SERUM ALBUMIN LEVEL AS A PREDICTOR OF ISCHEMIC STROKE OUTCOME

Dissertation submitted to

The Tamil Nadu Dr. M.G.R Medical University, Chennai

In fulfilment of the requirements for the award of the degree of

Doctor of Medicine in General Medicine

Under the guidance of

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THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI, TAMILNADU

MAY 2018

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This is to certify that the dissertation entitled, "**SERUM ALBUMIN LEVEL AS A PREDICTOR OF ISCHEMIC STROKE OUTCOME"** is the bonafide original work of **Dr.JOEL FRANKLIN.F,** done under my direct guidance and supervisionin the Department of General Medicine, PSG Institute of Medical Sciences and Research, Coimbatore in fulfilment of the regulations by The Tamil Nadu Dr.MGR Medical University, Chennai for the degree of Doctor of Medicine in General Medicine.

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I hereby declare that this dissertation entitled **"SERUM ALBUMIN LEVEL AS A PREDICTOR OF ISCHEMIC STROKE OUTCOME"** is a bonafide and genuine research work carried out by me under the guidance of **Dr .SUJAYA MENON, M.D., MRCP,**Professor of Medicine, PSG IMS&R, Coimbatore. This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University in fulfilment of the university regulations for the award of MD degree in General Medicine. This dissertation has not been submitted for award of any other degree or diploma.

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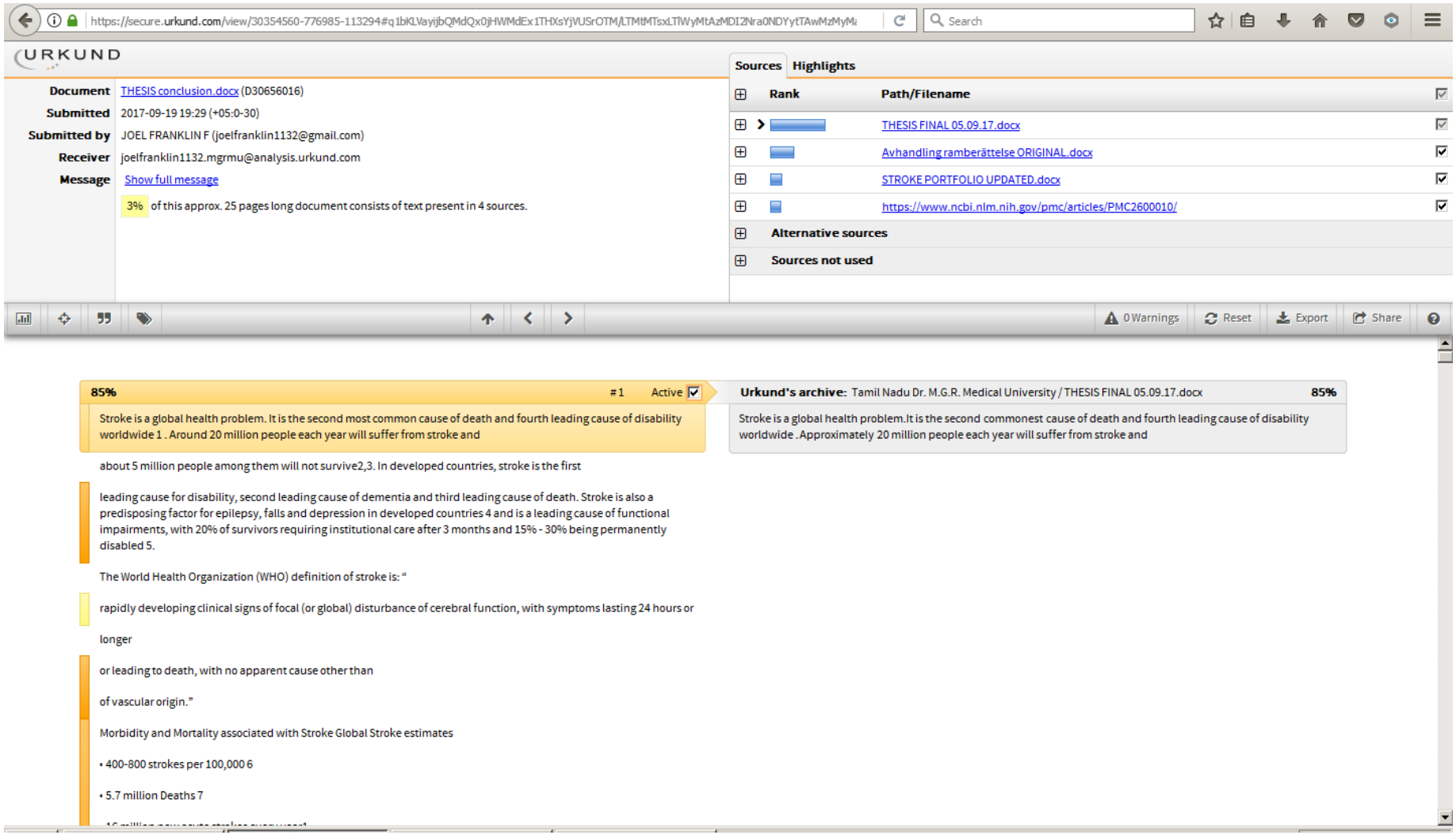
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Stroke is a global health problem. It is the second most common cause of death and fourth leading cause of disability worldwide 1 . Around 20 million people each year will suffer from stroke and
about 5 million people among them will not survive2,3. In developed countries, stroke is the first
leading cause for disability, second leading cause of dementia and third leading cause of death. Stroke is also a predisposing factor for epilepsy, falls and depression in developed countries 4 and is a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15% - 30% being permanently disabled 5.
The World Health Organization (WHO) definition of stroke is: “
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longer
or leading to death, with no apparent cause other than
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Morbidity and Mortality associated with Stroke Global Stroke estimates
• 400-800 strokes per 100,000 6
• 5.7 million Deaths 7
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TITLE

SERUM ALBUMIN LEVEL AS A PREDICTOR OF ISCHEMIC STROKE OUTCOME

INTRODUCTION

Stroke is a global health problem. It is the second most common cause of death and fourth leading cause of disability worldwide[1]. Around 20 million people each year will suffer from stroke and about 5 million people among them will not survive [2,3]. In developed countries, stroke is the first leading cause for disability, second leading cause of dementia and third leading cause of death. Stroke is also a predisposing factor for epilepsy, falls and depression in developed countries [4] and is a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15% - 30% being permanently disabled[5].

The World Health Organization (WHO) definition of stroke is: "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin."

Morbidity and Mortality associated with Stroke

Global Stroke estimates

- 400-800 strokes per 100,000 [6]
- 5.7 million Deaths [7]
- 16 million new acute strokes every year[1]
- 28,500,000 DALYs (disability adjusted life-year)[8]
- 28-30 day case fatality ranges from 17%-35% Stroke[9]

Morbidity and Mortality in India

- Prevalence 90-222 per 100,000 [2]
- 102, 620 million deaths [10]
- 1.44-1.64 million cases of new acute strokes per year[11,12]
- 6,398,000 DALYs[13]
- 12% of strokes occur in the population aged <40 years [14]
- 28-30 day case fatality ranges from 18-41% [2,3]

The most common cause of ischemic stroke in India is large vessel atherosclerosis. Common risk factors includehypertension, diabetes, smoking, alcohol anddyslipidemia. These risk factors are not properly controlled due to poor public awareness and inadequate infrastructure. Number of people who benefit from thrombolytic therapy is very small. Various trials are being conducted for stemcell therapy in ischemic stroke. At present the best way to prevent stroke in the Indian scenario is to control the the risk factors of stroke. Interventional studies are also required which may give better outcome in the future.

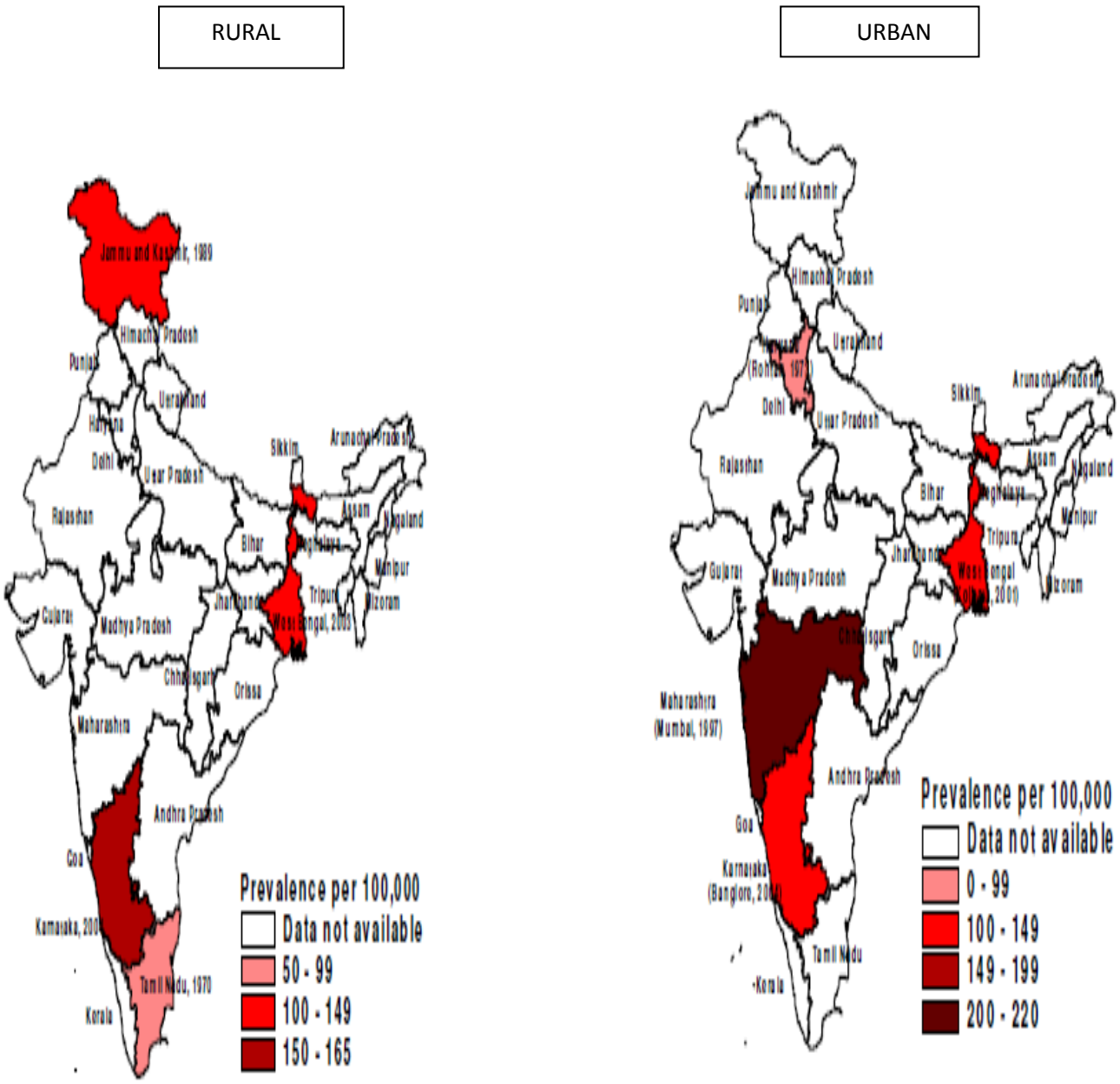


FIGURE 1Crude prevalence rates for stroke Rural India 1970-2004 Urban India 1973-2004

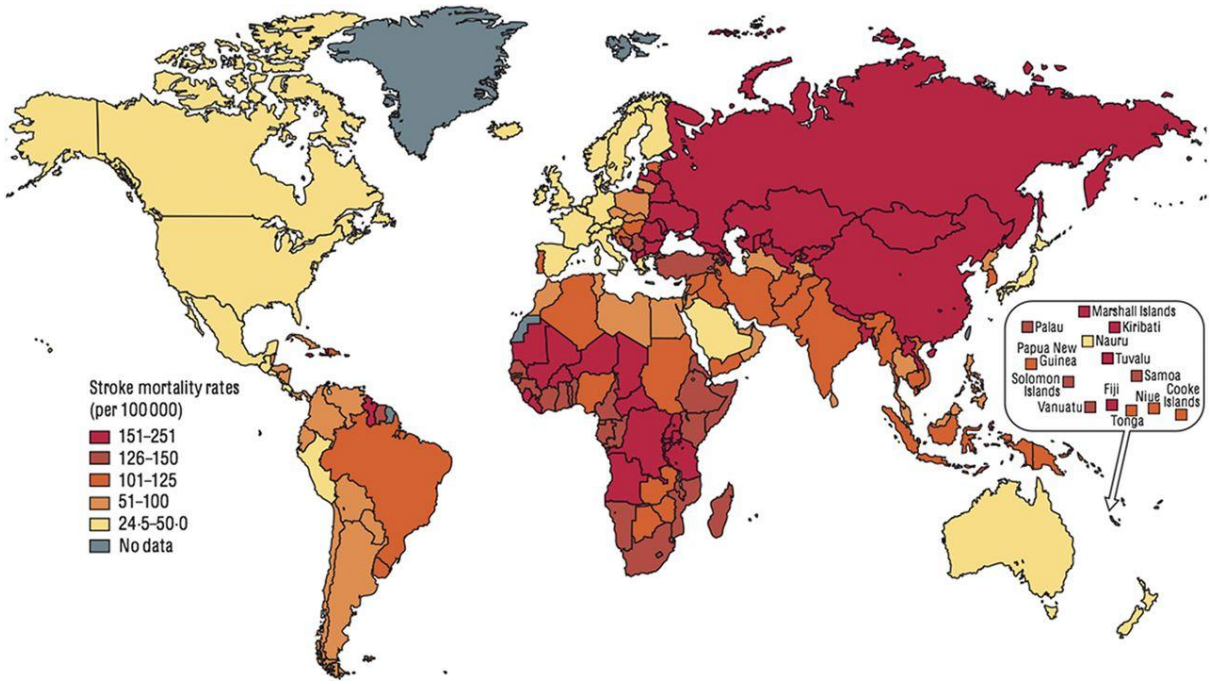


FIGURE 2: Stroke mortality rates across world

It is a well known fact that if stroke patients have associated protein energy malnutrition they tend have poor outcome.[25]Recent studies have shown that serum albumin level is an independent predictor of ischemic stroke outcome[26,27]. Albumin as an independent predictor in ischemic stroke has not been studied significantly in Indian population. Therapeutic interventions like albumin infusion with tissue-plasminogen activator has been tried in murine models of acute ischemic stroke where positive results have been obtained. Albumin In Acute Stroke (ALIAS) trial was an interventional trial conducted in ischemic stroke patients which didn't yield promising reports.If there is a suitable predictor of ischemic stroke outcome it will enable us to monitor and prognosticate.Later further studies may entail therapeutic interventions such as albumin infusion.

AIM

To determine the prognostic value of Serum Albumin levels in Acute Ischemic Stroke by correlating its levels with clinical outcome.

MATERIALS AND METHODS

STUDY DESIGN

Hospital based prospective study

SAMPLE SIZE: 50

INCLUSION CRITERIA:

All patients of age group more than 18 years with clinical and radiological evidence of acute ischemic stroke

EXCLUSION CRITERIA:

1) Cerebral hemorrhage of any etiology
2) Liver disease (Alcohol intake >20 units/week for males,>14 units/week for females)
3) Cardiac failure
4) Nephrotic syndrome/diabetic nephropathy(urine albumin >2+)
5) Protein losing enteropathies
6) Malignancy
7) Conditions mimicking stroke
    a) Metabolic

        -severe hyponatremia

        -hypoglycemia

        -hepatic encephalopathy

        -hyperglycemichyperosmolarnonketotic state

b) Psychiatric disorders

-conversion disorder

-malingering

-factitious disorder

c) Infectious conditions

-viral encephalitis

-Bacterial meningitis

-Brain abscess

d) Cardiovascular

- syncope

- hypertensive encephalopathy

e) Neurological conditions

-seizure with Todd's paralysis

-brain tumor

-demyelinating disorders

-myasthenia gravis

-Bell's palsy

METHODOLOGY:

The study is based on prospective collection of data in Ischemic stroke patients who fulfill the inclusion criteria stated above and who were admitted in medicine and neurology wards in a tertiary care centre(PSGIMSR) where systematic computer coding for registry is used.Diagnosis of ischemic stroke is based on clinical observation and radiological imaging.

Blood samples for assessment of albumin was collected at admission within 36 hours after stroke onset. Strokeseverity at presentation was determined by NIHSS score. Functional outcome was measured 1 week post admission and after 3 months during follow up using modified Rankin scale.

Favourable score mRS:0-3

Unfavourable score mRS:4-6

According to the imaging done at baseline and associated risk factors, the stroke subtypes were classified by using classification developed for Trial of Org 10172 in Acute Stroke Treatment (TOAST).

TABLE 1

TOAST Classification Of Subtypes Of Acute Ischemic Stroke
Large-artery atherosclerosis (embolus/thrombosis)
Cardioembolism (high-risk/medium-risk)
Small-vessel occlusion(lacunar)
Stroke of other determined etiology
Stroke of undetermined etiology a. Two or more causes identified b. Negative evaluation c. Incomplete evaluation

Patients are examined clinically in detail and their severity was assessed by National Institute of Health stroke scale (NIHSS) at baseline.

TABLE 2: National Institute of Health stroke scale (NIHSS):

STROKE	STROKE SEVERITY
0	No stroke symptoms
1-4	Minor Stroke
5-15	Moderate Stroke
16-20	Moderate to Severe Stroke
21-42	Severe Stroke

To assess the clinical outcome of the patients, mRS scoring is done after 1 week and after 3 months and are correlated accordingly. mRS ranges from 0-6, and includes people with no disability to death.

TABLE 3: Modified Rankin Scale

SCORE	SYMPTOMS
0	- No symptoms
1	- No significant disability. Able to carry out all usual activities, despite some symptoms
2	- Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
3	- Moderate disability. Requires some help, but able to walk unassisted
4	- Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted
5	- Severe disability. Requires constant nursing care and attention, bedridden, incontinent
6	-Dead

Statistical tools:

The data collected from the patients is tabulated using Microsoft Excel. The data has been reported in the tables as Percentages, Mean and Standard deviation. The data was analyzed using Chi-squaretest and ANOVA. Chi-square test has been used for categorical variables and ANOVA is applied forcomparison between groups. Statistical analysis for the data collected was done using SPSS(Statistical Package for Social Sciences) with the version of 16.0. The p value were tested at 5% levelof significance.

REVIEW OF LITERATURE

History and Background:

Stroke was first recognized by Hippocrates (460 to 370 BC), father of medicine some 2400 years ago. Initially it was termed apoplexy in Greek (meaning "struck down by violence").

Johann Jacob Wepfer (1620–1695) was the next well renowned person in the field of stroke. He studied the corpses deceased due to apoplexy. He discovered that blood supply might be disrupted to the brain due to blocked arteries in a few or due to massive bleeding into the brain tissue [28].

Rudolf Virchow, known as father of modern pathology, was the first to describe the mechanism of thromboembolism as a major factor causing stroke. In the mid nineteenth century , he described the term thrombosis which can detached to form an embolus causing cardio-embolic stroke[29].

Depending on the cause the term apoplexy was further categorised in the year 1928 and after which the term cerebrovascular accident came into play. In 2011, use of this term cerebrovascular accident was discouraged reasoning that the connotation of fortuitousness carried by the word *accident* insufficiently highlights the modifiability of the underlying risk factors[30,31].

EPIDEMIOLOGY

In India, the prevalence of stroke is increasing. The incidence of stroke increases exponentially from 30 years of age, and etiology varies by age. About two-thirds of strokes occur in those over the age of 65[23,24]. It has been observed now that the prevalence is becoming high among younger age group and those of low socioeconomic status[25]

The AIRs of stroke in India, as observed in the Kolkata, Mumbai, and Trivandrum studies are higher than that in United States (107 per100,000 per year), European countries (61-111 per 100,000 per year)[17,18,19],and Australia (99 per 100,000 per year)[21] but similar to that reportedfrom one Chinese city - Changasha. [35]

Joshi *et al*.,[14] did a study on mortality because of chronic diseases through verbal autopsy in a population of 180,out of which 162 were residing in 45 villages of Andhra Pradesh. Death due to stroke(13%) and cardiovascular disease were similar(14%).[14] Another community based prospective study done in kolkatta showed a 30-day case fatality rate (CFR) [15] of 41.08% (men, 38.18%; women, 43.24%), which showed a significant difference from that seen in the Western countries (17-33%).[16,17,18,19,21] High stroke related case fatality rate can be attributed to improper medical care among poor people and lesion severity.[20] Another study revealed that genetic factors may also play a role as there is greater susceptibility and higher mortality to stroke among UK residents

of Indian descent.[22] The fatality rates were higher among women, as women outnumber men and also have higher prevalence of uncontrolled hypertension than men.[24] In a study done in Trivandrum, the 28-day CFRs were 24.5% for urban and 37.1% for rural areas.[23]

TABLE 4: Prevalence (PR) of stroke in major Indian studies

Place	Rural/urban	Year	Population, *n*	PR per 1,000*	AS-PR per 1,000
North Rohtak, Haryana[3]	Urban	1971-1974	79,046	0.44	
Kuthar Valley, Kashmir[4]	Rural	1986	63,645	1.43	2.44#
Ballabgarh, Haryana[5]	Rural	1986	48,798	0.88	
West Mumbai (Parsis)[6]	Urban	1985	14,010	8.42	4.24#
Mumbai[7]	Urban	1997	145,456	2.20	
East Malda, WB[8]	Rural	1989-1990	37,286	1.26	
Baruipur, WB[9]	Rural	1992-1993	20,842	1.47	
Kolkata[10]	Urban	1998-1999	50,291	1.47	3.34‡
Kolkata[11]	Urban	2003-2004	52,377	4.72	5.45†
South Vellore[2]	Rural	1968-1969	258,576	0.57	
Gowribidanur, Karnataka[12]	Rural	1982-1984	57,660	0.52	
Bangalore[13]	Rural	1993-1995	51,055	1.65	2.62¦
Bangalore[13]	Urban	1993-1995	51,502	1,36	

PR = Prevalence rate, AS-PR = age-standardized PR, WB = West Bengal. *Crude PR, #US population of 1960, ‡US population of 1996, †world standard population, ¦not mentioned

TABLE 5:Data from Trivandrum stroke registry showing urban and rural distribution

Factors	Urban	Rural	*P* value
Crude annual incidence rate	116/100,000	119/100,000	NS
Risk factors present	94.9%	94.1%	NS
Ischaemic stroke	83.9%	82.3%	NS
Hemorrhagic stroke	16.1%	17.7%	NS
Smoking (men)	22.8%	39.3%	0.013
3 or more risk factors	12.7%	20.8%	0.034
Imaging available	71.9%	56.4%	0.003
28 day fatality rate	24.5%	37.1%	0.011
28 day disability rate-Mild	42.3%	43.2%	NS
Moderate disability	42.3%	47.7%	NS
Severe disability	15.4%	9.1%	NS

DEFINITION AND CLASSIFICATION:

Although more common in older adults, stroke also occurs in neonates, infants, children and young adults, resulting in significant morbidity and mortality[36].Stroke is a clinical syndrome which is classified broadly into:

- Ischaemic strokes – These are caused by sudden occlusion of arteries supplying the brain, either due to thrombus at the site of occlusion or formed in another part of the circulation causing restriction of blood supply to the part of brain causing cerebral infarction. It accounts for 50-85% of all strokes worldwide [37]
- Haemorrhagic strokes – defined as bleed which occurs within substance of the brain, intracerebral haemorrhage or contained within the subarachnoid space[38].

