A Study Of C-Reactive Protein In Acute Ischemic Stroke

by

DR.ANUSHA REDDY

Dissertation submitted to

In partial fulfillment for the degree of

DOCTOR OF MEDICINE
IN
GENERAL MEDICINE

Under the Guidance of

DR. VG WARAD M.D

PROFESSOR

DEPARTMENT OF MEDICINE

BLDE (DEEMED TO BE UNIVERSITY)

SHRI B. M. PATILMEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE

VIJAYAPUR – 586103

2019

LIST OF ABBREVIATIONS USED

Bg…….	Basalganglia
A/D/C……..	Alert/ Drowsy/Coma
CR……...	CoronaRadiata
CRP…….	C-reactive protein
ESM……	Ejection systolicmurmur
Fr…….	Frontal
Ft…….	Frontotemporal
I……	Infarct
IC……	Internalcapsule
L-h……	Lefthemiparesis
L-H……..	Lefthemiplagia
LUL…….	Left upperlimb
Oc…….	Occipital
Pa…….	Parietal
R-h……..	Righthemiparesis
	Righthemiplagia
RLL…….	Right lowerlimb
RUL…….	Right upperlimb
Te…….	Temporal
Th……	Thalamus

ABSTRACT

NEED FOR THE STUDY:

The role of the inflammation in the causation of the atherosclerotic changes has been proved. Various studies done have showed the role of C reactive protein as an early inflammatory mediator and its association with the stroke and its outcome has been done and is under research. Hence we evaluated the role of C reactive protein in acute ischemic stroke within 72hrs of the onset of the symptoms.

METHODS:

We studied prospectively 60 patients of stroke who were admitted in Shri B M Patil Medical College hospital who were diagnosed and admitted with ischemic stroke on the basis of the History, Clinical examination and proved on CT scan. CRP was measured on admission within 72hrs of the onset of the symptoms and patients were selected on the basis of the inclusion and exclusion criteria. This study was conducted between September 2017 to July 2019 .60 age and sex matched controls were considered for the study for comparison and these were patients admitted in the other wards of the hospital after matching the inclusion and exclusion criteria.

RESULTS:

The CRP value in our study was maximum in age group of 51-60yrs of age.Males were 39 cases and 21 were females. The mean age in females was 63.7±11.6 yrs and in Males was 60.4±9.3 i.e mean age was higher in females compared to males. The mean CRP among cases was 42.4±32.6 and among controls was 11.6±16.1 which showed a P value of <0.001 which was statistically significant.85% of the cases had elevated CRP and only 20% had normal values which was significant.

CONCLUSION:

CRP was elevated in patients with stroke when compared to controls and it was associated with poor outcome and was a poor prognostic indicator and patients with elevated CRP had increased risk of mortality

LIST OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Stroke is an important cause of mortality in elderly and increased rate of morbidity in elderly patients. In spite of understanding the physiology, pathology and incidence of cardiovascular and cerebrovascular disease developing advances in prevention and treatment, the burden of disease is increasing. Furthermore chronic conditions such as Diabetes mellitus and Hypertension which are considered as risk factor for stroke do not explain the occurrence of cardiovascular diseases and cerebrovascular disease in the different population groups.

There is no surprise that extensive research study is necessary for potential risk factors.

At the start of 20th century, Sir Williams Osler (1908) and Ophulus (1921) proposed that infection could be association in pathogenesis of atherosclerosis. In fact, research of more than a century has indicated various microorganisms as significant link between inflammation and the pathogenesis of atherosclerosis. Recent research show atherosclerosis as one of the cause of inflammation[1]. Researchers found a protein in the study of patients with cardiovascular and cerebrovascular disease which was named as C- reactive protein. C-reactive protein value estimation may help in the assessment of Atherosclerosis of vessels in healthy persons. Limited research has been done in our country despite of the increasing incidence of the cerebrovascular disease.

OBJECTIVES

Our study was undertaken with the following aim and objectives.

1. To study the C-Reactive protein (CRP) level in patients of acute ischemic stroke.
2. To assess role of C-Reactive protein (CRP) level in patients of acute ischemic stroke.

REVIEW OF LITERATURE

C-REACTIVE PROTEIN "C-reactive protein was discovered by Tillet and Francis in 1930"[2]. These scientists were working on serological response in patient with pneumonia with pneumococci extracts and identified a nonspecific polysaccharide which they named as fraction "C" which was obtained from serum of these patients. After the recovery of these patients the precipitancy of this protein with polysaccharide was absent and this protein was absent in these recovered patients. Scientist by name Avery and his colleagues described a substance and called it as material. C -reactive compound as a material that needed calcium ions for reaction with CPS and they described a term by name "acute phase" to describe serum obtained from the sick patients with infectious diseases and containing the material called C-reactive protein[3, 4].

Lofstrom did a study on the specific strains of pneumococci which showed capsular swelling which was nonspecific when the sera obtained from the patients was mixed with the strains of pneumococci and he named this substance as CRP[5].Semi quantitative analysis of CRP has been used as acute phase reactant and disease activity of many of the clinical conditions In the last couple of years there has been increased emergence in interest of structure and function of CRP, and with discovery of sensitive and specific tests, the estimation of CRP levels is useful in many of the scenarios, including ischemic stroke. In patients who were diagnosed with acute myocardial infarction or any coronary syndromes CRP an acute phase reactant was found to be elevated[6,7]. It has been reported that levels of C-reactive protein is directly related to severity and presence of coronary vessel thickening and are predictors of coronary events and mortality in patients with acute coronary syndromes[8,9]. Recently CRP was shown to be a predictor and risk for the future acute coronary events, stroke

and coronary heart disease death in apparently healthy persons[10,11].

This predictive capacity of the CRP levels warrants further evaluation. A feature of most forms of inflammation, infection and tissue damage is the increase in the circulating concentrations of various plasma proteins known as acute phase reactants[12].

These reactants are mainly produced by hepatocytes, and the increased expression of these acute phase protein genes is derived by cytokines, which are produced by activated macrophages and other cells[13]. "During inflammation, the plasma concentrations of CRP can rise by up to 10,000 folds[14].

The concentration of CRP level is determined only by its production rate[15], depends on cytokines and mediators that reach the hepatocytes. Thus, plasma CRP levels are indicator of inflammatory activity in the body as they increase cytokine levels.

Therefore, measurement of CRP enables low grade inflammation, which is usually not able to detect without invasive procedures. CRP levels indicate presence and severity of atherosclerotic changes in the cerebral, peripheral and the coronary circulation[16]

Structure and synthesis of C-reactive protein

CRP is being synthesized by liver cells called hepatocytes[17]. It is present in traces in the plasma. The normal range of C-reactive protein in healthy adults is less than 10mg/L and this is present in about 99 % of the individuals and levels as low as 0.07mg/L has been obtained in them. Normal levels are usually between 0.3-1.7mg/dl[18].

CRP will increase within aa few hours of the onset of the infection or inflammatory process[19], This increase in the CRP is due to the mediators of humoral

immunity that is endogenous pyrogen[20] and prostaglandin mediator PGE[21]. The CRP levels reach maximum within 24-48 hours.

CRP belongs to the pentraxin family of proteins with having a molecular weight of 1,05,500. Its structure is made of non-glycosylated polypeptide subunits which is arranged in shape of disc with cyclical and pentamer structure[22]. This arrangement of the sequence of amino acid are unique from all other known proteins, with serum amyloid P component being the exception[22],[23].

Along with the reaction with the pneumococcal C- polysaccharide which was responsible for its discoverey, CRP forms calcium dependent binding to cholinephosphatides such as sphingomyelin, lecithin, lysolecithin to other lipids which doesn't have phosphoryl choline (PC), to PC-containing and non-PC containing microbial polysaccharides and peptide polysaccharides, which are present in parasites, bacteria, fungi and to polyanions and also to dextran sulphate, nucleic acids and heparin. CRP also binds to substance lackingPC, In addition, CRP binds in the absence of calcium ions to polycations, including myelin basic protein, histomers, leucocyte cationic protein and protamine The binding site is different for these polycations compared to PC which have calcium dependent site[24,25.]

Functional structure of CRP:

CRP precipitates soluble ligand, and agglutinates particulate Ligands[24, 26].CRP activates classical complement pathway with c1q being activator. Complement activation progresses and causes precipitation of C4b and C3b, which causes fixation of the C5b-C9, and fixation of C5b-C9 which is the terminal component, causes lysis of cell. CRP opsonize materials for phagocytosis and initate the process of cell damage and inflammatory process Other functions of CRP are:

1. Binds to the T-lymphocyte and cause change in the function[27]
2. Platelet activation and aggregation reaction is supressed[28]
3. Increases the phagocytic activity

However, the above findings have obtained similar results with highly purified CRP, in the laboratories which reported the results or elsewhere[29]. CRP complexed in a suitable way may bind to lymphocyte bearing Fc (Y) receptors (including BT and non-B, non-T cells) both in vivo and in vitro, but the functional significance of this is not known[30,31].

The Role of C - reactive protein in Humans:

The response of C-reactive protein in tissue is not known it may cause inflammation. However, when injected in patients with acute illness causes wheal and flare followed by erythema and edema which is maximum in first 6 hours. cutaneous vasculitis lesions seen chronically in the patients may be due to the contribution of deposition of the CRP locally in the vessels[32].

CRP is known as a pathogenic factor in various inflammatory conditions in which levels are elevated The function of CRP is early recognition of the underlying inflammatory condition caused by the microorganism.

CRP levels will be increased in infectious and non-infectious conditions as it binds to various cell components during tissue damage which are exposed. However, the main role of CRP, for which it has been conserved and evolved, was to recognize in the plasma the potentially toxic materials released from damaged tissues, to bind them, and to help them to detoxify them and/ or facilitate their clearance[33].

Clinical use of CRP levels:

C- reactive protein is a cannot be used for diagnosis because it is nonspecific. C- reactive protein cannot be suppressed by any drugs unless the inflammatory response is suppressed which is provoked by the underlying pathologic process.

C- reactive protein is an indicator of the disease and its severity and the response after the therapy.

C-reactive protein when tested clinically when combined with the clinical history, examination and laboratory results when tested in different conditions gives valuable information[18].

It can be used for:

1. Screening for organic diseases: CRP production is sensitive index of organic diseases and raised CRP is unequivocal evidence of the active disease.
2. To monitor activity and extent of disease: it needs measurement of the levels continuously with multiple values
3. Detection and management of intercurrent infection: with treatment with antibiotics C-reactive protein should decrease if elevated persisantly indicates persisting infection.

Testing of C-reactive protein gives accurate information regarding the changes in the clinical examination and functioning of the organs which is difficult with other objective tests[18].

Elevated C-reactive protein is seen in following scenarios

I. Infection such as Rheumatic fever
II. Allergic complications of infection: Erythema nodosum leprosum
III. Inflammatory diseases: various connective tissue and autoimmune diseases
IV. Allograft rejection: Renal transplantation

V. Malignant neoplasia: Lymphoma leukemia, Hodgkin', carcinoma, Sarcoma

VI. Necrosis: Myocardial infarction Tumor embolization Acute pancreatitis

VII. Trauma : Surgery, Burns, Fractures[18] minor levels of C - reactive protein elevated in following condition:

- Systemic lupus erythematosus
- Systemic sclerosis
- Dermatomyositis
- Ulcerative colitis
- Leukemia
- Graft versus host disease (GVHA)[18].

ISCHEMIC STROKE

"Stroke is defined as rapidly developing clinical symptoms and/ or signs of focal, at times global loss of brain function, with symptoms lasting for more than 24 hours or leading to death, with no apparent cause other than that of vascular origin (WHO)"[34]. There is a wide range of severity, from recovery in a few days, through persistent disability, to death.

About 80 % of the cerebrovascular disease are due to cerebral vessels ischemia,10% due to primary hemorrhage and 5% constituted by subarachnoid hemorrhage and in the remainder there is uncertainty[35].

After coronary heart disease and all cancers, stroke is the third most common cause of death in the world causing about 4 million deaths, three-quarters of them in developing countries[36].

- Incidence of first ever stroke varies from 13 per lakh per year to 27 per lakh per year[34].
- Prevalence of stroke is around 84 per lakh[34].
- Stroke mortality in India is estimated to be about 73 per lakh population[34].

The Blood Supply to the Brain[37]:

Brain receives 20% of the cardiac output and is 2% body weight. The blood supply is delivered by the two internal carotid and two vertebral arteries, which anastomose at the basal part of the brain

The internal carotid artery starts forms carotid sinus at the level of thyroid cartilage, which doesn't give any branch in neck it passes via foramen lacerum and traverse petrous bone through carotid canal. It bifurcates into middle cerebral and anterior cerebral artery.

The eye and the orbit is supplied by ophthalmic artery which is the first branch. The posterior communicating artery joins posterior cerebral artery which forms the circle of Willis The anterior choroidal artery supplies internal capsule, thalamus, midbrain, temporal lobe medial part, lateral geniculate body.

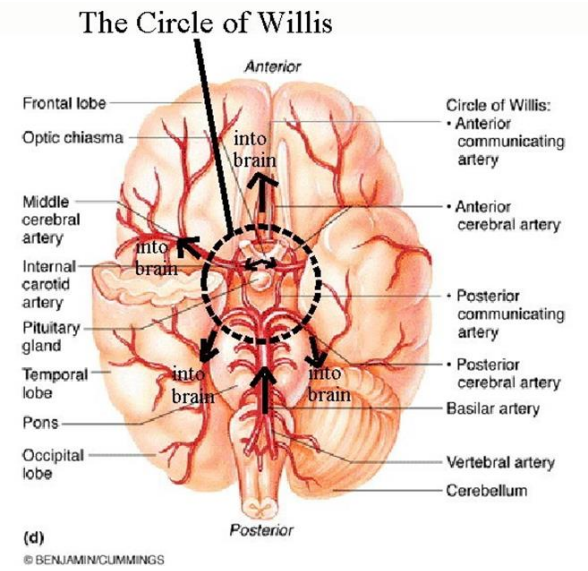
The anterior cerebral artery anastomoses with the other side through anterior communicating artery supplies anterior and medial side of cerebrum. The middle cerebral artery supplies the lateral part of cerebrum. Lenticulo striate arteries and arterioles from main branch supply basal ganglia and internal capsule.

The vertebral artery passes via transverse foramina of the sixth to second cervical vertebrae, which gives various branches to muscle. It then travels through process of the atlas to reach skull Via foramen magnum. It then forms basilar artery by joining with the opposite side on the ventral aspect of brain.

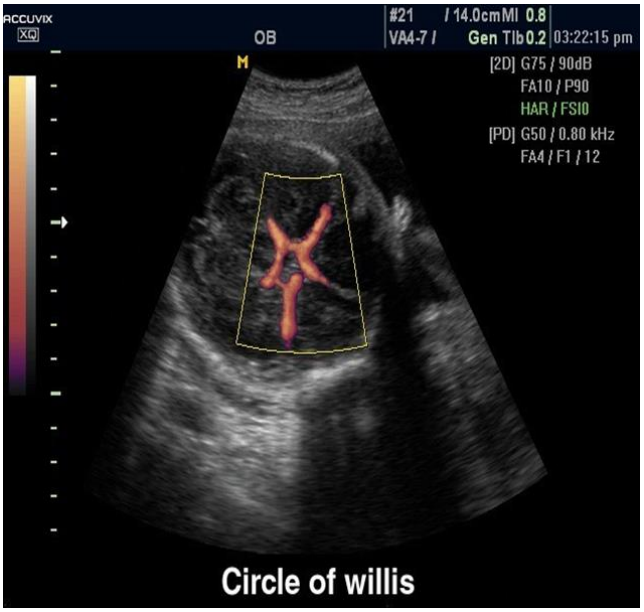
The vertebral artery gives branches such as posterior inferior cerebellar artery, anterior and posterior spinal artery, and various penetrating arteries which supply medulla. The basilar artery branches are posterior cerebellar artery supply temporal lobe inferior part, occipital lobe, small perforating branch from this supply midbrain, thalamus and hypothalamus. second branch anterior inferior cerebellar artery supply brainstem, cerebellum rostrum part. Third branch superior cerebellar artery supplies superior cerebellum and vermis. Various small branches penetrate cerebellum and brainstem.

Venous Drainage:

In general, venous blood flow from both superficial and deep system enter to the dural venous sinuses then into internal jugular veins. The cerebral veins are thin walled, have no valves. There are connections between dural and cerebral venous sinuses, so helping the propagation of thrombus or spread of infection between those vessels.



Ultrasound Brain Doppler Showing Circle of Willis



The Cerebral blood flow regulation:

In normal humans cerebral blood flow is about 50 ml/ 100 gms of brain per minute. It is very much influenced by small changes in PaCO2.Cerebral blood flow is inversely related to whole blood viscosity[37]. The whole blood viscosity depends non plasma fibrinogen, platelet aggregation, red cell aggregation etc.[38]. Increase in the regional functional activity of the brain increases the blood supply.

Autoregulation is damaged following damage to brain and it follows perfusion pressure[39]. Autoregulation is impaired of and the PaCO2 is very high and also in the elderly[40]

Pathophysiology of Acute Cerebral Ischemia:

The sequel of Ischemia:

The brain depends on glucose for energy. Fall in the cerebral blood flow cause decrease in the glucose supply to brain which causes ischemic, a series of metabolic changes occur to supply energy before cell death (infarction).

Various mechanism causes cell death which is reversible and loss of function of these cells and various different mechanisms cause death of the endothelial cells, glial cells and neurons and cells of grey and white matter[41,42.]

When CBF falls below about 20 ml/ 100 g brain / min, the oxygen delivery is maximal[43]. The EEG halters, evoked responses disappear and the neurological signs appear. If it is restored, functional recovery is still be possible.

With impairment in protein synthesis is the first change followed by the anaerobic metabolism of glucose, which causes a rise in the lactate production, fall in pH both inside and outside the cell and abnormality in phosphocreatine and ATP synthesis and so energy not generated in the cells.

As the flow falls further the energy dependent functions of the cell

membranes, sodium and chloride enter the cell, calcium also enters and which is cytotoxic and potassium leaks out.

Cellular transport mechanisms and neurotransmitter systems fails, potentially neurotoxic excitatory transmitters, such as glutamate and aspartate, are released from neurons into extracellular space, free oxygen radicals, nitric oxide and lipid peroxides are formed, which damages cell further; proteases are activated and lyse structural proteins, and neurons release platelet activating factor, which may be then neurotoxic[44].

At flows below about 10 ml/100 g brain/ min infarction occurs, and even if flow is then restored, function does not recover.

Later on apoptosis rather than necrosis may be then responsible for neuronal death[45].

The results of decrease in the CBF depend both on the duration and depth of the ischemic insult. When ischemia is due to the occluded artery, flow is almost never reduced to zero because of availability of some sort of collateral blood supply, which is therefore, a further factor on determining the metabolic consequences.

The local CBF may also be influenced by development of the cerebral edema and raised intracranial pressure, acid metabolites and increasing the extracellular potassium concentration, which cause the vasodilatation, the release of vasoconstrictor prostaglandins from aggregating platelets and damaged cell membranes and of other vasoconstrictors such as endothelin-1, whole blood viscosity, accumulation of leucocytes, aggregation of formed elements of blood in the sluggish microcirculation and eventually thrombosis and local ability of the ischemic tissue to auto regulate, which will then be impaired.

The ischemic penumbra:

Around, and presumably as islands around infarcted brain, there is an ischemic penumbra[46].

It is an area of "viable tissue" with decreased blood supply The tissue may die or survive which depends on restoration of the blood flow Hence any intervention done during this time may help in restoring of flow and prevent neuronal death or loss of neuron which occurs after stroke

Ischemic Cerebral Edema:

Cerebral ischemia causes cerebral edema in addition to reversible and irreversible loss of the cerebral functions[47].

It is both cytotoxic and vasogenic. cytotoxic affects grey matter and starts early which causes intravasation of water into cells.

Vasogenic edema affects white matter starts later and extravasation of fluid Ischemic cerebral edema is seen in CT in case of large infarcts Reperfusion, 2 hours after the stroke onset, can exacerbate edema[48].

Secondary Insults:

Damaged brain may have the impaired autoregulation. This makes brain very sensitive to any further insults, such as increased intracranial pressure, hypotension, hypoxia[49]. Hyperglycemia is associated with the poor outcome after stroke, because of consequences of the ischemia is exacerbated in presence of high blood glucose concentration, mediated by the excess lactate production[50].

Fever is associated with a worse outcome and hypothermia with a better outcome in the stroke. Dehydration, increasing hematocrit and raised whole-blood viscosity are the potential exacerbating factors.

Diaschiasis:

Cerebral injury in remote areas is called diaschiasis. In practice, the phenomenon is easy to demonstrate in the cerebellum contralateral to the large MCA territory infarct, but more difficult to show the convincingly in the contralateral cerebral hemisphere or in other parts of the ipsilateral cerebral hemisphere, which appear to be unaffected on CT, even on MRI[51]. The functional consequences, if any, of such metabolic and flow changes of the distance from the primary lesion are not at all clear[52].

