A STUDY OF SERUM FIBRINOGEN LEVEL AND ITS PROGNOSTIC SIGNIFICANCE IN ACUTE ISCHEMIC STROKE

A Dissertation Submitted to

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY

CHENNAI

In Partial Fulfilment of the Regulations

For the Award of the Degree of

M.D. (GENERAL MEDICINE) - BRANCH – I

REG. NO: 200120102505

THANJAVUR MEDICAL COLLEGE AND HOSPITAL,THANJAVUR-613004

CERTIFICATE FROM DEAN

THIS IS TO CERTIFY THAT THIS DISSERTATION ENTITLED

"A STUDY OF SERUM FIBRINOGEN LEVEL AND ITS PROGNOSTIC SIGNIFICANCE IN ACUTE ISCHEMIC STROKE"

IS THE BONAFIDE ORIGINAL WORK DONE BY **DR KUMAR S**, IN PARTIAL FULFILMENT OF THE UNIVERSITY REGULATIONS OF THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY, CHENNAI, FOR **M.D BRANCH - GENERAL MEDICINE** EXAMINATION OF THE TAMILNADU DR M.G.R MEDICAL UNIVERSITY TO BE HELD IN **MAY 2023.**

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(Reg. No: EC/NEW/INST/2020/1058)

CERTIFICATE

No: 847/2021

TITLE OF THE STUDY:

A study of serum fibrinogen level and its prognostic significance in patients with acute ischemic stroke in tertiary care center.

PRINCIPAL INVESTIGATOR:

Dr. S. Kumar, Postgraduate in Department of General Medicine, Thanjavur Medical College.

This to certify that the protocol submitted by the principal investigator of the above mentioned study has been reviewed as per standard ethical guidelines and the same has been **APPROVED** by the members of the Institutional ethical committee at its meeting held on **21.01.2021**.

Dr. N. Arumugam M.D.,
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DECLARATION

I, **DR.KUMAR S**, SOLEMNLY DECLARE THAT THIS DISSERTATION TITLED

"A STUDY OF SERUM FIBRINOGEN LEVEL AND ITS PROGNOSTIC SIGNIFICANCE IN ACUTE ISCHEMIC STROKE"

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DATE: 16/12/22

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DR KUMAR S

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Document Information

Analyzed document	Dr Kumar thesis SHORT.pdf (D153453394)
Submitted	2022-12-15 08:54:00
Submitted by	S.Kumar
Submitter email	kumarseetharaman93@gmail.com
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ACKNOWLEDGEMENT

I would like to thank **DR.R. BALAJI NATHAN**., Dean, Thanjavur medical college and hospital, for permitting me to utilize the facilities of Thanjavur Medical College and Hospital facilities for this dissertation.

I wish to express my respect, sincere gratitude and thanks to my beloved teacher and Head of The Department **PROF DR.C. PARANTHAKAN, M.D.**, and my Unit Chief, **PROF.DR. S. VETRIVEL, M.D**., for his valuable guidance and encouragement during the study and also throughout my course period.

I am extremely thankful to Assistant Professors of Medicine of my Unit **DR.S.VENNILA M.D, DR. V.NARESHKUMAR M.D,** for their valid comments and suggestions.

I profusely thank the Department of Cardiology and the Department of Biochemistry for their timely help, cooperation and support.

I sincerely thank all the staffs of Department of Medicine and Department Of Cardiology and Biochemistry for their timely help rendered to me, whenever needed.

I extend my thanks to all my friends, batch mates, any senior and junior colleagues who have stood by me and supported me throughout my study and course period.

I express my gratitude to all the patients who participated in the study for their extreme patience and co-operation.

I am extremely thankful to my Parents for their continuous support.

LIST OF ABBREVATIONS:

CRP	C-reactive protein
NIHSS	National institute of health stroke scale
TIA	Transient ischemic attack
RIND	Reversible ischemic neurological deficit
TCD	Transcranial Doppler ultrasound
NMDA	N-methyl-D-aspartate
NOS	Nitric oxide synthase
MMP	Matrix metalloprotease
APOE	Apolipoprotein E
ASA/AHA	American stroke association/American heart association
ICA	Internal carotid artery
CCA	Common carotid artery
ACA	Anterior cerebral artery
PCA	Posterior cerebral artery
ACoA	Anterior communicating artery
PCoA	Posterior communicating artery
SSS	Scandinavian stroke scale
MRS	Modified rankin scale
SBP	Systolic blood pressure
DBP	Diastolic blood pressure

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1 ABSTRACT:

Introduction:

One of the leading causes of illness and mortality worldwide is acute ischemic stroke. The incidence seems to always be on the rise due to changing lifestyles. The patient must receive prompt attention and the proper care to survive. Serum fibrinogen level is a prognostic biomarker for acute ischemic stroke patients because they had a higher mortality rate when they admitted with high levels of fibrinogen. Plasma fibrinogen level is a simple marker which can be used to identify patients who are at risk.

