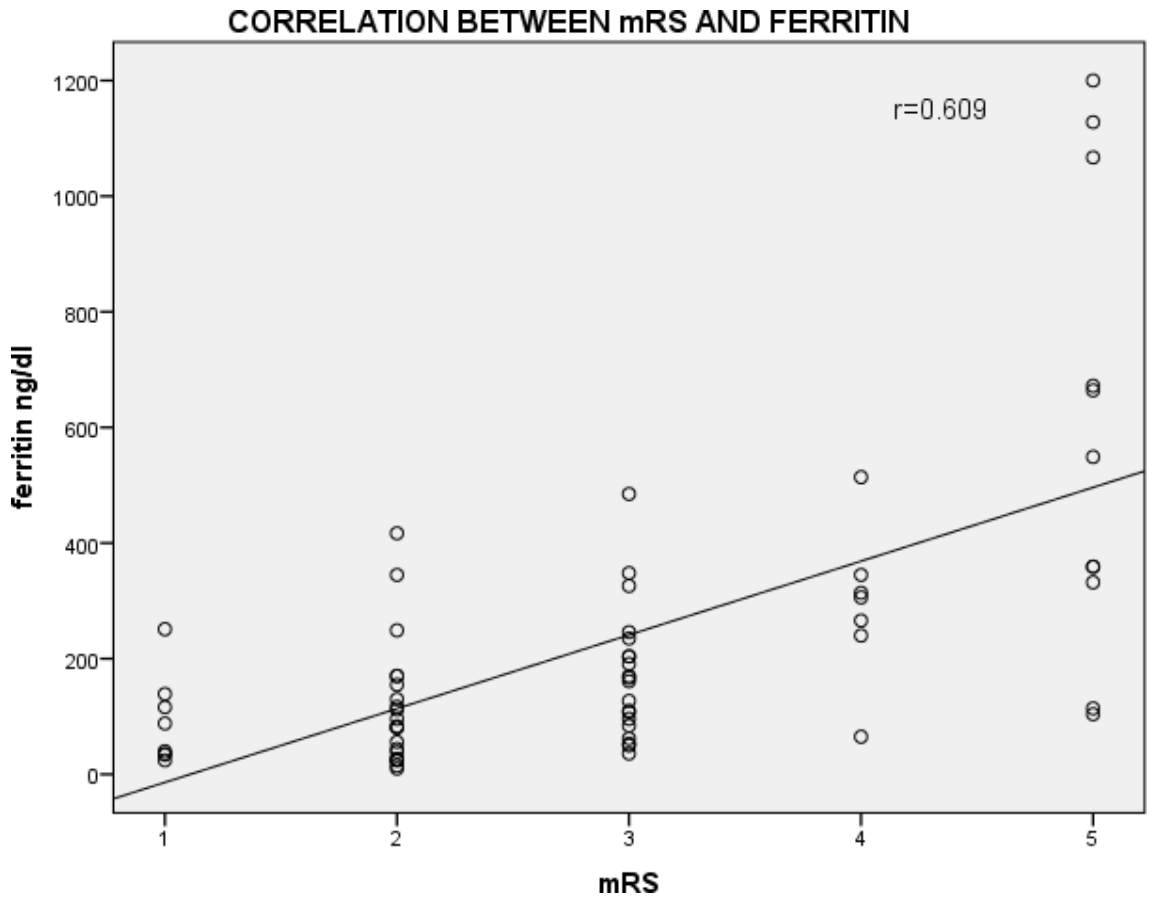


TABLE 19: CORRELATION OF DURATION OF STAY WITH MRS USING SPEARSON'S CORRELATION COEFFICIENT

CORRELATION BETWEEN	SPEARSON'S CORRELATION COEFFIENT	P VALUE	REMARK
mRSANDFERRITIN NG/DL	**r=0.609**	**P=0.0001***	**MODERATE CORRELATION & SIGNIFICANT**
*:STATISTICALLY SIGNIFICANT			

DISCUSSION

Study was carried out to correlate serum ferritin level to severity of ischemic stroke using modified Rankin Scale (mRS) in 68 patients who presented to our hospital within 24hrs of onset of symptoms.

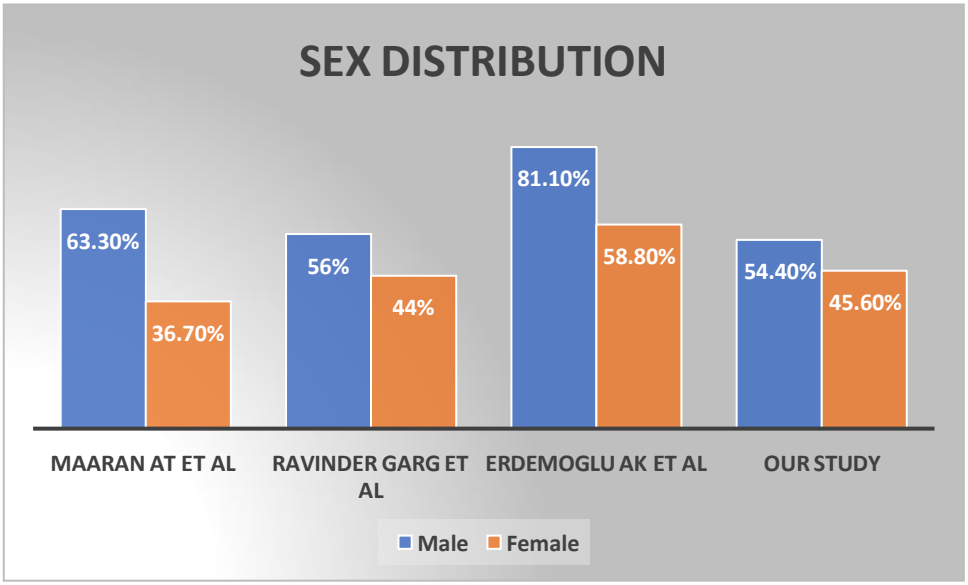
COMPARISON OF SEX DISTRIBUTION

In our study, the majority were male37(54.4%) and females constituted 31(45.6%) which is similar in the studies byMaaranATet al [81]with male 63.33% and Ravinder Garg et al [82] found 56% were males andErdemoglu AK et al [83] had female dominance of 58.8%.**TABLE 20 & FIGURE 27**