Risk Factors for Ischemic Stroke:

1. **Age**: It is risk factor which has strong association for stroke. Stroke in People aged 75-84 is about 25 times Most in people aged 45-54[53].
2. **Sex**: there is a small increase no of males, which is most prominent in the middle to old age, decrease in the very elderly and in the young[53].
3. **Blood pressure**: increasing blood pressure has major effect on the incidence of the stroke and the risk of the recurrent stroke in future[54].

The relationship between blood pressure during diastole in stroke is 'log linear' all throughout in normal range with no evidence of threshold value [55].

The risk of blood pressure with sex is similar in males and females, at all values and doubles with 7.5 mm Hg increase in diastolic blood pressure in western populations, and with each 5 mm Hg in Japanese and Chinese populations[56,57.] systolic blood pressure is having stronger relation, and presence of 'isolated', systolic hypertension has increased risk[58,59,60]. The blood pressure/ stroke association is so constant that the treatment of hypertension reduces stroke risk[61,62].

Hypertension is considered as a causal risk factor, at least for strokes in the general. For mild hypertension the population attributable risk is not only greater as

compared to severe hypertension, because it is so prevalent in the population at large, it is greater than any of the other risk factor.

Hypertension increases the prevalence of small vessel disease in the brain [67] and also increases the risk of atheroma[63,64,66,] formation and incidence of stroke.

4. **Smoking**: Males and females are equally affected, and there is an association with the passive smoking[68,69.]

   Ex-smokers have the sustained excess risk for some years[68].

   Smoking has been correlated to the extent of the atherosclerotic changes which is confirmed by ultrasound[66,70] and in identical twins discordant for the smoking[71].

5. **Blood Lipids**: The relationship between blood lipids and stroke is much weaker than that for the coronary artery disease[72,73] but for serum lipoprotein (a) is predictive[74]. Association exists between the atheroma and blood lipids[65,66]. This contrast between cardiovascular and cerebrovascular disease is unexpected, due to loss of stroke susceptible individuals from the populations by the prior coronary death etc.[57.]

6. **Diabetes Mellitus**: Diabetes has long been recognized as a risk factor for the vascular disease and stroke compared with of non-diabetics[75,76]. Stroke in diabetics are more likely to be fatal[77].

7. **Hemostatic variables**: "Increased fibrinogen by increasing viscosity increases the risk of stroke[78-80]. "Raised plasma factor VII coagulant activity, raised tissue plasminogen activator antigen, low blood fibrinolytic activity, and raised Von Willebrand factor are all risk factors for stroke[81,82.]

8. **Hematocri**t: Increasing hematocrit is a risk factor for the stroke confounded by smoking, blood pressure and plasma fibrinogen[83].

9. **Atrial fibrillation**: The most frequent potential cardiac source of embolism to the brain is atrial fibrillation by virtue of clot forming in the left atrium and its appendage[84-88.] Within the fibrillating population, individuals at particularly high risk of the stroke is those with a previous embolic event, increasing age, hypertension, diabetes, left ventricular dysfunction and enlarged left atrium[89,90,91].
10. Sex Hormones: Oral contraceptives about triple the risk of ischemic stroke, with no excess risk in theex-users[92-94]. Oral contraceptive users who are also carriers of mutations causing thrombophilia are likely to be affected by intracranial venous thrombosis[95].
11. Alcohol: Modest consumption of alcohol might be protective for ischemic stroke[96,98.] Confusion arises because any effect on stroke is due to alcohol per se or due to the type of the alcohol beverage, different patterns of drinking behavior may have the different effects; It is difficult to distinguish any casual pathway from alcohol consumption to stroke, because alcohol almost certainly raises the blood pressure [98]affects blood lipids[101] can cause atrial fibrillation and cardiomyopathy.[99-100],
12. **Obesity**: Risk of atherosclerotic vascular disease in men and women is greater in obese, particularly if the weight has been gained in middle age or has fluctuated substantially[102,103]. The higher risk of stroke in obese may be mediated by associated hypertension and diabetes[83,104,105.]
13. **Diet**: Omega-3 polyunsaturated fatty acids[106-108] and less saturated fatty acids consumption may reduce stroke risk. Excessive salt intake may increase blood pressure and increase stroke risk[109,110.] High intake of potassium reduces the stroke risk by lowering blood pressure[111,112.] Deficiency of antioxidant rich

food, which protect the arterial intima from oxidative damage to DNA and lipoproteins[113,114.]

14. **Exercise**: reduces the cholesterol levels, risk of diabetes, blood pressure. Thus absence of exercise is associated with stroke [115],[116,117].
15. **Homocysteinemia**: Homozygous patients with inherited deficiency of cystathionine synthesis develops severe homocysteinemia and homocystinuria and a tendency of venous and arterial thrombosis. Heterozygotes have modestly elevated levels of the blood homocysteine predisposing for ischemic stroke[118,119.]
16. **Non-stroke vascular diseases:**
    a. **Coronary artery diseases**: Independent of age, coronary artery disease is clearly associated with ischemic stroke[58,86,120-123.] There is correlation between coronary artery disease and carotid artery stenosis in ultrasound studies[124]. ECG abnormalities, left ventricular hypertrophy, cardiac failure reflecting coronary artery disease or hypertension is associated with stroke[58,122.]
    b. Claudicants and patients with the asymptomatic peripheral vascular disease are at excess risk of stroke[88,125.]
    c. **Carotid and supraclavicular arterial bruits**: due to stenosis are risk factors for subsequent stroke. The risk of stroke increases with severity of the stenosis and also with the progression of stenosis[126].
    d. **Transient ischemic attacks**: Increase stroke risk by 5-10 times than that of a non- TIA patient of the same age.
17. **Genetic Factors**: Which cause familial strokes[127] include vascular anomalies, connective tissue disorders like Ehler- Danlos syndrome, pseudoxanthoma

elasticum, Marfan's syndrome, fibromuscular dysplasia, mitral leaflet prolapses, hematological diseases like sickle cell disease/ trait, antithrombin III deficiency, protein C deficiency, activated protein C resistance, protein S deficiency, plasminogen abnormality/ deficiency, dysfibrinogenemia, familial hypercholesterolemia; cerebral amyloid angiopathy; homocysteinemia, fabry's disease, cardiac myxoma, cardiomyopathy, mitochondrial cytopathy, cerebral autosomal leukoencephalopathy. Paternal history of stroke is a risk factor[128].

The Causes of Ischemic Stroke:

Cerebral ischemia and infarction are usually caused by cutoff of the blood supply to the brain due to the occlusion of the arteries supplying the brain or due to the stenosis of the vessels

1. Atherothromboembolism:

Atheroma is most common arterial disorder and is most common cause of cerebral ischemia and infarction. Distribution of Atheroma: Atheroma is present in the area of tortusity of veesels and large and medium arteries which are site for hemodynamic stress, trauma, blood stagnation and accumulation of platelets; and of turbulence, all of which cause the thrombosis[129].

Natural history of atheroma:

Atheroma starts in the childhood[130]. Intimal fatty streaks appear first. In a general gradual process, circulating macrophages adhere to the arterial wall, which cause inflammatory response with T- lymphocyte activation, intra and later extra-cellular cholesterol and other lipids are deposited, particularly in the macrophages, which are then described as foam cells, smooth muscle cells proliferate and fibrosis occurs and so the fibro lipid plaques are formed[131,132.]

The atheromatous plaque becomes unstable as it progresses due to cracking of the

fibrous cap or due to bleeding within the plaque or due to ulceration[133,134.]

Any of above event expose unstable plaque which may Cause the thrombus to form and to embolize.

2. Cholesterol embolization syndrome:

This disorder seems to be due to the rupture of atheromatous plaques in elderly people with widespread disease, either spontaneous but perhaps more often as a result of complication of instrumentation or surgery of large atheromatous arteries such as the aorta and possibly the therapeutic due to thrombolysis[135].

3. small vessel disease:

The branches of the cerebral arteries do not have a good collaterals.so occlusion cause infarction in smaller territory supplied. Such 'lacunar' infarcts comprise about one-quarter of first ischemic strokes[136,137]. "Hypertension is common in patients with lacunar infarction[138,139.]

4. Rare arterial disorders causing ischemic stroke:

- Trauma – penetrating and non-penetrating.
- Fibromuscular dysplasia, congenital anomalies, Moya Moya syndrome.
- Inflammatory vascular disease like giant-cell arteritis, SLE, antiphospholipid antibody syndrome etc.
- Progressive systemic sclerosis.
- Burger's disease
- Irradiation.

5. Embolism from the heart:

In developed countries, about 20% of strokes are due to The embolism most common source of this is by the heart and is usually non rheumatic. Emboli vary in their composition from mostly fibrin to then mostly platelets to calcium, tumor or

infected vegetation. The emboli also vary in size so they may then impact in a medium-sized artery to cause a substantial infarct or in a smaller artery to cause merely a restricted defect. Some emboli may be completely be then asymptomatic[140].

Rheumatic valvular disease:

Mitral far more often than aortic, is well recognized as an embolic source, either because of thrombus in the left atrium or valvular debris[141].

Coronary artery disease:

mural thrombus in the heart in patients occurred within days of myocardial infarction and were common in patient who had anterior infarction and patient who had larger infarcts factors[142]. These thrombi may embolize, particularly if the protruding or mobile and these are associated with risk of stroke which is 5 times more in the first few days acute coronary event[143].

Mitral Leaflet Prolapse (MLP):

Common in persons who are tall and thin and is sometimes familial. It can be worsened by left atrial thrombus, lesions of the valves, atrial fibrillation which causes embolism to the brain[144].

Paradoxical Embolism:

From the venous system is a well-accepted mechanism of ischemic stroke, based on a number of convincing cases described at postmortem. The risk of recurrent stroke is very uncertain but probably not particularly high[145].

Diseases of the aortic and mitral valve.

Sinoatrial disease (sick – sinus syndrome)

Infective endocarditis.

Leukemia

Sickle cell disease

Paroxysmal nocturnal hemoglobinuria

Disseminated intravascular coagulation (DIC)

Thrombotic thrombocytopenic purpura (TTP).

Imaging in Stroke[34]:

The main aims of imaging are:

1. To determine the location and extent of the brain damage.

2. To differentiate between hemorrhagic from ischemic infarct.

3. To assess current or any impending herniation

4. To find out the cause of stroke.

The available modalities of Computed Tomography (CT), Magnetic Resonance Imaging (MRI) have their own advantages and disadvantages in the evaluation of stroke.

Imaging is the most supplementary examination in stroke because the diagnostic specificity is increased to over 80% with the imaging modalities, however, 20% of clinically diagnosed strokes are not seen by the usual imaging studies.

Ischemic Cerebrovascular Accident:

Acute infarcts are more frequently visible on MRI than on CT scans. On admission approximately 90% of the MRI scans are positive as compared to 60% of CT scans.

Computed Tomographic Scan:

The CT scan appearance of cerebral infarction is time dependent. Although the findings may be detected within 6 to 8 hours of the onset, the CT may be normal up to 24 hours. The earliest findings on CT scan may be sudden loss of grey-white matter contrast and effacement of the adjacent subarachnoid spaces. However, by 24 hours abnormal low attenuated area becomes obvious. The early findings on non- contrast

CT are the result of development of cytotoxic edema. The mass effect and decreased attenuation increases due to combination of cytotoxic and the vasogenic edema. At 10 to 21 days, the edema and the mass effect of the infarction begins to subside with the invasion of microglial cells, both of which may make the infarcted area isodense to normal brain on plain scans called 'fogging effect'.

When the lesion is about 21 days old, the edema has completely subsided and microglial cells have reabsorbed necrotic tissue and this tissue is replaced by the extracellular fluid and bridging glial fibers.

The plain CT will show a well-defined lucency involving both cortex and the white matter.

On post contrast scans the enhancement rarely occurs 24 to 48 hours after the onset of the disease, but is usually begins 3 to 6 days later. The amount and degree of the enhancement increases to its peak at about three weeks. Thereafter the enhancement declines and is usually absent buy 3 months, but may rarely persist up to 6 months. The enhancement is primarily due to breakdown in the blood-brain barrier although a component may also be from the luxury perfusion. The enhancement pattern is classically gyriform however, more solid ring like or the enhancement patterns may be seen.

CT in cerebral infarction:

Hyper acute infarct (<12 hours): Normal in large cases around 50%, hyper dense area may be seen in about few cases Acute (12 to 24 hours): Low density areas, loss of grey- white matter differentiation, sulcal effacement.

1 to 3 days: low density involving both grey and white matter.

4 to 7 days: mass effect and edema may be seen and sulci and gyri are enhancing.

1 to 8 weeks: mass effect is absent, chronic enhancement as hyper intensity is present

Months to years: Encephalomalacic change, volume loss

MATERIALS AND METHODS

The study "C Reactive protein in acute ischemic stroke" was conducted in Shri B M Patil Medical college Vijayapura, during the period from October 2017 to July 2019.

The study was done with the following aims.

1. To study Plasma CRP levels in acute ischemic stroke.

2. To evaluate the role of CRP in acute ischemic stroke

Selection of cases: The study was done in patients admitted and diagnosed with acute ischemic stroke in Shri B M Patil Medical college

Period of Study: From October 2017 to July 2019.

Sample Size: 60 patients who were age and sex matched among cases and controls admitted in Shri B M Patil Medical college

Study subjects: 60 cases of acute ischemic stroke admitted during the period of December 2017 to July 2019 Controls: 60 controls will be selected from the patients admitted in hospital, which were compared with study subjects in all factors except the disease under study.

Inclusion criteria:

1. Male and Female patients of 20-80yrs of age
2. CT scan show ischemia

Exclusion Criteria:

1. Other than age in inclusion criteria i.e. age <20yrs or >80yrs
2. Patients with history of cardiac disease such as myocardial ischemia, myocarditis and valvular heart disease
3. Any patient with previously diagnosed with TIA or stroke
4. Any patient having autoimmune disease, collagen vascular diseases

5. Patients with history of hemorrhage, tumors
6. Patient with RTA and head injury
7. Patients whose CT scan is normal
8. Patients with CNS infection that can alter the values of CRP.

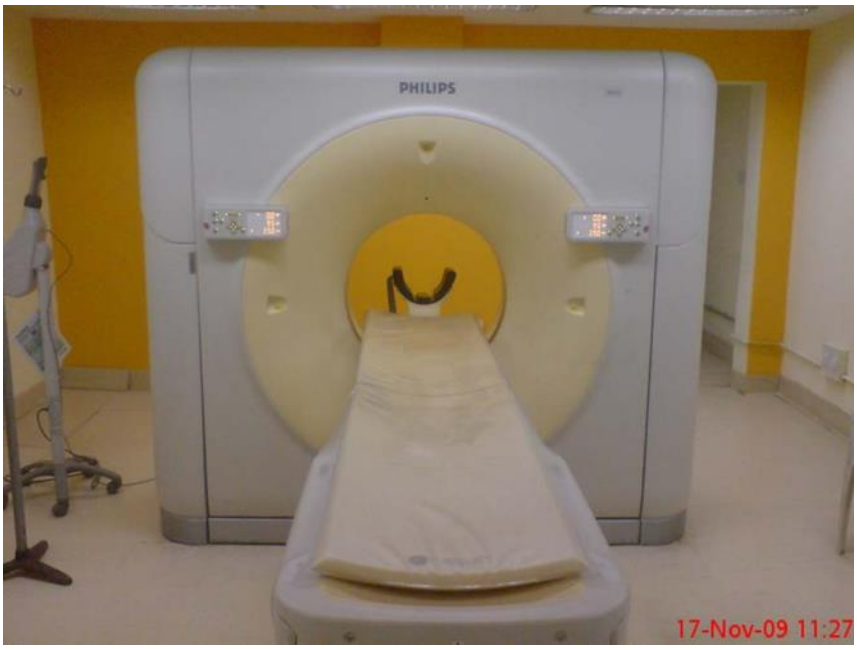
Protocol of the study:

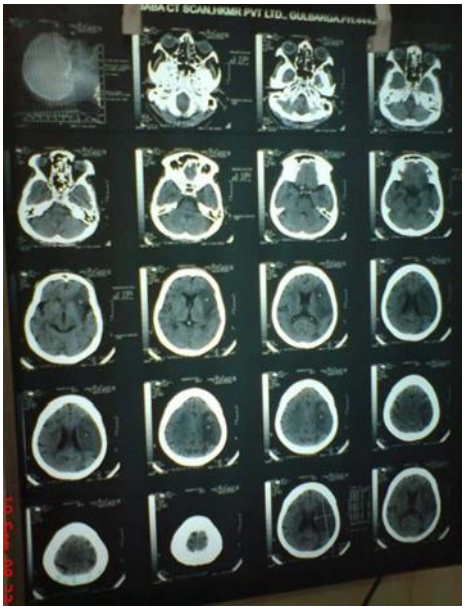
History was taken from patient and the attenders and important history regarding onset, duration of weakness any slurring of speech, deviation of angle of mouth any associated history of headache, vomiting, convulsions was taken.

- Past history regarding the presence of risk factors of the diabetes and hypertension in the past was taken
- Personal history related to addictive habits was also taken. Examination done according to proforma

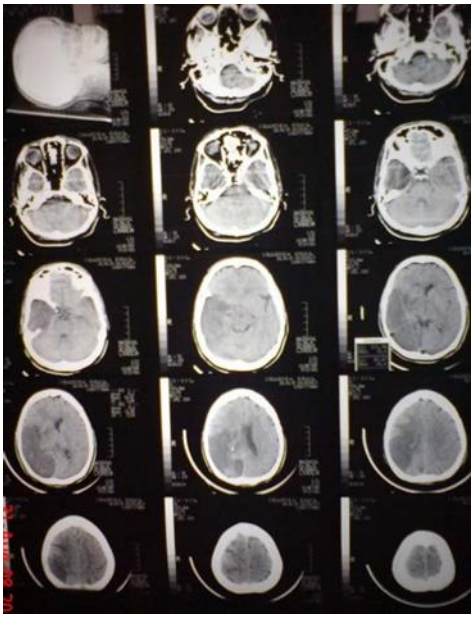
All the routine investigation including the complete blood counts, renal profile, urine routine, chest X-ray and ECG done. CT scan was done at the time of the admission to hospital and C-reactive protein levels were done on admission.

CT Scan Machine





Ct Scan Brain Showing Large infarct (7 x 4 cm) in the left Parietal Cortex



CT Scan Brain Showing Infarct in the Left Temporoparietal Region

Biochemical parameters:

Lipid profile: After overnight fasting of 12 hours blood collected in the morning about 5 ml and then serum centrifuged and kept for analysis.

Serum cholesterol estimation: The enzymatic colorimetric test was used.

Test principle:

1. Cholesterol ester + H2O + esterase Cholesterol RCOOH
2. Cholesterol + O2A4 Cholesterol + H2O2
3. 2H2O2 + 4 amino phenazone + 4p-benzoquinone – mono phenol amino phenazone Measured by colorimeter

Serum HDL Cholesterol (Phosphotungustate precipitation method): Chylomicron, VLDL and LDL are precipitated using phosphotungstic acid and Mg ions to the serum sample. The supernatant contains only HDL detected using THECHOD-PAP method.

Serum Triglyceride Estimation: Serum triglyceride estimation is done using GPO-PAP method which is an enzymatic colorimetric test.

Serum LDL Estimation: Serum LDL is calculated using Friedl-Walds formula. LDL

cholesterol = Total cholesterol – (HDL +Tg/5)

Routine tests for infection like DC, TLC, urine, chest X-ray, ESR were carried out.

Serum Urea: Serum urea is measured using urease method.

Serum Creatinine: It is measured using alkaline pictrate method.

CRP Estimation: CRP estimation is done using the following VITRIOS chemistry products

VITRIOS CRP slides provided

1FS and 4600 Chemistry Systems

Calibrator kit 7 on VITRIOS 250/350/950/5 and VITRIOS 5600 integrated system text.

Principle:

The CRP test is based on an enzymatic heterogeneous, sandwich immunoassay procedure. phosphoryl choline(PC) is bound to polystyrene beads and the capture agent used in procedure is calcium. Monoclonal anti-CRP antibody bound to horseradish peroxidase (HRP) serve as signal generator. A drop of patient sample is deposited on the slide and is spread CRP binds to PC linked capture beads and anti CRP antibody and form an insoluble complex. Addition of 12microL of VITRIOS Immune fluid to slide removes the material which is not bound. The reflection density is measured after addition of immune-wash fluid at end of incubation 2.The result obtained by the density y of the reflection indicates CRP in sample

Sample: 5 ml of patient blood was collected into the plane vial and centrifuged within 4hrs of collection and plasma separated Reagents

Slide ingredients

Reactive ingredients per cm2

Immobilized phosphoryl choline 0.07mg, mouse anti-CRP antibody labelled with horseradish peroxidase 0.0006u, calcium chloride 0.08mg, and 2-(3,5-dimethoxyl-4-hydroxyphenyl)-4,5- bis(4-dimethylaminophenyl) imidazole(leucodye)0.04mg

Other agents required are crosslinking agent, polymer beads, protein stabilizers, Binders, surfactants, buffers and wash detection dye

Interpretation: The CRP values are expressed as mg/dl

Observation	Conclusion
1. >10mg/dl	positive
2. 1-10mg/dl	negative

Statistics:

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square ($\chi 2$) test was used for association between two categorical variables. The difference of the means of analysis variables between two independent groups was tested by unpaired t test. The difference of the means of analysis variables between more than two independent groups was tested by ANOVA and F test of testing of equality of Variance. ROC analysis for Sensitivity- specificity was done to check relative efficiency. If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office 2007.

