A Study Of Association Of Mean Platelet Volume To Severity Of Ischemic Stroke

by

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LIST OF ABBREVIATIONS USED

ADP - Adenosine diphosphate

AGEs - Advanced Glycosylation End Products

AHA - American Heart Association

ANOVA - Analysis of variance

APLA - Antiphospholipid syndrome BT - Bleeding time

b-TG - Beta-thromboglobulin

Ca2+ - Calcium ion

CAD - Coronary artery disease

cAMP - Cyclic adenosine monophosphate

CAT - Computerized axial tomography

cGMP - Cyclic guanosine monophosphate

CHD - Coronary Heart Disease

CI - Confidence interval

CNS - Central nervous system

CT - Computed tomography

Cumm - Cubic millimetre

CVA - Cardiovascular accident

CVD - Cardiovascular disease

DALYs - Disability adjusted life-years

DM - Diabetes mellitus

DNA - Deoxyribonucleic acid

DVT - Deep venous thrombosi

ED - Emergency department

Fig - Figure

fL - Femto liters

FPG - Fasting plasma glucose

gm - Gram

GPE - General physical examination

HbA1c - Glycosylated haemoglobin

HDL - High density lipoprotein

IA - Intraarterial

ICH - Intracerebral hemorrhage

ITP - Idiopathic thrombocytopenic purpura

LAD - Large-artery disease

LDH - Lactate dehydrogenase

LDL - Low density lipoprotein

LOC - Level of consciousness

Mg^{2+} - Magnesium ion

MI - Myocardial infarction

MK - Megakaryocyte

mmol/L - Millimole per litre

MPHA - Megakaryocyte platelet haemostatic axis

MPV - Mean platelet volume

MRI - Magnetic resonance imaging

MRM - Modified Rankin Morbidity score

n - Total number

NIHSS - National Institute of Health stroke scale

OC - Oral contraceptive

OHA's - Oralhypoglycaemic

p	-	Probability
PAD	-	Peripheral Arterial Disease
PGI2	-	Prostacyclin
PKC	-	Protein kinase C
ROS	-	Reactive Oxygen Species
SD	-	Standard deviation
SE	-	Standard error
SCV	-	Small Cerebral Vessels
TIA’s	-	Transientischaemic
TXA2	-	Thromboxane A2
TXB2	-	Thromboxane B2
T2DM	-	Type 2 diabetes mellitus
UK	-	UnitedKingdom
WHO	-	World healthorganisation

ABSTRACT

BACKGROUND:

A Stroke or cerebrovascular accident (CVA) is defined by the abrupt onset of neurological deficit that is attributable to a focal vascular cause.

Because of the rise in the number of ageing population, the burden of stroke is likely to increase automatically in the near future. Mean platelet volume, a marker (and possibly a determinant) of platelet function is a physiological variable of haemostatic importance, as well as platelet count, are an index of haemostasis. Changes in MPV play a more important role in haemostasis than platelet count. very few studies has looked at the association between platelet size and ischaemic stroke

OBJECTIVE:

To assess whether mean platelet volume level is elevated and an independent risk factor in ischemic stroke.

To know the association of mean platelet volume with severity of stroke using modified Rankins score

METHODOLOGY:

All patients above 40 years of age , irrespective of sex with Ischaemic stroke identified based on clinical features and Radiological evaluation ie Magnetic Resonance Imaging of Brain admitted in _____ _____ Mean platelet volume on admission was documented & severity of stroke at the presentation was assessed using Modified Rankins scale.

RESULTS

Out of hundred patients 61% were males and 39% were females. 39% of the study patients were aged between 40-60 years and 38% were aged between 60-80

years. The co morbid conditions present were hypertension in 44% and diabetes mellitus in 20% followed by Chronic obstructive pulmonary disease and Ischemic heart disease . The clinical severity of stroke at presentation was determined by the Modified Rankin‘s score and severe disability was seen with 53% of the cases. There was no significant disability in 1% of the cases. In our study MPV has got no statistically significant correlation with ischemic stroke with a p value of 0.989.

CONCLUSION

This study did not find a statistically significant correlation between clinical severity of stroke and mean platelet volume.

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INTRODUCTION

Stroke is one of the common causes of morbidity and mortality. It is associated with increased long term mortality, Stroke is the most common cause of death after cardiac disease and cancer. They cause around 200,000 deaths in United States and 334-424/ 100,100 deaths each year in India and a major cause of disability. About 15% to 25% of stroke survivors become disabled permanently, while 20% remain in institutional care for three months after their stroke. The incidence of stroke increases with age and the number of strokes is projected to increase as the elderly population grows, with a doubling in stroke deaths in the India by 2030[1].It ranked as the sixth leading cause of disability-adjusted years (DALY; one DALY is one of the lost year of healthy life) in 1990 and is projected to rank fourth by the year 2020[2]. Because of the rise in the number of ageing population, the burden of stroke is likely to increase automatically in the near future. Most patients with stroke manifest by the abrupt onset of a focal neurologic deficit which results in residual physical, cognitive, and behavioral impairments.

MEAN PLATELET VOLUME (MPV), a marker (and possibly a determinant) of platelet function is a physiological variable of haemostatic importance [3.]Large platelets are more reactive, produce more prothrombotic factors and aggregate more easily in response to agonists such as ADP (adenosine diphosphate) and collagen.[4,5,6] They also contain more dense granules and release more serotonin and beta thromboglobulin than do small platelets [7] Mean platelet volume, as well as platelet count, are an index of haemostasis. Changes in MPV play a more important role in haemostasis than platelet count .Platelet volume is regulated by various intrinsic and extrinsic factors. The mean lifespan of light platelets is shorter than that of heavy platelets [8]. Perturbed megakaryocyte platelet haemostatic axis (MPHA),

results in the formation of hyper-functional platelets, which may contribute to the development of vascular disease or an acute thrombotic event such as ischemic stroke[9]. Increase in platelet volume has been reported as a risk factor for acute cerebral ischemia,[10,11] transient ischemic attacks. Higher levels of MPV in patients with acute ischemic stroke have been demonstrated than in control subjects [12] The severity and poor outcome of ischemic stroke patients with increased MPV has been reported in the literature [13,14,15]. Ischemic stroke patients with higher MPV tend to have poor outcome than their counterparts with low MPV . Mean platelet volume has been identified as an independent predictor of the risk of stroke.

Though there have been quite a few studies which have demonstrated an association between myocardial infarction and platelet size, very few studies has looked at the association between platelet size and ischaemic stroke. There are no documented studies in India comparing the association of mean Platelet volume with ischemic stroke among middle aged and elderly patients; hence an attempt has been made to study the association if any between mean platelet volume and stroke in an Indian population.

OBJECTIVE OF THE STUDY

1. To assess whether mean platelet volume level is elevated and an independent risk factor in ischemic stroke.
2. To know the association of mean platelet volume with severity of stroke using modified Rankins score.

REVIEW OF LECTURE

Definitions (WHO)-

1. ”Stroke is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause”.
2. Transient ischemic attack (TIA)- The neurological signs and symptoms last more than 24 hours without evidence of brain infarction on brain imaging.”
3. “Reversible ischemic neurologic deficit (RIND) – is a type of stroke due to occlusion of blood supply to brain leading to ischemia and neurological deficits which recover from 24 hours and upto few weeks .”
4. Stroke in evolution -is an evolving stroke is one in which neurological deficits appear to worsen over a given period after the initial stroke occurs, with or without the presence of appropriate medical intervention.”[16]

HISTORICAL BACKGROUND

The first concept of stroke was noted from 460 to 370 before the Common Era by Hippocrates.. Over the next several hundred years, scholars worked upon subjects and focused on physical symptoms and signs and their potential causes. At this time, the symptoms of convulsions and paralysis were referred to as apoplexy.

The historical events that took place are as follows –

1. The term “Apoplexy” can be followed from Antiquity ,passing through the middle ages and renaissance .The definition was stated by Hippocrates who took the word “Apoplexy” where it meant **“**Astonished**,** Suddenly benefit of one’s senses**”**
2. Jacob Werter, first person who was swiss physician to suggest that apoplexy was caused by disease of blood vessel in the brain.
3. Thomas Willis described the circle of wills in 1664.

4. Seddicot described spontaneous intracerebral haemorrhage in 1813.
5. Abberonbie, In 1828 described the arterial diseases of brain.
6. Johan Friedrich crell, 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 1860, Rudolf Virchow described imbibition theory that states there was deposition of blood constituents on the laminal surface of the arterial wall during the formation and growth of atheromatous plaques. He considered that the early lesions of atherosclerosis were based on a “loosening” of the connective tissue ground substance of the intima as a result of “imbibition” of constituents of the passing blood.
9. Von Rokitansky and the thrombogenic theory described the atheromatous deposition is by far the most frequent disease of the arteries and embodies the foundation of aneurysm formation and of many spontaneous arterial obliterations.
10. Virchow’s concept of atherogenesis was that, all the structural changes were initiated by an invading stream of plasma. This is the origin of the so called “infiltrative” theory of atherosclerosis which certainly, in so far as lipid accumulation is concerned, appears even now to have much truth in it.
11. Vogel in 1847 and Chalatow in 1913 observed that atherosclerotic plaques contained relatively large amounts of cholesterol.
12. In 1825, Bonillord described localisation of lesion and aphasia.
13. In 1860, Von Graafe used Helmoltz ophthalmoscope.

14. In 1895, Hamrich Quinn introduced the technique of lumbar puncture which is so vital in the diagnosis of neurological illness.
15. 1877 Osler reported a case of Subarachnoid and intracerebral haemorrhage due to ruptured aneurysm.
16. In 1914, Ramasay hunt described for the first time the comprehensive description of spontaneous carotid occlusion without CREST Trial (Carotid revascularization endarterectomy versus stenting trial) of the intracranial vessel producing cerebral infarction.
17. Dandy performed the first air ventriculogram.
18. Denny brown introduced the concept of vascular insufficiency.
19. Drugs like aspirin which was platelet antiaggregating was used in 1971 for TIA's by Karim in 1978.
20. Dr. God Frey Hounsfield, a British physicist in 1972 introduced computerized axial tomography (CAT) technique into neuro radiology which resulted in award of noble prize in 1979. This lead to more precise categorization of ischaemic and hemorrhagic cerebrovascular accident.
21. The first Magnetic resonance imaging (MRI) was recognized for his innovation and construction of full body scanning by Raymond Damadian .in 1971, but Nobel prize was awarded to Sir Paul Lauterbur in 2003 on first MRI.

The term apoplexy has faded, and the term stroke has become common place in the medical setting.[17]

Prevalence

Worldwide

Trials at International level show that rates grow exponentially with age, from 0.3% in the third and fourth decade of life, all the way to 30% in the eighth and ninth decade of life, which makes an average of 1–2%. It is estimated that approximately 4 million people suffer from stroke annually worldwide. Out of which , approximately 570,000 cases occur in Europe and approximately 500,000 in United States of America. Evidence shown by the recent data that the incidence of stroke in France is 114 cases per 100,000 persons per year, in Germany 350, in Italy 223, in Spain 141–220, and in UK 161[3] and in India it is 843 per 10000 population .[18]

Although rates of stroke mortality and burden vary greatly among countries, low-income countries are the most severely affected. There has been a 42% decrease in stroke incidence in high-income countries and >100% increase in low- to middle income countries.

Morbidity and Mortality [19]

It is estimated that around 400-800 strokes per 100,000 with 5.7 million Deaths. And 16 million new acute strokes every year with 28,500,000 DALYs (disability adjusted life-year). Several research have found out that 28-30 day case fatality ranges from 17%-35%.

Stroke in India[19]

With high stroke burden, in INDIA though significant advancements in treatment have been made there needs an in-depth study of genetic and epidemiological factors to understand the root of the problem.Notably, while communicable diseases continue to pose intermittent challenges to the country's health care infrastructure with seasonable epidemics, cases of non-communicable

diseases are mounting and constitute a much higher disease burden than communicable diseases.

The expected prevalence rate of stroke in India has recorded, in distinct studies, age-standardised prevalence rate of 145 and 154 per 1,00,000 per year. An intriguing finding rising from stroke occurrence studies in our world is that Indians are greater vulnerable to stroke than their Western counterparts.

This calls for powerful organisation of stroke care in multi-disciplinary stroke care units (SCU) in which patients are handled by coordinated efforts of medical doctors, nurses, physiotherapists and other healthcare employees as required.[20]

Morbidity and Mortality [21]

In INDIA , it is estimated that the Prevalence rate of 90-222 per 100,000, with 102,620 million deaths and 6,398,000 Disability adjusted life year which quantifies the burden of disease from mortality and morbidity. Out of which 12% of strokes occur in the population aged <40 years and studies have shown that 28-30 day case fatality ranges from 18-41%.

Classification of stroke[22]

Broadly, strokes are classified as either hemorrhagic or ischemic. Acute ischemic stroke refers to stroke caused by thrombosis or embolism and is more common than hemorrhagic stroke. There are many classifications according to etiology vascular territory and by time course[23].

1. Classification by time course:

a) Transient ischaemic attack.

b) Reversible ischaemic neurological deficit.

c) Stroke in evolution.

d) Completed stroke.

2. By arterial territory:

(As shown in figure 1)

a) Internal carotid artery territory.

b) Vertebrobasilar territory.(as shown in figure 2)

c) Lenticulo-striate branches.

d) Middle cerebral artery territory

e) Anterior cerebral artery territory.

3. By underlying pathology:

(As shown in figure 3)

a. Atheromatous occlusion of vessels anywhere in circuit leading hemorrhagic or ischemic stroke

b. Atheroembolism.

c. Lipohylinoid necrosis.

d. Charcot Bouchard aneurysm rupture.