TABLE 20: COMPARISON OF SEX DISTRIBUTION

SEX	Maaran AT et al	Ravinder Garg et al	Erdemoglu AK et al	Our study
Male	63.3%	56%	81.1%	54.4%
Female	36.7%	44%	58.8%	45.6%
TOTAL	100	100	100	100

FIGURE 27: COMPARISON OF SEX DISTRIBUTION



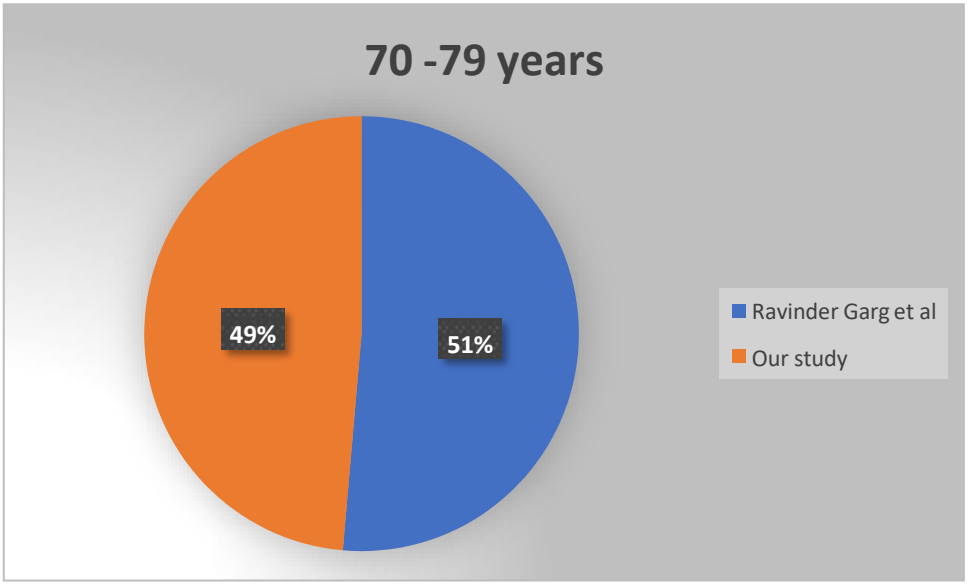
COMPARISON OF AGE DISTRBUTION

In our study mean age observed was 62.82 ±15.07 SD and majority were under 70 -79 years which was 26.5% which is similar in study by Ravinder Garg et al [82] that 28% were aged >70 years.**TABLE 21& FIGURE 28**