RESULTS

Our study was done in Shri. B. M. Patil Medical College Vijayapura during the period of September 2017 to July 2019 and consisted of 60 age and sex matched cases and controls after considering the inclusion and exclusion criteria.

The observations are as follows

TABLE 1: DISTRIBUTION OF AGE BETWEEN CASES AND CONTROLS

AGE (YRS)	CASES		CONTROLS	
	N	%	N	%
21-30	1	1.7%	1	1.7%
31-40	2	3.3%	2	3.3%
41-50	5	8.3%	5	8.3%
51-60	25	41.7%	25	41.7%
61-70	19	31.7%	19	31.7%
>70	8	13.3%	8	13.3%
Total	60	100.0%	60	100.0%

Mean±SD of age 61.6±10.3 years

Table 1 shows the comparison between the cases and controls with respect to age which were matched. Maximum cases of stroke patients were in the age group of 51-60yrs constituted 41 percent of study population. Young patients with stroke was present in only 5% of the cases.

FIGURE 1: DISTRIBUTION OF AGE BETWEEN CASES AND CONTROLS

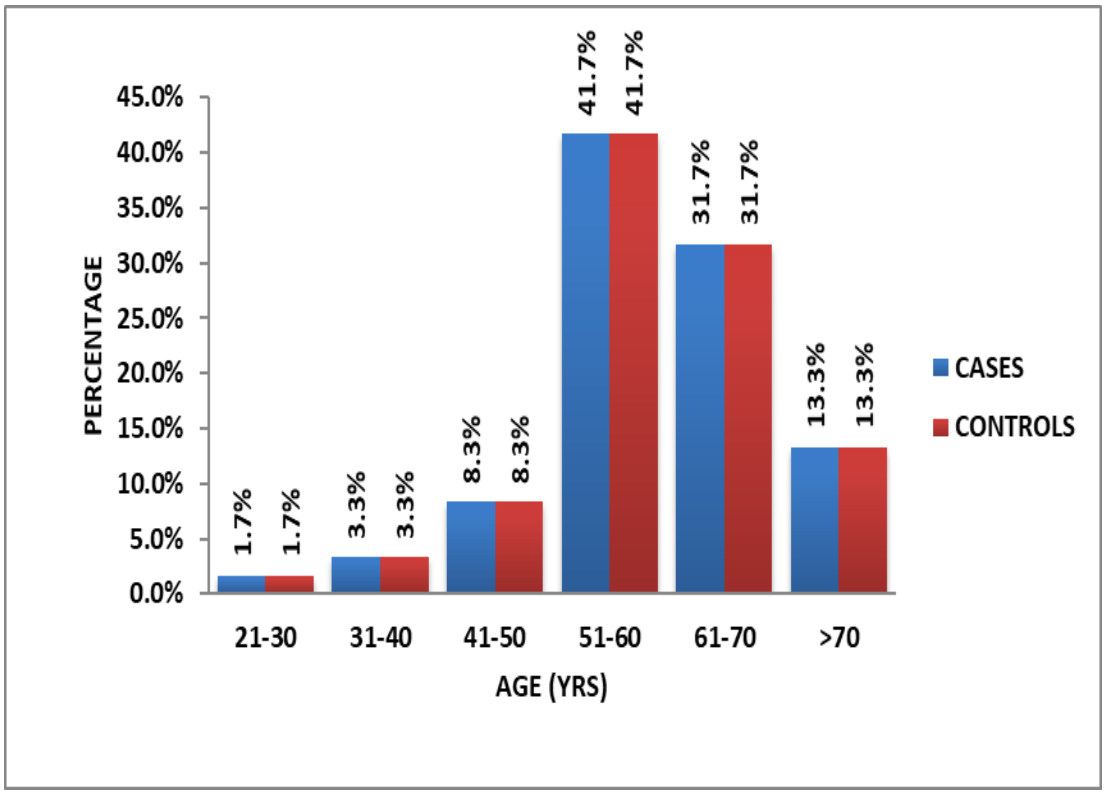


TABLE 2: ASSOCIATION OF AGE AND GENDER AMONG BOTH CASES AND CONTROLS

AGE (YRS)	MALE		FEMALE		p value
	N	%	N	%	
21-30	0	0.0%	1	4.8%	0.394
31-40	2	5.1%	0	0.0%	
41-50	4	10.3%	1	4.8%	
51-60	18	46.2%	7	33.3%	
61-70	11	28.2%	8	38.1%	
>70	4	10.3%	4	19.0%	
Total	39	100.0%	21	100.0%	

Table 2 shows the association of the age and gender among both cases and controls which were age and sex matched. It shows that the maximum thrombotic stroke was in the age group of 51-60yrs accounting for 46 percentage of study population in males i.e. 18 males accounted for cases and occurred maximum in same age group in females i.e. 51-60yrs accounted for 33 percent of the cases i.e. 7 females accounted for cases. stroke in young population was present in only 5 percent in males I.e. only two patients who were in age group of 31-40yrs of age and in female only 1 case was reported in age group of 21-30yrs which accounted for 4.8% of total cases

FIGURE 2: ASSOCIATION OF AGE AND GENDER AMONG BOTH CASES AND CONTROLS

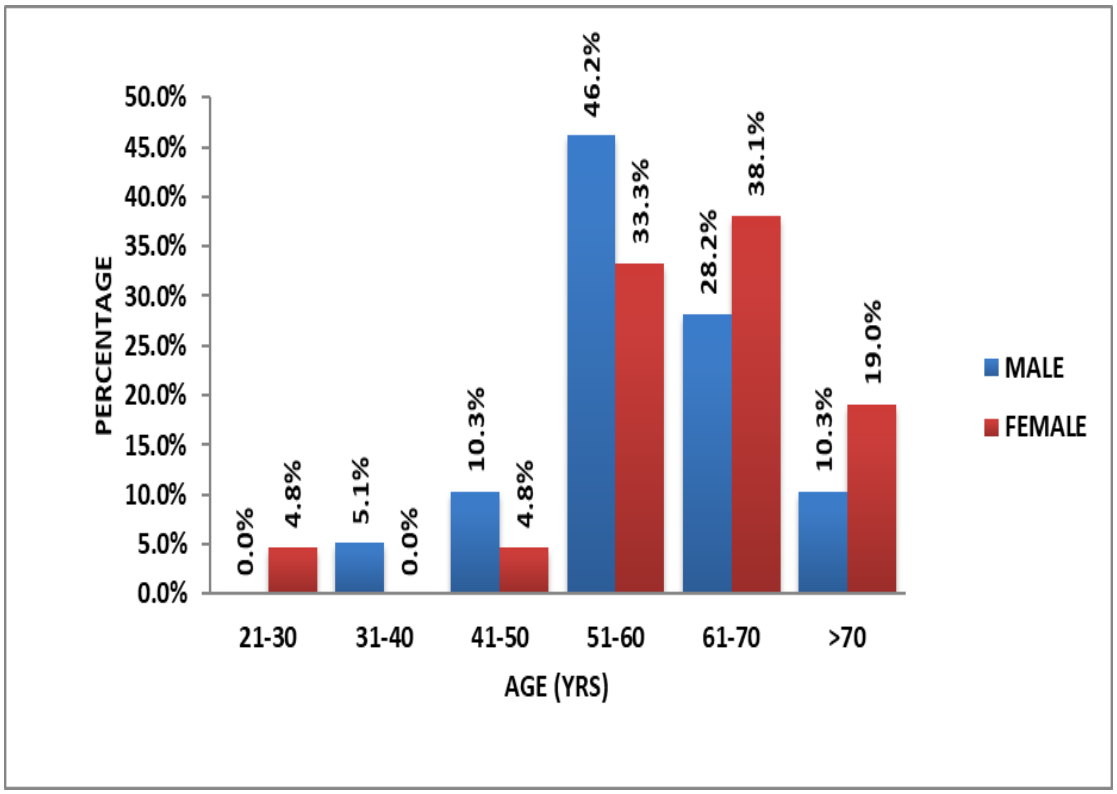


TABLE 3: LEVEL OF CONSCIOUS AMONG CASES

LEVEL OF CONSCIOUS	N	%
ALERT	30	50
COMATOSE	9	15
DROWSY	21	35
TOTAL	60	100

Table 3 shows the level of consciousness among the cases.50 percent of the patient were conscious and alert at the time of presentation while 35 percent were drowsy and 15 percent were comatose

FIGURE 3: LEVEL OF CONSCIOUS AMONG CASES

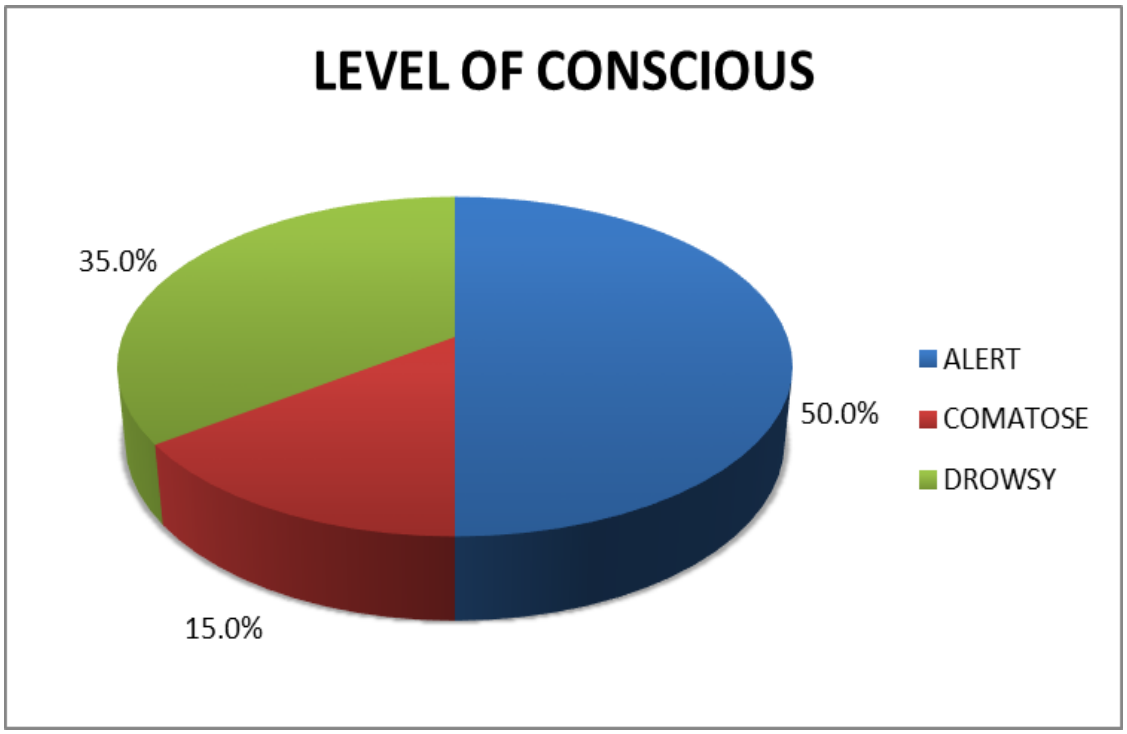


TABLE 4: DISTRIBUTION OF OTHERS COMPLICATIONS AMONG CASES

OTHERS COMPLICATIONS	MALE		FEMALE		TOTAL		p value
	N	%	N	%	N	%	
CONVULSIONS	5	12.8%	4	19.0%	9	15.0%	0.464
HEADACHE	6	15.4%	4	19.0%	10	16.7%	
VOMITING	2	5.1%	1	4.8%	3	5.0%	
NIL	26	66.7%	12	57.1%	38	63.3%	
TOTAL	39	100.0%	21	100.0%	60	100.0%	

Table 4 shows the other complications among the cases convulsion was present in 15 percent of cases. headache was present in 16 percent of cases .5 percent of the patients had vomiting and 60 percent of the cases didn't have the associated complications.

FIGURE 4: DISTRIBUTION OF OTHERS COMPLICATIONS AMONG CASES

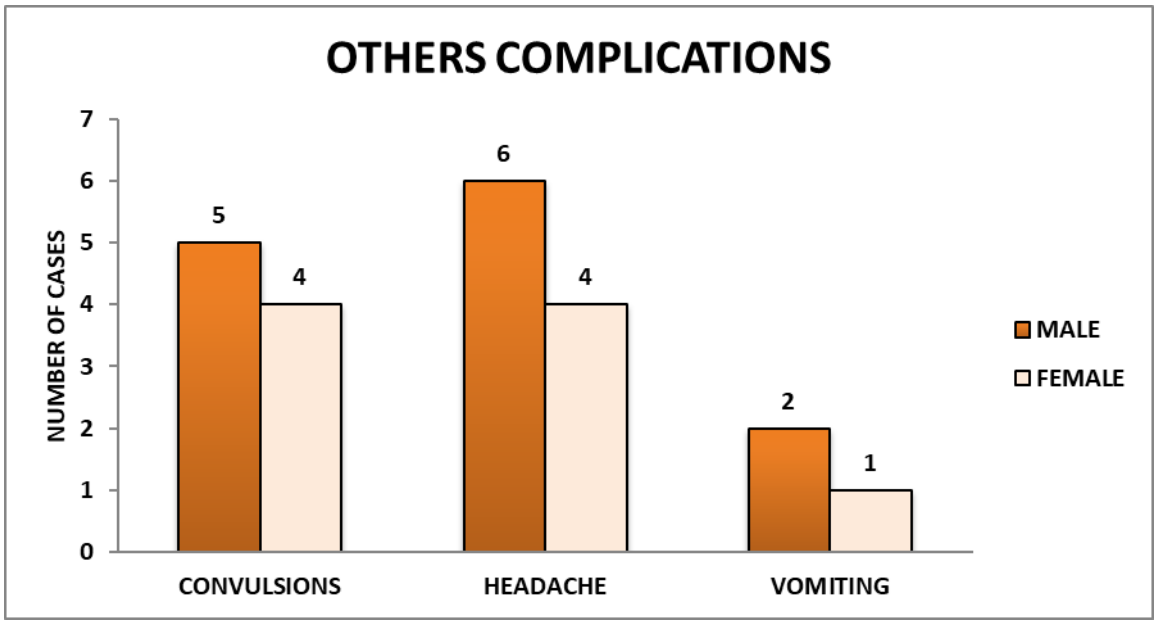


TABLE 5 : MOTOR SYSTEM EXAMINATION AMONG CASES

MOTOR SYSTEM	N	%
L-H	29	48.3
R-H	25	41.7
B/L-H	3	5
LUL PARESIS	2	3.3
RUL PARESIS	1	1.7
TOTAL	60	100

Table 4 shows the pattern of the motor symptoms among the cases.48 percent of the patients had right upper and lower limb hemiplegia and 41 percent of the patient had right upper and lower limb hemiplegia and 5 percent of the patient had bilateral hemiplegia and 3 percent of the patient had only left upper limb monoparesis and 1 percent of the patient had right upper limb monoparesis

FIGURE 5: MOTOR SYSTEM AMONG CASES

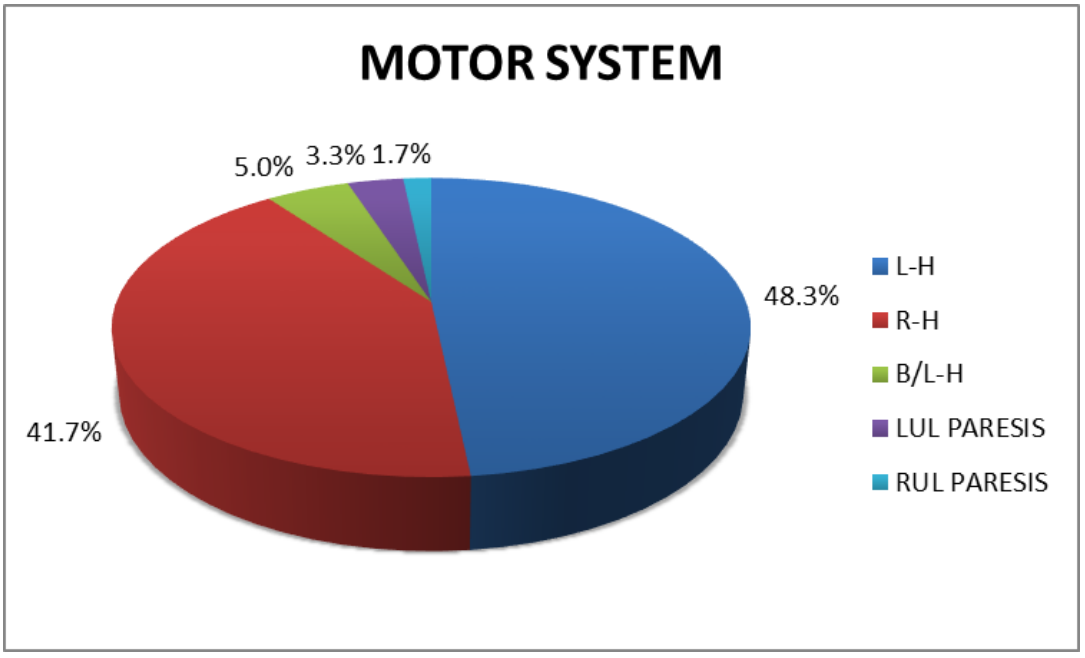


TABLE 6: FOOD HABITS AMONG CASES

FOOD HABITS	N	%
MIXED	33	55
VEG	27	45
TOTAL	60	100

Table 5 shows the food habits among the cases which showed mixed diet among 55 percent of the cases and vegetarian diet among 45 percent of the cases

FIGURE 6: FOOD HABITS AMONG CASES

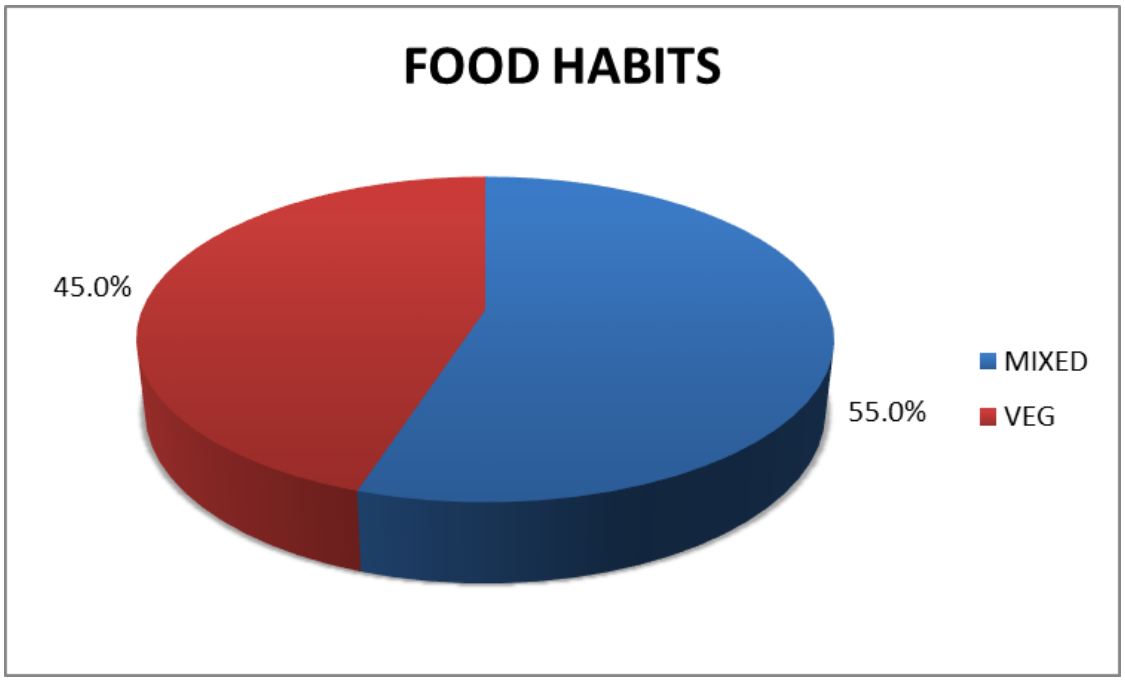


TABLE 7: HABITS AMONG CASES

HABITS	N	%
SMOKING	32	53.3
ALCOHOL	4	6.7
TOBACCO	3	5.0
MULTIPLE	17	28.3
NIL	4	6.7
TOTAL	60	100

Table 7 shows the habits among the cases which showed 53 percent of the cases were smokers and 6 percent of the cases were alcoholic and 5 percent were tobacco chewers and 28 percent of the cases had mixed habits of either smoking and alcohol or smoking, alcohol and tobacco and constituted the majority of the cases and 6.7 percent of the cases didn't have any of the addictive habits.