Objectives:

To study the prognostic importance of serum fibrinogen in acute ischemic stroke in a series of 70 cases

Methodology:

This is a Prospective cross-sectional study, among 70 patients both male and female presenting as Acute Stroke, admitted under the Department of Internal Medicine, Thanjavur Medical College and Hospital, Thanjavur. Relevant clinical history, clinical examinations, biochemical parameters especially the serum fibrinogen levels were compared with the outcomes of the study population. Prognostic value of the serum fibrinogen levels were analysed.

Results:

The mean Serum Fibrinogen (mg/dl) among the subjects was 396.36 (± 114.68) mg/dl ranging from 60 to 649 mg/dl. The mean Serum Fibrinogen (mg/dl) among Death was significantly higher compared to the subjects who Discharged. Age, smoking, alcoholism, blood pressure, hypertension status, blood sugar, Diabetic status were not associated with Serum Fibrinogen level. Female gender, ischemic stroke, severe cases in Scandinavian Stroke Scale, higher Modified Ranking Score at discharge and admission, had significantly higher levels of Serum Fibrinogen level.The cut off for predicting Outcome is 505 which had a sensitivity of 75%, specificity of 98.39%, positive predictive value of 85.71%, negative predictive value of 96.83% and a diagnostic accuracy of 95.71%.The area under the curve for Serum Fibrinogen (mg/dl) in predicting Outcome is 0.864 (0.637 - 1).

Conclusion:

Serum fibrinogen levels can be used to predict the prognosis in patients affected with acute ischemic stroke.

Keywords:

Fibrinogen, prognostic importance of serum fibrinogen, acute ischemic stroke, stroke prognosis, stroke outcomes.

2 INTRODUCTION

Stroke is the second leading cause of death and the third leading cause of disability worldwide. 5.3 million fatalities worldwide, or 1 in 11, were caused by stroke. Since 1990, the total number of stroke victims has risen, as have the numbers of stroke victims who are incapacitated and the number of stroke deaths. If current trends hold, it is predicted that there will be 70 million stroke survivors and 20 million yearly stroke fatalities worldwide by 2030.(1,2)

The patient's family, other healthcare professionals, insurance companies, and patients frequently ask clinicians to forecast outcomes following a stroke. (3,4)Age, stroke severity, stroke mechanism, infarct site, concomitant diseases, clinical findings, and associated sequelae are only a few of the many variables that affect a stroke patient's prognosis. (5–7)Additionally, interventions such as thrombolysis, mechanical thrombectomy, care in a stroke unit, and rehabilitation can all have a significant impact on how an ischemic stroke turns out. (8–10)

For a clinician to give an accurate prognosis for a specific patient, to offer a logical approach to patient management, and to assist the patient and family in understanding the course of the disease, they must be aware of the key variables that determine prognosis.The severe emotional and socioeconomic impacts of stroke on patients, their families, and the healthcare system is significant and is the leading cause of disability and mortality worldwide.(11)

Ischemic strokes account for 59% to 93% of all cerebrovascular incidents.A risk factor for atherosclerosis and ischemic events is inflammation. Numerous inflammatory

markers, including fibrinogen and high sensitivity C-reactive protein (hs-CRP), have been identified as reliable indicators of the severity and prognosis of stroke.(12–16)

The three main cardiovascular disorders (CVD)—ischemic heart disease, stroke, and venous thromboembolism—all involve thrombosis. While venous thrombosis is connected to endothelial dysfunction and blood stasis, which cause the aggregation of fibrin and red blood cells, arterial thrombosis is associated with the creation and rupture of an atherosclerotic plaque leading to the accumulation of platelets.(17,18)

The main determinant of plasma and whole blood viscosity is fibrinogen. Elevated levels are linked to carotid stenosis, peripheral vascular disease, atherosclerosis, and coronary heart disease.(19)The association between elevated fibrinogen levels and stroke persisted even after controlling for other confounding variables such as age, smoking, high blood pressure, and high cholesterol.(20)

Need for the study / Justification of the study:

One of the leading causes of illness and mortality worldwide is acute ischemic stroke. The incidence seems to always be on the rise due to changing lifestyles. The patient must receive prompt attention and the proper care to survive. Serum fibrinogen level is a prognostic biomarker for acute ischemic stroke patients because they had a higher mortality rate when they admitted with high levels of fibrinogen. Plasma fibrinogen level is a simple marker which can be used to identify patients who are at risk.Therefore this study aims to study the prognostic importance of serum fibrinogen in acute ischemic stroke in a series of 70 cases.

3 AIM AND OBJECTIVES

3.1 **AIM:**

To study the prognostic importance of serum fibrinogen in acute ischemic stroke in a series of 70 cases in thanjavur medical college.