TABLE 21: COMPARISON OF AGE DISTRBUTION

AGE	Ravinder Garg et al	Our study
70 -79 years	28%	26.5%

FIGURE 28: COMPARISON OF AGE DISTRBUTION



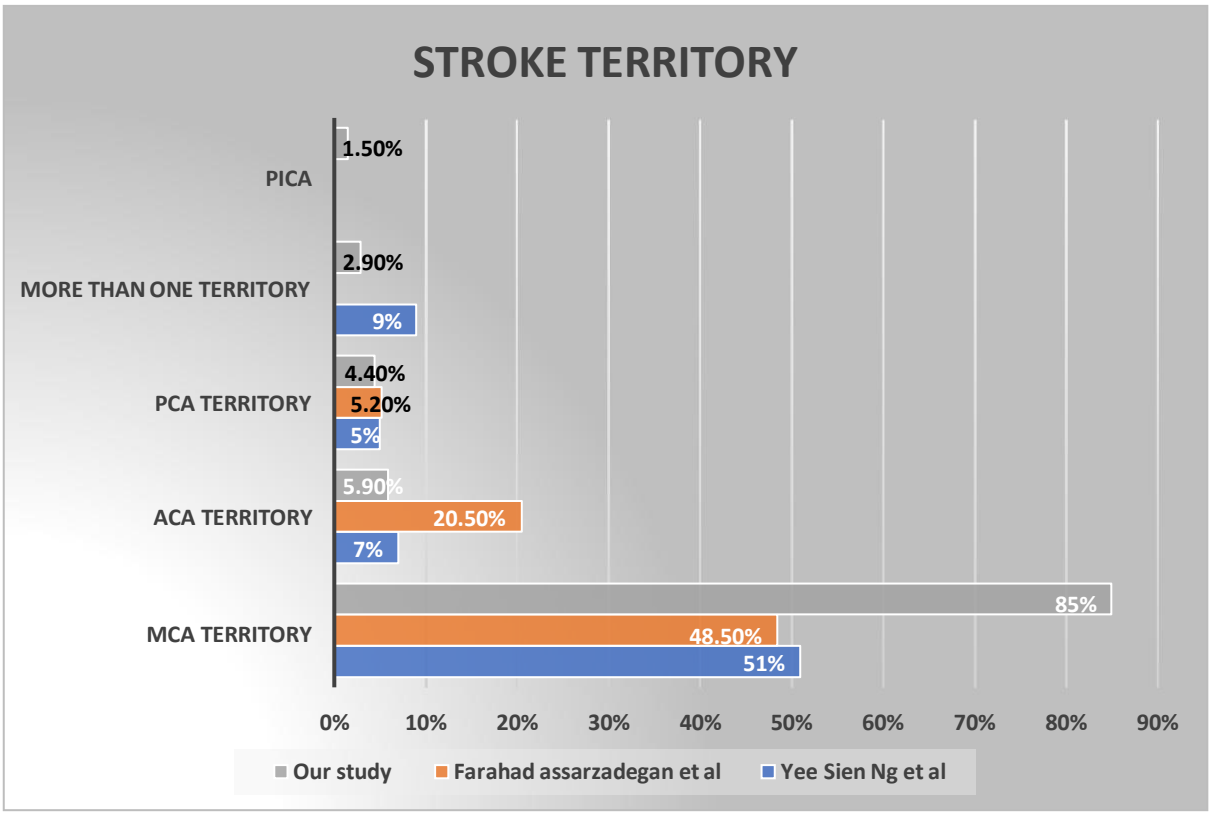
COMPARISON OF TERRITORY OF INVOLVEMENT

In our study most common territory involved was MCA territory 85% followed by ACA territory involved in 5.9%, PCA territory was involved in 4.4%, multiple territories was involved in 2.9% and PICA was involved in 1.5%. Which is similar in study by Yee Sien Ng et al [84]had MCA 51% PCA 7% and ACA 5% more than one territory was in 9%. And study by FarhadAssarzadegan et al [85] found MCA 48.5%, PCA 20.5% and ACA 5.2%. **TABLE 22& FIGURE 29**

TABLE 22: COMPARISON OF TERRITORY OF INVOLVEMENT

TYPE	Yee Sien Ng et al	Farahadassarzadegan et al	Our study
MCA TERRITORY	51%	48.5%	85
ACA TERRITORY	7%	20.5%	5.9
PCA TERRITORY	5%	5.2%	4.4
MORE THAN ONE TERRITORY	9%		2.9
PICA			1.5

FIGURE 29: COMPARISON OF TERRITORY OF INVOLVEMENT



COMPARISON OF COMORBIDITIES

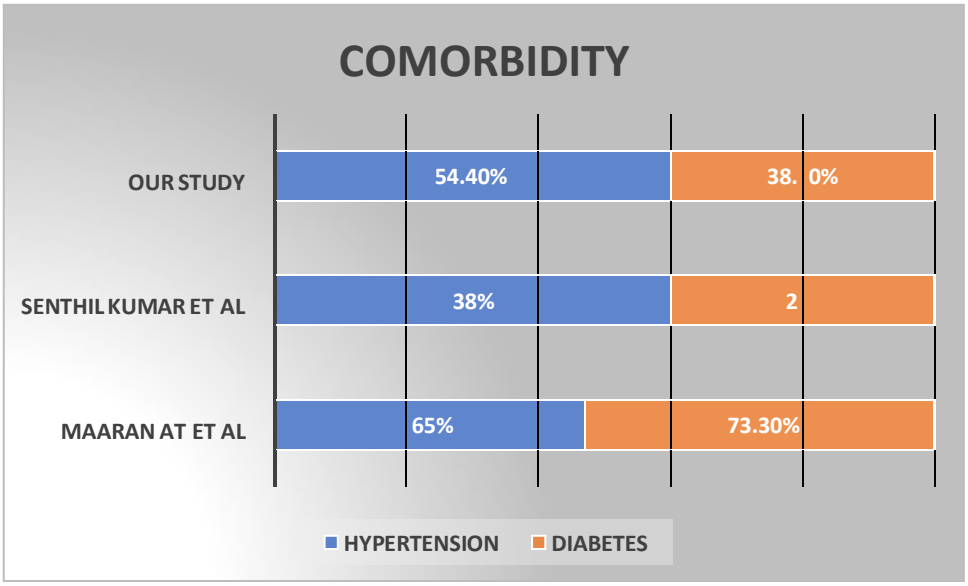
In our study the comorbidities in single or combinations of two or more was observed and commonest comorbidity was found to be hypertension 54.4% followed by diabetes 38.2% which is also similar in study conducted by Senthil Kumar PK et al [86] had hypertension in 38% and diabetes

in 26%, where MaaranATet al [81]showed commonest symptom as diabetes73.3% followed by hypertension in 65.0%.**TABLE 23& FIGURE 30**

TABLE 23: COMPARISON OF COMORBIDITIES

TYPE	MaaranAT et al	Senthilkumar et al	Our study
HYPERTENSION	65%	38%	54.4%
DIABETES	73.3%	26%	38.2%