- Transient ischemic attacks (TIAs) are defined as temporary neurological deficit with symptoms lasting less than 24hrs which is thought to be due to inadequate cerebral or ocular blood supply as a result of thrombosis or embolism associated with arterial, cardiac or haematological disease. It serves as a warning signal for impending stroke. It leaves no clinical residue or abnormality on imaging [39].

Risk factors :

Risk factors are defined as any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury. Risk factors may be further classified as modifiable or non-modifiable.

Non modifiable risk factors:

Risk factors like age, gender, race/ethinicity and family genetics come under non modifiable risk factors.

1. **Gender:** Globally, males are affected predominantly regardless of age and stroke subtype. In the Indian scenario, this difference observed is due to high prevalence of smoking and alcohol among males. The male :female sex ratio among affected individuals is 7:1 in India.[40,41]

   A few etiologies are confined to the female population. Most of the strokes observed commonly among the reproductive age group are due to pregnancy or oral contraceptive usage. Though prevalence of occurrence of stroke is high among males, prevalence of death is higher among females.

2. **Race and ethnicity:** Blacks are more commonly affected with stroke compared to whites. Lack of proper awareness, affordability and no insurance are among the contributory factors to this observed difference.[42,43]
3. **Family genetics:** Family members may have a genetic tendency or share lifestyles and behavioural patterns that significantly contribute to the occurrence of stroke. Genetic factors for hypertension, Von Willebrand disease, Sickle cell disease may also contribute to increased risk of stroke. Risk of stroke further increases with a past history of stroke. Although heredity plays only a minor role in the pathogenesis of stroke, an increased risk is seen among first-degree relatives with a family history of stroke. Heredity factors when combined with an unhealthy lifestyle leads to increased risk among individuals. [44,45]

Modifiable

- **Cigarette smoking** – It is one of the most important risk factors of stroke among young adults. Risk of stroke increases by four fold among young adults in smokers compared to non-smokers. The risk depends on both duration and dosage. Smoking more than 20 cigarettes per day carries a higher risk of developing ischemic stroke. The risk of stroke increases by enhancing atherogenesis, triggering cardiac arrhythmias, arterial thrombosis and vasospasm. It also adds to the economic burden. If associated with other risk factors there will be synergistic effect on risk of stroke occurrence.[46]

- **Alcohol consumption** – This is another modifiable and preventable risk factor for stroke in young adults. It differs among men and women. In men, binge drinking of alcohol carries a higher risk of developing ischemic stroke than in non -alcoholics or alcoholic abstainers. Binge drinking has the effect of raising blood pressure which further increases risk of stroke[47].In men, binge drinking is defined as six or more alcoholic drinks whereas it is four or more in women. In women the risk increases with increase in intake of alcohol. Consumption of wine has a protective effect.

- **Dyslipidaemia** – Atherogenic dyslipidaemia is an independent risk factor of stroke among young adults and also plays a role in causing higher prevalence of recurrent stroke. Atherogenicdyslipidemia is defined as high levels of low-density lipoprotein cholesterol (LDL-C) along with other factors such as high triglycerides (TGL) (TGL ≥150 mg/dL) and low high-density lipoprotein cholesterol (HDL-C) (HDL-C ≤40 mg/dL)[48]. Elevated apolipoprotein B and A1 levels are also associated with young stroke. Elevated LDL and TGL levels increase the intimal thickness of carotid artery thereby increasing atherosclerosis. It is associated with symptomatic intracranial stenosis identified by computed tomography (CT) imaging or magnetic resonance imaging of cerebral blood vessels (MRI). They comprise a metabolic pattern that may be driven by insulin resistance, which ultimately leads to accelerated progression of atherosclerotic vascular disease.

- **Abdominal obesity** – defined as BMI more than 30kg/sq.m. Predisposing mechanism of stroke in obese individuals is likely due to its effect on arterial hypertension associated with elevated cholesterol levels. It mainly plays an important contributory factor for stroke. Upper body obesity is more important than lower body obesity as a risk factor[49]. Increased waist hip ratio is associated with early death. People should be encouraged to increase daily physical activity and reduction of weight in order to lessen the risk of stroke.Increased physical activity also decreases platelet aggregation and increase insulin sensitivity[50].

- **Sedentary life style** – It has been a contributory factor for occurrence of stroke in young individuals. Blood pressure, impaired glucose tolerance, insulin resistance are associated with altered lipid profile with increasing risk for stroke. Lifestsyle modifications like regular exercise, weight reduction measures and dietary modifications may help decrease incidence.

- **Hypertension** – It is defined as systolic blood pressure (SBP) more than 140 mm Hg or diastolic blood pressure (DBP) more than 90 mm Hg. It is considered both primary as well secondary cause of death among stroke in young adults. 70% of hypertensives develop stroke. Hypertension increases wall stress and causes damage of vascular endothelium. This damage causes thrombi formation and ischemic lesions mainly affecting large extra-cranial vessels. Both elevated diastolic and systolic blood pressures are associated with increased concentrations of haemoglobin, which is a risk

factor for ischaemic stroke[51,52]. Isolated systolic blood pressure and wide pulse pressures are at greater risk.

In chronic hypertension, there is vessel wall thickening and luminal narrowing which limit the capacity of the resistance vessels for dilation. In acute stroke, auto-regulation may be impaired in regions surrounding an acute lesion and even in the hemisphere contralateral to the lesion because of dilation of cerebral resistance vessels in an attempt to increase blood flow in response to tissue ischemia and acidosis. About 10-20 mm of Hg decrease in SBP causes reduction of incidence of stroke of 28% in young adults[53].

- **Diabetes mellitus:** Increasing prevalence of diabetes results in an increase of macro-vascular complications. Thus stroke is one of the long termcomplication of diabetes mellitus[54]. Three factors fasting blood glucose (FBS), glycosylated haemoglobin (HbA1c) and duration of diabetes have significant impact on risk of stroke among young adults. FBS more than 241 mg/dl, HbA1c more than 6.5% and duration of diabetes for more than 7 years. Stroke occurring in diabetic individuals is usually not reversible. Persons with both type 1 and type 2 diabetes mellitus (DM) have increased susceptibility affecting both large and small vessels. Diabetes increases fibrinogen and clotting factors thereby causing increasing platelet aggregation promoting formation of arterial thrombosis[55]. There is 11 times higher risk of stroke in young adults compared to older age group. Hyperglycemia does not present with signs typical of stroke whereas hypoglycaemia can mimic as stroke causing neurological

deficits. It is therefore said that prompt treatment of hypoglycaemia in emergency conditions in suspicion of stroke.

- **Oral contraceptives** – risk of stroke in young women taking oral contraceptives is four times higher. High dose oestrogen doubles the risk of stroke [56]in women with other associated factors like smoking, pro-thrombotic genetic variants and migraine. High prevalence of thromboembolic stroke is seen in these conditions[57]. Newer oral contraceptives with low levels of estrogen are being used to decrease the incidence of stroke in women.

- **Pregnancy:** Pregnancy and puerperium - Estrogen related stroke – Risk of stroke is high in third trimester and 6 weeks of post-partum period[58]. Preeclampsia and eclampsia play a synergistic role leading to nine fold increase in stroke occurrence[59]. Amniotic fluid embolism, postpartum angiopathy and postpartum cardiomyopathy can result in cardio-embolism or infarction due to hypotension. It may also be influenced by underlying haemotological or thrombotic conditions

- **Illicit drug abuse:** Recreational drug abuse in young adults increases the susceptibility of stroke in young adults. Injectable drugs are more prone for embolic stroke[60]. Use of certain drugs (eg, cocaine, amphetamines, crack) having sympathomimetic activity causing hypertension, platelet aggregation leading to endocarditis causing embolic stroke[61]. Attimes, they may cause vasculitis of arteries

and arterioles causing stroke. Drugs like heroin, opiates, cannabinoids also play a role in etiology of ischemic stroke.

- Migraine headache – There is increased risk of ischemic stroke among young women (35-45years) with migraine headache with aura (MA). The risk is accelerated with concomitant use of oral contraceptives, smoking and blood pressure. Cerebral ischemia may induce migraine headache[62,63]. Most commonly occipital headaches are present. It is seen in about one third of total cases.

ETIOLOGY:

- Atherosclerotic – thrombotic and cerebral embolic stroke are the predominant cause of AIS.

  Atherosclerosis:

  It mainly involves large vessels both intra-cranial and extra-cranial arteries and small vessels (lacunar arteries)[64]. It begins with damage to the endothelial lining of vessel wall. The damaged area attracts platelets, calcium, fatty substances, fibrin and cellular debri which accumulate to form an atherosclerotic plaque. These plaque eventually increase in size and block the blood flow through the vessel thereby decreasing the blood supply leading to hypoxia.

  These plaques become more vulnerable, when the lipid content increases in the plaque within the fibrous core. They become easily friable and get detached from the vessel form blood clots pass in to the circulation and reach other areas and block the

blood vessel[65]. The second type of mechanism of stroke called cardio-embolic stroke. Cardioembolism is responsible for 20% of all ischemic strokes. Stroke caused by heart disease is primarily due toembolism of thrombotic material forming on the atrial or ventricular wall or the left heart valves. These thrombi then detach and embolizeinto the arterial circulation. The thrombus may fragment or lyse quickly, producing only TIA. Alternatively, the arterial occlusion may last longer, producing stroke. Embolic strokes tend to occur suddenly with maximum neurologic deficit present at onset. Nonrheumatic atrial fibrillation is the most common cause of cerebral embolism overall. The presumed stroke mechanism is thrombus formation in the fibrillating atrium or atrial appendage, with subsequentembolization. Atrial fibrillation causes stasis of blood due to hypocontractile nature of atrium. There occurs atrial remodeling, endothelial dysfunction, release of coagulation factors like Xa and thrombin. All these factors promote thrombus formation and ultimately lead to cerebral embolism.Patients with atrial fibrillation have an average annual risk of stroke of -5%[66].Recent MI may be a source ofEmboli, especially when transmural and involving the anteroapical ventricular wall, and prophylactic anticoagulation following MI has been shown to reduce stroke risk. Mitral valve prolapse is not usually a source of emboli unless the prolapse is severe. Paradoxical embolization occurs when venous thrombi migrate to the arterial circulation, usually via a patent foramen ovale or atrial septal defect.

FIGURE 3 : Mechanism of thrombotic process in stroke

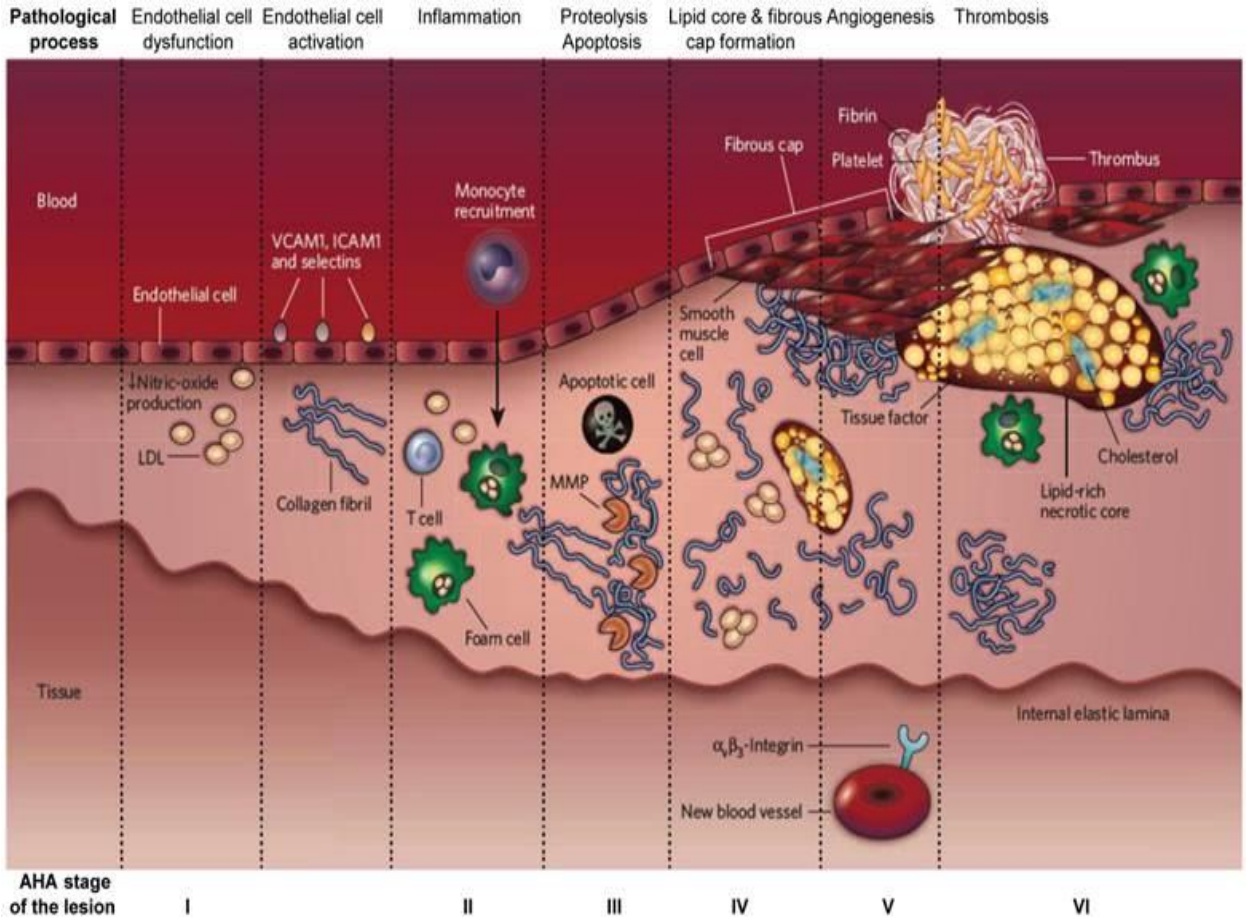
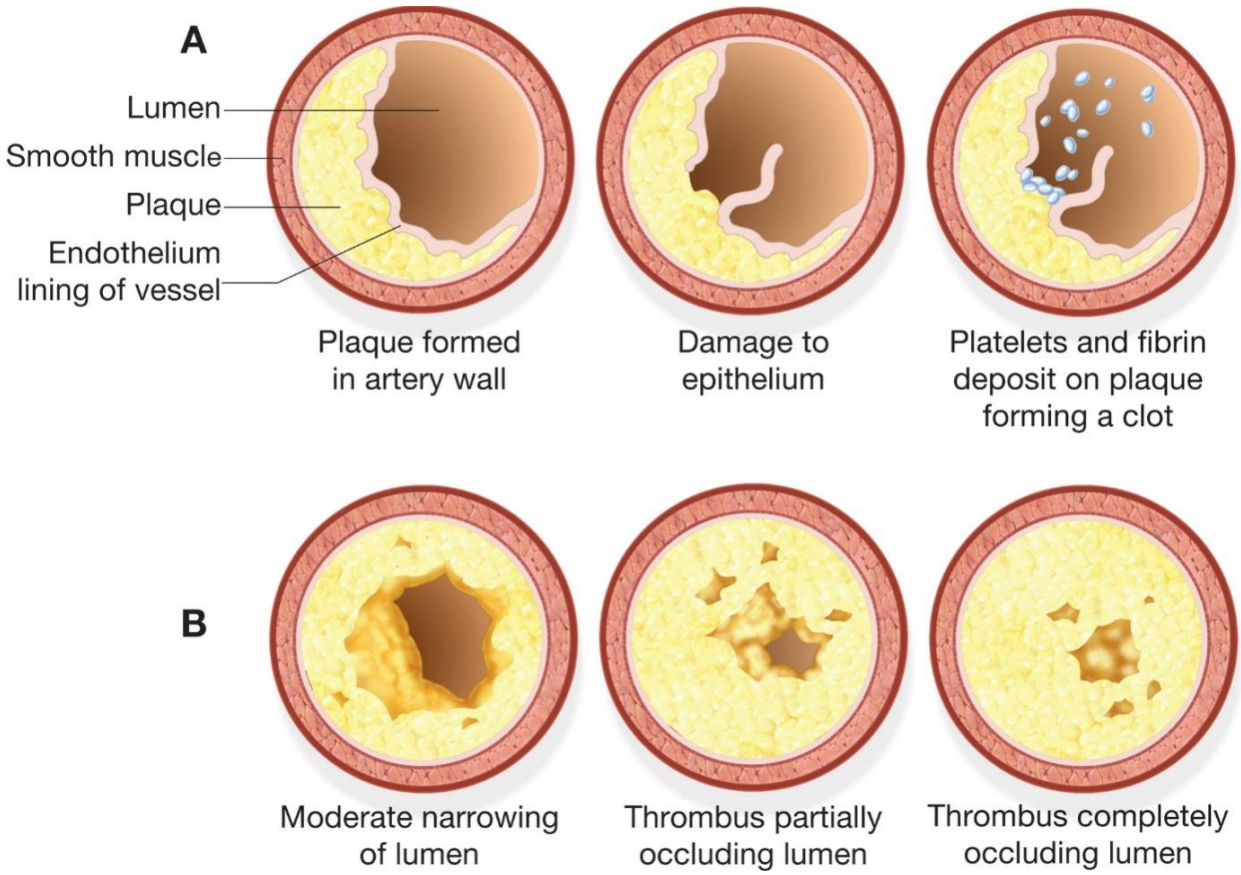


FIGURE 4 : Atherosclerosis



Atheromatous plaques mostly form preferentially at branching points and curves of cerebral arteries. The most frequent sites involved are

- Internal carotid artery at its origin from the common carotid artery
- In the cervical part of vertebral arteries and at their junction to form basilar arteries
- In the stem or at the main bifurcation of middle cerebral arteries
- In the proximal posterior cerebral arteries as they wind around the midbrain
- In the proximal anterior cerebral arteries as they pass anteriorly and curve around corpus callosum.

- **Large artery disease:**

  Carotid and vertebral dissections - Defined as tear in intimal layer of vessel leading to blood flow in between the layers of vessel wall. The stasis of blood in between the vessel layers leads to formation of a clot which can embolise leading to formation of stroke[67]. It is one of the factors in causing stroke in the young though it becomes a rarer cause in older age group. It is commonly caused by trauma to blood vessel. It also causes haemorrhagic stroke in young adults. Spontaneous dissection is also seen in few individuals, especially in those with connective tissue disorders, increases predisposition to stroke.

- **Small artery disease:** systemic hypertension and migraine effect the small microvasculature causing lacunar infarcts in individuals.

- **Cardioembolism:** It is the most common cause of arterial ischemic stroke (AIS) of all ages. It occurs very rapidly within seconds. The most common cause is

atherosclerosis in older age group. It accounts for about one fifth of ischemic stroke [68]. Most of the cases the emboli arises from a thrombus within heart. The arterial ischemic stroke caused by embolism from the heart can only be diagnosed, if there is an identifiable cardioembolic source, by using transoesophageal echocardiography. It can provide the anatomic location regarding the source of emboli.

Cardiac diseases – they may classified as congenital and acquired.

- Congenital heart disease is a major risk factor for cardio-embolic stroke especially in the perioperative period or following catheterization or extracorporeal membrane oxygenation (ECMO).
- **Rheumatic Heart Disease**(RHD) – it plays a significant role in causing stroke in young adults in developing countries. About 3-8% strokes are attributed to RHD. It also plays a role in recurrent stroke. It remains as an occult cause where early identification and preventive measures must be taken to reduce the incidence and recurrence[69].
- **Acquired conditions** –These commonly include Dilated cardiomyopathy (DCM), acute myocardial infarction (AMI), infective endocarditis (IE), Atrial Fibrillation (AF) and prosthetic valve placement. Coronary artery disease (CAD) share similar risk factors as that of stroke. Left ventricular hypertrophy (LVH) and left atrial enlargement (LAE) further increases the relative risk of development of stroke[70].

- **Elevated Homocysteinelevels:** Inborn errors of metabolism characterized by defect in methionine metabolism due to deficiency of enzyme cystathione b-synthase(CBS). Common pattern of inheritance is autosomal recessive. Deficiency of vitamin B12 and serum folate levels is another factor having a contributory role. These enzyme and vitamin deficiencies cause increased accumulation of homocysteine levels in plasma and urine. Elevated homocysteine levels causes endothelial dysfunction and thromboembolic events affecting both small and large vessels causing cerebrovascular ischemia[71]. It is mainly diagnosed by measuring the levels of homocysteine in urine and plasma. Most of them respond to vitamin supplements.

- **Fibromuscular dysplasia** – This condition mainly affects the medium sized vasculature in young women of childbearing age group. It causes medial fibrosis of vessel wall due to an unknown mechanism, predominantly involving the carotid vasculature[72]. Stroke may be thromboembolic or vascular stenosis may be the underlying cause. On angiography, a typical beading pattern of involved vessel is formed.