3.2 **OBJECTIVES:**

I. Primary Objectives:

To study the prognostic importance of serum fibrinogen in patients with acute ischemic stroke.

II. Secondary Objectives:

To study the prognostic importance of serum fibrinogen level in acute ischemic stroke with age and sex distribution and various risk factors.

To compare the measures to decrease plasma fibrinogen levels can be included in preventive strategies against stroke.

4 REVIEW OF LITERATURE

Review of Literature of this study on prognostic role of serum fibrinogen in patients affected with acute ischemic stroke is discussed under the following heads:

a. Stroke
    i. Definition of stroke.
    ii. Classificationof stroke.
    iii. Risk-factorsof stroke.
    iv. Diagnosisof stroke.
    v. Managementof stroke.
b. Acute ischemic stroke
    i. Classification of acute ischemic stroke.
    ii. Pathophysiologyof acute ischemic stroke.
    iii. Management of acute ischemic stroke.
c. Fibrinogen
d. Similar studies on prognostic role of serum fibrinogen in patients affected with acute ischemic stroke

a. Stroke:

Definitionof stroke:

"Rapidly developing symptoms and/or evidence of focal and global loss of brain function persisting for at least 24 hours with no evident explanation other than of vascular origin" are considered to be strokes.(21)

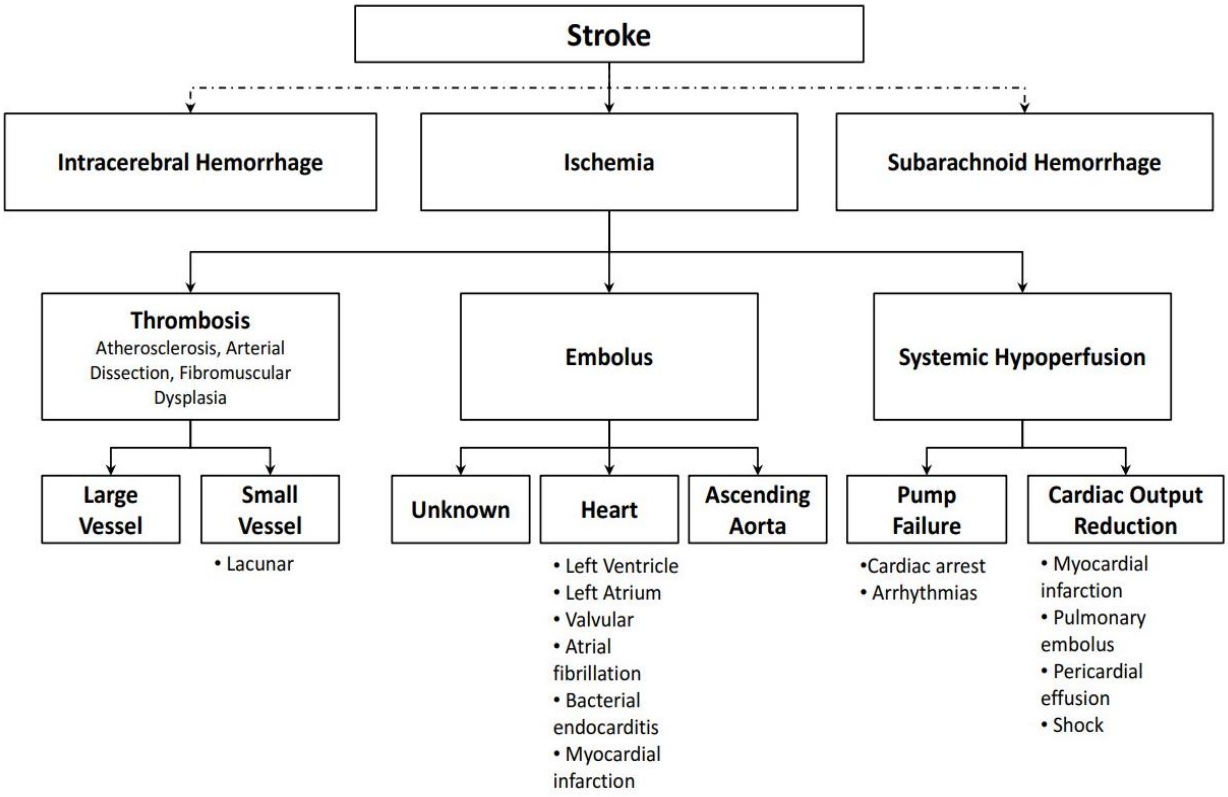
Typesof stroke:

Generally, there are two main forms of presentation of stroke:

I. An ischemic stroke causes a portion of the brain's blood supply to be cut off, which causes a sudden loss of function (80 percent of cases of stroke)
II. Haemorrhagic stroke (caused by a blood vessel rupturing or a vascular anomaly) (20 percent of cases of stroke).(22)