FIGURE 30: COMPARISON OF COMORBIDITIES



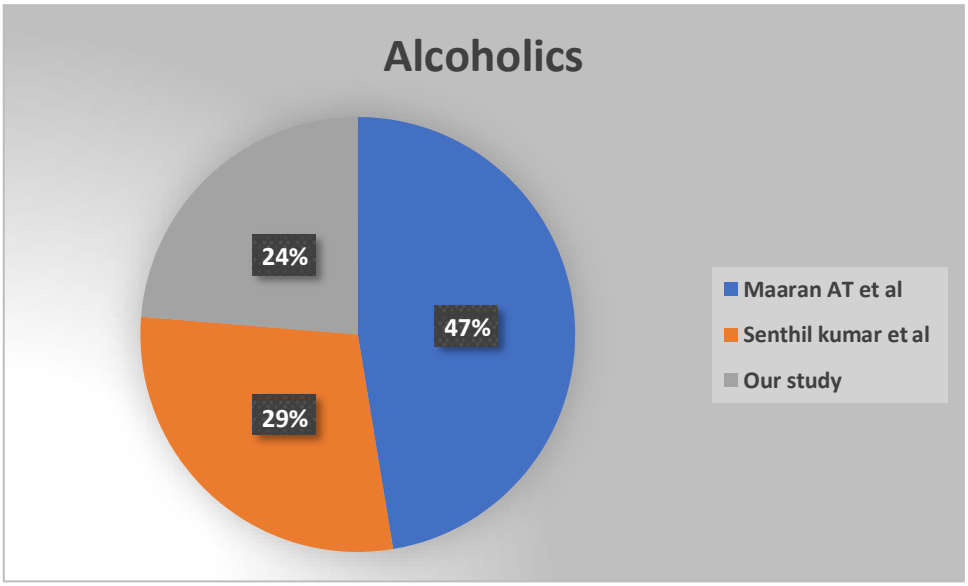
COMPARISON OF ALCOHOLICS

In our study, it was found that out of 68 patients, 14 (20.5%) patients were alcohol abusers. Similarly study by Senthil Kumar PK et al [86] had 25% of alcohol abusers and 41 % of alcohol abusers were in the study by MaaranATet al [81]**TABLE 24& FIGURE 31**

TABLE 24: COMPARISON OF ALCOHOLICS

TYPE	MaaranAT et al	Senthilkumar et al	Our study
Alcoholics	41%	25%	20.5%

FIGURE 31: COMPARISON OF ALCOHOLICS



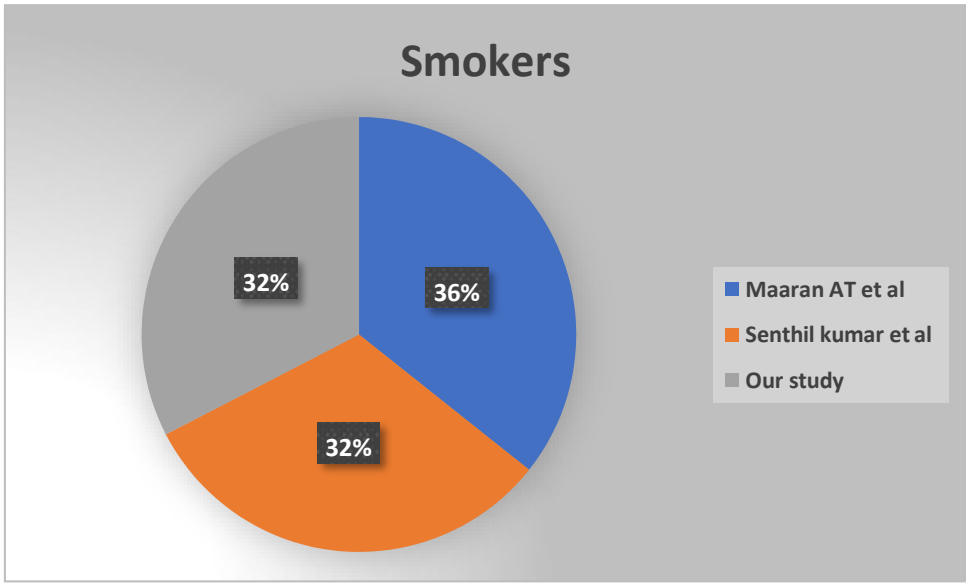
COMPARISON OF SMOKERS

In our study, it was found that out of 68 patients, 28 (41.1%) patients were smokers. Similarly study by Senthil Kumar PK et al [86] had 40% of smokers and 45 % of smokers were in the study by MaaranATet al[81]**TABLE 25& FIGURE 32**

TABLE 25: COMPARISON OF SMOKERS

TYPE	MaaranAT et al	Senthilkumar et al	Our study
Smokers	45%	40%	41.1%

FIGURE 32: COMPARISON OF SMOKERS



SERUM FERRITIN LEVEL AND SEVERITY

In our study serum ferritin was assessed in all eligible patients and correlated to the severity of stroke using mRS scale, we have got positive correlation between serum ferritin and severity of ischemic stroke with significant p value <0.0001 which was found in other studies as follow

TABLE 26.

TABLE 26: COMPARSSION OF SERUM FERRITIN AND SEVERITY

SL.NO	AUTHOR	YEAR
1	Erdemoglu AK et al [83]	2002
2	Senthil Kumar PK et al [86]	2006
3	MaaranATet al[81]	2014
4	Koul RK et al [87]	2017
5	Narayan M et al [88]	2018
6	Ravinder Garg et al [82]	2020

CONCLUSION

The present study conducted to evaluate Serum ferritin level as a severity marker in patients with ischemic stroke using modified Rankin Scale (mRS) revealed a significant correlation of serum ferritin with severity of ischemic stroke, illustrating higher the level of serum ferritin, more the severe stroke. Patients with higher levels of serum ferritin at admission tend to deteriorate more as compared to those with lower serum ferritin levels. Thus, serum ferritin can be used as a severity marker in patients with acute ischemic stroke and iron chelation therapy can be considered for the better outcome. To improve the outcome many studies must be conducted in large scale using iron chelator in stroke patient. And we conclude serum ferritin to be evaluated in ischemic stroke patients at admission as a routine investigation.