- **Radiotherapy** – Patients who have received radiation for head and neck malignancies are more prone to develop delayed onset of arterial ischemicstroke[73]. Relative risk is doubled with radiotherapy.

- **Haematological disorders:**

- **Thrombophilia**: Defined as a group of condition related to the impairment of haemostatic mechanism which manifest as an increased tendency to form thrombus. They may be classified as inheritable or acquired conditions. Deficiency in natural coagulants like protein C, protein S and antithrombin III deficiency, polymorphisms in activated protein C and disturbance of clotting mechanisms by mutation in prothrombin gene 20210G/A are classified under the inheritable causes. Among the inherited conditions, Factor V leiden and prothrombin 20210 mutation are most commonly associated with arterial ischemia stroke(AIS)[74]. Among acquired conditions, Anti-phospholipid antibody syndrome (APLA) is most commonly associated with AIS. Acquired conditions are relatively at higher risk of causing stroke than inherited conditions. Workup for these conditions with a background of prior episode suggestive of thromboembolic event or having a positive family history or recurrent pregnancy loss or absence of other identifiable risk factors[75]. Family members and siblings should be screened.
- **Myeloproliferative syndromes** – They mainly include polycthemiavera (PV), myelofibrosis and essential thrombocythemia (ET). They are described to have high prothrombotic states which occurs due to inflammatory insult to the vessel wall by host immune response towards malignant cells. About 60-70% have arterial thrombosis. The risk of thrombosis further increases with the use of myelo-suppressive drugs[76]. If associated with underlying valvular heart disease, there is a high risk of cardio-embolic stroke.

- **Sickle cell anaemia** – Stroke in this condition is a near fatal complication. Considered mechanism in the etiology of stroke in this condition is that, the deformed sickle cells cause vaso-occlussion of vessels leading to stroke. Another mechanism is by hemolysis within the vasculature altering the endothelial structure of vessel wall[77]. This condition mainly affects the large arteries.
- **Vasculitides:** Defined as occurrence of inflammation and formation of necrosis of vessel wall. It is classified as primary or secondary in nature. Among the primary conditions Takayasu'sarteritis,Polyarteritisnodosa (PAN), Wegener's granulomatosis (WG), Behcet's are common conditions associated with stroke in young individuals. Another rare disorder called primary angitis of central nervous system (CNS) a multifocal disorder considered one of the cause of stroke in young[78]. In these conditions, there is inflammation of blood vessel wall which increases the thrombogenecity and alter the vessel tone predisposing to stroke.
- **Genetics:** It may be single gene disorder or polygenic disorder or metabolic in nature.

TABLE 6

TYPES:	GENE MUTATION	VESSEL AFFECTED
CADASIL	Notch 3 receptor	Small vessel disease
CARASIL	Notch 3 receptor	Small vessel disease
Fabry disease (X-linked recessive)	α-galactosidase A	Large and small vessel disease
MELAS (maternal)	Transfer RNA	Complex
Marfan syndrome (autosomal dominant)	Fibrillin 1	Cardioembolism and arterial dissection
Ehlers–Danlos syndrome (autosomal dominant) – type IV	Collagen type III	

- CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)- mutation causes progressive degeneration of smooth muscle cells in vessel wall causing stroke in late childhood or early adulthood[79]. High risk for recurrent stroke in young. It is identified by classical MRI changes which shows bilateral temporal pole hyperintensity – punctate and nodular lesions.

- CARASIL(cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy) – autosomally recessively inherited CADASIL associated with acute features of lumbago, spondylosisdeformans, diffuse baldness and progressive mental and motor deterioration. Most common age of onset is 25-30years of age (younger age comparatively to CADASIL). On imaging, it is typically identified as diffuse and homogenous lesions.

- MELAS – mitochondrial myopathy, encephalopathy, lacto-acidosis and stroke. It is a multisystemicmaternally inherited disorder which are characterised by stroke like episodes[80]. In this condition mostly posterior regions like temporo-parietal and occipital regions are involved. Due to mitochondrial dysfunction, nitric oxide metabolism is impaired and free radicals are released which cause impaired auto-regulation. Cardiomyopathy due to mitochondrial disease may cause cardio-embolic stroke. They are transient in nature and reflected in abnormalities on neuroimaging[81]. Muscle biopsy helps in diagnosis, by identifying the abnormal proliferation of mitochondria.

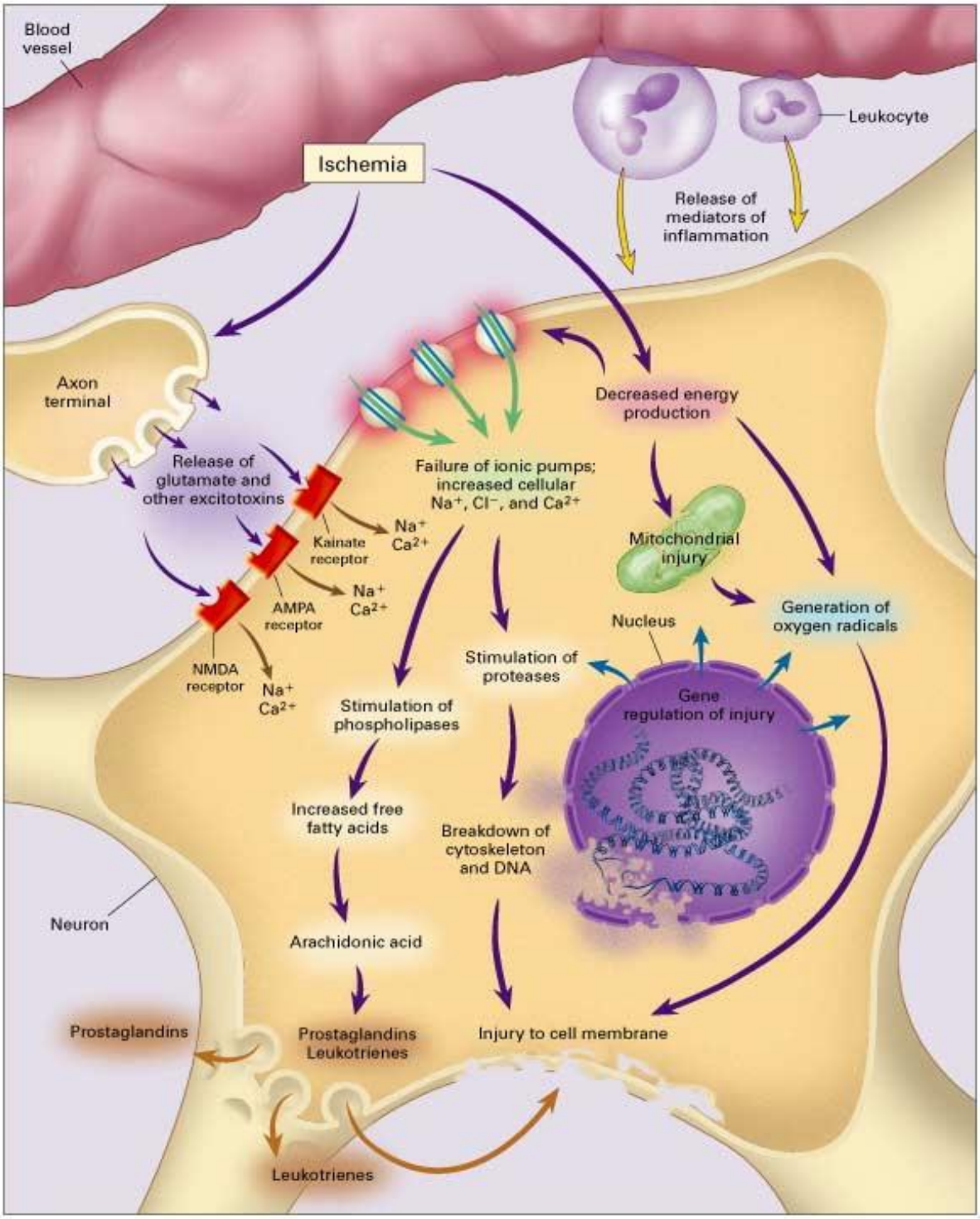
- Fabry's disease – X-linked genetic disorder where there is accumulation of lysosomes in vascular endothelium leading to narrowing of the vessels and infarction in affected young adult males[82]. It involves brain, kidney, heart and skin. About 25% of individuals with Fabry's disease develop stroke involving both carotid and vertebrobasilarregions[83]. Alpha galactosidase replacement decreased the incidence of cerebrovascular incidents.

- Heritable disorders of connective tissue – this mainly involves the mutation in collagen and elastin content which constitute the vessel wall. Of the disorders affecting collagen fibres, Ehlers Danlos syndromes (EDS), osteogenesisimperfecta (OI), autosomal dominant polycystic kidney disease (ADPKD) and collagen type IV related small vessel disease are most commonly associated with stroke[84]. These are associated with formation of aneurysms in the vessel wall and are complicated with carotid and vertebral artery dissections. Among those affecting the elastin content of vessel wall, Marfan's syndrome, Loeyz Dietz syndrome (LDS type I and II) and Pseudoxanthomaelasticum are commonly associated with occurrence of stroke in young.

- **Amyloid angiopathy:** it is associated with amyloid deposition in leptomeningeal walls and cerebral arteries and arterioles. Most commonly involves the occipital region and considered severe if it involves the same region. Mostly it causes haemorrhagic stroke.

- **Moyamoyadisease:** It is a genetic disorder with AD pattern of inheritance characterised by thickening of intimal carotid vessels. It has a bimodal age pattern at age of 5 years and 30-50years of age[85]. It causes ischemic stroke in younger age groups whereas it is associated with haemorrhagic stroke in adults.

FIGURE 6: PATHOPHYSIOLOGY OF STROKE



ROLE OF ALBUMIN IN ACUTE ISCHEMIC STROKE

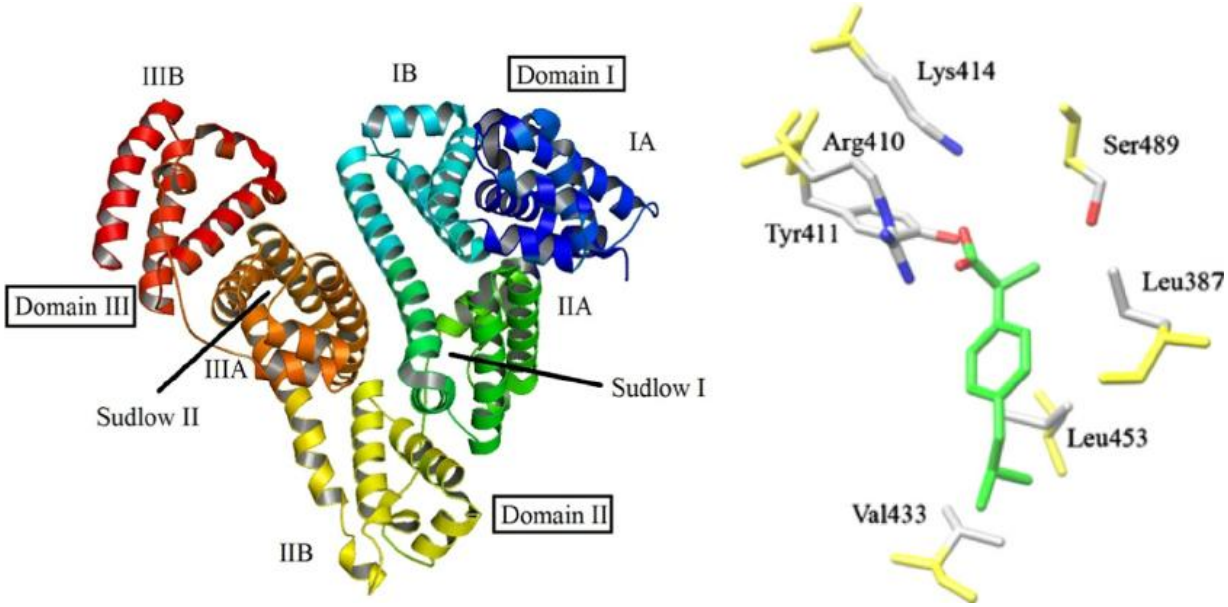
ALBUMIN:

A) SYNTHESIS:

Albumin is quantitatively the most important plasma protein. Adult liver synthesizes around 15 grams per day. Approximately 300 to 500 grams of albumin is distributed in the body fluids. The synthesis rate can double in situation in which there is rapid albumin loss or a fall in serum albumin concentration. Rate of albumin transcription can be affected due to trauma, sepsis, hepatic disease, diabetes , fasting.

B) STRUCTURE:

It is a single polypeptide chain of 585 aminoacids with a molecularmass of 67 KDa.



C) FUNCTION:

Major functions of albumin include regulation of colloid osmotic pressure of plasma,transportation of hormones,fattyacids,drugs and metabolites across plasma,regulation of microvascularpermeability,anti-oxidant activity,anti thrombotic and anti inflammatory activity.

D) DISTRIBUTION:

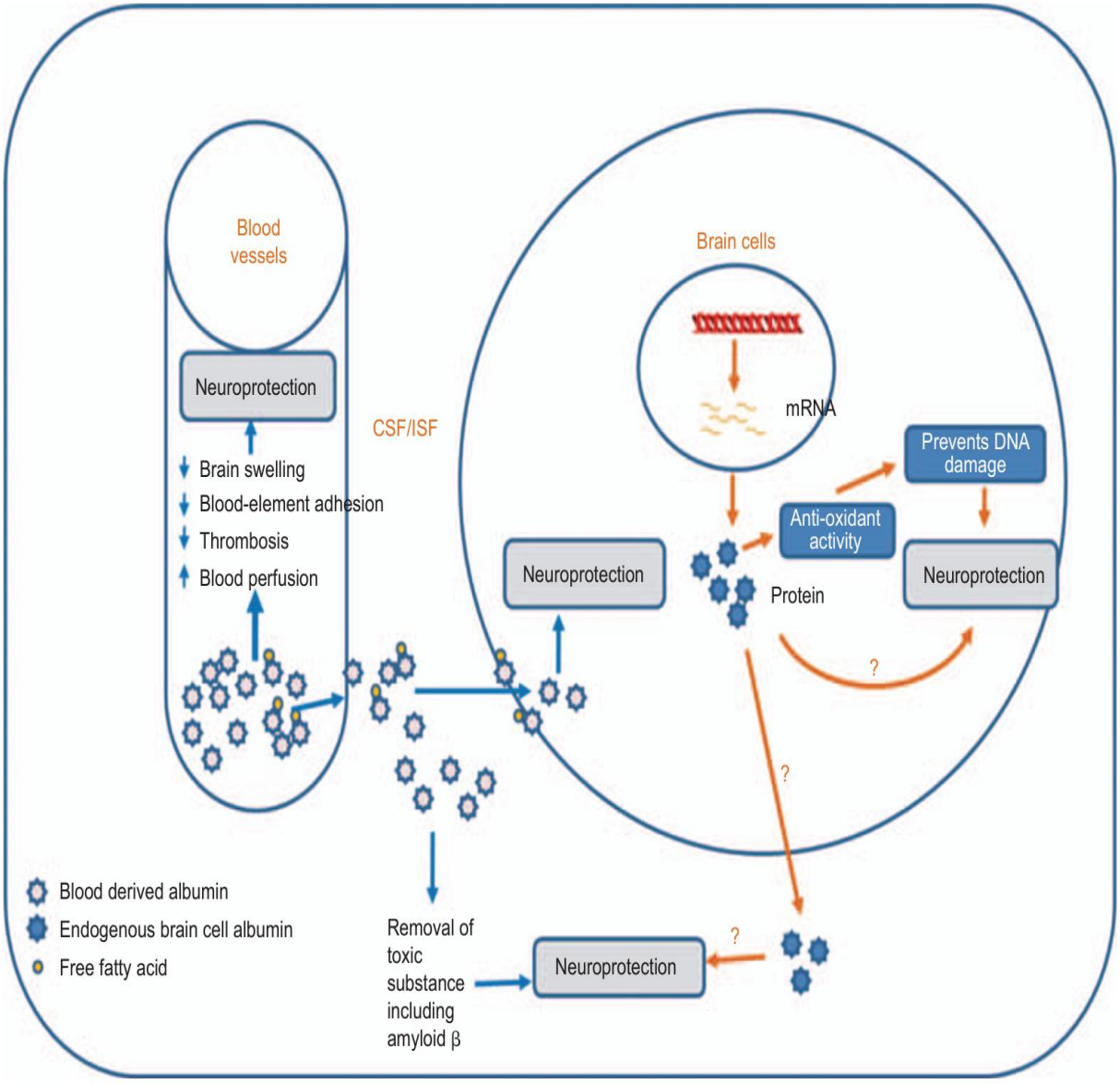
It is a major component of ECF including CSF,interstitial fluid and lymph.Around 40-60% albumin is degraded in muscle and skin,15% in liver,10% in kidney and 10% in GI tract.

E) USES:

Because of its unique properties,albumin has been used as therapeutics in the field of hepatology. The volume expanding property of albumin is widely used for benefit of patients with cirrhosis. Among neurological diseases albumin has a role in ischemic stroke,Alzhemier's disease and epilepsy. Human albumin in high doses has been used in clinical trials for acute ischemic stroke based on its neuroprotective effects.

The Albumin In Acute Stroke (ALIAS) clinical trial was conducted based on the fact that albumin in high doses decreases infarct volume and cerebral edema and improves behavioural function.

FIGURE 7NEUROPROTECTIVE ROLE OF ALBUMIN



VOLUME OF INFARCT AND CLINICAL OUTCOME

The standard measure of therapeutic success in animal stroke models is reduction in infarct volume. As a replacement for disability and global clinical scales, reduction in infarct volume can be considered an auxiliary outcome measure for human stroke clinical trials. Few studies have compared infarct volume and clinical outcome.

Several small series showed that infarct volume and clinical outcomein terms of BI, NIHSS, Rankin Disability Scale had no statistical significance.[91,92]Some larger series , revealed correlations between infarct volume and clinical scales (NIHSS, Rankin Disability Scale, Oxford Disability Scale, aphasia severity scale).[93–95]

Volume of infarct is calculated using the formula ABC/2. The infarct was measured in three perpendicular axes A,B and C

A = Longest dimension in axis x

B = Longest perpendicular dimension to axis x (y)

C = Total length in z dimension

Most of the studies in which serum albumin was studied as a predictor of ischemic stroke outcome didn't include volume of infarct . This study compared serum albumin and clinical outcome and also volume of infarct and clinical outcome.

ANATOMY AND CLINICAL MANIFESTATIONS

- **ANATOMY OF CEREBRAL CIRCULATION:**

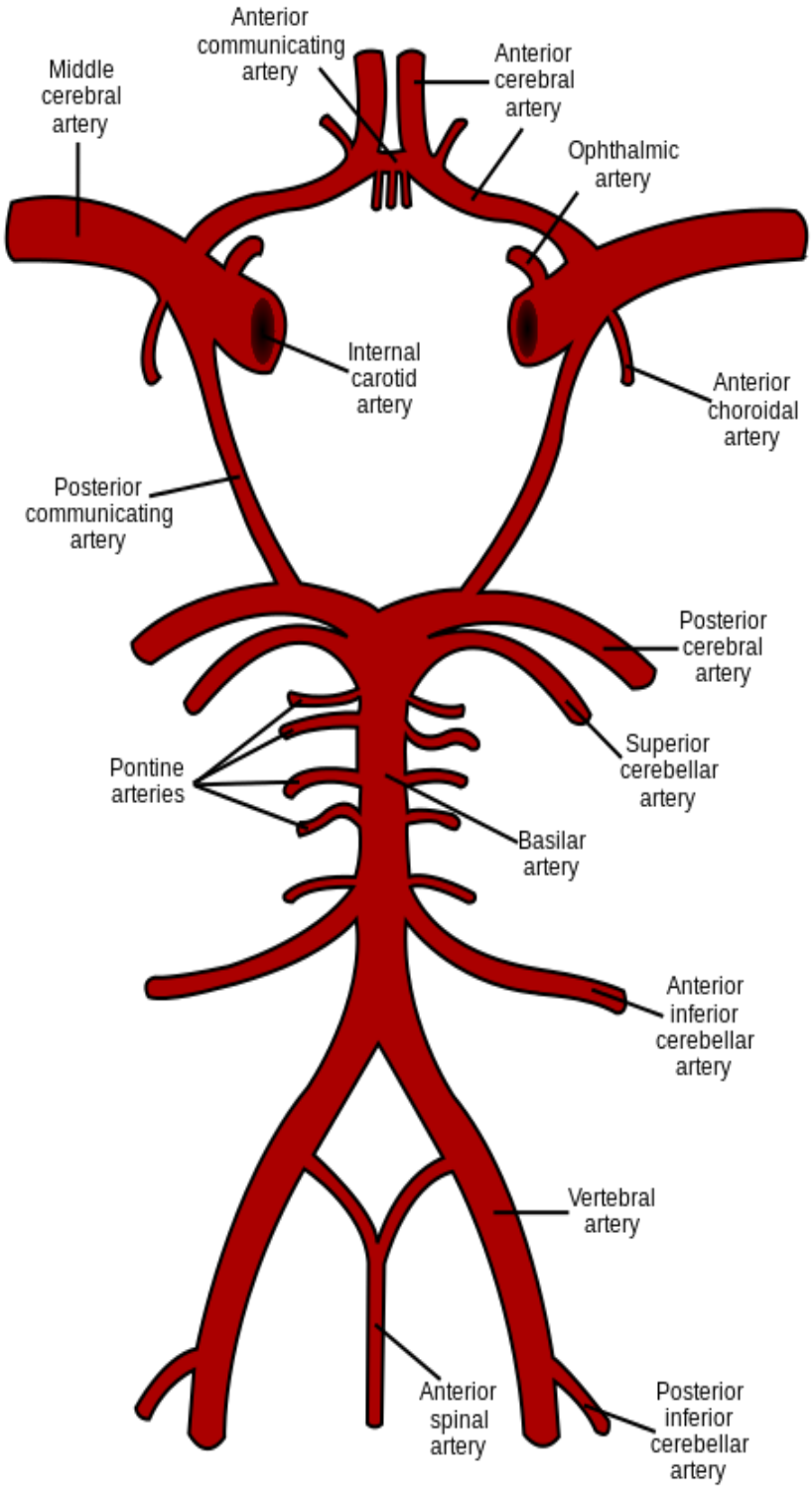
Brain is the highest perfused organ in the body. It receives about 20% of total circulation and also has the maximum consumption of oxygen in the blood. It is supplied by two pairs of large arteries – internal carotid arteries and vertebral arteries[78].