80 percent of haemorrhagic strokes are caused by intracerebral and subarachnoid haemorrhages. Subarachnoid haemorrhage is primarily caused by saccular aneurysms, but it is also linked to arteriovenous malformation, intracranial neoplasm, and some medications like anticoagulants. Intracerebral haemorrhage results from uncontrolled hypertension that causes small vessels to burst, whereas intracerebral haemorrhage is caused by uncontrolled hypertension.(23,24)The following picture shows how strokes are classified., (25)

Figure 1.Stroke-Classification:



Risk factorsof stroke:

The risk factors for stroke that can be modified and those that cannot be modified are shown in the following table, (26)

Table 1.Risk factors associated with Stroke:

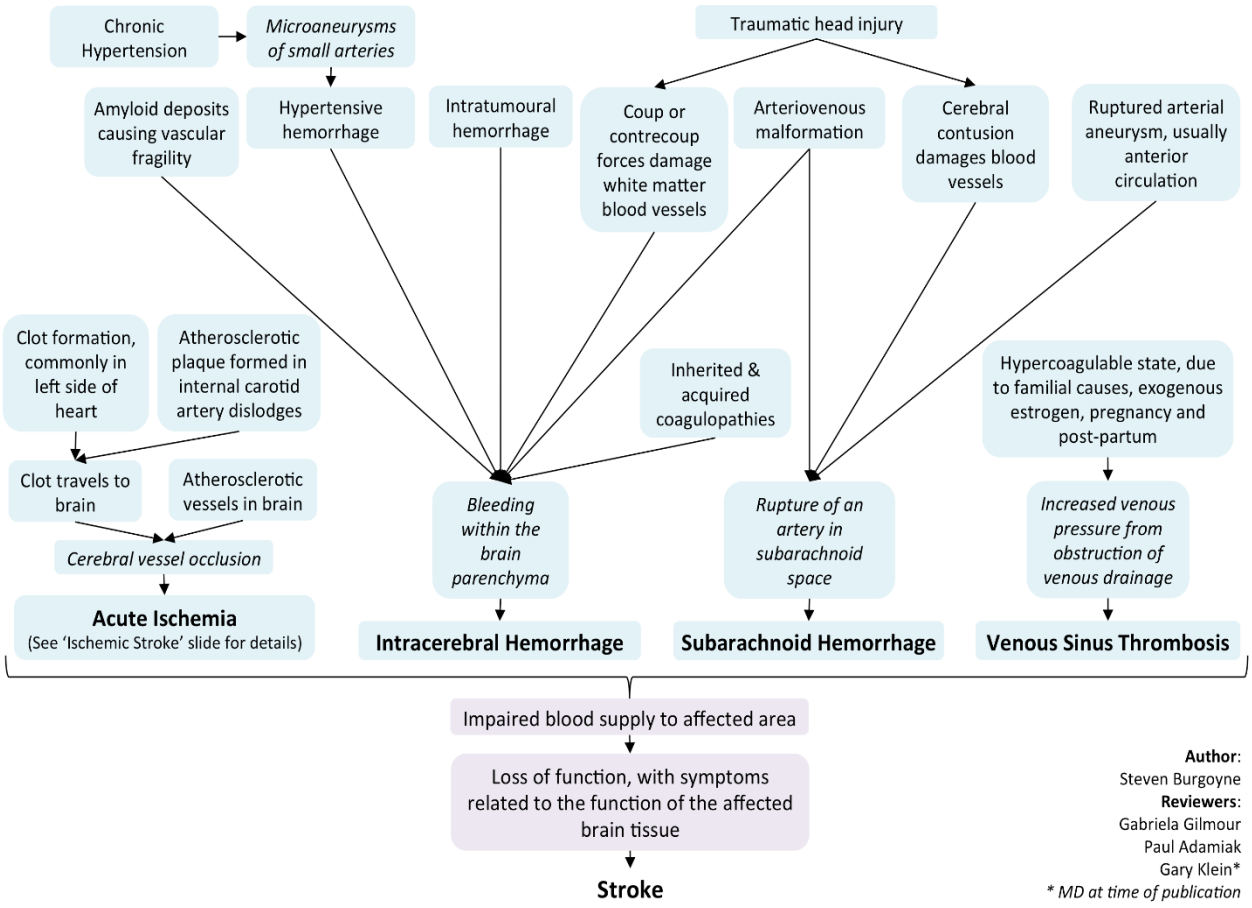
Nonmodifiable risk factors	Modifiable risk factors
Age	Hypertension
Sex	Diabetes
Low birth weight	Dyslipidemia
Race/ethnicity	Obesity
Family history (including intracranial aneurysms)	Metabolic syndrome
Genetic predisposition (including Fabry disease, sickle cell disease, CADASIL, coagulopathies)	Diet and nutrition
	Cigarette smoking
	Alcohol consumption
	Physical inactivity
	Obstructive sleep apnea
	Large artery atherosclerosis:
	Extracranial carotid disease
	Extracranial vertebrobasilar disease
	Intracranial atherosclerosis
	Arterial fibrillation
	Aortic atherosclerosis
	Patent foramen ovale
	Prosthetic heart valves
	Valvular heart disease
	Cardiomyopathy
	Acute myocardial infarction
	Hypercoagulability
	Hyperhomocysteinemia
	Antiphospholipid antibody syndrome

Abbreviation: CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy.