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ANNEXURE I

B.L.D.E. (DEEMED TO BE UNIVERSITY) IEC/No-9/2021 Date-22/01/2021

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: Serum Ferritin level as severity marker in patients with ischemic stroke using modified rankin scale

Name of PG student: Dr Santhosh.B.T, Department of Medicine

Name of Guide/Co-investigator: Dr Anand.P.Ambali, Professor of Medicine

DR .S.V.PATIL
CHAIRMAN
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

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ANNEXURE II

SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE,VIJAYAPURA-586 103

RESEARCH INFORMED CONSENT FORM

TITLE OF THE PROJECT :"Serum ferritin level as a severity marker in patients with ischemic stroke using modified Rankin Scale (mRS)"

PG GUIDE : DR. ANAND P AMBALI

PG STUDENT : DR. SANTHOSH.B.T

PURPOSE OF RESEARCH: I have been informed about this study. I have also been given a free choice of participation in this study.

BENEFITS:-

I understand that my participation in this study will help the investigator to diagnose the disease better and will help in the management of the disease.

PROCEDURE:-

I understand that relevant history will be taken and I will undergo detailed clinical examination after which necessary investigations will be done and accordingly treatment will be given.

RISK AND DISCOMFORTS:-

I understand there is no risk involved and I will experience no pain during the procedures performed.

CONFIDENTIALITY:-

I understand that medical information produced by this study will become a part of my hospital records and will be subjected to the confidentiality and privacy regulation of the said hospital. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file.

If the data are used for publication in the medical literature or for teaching purposes no names will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand I may see the photographs, videotapes and hear the audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:-

I understand that I may ask more questions about the study at any time Concerned. The researcher is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which may influence my continued participation.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:-

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in this study at any time without prejudice. I also understand that the researcher may terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician, if this is appropriate.

INJURY STATEMENT:-

I understand that in the unlikely event of injury to me resulting directly from my participation in this study and if such injury were reported promptly, then medical treatment will be available to me, but no further compensation will be provided. I understand that by my agreement for my participation in this study, I am not waiving any of my legal rights.

I have explained to (patient's / relevant guardian's name) the purpose of the research, the procedures required, and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Investigator / P. G. Guide Date

I confirm that …….(Name of the PG guide / chief researcher) has explained to me the research, the study procedures that I undergo and the possible risks and discomforts as well as benefits that I may experience. I have read and I understand this consent form. Therefore, I agree to give my consent for my participation as a subject in this research project.

_____ _____

Participant / guardian Date

_____ _____

Witness to signature Date

ANNEXURE III

B.L.D.E (DEEMED TO BE UNIVERSITY)

SHRI B M PATIL MEDICAL COLLEGE

VIJAYAPURA, KARNATAKA

SCHEME OF CASE TAKING

Informant :

Name: CASE NO:Past Occupation:

Age: IP NO: Present Occupation:

Sex: DOA: Residence:

Religion: DOD:

Chief complaints:

History of present illness:

Past History:

H/O of stroke in past

H/O of Diabetes mellitus, hypertension, asthma, tuberculosis, allergy

H/O of recent hospitalization

H/O of surgeries

Personal History:

- **DietAppetiteSleepBladder Bowel**
- **Habits**

Family History:

General Physical Examination

Height: Weight:Body Mass Index:

Vitals = PR: BP: RR: Temp:

Head to toe examination:

Scalp: **Eyes:Nose:Ears:** **Oral cavity:**

Face: **Neck:**

Upper limb & Lower limb:

Nails -Edema -Pigmentation –

Chest and abdomen:

SYSTEMIC EXAMINATION.

CENTRAL NERVOUS SYSTEM:

I. **Handedness**

II. **Higher mental function**

Conscious: Orientation:

Delusion and hallucinations: **Memory: Past, Present and Remote**

III. **Speech:**
Dysarthria - Repetition –

Comprehension - Reading -

Fluency –Writing -

IV. Cranial nerves – 1 2 3 4 5 6 7 8 9 10 11 11 12

V. Motor system

- **Power –**

Shoulder **Hip**

Elbow **Knee**

Wrist **Ankle**

- **Nutrition/bulk of muscle**
- **Tone**

- **Reflexes**

SUPERFICIAL

Plantar **abdominal** **sphincter reflex**

DEEP

Biceps **Triceps** **Supinator** **Knee** **Ankle**

- **Co-ordination of movement**

- **Gait**

- **Involuntary movements**

VI. Sensory system

- **Tactile sensibility –** light touch and pressure, and tactile localization and discrimination
- **Recognition of size, shape, weight and form –**
- **Vibration –**
- **Pain –**
- **Temperature –**

VII. Autonomic function

Bladder and bowel control

Postural hypotension

VIII. Signs of meningeal irritation

RESPIRATORY SYSTEM: CARDIOVASCULAR SYSTEM:

PER ABDOMEN

INVESTIGATIONS

1. HAEMATOLOGY –

Hemoglobin	gm. %
Total WBC counts	Cells/mm^3
Differential counts	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	%
Basophils	%
Platelet count	
ESR	At the end of 1st hour

TOTAL CHOLESTEROL-	
TRIGLYCERIDES-	
LDL-	
HDL -	
NON HDL CHOLESTEROL-	
VLDL -	
CHOL/HDL RATIO -	
SERUM FERRITIN	
CREATININE	
UREA	
GRBS	

2.Radiological investigations:

- **CT brain :**

- **MRI Brain**

- **URINE ROUTINE : albumin sugars pus cell RBC**
- **ECG**

- **2D-ECHOCARDIOGRAPHY**

- **Modified rankin scale score**

CONCLUSION:

Date:-

Signature:-

Master chart

SL.N	OF STA	NAME	AGI	SE	complaint	type	CT	MRI	site	mR	ferritin ng	RBS mg	DM	HTN	OTHERS	ALCOH	SMOKI	outcome
1	3	HUSHEN SAB NADAF	70	M	L/Lweakness & deviation of angle of mouth	right hemiparesis	NORMAL	ACUTE INFARCT	LEFT MCA TERRITORY	3	95.6	234	YES	YES	IHD	YES	YES	IMPROVED
2	5	DUNDAWWA	80	F	left U/L L/Lweakness & giddiness	left hemiparesis	LACUNAR INFARCT	NA	RIGHT MCA TERRITORY	2	26.4	541	YES	YES		NO	NO	IMPROVED
3	7	LAXMIBAI	58	F	inability to swallow	Wallenberg's syndrom	NORMAL	ACUTE INFARCT	PICA	1	116	278	YES	YES		NO	NO	IMPROVED
4	3	ANNAPPA SANGAPPA HALAKE	70	M	irrelevant speech	right hemiparesis	ACUTE INFARCT	NA	LEFT MCA TERRITORY	3	246	100	NO	NO		YES	YES	IMPROVED
5	7	CHANDRASHEKAR M DEVAREDDY	65	M	right U/L L/Lweakness & unable to talk	right hemiparesis	NA	ACUTE INFARCT	LEFT MCA TERRITORY	3	49.5	256	YES	YES	IHD	NO	YES	IMPROVED
6	5	SHIVALINGAYYA BASAYYA MANTI	65	M	B/L U/L & L/Lweakness	right hemiplegia	LACUNAR INFARCT	ACUTE INFARCT	LEFT ACA & MCA TERRITOR	5	549.4	105	NO	NO		YES	YES	BEDRIDDEN
7	2	SHARANAPPA SIDRAMAPPA KOTL	65	M	left U/L L/Lweakness & swaying to left	left hemiparesis	NORMAL	MULTIPLE LAUNAR INFARCT	RIGHT MCA TERRITORY	3	161	110	NO	NO		NO	NO	IMPROVED
8	4	RAMESH GANAPATHI BADIGERE	40	M	right U/L L/Lweakness	right hemiparesis	ACUTE INFARCT	NA	LEFT MCA TERRITORY	3	61.7	200	NO	NO		NO	YES	IMPROVED
9	7	DRAKSHYANI BASAYYA GANCHAF	67	F	right U/L L/Lweakness	right hemiplegia	NA	ACUTE INFARCT	LEFT MCA TERRITORY	4	64.8	402	YES	YES	IHD	NO	NO	BEDRIDDEN
10	3	SRIMANTH LOKAPPA NIVARAGI	70	M	decreased response	parapleagia	ACUTE INFARCT	ACUTE INFARCT	B/L ACA TERRITORY	5	672	351	NO	NO	COPD	NO	YES	BEDRIDDEN
11	7	SHIVANAD I TAPAPUR	55	M	left U/L L/Lweakness	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	3	84	278	YES	YES		NO	NO	IMPROVED
12	9	SHAVANTRAWWA D PATIL	65	F	giddiness & altered sensorium	right hemiplegia	NORMAL	ACUTE INFARCT	LEFT MCA TERRITORY	5	113.8	111	NO	NO		NO	NO	BEDRIDDEN
13	6	JAIBANBEE HUSANSAB PADASAL	55	F	altered sensorium & slurred speech	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	3	52.9	162	NO	YES	EPILEPSY	NO	NO	BEDRIDDEN
14	9	BASAMMA	74	F	left U/L L/Lweakness	right hemiparesis	NORMAL	ACUTE INFARCT	LEFT MCA TERRITORY	2	80.6	150	NO	YES		NO	NO	IMPROVED
15	5	SHIVAYOGI SIDRAM HATI	70	M	right U/L L/Lweakness	right hemiparesis	NORMAL	ACUTE INFARCT	LEFT MCA TERRITORY	2	55.5	147	NO	NO		YES	YES	IMPROVED
16	4	RAMU THULAJU RATHOD	55	M	L/Lweakness & deviation of angle of mouth	left hemiplegia	NORMAL	LARGE ACUTE INFACT	RIGHT MCA TERRITORY	5	359	166	NO	NO		YES	YES	BEDRIDDEN
17	14	SHANTAPPA laxman banikolu	70	M	right U/L L/Lweakness & slurred speech	left hemiplegia	NA	ACUTE INFARCT	RIGHT MCA TERRITORY	4	313.74	176	NO	NO	osteoarthritis	YES	YES	BEDRIDDEN
18	13	KASHIBAI SHARANAPPA PALKI	61	F	giddiness	right hemiparesis	NORMAL	ACUTE INFARCT	LEFT MCA TERRITORY	3	106.64	141	NO	NO		NO	NO	IMPROVED
19	4	SHARADABAI MALLAPPA KOTANA	30	F	loss of balance	right hemiparesis	NA	ACUTE INFARCT	LEFT MCA TERRITORY	1	250.77	89	NO	NO		NO	NO	IMPROVED
20	2	APPASAHEB KUCHANUR	59	M	right U/L L/Lweakness & slurred speech	right hemiparesis	NORMAL	ACUTE INFARCT	LEFT MCA TERRITORY	2	14.97	265	YES	YES		NO	YES	IMPROVED