4. According to the cause

a) Atherosclerosis.

b) Embolism of cardiac origin.

c) Vasculitis: Polyarteritis nodosa, Collagen Vascular Disease, temporal arteritis

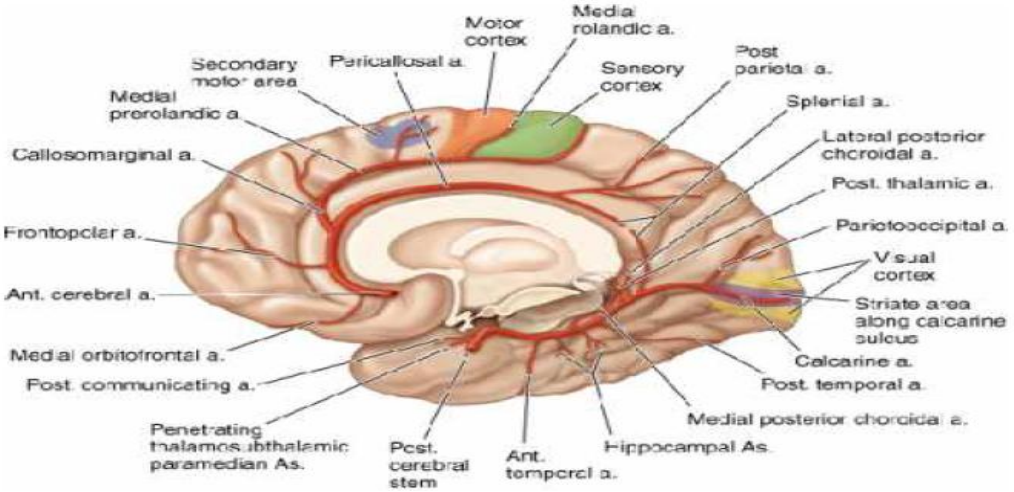
d) Hematological Disorders: Hemoglobinopathies, hyperviscosity syndrome,hypercoagulability states, protein C and S deficiency, AntiPhospholipid Antibody syndrome.

e) Drugs: Cocaine, alcohol, amphetamines, Oral Contraceptive pills.

f) Others: MoyaMoya disease , migraine, fibromuscular dysplasia.

g) Cerebral Venous Thrombosis.

Figure1. Cerebral hemisphere showing medial aspect – Branches of Anterior cerebral artery



Courtesy Harrison principles of internal medicine

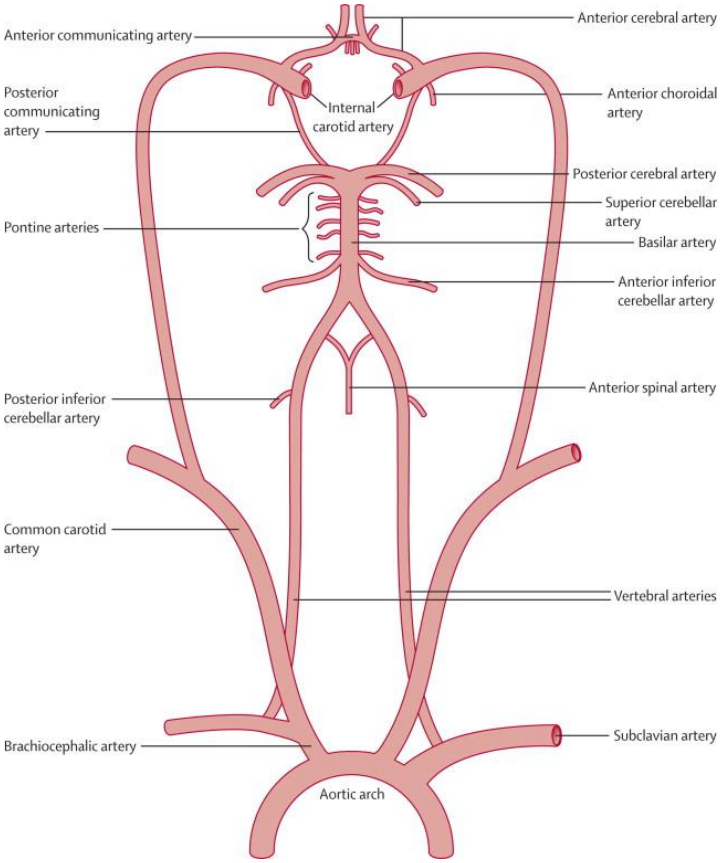
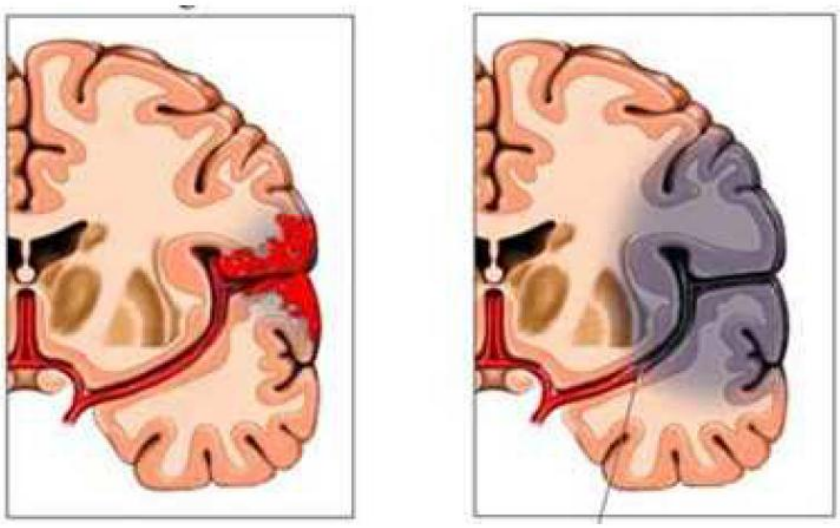


Figure 2. Circle of Willis /Vertibrobasilar system

Figure 3 Pathology haemorrhagic and ischaemic stroke

(courtesy Harrison principles of internal medicine**)**



ISCHEMIC STROKE

Occlusion cerebral pathology is because of embolism of a clot within the cerebral arteries coming back from different elements of the blood vessel system, as an example, from viscus lesions, either at the location of the valves or of the center viscus cavities, or because of rhythm disturbances with stasis of the blood, that permits action among the center as seen in arrhythmia.

Lacunar cerebral infarctions are tiny deep infarcts within the territory of small penetrating arteries, because of an area un wellness of those vessels, in the main associated with chronic high blood pressure. many different causes of cerebral infarct exist and are of great sensible importance for patient management.

In India frequency of cerebrovascular accident is between sixty to eighty percent[24,25,26]. Further, lacunar giant vessel and cardioembolic varieties occur at 18% , 40%, 10% severally whereas different determined and undetermined varieties occur in 10% and 20% respectively.

Etiology[27]

As blood flow decreases, neurons stop functioning, and irreversible neuronal ischemia and damage begin at blood flow rates of much less than 18 mL/100 g of tissue/min. Ischemic strokes result from occasions that restrict or prevent blood go with the flow, along with extracranial or intracranial thrombo-embolism, thrombosis in situ, or relative hypoperfusion.

Pathophysiology

Ischemic stroke may be a complicated entity with multiple etiologies and variable clinical manifestations. about 45% of ischemic strokes are caused by little or giant artery thrombus, 20% are clot in origin, and others have an unknown cause **.**When an ischemia happens, the blood supply to the brain is interrupted,and brain cells are bereft of the glucose and oxygen they have to operate**.**During an embolic stroke, a clot travels from a far off supply and resorts in cerebral vessels.

As thrombosis or emboli cause a decrease in blood provide to the braintissue, occasions arise at the cell stage, referred to due to the fact the ischaemic cascade. Neurons and support cells need a careful balance of variables like temperature, pH,nutrients, and waste elimination in their placing to carry out optimally. extensive fundamental clinical studies over the last a long time has given health care professionals an extended understanding of the ischemic cascade in the format of the best environmental adjustments worried within the pathophysiology of ischemic damage on the cell stage . often, there may be a middle vicinity of vain cells encircled by a place of hypoperfused tissue. The hypoperfused place can also be rescued;this location is called the penumbra location.[28,29]((As proven in figure 4)

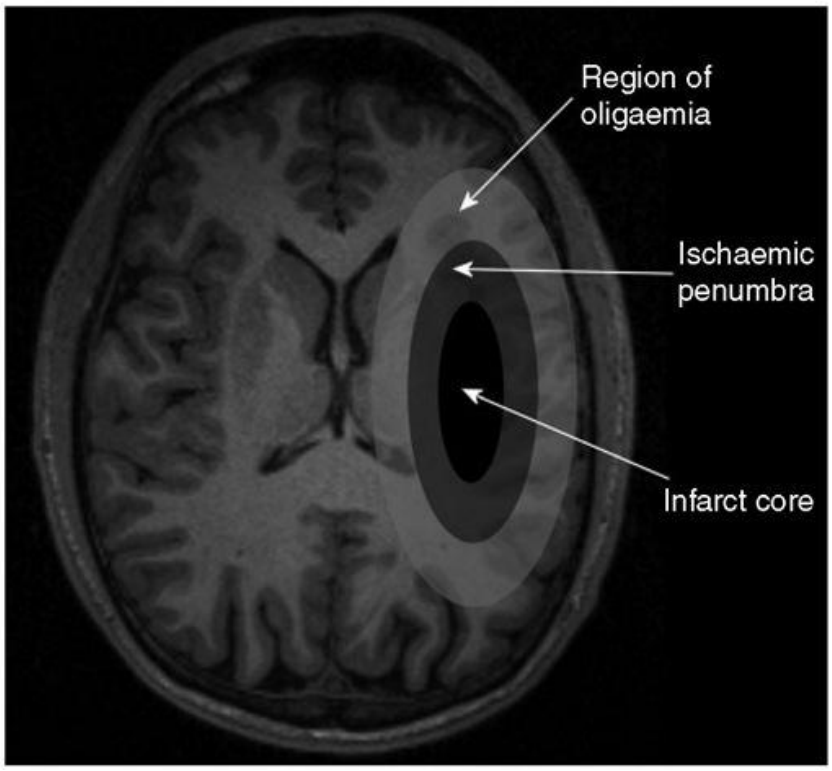


Fig 4 penumbra[30]

Risk factors for stroke in older people [31]

Sex

Atrial fibrillation

Ischemic heart disease

Heart failure

Carotid stenosis

Hypertension

Hypertriglyceridemia

Pathophysiologic changes[32]

Cardiovascular changes

In disease-free older people aging has no or little effect on cardiac function. In the West, however, over 50% of people over 50 years of age who have died have shown evidence of ischemic vascular disease. The presence of atherosclerosis in one region of the vasculature is associated with an increased prevalence of similar changes in other organs. Also, most patients with stroke have some degree of coronary atherosclerosis.

In the absence of coronary artery disease the cardiac muscle in the aging heart maintains its ability to develop tension, but cardiac responses decrease strikingly with age. This decreased responsiveness is manifested by a reduced inotropic response, arterial vasodilating response and heart rate.

Arrhythmia:

There is a progressive loss of conduction tissue cells and pacemaker function with aging.This predisposes to sinus node dysfunction and abnormal conduction in the atrioventricular node and bundle-branch fibres. In addition, the frequency of supraventricular arrhythmia has been found to be increased among elderly people.These changes may be present without associated ischemicheart disease.The detection of cardiac arrhythmia has improved with the increased availability of 24-hourHolter monitoring. Cardiac arrhythmia, especially atrial fibrillation, is a common cause of cardioembolic stroke.Also, elderly stroke patients with atrial fibrillation have been found to have a poorprognosis.

Valvular heart dysfunction:

The occurrence of primary degenerative changes in the aortic valve increases with age, and in the elderly such changes lead to calcific aortic stenosis. This sometimes leads to significant compromise within a short time. The impact of these valvular changes on cardioembolic stroke may contribute to its rising incidence with age.

Hypertension

Like cardiac tissue peripheral vasculature becomes increasingly stiff with age and less responsive to stimulation. The resultant increase in bloodpressure, especially systolic, has been found to peak among patients 75 to 84 years of age. In the Framingham study 57% of the men and 65% of the women with hypertension who were 66 to 89 years of age had isolated systolic hypertension (systolic pressure greater than 160 mm Hg and diastolic pressure less than 90 to 95 mm Hg). Isolated systolic hypertension has recently become recognized as an important risk factor for both cardiovascular and cerebrovascular disease.

Control of hypertension has been an important factor in the decreased incidence of various vascular diseases in the last four to five decades. The treatment of hypertension in elderly patients reduces the incidence of death from cardiac and cerebrovascular diseases.

Overzealous or inappropriate treatment of hypertension often leads to serious complications, and the protective effects of hypertension therapy may not be as obvious in the elderly. Elderly people may be more prone than younger patients to the side effects, including hypotension. Meissner, Whisnant and Garraway[33] conducted a community-based study involving 1680 patients with stroke (mean age72 years), of whom 368 suffered a second stroke during follow-up. The rate of recurrence was

unaffected by the presence of hypertension before the stroke or the subsequent management of the hypertension.

Stroke as a complication of aggressive treatment of hypertension has been reported and appears to be an important problem among elderly patients admitted with acute stroke.

Although evidence is scant the blood pressure should probably be reduced gradually several days after the stroke. In many cases as the stress and sympathetic activity settle down the blood pressure may decrease without any intervention. Acute cerebral ischemic events are frequently associated with blood pressure elevations that tend to settle with time.