Pathogenesis of stroke:

The pathogenesis of a stroke is depicted in the following picture., (27)

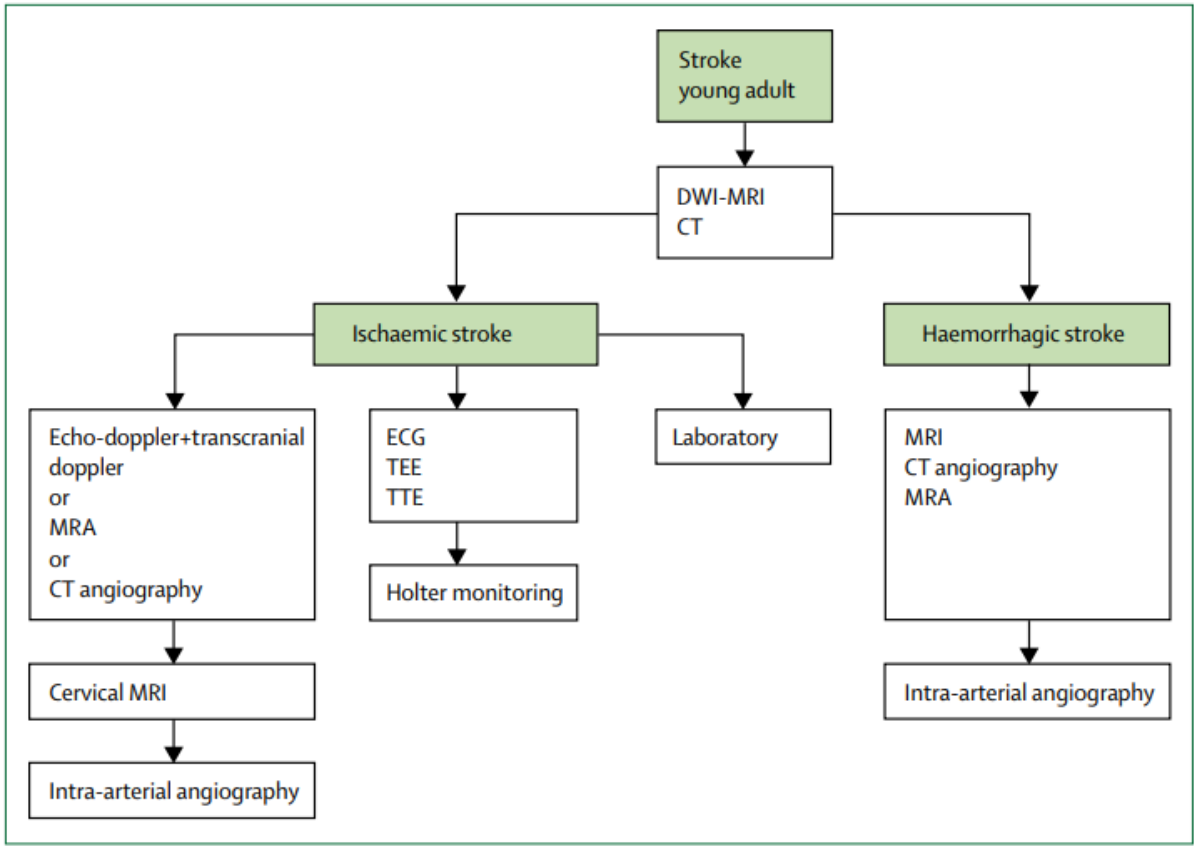
Figure 2.Stroke-Pathogenesis:



Diagnosisof stroke:

The diagnosis of ischemic stroke to determine its arterial and cardiac causes is represented by the next image. (28)

Figure 3. Diagnosis of ischemic stroke to determine its arterial and cardiac causes:



Both magnetic resonance imaging (MRI) and computerised tomography (CT) imaging are effective diagnostic methods. Although CT imaging is more often utilised, MRI provides information that is more precise and dependable. MRI imaging can distinguish between thrombus and haemorrhage.(29)the left middle cerebral artery (MCA) infarction is shown in the computer tomography scan below as axial nonenhanced hypoattenuating