Internal carotid artery supplies about 3/5th of cerebrum. The two vertebral arteries join together to form basilar artery which supplies cerebellum and brain stem. These two arterial circulation join together with the help of communicating branches to form circle of willis (COW)[79]

- The internal carotid group produce three main vessel branches which include –

1. Ophthalmic artery – supplies the meninges, contents of orbit.
2. Anterior cerebral artery (ACA) – These are a pair of arteries supplying the medial portions of frontal lobes along with prefrontal and supplementary motor cortex and superior medial parietal lobes. They are further subclassified into 5 smaller branches called callosal arteries as they also supply the carpus callosum. Due to collateral supply by anterior communicating artery, stroke due to ACA is very rare.

FIGURE 8: Circle of Willis



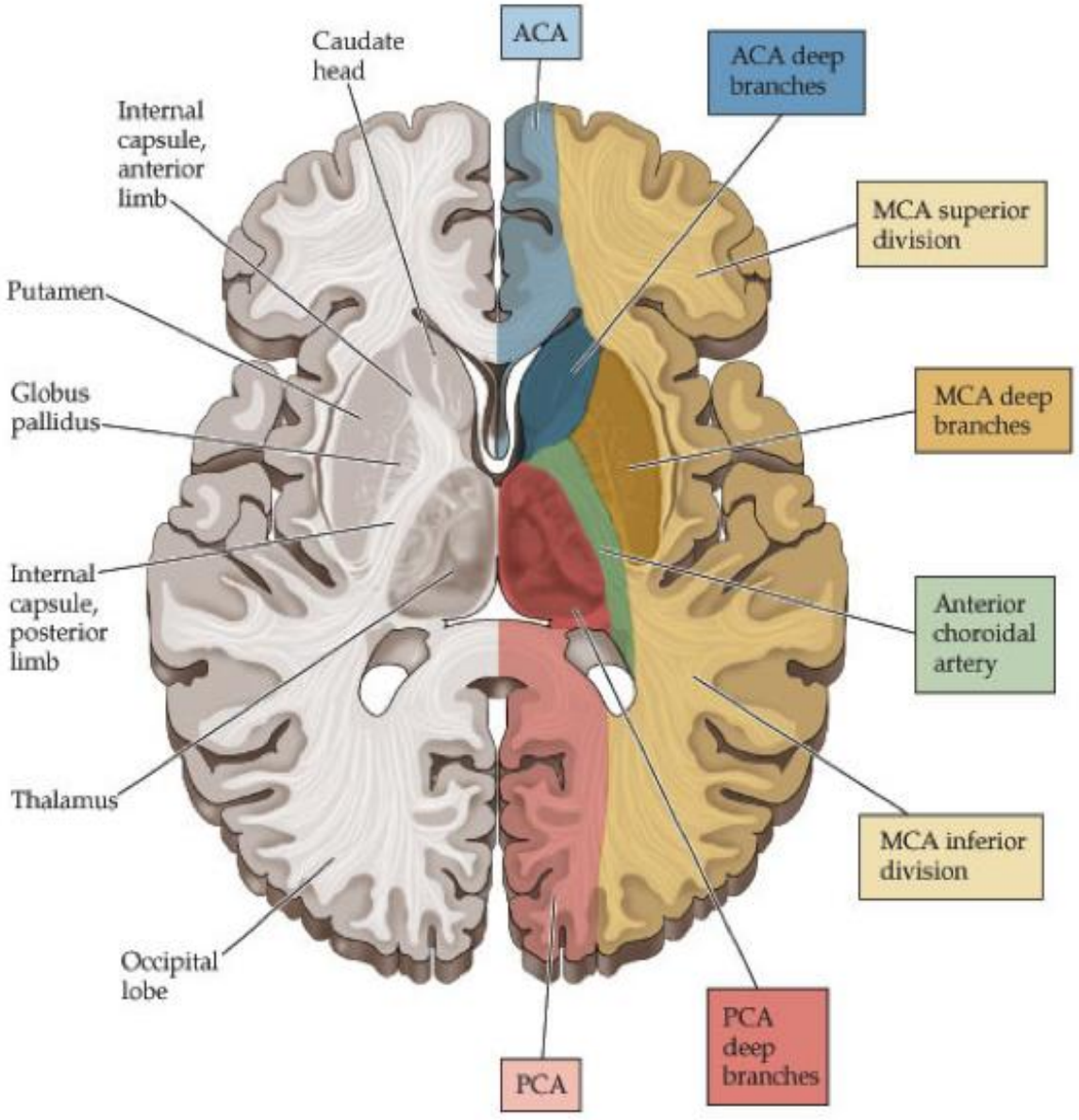
- Clinical relevance –
    - Occlusion of ACA may cause following symptoms:
    - Contralateral lower limb upper motor neuron type (UMN) of weakness
    - Contralateral sensory loss in lower limb
    - Due to frontal lobe involvement – Behavioural abnormalities, cortical release reflexes – grasp reflex, sucking reflex, gegenhalten phenomenon.
    - Transcortical aphasia.

3. Middle cerebral artery (MCA) – It is also a paired artery which supplies anterior temporal and insular cortices. They are connected to ACA with the help of anterior communicating branches and connected with PCA with the help of posterior communicating branches. They are further divided into 4 parts or segments in their course of supply. They supply the bulk of lateral surface of the hemispheres along with speech areas (Broca's and Wernicke's areas)
    - Clinical relevance –
        - Contralateral upper and lower limb UMN type of paralysis
        - Contralateral sensory loss over face and arm
        - If lenticulostriate branches of MCA are involved –
            - If involvement of dominant hemisphere → aphasia
            - Involvement of non-dominant hemisphere → contralateral neglect syndrome

4. Posterior cerebral artery (PCA) – it is one of the paired arteries which supply the posterior part of the brain which includes occipital lobe. It is divided into 2 branches – cortical and ganglionic vessels.

- Clinical relevance –
    - Contralateral loss of pain and temperature
    - Contralateral homonymous hemianopia with macular sparing
    - Alexia and agraphia
    - Weber's syndrome – third cranial nerve palsy with contralateral hemiplegia
    - Horner's syndrome

FIGURE 9: Blood supply of brain



MANAGEMENT:

NON INVASIVE METHODS:

In patients with AIS, diagnosing stroke early plays a key role in many ways:

- ✓ To assess the clinical outcome and prognostication of the condition.
- ✓ To institute thrombolysis whenever possible.
- ✓ It helps further management – mainly in the ED, where it plays a crucial role in order to decide about further management.

Therefore, a standard approach for diagnosis and treatment for stroke must be established in primary health care centres and educational institutions for management of stroke in emergency.It also helps in assessing the arterial territory involved and area of brain affected by examining clinically.Identification and control of modifiable risk factors and especially hypertension, is the best strategy to reduce the burden of stroke, and the total number of strokes could be reduced substantially by these means.

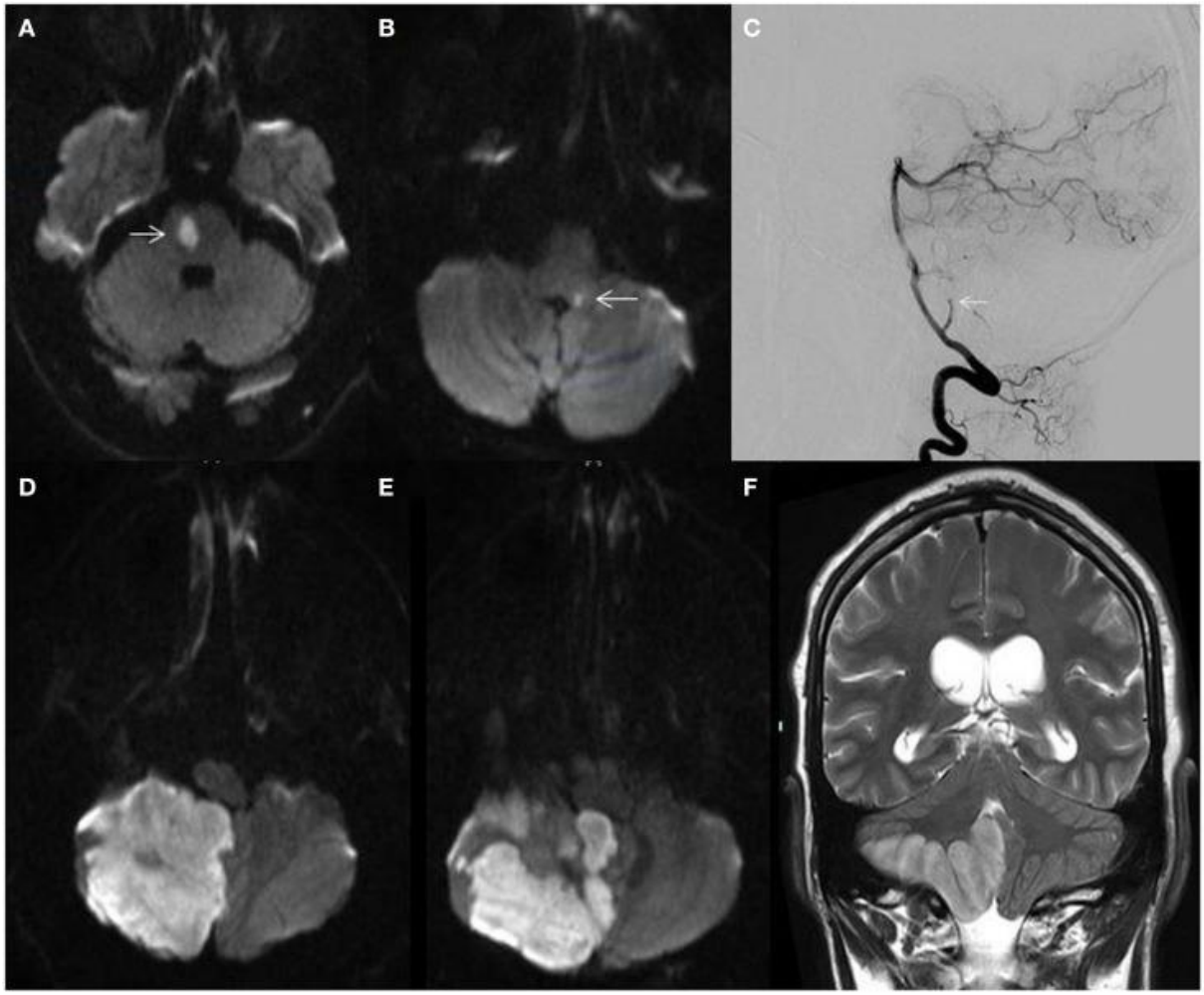
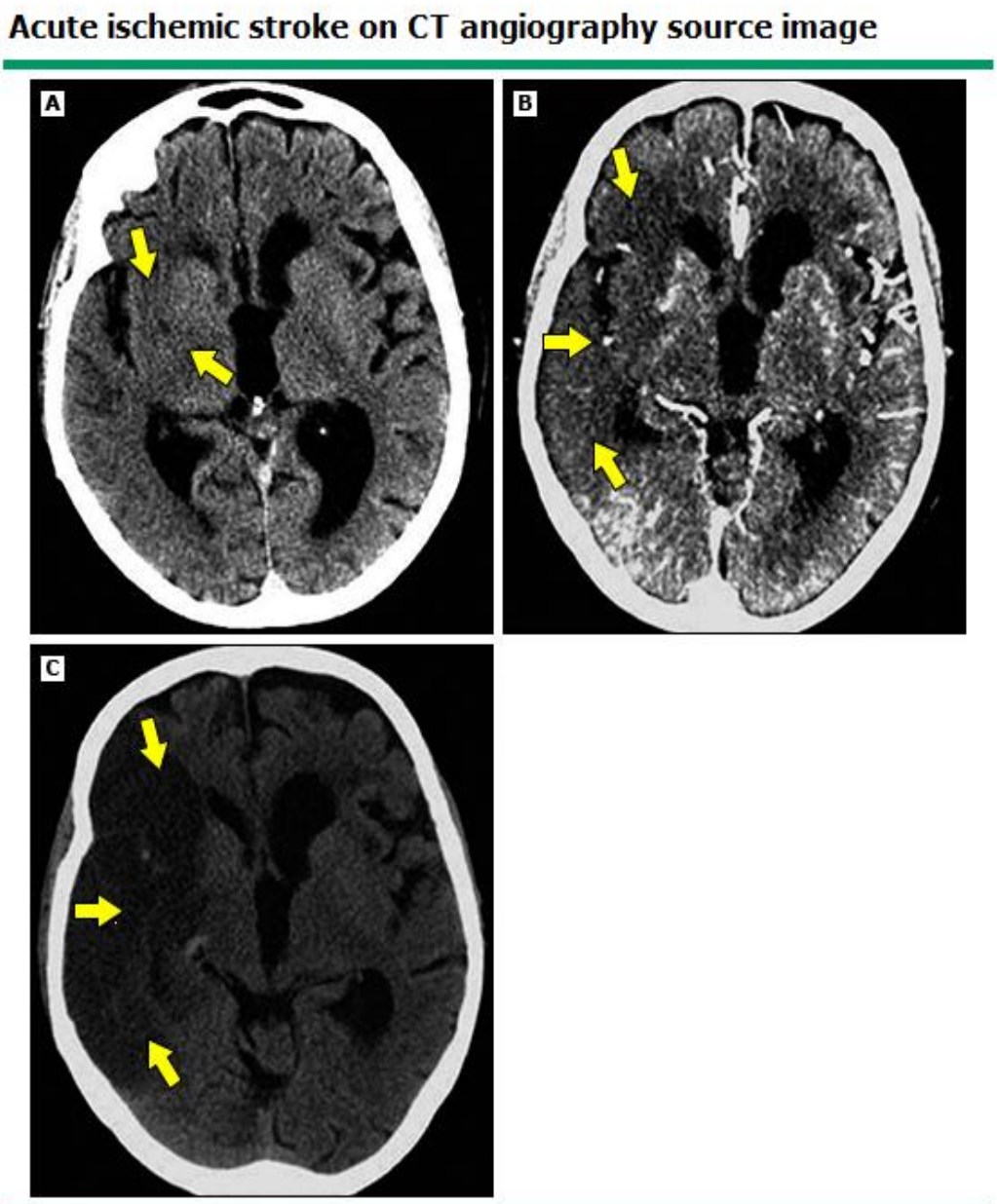


FIGURE 10: (A) MRI diffusion-weighted image (DWI) demonstrating a right ventral pontine infarction (arrow); **(B)** MRI-DWI showing a small dorsal left medullary infarction (arrow) in a patient presenting with acute isolated vertigo; **(C)** catheter angiogram showing cut-off of the right posterior inferior cerebellar artery (arrow); **(D,E)** MRI-DWI showing massive right cerebellar hemispheric and vermian infarction; **(F)** MRI T2-weighted sequence demonstrating right cerebellar infarction with edema and mass effect

FIGURE 11



An 88-year-old woman admitted with acute left hemiparesis and dysarthria 90 minutes after the onset of symptoms. Baseline noncontrast head CT (A) shows early ischemic changes in the right MCA territory (arrows). CTA-SI image (B) reveals hypoattenuation in the right MCA territory (arrows), which corresponds to the final infarct (C) on follow-up CT scan (arrows).

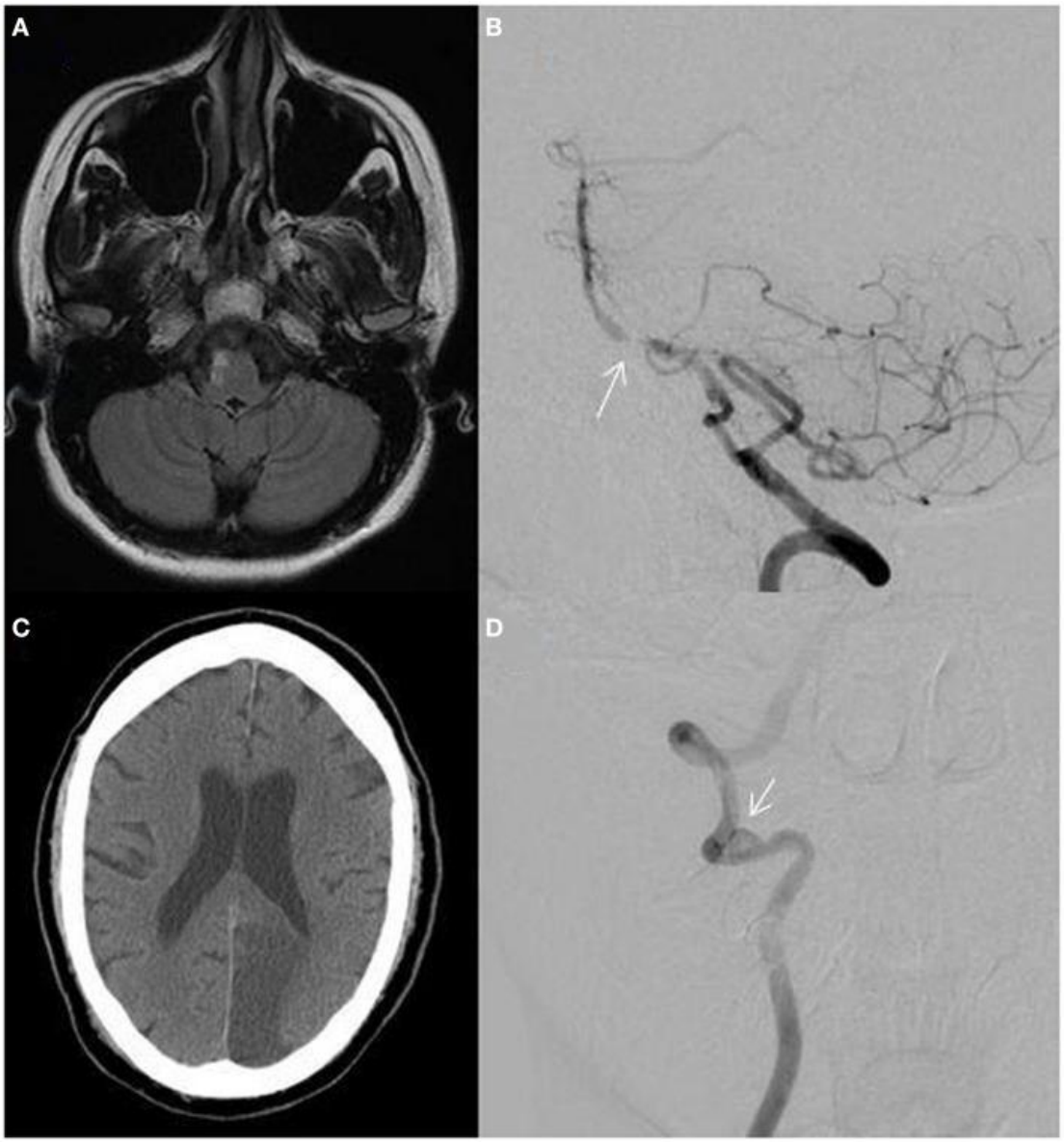
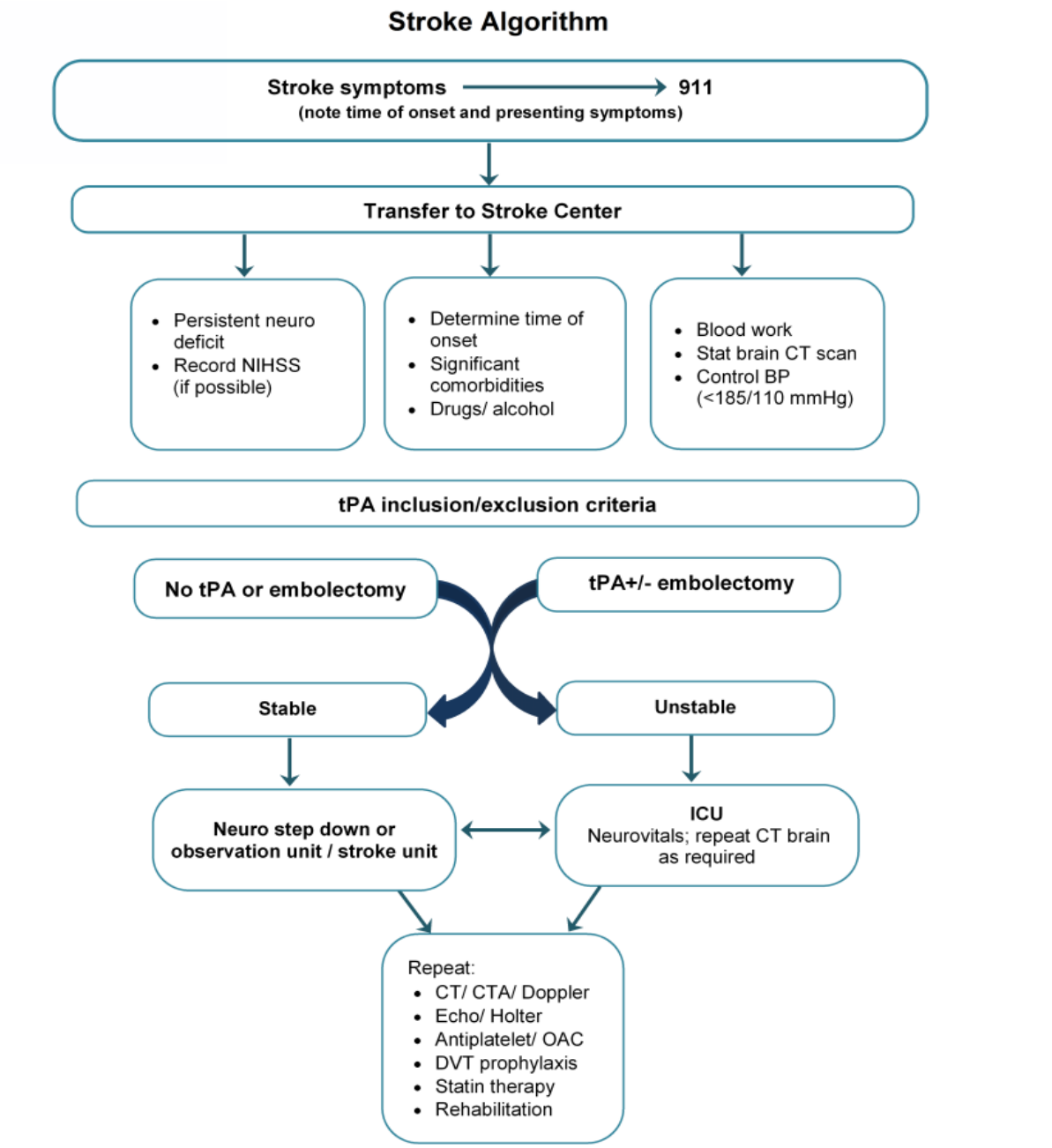


FIGURE 12 :MRI (A) MRI fluid-attenuated inversion recovery (FLAIR) sequence showing a right lateral medullary infarction with a hypoplastic right vertebral artery.**(B)** catheter angiogram showing stenosis at the vertebrobasilar junction (arrow); **(C)** non-contrast CT showing a left posterior cerebral artery territory infarction **(D)** catheter angiogram showing a right distal vertebral dissecting aneurysm with intraluminal thrombus (arrow) presenting with vertigo, ataxia, and a right cerebellar infarction.