Pseudohypertension results from poor contraction of stiff atherosclerotic blood vessels and is frequently seen in the elderly. It should be considered when the blood pressure differs significantly between the two arms, there is no evidence of end-organ damage despite a long history of "poorlycontrolled" hypertension, multiple drugs are ineffective in controlling the blood pressure, and orthostatic problems complicate treatment. It is important to recognize pseudohypertension, because inappropriate treatment may result in dangerous reduction of the cerebral perfusion pressure.

Carotid sinus hypersensitivity

Massage or compression of the carotid sinus in healthy people is frequently associated with slowing of the heart rate and a mild decrease in blood pressure. In some people, especially the elderly, there is marked slowing of the heart rate and severe hypotension; this condition, known as carotid sinus hypersensitivity, can lead to syncope. Diffuse atherosclerosis or other cardiac disease is also common in such patients. The combination of acute slowing of the heart rate and hypotension after

stroke can exacerbate the neurologic deficit. Severe cases that do not respond to preventive measures may require medical therapy with sympathomimetic agents or pacemaker implantation. Before such aggressive measures are taken a cardiologist should evaluate the condition, because not all types of carotid sinus syndromes respond to pacemakers.

Baroreceptor function

One of the main afferent pathways for control of circulatory dynamics originates in mechanoreceptors in the aortic arch and the carotid sinus. As the arterial pressure increases there is increased activation of the nerve fibres arising from these receptors, this results in a decrease in the muscle tone of the blood vessels and in the heart rate. The reverse occurs if the blood pressure suddenly decreases. With aging there is a progressive loss in function of the mechanoreceptors, especially in the aortic arch. A similar decrease in sensitivity also occurs in patients with hypertension.

The mechanism for the lowered sensitivity is not well understood. Some evidence suggests that the decrease may be due to reduced distensibility of the aortic vessel wall at the site of the baroreceptor. There has been autopsy evidence of such decreased distensibility of the carotid sinus. Physicians should realize the clinical importance of the decreased baroreceptor sensitivity when they consider lowering the blood pressure in elderly patients with acute stroke.

Cerebral autoregulation

There is a gradual decrease in the cerebral bloodflow with increasing age. This can be explained as (a) a progressive loss of neurons and (b) a loss of hemodynamic reserve. Failure of cerebral autoregulation can result in symptomatic cerebrovascular ischemic disease. In a study involving 11 elderly patients with postural hypotension Wollner and associates[34] found 7 with relatively minor hypotension who had

symptoms of cerebral ischemia. All seven had altered cerebral autoregulation in the form of cerebral atrophy. In the other four patients the cerebral autoregulation was intact. Patients with acute stroke have been found to have altered cerebral blood flow, the cerebral blood vessels are maximally dilated, and any decrease in blood pressure may then result in serious compromise. This should be kept in mind when hypertensive patients with acute stroke are given medication to lower their blood pressure.

Altered metabolism and drug interactions

Drug pharmacokinetics

Most of the information on the efficacy and adverse effects of medications comes from experiments involving young volunteers. The assumption that the drug will have similar effects in the elderly can be potentially dangerous. Because gastric acidity, gastric emptying, the intestinal absorptive surface ,liver size and blood flow are affected by aging, absorption and elimination of commonly used medications can be particularly unpredictable in the elderly. In addition, drug distribution can be similarly affected, for a variety of reasons, including decreased total body size and lean body mass,increased body fat stores and declining renal function.

With the decrease in the plasma albumin level drugs such as warfarin that are strongly bound to plasma proteins can become increasingly "free and unbound" and cause "over anticoagulation" and potentially serious bleeding. The anticoagulant effect of warfarin has been found to be higher in the elderly than in other age groups. Many such medications, including diazepam, haloperidol and phenytoin, have been shown to slow recovery of function after experimental brain injury.

Altered pharmacodynamics

Pharmacodynamics involves the measurement of the duration and intensity of a drug's effects at a particular concentration. Several age-related changes have been noted in homeostatic mechanisms,including derangement in postural control,thermoregulation, visceral muscle function and orthostatic circulatory responses.These changes are believed to lead to a gradual reduction in homeostatic reserve - in other words a diminished ability to adapt to changing environmental stresses. In terms of pharmacodynamics this means that there is a general decrease in handling the effects of drugs at their target organs.

There is an increase in the corrective responses to standing up as a person grows older. The mechanisms are not well understood but may be related to striatal dysfunction with a reduction in D2 receptors in the basal ganglion. This results in an increased risk of postural instability and falls with the use of sedatives. Epidemiologic data have shown an association between the use of sedatives and an increased incidence of falls in the elderly.Orthostatic circulatory responses are important in maintaining normal blood pressure when a person rises to an upright position. With increasing age such reflexes slow, the result being a postural fall in bloodpressure of over 20 mm Hg in 17% of elderly people and over 40 mm Hg in 5%. These effects become particularly important in those taking drugs to control hypertension. Other medications such as phenothiazines, tricyclic antidepressants, antihistamines and barbiturates that are commonly used in patients with acute stroke can similarly affect orthostatic postural responses.

Elderly people have an increased sensitivity to benzodiazepines. Several studies have shown changes in cognitive function with commonly used compounds such as lorazepam,diazepam, nitrazepam in elderly patients, even though there

appeared to be no differences between the young and elderly patients in the serum levels of the drugs. The mechanism for this age-related difference is not well understood, however, a decrease in central GABA receptors, are distribution in the regional concentration of benzodiazepines in the brain and an alteration in postreceptor function have all been considered.

Angiotensin-converting-enzyme inhibitors are now becoming the drug of choice in the management of hypertension and are frequently prescribed for the elderly. The fall in blood pressure associated with enalapril has been found to be greater in elderly patients than in younger volunteers. The lower rate of elimination of enalaprilat (an active metabolite of enalapril) in the elderly accounts for the greater activity of a given dose.

Adverse drug reactions

However, this maybe the tip of the iceberg, as physicians tend to underreport such complications. Physicians must beware of such problems developing in acutely ill elderly patients with cerebrovascular disease. Risk factors of adverse reactions include female sex, polypharmacy, previous reactions and progressive decrease in cognitive function with increasing dosage .

History and clinical presentation

Assessment of the patient with a stroke begins with recognition of the event as a stroke with detailed history . Assessing the patients general conditions with Glasgow coma score and Disability with help of stroke severity score-Modified rankings score[35].

Essential data to include are a quick history of timing of the event, pertinent past medical history, and risk factors .Careful medical history is crucial to establish the exact time of onset of stroke signs and symptoms..

Symptoms of Ischemic Stroke According to Cerebral Circulation[36,37]

“Brainstem

a. Hemiparesis or quadriparesis
b. Motor or sensory loss in all four limbs
c. Eye movement abnormalities, such as diploplia and dysconjugate gaze
d. Oropharyngeal weakness
e. Vertigo, tinnitus
f. Nausea, vomiting
g. Dysmetria

Cerebellum

a. Ipsilateral limb ataxia
b. Gait ”

“Vetebrobasilar circulation

a. Symptoms correlate with brainstem and cerebellar functions as above
b. Cranial nerve deficits in cranial nerves III – XII

Anterior Circulation Symptoms

a. Carotid artery
b. Contralateral motor and sensory loss
c. Amaurosis fugax or transmonocular blindness (caused by emboli to retinalartery)

Anterior Cerebral Artery

a. Confusion
b. Personality change

c. Incontinence

d. Contralateral motor or sensory loss in leg greater than arm”

Middle Cerebral Artery

a. “Contralateral motor or sensory loss (arm greater than leg)

b. Contralateral motor loss in lower face

c. Contralateral visual field loss

d. Language deficit (dominant hemisphere)

e. Spatial-perceptual deficit (nondominant hemisphere)”

”Posterior Cerebral Artery

a. Contralateral sensory loss

b. Ipsilateral visual field deficit

c. Cortical blindness”

“Conditions that Mimic Ischemic Stroke

a. Unrecognised seizures

b. Coma like state

c. Syncope

d. Poisonous or metabolic disorders

e. Hypoglycaemia

f. Drug overdose

g. Hyponatraemia

Diagnosis[39]

The diagnostic tests are available in most Emergency Departments (ED)over twenty hours a day. A computed tomography (CT)scan without contrast (example shown in figure 5) is recommended to rule out the presence of a

hemorrhagic stroke . Additional studies may include CT angiogram, cerebral angiography ,magnetic resonance imaging (MRI),(as shown in figure 6)and. A CTangiogram can be used to identify large vessel stenosis or occlusion. MRI permits for better visualization of viable infarcted areas, and angiography is used whilst intraarterial (IA) thrombolysis is indicated or when surgical interventions are being considered.[40]

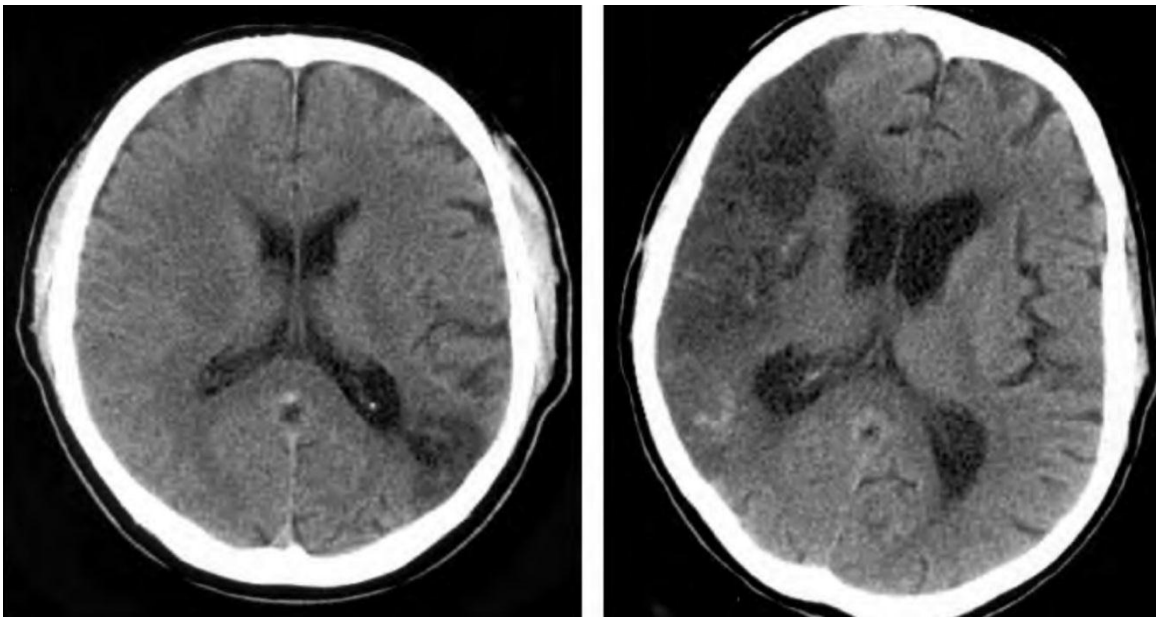


Figure 5 CT brain hypodense area in right fronto parietal area

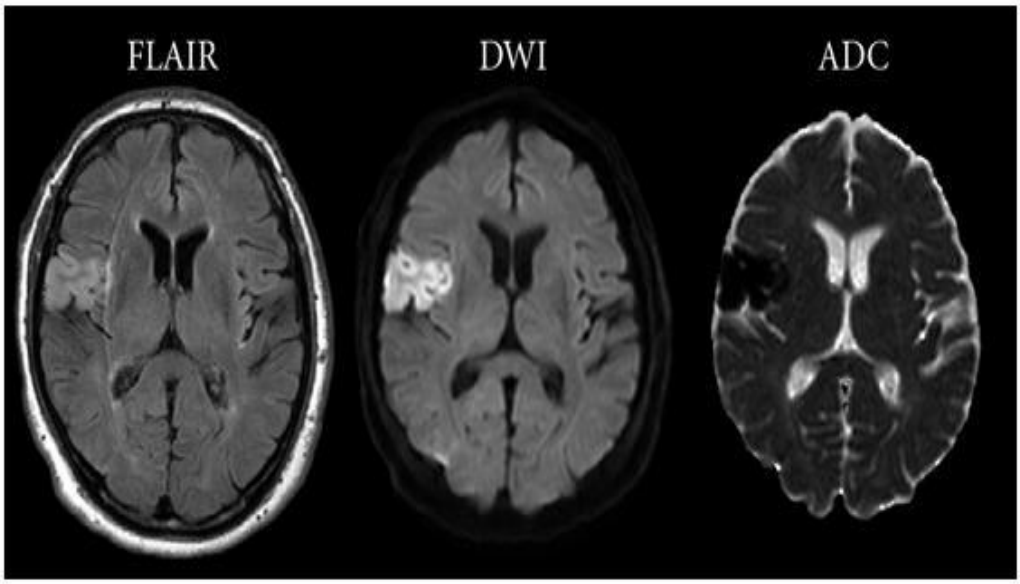


Fig 6 MRI with diffusion scan showing right fronto parietal hyperintensity

"Recommended Tests in Evaluation of Acute Ischemic Stroke[41]

All Patients

1. Computed Tomography of brain
2. MRI and stroke protocol
3. Electrocardiogram
4. Complete blood count with platelet count including Mean platelet volume
5. Serum electrolytes
6. Blood glucose
7. Renal function tests
8. Oxygen saturation
9. Chest X ray
10. Liver function tests if history of alcoholism is present
11. Arterial blood gas levels (if hypoxia suspected)
12. Markers of cardiac ischemia- CPK MB,Troponin
13. Erythrocyte sedimentation rate (ESR)
14. Lipid profile
15. Carotid doppler"

Risk factors of stroke[42]

A risk factor is a characteristic of an individual or population associated with increased risk of disease compared to those without it. Multiple risk factors are associated with cerebral infraction and have been studied in great detail. Various proatherothrombotic processes leading to macrovascular complications are well known. Risk factors for ischemic stroke include modifiable and nonmodifiable etiologies and is variable in young and older people . Modifiable risk factors include Diabetes mellitus, hypertension, smoking, alcoholism and dyslipidemia ,raised homocysteine ,obesity, inadequate physical activity, migraine,oral contraceptives and hormonal supplements, fibrinogen and clotting factors,vasculitis, collagen vascular diseases and cardiac disorders include atrial fibrillation. Age, gender,ethnic and geographical background, genetic inheritance and familial predisposition are some of the non-modifiable risk factors of ischaemic stroke.(Table 1) In spite of the adequate control of these conventional risk factors, the incidence of cerebral infarction is not curbed, emphasizing a need to look into novel and unrecognized risk factors. Identification of risk factors in each patient can uncover clues to the cause of the stroke and the most appropriate treatment and secondary prevention plan.