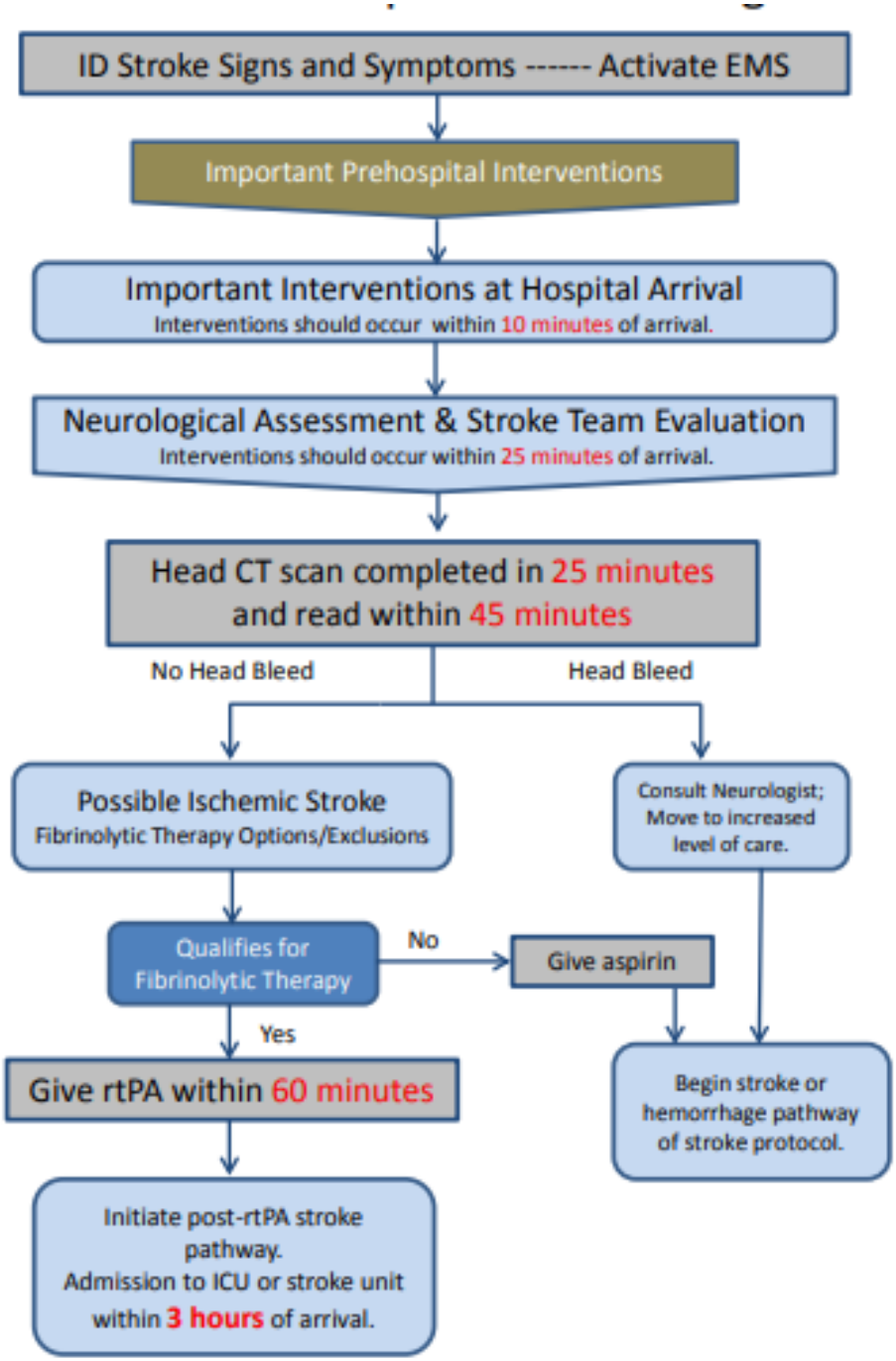
foci all along the left side of the white matter (with arrows) and sulcal effacement in the left MCA region, both of which are compatible with infarction..(30)

Figure 4.Appearance of infarction in Left middle-cerebral artery (MCA) in CT:

Managementof stroke:

The AHA ACLS adult suspected stroke algorithm is represented by the following algorithm., (31)

Figure 5.AHA ACLS algorithm for the suspected stroke in adults:

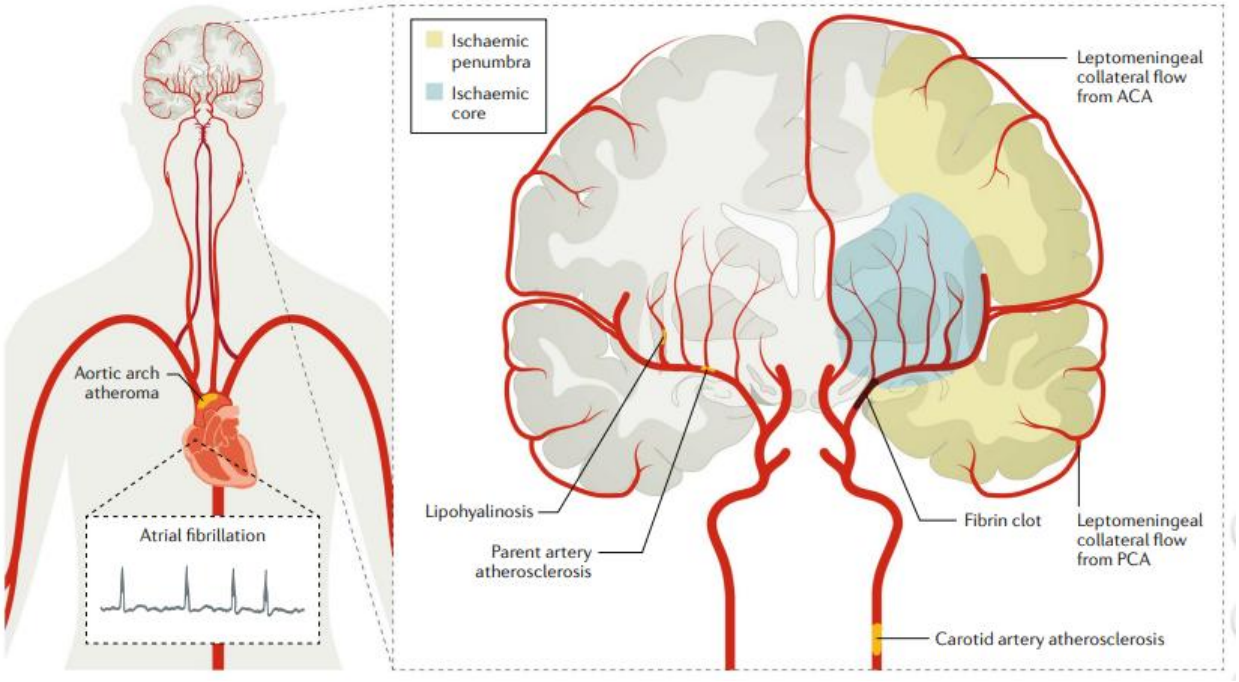


b. Acute ischemic stroke:

Mechanism of acute ischemic stroke:

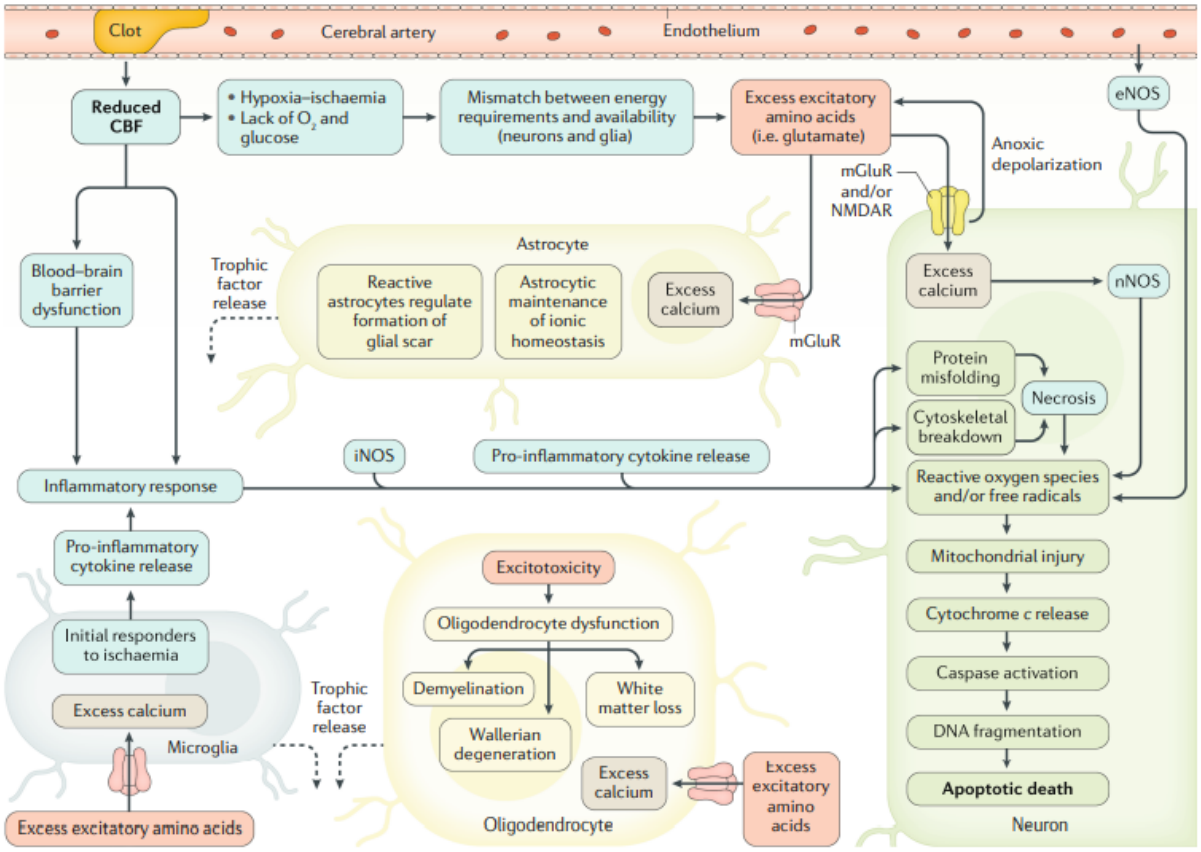
The mechanism of an ischemic stroke is shown in the illustration below., (32)