21	6	MOHAN VAMAN TILGUL	76	M	L/Lweakness & deviation of angle of mouth	left hemiplegia	NORMAL	ACUTE INFARCT	RIGHT MCA TERRITORY	4	266.02	216	YES	YES		NO	YES	BEDRIDDEN
22	16	BASAVARAJ KATTIMANI	40	M	left U/L L/Lweakness & giddiness	left hemiparesis	NA	ACUTE INFARCT	RIGHT MCA TERRITORY	3	235.01	82	NO	NO		YES	YES	IMPROVED
23	3	HANAMANTH BHIMASHI MARADI	46	M	left U/L L/Lweakness	left hemiplegia	ACUTE INFARCT	NA	RIGHT MCA TERRITORY	4	240	118	NO	NO	IHD,osteoarthritis	YES	YES	BEDRIDDEN
24	10	PREMASINGH KATHEWAL	85	M	left U/L L/Lweakness	left hemiplegia	SUBACUTE INFARCT	NA	RIGHT MCA TERRITORY	5	1200	110	NO	NO		NO	YES	BEDRIDDEN
25	3	LACHAPPA YALLAPPA CHIGARI	44	M	swaying while walking & slurring of speech	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	2	116.67	127	NO	NO		NO	NO	IMPROVED
26	42	VIDYA RAMESH BYAKOD	32	F	decreased response	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	3	326	109	NO	NO		NO	NO	IMPROVED
27	2	SHEKAPPA HUKKERI	55	M	giddiness & swaying to right	right hemiparesis	ACUTE INFARCT	NA	LEFT MCA TERRITORY	2	249	287	YES	YES		NO	YES	IMPROVED
28	6	MANJULA BHIMANNA JABENAVAR	55	F	left U/L L/Lweakness	left hemiparesis	NA	ACUTE INFARCT	RIGHT MCA TERRITORY	2	10.06	121	YES	NO	osteoarthritis	NO	NO	IMPROVED
29	5	MAMATAJBEGAM NAZEERAHEMA	50	F	eft U/L L/Lweakness & involuntary movement	left hemiplegia	SUBACUTE INFARCT	ACUTE INFARCT	RIGHT ACA & MCA TERRITOR	5	1067	258	YES	YES		NO	NO	IMPROVED
30	3	SHIVASHANKAR SHIVAN& ALAGUI	62	m	left U/L L/Lweakness	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	2	83	96	NO	NO		NO	NO	IMPROVED
31	11	BAPU MANE	56	M	right U/L L/Lweakness & gen weakness	right hemiparesis	NA	SUBACUTE INFARCT	LEFT MCA TERRITORY	3	485	114	NO	YES		NO	YES	IMPROVED
32	6	ASHOK SIDAPPA PATTASHETTI	55	M	right U/Lweakness & slurred speech	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	2	170	182	YES	YES		YES	NO	IMPROVED
33	4	SHRISHAIL D RACHAGOND	65	M	involuntary movements	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT PCA TERRITORY	3	204.5	161	NO	NO		YES	YES	IMPROVED
34	5	GANGARAM IRASOOR	68	M	left U/L L/Lweakness & giddiness	left hemiparesis	NORMAL	ACUTE INFARCT	RIGHT MCA TERRITORY	2	25.62	100	NO	NO		NO	YES	IMPROVED
35	3	SARUBAI SHIVANAD	68	F	left U/L L/Lweakness	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	2	23.7	107	NO	YES	COPD	NO	NO	IMPROVED
36	11	SHARANAPPA NARASKOPPA	60	M	right U/L L/Lweakness & slurred speech	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT PCA TERRITORY	2	129.79	126	NO	YES		NO	NO	IMPROVED
37	6	KASHIMSAB DAWALSAB	62	M	left U/L L/Lweakness & giddiness	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	3	170	189	YES	YES		NO	YES	IMPROVED
38	4	VISHVARAPPA	72	M	left U/L L/Lweakness	left hemiplegia	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	4	513.81	425	YES	YES		YES	YES	BEDRIDDEN
39	5	TOOLAMMA	45	F	left U/L L/Lweakness & giddiness	left hemiparesis	NA	ACUTE INFARCT	RIGHT MCA TERRITORY	3	127.46	300	NO	NO	IHD	NO	NO	IMPROVED
40	3	RATANABI	85	F	right U/L L/Lweakness	right hemiparesis	NA	ACUTE INFARCT	LEFT MCA TERRITORY	2	345	107	NO	YES		NO	NO	IMPROVED