Table no 1 Risk factors

Risk factors	**NON MODIFIABLE**	**MODIFIABLE**
ISCHEMIC STROKE	Age	Hypertension
	sex	Smoking
	Race/ethnicity	Waist to hip ratio
	Genetic factors -Ehlers Danlos type4 ,Fabry disease,sickle cell disease	Diet, food habits
		Physical inactivity
		hyperlipidemia
		Diabetes mellitus
		Alcohol consumption
		Lifestyle issues- tobacco use,illicit drug use
		Atrial fibrillation

Table no 2 Difference between stroke in young and old[43]

Parameters	**Young**	**old**
Mean platelet volume (MPV)	Normal or raised	May be raised or normal
Factors	Arteriopathy Premature atherosclerosis Homocystinuria Mitochondrial encephalopathy lactic acidosis Fibromuscular dysplasia Vasculitis Toxins;cocaine, heroin Carotid dissection Sickle cell disease Disseminated intravascular	Diabetes mellitus Hyperlipidemia Hypertension Cigarette smoking Atrial fibrillation Physical inactivity Medications Falls in elderly

	Coagulation Protein c or S deficiency AV malformation	
Presentation	Not unique to age group	
Investigation	Coagulation profile and screening for homocystiene Anti nuclear antibodies fibrinogen Toxicology screening	Stroke protocol MRI + CT scan
Management	Antiplatelets , antilipid and physiotherapy	Antiplatelets,antilipid physiotherapy, Rehabilitation
Prognosis	Better than older adults	Poor
Long term complications	Depression Bed sores Disability	Depression Bed sores Abuse Urinary tract infections Pneumonia

Table no 3 Differences between various types of stroke [44]

Type	Thrombosis	Embolism	Hemorrhage
Age	Old age	young	young
Time of onset	subacute	hyperacute	hyperacute
Weakness	Progressing over hours	Full at onset	Progressing over hours
Headache	+/-	-	+++
Seizures	+/-	+	++
Progression	Can progress over 72hours	High at onset	Upto 6 hours
Mortality	less	more	more
Morbidity	more	less	more

Mean platelet volume[45]

Platelets play an crucial position in the integrity of ordinary homeostasis, and suggest platelet volume (MPV) is the indicator for its characteristic.. both the size and variety of granules in platelets in stream are under unbiased hormonal control and do no longer change at some point of the life span of the platelet. The large platelets contain extra dense granules, are more potent than the smaller platelets, and are hence greater thrombogenic.

MPV, a determinant of platelet function, is a newly emerging risk factor for atherothrombosis. platelets can be separated using Counter flow centrifugation into fractions by differences in platelet volume. these variations in platelet quantity correlate with differences in density, dense frame content material, enzymatic activity of LDH(lactate dehydrogenase), platelet aggregation to ADP (adenosine diphospate), and serotonin uptake and release, helping the relevance of the mean platelet quantity(MPV) as a measure of platelet practical functionality.

Platelet size (MPV), a marker (and likely a determinant) of platelet characteristic is a physiological variable of haemostatic significance. In addition they include greater dense granules and release more serotonin and beta thromboglobulin than do small platelets. suggest platelet extent, as well as platelet depend, are an index of haemostasis and its disorder i.e. thrombosis. Large platelets are metabolically greater reactive, produce extra prothrombotic factors and combination extra without problems and are metabolically and enzymatically more active, and have greater prothombotic potential.[46]

Mean platelet volume (MPV), the most commonly used measure of plateletsize, is a potential marker of platelet reactivity. MPV is regular laboratory test in the panel of haemogram easily available with no added cost.

Modifications in MPV play a greater vital position in haemostasis than platelet count. Platelet extent is regulated by diverse intrinsic and extrinsic elements. The mean lifespan of light platelets is shorter than that of heavy platelets.[47]

Elevated MPV is related to other markers of platelet activity, together with expanded platelet aggregation, increased thromboxane synthesis and β-thromboglobulin release, and elevated expression of adhesion molecules. [48]

Hyper-functional platelets are formed due to Perturbed megakaryocyte platelet haemostatic axis (MPHA) which may additionally make a contribution to the improvement of vascular ailment or an acute thrombotic occasion which includes ischemic stroke or myocardial infarction. higher degrees of MPV in sufferers with acute ischemic stroke have been demonstrated in various studies [49,50]

The megakaryocyte-platelet-haemostatic axis(MPHA).

Platelets are anucleate cells and, as such, have little or no protein synthetic capability. Platelet size (imply platelet extent, MPV) is a marker (and in all likelihood determinant) of platelet function, big platelets being potentially more reactive. In addition they produce more thromboxane A2 (TXA2) which is consistent with unit extent and are associated with a decreased bleeding time (BT; a degree of in vivo haemostatic function).For example, they comprise extra dense granules, go through greater in vitro aggregation in response to agonists together with ADP and collagen, and release greater serotonin and b -thromboglobulin(b-TG)[51].

Measurements of platelet and MK parameters in human beings suggest that they're so closely related that they may be considered a single gadget: the megakaryocyte-platelet haemostatic axis .

Despite the fact that platelets are incapable of de novo protein synthesis they're very active metabolically and respond rapidly to vascular damage or trauma via undergoing a series of reactions (adhesion, release of granule contents, form alternate and aggregation), which ultimately bring about the formation of a platelet–fibrin plug [30] as (shown in figure 7 &8). Variation in MPV is a result of a exchange within the rate of platelet destruction, while altered MK ploidy, and concomitant modifications in MK length and cytoplasmic extent are related to a alternate inside the price of platelet production[54]

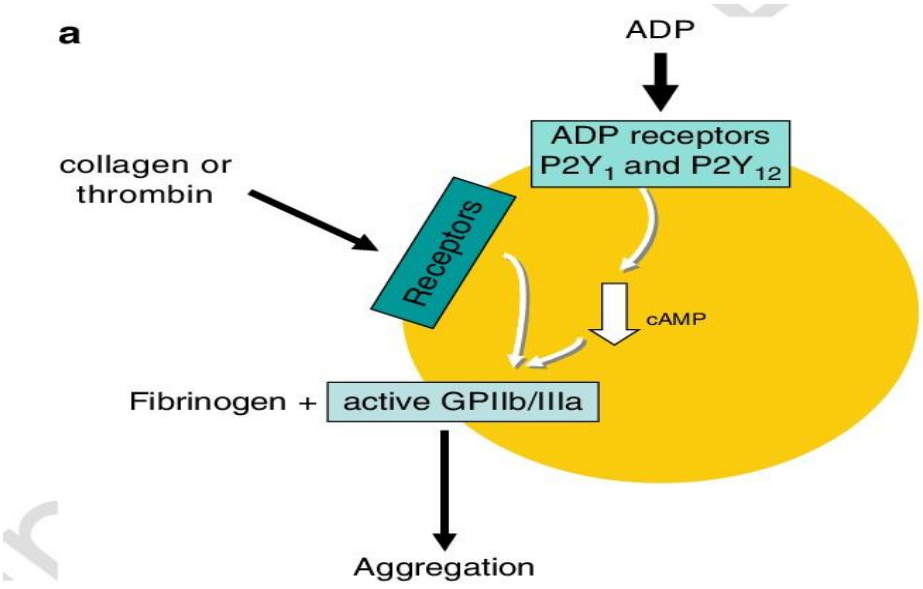


Fig 7 platelet aggregation [54]

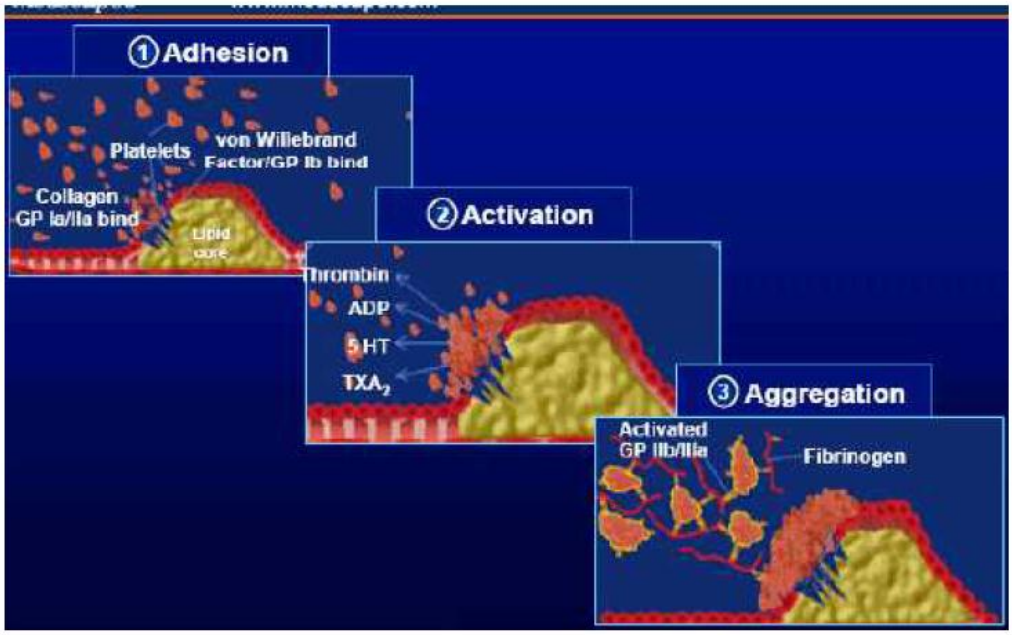


Figure 8 platelet activation cascade[55]

O'Brien[56] and associates have conducted aggregation experiments which imply that shear pressure alone can purpose platelet activation and aggregation accompanied rapidly afterwards by way of the platelets returning to the quiescent state – a phenomenon they termed 're-bleeding'

MPV measured at this level can also nicely replicate (at least in part) the ability reactivity of platelets previous to the stroke. but, the dynamics of platelet intake and manufacturing in the intense section of stroke aren't yet understood properly enough to rule out the possibility that MPV is being modified to some extent through the extreme destruction of platelets and next trade in the fragmentation of MK cytoplasm. If MK parameters could be proven to be peculiar rapidly following the stroke this will strongly recommend that the MPHA became chronically perturbed previous to the stroke.

Increased platelet function and, in some cases, a shift in MK indices in a prothrombotic direction has been shown in stroke risk factors such as hypertension ,

diabetes mellitus and smoking, and in vascular conditions associated with stroke.Levels of cAMP and cGMP because of rise in Prostaglandin I2 and Nitric Oxide resulting inactivation of cAMP- or cGMP-dependent protein kinases and inhibition of the platelet activation pathways. [57]

Relationship between antithrombotic drug usage and MPV[58]

Studies have shown some platelet indices differed between the anti-thrombotic drug customers and the non-customers . Patients taking aspirin or clopidogrel had significantly lower MPV compared with non-customers .In addition, patients taking warfarin had a decrease platelet matter and higher MPV in comparison with non-users.

Relationship of mean platelet volume in patients with acute ischaemic stroke

The majority of research have found that the MPV is significantly increased in acute ischemic stroke, with a concomitant lower in platelet count number. The exceptions to this include a study by Tohgi et al[59] wherein MPV was no longer notably associated in patients with Ischemic Stroke than in controls.

D'Erasmo et al[60] discovered a appreciably decrease platelet matter in patients that died, while O'Malley et al. discovered that platelet modifications were no longer related to clinical final results after 6 months. It has been discovered that patients that do badly(determined as death or dependency) have a substantially increased MPV in the extreme section of stroke than those who do well (independence) and have a tendency to have a lowerplatelet count.

A persistently raised MPV following ischaemic stroke may well be associated with recurrent vascular events and death. This has been assessed as a substudy of the PROGRESS trial.[61]

O'Malley et al[62] found no significant differences in platelet count between subtypes; results that concur with our own. Fisher and Zipser [63] found that urinaryTXB2 levels were raised in large vessel and cardiogenic but not lacunar strokes compared with normal controls.

Woo and colleagues[64] observed that plasma beta-Thromboglobulin (b-TG) became raised following large vessel atherosclerotic and cardioembolic strokes but no longer lacunar infarcts.

Shah et al[65]. made similar findings and moreover observed that Plasma Platelet aspect F4 was accelerated after thromboembolic but not cardioembolic or lacunar strokes. In contrast, Iwamoto[66] and colleagues discovered elevated levels of b-TG in all subgroups of patients as compared with controls.

So, it could be seen that the bulk of the proof factors to there being greater platelet pastime following cortical than lacunar stroke and it is in all likelihood that this is associated with their respective pathophysiologies.