TABLE 7



NIHSS: The National Institutes of Health Stroke Scale; **tPA:** Tissue plasminogen activator; **ICU:** Intensive care unit; **CT:** Computed tomography; **CTA:** Computed tomography angiography; **OAC:** Oral anticoagulant; **DVT:** Deep vein thrombosis

Stroke scoring systems:

Rapid assessment with the help of scoring systems is needed in the patients with suspicion of stroke. Several scoring scales are mainly used to assess the baseline characteristics for treatment outcome [81].In this study, clinical assessment by NIHSS scoring scale wasused in Emergency Department to know the severity of stroke at onset and used for prognosis and to assess clinical outcome. These scales mainly help in the accuracy of diagnosis of AIS and also help in determining the appropriate treatment and predicting the outcome. No single scale will be able to assess all the effects of stroke that is to say not all parameters of stroke can be assessed completely by these scales. Several scoring scales have been designed and standardized. Early imaging of brain either CT or MRI with or without angiography has to be done in the ED presented when a patient presents with stroke. Thus, haemorrhagic stroke is ruled out wherein the line of management differs from that of AIS.

Routine baseline investigations to be done are **(TABLE 8):**

Complete haemogram	
Blood sugars	Hypo or hyperglycemia
Urine routine	Diabetes, infection
Serum electrolytes	Hyponatremia or hypokalaemia or hyperkalaemia
Renal function tests	Renal failure
Fasting lipids	Dyslipidemia
Homocysteine levels	Homocystinemia
Serology	Vasculitis , Infections, HIV, VDRL
ECG	Left ventricular hypertrophy (LVH), Atrial fibrillation, arrhythmias, AMI
Echocardiography	Infective endocarditis, atrial myxoma,mural thrombus
ESR, CRP	Autoimmune causes-vasculitis, SLE
To do in young stroke	
ANA profile, APLA	APLA syndrome, SLE, vasculitis
Coagulation profile	Protein C and S deficiency, anti thrombin III deficiency, hyperfibrinogenemia.
Genetic studies (optional)	CADASIL, MELAS, CARASIL.,etc

TREATMENT:

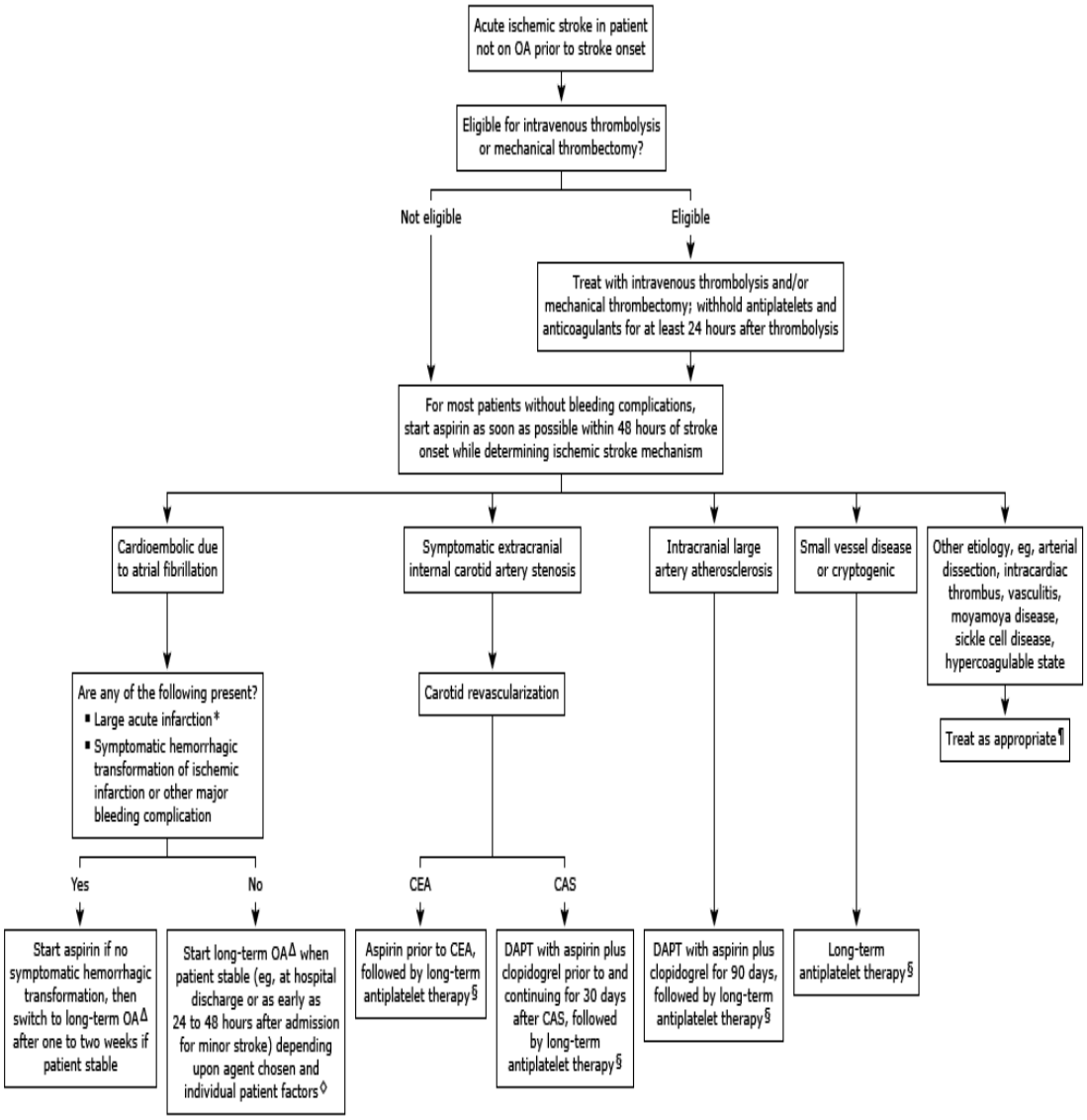
Treatment is mainly aimed at reversing the hypoxic brain injury and lessen further damage of brain from hypoxia caused by decreased blood supply due to occlusion of the blood vessels supplying the brain.

At the presentation to ED with acute stroke, the primary management is to assess the airway, breathing and circulation initially[81].Treat the hypoglycaemia (<60mg/dl) identified on presentation as it may act as a stroke mimic. Hyperglycemia leads to poor outcomes in stroke. Hence, early treatment of blood sugars is needed.

Blood pressure: Reduce the blood pressure by 15% of that of initial presentation within 24hrs of onset if SBP > 220 mm Hg and DBP >120 mm Hg

TABLE 8

General approach to antithrombotic therapy for acute ischemic stroke in patient not on anticoagulation prior to stroke onset



❖ ***Early fibrinolysis :***

According to AHA/ASA guidelines for the management of AIS, thrombolysis is indicated in order to restore the blood flow to the brain and early resolution ofneurological deficits. For this purpose, the most commonly used fibrinolytic drug is r-

tPA(recombinant tissue plasminogen activator). Streptokinase which has a major role in AMI, has high incidence of complications in acute AIS. Hence this drug is of not in regular use for AIS. It must be decided whether a patient is a feasible candidate for fibrinolysis[81].They must be thrombolysed within a window period of maximum of 4.5hrs from the onset of symptoms.

The FDA approved dose of IV r-tPA is 0.9 mg per kilogram of body weight, withamaximum dose of 90 mg. A bolus of 10% of the dose to be given over 1 minute, with the remaining 90% to be infused over 60 minutes. Weight should be determined reliably. Treatment with a lower dose of r-tPA (0.6 mg per kilogram) in Japan suggest that it had similar efficacy but the lower dose has not yet been assessed in large, randomized trials.

Third-generation plasminogen activators, such as Tenecteplase and Desmoteplase, are more fibrin specific than second generations r-tPA and cause less activation of systemic lytic activity.

Symptomatic intracranial hemorrhage occurs in 1.7 to 8.0% of treated patients.[87,88]Recommendations for the treatment of intracranial or major systemic bleeding after thrombolytic therapy often includes administration of cryoprecipitate and platelets,although evidence-based guidelines for such an approach are lacking[89,90]

- 10 units of cryoprecipitate (to increase fibrinogen and factor VIII)
- 6-8 units of platelets to be given

- In patient receiving UFH consider giving protamine 1mg for every 100 U UFH

INCLUSION AND EXCLUSION CRITERIA FOR THROMBOLYSIS IN AIS:

INCLUSION CRITERIA:

- ✓ Onset of symptoms <3 hours before beginning treatment (Onset time is defined as either the witnessed onset of symptoms or the time last known normal)
- ✓ Age ≥18 years
- ✓ Potential risks and benefits of IV t-PA treatment discussed with patient and/or family members and they have verbalized understanding (to be documented in patient's record). If patient unable to give verbal consent and no family available, IV t-PA can be given under Emergency Doctrine. Written informed consent not required for IV tPA when given within 3 hours of symptom onset.

EXCLUSION CRITERIA:

- ✓ Significant head trauma or prior stroke in previous 3 months
- ✓ Any history of haemorrhage stroke
- ✓ Intracranial neoplasm, arteriovenous malformation, or aneurysm
- ✓ Recent intracranial or intra-spinal surgery
- ✓ Elevated blood pressure (systolic >185 mm Hg or diastolic >110 mm Hg)
- ✓ Active internal bleeding
- ✓ Blood glucose concentration <50mg/dl (2.7mmol/L)
- ✓ Acute bleeding diathesis, including but not limited to: Platelet count <1,00,000/mm^3 (In patients without history of thrombocytopenia, treatment with

IV rtPA can be initiated before availability of platelet count but should be discontinued if platelet count is <100 000/mm³.)

- ✓ Heparin received within 48 hours, resulting in abnormally elevated aPTT greater than the upper limit of normal
- ✓ Current use of anticoagulant with INR >1.7 or PT >15 seconds and current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT; TT; or appropriate factor Xa activity assays)
- ✓ CT demonstrates multilobar infarction (hypodensity>1/3 cerebral hemisphere)

RELATIVE EXCLUSION CRITERIA:

- ✓ Only minor or rapidly improving stroke symptoms (clearing spontaneously)
- ✓ Seizure at onset with postictal residual neurological impairments
- ✓ Major surgery or serious trauma within previous 14 days
- ✓ Recent gastrointestinal or urinary tract haemorrhage (within previous 21 days)
- ✓ Pregnancy

To extend IV tPA to 4.5 hours from symptom onset/last known normal, the following additional criteria MUST be met:

- ✓ Patient is < 80 years of age
- ✓ Patient does not have a history of both diabetes AND stroke

- ✓ Patient is not taking Warfarin (Coumadin) or any other anticoagulant regardless of INR/coagulation results
- ✓ NIHSS is < 25
- ✓ Written informed consent obtained from patient and/or family – required when IV tPA given within the 3-4.5 hour window.

❖ ***Anti coagulants:***

Anticoagulation is not recommended in all patients with AIS in emergency condition. Drugs most commonly used are low molecular weight heparin (LMWH) or unfractionated heparin (UFH)[84]. They can be used to prevent venous thromboembolism. Only in the below mentioned specified clinical situations, anticoagulation therapy is indicated :

- Conditions with potential high risk of early cardiogenic reembolization
- Symptomatic dissection of arteries supplying the brain
- Symptomatic extra-cranial or intra-cranial atherosclerotic stenosis
- Basilar artery occlusion before or after intra-arterial pharmacological or mechanical thrombolysis
- Known hypercoagulable states
- Cerebral venous sinus thrombosis

❖ ***Anti-thrombotic agents :***

They are mainly used for secondary prevention of stroke. Drugs most commonly used are aspirin,clopidogrel and extended release dipyridamole. Newer antiplateletsdabigatran, apixaban and rivaroxaban are being studied for anticoagulation comparing with warfarin [85].According to guidelines, aspirin should be given within 24 to 48hrs of onset of stroke to prevent mortality and primary end point.

Endovascular techniques – intra-arterial fibrinolysis, thrombo-embolectomy, suction thrombectomy, angioplasty and revascularisation are among the common endovascular procedures. The main aim of these is to recanalise the thrombosed vessel to improve the blood flow. For this a team of skilled neurologists, interventional radiologists, anaesthesiology, nursing and technical support is required for optimal success.

❖ ***Neuro protection:***

Several novel neuro-protective agents like citicholine, traxoprodil, ONO-2506, magnesium, DP-b99 and NXY-059 have been identified. They limit the infarct size and improve functional outcome (primary end point)[85]. They act as free radicals scavengers and inhibit further occurrence of neuronal cell death.

❖ ***Rehabilitation centres :***

The main aim of these centres is to improve the quality of life of stroke survivor by improving the skills to perform activities of daily living. A team of neurologist, psychiatrist, occupational therapist, speech language therapists, dieticians and social workers play an important role in achieving the desired result[86]

RESULTS

In this study, about 50 consecutive cases admitted with AIS, which met inclusion and exclusion criteria were evaluated. At presentation, along with complete history taking, relevant clinical examination, scoring was done based on NIHSS score.mRSscoring 1 week post admission,3 months later and Volume of infarct in CT scan and clinical outcome were analysed in this study.

GENDER

Among the study population of 50 patients, 44(88%) were males and 6(12%) were females. Out of 50 patients,3 patients were lost to followup.

FIGURE 12: Sex Distribution

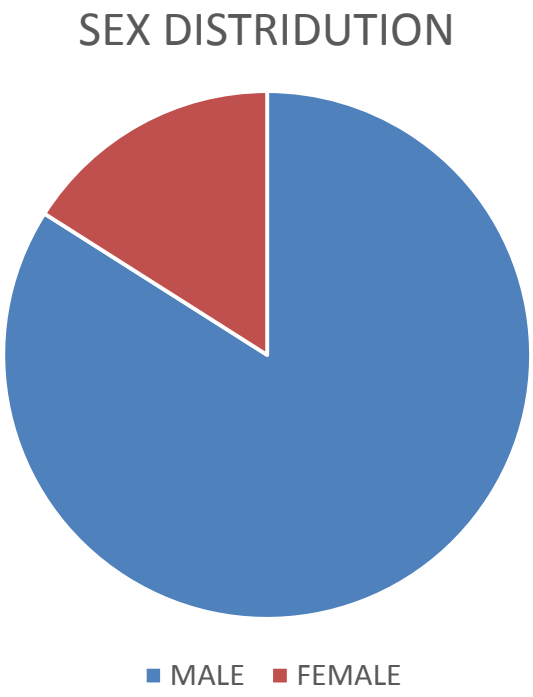


TABLE 9: Presenting symptoms in study population

SYMPTOMS	NO OF PATIENTS	%
HEADACHE	5	10
VOMITING	4	8
MOTOR WEAKNESS	18	36
UNCONSIOUSNESS	6	12
DYSARTHRIA	11	22
VERTIGO	3	6
TINGLING	2	4
DIPLOPIA	0	0
CONVULSIONS	1	2

TABLE 10: Distribution according to systolic blood pressure (SBP) on admission

SBP	MALE	FEMALE	TOTAL	%
< 138	5	1	6	12
140 – 158	21	2	23	46
160 – 178	9	2	11	22
180 – 198	7	1	8	16
>200	2	0	2	4
TOTAL	**44**	**6**	**50**	**100**

TABLE 11:Distribution according to diastolic blood pressure (DBP) on admission

DBP	MALE	FEMALE	TOTAL	%
<78	4	0	4	8
80 – 88	13	2	15	30
90 – 98	18	3	21	42
100 – 108	7	1	8	16
>110	2	0	2	4
TOTAL	**44**	**6**	**50**	**100**

TABLE 12:Past medical history on study population

RISK FACTORS	TOTAL	MALE	FEMALE
TOBACCO	1	0	1
OLD CVA	5	4	1
ALCOHOLISM	11	11	0
IHD	12	12	0
SMOKING	12	12	0
DLP	14	13	1
DM	20	19	1
SHT	34	30	4

FIGURE 13:

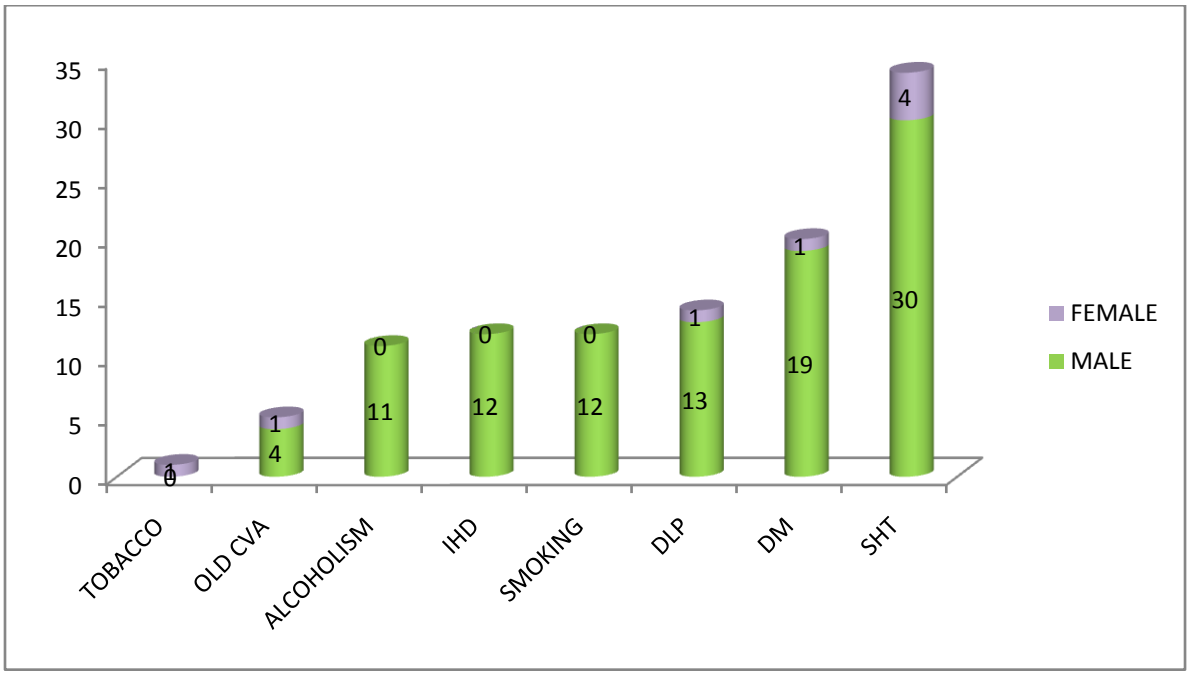


TABLE 13: Frequency of lesion in MRI / CT brain

FREQUENCY OF LESION IN MRI/CT	NO OF PATIENTS
MCA INFARCT	30
MULTI INFARCT	9
POSTERIOR CIRCULATION INFARCT	5
LACUNAR INFARCT	6
TOTAL	50

FIGURE 14:

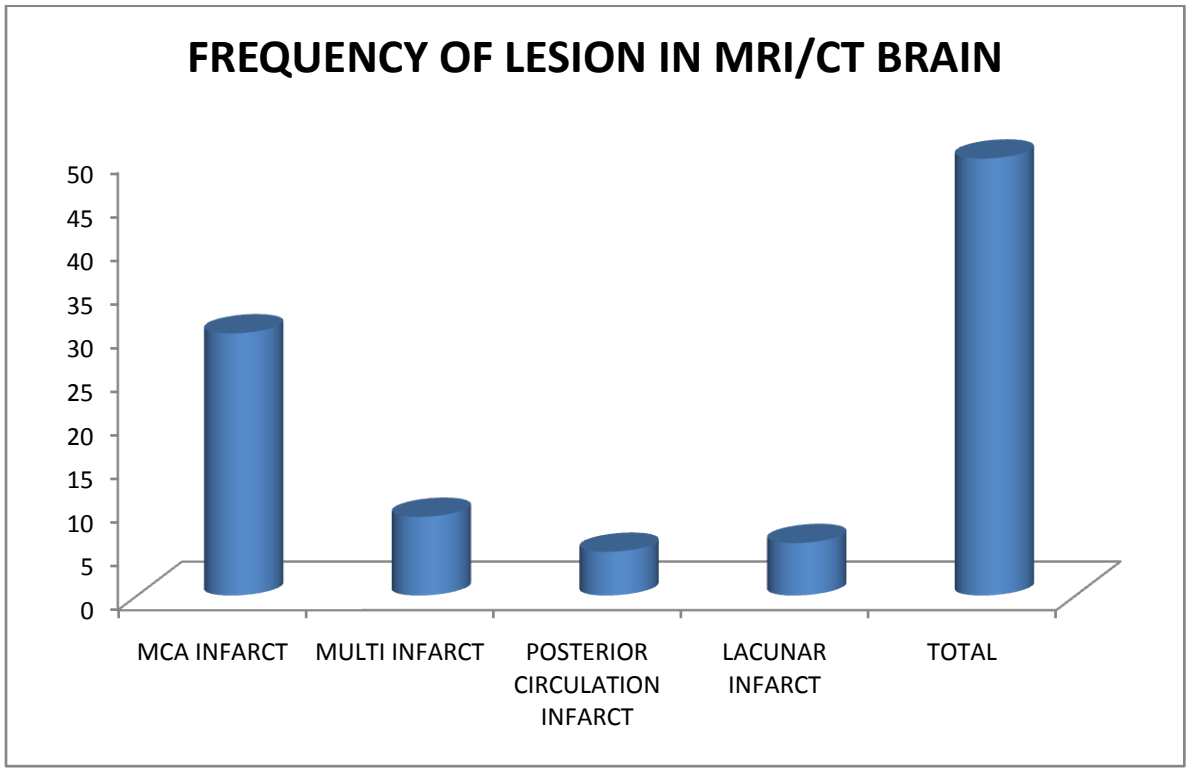
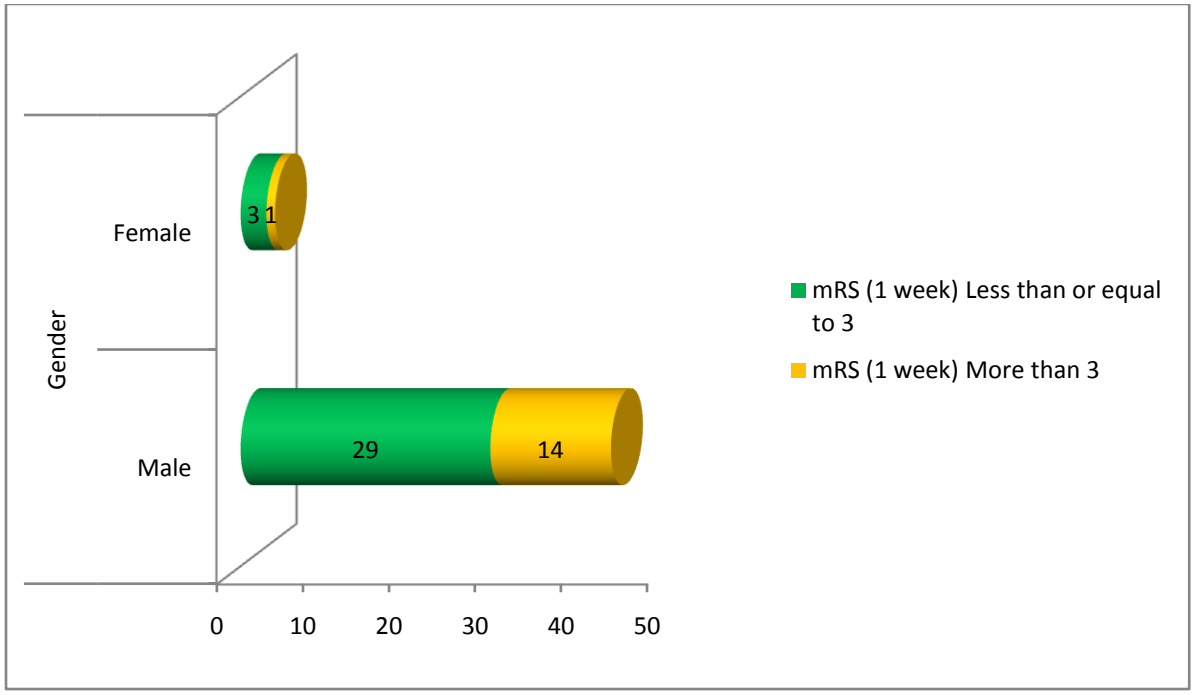


TABLE 14: Gender and mRS @ 1 week

Gender	mRS (1 week)		Total
	Less than or equal to 3	More than 3	
Male	29	14	43
Female	3	1	4
Total	**32**	**15**	**47**

FIGURE 15:

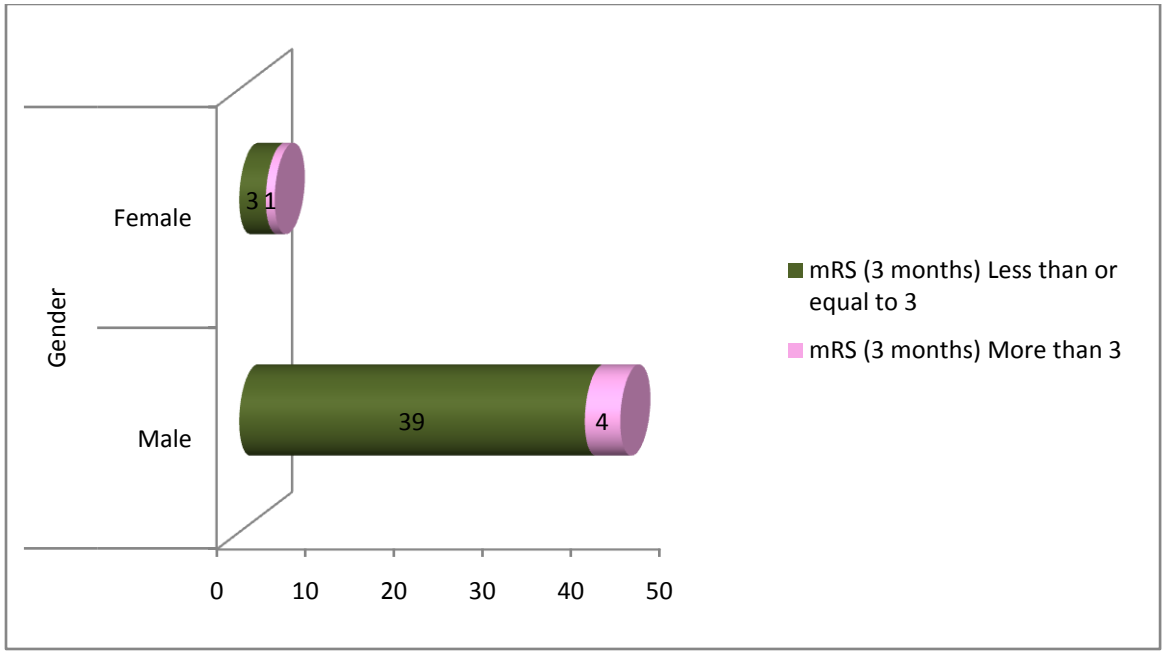


Out of the 43 male patients , 14 patients had significant disability. Among the 14, 3 had death as outcome. 29 patients had mild disability. Out of the 4 female patients, 1 had significant disability and died during the first week. Remaining 3 patients had mild disability.

TABLE 15: Gender and mRS @ 3 months

Gender	mRS (3 months)		Total
	Less than or equal to 3	More than 3	
Male	39	4	43
Female	3	1	4
Total	42	5	47

FIGURE 16:

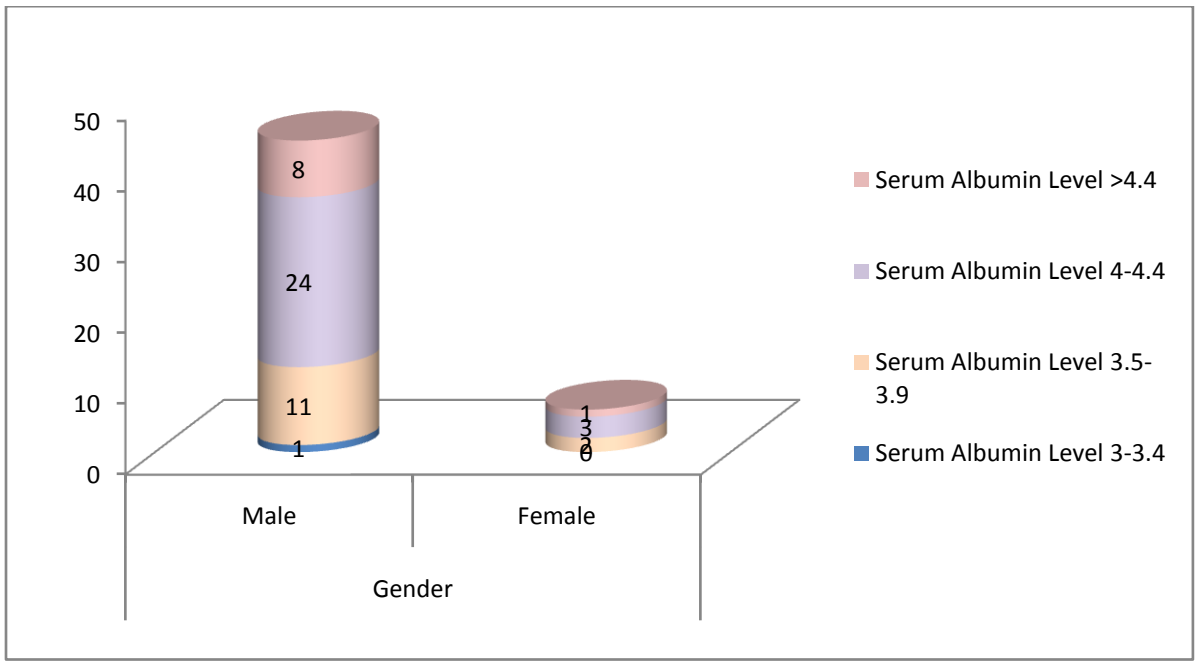


Among the male patients, no of patients with significant disability dropped from 14 to 4.In the female group,the 3 patients with mild disability had improvement in the mRS score and didn't worsen.

TABLE 16 :Gender and serum albumin level

Gender	Serum Albumin Level				Total
	3-3.4	3.5-3.9	4-4.4	>4.4	
Male	1	11	24	8	44
Female	0	2	3	1	6
Total	1	13	27	9	50

FIGURE 17:

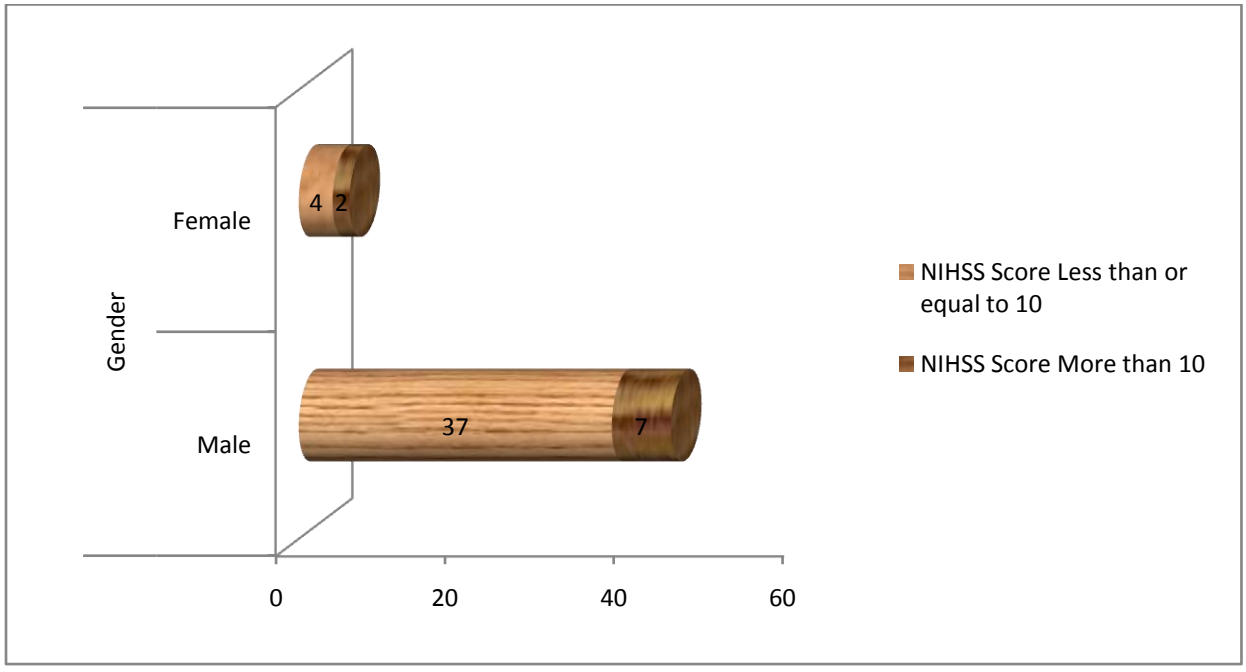


Among 50 patients , only one patient had low serum albumin levels. Majority of patients had albumin levels between 4 to 4.4.Both male and female groups were similar.

TABLE 17: Gender and NIHSS score

Gender	NIHSS Score		Total
	Less than or equal to 10	More than 10	
Male	37	7	44
Female	4	2	6
Total	41	9	50

FIGURE 18:

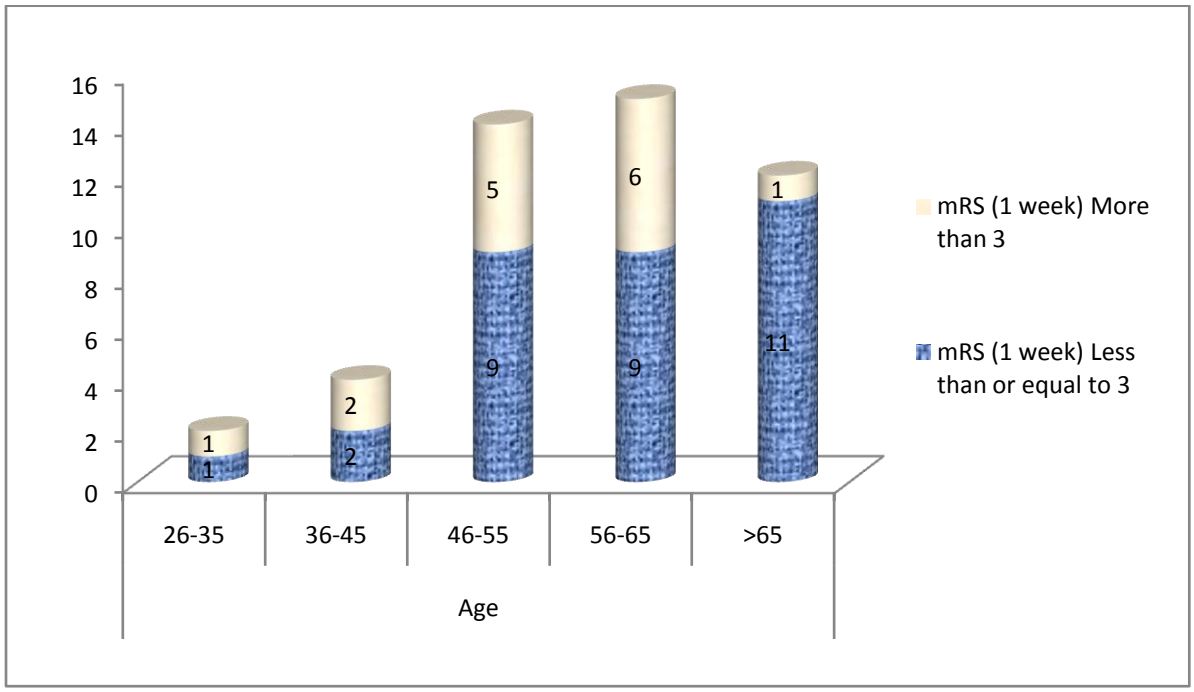


On admission, no. of males who had NIHSS more than 10 were 7. No of females who had NIHSS more than 10 were 2.

TABLE 18: Age and mRS @ 1 week

Age	mRS (1 week)		Total
	Less than or equal to 3	More than 3	
26-35	1	1	2
36-45	2	2	4
46-55	9	5	14
56-65	9	6	15
>65	11	1	12
Total	32	15	47

FIGURE 19:

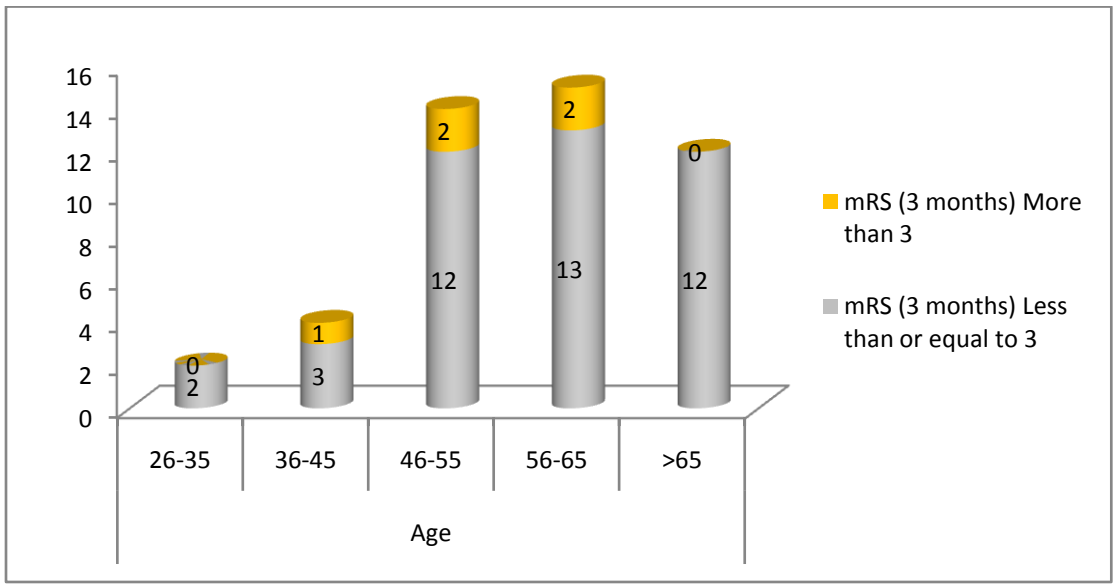


Among the 47 patients , no of people who had significant disability were 15.Among them 6 were in the age group of 56 to 65. No of people who had mild disability were 32.Among them about 11 people were in the age group more than 65.

TABLE 19: Age and mRS @ 3 months

Age	mRS (3 months)		Total
	Less than or equal to 3	More than 3	
26-35	2	0	2
36-45	3	1	4
46-55	12	2	14
56-65	13	2	15
>65	12	0	12
Total	42	5	47

FIGURE 20:

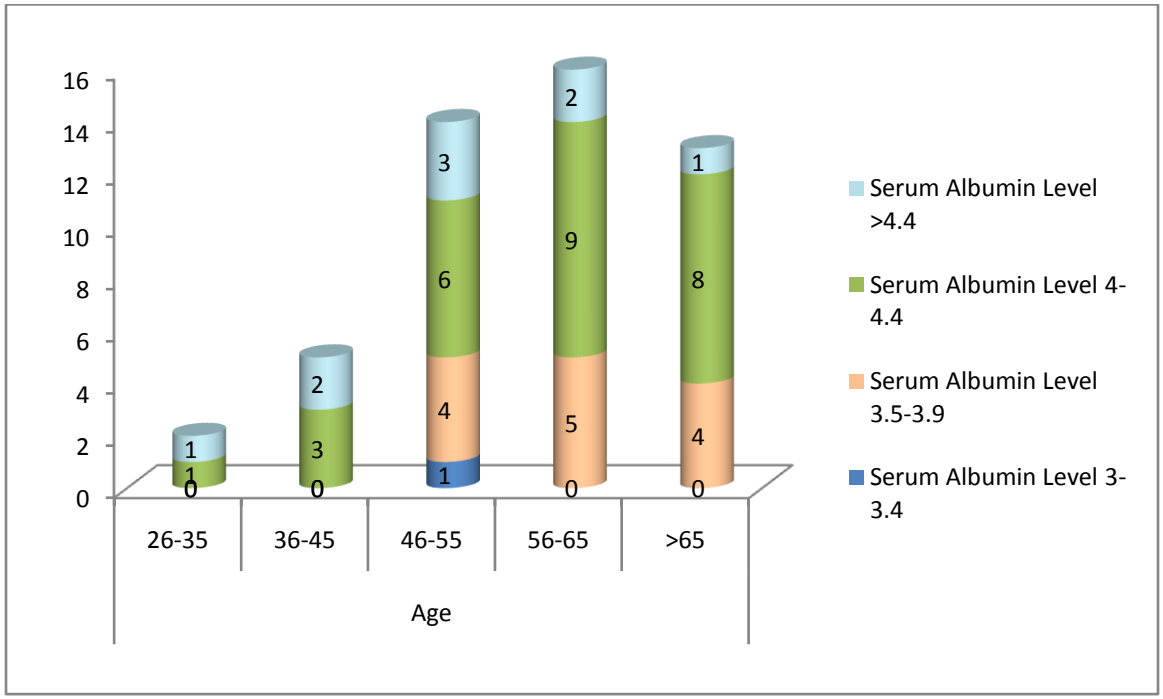


After 3 months , number of people with significant disability were 5 and number of people with mild disability were 42.Significant improvementwas seen in the age group of 56 to 65 (9 to 13).