FIGURE 7: HABITS AMONG CASES

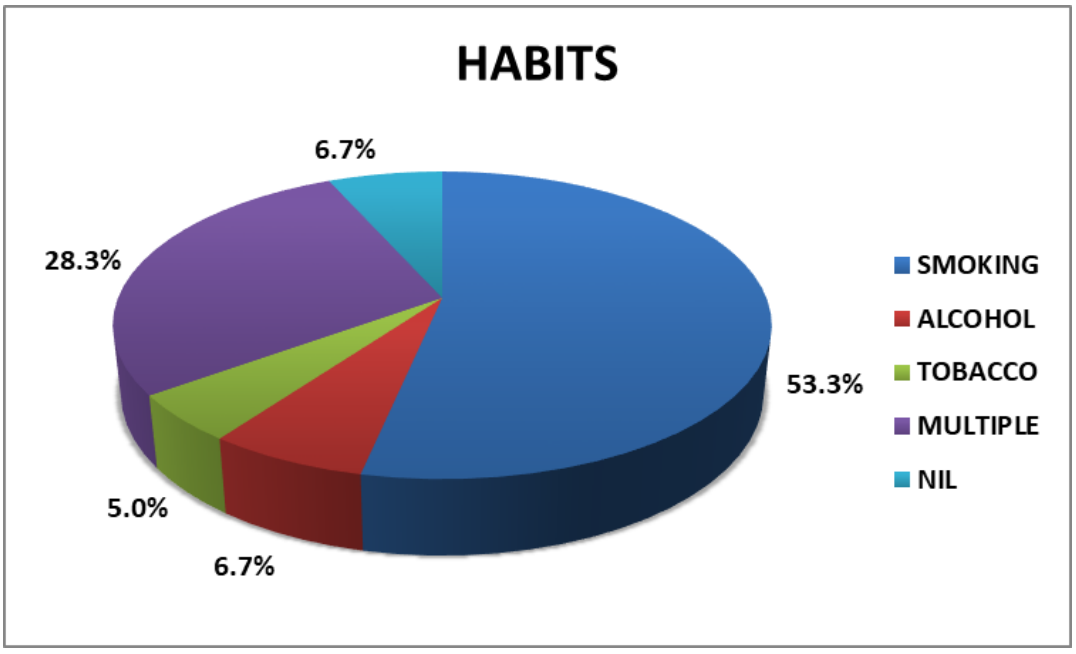


TABLE 8: CVS INVOLVMENT AMONG CASES

CVS	N	%
ECTOPIC	4	6.7
ESM	7	11.7

Table 8 shows the CVS involvement among cases 6 percent of the patient had ectopic and 7 percent of the patient had ejection systolic murmur.

FIGURE 8: CVS INVOLVMENT AMONG CASES

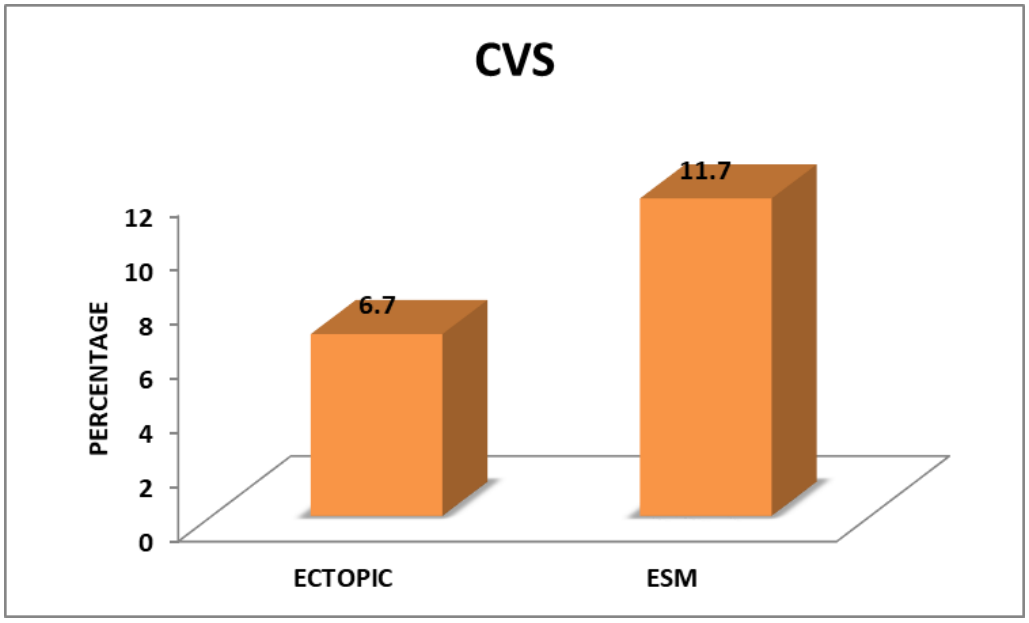


TABLE 9: CRANIAL NERVE INVOLVMENT AMONG CASES

CRANIAL NERVE	N	%
LEFT	1	1.7
RIGHT	6	10

Table 9 shows cranial nerve involvement among cases 10 percent of patient had right seventh nerve palsy and 1 percent of the cases had left seventh nerve palsy

FIGURE 9: CRANIAL NERVE INVOLVMENT AMONG CASES

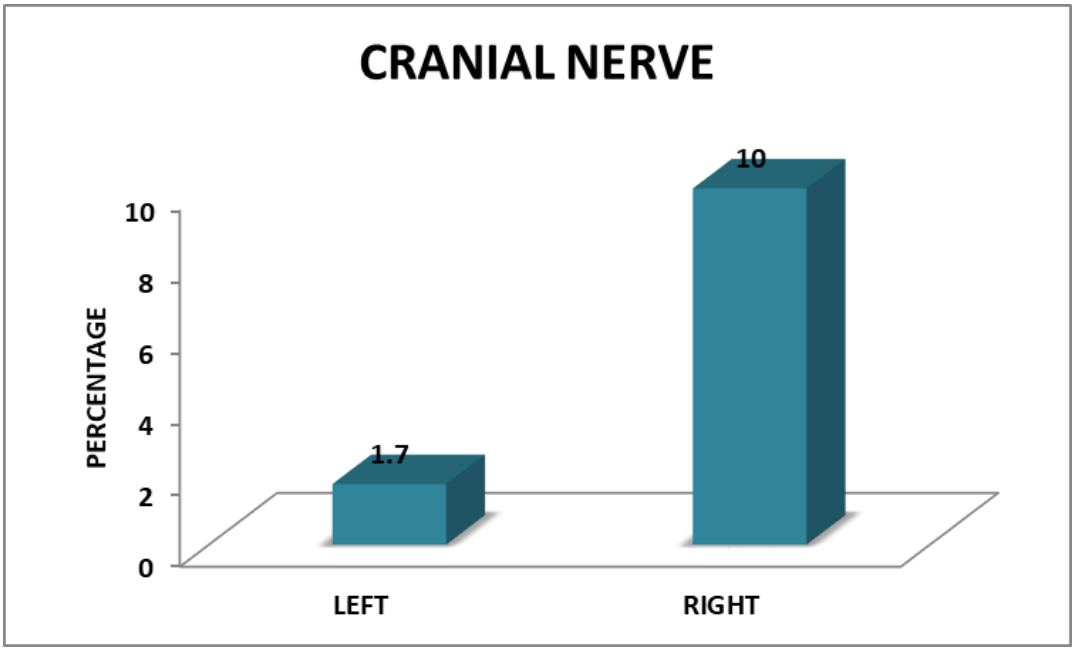


TABLE 10: RISK FACTORS AMONG CASES

RISK FACTORS	N	%
NIL	6	10
HTN	12	20
DM	6	10
BOTH	36	60
TOTAL	60	100

Table 10 shows the risk factors among the cases which shows that hypertension was the risk factor in 20 percent of the cases and diabetes mellitus was risk factor among 10 percent of the cases and majority of the cases that is 60 percent had both diabetes and hypertension as a risk factor for the stroke and 10 percent of the cases in our study did not have any risk factor of diabetes or hypertension.

FIGURE 10: RISK FACTORS AMONG CASES

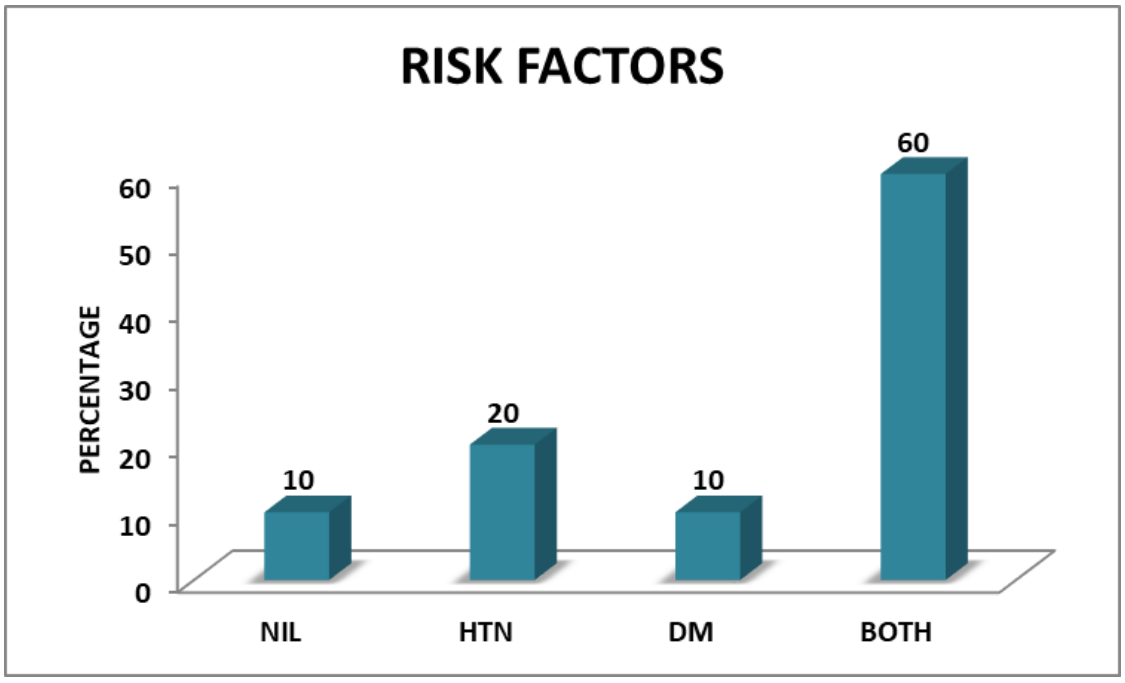


TABLE 11: MEAN BP BETWEEN CASES AND CONTROLS

PARAMETERS	CASES		CONTROLS		t value	p value
	Mean	SD	Mean	SD		
SBP	157.4	25.5	124.6	5.9	9.701	<0.001*
DBP	93.4	13.3	77.5	6.1	8.435	<0.001*

Note: * significant at 5% level of significance (p<0.05)

Table 11 shows the mean blood pressure among the cases and controls the average systolic blood pressure was 157.4+_25.5 in the study group whereas in the control group it was 124.6+-5.9 which showed that the systolic blood pressure was significantly raised in study group and was statistically significant with p value <0.001.The diastolic blood pressure was 93.4+_13.3 in the study group while in the control group it was 77.5+_6.1 with a p value of <0.001 which showed that diastolic blood pressure was significantly elevated in the study group

FIGURE 11: MEAN BP BETWEEN CASES AND CONTROLS

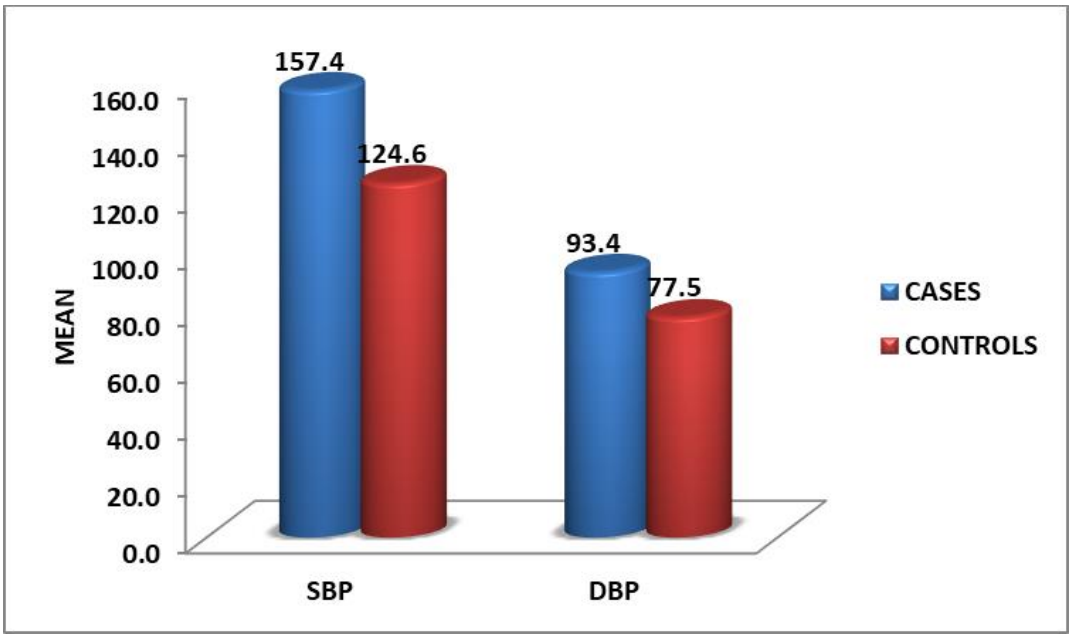


TABLE12: MEAN BIOCHEMICAL PARAMETERS BETWEEN CASES AND CONTROLS

PARAMETERS	CASES		CONTROLS		t value	p value
	Mean	SD	Mean	SD		
Sr. Urea	35.5	22.7	24.9	11.5	3.243	0.002*
Sr. Creatinine	1.0	0.4	0.8	0.3	3.947	<0.001*
Sr. Cholesterol	169.6	44.8	174.8	21.7	-0.807	0.421
HDL	52.5	21.0	66.0	19.1	-3.683	<0.001*
LDL	91.7	38.0	81.8	32.1	1.542	0.126
TG	146.2	55.1	137.4	27.9	1.114	0.267

Note: * significant at 5% level of significance ($p<0.05$)

Table 12 shows the mean biochemical parameters among the cases and controls mean serum urea was 35.5+_22.7 in the cases and 24.9+_11.5 in the control group with p value of 0.002 which was statistically significant value between cases and control. Mean creatinine was 1+_0.4 in the cases and 0.8+_0.3 in the control group with p value of <0.001 which was statistically significant. The lipid profile in the study group showed HDL value to be statistically significant with p value <0.001 which showed that HDL values were lower in the study group compared to the controls. Other parameters like total cholesterol and LDL, Triglycerides were statistically insignificant between the cases and the controls.

FIGURE 12: MEAN BIOCHEMICAL PARAMETERS BETWEEN CASES AND CONTROLS

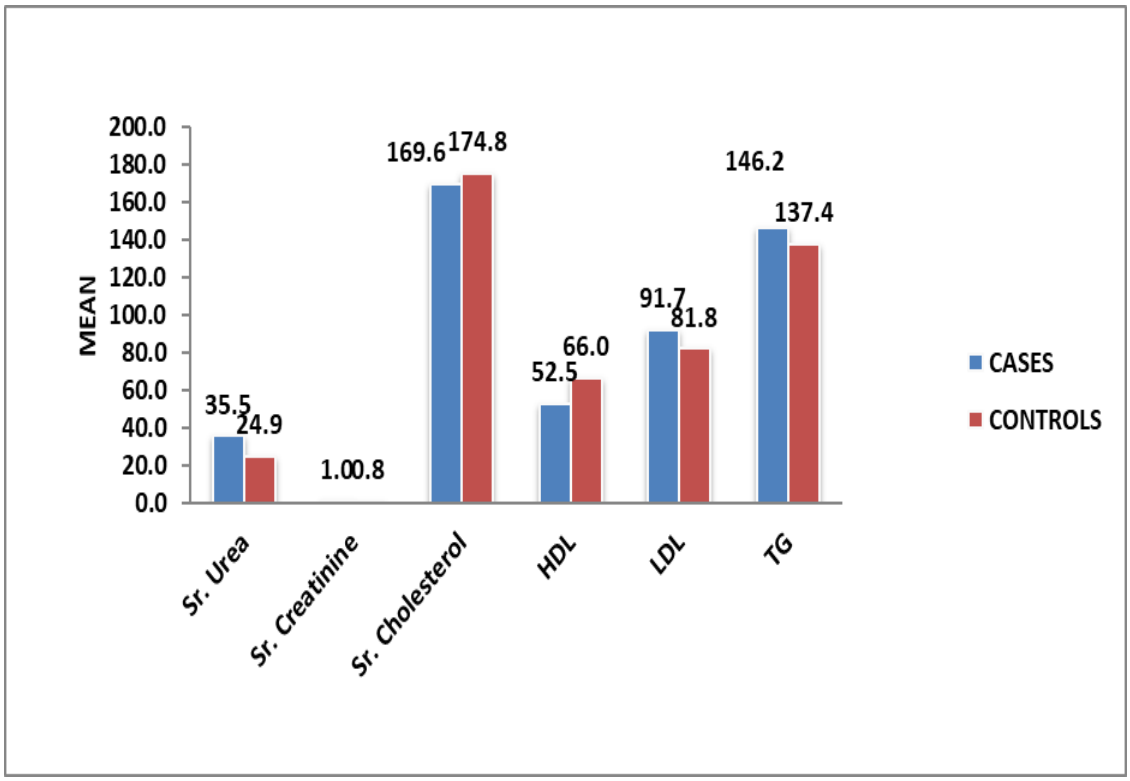


TABLE 13: Localization of the lesion on CT scan

LOCALIZATION ON CT		N	%
CORTICAL	FRONTAL	2	3.3
	PARIETAL	9	15.0
	TEMPORAL	1	1.7
	MUTIPLE	28	46.7
	TOTAL	40	66.7
SUB CORTICAL	IC	2	3.3
	BASAL GANGIA	1	1.7
	THALAMUS	1	1.7
	MUTIPLE	12	20.0
	TOTAL	16	26.7
MIXED		4	6.7

Table 13 shows the localization of the lesion on the CT scan which shows cortical infarction accounted for about 66 percent of the cases in which the maximum patients 46 percent were having multiple cortical site involvement that is either fronto parietal, parieto temporal or frontal parietal and temporal .sub cortical infarction constituted for about 26 percent of the cases in the study and majority had multiple site involvement with either internal capsule, basal ganglia or thalamus and Mixed group constituted for 6 percent of the cases who had both cortical and subcortical involvement

FIGURE 13 SHOWS THE LOCALIZATION OF THE LESION ON CT SCAN

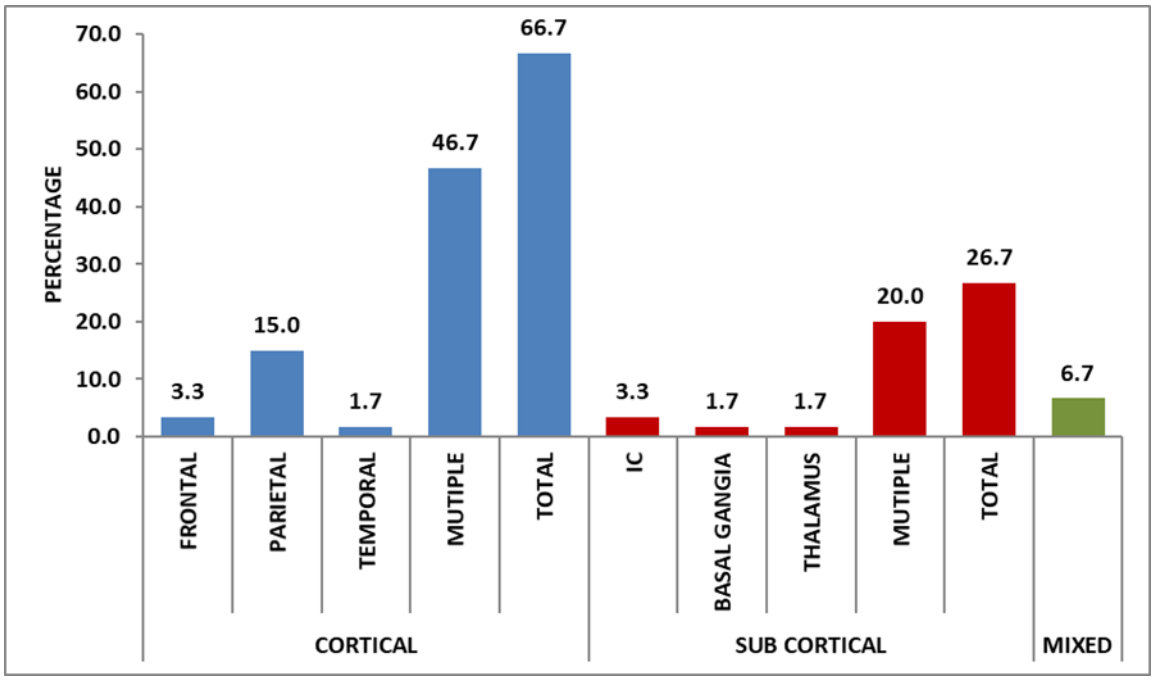


TABLE 14: OUTCOME AMONG THE CASES BASED ON LOCATION OF LESION

LOCALIZATION ON CT	OUTCOME		TOTAL
	IMPROVED	EXPIRED	
CORTICAL	34	6	40
SUB CORTICAL	12	3	16
MIXED	0	4	4

Table 14 shows the outcome among the cases according the site of the lesion 40 percent of the cases had cortical involvement in which 34 cases improved and 6 cases expired.16 percent of the cases had subcortical involvement out of which 3 expired and 12 improved and 4 percent of the cases had both cortical and subcortical involvement and all 4 patients expired.