The severity and poor outcome of ischemic stroke patients with increased MPV has been reported in the literature. Stroke patients with high mortality have been found to have low platelet count. Again, ischemic stroke patients with higher MPV tend to have poor outcome than their counterparts with low MPV.

SEVERITY of stroke is evaluated with the help of MRS which is internationally accepted scoring scale

MODIFIED RANKINS SCORE (MRS)

The association of MPV with severity of stroke will be determined by comparing the modified Rankin score with corresponding mean values of MPV in each group.

Score Description

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

MATERIALS AND METHODS

STUDY DESIGN:

HOSPITAL BASED CROSS SECTIONAL STUDY

SOURCE OF DATA:

The study will include patients presenting to the hospital diagnosed with an acute ischemic stroke and satisfying inclusion and exclusion criteria. Study is carried out in

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between November 2017 to October 2019.

SAMPLE SIZE: The average mean platelet volume (MPV) – 8.92 ±1.74 at 95% confidence interval and 5% margin of error , minimum sample size is 60.

$$n = \frac{(Z)^2 \times SD^2}{d^2}$$

Zα- Z value for α error

SD- Common standard deviation between two groups

d- margin of error

Total sample size = 60 [18]

STATISTICAL ANALYSIS:-

Data will be presented using Mean± SD (continuous data) and percentages (categorical data) and diagrams.

Association of MPV and stroke using modified Rankins scores will be carried out using Chi-square test.

METHOD OF COLLECTION OF DATA:

Information will be collected through prepared proforma from each patient. Clinical severity will be assessed using MODIFIED RANKIN'S scale. Mean platelet volume will be measured using an automated analyser available in central lab of _____.

Inclusion criteria: 1. All patients above 40 years of age , irrespective of sex with Ischaemic stroke identified based on clinical features and Radiological evaluation ie Magnetic Resonance Imaging of Brain admitted in _____

_____

Exclusion criteria:

Patients with

1. Thrombocytopenia.
2. Known cases of hereditary disorders of large platelets.
3. Medications that can reduce the platelet count: hydroxyurea, antineoplastic agents, and inhibitors of the platelet integrin αIIbβ3 ie Abiximab.
4. Haemorrhagic stroke.
5. Patients unable to communicate because of severe stroke, aphasia or dementia without a valid surrogate respondent. (A valid surrogate respondent is considered a spouse or first degree relative that is living in the same home or is self- identified as aware of the participant's previous medical history and current therapies)

RESULTS

AGE

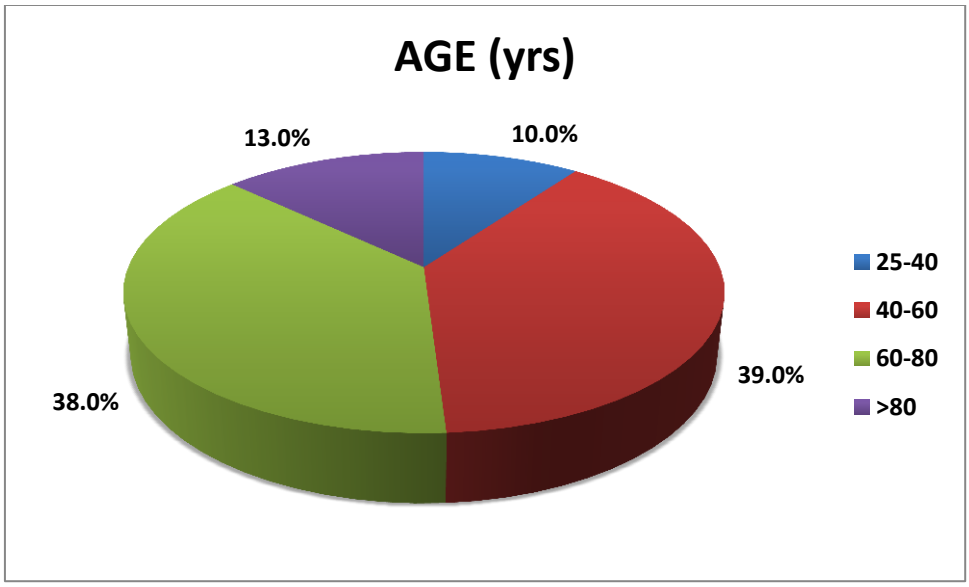
TABLE 4: DISTRIBUTION OF CASES ACCORDING TO AGE

AGE (yrs)	N	%
25-40	10	10
40-60	39	39
60-80	38	38
>80	13	13
Total	100	100

A Total of 100 patients with stroke admitted to the medical wards meeting eligibility criteria. The mean age for the cases was 62.70 ± 15.6 . The maximum number of cases in this study were in the age group between 40-60 years which was followed by age group of 60-80 years .

PARAMETERS	Mean	SD	RANGE
Age (yrs)	62.7	15.6	26-92

FIGURE 9: DISTRIBUTION OF CASES ACCORDING TO AGE



Gender

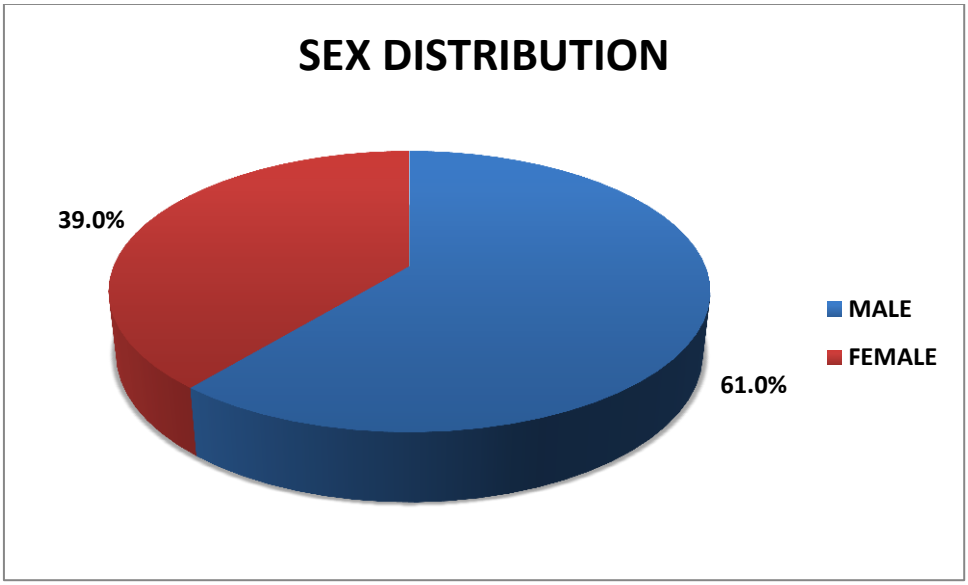
TABLE 5: DISTRIBUTION OF CASES ACCORDING TO SEX

SEX	N	%
MALE	61	61
FEMALE	39	39
Total	100	100

MALE TO FEMALE RATIO= 1.6:1

Out of study population males were predominant with 61% and females were 39% .

FIGURE 10: DISTRIBUTION OF CASES ACCORDING TO SEX



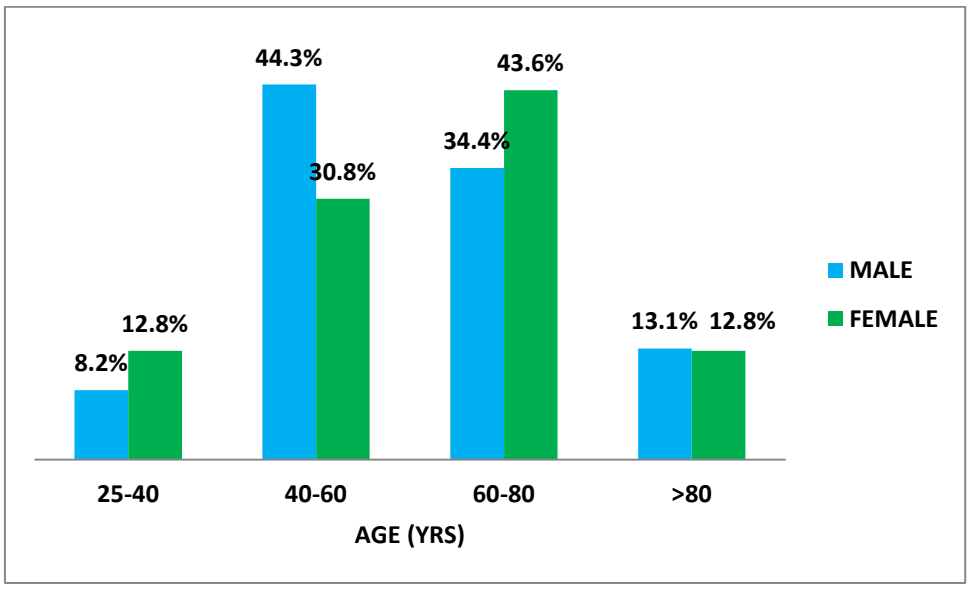
Age and Sex

TABLE 6: ASSOCIATION OF AGE AND SEX

AGE (yrs)	MALE		FEMALE		p value
	N	%	N	%	
25-40	5	8.2%	5	12.8%	0.543
40-60	27	44.3%	12	30.8%	
60-80	21	34.4%	17	43.6%	
>80	8	13.1%	5	12.8%	
Total	61	100.0%	39	100.0%	

Males with stroke were having higher age of 80 years and above 13.1% when compared to females .

FIGURE 11: ASSOCIATION OF AGE AND SEX



Risk Factors

TABLE 7: DISTRIBUTION OF CASES ACCORDING TO COMORBID CONDITIONS

PAST HISTORY	N	%
COPD	1	1
DM	20	20
HTN	44	44
IHD	1	1

COPD -Chronic Obstructive Pulmonary Disease

DM- Diabetes Mellitus

HTN-Hypertension

IHD -Ischemic Heart Disease

Out of the many risk factors for stroke, Hypertension was the most common risk factor in this study group with 44% .Diabetes mellitus being second with 20 % followed by Chronic obstructive pulmonary disease and Ischemic heart disease .

FIGURE 12: DISTRIBUTION OF CASES ACCORDING TO COMORBID CONDITIONS

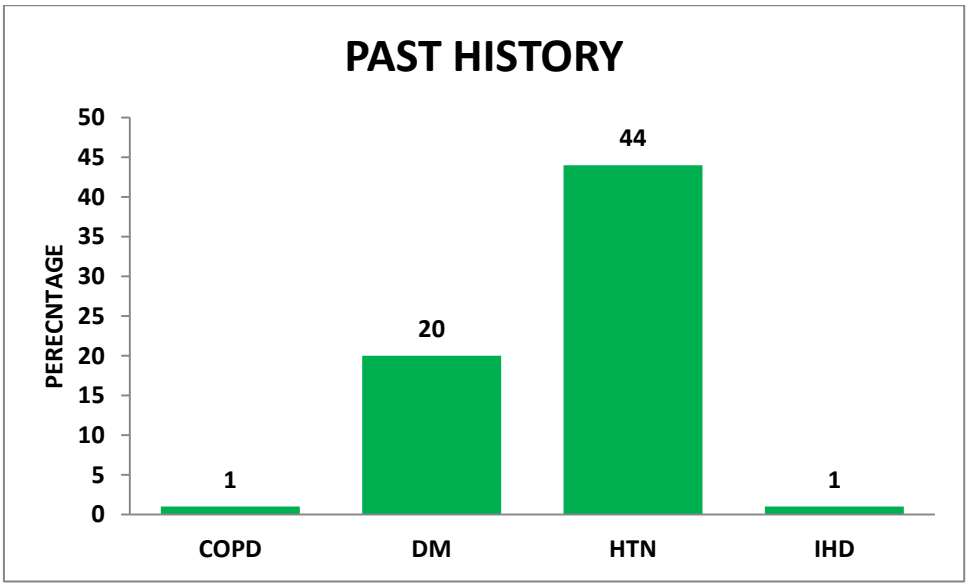
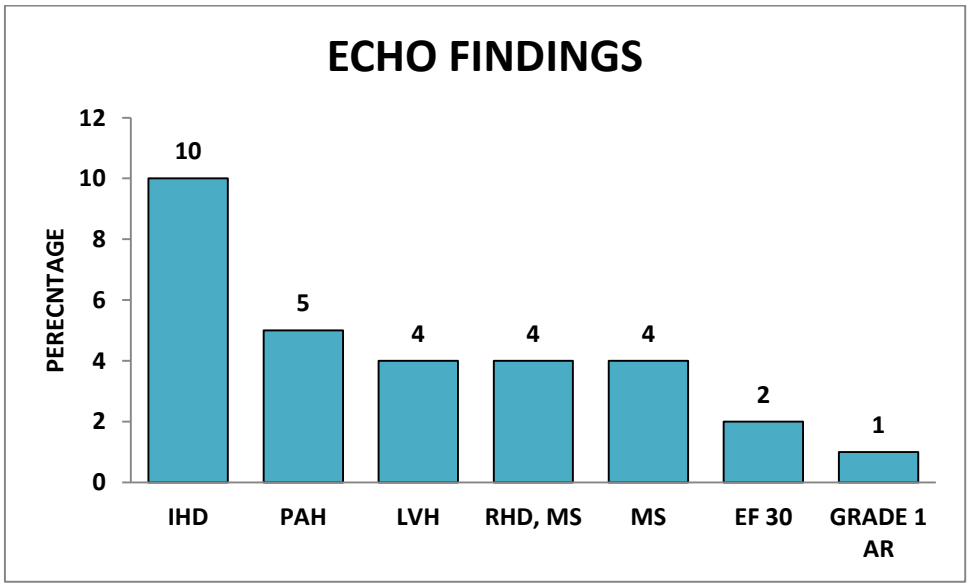