SL_N	DUR O	NAME	AGE	SEX	complaint	type	CT	MRI	site	mRS	ferritin ng	RBS mg	DM	HTN	OTHERS	ALCOH	SMOKE	outcome
39	5	TOOLAMMA	45	F	left U/L L/Lweakness & giddiness	left hemiparesis	NA	ACUTE INFARCT	RIGHT MCA TERRITORY	3	127.46	300	NO	NO	IHD	NO	NO	IMPROVED
40	3	RATANABI	85	F	right U/L L/Lweakness	right hemiparesis	NA	ACUTE INFARCT	LEFT MCA TERRITORY	2	345	107	NO	YES		NO	NO	IMPROVED
41	2	PARASHURAM	40	M	ght U/L L/Lweakness with urinary incontinen	monoparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT ACA TERRITORY	2	80.86	219	YES	YES		NO	NO	IMPROVED
42	8	JAYASHREE	50	F	difficulty in swallowing	right hemiparesis	NORMAL	ACUTE INFARCT	LEFT PCA TERRITORY	3	191.3	104	YES	YES	IHD	NO	NO	IMPROVED
43	7	HANAMAWWA	97	F	slurred speech & altered sensorium	right hemiparesis	ACUTE INFARCT	NA	LEFT MCA TERRITORY	2	111.9	520	YES	YES		NO	NO	IMPROVED
44	25	INDUMANTI	75	F	decreased response	right hemiplegia	ACUTE INFARCT	NA	LEFT MCA TERRITORY	4	306.5	126	YES	YES		NO	NO	BEDRIDDEN
45	1	SHRIMANTH LAGAMMA	60	F	left U/L L/Lweakness	right hemiparesis	NORMAL	ACUTE INFARCT	LEFT MCA TERRITORY	1	139	120	NO	YES		YES	YES	IMPROVED
46	24	MANOHAR BASAPPA	76	M	left U/L L/Lweakness	left hemiparesis	ACUTE INFARCT	NA	RIGHT MCA TERRITORY	3	166.8	200	NO	NO		NO	NO	IMPROVED
47	8	SHANKAR GOWDA R PATIL	40	M	loss of consciousness	right hemiplegia	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	5	663.9	300	YES	YES		YES	YES	BEDRIDDEN
48	4	NOORJHAN	55	F	left U/L L/Lweakness	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	3	36.4	250	NO	NO	RHD	NO	NO	IMPROVED
49	14	ISMILSAB M CHOUDHARI	70	M	left U/L L/Lweakness & slurred speech	left hemiparesis	NA	ACUTE INFARCT	RIGHT MCA TERRITORY	3	109.7	104	NO	YES	COPD	NO	YES	IMPROVED
50	4	AHILYA BABURAO MAHINDAKAR	93	F	left U/L L/Lweakness & slurred speech	left hemiplegia	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	5	359	400	YES	YES		NO	NO	BEDRIDDEN
51	7	SAROJANADEVI	76	F	altered sensorium	right hemiparesis	ACUTE INFARCT	NA	LEFT MCA TERRITORY	2	417	130	NO	NO		NO	NO	IMPROVED
52	8	NIJAWWA MALLAPPPA	65	F	altered sensorium	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	2	170	150	NO	NO		NO	NO	IMPROVED
53	6	RACHAWWA VERRAPPA	83	F	giddiness & altered sensorium	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	2	43.5	140	NO	NO		NO	NO	IMPROVED
54	1	KAMALABAI PATIL	85	F	tered sensorium & deviation of mouth to rig	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	2	25.1	145	YES	YES		NO	NO	IMPROVED
55	13	LAGAMAVVA SAMGAMAD	75	F	right U/L& L/Lweakness & giddiness	right hemiparesis	NA	ACUTE INFARCT	LEFT MCA TERRITORY	2	39.1	160	NO	YES		NO	NO	IMPROVED
56	5	ASHOK S MANUS	60	M	right U/L L/Lweakness	QUADRIPARESIS	ACUTE INFARCT	ACUTE INFARCT	B/L MCA TERRITORY	5	1128	211	NO	YES	HIV	NO	NO	BEDRIDDEN
57	9	LALITABAI	71	F	involuntary movements	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	3	348	226	NO	YES	EPILEPSY	NO	NO	IMPROVED
58	7	SAVITRIBAI	72	F	left U/L L/Lweakness & giddiness	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	2	95.7	150	YES	YES	RONCHIAL ASTHN	NO	NO	IMPROVED
59	6	SHANTA NIMBARAGI	48	F	involuntary movements	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	1	40.3	180	YES	YES		NO	NO	IMPROVED
60	6	SHIVAHARAPPA M BIRADAR	74	M	left U/L L/Lweakness & slurred speech	left hemiplegia	NA	ACUTE INFARCT	RIGHT MCA TERRITORY	5	331.7	250	NO	NO		NO	YES	BEDRIDDEN
61	5	SHANTABAI	75	F	right U/L L/Lweakness & slurred speech	right hemiparesis	NA	ACUTE INFARCT	LEFT MCA TERRITORY	1	24.2	123	NO	NO		NO	NO	IMPROVED
62	4	PARASAPPA BASAPPA WALIKAR	61	M	giddiness & left U/L weakness	monoparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT ACA TERRITORY	1	34.5	270	YES	YES		NO	YES	IMPROVED
63	10	BASAVARAJ RANMAPPA CHALAW	40	M	right U/L L/Lweakness	right hemiplegia	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	4	345	400	NO	NO		NO	YES	BEDRIDDEN
64	10	SUNIL D KOTYAL	45	M	involuntary movements & slurring of speech	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	1	87.5	100	NO	YES	IHD	NO	NO	IMPROVED
65	6	ANIL KUMAR	31	M	involuntary movements	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	1	34.9	110	YES	NO		YES	YES	IMPROVED
66	27	SIDDAMMA	65	F	decreased response	parapleagia	ACUTE INFARCT	ACUTE INFARCT	B/L ACA TERRITORY	5	104.4	250	YES	YES	BRONCHIAL AST	NO	NO	BEDRIDDEN
67	5	SHARANAPPA BHIRAPPA PUJARI	70	M	altered sensorium	left hemiparesis	ACUTE INFARCT	ACUTE INFARCT	RIGHT MCA TERRITORY	3	204.1	124	NO	NO	COPD	NO	YES	IMPROVED
68	7	SHIVABHAI NANDABASAPPA BIRA	95	F	slurred speech & altered sensorium	right hemiparesis	ACUTE INFARCT	ACUTE INFARCT	LEFT MCA TERRITORY	2	155.2	150	NO	YES		NO	NO	IMPROVED