TABLE 15: DEATH AMONG THE CASES BASED ON LOCATION OF LESION AND RISK FACTORS

LOCALIZATION	NUMBER OF DEATHS WITH RISK FACTORS			
	HTN	DM	BOTH	Total
CORTICAL	1	1	4	6
SUB CORTICAL	0	0	3	3
MIXED	1	1	2	4
Total	2	2	9	13

Table 15 showed the association of the risk factor and the extent of the lesion on the CT scan with regarding to the death among the cases.6 of the cases who were having cortical infarct and died in that 4 cases had diabetes and hypertensive as the risk factor and one patient was only hypertensive and one patient was only diabetic.3 of the cases who had sub cortical infarct expired in which all 3 patient had the risk

factor of both diabetes mellitus and hypertension. 2 of the cases had both cortical and sub cortical involvement expired in which one was only hypertensive and one was only diabetic.

TABLE 16: DISTRIBUTION OF CASES ACCORDING TO RAISED CRP BY LOCALIZATION

LOCALIZATION	RAISED CRP	
	N	%
COR	32	66.7%
SC	13	27.1%
MIXED	3	6.3%
Total	48	100.0%

Table 16 shows the association of localization of the lesion with the elevation of the CRP levels among the cases which shows that 66.7% of the cases with elevated CRP levels had lesion in the cortex and 27.1% had lesion in subcortical level and 6.3% cases had mixed lesion in both cortical and subcortical level

FIGURE 14: DISTRIBUTION OF CASES ACCORDING TO RAISED CRP BY LOCALIZATION

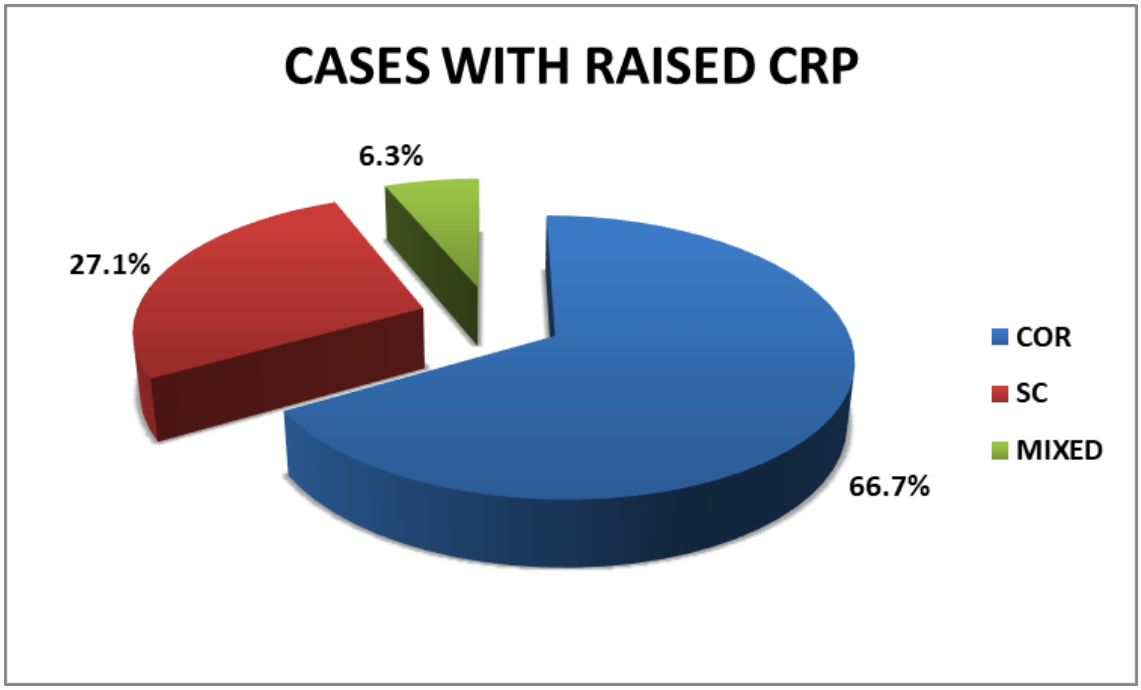


TABLE 17: CRP LEVEL BETWEEN CASES AND CONTROLS

CRP LEVEL	CASES		CONTROLS		p value
	N	%	N	%	
≤10	12	20.0%	51	85.0%	<0.001*
>10	48	80.0%	9	15.0%	
Total	60	100.0%	60	100.0%	

Note: * significant at 5% level of significance (p<0.05)

Table 17 depicts the level of C-reactive protein between the cases and the controls 80 percent of the cases showed elevated level of the C-reactive protein and only 20 percent cases had values In the normal range. Among the controls 85 percent of them had C-reactive protein In the normal range and about 15 percent of the patients had elevated values.

FIGURE 15: CRP LEVEL BETWEEN CASES AND CONTROLS

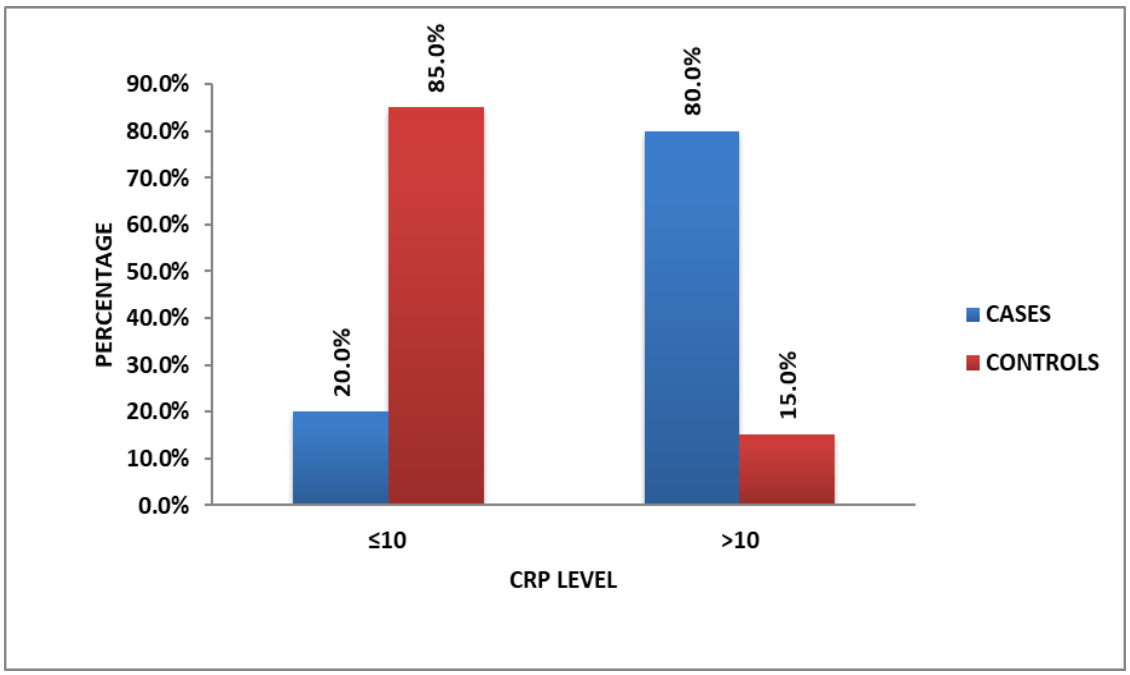


TABLE 18: MEAN CRP LEVEL BETWEEN CASES AND CONTROLS

PARAMETERS	CASES		CONTROLS		t value	p value
	Mean	SD	Mean	SD		
CRP VALUE	43.4	32.6	11.1	16.1	6.871	<0.001*

Note: * significant at 5% level of significance (p<0.05)

Table 17 shows the mean CRP values among the cases and the controls. cases had a mean CRP value of 43.4+_32.6 and controls had a mean CRP value of 11.1+_16.1. The p value is <0.001 which is statistically significant

FIGURE 16: MEAN CRP LEVEL BETWEEN CASES AND CONTROLS

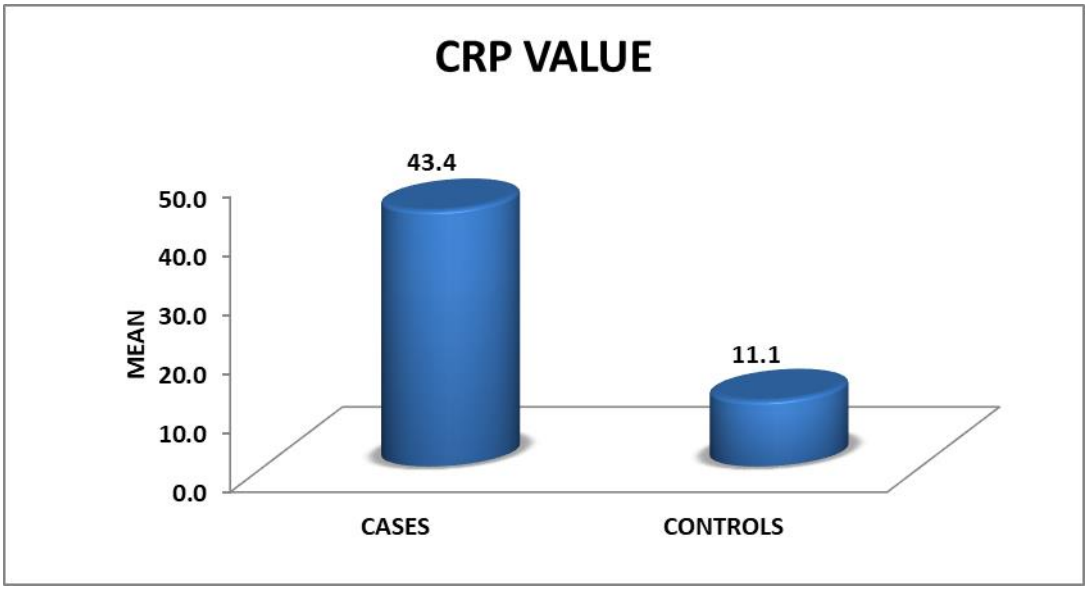


TABLE 19: MEAN CRP LEVEL BETWEEN CASES AND CONTROLS BY AGE

AGE(YRS)	CASES		CONTROLS		p value
	Mean CRP	SD	Mean CRP	SD	
21-30	21.1	0.0	3.0	0.0	-
31-40	50.0	14.1	0.6	0.6	0.039*
41-50	57.0	14.0	5.6	3.9	0.010*
51-60	48.8	10.8	7.7	6.9	<0.001*
61-70	34.6	14.7	8.5	7.2	0.003*
>70	42.1	14.4	6.1	3.3	0.011*
TOTAL	43.4	32.6	11.1	16.1	<0.001*

Note: * significant at 5% level of significance ($p<0.05$)

Table 18 shows the mean CRP level between cases and controls by age which showed that the levels of C-reactive protein was maximum in the age group of 41-50 among the cases i.e. 57+_14and and was less in young people who had stroke who were less than 3oyrs which was 21+_0.0. Among the controls maximum values were in age group of 61-70 which was 8.5+_7.2 and young controls has the lower values of 3.0+_0.0.

FIGURE 17: MEAN CRP LEVEL BETWEEN CASES AND CONTROLS BY AGE

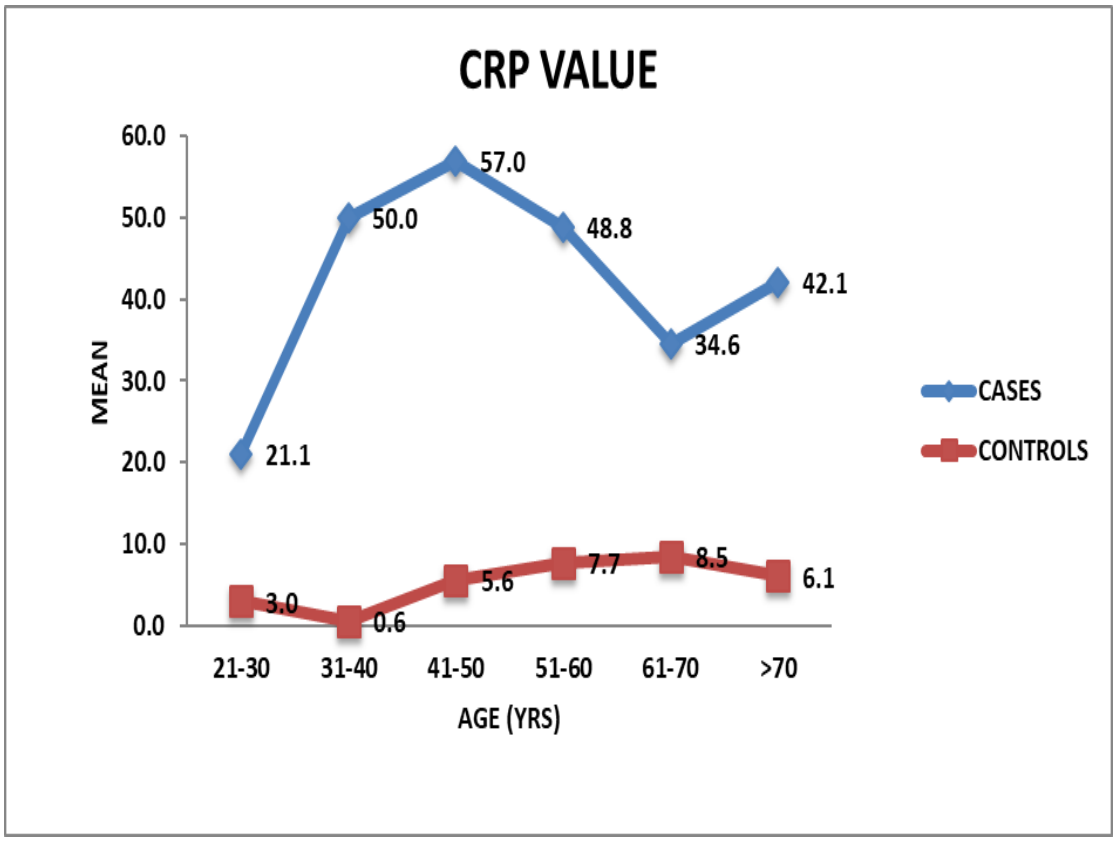


TABLE 20: ASSOCIATION OF CRP LEVEL AND AGE AMONG CASES

AGE (YRS)	CRP LEVEL ≤10		CRP LEVEL >10		p value
	N	%	N	%	
21-30	0	0.0%	1	2.1%	0.261
31-40	0	0.0%	2	4.2%	
41-50	0	0.0%	5	10.4%	
51-60	3	25.0%	22	45.8%	
61-70	7	58.3%	12	25.0%	
>70	2	16.7%	6	12.5%	
Total	12	100.0%	48	100.0%	

Table 20 shows the association of CRP levels among different age groups in the cases which showed that CRP levels more than 10 was found in the maximum age group was 51-60yrs and it constituted about 45 percent of the cases and young patients had a C reactive protein elevation of only 6.3 percent of the cases.

FIGURE 18: ASSOCIATION OF CRP LEVEL AND AGE AMONG CASES

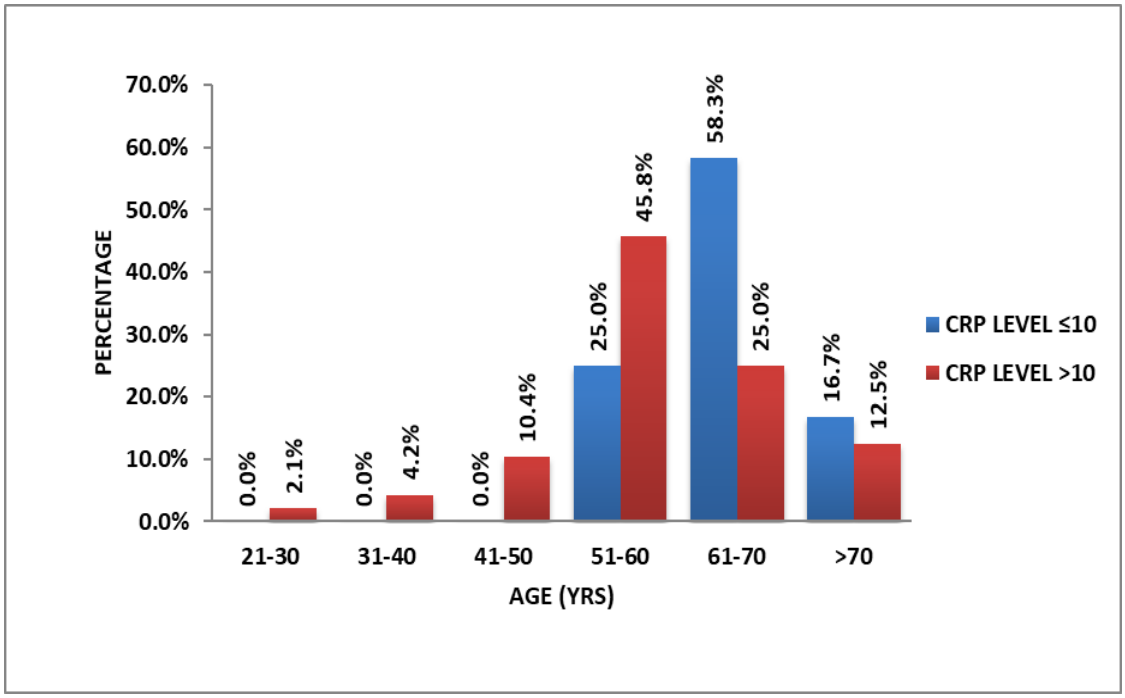


TABLE 21: ASSOCIATION OF CRP LEVEL AND AGE AMONG CONTROLS

AGE (YRS)	CRP LEVEL ≤10		CRP LEVEL >10		p value
	N	%	N	%	
21-30	1	2.0%	0	0.0%	0.761
31-40	2	3.9%	0	0.0%	
41-50	4	7.8%	1	11.1%	
51-60	21	41.2%	4	44.4%	
61-70	15	29.4%	4	44.4%	
>70	8	15.7%	0	0.0%	
Total	51	100.0%	9	100.0%	

Table 21 shows association between CRP levels and age among controls shows that C reactive protein of <_10 was present maximum in the age group of 51-60yrs of age i.e 41 percent of the cases and young patients with CRP elevation among controls was 0 percent and CRP less than 10 in young patients accounted only 5.9 percent i.e. age group of less than 30yrs of age.