TABLE 20: Age and Serum Albumin Level

Age	Serum Albumin Level				Total
	3-3.4	3.5-3.9	4-4.4	>4.4	
26-35	0	0	1	1	2
36-45	0	0	3	2	5
46-55	1	4	6	3	14
56-65	0	5	9	2	16
>65	0	4	8	1	13
Total	1	13	27	9	50

FIGURE 21:

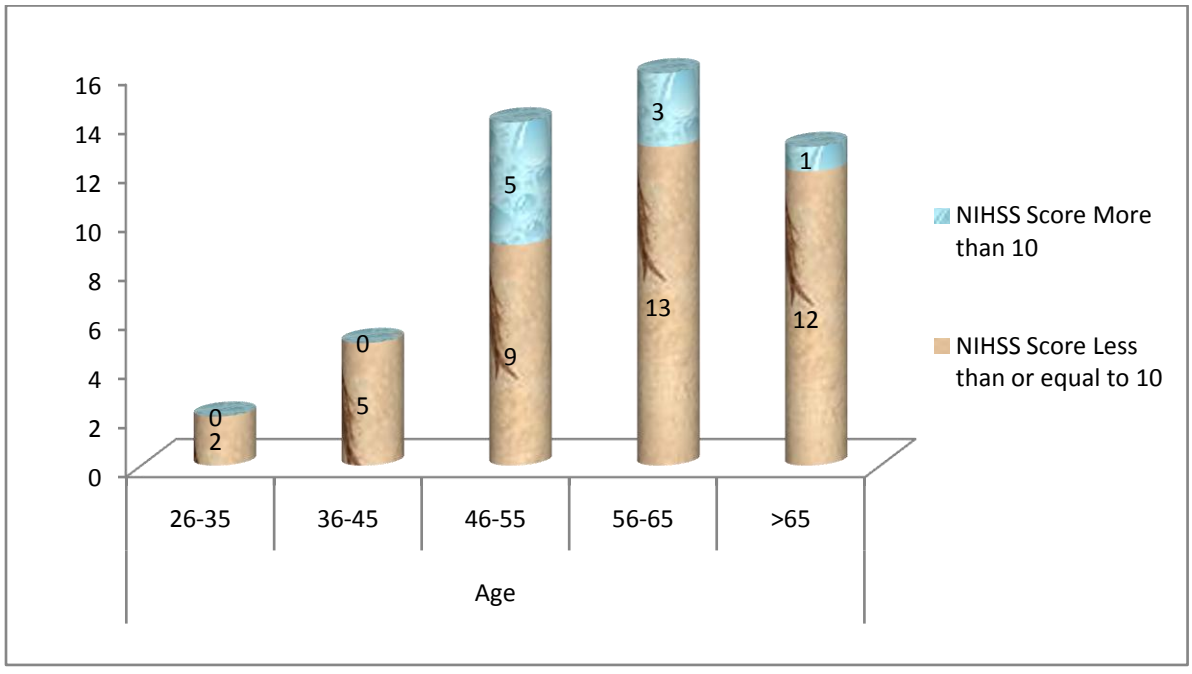


Mean albumin is 3.8.Only one patient in the age group of 46 to 55 had low serum albumin .Each group had high no of patients in the albumin range 4 to 4.4.

TABLE 21: Age and NIHSS score

Age	NIHSS Score		Total
	Less than or equal to 10	More than 10	
26-35	2	0	2
36-45	5	0	5
46-55	9	5	14
56-65	13	3	16
>65	12	1	13
Total	41	9	50

FIGURE 22:

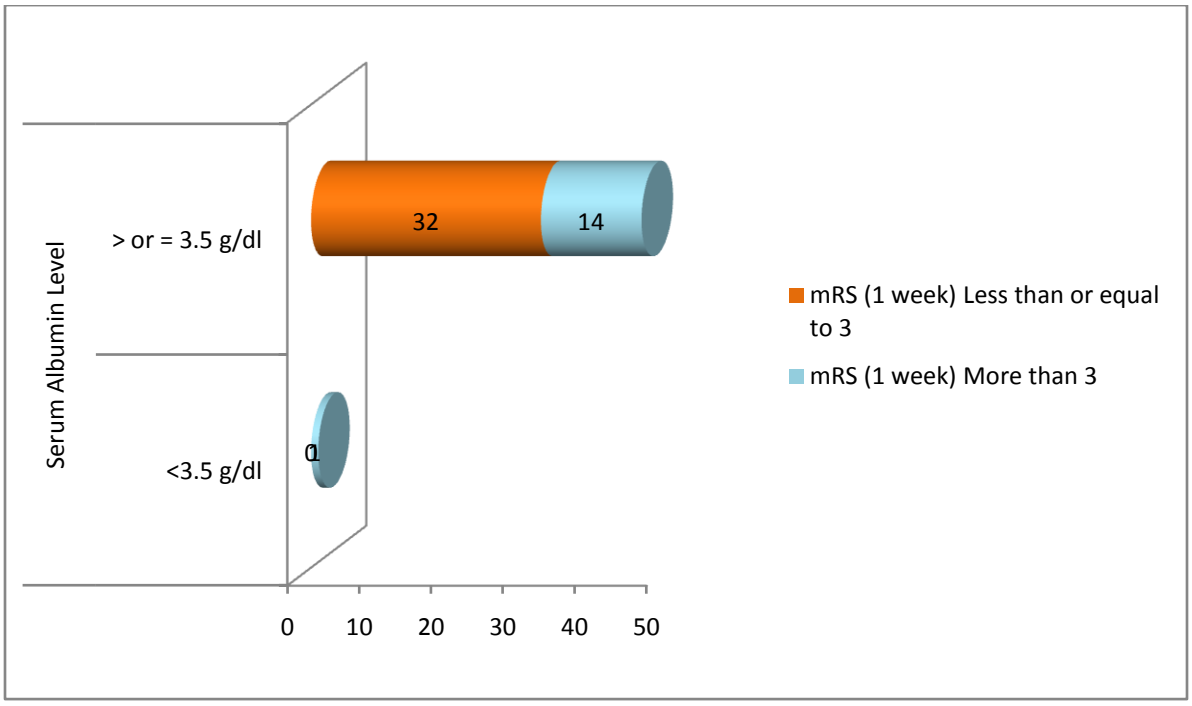


No. of people with NIHSS score less than or equal to 10 was 41 and more than 10 was 9. NIHSS score of 10 or less than 10 was seen in high numbers in 56-65 and >65 years age group.

TABLE 22:Serum Albumin with mRS after 1 week

Serum Albumin Level	mRS (1 week)		Total	P value
	Less than or equalto 3	More than 3		
<3.5 g/dl	0	1	1	0.319
> or = 3.5 g/dl	32	14	46	
Total	32	15	47	

FIGURE 23:

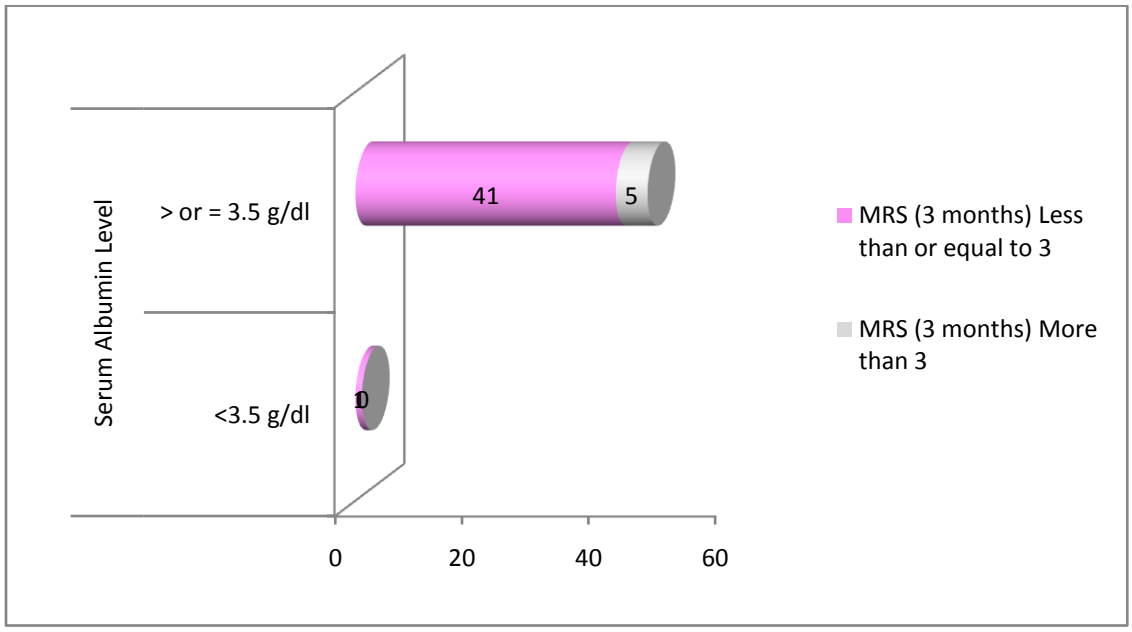


Serum albumin level was compared with mRSscore. No of people with serum albumin >3.5 and mRS less than or equal to 3 are 32 and with mRS> 3 are 14. No of people with serum albumin<3.5 and mRS>3 are 1. Pvalue was 0.319. Hence there was no significant correlation.

TABLE 23: Serum Albumin with mRS after 3 months

Serum Albumin Level	mRS (3 months)		Total	P value
	Less than or equal to 3	More than 3		
<3.5 g/dl	1	0	1	0.894
> or = 3.5 g/dl	41	5	46	
Total	42	5	47	

FIGURE 24:



Serum albumin level and mRS score after 3 months were compared. Number of patients with serum albumin >3.5 and mRS< 3 increased from 32 to 41. The patient with serum albumin <3.5 had an improvement in mRS score. Eventhough there was improvement in patients clinically, statistically there was no significant correlation as the p value was 0.894.

TABLE 24: Volume of Infarct in CT Scan withmRS after 1 week

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	P value
					Lower Bound	Upper Bound			
Less than or equal to 3	32	5.5948	12.00600	2.12238	1.2662	9.9234	.11	52.54	.001
More than 3	14	26.5182	26.47135	7.07477	11.2341	41.8023	.30	81.60	
Total	46	11.9628	19.91184	2.93584	6.0497	17.8759	.11	81.60	

FIGURE 25:

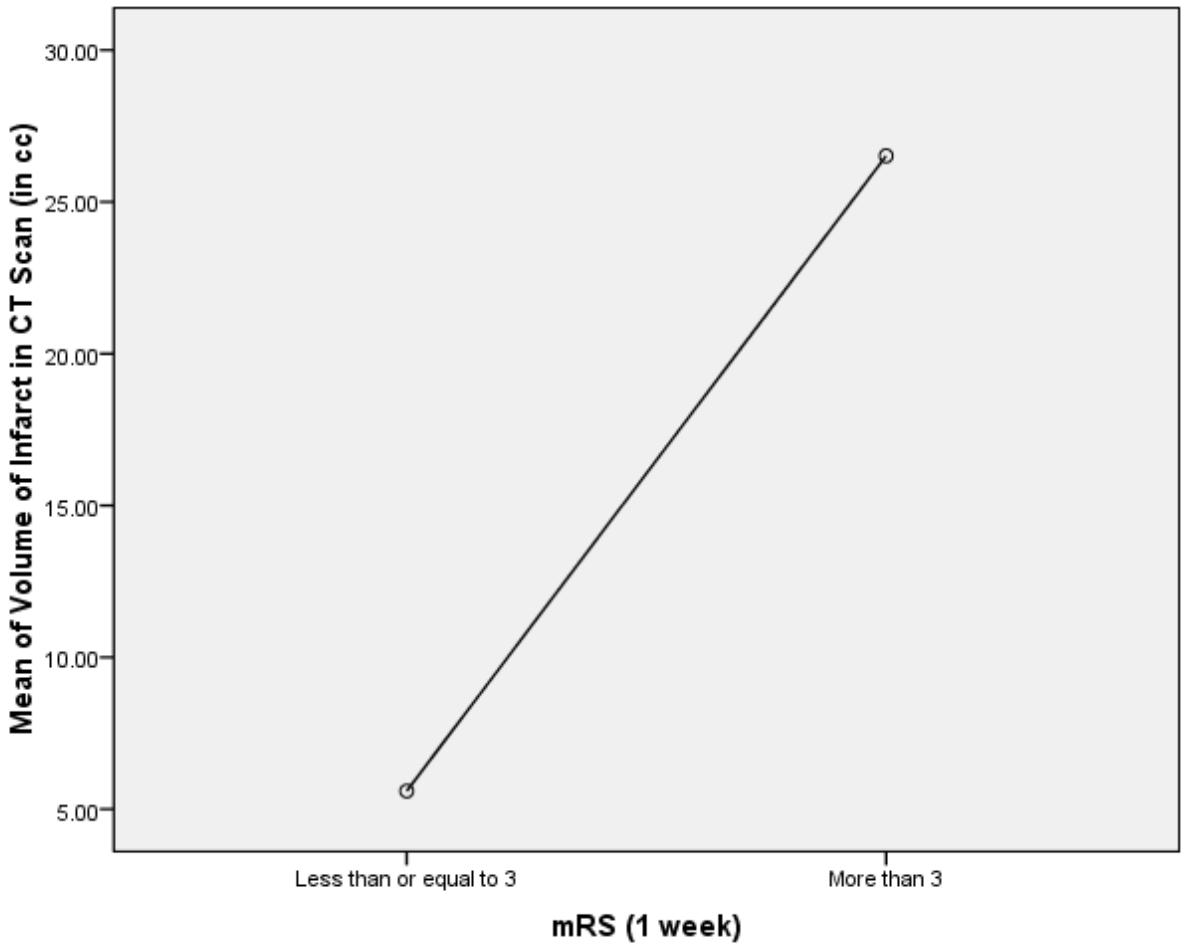
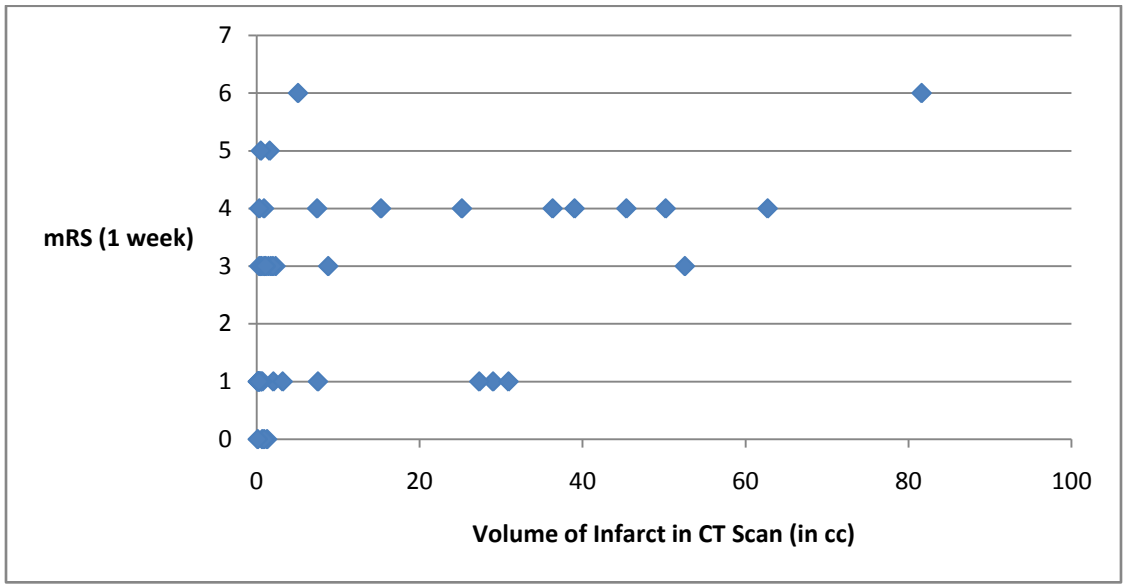


FIGURE 26:**Scatter Plot of infarct volume VsmRS @ 1 week**



Out of 47 patients , volume of infarct could not be calculated for one patient . For remaining patients volume of infarct and mRS scale was compared using ANOVA method. P value was 0.001.This shows that there was significant correlation between the volume of infarct and outcome during first week.

TABLE 25: Volume of Infarct in CT Scan with MRS after 3 months

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	P value
					Lower Bound	Upper Bound			
Less than or equal to 3	42	10.6385	17.63608	2.72131	5.1428	16.1343	.11	62.70	0.146
More than 3	4	25.8675	37.60486	18.80243	-33.9702	85.7052	1.57	81.60	
Total	46	11.9628	19.91184	2.93584	6.0497	17.8759	.11	81.60	

FIGURE 27:

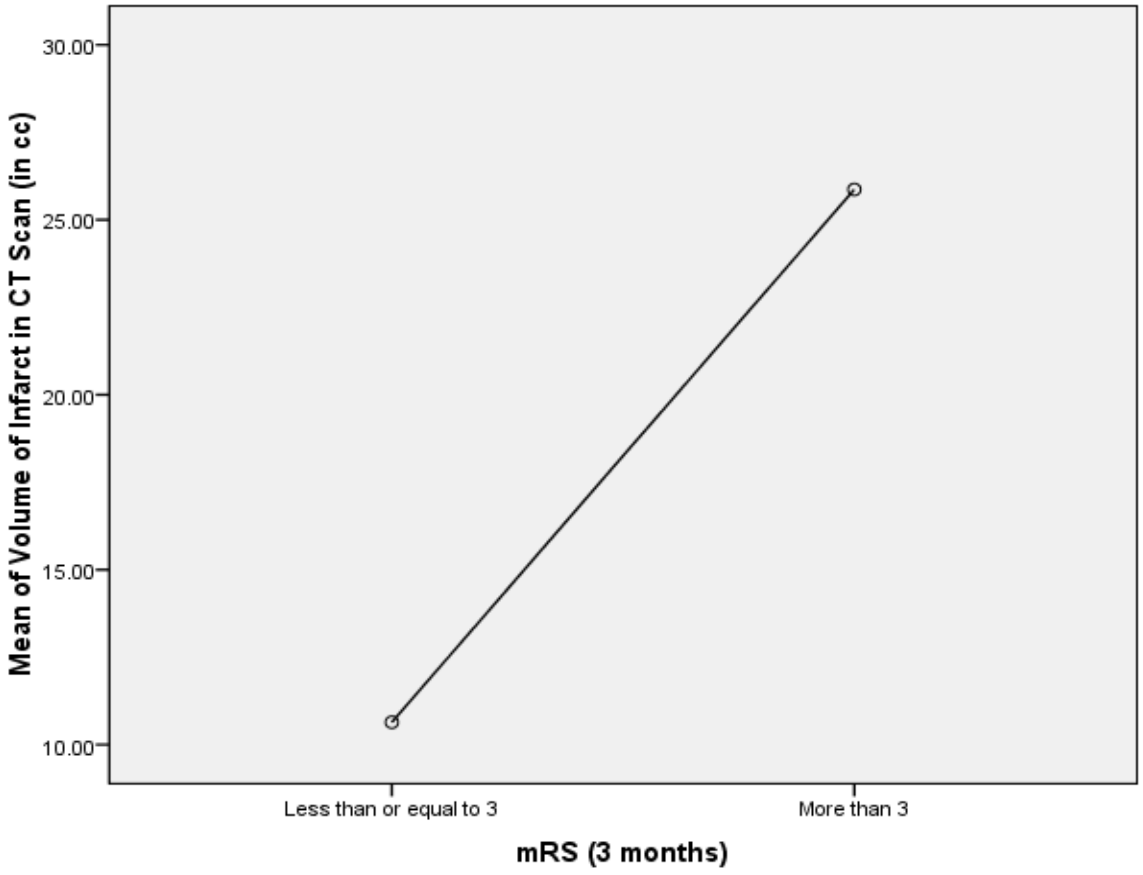
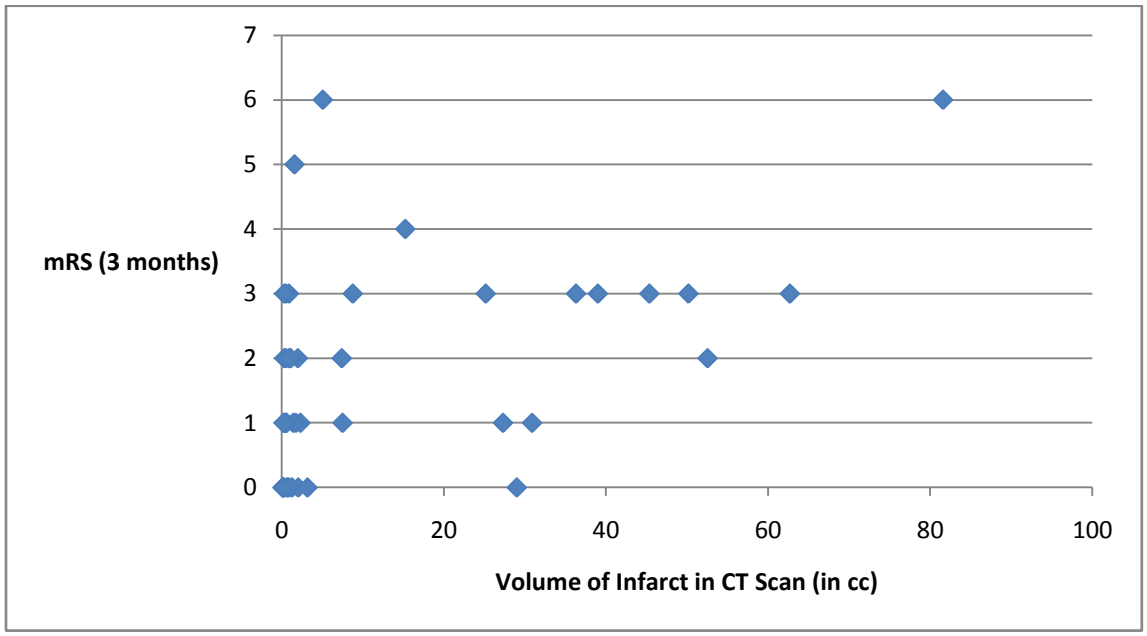


FIGURE 28:**Scatter Plot of infarct volume VsmRS @ 3 months**

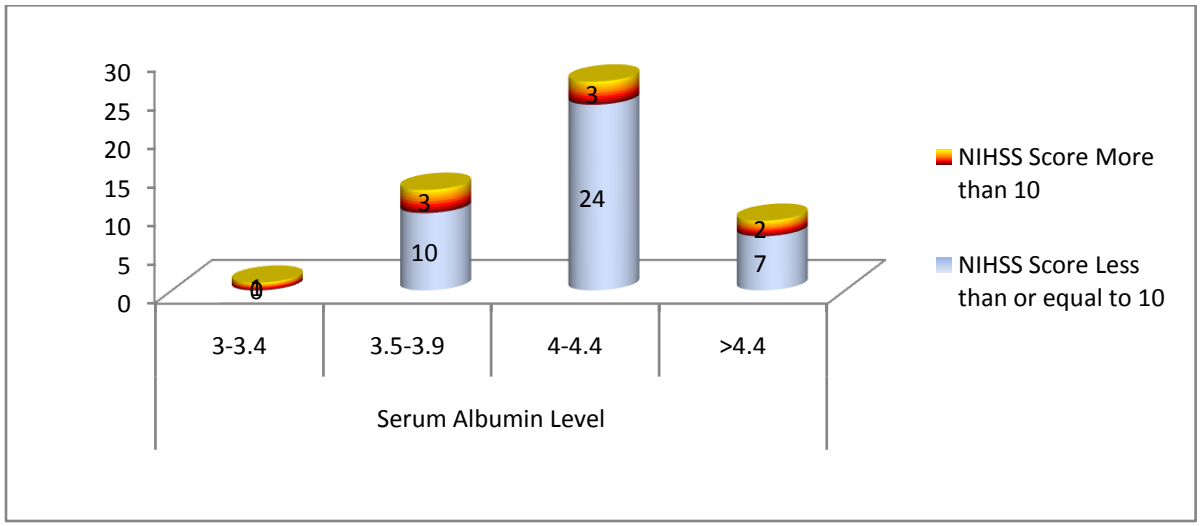


The volume of infarct and mRS scale was compared during 3rd month using ANOVA method. P value was 0.146 . This showed there was no correlation between volume of infarct and outcome during third month.