TABLE 8 : DISTRIBUTION OF CASES ACCORDING TO ECHOCARDIOGRAPHY FINDINGS

ECHO FINDINGS	N	%
Ischemic heart disease	10	10
Pulmonary arterial hypertension	5	5
Left ventricular hypertrophy	4	4
Rheumatic heart disease with Mitral stenosis	4	4
Mitral stenosis		
Low ejection fraction (30%)	2	2
Aortic regurgitation	1	1

FIGURE 13: DISTRIBUTION OF CASES ACCORDING TO ECHO FINDINGS



Stroke- MRS (Modified Rankin's score)

The clinical severity of stroke at presentation was determined by the Modified Rankin's score and severe disability was seen with 53% of the cases. There was no significant disability in 1% of the cases

TABLE 9: DISTRIBUTION OF CASES ACCORDING TO MRS

MRS	N	%
1	01	01
2	10	10
3	15	15
4	21	21
5	53	53
Total	100	100

FIGURE 14: DISTRIBUTION OF CASES ACCORDING TO MRS

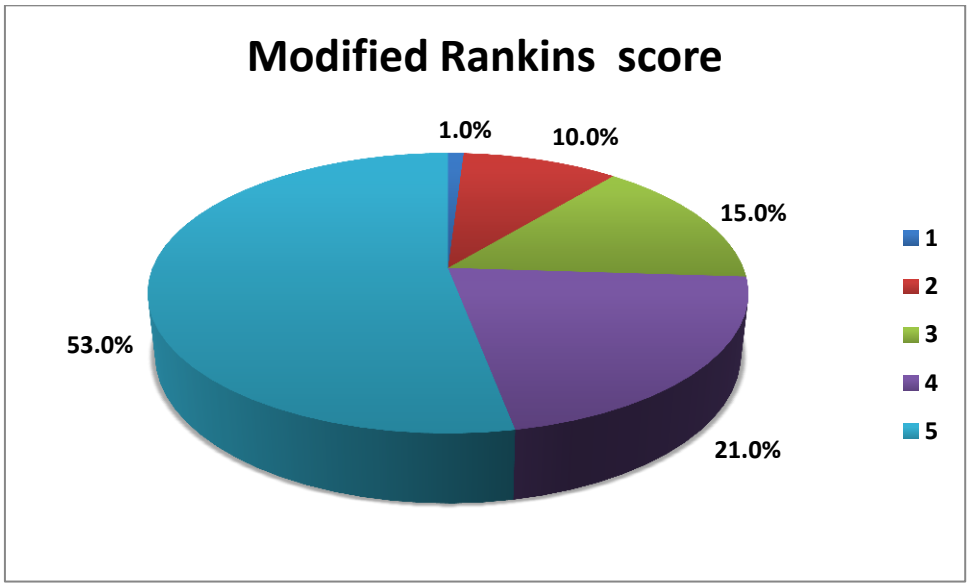


TABLE 10Association of MPV and stroke severity

MRS	N	MPV		p value
		Mean	SD	
1	1	10.40	0.00	0.842
2	10	10.22	1.34	
3	15	10.11	0.85	
4	21	10.55	1.49	
5	53	10.26	1.12	
Total	100	10.30	1.18	

TABLE 11: COMPARISON OF MEAN PARAMETERS ACCORDING TO AGE

MPV was almost same between middle aged and in older people with mean value of 10.29 and 10.30 respectively and MRS score of 4.1 and 4.2 respectively which indicates severity and disability of stroke patients .

	Parameter	Middle aged			Elderly			Total			p value
		Mean	SD	Range	Mean	SD	Range	mean	SD	Range	
a	MPV	10.29	1.3	8.5-13.7	10.3	1.1	7.9-13.5	10.3	1.2	8.5-13.7	0.952
b	Plt (lac)	2.6	0.8	0.47-4.52	2.3	1.1	0.24-6.2	2.5	1.0	0.24-6.2	0.205
c	PDW	11.8	3.2	8.7-24.5	12.1	2.4	9.2-20	12.0	2.8	8.7-24.5	0.541
d	MRS	4.1	1.1	1-5	4.2	1.0	2-5	4.2	1.1	1-5	0.536
e	Sodium	133.8	7.1	114-146	134.0	8.9	115-165	133.9	8.0	114-165	0.929
f	Potassium	3.8	0.8	2.6-6.3	3.7	0.7	2.3-5.3	3.7	0.7	2.3-6.3	0.545