FIGURE 19: ASSOCIATION OF CRP LEVEL AND AGE AMONG CONTROLS

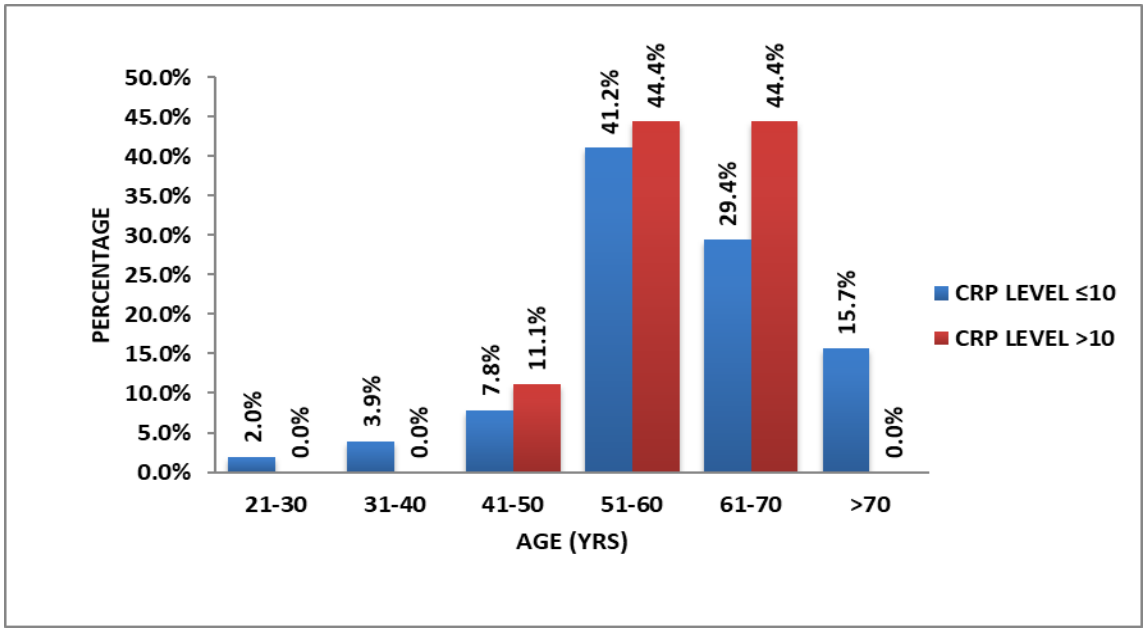


TABLE 22: ASSOCIATION OF CRP LEVEL AND SEX AMONG CASES

SEX	CRP LEVEL ≤10		CRP LEVEL >10		p value
	N	%	N	%	
MALE	7	58.3%	32	66.7%	0.588
FEMALE	5	41.7%	16	33.3%	
Total	12	100.0%	48	100.0%	

Table 22 shows the association of CRP level and sex among the cases which showed that CRP levels among males constituted having higher levels both among cases and controls as the percentage of males among our study was more than females this result was inconclusive and was not statistically significant

FIGURE 20: ASSOCIATION OF CRP LEVEL AND SEX AMONG CASES

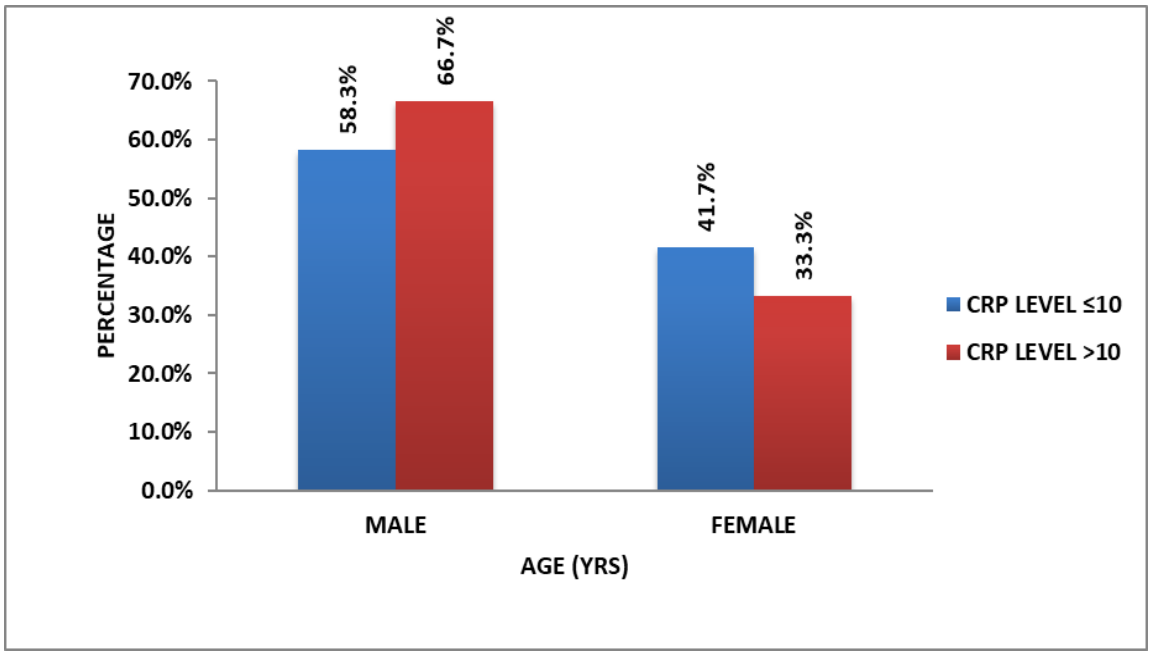


TABLE 23: ASSOCIATION OF CRP LEVEL AND SEX AMONG CONTROLS

SEX	CRP LEVEL ≤10		CRP LEVEL >10		p value
	N	%	N	%	
MALE	31	60.8%	1	11.1%	0.103
FEMALE	20	39.2%	8	88.9%	
Total	51	100.0%	9	100.0%	

Table 23 shows the association of CRP level and sex among the controls CRP levels of <10 was present in 60 percent of the males and 39 percent of the females and CRP values of > 10 was present in 88 percent of the females and 11 percent of the males with a p value of 0.103 which was statistically insignificant

FIGURE 21: ASSOCIATION OF CRP LEVEL AND SEX AMONG CONTROLS

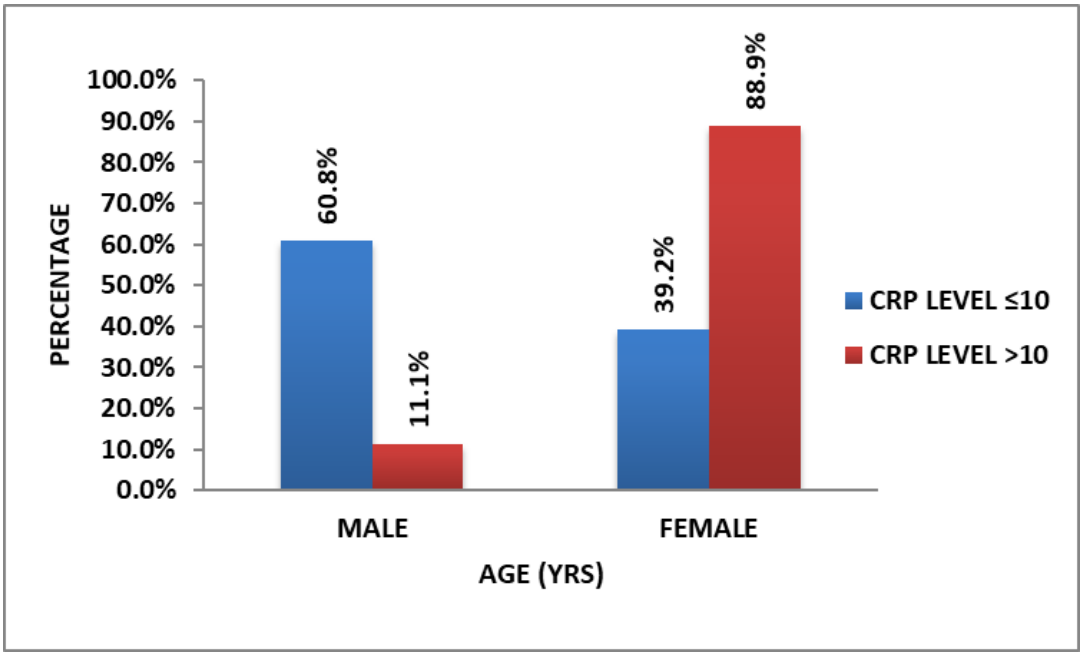


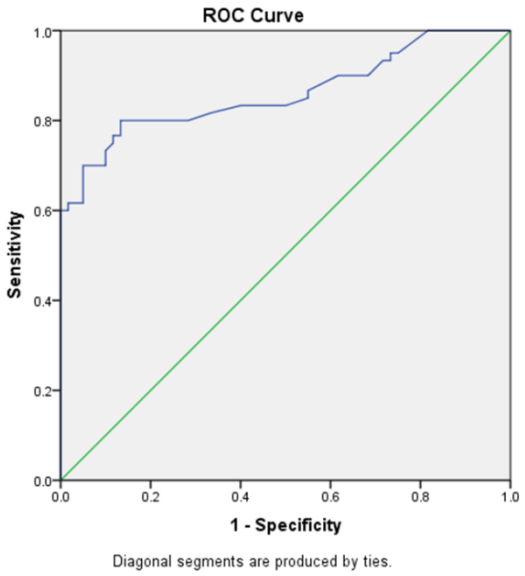
TABLE 24: ROC ANALYSIS OF CRP VALUE BETWEEN CASES AND CONTROLS

Parameters	Area Under the Curve	Std. Error	p value	95% Confidence Interval	
				Lower Bound	Upper Bound
CRP VALUE	0.861	0.035	<0.001*	0.792	0.93

Note: * significant at 5% level of significance (p<0.05)

Parameters	Positive if greater than or Equal to	Sensitivity	Specificity
CRP VALUE	9.25	80.0%	71.7%

FIGURE 22: ROC CURVE OF CRP VALUE BETWEEN CASES AND CONTROLS



Above tables shows the results from receiver operating characteristic curve (ROC) analysis. The area under the curve (AUC) was found 86.1% for CRP values which was statistically significant. AUC is equal to the probability that a classifier will rank a randomly chosen positive instance of mortality higher than a randomly chosen negative one. Cut off value of CRP values (more than 9.25) yields the chance of predicting the stroke cases with morbidity and mortality with sensitivity 80% and specificity 71.7%.

DISCUSSION

Our study is a hospital based case control study with 60 cases and 60 age and sex matched controls admitted in Shri B M Patil medical college Vijayapura. our study was compared with the different parameters with the different studies done as follows

TABLE 25: Shows comparison of mean age in different studies (mean age+_SD)

GROUP	Our study	Dhamija R.K.et al[148]	Agarwal et al[147]	David curb et al[146]	Natalia Rost et al[149]
CASES	61±10yrs	56.48	65.3±9.07	58.1±5.7	69.7
CONTROLS	61±10yrs	54.20	65.3±8.88	55.8±5.4	

In our present study mean age of cases and contols was 61±10yrs of age which was

comparable with David curb et al[146] which showed mean age among cases 58.1±5.7yrs and among controls 55.8±5.4yrs, Agarwal et al[147] having shown 65.3±9.07yrs and 65.3±8.88yrs, Dhamija R K et al[148] showing 56.48yrs and 54.20yrs, respectively among the cases and the controls, Natalia Rose et al[149] showing 69.7yrs.

TABLE 26: Shows comparision of stroke among the young

OUR STUDY	Kristensen B et al[150]	T Song-Hai Lee et al[151]
5.1%	5%	6.8 %

In our present study incidence of stroke among the young patients was about 5.1 percent which was in comparision to studies done by Kristensen B et al[150] which showed 5 percent and T song Hai Lee et al[151] which showed about 6.8 percent of the cases

TABLE 27: comparision of age of stroke among men and women

GROUP	Our study	Jaume Roquer et all[152]
MALE	60.4±9.3	68.8±11.9
FEMALE	63.7±11.6	74.6±11.4

The greater incidence of stroke among men compared to women is well established. But according to recent studies emphasis has been made upon the increasing incidence of stroke in women[165] with respect to the age. Entire life time risk 16% of women & 8 % men die of stroke[166] Knowledge of the difference in the sex incidence is of importance for the management of the admitted patients with the stroke. Our study showed the increased incidence of thrombotic stroke in male in mean age group of 60.4±9.3 and females in the mean age group of 63.7±11.6yrs showing highest incidence which was comparable with the study done by James Roquer et al[152]. Who documented mean age of stroke was higher in females than compared to males Smoking is considered as a risk factor for acute stroke in the population. smoking is considered to affect the cerebral circulation through the mechanism of arterial vasoconstriction and increased platelet aggregation.

TABLE 28: Showing comparision of smoking

Smoking	J David Curb et al[146]	Natalia S Rost et al[149]	Our study
Cases	54.4 %	22.7%	53.3%

Smokers in our study were 53.3 % of the cases which was comparable to the study done by J David Curb et al[146] which showed 54.4 % of the cases in the study to be smokers and study done by Natalia S Rost et al[149] which showed 22.7 percent of the smokers among the study group. Hence smoking was an important risk factor for

the occurrence of the stroke.

Our study showed that both hypertension and diabetes mellitus increased the incidence if the stroke independently and having been diagnosed with both diabetes mellitus and hypertension together increased the risk dramatically this was in accordance with the study by Gang Hu et al[153] which was one of the fewer studies which showed the combined effect of the diabetes mellitus and hypertension occurring concomitantly, Kissela B M et al[154] also studied the concomitant effect of diabetes mellitus and hypertension in patients with ischemic stroke in North kentuky stroke study.

In our study cases diagnosed with both diabetes mellitus and hypertension with ischemic infarct showed 9 deaths among the total 13 deaths which further indicates the increased risk of mortality of patients with both the risk factors of hypertension and diabetes mellitus which was in accordance with the study done by Gang Hu et al[153], Kissela B M et al[154] which showed increased incidence and mortality among patients diagnosed with both diabetes mellitus and hypertension rather than either diabetes mellitus or hypertension alone and this may be because of the undiagnosed disorder of glucose metabolism in patients diagnosed with hypertension.

Our study showed that the cases had a significant lesser HDL levels compared to the controls with a p value being significant of $p<0.001$ which was in accordance to the studies done by Samantha A Reina MS et al[155] which showed that lower level of HDL was associated with elevated risk of stroke.

However, our study did not notice any significant difference in the Total cholesterol, LDL and triglycerides among the cases and the controls.

In contrary study done by Thomas S Bowman et al[156] did not show any

association of Total cholesterol, HDL, LDL, TG in relation to any increased incidence of the stroke among the cases and the controls.

C-reactive protein is one of the important marker of the inflammation and its role in the atherothrombotic event has been well established. C reactive protein has an important role in the recognition of the foreign particles and phosplipid and various glycolipid of the cell wall.

Table 29 showing comparision of the mean C reactive protein in different studies (mean ±SD) mg/dl

CRP mg/dl	Agarwal et al[147]	J David Curb et al[146]	Natalia S Rose et al[149]	Our study
Cases	**25±24.78**	**14.3**	**5.8±7.8**	**42.4±32.6**
Controls	**4.00±1.48**	**11.6**		**11.1±16.1**

Our study showed the mean C reactive protein among the case to be 42.4±32.6 11.1±16.1 among the control group which showed that there was significant elevation of the levels of the C reactive protein among the cases compared to the controls which was comparable to the study done by Agarwal et al[147] which showed 25±24.78 among the cases and 4.00±1.48 among the controls, J David curb et al[146] showed values of 14.3 among the cases and 11.6 among the controls which was comparable with our study, Natalia S Rose et al[149] showed the values of 5.8±7.8 among the cases.

Table 30 showing the positive C reactive protein values in cases and controls in different study groups

CRP	Dhamaja R K et al[148]	S C Mahapatra et al[157]	Our study
Cases	**77.3%**	**80%**	**85%**
Controls	**12.54%**	**10%**	**15%**

The table shows the comparision of the studies showing elevated C reactive protein among different studies between the cases and the controls. Our study showed 85% of the cases had elevated C reactive protein and 15 % of the controls had the elevated values which was comparable to the study done by Dhamaja R K et al[148] which showed 77.3% of the cases had raised values and 12.54% of controls had elevated values, S C Mahapatra et al[157] showed 80 percent of the cases had raised values and 1o percent of the controls had elevated values.

Mario Di Napoli[158] et al studied the values of C reactive protein levels in 473 patients of acute ischemic stroke and showed that 72% had an elevated value of the C reactive protein and showed the association of C reactive protein as a marker of the underlying inflammatory process leading to athero thrombotic event.

A study done by Montanear et al[159] showed the rise of the acute inflammatory mediators such as interleukin-6 after the onset of the ischemic stroke.

Mahapatra SC et al[157] did a study on 80 of the thrombotic stroke patients and showed that 64 patients had an elevated value of the C reactive protein. The purpose of the study done was to assess the role of the underlying inflammation in the pathogenesis of the stroke.

Rathore HS et al[160] did a study on the in the ischemic infarct patients consisting of the lacunar and cortical infarct and the role of the early inflammatory

mediators in these patients of stroke and showed that the C reactive protein levels was raised in about 80 percent of the cortical infarcts and 12 percent of the lacunar infarcts and this was carried out in 25 each cases of the cortical and lacunar infarct patients.

In a study done by L Masoti et al[161] they measured C reactive protein values in 196 elderly patients and observed the short term prognosis in these patients with stroke and they observed that elevated C reactive protein levels was associated with the poorer prognosis.

In our study C reactive protein was measured in the patients admitted and who were proven to be having ischemia by CT scan which was done at the time of the admission to the hospital and the levels of CRP was estimated after 12hrs and within 72 hrs of the onset of the symptoms.

This observation was in accordance to the study done by Kerstin winbeck et al[162] who did study on 127 patients of stroke and showed that CRP levels estimated between 12-24hrs of the onset of the symptoms indicates poor prognosis and estimation before 12hrs did not show any significant changes.

Our study showed that 66.7 % cases with elevated CRP levels had cortical infarcts,27.1% cases with subcortical infarct had elevated CRP levels and 6.3% cases with elevated CRP levels had both cortical and subcortical level

In study done by Irene et al[163] study, CRP levels was measured in 773 cases who were more than 55yrs of age and these cases were followed up for the next 6.5yrs The study documented the progression of the atherosclerotic changes and the change in the values of the CRP observed in them which predicted the risk of stroke or cardiovascular diseases in these individuals.

In our study the control group showed an elevation in the C reactive protein in about 15 percent of them the further risk prediction of myocardial infarction and the

risk of stroke could not be assessed in these people because our study didn't do follow up of these patients which needed a longer duration for the follow up.

In our study 13 deaths occurred in which 9 were males and 4 were females and in this 6 had cortical infarcts and 4 patients had both cortical and subcortical infarcts and 3 patients had subcortical infarct. All patients who died showed an elevated levels of C reactive protein and elevated levels showed a bad prognostic indicator.

In our study 40 patients had cortical infarction out of which 6 patients expired and 16 patients had subcortical infarct out of which 3 patients expired and 4 patients had both cortical and subcortical infarcts out of which all the patients expired. This was compared to the study done by Sukdeb Das et al[164] on the short term mortality prediction in patients with stroke which showed that 30% of the cortical lesion contributed for mortality and 22 % for subcortical and 32% were combined overall it showed that mortality increases when it is combined whether it is ischemic or haemorrhagic stroke which was similar to our study.

SUMMARY

Our study is a hospital based case control study of 6o patients with acute ischemic stroke and 60 age and sex matched controls admitted in Shri B M Patil medical college Vijayapura between the period of September 2017 to July 2019 Summary of results

1. Among the 60 cases, and controls 39 were males and 21 were females in the both the groups as it was age and sex matched study
2. The mean age of the both cases and controls was 61.6±10.3 years. Majority were in the age group of 51-60yrs of age
3. The increased incidence of thrombotic stroke in male in mean age group of 60.4±9.3 and females in the mean age group of 63.7±11.6yrs which showed that mean age was higher in females compared to males in our study
4. Most common addictive risk factor among the cases was smoking which constituted about 53 percent of the cases followed by multiple risk factor in 28.3 % and only alcohol in 6.7% of the cases
5. Most common associated risk factor for stroke in our study among the cases was combination of the Diabetes mellitus and Hypertension which was present in 60 percent of the cases followed by hypertension only in 20% cases and only diabetes mellitus in 10% of the cases.
6. Our study showed that the cases had a significant lesser HDL levels compared to the controls as one of the risk factor for the stroke
7. Serum total cholesterol, LDL and triglycerides as a risk factor was insignificant in our study
8. Mean blood urea and serum creatinine was higher among the cases compared to the controls.

9. Our study showed study showed the mean C reactive protein among the case to be 42.4±32.6 and among the control group which showed 11.1±16.1 that there was significant elevation of the levels of the C reactive protein among the cases compared to the controls
10. Our study showed elevated C reactive protein in 80% of the cases and 15% of the controls hence showed a significant elevation among the cases.
11. Maximum number of the cases showed elevated C reactive protein level in the age group of 51-60yrs and younger cases less than 40yrs had less significant rise in the C reactive protein level
12. Our study showed C reactive protein levels were more in the age group of 41-6yrs of age among the cases and was less in patients with young stroke.
13. Mortality was higher in the cases who had higher C reactive protein levels and both diabetes mellitus and hypertension as a risk factor, associated smoking and who had cortical infarcts and mixed infarcts compared to other cases.

CONCLUSION

1. Our study showed that the C reactive protein was elevated in patients diagnosed with stroke when it was compared with the control group
2. Our study also showed that elevated C reactive protein was associated with the poor outcome in patients with acute ischemic stroke and is poor prognostic indicator.
3. Our study also showed that the mortality in the study group of patient who died with acute ischemic stroke in them all had elevated values of C reactive protein.

LIMITATIONS OF OUR STUDY

1. Our study is a hospital based case control study which was done on a smaller population and hence results cannot be generalized and it needs to be done in larger populations for stronger correlation of the outcome of the study
2. Our study measured C reactive protein only on admission at a single point where as serial measurement of the CRP levels would be a better indicator of the outcome which was not done in our study

BIBLIOGRAPHY

1. Ridker et al. Inflammation, atherosclerosis, ischemic episode exploring hidden side of the moon", NEJM 1997, Vol. 336: 1014.
2. Tillet WS, Francis T. Serological reactions in pneumoniae with a non-protein somatic fraction of pneumococcus. J. Exp. Med. 1930; 52: 561-571.
3. Abernethy TJ, Avery OT. The occurrence during acute infections of protein not normally present in the blood. I Distribution of the reactive protein in patients sera and the effect of calcium ions on the flocculation reaction with C-polysaccharide of pneumococcus. J Exp Med 1941; 73: 173.
4. Maclead CM, Avery OT. The occurrence during acute infections of a protein not normally present in the blood. II Isolation and properties of the reactive protein. J. Exp. Med. 1941; 73: 183.
5. Loftstrom G. Comparison between the reactions of acute phase serum with pneumococcus C-polysaccharide and with pneumococcus type-27. Br. J. Exp. Pathol 1994; 25: 21-26.
6. Berk BC, Weintraub WS, Alexander RW. Elevation of C-reactive protein in acute coronary artery disease. Am. J. Cardiol 1990; 65: 168-72.
7. De Beer FC, Hind CR, Fox KM, Allan RM, Maseri A, Pepys MB. Measurement of serum C-reactive protein in myocardial ischemia and infarction. Br. Heart J, 1982; 47: 239-43.
8. Liuzzo G, Biasucci LM, Gallimore JR, Grillo RL, Rebuzzi AG, Pepys MB and Maseri A. The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. N Engl J Med 1994; 331: 417-24.
9. Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP, Braunwald E. C-reactive protein is a potent predictor of mortality

independently of and in combination with troponin T in acute coronary syndromes: A TIMI 11A Sub-Study. J Am. Coll. Cardiol 1998; 31: 1460-5.

10. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, aspirin and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1996; 336: 973-9.
11. Kuller LH, Tracy RP, Shaten J, Meilahn EN. Relation of C-reactive protein and coronary heart disease in the MRFIT nested case control study. Am J. Epidemiol 1996; 144: 537-47.
12. Pepys MB, Baltz ML. Acute phase proteins with special reference to Creactive protein and related proteins (pentaxins) and serum amyloid A protein. Adv. Immunol 1983; 34: 141-212.
13. Pepys MB. Acute phase proteins in the acute response. London: SpringerVerlag, 1989.
14. Shine B, deBeer FC, Pepys MB. Solid phase radioimmuno-assays for Creactive protein. Clin. Chim Acta 1981; 117: 13-23.
15. Vingushin DM, Pepys MB, Hawkin PN. Metabolic and scintigraphic studies of radio-iodinated human C-reactive protein in health and disease. J. Clin Invest 1993; 91: 1351-57.
16. Heinrich J, Schuttle H, Schonfeld R, Kohler E, Assmann G. Association of variables of coagulation, fibrinolysis and acute phase with atherosclerosis in coronary and peripheral arteries and those arteries supplying the brain. Thromb Haemostas 1995; 73: 347-78.
17. Hurlimann J, Thasbeeke G, Hochwald G. The liver as the site of C-reactive protein formation. J Exp Med 1996; 123: 365-78.
18. Pepys MB. The acute phase response and C-reactive protein. Chapter No.

11.13.3 in Oxford Textbook of Medicine, Third Edition. Weatherall AJ, Ledingham JGG, Warrell DA. Tokyo. Oxford University Press, 1996; 1527-1533 pp.

19. Kushner I, Feldmann G. Control of the acute phase response. Demonstration of C-reactive protein synthesis and secretion by hepatocytes during acute inflammation in the rabbit. J. Exp. Med. 1978; 148: 466-77.

20. Merriman CR, Pullaim LA, Kampschmidt RF. Effect of leucocytic endogenous mediators on C-reactive protein in rabbits. Proc Soc Exp Biol Med 1975; 149: 782-84.

21. Whicher JT, Martin JFR, Dieppe PA. Prostaglandin-stimulated increase in acute phase proteins in man and its failure in systemic sclerosis. Lancet 1980: 11: 1187.

22. Osmand AP, Friedenson B, Gewurz H, Painter RH, Haffmann T, Shelton E.Characterization of C-reactive proteins and the complement subcomponent Clt as homologous proteins displaying cyclic pentameric symmetry (Pentraxins). Proc Nat Acad Sci USA 1977; 74: 739-43.

23. Oliveria EB, Gotschlich EC, Liu T. Primary structure of human C-reactive protein. Proc. Nat Acad Sci USA, 1977; 74: 3148-51.

24. Tsujimoto m, Inoue K, Nojima S. C-reactive protein induced agglutination of lipid suspensions prepared in the presence and absence of phosphatidylcholine. J. Biochem 1980; 87: 1531-37.

25. Oliveria EB, Gotschlich EC, Liu TY. Comparative studies on the binding properties of human and rabbit C-reactive protein. J. Immunol 1980; 124: 1396-402.

26. Osmand AP, Mortensen RF, Siegel J, Gewrz H. Interaction of C-reactive

protein with the complement system III. Complement dependent passive hemolysis initiated by CRP. J. Exp Med 1975; 142: 1065-72.

27. Mortensen RF, Osmand AP, Gewurz H. Effects of C-reactive protein on the lymphoid system-I. Binding to thymus dependent lymphocytes and alteration of their functions. J. Exp Med 1975; 141: 821-39.
28. Fiedel BA, Gewurz H. Effects of C-reactive protein on platelet functions I. Inhibition of platelet aggregation and release reactions. J. Immunol 1976; 116: 1289-94.
29. Hokama Y, Nagasawa LS, Uchida DA, Morita AH, Abad MA, Michimoto. Suppression of arachidonic acid and endoperoxide-analog stimulated platelet aggregation by sodium azide protection of this effect by Creactive protein. Fed Proc 1978: 1437-55.
30. Williams RC Jr, Kilpatric KA, Kassaby M, Abdin ZH. Lymphocytes binding C-reactive protein during acute rheumatic fever. J Clin Invest 1978; 61: 1384-93.
31. James K, Hansen B, Gewurz H. Further studies of the binding of C-reactive protein (CRP) to human lymphocytes: development of a radioassay and requirement for a multivalent binding specificity. Fed. Proc 1980; 39: 945.
32. Parish WE. Studies in vasculities VII. C-reactive protein as a substance perpetuating chronic vasculities. Occurrence in lesions and concentrations in sera. Clin Allergy 1976; 6: 543-50.
33. Pepys MB. C-reactive protein fifty years on. The Lancet 1981; I: 653-6.
34. Bansal BC, Agrawal AK. Recent concepts in stroke 1999; Published by ICPAPI.
35. Sudlow CLM et al comparable studies of the incidence of stroke and its

pathological types results from an international collaboration. Stroke 28: 491-9.

36. Murray et al. Mortality by cause for 8 regions of the world: Global burden of the disease study. Lancet, 349: 1269-76.
37. Michael Donaghy et al. Brain's disease of the nervous system, 11th Edition, 2001; Oxford University Press.
38. Weaver JPA et al. The effect of increased fibrinogen content on the viscosity of blood. Clin Sci. 1969; 36: 1-10.
39. Symon L et . Autoregulation in acute focal ischemia. An experimental study. Stroke 1976; 7: 547-54.
40. Wollner L et al. Failure of auto-regulation as a cause of brain dysfunction in the elderly. BMJ 1979; 1: 1117-18.
41. Dearden NM. Ischemic Brain. Lancet 1985; 2: 225-9.
42. Pulsinelli W. Pathophysiology of acute ischemic stroke. Lancet 1992; 339: 533-6.
43. Wise RJS et al. Serial observations on the pathophysiology of acute stroke brain. 1983; 106: 197-222.
44. Kristian T et al. Calcium in ischemic cell death. Stroke, 1998; 29: 705-18.
45. Miles AN et al. Apoptotic neuronal death following cerebral ischemia. J. Clin. Neurosci, 1988; 5: 125-45.
46. Astrup J et al. Thresholds in cerebral ischemia. The ischemic pneumbra. Stroke, 1981; 723-5.
47. Symon L et al. Ischemic brain edema following middle cerebral artery occlusion. Stroke 1979; 10: 184-91.
48. Bell Be et al. CBF and time thresholds for formation of ischemic cerebral

edema. J Neurosurg 1985; 02: 31-41.

49. Cormio M et al. Secondary insults to the injured brain. J. Neurosurg. 1997; 4: 132-48.

50. Weir CJ et al. Is hyperglycemia an independent predictor of poor outcome after acute stroke? AMJ 1997; 314: 1303-6.

51. Andrews RJ. Transhemispheric diaschisis: Review and comment. Stroke, 1991; 22: 943-9.

52. Bowler JV et al. Contribution of diaschisis to the clinical deficit in human cerebral infarction. Stroke 1995; 26: 1000-6.

53. Bamford JM et al. A prospective study of acute cerebrovascular disease in the community: The Oxfordshire Community Stroke Project. J Neurol. Neurosurg. Psychiatry 1988; 51: 1373-80.

54. Whelton PK. Epidemiology of hypertension. Lancet 1994; 344: 101-6.

55. Rodgers A et al. Blood pressure and the risk of stroke in patients with cerebrovascular disease. BMJ 1996; 313: 147.

56. MacMohan S et al. Blood pressure, stroke and CHD. Lancet 1990; 335: 76574.

57. Eastern stroke and CHD Collaborative Research Group. Blood pressure, cholesterol and stroke in Eastern Asia. Lancet 1998; 352: 180-7.

58. Shaper AG et al. Risk factors for stroke in middle aged British men. BMJ 1991; 302: 1111-15.

59. Keli S et al. Predictive value of repeated blood pressure measurements for stroke risk. The Zutphun Study, Stroke 1992; 23: 347-51.

60. Sagie A et al. The natural history of borderline isolated systolic hypertension. N Engl. J Med. 1993; 329: 1612-17.

61. Collins R et al. Blood pressure, antihypertensive drug treatment and the risks of stroke and CHD. Br. Med. Bull. 1994; 50: 272-98.

62. Mulrow CD et al. Hypertension in the elderly. JAMA 1994; 272: 1932-8.

63. Chobanian AR. The influence of hypertensive and other hemodynamic factors in atherogenesis. Progr. Cardiovasc Dis. 1983; 26: 177-96.

64. Lusiani L et al. Prevalence of atherosclerotic involvement of the internal carotid artery in hypertensive patients. Int. J. Cardiology 1987; 17: 516.

65. Reed DM et al. A prospective study of artery atherosclerosis. Stroke 1988; 19: 820-5.

66. Fine Eldelstein JS. Precursor of extracranial carotid atherosclerosis in the Framingham study. Neurology 1994; 44: 1046-50.

67. Ross Russell RW. How does blood pressure cause stroke? Lancet 1975; 2: 1283-5.

68. Shinton R et al. Meta-analysis of relation between cigarette smoking and stroke. BMJ 1989; 298: 789-94.

69. Donnan GA et al. Smoking as a risk factor for stroke. Cerebrovasc Dis 1993; 3: 129-38.

70. Howard G et al. Cigarette smoking and progression of atherosclerosis. JAMA, 1998; 279: 1189-24.

71. Haapanen A et al. Carotid atherosclerosis in identical twins discordant for cigarette smoking. Circulation 1989; 80: 10-16.

72. Lindenstrom E et al. Influence of total cholesterol, HDL and triglycerides on risk of CVD. The Copenhagen City Heart Study, AMJ 1994; 309: 1115.

73. Prospective studies collaboration. Cholesterol, diastolic blood pressure and stroke. Lancet 1995; 346: 1647-53.

74. Jurgens G et al. Lipoprotein (a) Serum concentration and apolipoprotein (a) phenotype correlate with severity and presence of ischemic CVD. Stroke 1995; 26: 1841-8.

75. Manson JE et. A prospective study of maturity onset diabetes mellitus and risk of CHD and stroke in women. Arch. Intern Med 1991; 151: 11417.

76. Burchfiel CM et al. Glucose intolerance and 22 years stroke incidence. The Honolulu Heart Program. Stroke, 1994; 25: 951-7.

77. Jorgensen HS et al. Intracerebral hemorrhage versus infarction: Stroke severity, risk factors and prognosis. Ann Neurol., 1995; 38: 45-50.

78. Cook NS et al. Fibrinogen as a major risk factor in cardiovascular disease. Trends Pharmacol Sci 1990; 11: 444-51.

79. Rosengren A et al. Social influences and cardiovascular risk factors as determinants of plasma fibrinogen concentration in a general population sample of middle aged men. BMJ 1990; 330: 634-8.

80. Quizilbash N et al. Fibrinogen and lipid as risk factors for transient ischemic attacks and minor ischemic stroke. BMJ 1991; 303: 605-9.

81. Quizilbash N et al. Von Willebrand factor and risk of ischemic stroke. Neurology 1997; 49: 1552-6.

82. Macko RF et al. Elevated tissue plasminogen activator antigen and stroke risk. Stroke 1999; 30: 7-11.

83. Welin L et al. Analysis of risk factors for stroke in a cohort of men born in 1913. N Engl J Med 1987; 317: 521-6.

84. Yamanouchi H et al. Embolic brain infarction in non-rheumatic atrial fibrillation: A clinicopathological study in the elderly. Neurology 1997; 1593-7.

85. Wolf PA et al. Atrial fibrillation as an independent risk factor for stroke. The Framingham study. Stroke, 1991; 22: 312-18.

86. Friedman GD et al. Relationship of stroke to other cardiovascular disease. Circulation 1968; 38: 533-41.

87. Wolf PA et al. Epidemiological assessment of chronic atrial fibrillation and risk of stroke. The Framingham Study. Neurology 1978; 28: 973-7.

88. Harmsen P et al. Risk factors for stroke in middle aged men in Gotheburg, Sweden. Stroke 1990; 21: 223-9.

89. Stroke Prevention in Atrial Fibrillation Investigator. Predictors of Thromboembolism in Atrial Fibrillation. Ann Int. Med. 1992; 116: 612.

90. Atrial Fibrillation Investigators: Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Arch. Int Med 1994; 154: 1449-57.

91. Di Pasquale G et al. New cardiographic markers of embolic risk in atrial fibrillation. Cerebrovascular disease 1995; 5: 315-22.

92. Stampfer MJ et al. Past use of oral contraceptives and cardiovascular disease: a meta-analysis in the context of the nurses Health study. Am J Obstet Gynecol 1990; 163: 285-91.

93. WHO collaborative study of cardiovascular disease and steroid hormone contraception. Ischemic stroke and combined contraceptives; results of an international multicenter case-control study. Lancet 1996; 348: 498-505.

94. Heinemann LAJ et al. Case-control study of oral contraceptives and risk of thromboembolic stroke: Results from international study on oral contraceptives and health of young women. BMJ 1997; 315: 1502-4.

95. Vandenbroucke JP. Cerebral sinus thrombosis and oral contraceptives. BMJ 1998; 317: 483-4.

96. Kiyohara Y et al. The impact of alcohol and hypertension on stroke incidence in a general Japanese population. Stroke 1995; 26: 368-72.

97. Wannamethee S et al. Patterns of alcohol intake and risk of stroke in middle aged British men. Stroke 1996; 27: 1033-9.

98. Malhotra H et al. Pressor effects of alcohol in normotensive and hypertensive subjects. Lancet 1985; 2: 584-6.

99. MacMohan SW et al. Alcohol and hypertension. Ann Int. Med. 1986; 105: 124-6.

100. Kaplan NM. Alcohol and hypertension. Lancet 1995; 345: 1588-9.

101. Gaziano JM et al. Moderate alcohol intake, increased levels of HDL and its sub-fractions and decreased risk of MI. N Engl. Med. 1993; 329: 1829-34.

102. Manson JE et al. A prospective study of risks of CHD in women. N Engl J Med. 1990; 322: 882-9.

103. Lissner L et al. Variability of body weight and health outcomes in the Framingham population. N Engl J Med. 1991; 324: 1839-44.

104. Shinton R et al. Body fat and stroke. J Epidemiol Community Health. 1995; 49: 259-64.

105. Rexrode KM et al. A prospective study of body mass index, weight change and risk of stroke in women. JAMA 1997; 277: 1539-45.

106. Katan MJ. Fish and Heart Disease. N Engl J Med 1995; 332: 1024-5.

107. Prichard BNC et al. Fish oils and CVD. BMJ 1995; 310: 819-20.

108. Orencia AJ et . Fish consumption and stroke in men. Stroke 1996; 27: 204-9.

109. Midgley JP et al. Effect of reduced dietary sodium on blood pressure. JAMA 1996; 275: 1590-7.

110. Thelle DS. Salt and blood pressure revisited. BMJ 1996; 312: 1240-1.

111. Khaw KT. Epidemiology of stroke. J Neurol. Neurosurg Psychiatry 1996; 61: 333-80.

112. Whalton PK et al. Effects of oral potassium on blood pressure. JAMA 1997; 277: 1624-32.

113. Witztum JL. The oxidation hypothesis of atherosclerosis. Lancet 1994; 344: 793-5.

114. Greenberg ER et al. Antioxidant vitamins, cancers and CVD. N Engl J Med 1996; 334: 1189-90.

115. Connelly JP et al. Strenuous exercise, plasma fibrinogen and factor VII activity. Br Heart J 1992; 67: 351-4.

116. Curfman GD. The health benefits of exercise. N Engl J Med 1993; 328: 574-6.

117. Lee JM et al. Exercise and risk of stroke in male physicians. Stroke, 1999; 30: 1-6.

118. Welch GN. Homocysteine and atherosclerosis. N Engl J Med 1998; 338: 1042-50.

119. Yoo JH et al. Relation of plasma homocysteine to cerebral infarction and cerebral atherosclerosis. Stroke 1998; 29: 2478-83.

120. Stemmermann GH et al. Risk factors related to ischemic and hemorrhagic cerebrovascular disease at autopsy. Stroke 1984; 15: 23-8.

121. Dipasquale G et al. Cerebral ischemia and asymptomatic CHD. Stroke, 1986; 17: 1098-101.

122. Kannel WB et al. Manifestations of CHD predisposing to stroke. JAMA 1983; 250: 2942-6.

123. PA et al. Probability of stroke. Stroke 1991; 22: 312-18.

124. Craven TE et al. Evaluation of atherosclerosis between carotid artery atherosclerosis and coronary artery stenosis. Circulation 1990; 82: 1230-42.

125. Orgen M et al. Non-invasively detected carotid stenosis and IHD in men with leg atherosclerosis. Lancet 1993; 342: 1138-41.

126. Mackey AE et al. Outcome of asymptomatic patients with carotid disease. Neurology 1997; 48: 896-903.

127. Natowicz M et al. Mendelian etiologies of stroke. Ann Neurol 1987; 22: 17592.

128. Liao D et al. Family history of stroke and stroke risk. Stroke 1997; 28: 190812.

129. Grady PA. Pathophysiology of extracranial cerebral arterial stenosis. Stroke, 1984; 15: 224-36.

130. Ross R. Atherosclerosis – An inflammatory disease. N Engl J Med 1999; 340: 115-26.

131. Fuster V et al. The pathogenesis of CHD and the acute coronary syndromes. N Engl J Med 1992; 326: 310-18.

132. Libby P. Atheroma more than mush. Lancet 1999; 348: 54-57.

133. Torvik A et al. Pathogenesis of carotid thrombosis. Stroke 1989; 20: 147783.

134. Lammie GA et al. Recently occluded intra and extracranial carotid arteries. Stroke 1999; 30: 1319-25.

135. Rhodes JM. Cholesterol crystal embolism. Lancet 1996; 347: 1641.

136. Millikan C et al. The fallacy of lacunae hypothesis. Stroke 1990; 21: 1251-7.

137. Fisher CM Lacunar infarcts – a review. Cerebrovasc Dis 1991; 1: 311-20.

138. Sacco SE et al. Epidemiological characteristics of lacunar infarcts in a

population. Stroke 1991; 22: 1236-41.

139. You R et al. Risk factors for lacunar infarction syndromes. Neurology 1995; 45: 1483-7.
140. Caplan LR. Brain enbomlism revisited. Neurology 1993; 43: 1281-7.
141. Daley R et al. Systemic arterial embolism in RHD. Am heart J 1951: 42: 56681.
142. Meltzer RS et al. Intracardiac thrombi and systemic embolization. Ann Int Med 1986; 104: 689-98.
143. Vaitkus PT et al. Embolic potential, prevention and management of mural thrombus complicating anterior wall MI. J Am Coll Cardiol 1993; 22: 1004-9.
144. Levy D et al. Prevalence and clinical features of mitral valve prolapse. Am Heart J 1987; 113: 1281-90.
145. Bogousslavsky J et al. Stroke recurrence in patients with patent foramen ovale. Neurology 1996; 46: 1301-5
146. Curb JD, Abbott RD, Rodriguez BL, Sakkinen P, Popper JS, Yano K, Tracy RP. C-reactive protein and the future risk of thromboembolic stroke in healthy men. Circulation. 2003 Apr 22;107(15):2016-20
147. Agarwal MP, Singh NR, Kaur IR. C-Reactive Protein in acute cerebral infarction. JAPI. 2003 Dec;51.
148. Dhamija RK, Arora S, Gaba P, Jais M, Kaintura A, Kumar M, Bhattacharjee J. Study of genetic, metabolic and inflammatory risk factors in patients of acute ischemic stroke. Indian Journal of Clinical Biochemistry. 2008 Apr 1;23(2):136-43.
149. Rost NS, Wolf PA, Kase CS, Kelly-Hayes M, Silbershatz H, Massaro JM, D'Agostino RB, Franzblau C, Wilson PW. Plasma concentration of C-reactive

protein and risk of ischemic stroke and transient ischemic attack: the Framingham study. Stroke. 2001 Nov 1;32(11):2575-9.