TABLE 26 :Serum Albumin with NIHSS Score

Serum Albumin Level	NIHSS Score		Total	P value
	Less than or equal to 10	More than 10		
3-3.4	0	1	1	0.124
3.5-3.9	10	3	13	
4-4.4	24	3	27	
>4.4	7	2	9	
Total	41	9	50	

FIGURE 29:



Most of the previous studies showed that patients with good outcome had lower NIHSS score and high serum albumin level on admission and those with worst outcome showed high NIHSS score and low serum albumin level. In this study also patient with good outcome had low NIHSS and high albumin. Only one patient had low albumin and high NIHSS score. P value was 0.124.Hence there is no significant correlation between serum albumin and NIHSS score in this study, contrary to other studies.

DISCUSSION

The mean age group of the study population was 53 years, predominantly middle aged group which is a decade lower than the peak group of stroke in western countries.[96]

In this study, male patients had more severe stroke compared to female patients. Diabetes mellitus and systemic hypertension were the most common risk factors observed in the study. Around 42 patients had good outcome in this study and only 5 patients had poor outcome. The patients with poor outcomes had a mean volume of infarct of around 26.51 and those with good outcome had a mean volume of infarct of around 5.59. Eventhoughthere was significant correlation between volume of infarct and mRS score at 1 week there was no significant correlation between them at 3 months. Earlier studies showed that increasing age was associated with increased hospital stay and poor outcome. This study was contrary to the above reports. All the patients above 65 years at 3 months had mRS score<3.

STUDY	NO OF PATIENTS	MEAN ALBUMIN	P VALUE
Reeta et al[100]	100	3.73	Significant
Idicula et al[98]	444	3.76	<0.05
Dziedzic et al[97]	759	3.55	<0.01
Gaurav et al[99]	50	3.81	<0.001
Present study	50	3.85	0.894

In 2004 Dziedzic et al conducted a study in Poland. Around 759 patients with ischemic stroke were taken up for study. Using modified Rankin Scale outcome was measured 3 months post stroke. Serum albumin levels were compared with functional outcome at third month. This study reported that those patients with poor outcome had a lower serum albumin levels compared to those with non poor outcome. The study by Idicula et al observed that Ischemic stroke patients with high serum albumin had better outcome and low mortality. This study also showed that there is significant association between serum albumin and age. Hardly few studies have been done in India comparing serum albumin levels and functional outcome. To the best of our knowledge we could find only two studies regarding the same in India. Both studies compared serum albumin levels with short term functional outcome in ischemic stroke patients. Reeta et al conducted a study in Kerala. 100 patients were included in the study. This study concluded that serum albumin has an influence in stroke severity and outcome. The other Indian study was conducted by Gaurav et al in Jodhpur. 50 patients were included in the study. This also found a significant association between serum albumin levels and short

term functional outcome. These two studies didn't compare serum albumin levels with functional outcome at third month. Most western studies and Indian studies didn't take volume of infarct into account which also plays a significant role in the outcome. A study by Mallemoggala et al has found that patients with low albumin levels had high incidence of recurrence.

In this study, most patients with a good outcome had lower NIHSS score,low mRS score,high albumin and low volume of infarct. Those with worst outcome had higher NIHSS, high mRS,high volume of infarct and high albumin. The one patient with low serum albumin also had a good outcome in 3 months. As opposed to study by Idicula et al this study didn't show any association between serum albumin and age. Thus not only serum albumin but volume of infarct also plays a role in the final outcome of the patient - this was not considered in other studies .Those who had poor outcome had a mean volume of infarct of around 25 cc and also there was stastistical significance between volume of infarct and mRS at 1 week. Eventhough clinically most of the patients had good outcome after 3 months based on mRSscore, statistically p value was not significant. Hence this study is contrary to the evidence that serum albumin is a long term predictor of ischemic stroke outcome. The disadvantage of this study was that of sample size which was low compared to other western studies and the number of people with low albumin levels were low.

Albumin has a wide range of intravascular effects. It reduces hematocrit level and also plays a vital role in aggregation of erythrocytes by increasing low shear viscosity and decreasingerythrocyte sedimentation under no-flow conditions. Albumin has a good antioxidant property. Other neuroprotective effect of albumin in stroke includes

A) Prevention of thrombosis and
B) Prevention of leukocyte adhesion within postcapillary microcirculation in the early reperfusion phase.

Albumin captures the oxygen free radicals and slows the production of reactive hydroxyl radical species. Albumin has a peculiar property of binding to copper ions by doing so it inhibits the process of copper ion dependent lipid peroxidation at cell membrane. It has also been postulated that albumin exerts neuroprotection by binding to lysophosphatidylcholine. Free lysophosphatidylcholine increases leukocyte adhesion molecules which leads to inflammatory mediated damage on vascular endothelium. It also causes apoptosis when it is present in high concentration. Based on the above properties it was postulated that albumin infusion post ischemic stroke may be beneficial in long term outcome.

Research studies in rats done by Belayev et al. showed that functional outcome, volume of infarct and brain edema had a significant improvement after high-dose human albumin therapy, when administered within 2 to 4 hours after onset of stroke. Based on all the evidences human trial known as ALIAS (AlbuminIn Acute Ischemic Stroke) was conducted. Dosage of albumin (Intravenous 25%) used in this trial was 2g/kg. There was

no significant outcome after 90 days. High incidence of intracerebral haemorrhage and pulmonary edema were noted[100]. Further research is required to come to a definite conclusion that human albumin infusion can improve the clinical outcome of stroke patients.

CONCLUSION

Stroke being a major health concern in developing countries it is high time we get a suitable predictor for its outcome.Diabetes and systemic hypertension were the most common risk factors associated.This study indicates that higher levels of serum albumin is**NOT** a predictor of ischemic stroke outcome .It is contrary to the literature already present. Further larger studies are required to come to ascertain the facts and its implications for therapy.

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PROFORMA

- Name
- Age
- Sex
- Address
- Occupation
- Chief complaints
- H/o cocaine abuse or any other substance abuse or use of oral contraceptives
- H/o smoking, alcohol, diabetes, hypertension, seizure disorder, bleeding disorders, migraine, thrombosis, rheumatic heart disease, ischaemic heart disease, severe LV dysfunction, arrhythmias (mainly atrial fibrillation)
- H/o head trauma
- Family history of thrombosis, hyperlipidaemia, hypertension, diabetes

CLINICAL EXAMINATION

- General examination
- CNS examination:
  - Speech – dysarthria or aphasia (motor / sensory/ global)
  - Cranial nerves
  - Weakness of limb
  - Power – UL and LL
  - Sensory
  - Cerebellar
  - Carotid and subclavian bruits, murmurs
  - Peripheral pulses
  - NIHSS on admission
  - mRS after 1 week and after 3 months

- Routine investigations:
  - Complete blood count, Diabetic profile
  - Serum albumin, electrolytes, urine routine and microscopy
  - ECG, ECHO, serum homocysteine levels

CT- brain plain, MRI brain with angiography

ABBREVIATIONS

AIS – Arterial ischemic stroke

WHO - World Health Organization

TOAST - Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.

ANA – Anti nuclear antibody profile

APLA – Anti-phospholipid antibody

CT – Computed tomography

MRI – Magnetic resonance imaging

NIHSS - National Institute of Health stroke scale

mRS – modified rankin scoring

TIA - Transient ischemic attacks

LDL-C - low-density lipoprotein cholesterol

TGL - Triglycerides

HDL-C - High-density lipoprotein cholesterol (HDL-C)

BMI – Body mass index

SBP – Systolic blood pressure

DBP – Diastolic blood pressure

FBS - fasting blood glucose

HbA1c - glycosylated haemoglobin

DM – Diabetes mellitus

MA – Migraine headache with aura

RHD - Rheumatic heart disease

DCM - Dilated cardiomyopathy

AMI – Acute myocardial infarction

IE – Infective endocarditis

AF – Atrial Fibrillation

CAD – Coronary artery disease

LVH – Left ventricular hypertrophy

LAE – Left atrial enlargement

PV – Polycthemiavera

ET - Essential thrombocythemia

PAN – Polyarteritisnodosa

WG – Wegener’s granulomatosis

CNS - Central nervous system

CADASIL – Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy

CARASIL – Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy

MELAs – Mitochondrial myopathy, encephalopathy, lacto-acidosis and stroke

EDS – Ehlers Danlos syndromes

OI – Osteogenenis imperfect

ADPKD - Autosomal dominant polycystic kidney disease (ADPKD)

LDS - Loeyz Dietz syndrome

AD – Autosomal dominant

COW – Circle of willis

ACA – Anterior cerebral artery

MCA – Middle cerebral artery

PCA – Posterior cerebral artery

UMN – Upper motor neuron type

ED – emergency department

HIV – human immunodeficiency virus

ECG – Electrocardiogram

ECHO – Echocardiography

AHA/ASA – American heart association / American stroke association

r-tPA – Recombinant tissue plasminogen activator

NINDS – National institute of Neurological Disorders and Stroke

aPTT – Activated partial thromboplastin time

INR – International normalised ratio

PT – Prothrombin time

UFH – Unfractionated heparin

LMWH – Low molecular weight heparin

PSG Institute of Medical Science and Research, Coimbatore

Institutional Human Ethics Committee

INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

I Dr. JOEL FRANKLIN F am carrying out a study on the topic:SERUM ALBUMIN LEVEL AS A PREDICTOR OF ISCHEMIC STROKE OUTCOME as part of our research project being carried out under the aegis of the Department of General Medicine.

My research guide is: Dr. SUJAYA MENON

The justification for this study is: Cerebrovascular diseases include some of the most common and devastating disorders:Ischemic stroke and haemorrhagic stroke.Stroke is the second leading cause of death worldwide.So if there is a suitable predictor for ischemic stroke outcome it will enable us to monitor the patients closely and also can be applied it for therapeutic intervention as in the case of albumin.

Location: PSG Hospitals

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out: Clinical examination on admission and serum albumin levels will be taken within 36 hours.mRS scale will be done one week and 3 months later.

Data collected will be stored for a period of three years. We will not use the data as part of another study.

INITIAL INTERVIEW: Approximately 15 minutes

Clinical examination will be done to asses other clinical findings

Risks involved by participating in this study: Blood prick for collecting sample

How the **results** will be used: The results of the study will be submitted to THE TAMILNADU DR MGR MEDICAL UNIVERSITY as a part of thesis programme in post graduate course of general medicine

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new

findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Contact number of PI: 9894927206

Contact number of Ethics Committee Office: 0422 2570170 Extn.: 5818

LIST OF FIGURES

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MASTER CHART

S.No	SEX	AGE	CHIEF COMPLAINTS	COMORBID CONDITIONS	DIAGNOSIS	VOLUME OF INFARCT IN CT SCAN	NIHSS SCORE	SERUM ALBUMIN LEVEL	MRS AFT 1 WEEK	MRS AFTER 3 MONTHS	MRS AFT 3 MONTHS
1	M	56	DIFFICULTY IN USING OF RT UL & LL, SLUURING OF SPEECH	RHD, MVR, AF+CVR, MOD.LVD	RT HEMIPLEGIA+ MOTOR APHASIA	39	13	3.9	4	3	3
2	M	62	GIDDINESS,SWAYING WHILE WALKING,SLURING OF SPEECH.	NO COMBID CONDITION	POSTERIOR CIRCULATION STROKE	7.4	3	4.3	4	2	2
3	M	40	WEAKNESS IN LEFT UPPER AND LOWER LIMBS	T2DM,SHTN,ALCOHLIC,DLP.	LEFT HEMIPLEGIA	25.17	8	4.6	4	2	3
4	M	80	DIFFICULITY IN USING RIGHT UPPER AND LOWER LIMBS	T2DM,SHTN,CAD,MILD LVD.	CVA WITH RIGHT HEMIPARESIS	2.3	6	4	3	2	1
5	M	58	DIFFICULITY IN USING RIGHT UPPER LIMBS	HTN,,ALCOHOLIC,DLP	CVA WITH RIGHT MONOPARESIS.	7.5	5	4.4	1	3	1
6	M	53	WEAKNESS IN RIGHTUPPER AND LOWER LIMBS	DM,SHT	CVA WITH RIGHT HEMIPLEGIA	50.18	12	3.9	4	2	3
7	M	49	DIFFICULITY IN USING RIGHT UPPER AND LOWER LIMBS,DIFFICULITY IN SPPEC	DM,DLP.	CVA WITH RIGHT HEMIPLEGIA.	45.36	13	3.1	4	3	3
8	M	65	DIFFICULITY IN USING LEFT UPPER AND LOWER LIMBS.	HTN,IHD	CVA WITH LEFT HEMIPLEGIA	29	10	4.3	1	0	0
9	F	47	DIFFICULITY IN USING RIGHT UPPER AND LOWER LIMBS.SLURRING OF SPEECH HTN	HTN	CVA WITH RIGHT HEMIPLEGIA.	1.72	8	4.3	3	1	1
10	M	32	DIFFCULITY IN USING LEFT UPPER AND LOWER LIMBS,FASCIAL PALSY	SMOKER,ALCHOLIC	CVA WITH LEFT HEMIPLEGIA	0.88	10	4.1	4	3	3
11	M	27	DIFFICULITY IN USING RIGHT UPPER AND LOWER LIMBS	SMOKER,ALCHOLIC	YOUNG STROKE	8.76	9	4.6	3	3	3
12	M	42	DIFFICULITY IN USING RIGHT UPPER AND LOWER LIMBS	SHT,CVD	CVA WITH RIGHT HEMIPARESIS	0.3	7	4.1	3	2	2
13	M	44	DIFFICULITY IN USING RIGHT UPPER AND LOWER LIMB	NO COMBID CONDITION	CVA WITH RIGHT HEMIPARESIS	1.42	10	4.6	3	2	1
14	M	72	WEAKNESS IN RIGHT UPPER AND LOWR LIMBS.	SHT,ALCOHOLIC,SMOKER	CVA WITH LEFT HEMIPARESIS	1.98	7	4.6	3	0	2
15	M	45	WEAKNESS IN LEFT UPPER AND LOWER LIMBS,SLURRING OF	OLD CVA,,SHT,DLP,SMOKING,SPEECH,FASCIAL PALSY	RECURRENT CVA	1.57	10	4.4	5	3	5
16	M	58	WEAKNESS IN RIGHT UPPER AND LOWER LIMBS,SLURRINGOF SPEECH,FACIAL PALSY.	HT,IHD,		52.54	8	4.1	3	2	2
17	M	48	MILD FASCIAL PARESIS,SWAYING IN ONE LIMB,	HT,IHD,DM,EX SMOKER& ALCOHOLIC		1.26	3	3.5	0		0
18	M	54	DROWSINESS,		DECLARED	5.06	30	3.8	DECLARED		
19	M	75	WEAKNESS IN RIGHT UPPER AND LOWER LIMB	SHT,DM,DLP	POSTERIOR CIRCULATION STROKE.	0.2	7	4.3	1		0
20	M	55	WEAKNESS IN LEFT UPPER LIMB	DM,SHT,	CVA WITH LEFT HEMIPARESIS	2.03	1	4.3	1		0
21	M	55	WEAKNESS IN LEFT UPPER AND LOWER LIMB	NO COMBID CONDITION	ACUTE INFRACT IN RT FRONTAL BONE	1.08	10	4.2	3		2
22	M	62	SWAYING WHILE WALKING,SLUURING OF SPEECH.	SHT,DLP.SMOKER	ACUTE INFRACT INRT CEREBELLAR REGION	30.89	3	4.1	1		1
23	M	65	WEAKNESS IN LEFT UPPER AND LOWER LIMB	NO COMBID CONDITION	ACUTE INFRACT IN RT MCA TERRITORY.	0.52	2	4.1	1		1
24	M	60	SWAYING WHILE WALKING	SHT,TOBACCO CHEWER	ACUTE INFRACT LEFT MEDULLARY INFARCT	0.24	4	4.2	1		1
25	M	50	WEAKNES RIGHT IN UPPER LIMB	SHT/DM	RIGHT UPPER LIMB MONOPARESIS.	0.45	4	3.6	1		1
26	F	64	ATAXIA,	TOBACCO CHEWER	LEFT CEREBELLAR INFARCT		4	3.8	LOST FOLLOW UP		LOST TO FOLLOW UP
27	F	70	WEAKNESS IN B/L LIMBS	NO COMBID CONDITION	ACUTE INFRACT LEFT INTERNAL CAPSULE A	0.11	13	4.4	1		0
28	M	51	WEAKNESS IN RIGHT UPPER AND LOWR LIMB,FACIAL PALSY	TYPE 2 DM	CVA WITH RIGHT HEMIPLEGIA	0.66	11	4	0		0
29	F	70	FACIAL PALSY,LIMBATAXIA,DYSARTHRIA	SYSTOLIC HT,	CEREBELLAR STROKE	0.67	3	4	1		0
30	M	66	FACIAL PALSY,WEAKNESS IN RIGHT UPPER AND LOWER LIMB	NO COMBID CONDITION	CVA WITH RIGHT HEMIPARESIS	0.58	5	4.1	3		1
31	M	60	FACIAL PALSY,LIMBATAXIA	HTN,SMOKER,ALCOHLIC	INFRACT IN RIGHT OCCIPITAL AND RIGHT CI	0.9	2	5	0		0
32	M	50	FACIAL PALSY,LIMB ATAXIA,DYSARTHRIA	SHT,	LEFT ATAXIC HEMIPARESIS	0.271	3	4.3	1		1
33	M	60	FACIAL PALSY ,WEAKNESS IN LT UL AND LL ,DYSARTHRIA	SHT,T2DM,SMOKER	RT CAPSULOGANGLIONIC INFRACT	0.52	6	3.6	3		2
34	M	50	SLURRING OF SPEECH,GIDDINESS AND UNRESPONSIVENESS	HT ON IRRX	BRAIN DEAD	NOT ABLE TO ASSESS	30	4.5			BRAIN DEAD
35	M	70	FACIAL PALSY AND DYSARTHRIA	T2DM,SHT,DLP,TIA	CVA RT THALAMIC INFRACT	0.163	2	4.2	1		0

S.No	SEX	AGE	CHIEF COMPLAINTS	COMORBID CONDITIONS	DIAGNOSIS	VOLUME OF INFARCT IN CT SCAN	NIHSS SCORE	SERUM ALBUMIN LEVEL	MRS AFT 1 WEEK	MRS AFTER 3 MONTHS	MRS AFT 3 MONTHS
36	M	49	FACIAL PALSY ,WEAKNESS IN RT UL AND LL,	SHT,IHT,POST CABG,DLP	SEVERE RT HEMIPARESIS	0.9	6	4.7	3		2
37	M	73	POSTERIOR CIRCULATION STROKE	SHT,DM,DLP	POSTERIOR CIRCULATION STROKE	0.11	0	4.1	0		0
38	M	50	FACIAL PALSY,DECREASED SENSATION AND DYSARTHRIA	DM,SHT.ALCOHOLIC,SMOKER,IHT	RT WALLENBURGH SYN,BILATERAL CEREBEL	62.7	3	4.5	4		3
39	M	56	LIMB ATAXIA	SHT,T2DM,ALCOHOLIC	CEREBELLAR STROKE	36.31	2	4	4		3
40	F	65	FACIAL PALSY,DROWSINESS,WEAKNESS IN RT UL AND LL	NONE	CVA WITH RT HEMIPLEGIA	81.6	17	4.7	DECLARED		DECLARED
41	M	75	ATAXIA,DYSARTHRIA	T2DM	ISCHEMIC STOKE IN LT PONTINE	0.2	2	3.8	1		0
42	M	55	DIFFICULITY IN USING BOTH UL &LL.	HT,DM	CVA	1.05	10	3.9	3		2
43	M	71	WEAKNESSIN LEFT UPPER LIMB	SHT,DLP,CAD,TVD,T2DM	CVA WITH RT PARIETAL INFARCT	3.17	2	3.8	1		0
44	M	68	WEAKNESS IN THE LT UL AND LL ,DYSARTHRIA	DLP,OLD CVA	RECURRENT CVA ,PARIETAL INFRACT	0.485	9	4	5		3
45	M	55	DIFFICULITY IN USING LEFT UPPER LIMB AND LOWER LIMB	SMOKER,ALCHOLIC,SHT,CAD,DYSLIPIDEMIA	ACUTE CVA -LEFT MEDULLARY INFRACT.	0.24	4	4.2	1	1	0
46	M	60	WEAKNESS IN THE LT UP AMD LL AND DYSARTHRIA	DLP,SMOKER,ALCOHOLIC	RT MCA INFRACT	15.24	9	4.1	4		4
47	M	72	FACIAL PALSY &DYSARTHRIA	HTN,DM	CVA	27.3	2	4.3	1		1
48	M	44	WEAKNESS IN LEFT UPPER AND LOWER LIMBS	NO COMBID CONDITION	CVA WITH RIGHT HEMIPLEGIA		9	4.3	LOST FOLLOW UP	LOST TO FOLLOW UP	LOST TO FOLLOW UP
49	F	74	DIFFICULITY IN BOTH UPPER AND LOWER LIMBS.FASCIAL PALSYTYPE 2DM HTN, BA,HYPOTHYROID		CVA		10	3.6	OST FOLLOW UP	LOST FOLLOW UP.	LOST TO FOLLOW UP
50	M	60	WEAKNESS IN THE RT UL,DYSARTHRIA,FACIAL PALSY	SHT,IHT,DM,PTCA	CVA RT HEMIPLEGIA	0.3	14	4.4	4		3