FIGURE 15 a : COMPARISON OF MEAN PARAMETERS ACCORDING TO AGE

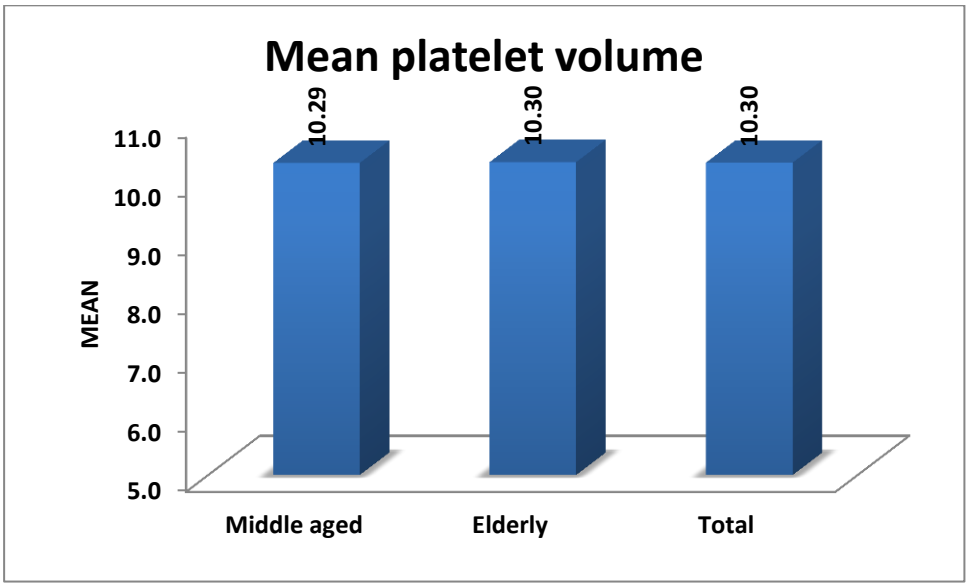


Fig 15 b

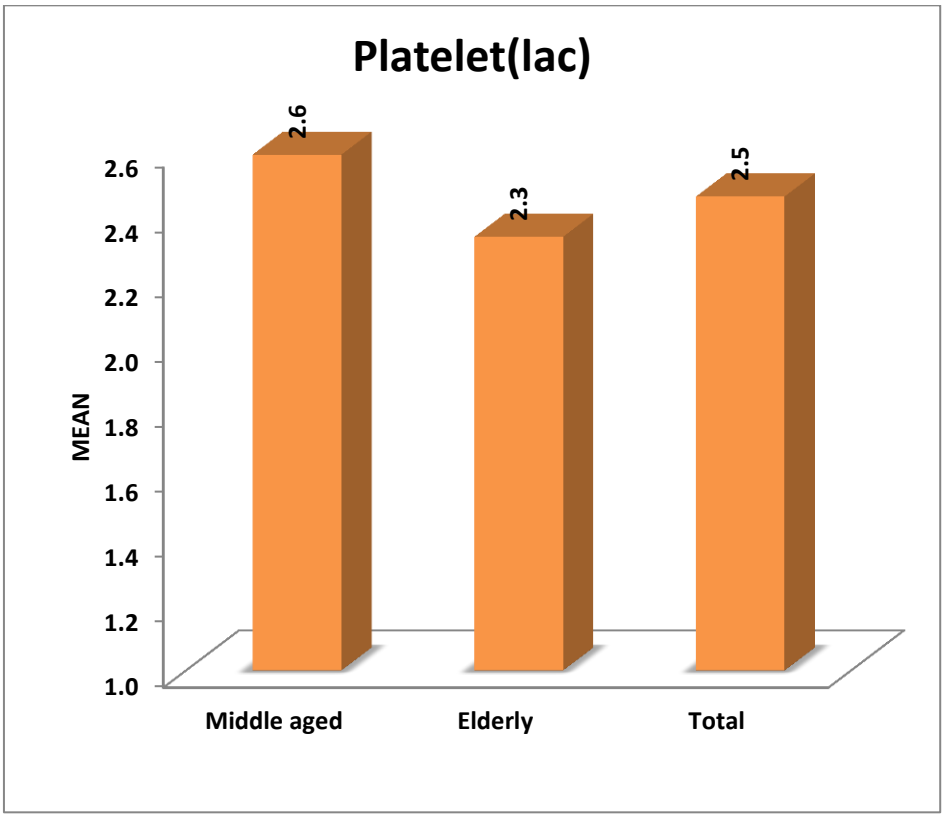


Fig 15 c

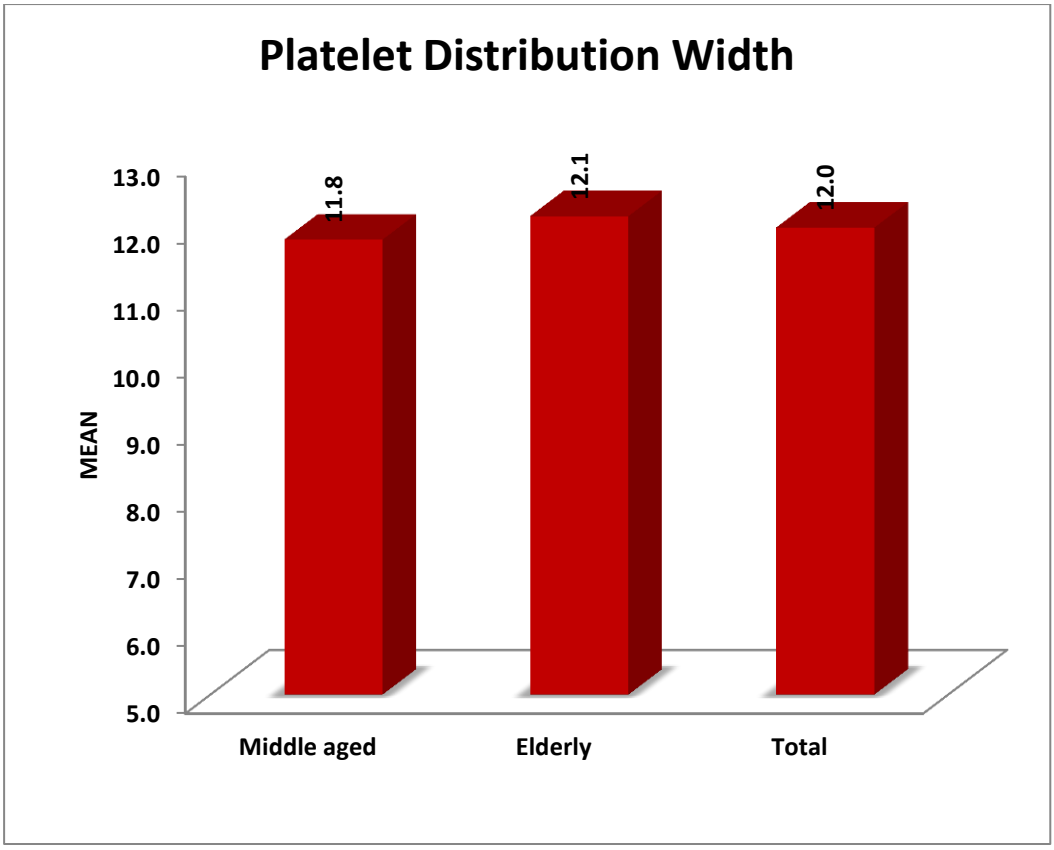


Fig 15 d

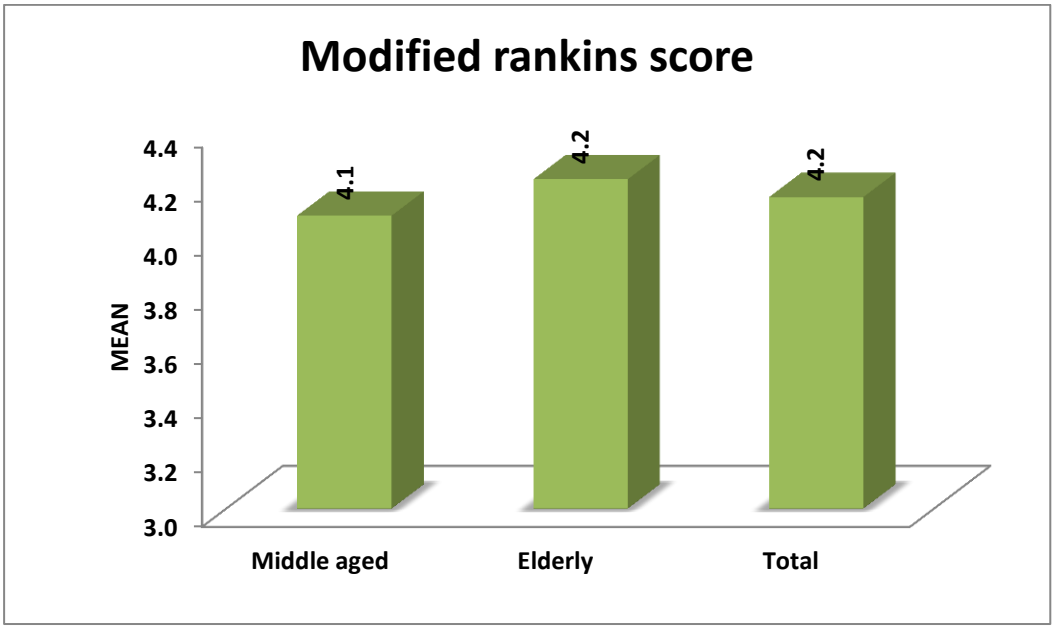


Fig 15 e

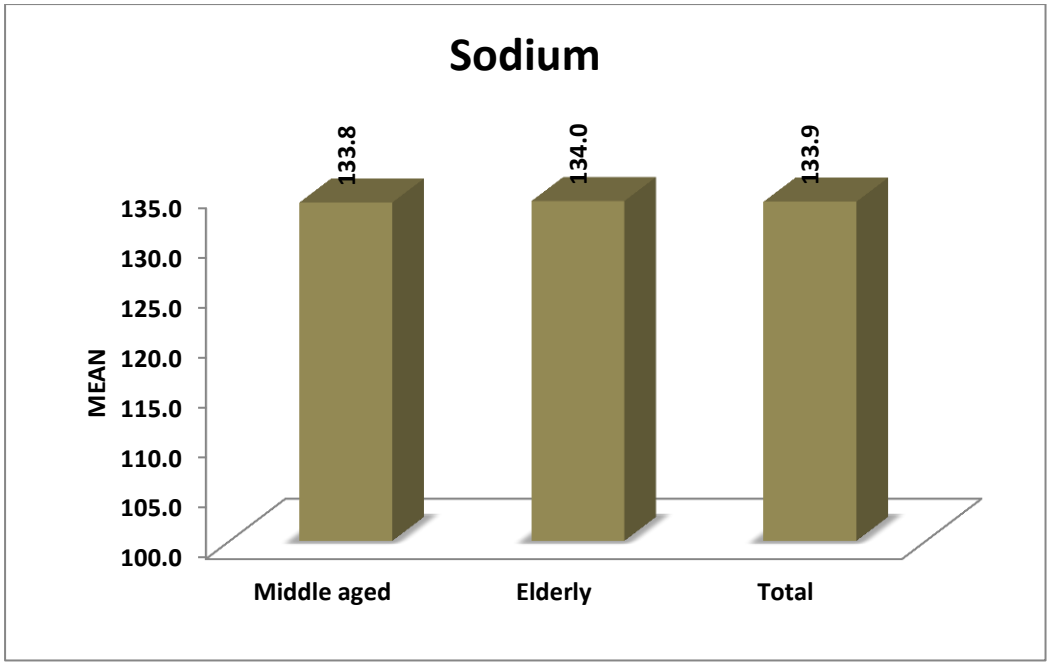


Fig 15 f

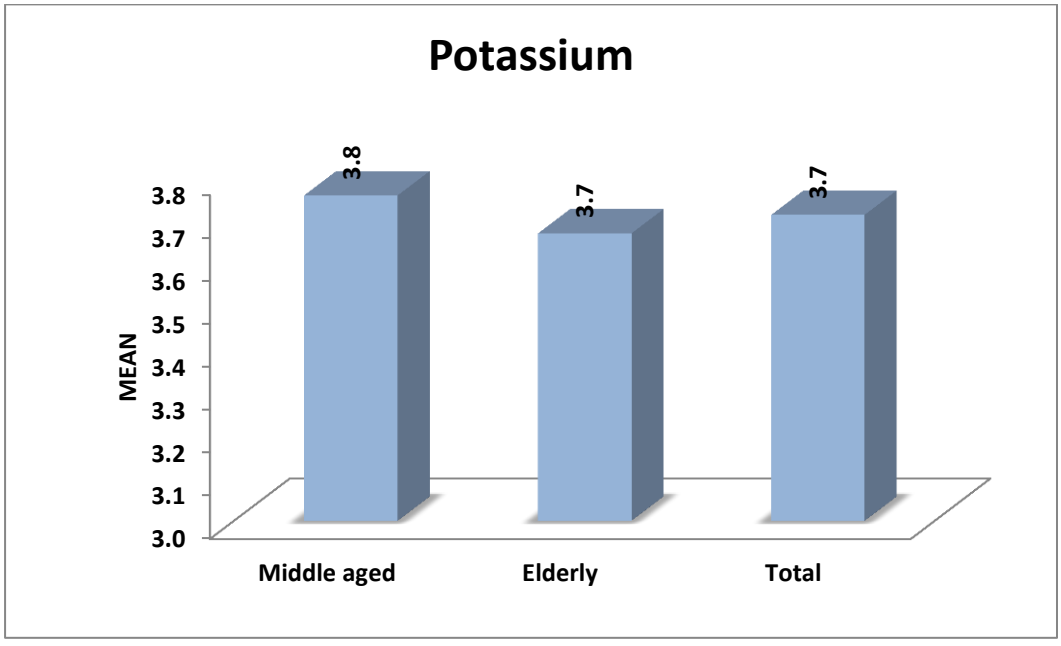


Table 12 DEMOGRAPHIC COMPARISON WITH OTHER STUDIES

Study	**O'Malley et al[62]**	**Butterworth HH et al[14]**	**Bath et al[15]**	**Pikija et al[67]**	**Muscari et al[68]**	**Current Study**
No of cases recruited	58	137	301	81	137	100
Age in years	79.5 ± 6.5	71.9 ± 10.8	65 ±9	76	78	62.7 ± 15.6
Women	39 (67%)	55 (40%)	87 (29%)	49 (60%)	65 (47%)	39 (39%)
Men	19 (33%)	82 (60%)	214 (71%)	32 (39%)	72 (52%)	61 (61%)

Table no 13 MPV COMPARISON WITH OTHER STUDIES IN STROKE

Study	Neki et al [35]	Thankappan PK et al [71]	Sridharan et al [72]	Current study
MPV association with stroke	Yes /ischemic stroke	Yes/ thrombotic stroke	Yes	Yes
MPV in stroke	Elevated	Elevated	Elevated	Elevated
MPV and severity stroke	Not significant	Not significant	Significant	Not significant

DISCUSSION

Discussion

This hospital based cross sectional study was conducted at _____ _____ .A total of 100 patients who presented with acute ischaemic stroke from november 2017 to to October 2019 were studied.

In this study, acute ischemic stroke was widely prevalent among 61% of males and 39% in females. The male to female ratio was 1.6:1 .These findings suggest male preponderance in acute ischaemic stroke patients which was consistent with a study by Shah PA. et al. who reported that, males constituted 59% of ischemic stroke patients. Similar findings have been reported in other studies from India by Khan et. al.

Age is an important non-modifiable risk factor for stroke.In the present study nearly one third of the study patients were aged between 40 to 60 years followed by 60 to 80 years . However statistically the age distribution was comparable among male and female patients (p=0.543). In this study the mean age among patients was 62.7 ± 15.6 years . These observations showed that, acute ischemic stroke in this study was common in middle age group. A study to assess the role of MPV in ischemic stroke by Shah PA. et al. has reported mean age as 58 years which is lower compared to our study .

RISK FACTORS FOR STROKE

Out of the many risk factors for stroke, hypertension was noted in 44 % of the patients followed by 20 % of diabetes mellitus .Similarly hypertension was the most prevalent risk factor in study by Muscari et al with 84.7% and 82.7% in Pikija et al.

Diabetes mellitus had a representation of 20% of the patients . Most previous studies have included hypertension as risk factor .

In our study echocardiography in ischemic stroke revealed that ischemic heart disease was seen in 10% of the cases followed by pulmonary arterial hypertension in 5% of the cases and left ventricular hypertrophy and rheumatic heart disease with mital stenosis in 4% of cases respectively .

MEAN PLATELET VOLUME AND STROKE

The Platelet parameters assessed was mean platelet volume (MPV). MPV has got no statistically significant correlation with ischemic stroke with a "p" value of 0.989 and MPV was compared among two age group out curiosity with an average MPV in middle aged people being 10.29±1.3fl compared to older people in which average being 10.30±1.1fl. The range of MPV in middle aged was 8.50 to 13.70 .The range of MPV in older people was 7.90 to 13.50 . This pattern has been derived for the first time in our study .The result of our study was contrary to study by Neki et al which said that MPV has got significant correlation with acute ischemic stroke as independent risk factor .

The association of ischemic stroke with MPV observed in the present study is in discord with the known facts that there is more reactivity of large platelets, the pathophysiological position of platelets in the prevalence of ischemic stroke, and the identified results of antiplatelet remedy on the chance of ischemic stroke.

Findings in study by PROGRESS collaborative group follows stroke rates were greater among individuals with higher measurements of MPV, The study identified MPV as an independent predictor of the risk of stroke among high-risk individuals.

Slavka et al.[70] showed that subjects with higher MPV (>11.01 fL) had 1.5 times higher vascular mortality risk than patients with low MPV (<8.7 fL) value. In the same study, significant positive relationship between high MPV and the risk of ischemic heart disease was identified.

STROKE SEVERITY AND MPV

The clinical severity of stroke at presentation was determined by the Modified Rankin's scale and severe disability was seen with 53% of the cases. 21% of the cases had moderately severe disability, 15% with moderate disability and 10% with slight disability. There were no deaths recorded during hospital stay .Mean duration of stay at hospital was 4.6 days. The association of MPV with severity of stroke was determined by comparing the modified Rankin's score with corresponding mean values of MPV in each group. MPV showed a 'p' value of 0.982 which was statistically insignificant. O'Malley [62] conducted similar studies and divided the outcomes as independent (Rankin's grade 0 to 2), dependent (Rankin's grade 3 to 5) and dead (Rankin's grade 6). However no statistical significance with MPV was obtained. Butterworth et al studied patients who were dead or dependent at 3 months, using the Lindley score, and they had a significantly higher platelet volume, and a tendency to a lower platelet count, as compared with those who fared well. However statistical significance was not found.

Our study showed no statistical significance between MPV and severity of stroke which was similar to study by Neki et al .

This pattern has been seen in another study by Prasantha Kumar et al[71] which proved no correlation between clinical severity of stroke and mean platelet volume.

The studies which has shown results like Neki et al in which MPV was significantly higher in patients of ischemic stroke which suggest a association of MPV

with ischemic stroke. Further there was no significant association between severity of ischemic stroke and MPV.

The study done by Sridharan M et al [72] showed that MPV is independent of age, sex, smoking status, systemic hypertension and diabetes mellitus in stroke patients and MPV was higher in ischemic stroke patients compared to haemorrhagic stroke.

LIMITATIONS

This study has some obstacles that need to be taken under consideration in assessing the results. We measured MPV best at admission, and did no longer carry out similarly serial measurements at some point of the evolution of stroke. consequently, according to our outcomes, we advocated in addition studies to analyze the role of this index as a predictive thing in the severity of ischemic stroke.

CONCLUSION

1. The study identified MPV as an independent predictor of the risk of stroke among high-risk individuals.
2. This study did not find a statistically significant correlation between clinical severity of stroke and mean platelet volume.

SUMMARY

Atherothrombosis is the main cause for most of vascular complications. Platelet size, measured as mean platelet volume (MPV), is a marker of platelet function and is positively associated with indicators of platelet activity, including aggregation and release of thromboxane A2, platelet factor 4, and thromboglobulin.

Studies have shown MPV to predict the severity of ischemic strokes. Therefore, in this study we associated MPV on admission and to assess severity of stroke and also predict the outcome of stroke we used MR SCORE.

In this 20 months hospital based cross sectional study, total of 100 patients with acute ischemic stroke were enrolled of which hypertension was noted in 44 % of the patients followed by 20 % of diabetes mellitus

In this study, acute ischemic stroke was widely prevalent among 61% of males and 39% in females and nearly one third of the study patients were aged between 40 to 60 years followed by 60 to 80 years , In this study the mean age among patients was 62.7 ± 15.6 years .

MPV was compared among two age group out curiosity with an average MPV in middle aged people being 10.29±1.3fl compared to older people in which average being 10.30±1.1fl. The range of MPV in middle aged was 8.50 to 13.70

The range of MPV in older people was 7.90 to 13.50

The clinical severity of stroke at presentation was determined by the Modified Rankin‘s scale and severe disability was seen with 53% of the cases. 21% of the cases had moderately severe disability, 15% with moderate disability and 10% with slight disability.

To conclude, This study did not find a statistically significant correlation between clinical severity of stroke and mean platelet volume.

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ETHICAL CLEARANCE CERTIFICATE

INFORMED CONSENT FORM

TITLE OF THE PROJECT - "A STUDY OF ASSOCIATION OF MEAN PLATELET VOLUME TO SEVERITY OF ISCHAEMIC STROKE ''

PRINCIPAL INVESTIGATOR -

P.G.GUIDE NAME -

CHAIRMAN ETHICAL COMMITTEE

All aspects of this consent form are explained to the patient in the language understood by him/her.

1) PURPOSE OF RESEARCH:

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

2) PROCEDURE:

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.

3) RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

4) BENEFITS:

I understand that my participation in this study will help to patients survival and better outcome.

5) CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. 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 and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location.

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

6) REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at anytime . 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 the study, which might influence my continued participation.

If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. A copy of this consent form will be given to me to keep for careful reading.

7) REFUSAL OR WITHDRAWAL OF PARTICIPATION:

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

8) INJURY STATEMENT:

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

_____ _____

Signature of the Patient

(Investigator) (if the patient is conscious , oriented)

Date:

Signature Date:

PROFORMA

Informant :

Name: CASE NO:

Age: IP NO:

Sex: DOA:

Religion: DOD:

Past Occupation:

Present Occupation:

Residence:

Chief complaints:

History of present illness:

Past History:

Personal History:

Family History:

Treatment History:

General Physical Examination

Height:

Weight:

Body Mass Index:

Vitals

PR:

BP:

RR:

Temp:

Head to toe examination:

SYSTEMIC EXAMINATION.