150. Kristensen B et al. Epidemiology and etiology of ischemic stroke in young adults aged 18-44 years in Northern Sweden. Stroke 1997; 28: 17021709.
151. Tsong-Hai Lee et al. Etiologic study of young ischemic stroke in Taiwan. Stroke 2002; 33: 1950-1955.
152. Jaume Roquer, Ana Rodriguez Campello, Meritxell Gomis. Sex differences in first-ever acute stroke. Stroke 2003; 34: 1581-1585
153. Hu G, Sarti C, Jousilahti P, Peltonen M, Qiao Q, Antikainen R, Tuomilehto J. The impact of history of hypertension and type 2 diabetes at baseline on the incidence of stroke and stroke mortality. Stroke. 2005 Dec 1;36(12):2538-43.
154. Kissela BM, Khoury J, Kleindorfer D, Woo D, Schneider A, Alwell K, Miller R, Ewing I, Moomaw CJ, Szaflarski JP, Gebel J. Epidemiology of ischemic stroke in patients with diabetes: the greater Cincinnati/Northern Kentucky Stroke Study. Diabetes care. 2005 Feb 1;28(2):355-9.
155. Reina SA, Llabre MM, Allison MA, Wilkins JT, Mendez AJ, Arnan MK, Schneiderman N, Sacco RL, Carnethon M, Delaney JC. HDL cholesterol and stroke risk: the Multi-Ethnic Study of Atherosclerosis. Atherosclerosis. 2015 Nov 1;243(1):314-9.
156. Gaby C, Kushner I. Acute phase proteins and other systemic responses of inflammation. N Engl J Med 1999; 340: 448-454.
157. Mahapatra SC, Pillai PK, Hui PK, Tripathy SK, Behera BK, Samal KK. C-reactive protein in thrombotic stroke. JAPI Dec. 2002;50:1512.
158. Mario Di Napoli, Francesca Papa. Inflammation, hemostatic markers and antithrombotic agents in relative to long-term risk of new cardiovascular

events in first-ever ischemic stroke patients. Stroke 2002; 33: 1763-1771.

159. Montaner J et al. Correlation between the expression of proinflammatory cytokines and matrix metalloproteinases in the acute phase of an ischemic stroke. Rev Neurol 2001; 33: 115-118.
160. Rathore HS et al. Role of C-reactive protein estimation in early diagnosis of cortical and lacunar infarct. JAPI Dec. 2002; 50: 1516.
161. L.Masotti et al. Prognostic role of C-reactive protein in very old patients with acute ischaemic stroke. Journal Of Internal Medicine 2005; 258: 145152.
162. Kerstin Winbeck et al. Prognostic relevance of early serial C-reactive protein measurements after first ischemic stroke. Stroke 2002; 33: 2459-2464.
163. Irene M et al. C-reactive protein predicts progression of atherosclerosis measured at various sites in the arterial tree. The Rotterdam Study. Stroke 2002; 33: 2750-2755.
164. 164. Das S, Ghosh KC, Malhotra M, Yadav U, Kundu SS, Gangopadhyay PK. Short term mortality predictors in acute stroke. Annals of neurosciences. 2012 Apr;19(2):61.
165. Bousser MG. Stroke in women. Circulation 1999; 99: 463-467.
166. Bonita R. Epidemiology of stroke. Lancet 1992; 339: 342-344.

ANNEXURE -I

ETHICAL CLEARENCE CERTIFICATE

ANNEXURE II

INFORMED CONSENT FORM:

TITLE OF RESEARCH: **A STUDY OF C-REACTIVE PROTEIN IN ACUTE ISCHEMIC STROKE**

GUIDE :

P.G. STUDENT:

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

PURPOSE OF STUDY:

I have been informed that the purpose of this study is to study diagnostic importance of platelet volume indices in patients with acute chest pain suggesting acute coronary syndrome.

PROCEDURE:

I understand that I will undergo detailed history and clinical examination and investigations

BENEFITS:

I understand that my participation in this study will have no direct benefit tome other than the potential benefit of treatment which is planned to prevent further morbidity and mortality in me.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulation of hospital. If the data is used for publication the identity will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw from study at any time.

(Signature of Guardian) (Signature of patient)

STUDY SUBJECT CONSENT FORM:

I confirm that _____ has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all above in detail in my own language and I understand the same. I agree to give my consent to participate as a subject in this research project.

DATE SIGNATURE OF PARTICIPANT

DATE SIGNATURE OF WITNESS

ANNEXURE III

PROFORMA

SCHEME OF CASE TAKING

Name: CASE NO:

Age: OP/IP NO:

Sex: DOA:

Religion: DOD:

Occupation:

Address:

Presenting Complaints:

History of presenting complaints:

Past History:

Family history:

Personal History:

Diet –

Appetite –

Sleep –

Bowel –

Bladder –

Habits –

Obstetric and menstrual history (in females):

Physical Examination:

1. .Built :
2. .State of Nutrition :
3. Hydration status :
4. .Eyes :
5. Ears:
6. .Oral cavity:
7. .Lymphadencopathy :
8. .Pedal Edema:
9. .Examination of peripheral vessels and neck vessels

Vitals:

Pulse rate:	Respiratory rate:
Blood pressure:	Temperature:

Systematic Examination:

1.Nervous system examination:

a.Handed ness:

b.Mental status examination

i.Memory :

iiOrientation :

iii.Speech and language :

iv intelligence:

v.level of consciousness:

c.Cranial nerves examination

d.Motor system examination:

	Right		Left	
	UL	LL	UL	LL
a.Nutrition				
b.Tone				
c.Power				
d.Coordination				
e.Involuntary movements:				
f.Reflexes:	Right		Left	
a.Superficial				

i.Abdominal

ii.Cremastric

iii Corneal

iv Conjunctival

v .Plantar

b.Deep

i.Biceps

ii.Triceps

iii.Supinator

iv.Knee

v.Ankle

c.Primitive reflex –

d.Sensory system examination:

	Right	Left
Touch		
Pain		
Temperature		
Vibration		
Joint sense		
Cortical sensation		

e.Cerebrallar system examination:

	Right	Left
Finger Nose test		
Knee Heel test		
Dysdiadokinesia		

g.GAIT:

h.Signs of Autonomic Disturbances – Present/Absent

i.Signs of Meningeal iriitation

Neck Rigidity/Kernings sign/Brudzenski sign

j.Examination of skull and spine – Deformity Present /Absent

2. Cardiovascular System:

3. Respiratory System:

4. Per Abdomen Examination:

Final diagnosis:

INVESTIGATIONS

PATHOLOGY:

1.)Complete blood count:	
Hb	gm/dl
Total count	Cells/cumm
Differential count Neutrophils	%
Lymphocytes	%

Eosinophils	%
Basophils	%
Monocytes	%
2.) ESR	At the end of 1st hour.
3.)Platelet Indices	
Platelet Count	
4.) Urine Routine	
Sugar	
Albumin	
Pus cell	
Epithelial cell	

BIOCHEMISTRY:

B urea	
S creatinine	
Total cholesterol	
Ldl	
Vldl	
Hdl	

S triglycerides	
Rbs	
Serum Electrolytes	
Serum CRP level	

ECG

CHEST XRAY PA VIEW

CT BRAIN PLAIN

Other relevant investigations will be done when required.

CONCLUSION:

DATE:

SIGNATURE

MASTERCHART

SN	GRP (1 CASE 2 CONTROL)	AGE	SEX	Conscious	Motor	CRANIAL NERVE	OTHERS	MIXED	VEG	SMOKING	ALCOHOL	TOBACCO	SBP	DBP	HTN	CVS	Ct-Scan diagnosis	RBS	DM	Sr. Urea	Sr. Creatinine	Sr. Cholesterol	HDL	LDL	TG	CRP VALUE	CRP
1	1	68	M	A	L-H		headache	+	-	+	+	-	140	90	1		Fr-Tmp	140	1	31	1.4	140	68	82	136	60	2
2	1	60	M	C	B/L-H			-	+	+	+	-	130	90	0		Pa,Temp occiptal	160	1	20	2	186	86	106	120	90	2
3	1	55	M	A	R-H			-	+	+	-	-	140	80	1		Bg,,Thalamus,Int Cap	180	1	20	0.8	186	68	101	132	60	2
4	1	55	M	A	L-H			-	+	-	-	-	130	90	0		B/l parietall	72	0	10	1	90	25	43	109	20	2
5	1	72	F	D	R-H			+		-	-	-	180	100	1	ectopic	Ic	240	1	17	0.8	283	38	190	275	50	2
6	1	75	M	A	L-H	R		-	+	-	-	-	150	70	1		Pa	90	0	20	1.5	170	38	82.4	248	42	2
7	1	60	F	C	R-H	L	convulsions	+	-	-	-	-	130	70	0		Fr,Pa	112	0	20	1.2	229	59	148	113	50	2
8	1	72	M	C	L-H		vomitting	+	-	+	-	-	140	84	1		Bg,Caudate nucleus	105	0	38	0.5	97	18	54	92	90	2
9	1	60	M	D	L-H			+	-	-	-	+	180	90	1		Fr Pa Temp	138	1	20	0.8	188	31	125	158	47	2
10	1	60	M	D	L-H			+	-	+	-	-	130	70	0		Fr,Pa	148	1	20	0.8	124	41	69	69	48	2
11	1	55	F	A	L-H			-	+	-	-	-	140	90	1		Fr,Pa	180	1	23	0.7	188	42	95	257	50	2
12	1	60	F	D	L-H		headache	+	-	-	-	-	190	110	1	ectopic	Fr	136	1	70	2	174	44	103	137	43	2
13	1	65	F	A	L-H		convulsions	+	-	-	-	-	116	76	0		Fr-Prt-Temp	131	1	20	0.6	140	42	73	144	8	1
14	1	60	M	A	LULparesis			+	-	+	-	-	150	110	1		Rt frontal	244	1	18	0.7	245	36	187	106	90	2
15	1	70	M	D	R-H			+	-	+	+	+	220	110	1	ESM	Pa	130	1	20	1	235	37	152.6	230	44	2
16	1	57	M	C	L-H		headache	-	+	-	-	-	180	120	1		Frnt Pa,Te	82	0	67	1.4	118	22	61	176	42	2
17	1	40	M	A	R-H			+	-	-	-	-	170	100	1		Frontal	96	0	26	1	159	40	101	144	60	2
18	1	40	M	A	R-H			+	-	+	+	+	180	100	1		Fr	180	1	20	0.8	171	29	171	286	40	2
19	1	60	M	D	L-H	R	convulsions	-	+	+	-	+	130	86	0		Pa,Bg	110	0	20	0.8	148	84	102	108	90	2
20	1	80	F	D	L-H			+	-	+	+	+	170	90	1		Fr,Pa	130	1	20	0.6	200	68	122	104	3	1
21	1	50	M	D	L-H		vomitting	+	-	+	-	-	180	90	1		Temp,Pa	90	0	20	1.1	150	32	88	149	17	2
22	1	60	M	A	R-H			+	-	-	-	-	130	80	0		Pa	140	1	20	1.01	186	82	110	130	90	2
23	1	58	M	D	LULparesis			-	+	+	-	-	140	100	1		Pa	136	1	39	1	163	29	105	144	90	2
24	1	65	M	A	L-H	R	headache	-	+	-	-	-	150	100	1		Pa,Occp,IC	180	1	20	0.8	140	42	73	144	6	1
25	1	60	M	C	R-H			-	+	+	-	-	170	100	1		Pa	130	1	127	2	212	42	86	148	90	2
26	1	50	M	A	R-H			-	+	+	+	-	144	90	1		IC,Corona radiata	162	1	58	0.7	196	48	122	129	28	2
27	1	68	M	A	L-H			+	-	-	-	-	110	70	0	ESM	Bg,IC,Fr,Prt	130	1	25	1	176	39	127	130	2.7	1
28	1	70	F	D	R-H		convulsions	+	-	-	-	-	146	96	1	ESM	Pa,Temp,Occp	132	1	20	1.1	176	39	127	45	90	2
29	1	60	M	D	B/L-H			-	+	+	+	-	150	80	1		Fr,Occp,Pons,Bg	110	0	27	1	142	92	82	138	40	2
30	1	78	M	D	R-H		headache	-	+	+	-	-	170	110	1		Pa,Te	90	0	20	1.5	170	38	82	248	42	2
31	1	26	F	A	L-H		headache	+	-	+	+	-	170	106	1		Pa,Rt Pons	148	1	20	0.8	180	80	106	126	21.1	2
32	1	58	M	C	R-H		convulsions	-	+	+	+	-	220	110	1		L Front	136	1	28	0.9	138	48	108	148	5.5	1
33	1	78	M	C	R-H			-	+	+	-	-	170	80	1	ESM	Rt pons	168	1	16	1.1	186	52	110	138	5	1

34	1	68	F	A	R-H			-	+	-	-	-	170	94	1		Fr,Pr,Temp	130	1	20	0.6	156	28	91	134	90	2
35	1	60	F	A	L-H			-	+	-	-	-	180	100	1		Thalamus	128	1	35	1.3	196	56	118	119	30	2
36	1	65	F	A	L-H			-	+	-	-	-	150	70	1	ESM	Pa	113	0	37	1.2	108	83	44	133	66	2
37	1	60	F	A	L-H			+	-	-	-	-	180	100	1		IC	176	1	40	0.7	135	39	65	158	13.2	2
38	1	56	M	A	RULparesis			+	-	+	-	-	140	80	1		Bg,Fr,Part,Occp	120	0	20	0.8	59.8	53	153	328	30	2
39	1	60	F	D	R-H			+	-	-	-	+	180	90	1		Fr,Temp	141	1	20	0.8	196	57	125	66	20	2
40	1	56	M	C	R-H			+	-	+	-	-	170	110	1	ectopic	Fr,Pa	129	1	31	1.4	280	42	102	138	24	2
41	1	67	M	D	L-H		convulsions	-	+	-	-	-	140	90	1		Fr,Temp	120	0	100	2	150	60	25	180	90	2
42	1	60	M	D	L-H		headache	+	-	-	-	-	200	110	1		FrTempPrt	131	1	48	0.7	155	57	80	90	2	1
43	1	65	M	A	L-H			+	-	-	-	-	116	74	0		Pa	87	0	40	0.8	200	80	50	158	2	1
44	1	68	M	A	L-H			+	-	+	-	-	150	110	1	ectopic	Temp	200	1	40	0.7	250	22	25	85	9	1
45	1	52	M	D	L-H	R	headache	+	-	+	+	+	210	110	1		Fr,Prtal	142	1	40	1.2	200	80	50	160	63	2
46	1	70	M	D	L-H		convulsions	-	+	-	-	-	180	120	1		Pa,Te,Occp	149	1	40	1.1	180	63	80	184	90	2
47	1	65	F	D	R-H			+	-	-	-	-	170	110	1		Pons,occip	140	1	30	0.5	200	40	15	100	5	1
48	1	68	M	A	R-H			+	-	+	+	+	180	100	1		occip,Part	140	1	60	1	200	85	65	124	14.6	2
49	1	63	F	A	L-H		vomiting	-	+		-	+	130	86	0		Fronto-Part	140	1	60	0.5	191	51	96	218	11	2
50	1	68	F	A	R-H			+	-	+	+	+	170	90	1		Fr,Pa	130	1	30	0.9	182	32	112	187	2	1
51	1	80	F	A	R-H			+	-	+	-	-	180	90	1	ESM	IC,Bg	132	1	20	1	169	82	70	83	15	2
52	1	45	M	A	L-H			+	-	-	-	-	130	90	0		Pa	94	0	30	0.7	94	92	80	162	90	2
53	1	45	M	A	L-H	R	convulsions	-	+	+	-	-	140	100	1		IC,CR	148	1	60	0.8	148	103	52	148	60	2
54	1	80	F	C	R-H	R	headache	-	+	-	-	-	150	100	1	ESM	Pons,Cerebellum	151	1	21	0.6	76	59	31	86	90	2
55	1	62	M	A	R-H			-	+	+	-	-	160	100	1		Bg,CR	180	1	60	0.8	120	62	48	104	16.9	2
56	1	55	M	A	L-H			-	+	+	+	-	144	90	1		CR,IC	84	0	90	1	160	41.2	92.2	130	90	2
57	1	70	M	A	R-H			+	-	-	-	-	110	70	0		Bg	125	0	19	1	165	38.6	93.3	165	20	2
58	1	70	F	D	B/L H			+	-	-	-	-	146	96	1		Fr,Pa,cR	110	0	60	0.8	200	82	60	124	30	2
59	1	50	F	D	R-H		headache	-	+	-	-	-	150	80	1		CR	140	1	60	1.3	115	36	58	101	90	2
60	1	60	F	D	R-H		convulsions	-	+	+	-	-	170	104	1		Pa,Te	150	1	60	0.8	206	47	130	148	3	1
1	2	68	M										124	86	0			95	0	21	0.9	162	68	42	132	1	1
2	2	60	M										126	54	0			88	0	21	0.9	180	86	84	126	1	1
3	2	55	M										120	84	0			120	0	20	0.8	186	82	90	138	19	2
4	2	55	M										124	82	0			127	1	14	0.6	186	88	62	136	0.5	1
5	2	72	F										130	80	0			99	0	24	1	144	25	92	134	2.8	1
6	2	75	M										126	82	0			95	0	20	1.2	182	55	96	156	4	1
7	2	60	F										130	80	0			122	0	23	0.7	144	26	106	61	4.7	1
8	2	72	M										126	80	0			140	1	20	1.4	186	86	52	132	9	1
9	2	60	M										118	72	0			135	1	20	0.6	182	62	42	132	2	1
10	2	60	M										114	70	0			130	1	25	0.6	186	48	110	186	7	1
11	2	55	F										121	86	0			110	0	20	0.8	160	68	110	148	6	1
12	2	60	F										130	80	0			101	0	33	0.8	186	48	120	110	7	1
13	2	65	F										124	80	0			110	0	19	0.8	180	62	100	136	8	1
14	2	60	M										116	70	0			146	1	15	0.9	182	64	42	130	2.6	1
15	2	70	M										126	72	0			134	1	19	0.8	188	62	42	134	3	1
16	2	57	M										120	72	0			91	0	20	0.8	168	60	100	148	9	1
17	2	40	M										120	72	0			98	0	20	0.8	180	80	120	128	0.2	1

18	2	40	M										120	70	0			170	1	20	0.8	160	41	108	54	1	1
19	2	60	M										120	70	0			110	0	20	0.6	100	22	25	100	9.5	1
20	2	80	F										118	74	0			114	0	15	0.5	200	68	55	200	1	1
21	2	50	M										116	74	0			190	1	50	0.7	180	68	110	136	2	1
22	2	60	M										120	84	0			140	1	26	0.8	180	80	100	136	25	2
23	2	58	M										120	72	0			121	0	70	0.8	151	58	77	81	1	1
24	2	65	M										124	74	0			180	1	20	0.5	180	68	110	136	19	2
25	2	60	M										130	80	0			80	0	27	0.8	130	60	110	136	15	2
26	2	50	M										140	88	1			131	1	20	0.7	168	66	44	146	10	2
27	2	68	M										136	84	0			115	0	45	1.1	168	40	132	136	29	2
28	2	70	F										126	76	0			110	0	10	0.5	168	68	110	178	19	2
29	2	60	M										120	84	0			110	0	60	0	160	80	60	138	25	2
30	2	78	M										120	70	0			110	0	60	2	186	68	110	136	9.5	1
31	2	26	F										130	70	0			94	0	20	0.8	186	88	110	138	3	1
32	2	58	M										120	84	0			82	0	27	0.7	186	88	44	186	7	1
33	2	78	M										130	80	0			132	1	20	0.8	158	68	114	132	5	1
34	2	68	F										130	84	0			130	1	20	0.8	168	68	42	132	9.5	1
35	2	60	F										120	82	0			132	1	28	0.6	186	62	42	130	9.5	1
36	2	65	F										124	82	0			118	0	28	0.6	182	82	42	142	3.8	1
37	2	60	F										130	70	0			130	1	28	0.8	136	48	68	136	0.9	1
38	2	56	M										126	76	0			142	1	32	0.6	186	82	46	138	5	1
39	2	60	F										130	80	0			134	1	14	0.6	182	82	42	126	9	1
40	2	56	M										120	70	0			130	1	17	0.6	138	40	110	126	6	1
41	2	67	M										120	76	0			112	0	18	0.8	186	68	42	120	6	1
42	2	60	M										130	86	0			130	1	20	0.6	146	48	110	136	9.5	1
43	2	65	M										114	76	0			136	1	28	0.6	182	82	42	138	4	1
44	2	68	M										118	84	0			130	1	20	0.8	186	46	116	136	2	1
45	2	52	M										134	84	0			115	0	31	0.6	182	68	110	136	9.5	1
46	2	70	M										124	76	0			93	0	20	0.8	186	88	110	136	9.5	1
47	2	65	F										130	80	0			97	0	15	0.6	186	82	42	132	5	1
48	2	68	M										126	76	0			87	0	19	0.8	186	88	42	132	8	1
49	2	63	F										118	80	0			86	0	20	0.8	186	82	106	138	7	1
50	2	68	F										130	84	0			120	0	30	1	186	82	110	136	7	1
51	2	80	F										126	74	0			115	0	20	0.6	188	68	48	136	8	1
52	2	45	M										130	80	0			130	1	26	0.8	182	68	28	132	1	1
53	2	45	M										110	70	0			110	0	36	0.7	136	86	100	146	7	1
54	2	80	F										130	76	0			136	1	24	0.8	180	58	126	168	9.5	1
55	2	62	M										132	76	0			124	0	32	0.8	166	40	86	111	1.2	1
56	2	55	M										130	74	0			120	0	17	0.6	180	86	104	134	2	1
57	2	70	M										128	76	0			83	0	20	0.6	200	108	52	138	14	2
58	2	70	F										126	76	0			81	0	10	0.7	172	35	105	160	5	1
59	2	50	F										124	80	0			157	1	20	0.7	252	25	80	252	8	1
60	2	60	F										132	84	0			210	1	34	1	200	86	130	158	1	1