Central Nervous System

MODIFIED RANKIN'S SCALE (Mrs)

Is commonly used scale for measuring the degree of disability or dependence daily activities of people who have suffered a stroke or the causes of neurological disability .It runs from 0-6 , running from perfect health without symptoms to death

Score:

0 - No symptoms at all

1. No significant disability despite symptoms; able to carry out all usual duties and activities
2. Slight disability; unable to carry out all previous activities, but able to look after own affair without assistance
3. Moderate disability; requiring some help, but able to walk without assistance
4. Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.
5. Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6. Dead

Cardiovascular System

Respiratory System

Per abdomen

INVESTIGATIONS

HAEMATOLOGY –

1) Hemoglobin	gm. %
2) Total WBC counts	Cells/mm^3
3) Differential counts -	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	%
Basophils	%
4) ESR	At the end of 1st hour
5) Platelet indices	
Mean platelet volume	
Platelet distribution width	
Platelet count	

Radiological investigations

Stroke protocol

1) **CT brain:**
2) **MRI brain**

3. BIOCHEMISTRY:

a. Serum electrolytes:

b. Lipid profile:

4. Others:

a. ECG

b. Echo

CONCLUSION:

Date:-

Signature:-

KEY TO MASTER CHART

For SEX		
Male	M	
Female	F	
For comorbid conditions		
Hypertension	HTN	
Diabetes mellitus	DM	
Chronic obstructive pulmonary disease	copd	
Ischemic heart disease	ihd	
For ECHO findings		
Right bundle branch block	rbbb	
Left ventricular hypertrophy	lvh	

MASTER CHART

	IP NO	PATIENT NAME	AGE	SEX	MPV	plt (lac)	PDW	MRS	ECG	sodium	potassium	DIAGNOSIS	Past h/o
1.	13235	BHIMAPPA	45	m	10.4	3.2	11.2	5	lvc	124	3.6	ischemic	h,d,
2.	2886	SHIVAPPA	58	m	11.3	1.16	12.6	5	normal	140	3.6	ischemic	copd
3.	2873	MAHADEVI	65	f	11.7	1.54	14.3	5	af	139	5	ischemic	
4.	3064	KAMALABAI	75	f	10.2	2.83	11.5	5	normal	139	3.4	ischemic	
5.	3099	SHRISHAIL	60	m	9	2.15	9.5	4		146	3.2	ischemic	h
6.	4249	BORAMMA	80	f	10.8	1.95	13.1	5		143	3.8	ischemic	h
7.	3715	RAYAPPA	65	m	10.2	2.16	12.1	4	normal	136	2.8	ischemic	
8.	3496	GOLLALAPPA	65	m	9.2	2.6	10.1	5	rbbb	137	3.6	ischemic	h,d
9.	2089	VIDYASHREE	16	f	10.5	3.23	11.3	4	lvc	136	3.1	ischemic	
10.	4812	MALLAPPA	92	m	10.2	3	11.8	4	normal	136	2.9	ischemic	h,d
11.	3692	SOMAPPA	90	m	9	3.26	9.3	5	normal	141	3.2	ischemic	
12.	4386	SIDDAPPA	70	m	12.5	2.16	11.5	2	rbbb	131	2.6	ischemic	
13.	9301	SHANKARAPPA	90	m	9.5	5.33	10	5	vpc	126	4.4	ischemic	h
14.	40229	CHANNAPPA	50	m	9	3.19	9.1	2		129	4.4	ischemic	
15.	10100	SHAINAZBEE	40	f	9.3	2.4	15.1	5	lvh	126	4.4	ischemic	h
16.	40525	KAMALAMMA	672	f	10.4	4.08	11.3	5	normal	131	4.4	ischemic	h,d
17.	9465	MAHADEVI	30	f	11.5	1.79	10.9	5	normal	128	4.4	ischemic	
18.	40751	KAMALA	60	f	10.3	2.75	12.5	5	lvh	137	3.7	ischemic	h
19.	40565	SIDDAPPA	80	m	10.1	1.99	11.7	5	lvh	134	4.7	ischemic	
20.	7697	DEVAKAMMA	60	f	10.5	3.69	11.1	2	normal	146	3.2	ischemic	
21.	13678	SHARANAPPA	35	m	10.5	3.24	12.9	3	normal	127	3.6	ischemic	
22.	14425	CHANDRASHEKHAR	68	m	11.3	1.16	13.4	4	normal	126	3.4	ischemic	
23.	14355	SUMITHRA	75	f	10.7	1.36	11.4	5		116	2.6	ischemic	d
24.	7502	KAMALABAI	56	f	11.1	1.9	13	5	lvh	133	3.6	ischemic	
25.	5952	RUDRAPPA	82	m	9.4	2.3	10.1	2	normal	141	3.6	ischemic	h
26.	5611	SHANTAWWA	55	f	10.8	4.06	13.6	3	u waves	135	2.6	ischemic	

27.	40693	SHIVAJI	68	m	8.9	1.96	9.2	5		127	4.1	ischemic	
28.	40860	DILEEP	52	m	9.6	2.63	11.4	4		133	4.8	ischemic	h,d
29.	8062	SONABAI	75	f	8.8	2.06		5		125	4.5	ischemic	h
30.	37077	KALYANAPPA	55	m	10.6	1.16	11.5	3	lvh	141	3.6	ischemic	h, ihd
31.	38443	NAGAWWA	55	f	9	2.16	9.5	5		129	4.9	ischemic	h,d
32.	38304	KAMALABAI	65	f	10.7	2.61	11.6	5	lvh	131	3.9	ischemic	
33.	5750	MUDDANNA	52	m	10.7	3.46	12.5	2	rbbb	132	5.1	ischemic	h
34.	37552	TARABAI	61	f	8.9	0.24	10.1	5	normal	141	2.6	ischemic	
35.	36294	FARIZANA	55	f	9.1	4.52	9	5	lvh	126	3.1	ischemic	
36.	5777	VISHWANATH	60	m	10.9	2.32	14.5	5	normal	141	2.6	ischemic	h
37.	36421	DEVAKAMMA	82	f	8	2.85	16	3	tachycard	132	4.3	ischemic	
38.	36906	BHARATHI	62	f	10.1	2.29	11.5	5	lv strain	131	4.1	ischemic	
39.	37022	BHIMASHA	85	m	9.7	2.51	10.6	3	strain	115	2.6	ischemic	
40.	34185	JAYBHIM	50	m	9.1	2.81	8.9	5	lvh	142	3.8	ischemic	
41.	2344	YAMANAWWA	74	f	12.4	0.85	19.5	4	strain	140	2.6	ischemic	
42.	2823	SAYEBASHA	74	m	10.6	4.19	12.3	5	lvh	121	4	ischemic	h,d
43.	1721	SHANKAR	46	m	13.2	1.1	24.5	5	lvc	145	3.9	ischemic	
44.	43282	HANMANTHA	85	m	9.6	2.98	10.1	6	lvc	126	4.6	ischemic	
45.	2221	PRAHALLAD	72	m	10.5	1.61	12.4	5	rbbb	146	3.6	ischemic	
46.	2918	SHATTEPPA	50	m	10.5	2.99	10.8	4	rbbb	131	3.2	ischemic	h
47.	43968	SAIFANSAB	60	m	8.8	2.3	9.3	5	rv strain	136	3.5	ischemic	
48.	625	MALLEPPA	45	m	9.3	2.19	9.2	4	tall t wave	136	6.3	ischemic	h
49.	695	KALLAWWA	82	f	10	3.1		2	normal	136	3.6	ischemic	
50.	100219	IRAGONDAPPA	65	m	11.1	1.35	13.1	5	ihd	136	3.2	ischemic	h,d
51.	798	PATTARAY	60	m	9.2	1.62	9.3	5		130	5.5	ischemic	
52.	26542	SHANKAREPPA	63	m	10	2.87		5		126	2.3	ischemic	h,d
53.	13073	IRAYYA	60	m	9.2	3.15		4		114	2.6	ischemic	h
54.	25501	SHANKERAPPA	60	m	13.7	0.47	21	5		128	2.6	ischemic	h,d
55.	12966	GURULINGAYYA	56	m	10.9	1.97		2	lvh	128	2.6	ischemic	

56.	25596	MALKAMMA	64	f	9.7	1.82	9.9	3		126	4.4	ischemic	
57.	10645	HARISH	48	m	10.8	3.15		4		128	3.7	ischemic	h,d
58.	7816	GURUSANGAMMA	84	f	10.7	1.96		5		130	3.6	ischemic	
59.	25561	BHIMARAYA	55	m	9.1	2.87		5	lvh	130	3.3	ischemic	
60.	25501	SHANKARAPPA	60	m	13.1	0.72		4		126	3.6	ischemic	
61.	18450	ANNAPPA	78	m	9.5	1.53	9.9	5	lvh	147	3.6	ischemic	
62.	17932	MALLAPPA	55	m	13.4	2.27	22.3	4		137	3.7	ischemic	h,d
63.	17745	YALLAWA	30	f	11.4	2.02	13.6	5		146	3.7	ischemic	
64.	18754	SHIVAMMA	55	f	10.5	2.97	11.5	5		140		ischemic	
65.	18764	ANNAPPA	75	m	9.5	1.6	11.5	4		116	3.9	ischemic	
66.	18765	SHIVACHANDRA	30	m	9.3	3.26	9.3	5		140	3.5	ischemic	h
67.	19766	ASHOK	50	m	9.5	2	8.8	5		119	3.6	ischemic	
68.	2110	BASAVARAJ	65	m	10	6.2	11.7	4	lvh	136	2.7	ischemic	h
69.	17265	AMBUBAI	70	f	10.8	2.45	11.2	3	normal	146	3.7	ischemic	h
70.	17183	SANGANGOUDA	55	m	10.6	2.31	11.7	5		144	4.5	ischemic	
71.	24911	ASHOK	74	m	11	0.96	13.6	5		136	2.9	ischemic	h
72.	89863	BHEEMAPPA	65	m	9.3	1.7	10.1	5		131	2.7	ischemic	h
73.	12964	GURULINGAYYA	56	m	10.9	1.97	11.6	5	normal	130	3.2	ischemic	
74.	12961	MAHADEV	57	m	9.5	2.71	9.8	4	normal	133	3	ischemic	d
75.	13017	NEELAMMA	62	f	9.5	4		3		135	3	ischemic	h
76.	10442	TIPANNA	75	m	9.5	2.79	9.9	5	normal	141	4.4	ischemic	h
77.	10890	SONABAI	80	f	7.9	1.76	16.3	2	normal	136	3.6	ischemic	h
78.	6644	MAHADEVI	19	f	11.7	2.72	13.1	2	normal	134	3.9	ischemic	
79.	6031	DUNDAPPA	40	m	10.4	1.88	11	1	lvh	130	3	ischemic	
80.	6459	PARVATI	70	f	13.5	2.27	20	4		130	4.1	ischemic	h,d
81.	10278	HUSNAPPA	57	m	11.2	3.03	13.5	3	normal	126	3.7	ischemic	
82.	10112	RAJESAB	67	m	10.5	3.12	11.8	5		142		ischemic	h
83.	2236	MALLAMMA60	60	f	9	3.05	9.2	4	normal	136	4.6	ischemic	
84.	1249	SAHIDA	60	f	8.5	4.01	8.7	4		132		ischemic	h,d

85.	1390	BAGAWWA	85	f	10.8	2.67	13	5	af	142	4.3	ischemic	h,d
86.	32496	SHIVAJI	26	m	9.5	3.45	10.4	5	normal	138	3.9	ischemic	
87.	1857	LAXMAN	80	m	9.9	1.8	11.3	3	normal	144	4.4	ischemic	d
88.	3160	SHIVAPPA	70	m	10	2.62	10.2	4	normal	133	5.3	ischemic	h
89.	4469	SADASHIV	75	m	11.3	1.73	13.6	4	lvh	129	3.6	ischemic	
90.	12125	NEELAMMA	50	f	9.4	2.46	10.3	3	normal	134	3.6	ischemic	h
91.	5985	SATAWWA	50	f	9.3	2.94	9.6	5	lvc	136		ischemic	h
92.	4733	SHANTABAI	91	f	11.8	0.73	9.8	5	lvc	128	3.4	ischemic	d
93.	5745	JANAKIBAI	76	f	9.6	2.8	10.8	2	lvh	128	3.4	ischemic	h
94.	4501	MUDAKAPPA	90	m	11.5	1.36	16.1	5	lvc	129	3.3	ischemic	
95.	1924	NEELABAI	75	f	10.9	3.5	11.7	3	normal	129	3.7	ischemic	h
96.	44857	SHANTABAI	60	f	10.6	3.53	12.2	3	normal	137	4.4	ischemic	
97.	43064	SHRINATH	85	m	10.9	1.64	14.7	4	normal	143	4	ischemic	
98.	41613	VITTAL	75	m	12.3	1.06	17.9	5	normal	165	3.8	ischemic	
99.	40688	RAVI	29	m	9.3	2.89	10.8	3	ihd	142	4.7	ischemic	
100.	39453	DHARAMSINGH	65	m	10.7	1.96	12.2	3	lvh	137	3.7	ischemic	h,d
101.	38453	HANAMANTH	60	m	9.1	2.93	10.1	5	ihd	140	3.2	ischemic	h