Figure 6. Ischaemic stroke-Mechanism:



A cascade of cellular events that result in necrosis and apoptosis are brought on by cerebral ischemia, which reduces the availability of glucose and oxygen to the brain. The cellular events that occur after cerebral ischemia are shown in the accompanying image., (33)

Figure 7. Cellular effects associated with brain ischemia:



The major arteries supplying the brain includes,

a) ACA-anterior cerebral artery.

b) AICA - anterior inferior cerebellar artery.

c) ACHA - anterior choroidal artery .

d) MCA - middle cerebral artery.

e) LSA - lenticulostriate artery.

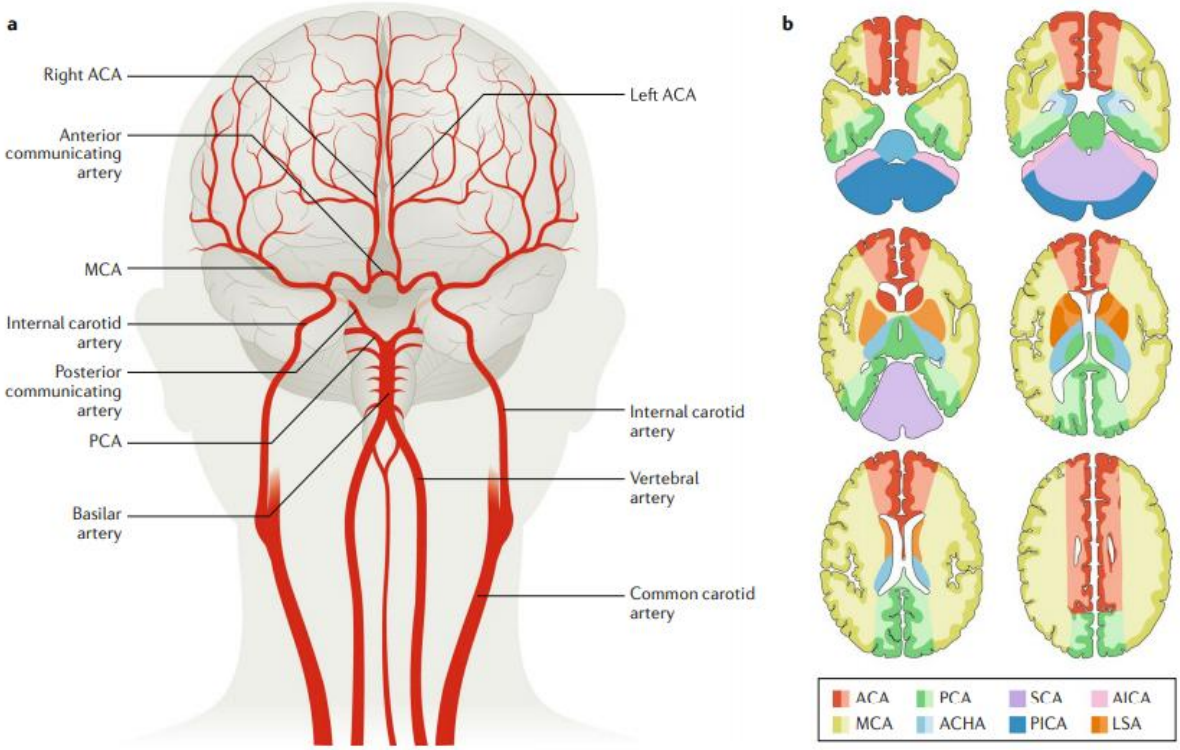
f) PICA-posterior inferior cerebellar artery.

g) PCA - posterior cerebral artery.

h) SCA-superior cerebellar artery.

The below image summarises the cerebral vasculature and the circulation,(34)

Figure 8. Cerebral vasculature:



Classificationof acute ischemic stroke:

The TOAST classification, which uses Trial of ORG 10172 in Acute Stroke Treatment, is the one most frequently used for ischemic stroke. According to the TOAST classification, the following table shows the pathological or etiological kinds of ischemic stroke, along with its causes and prevalence., (35)

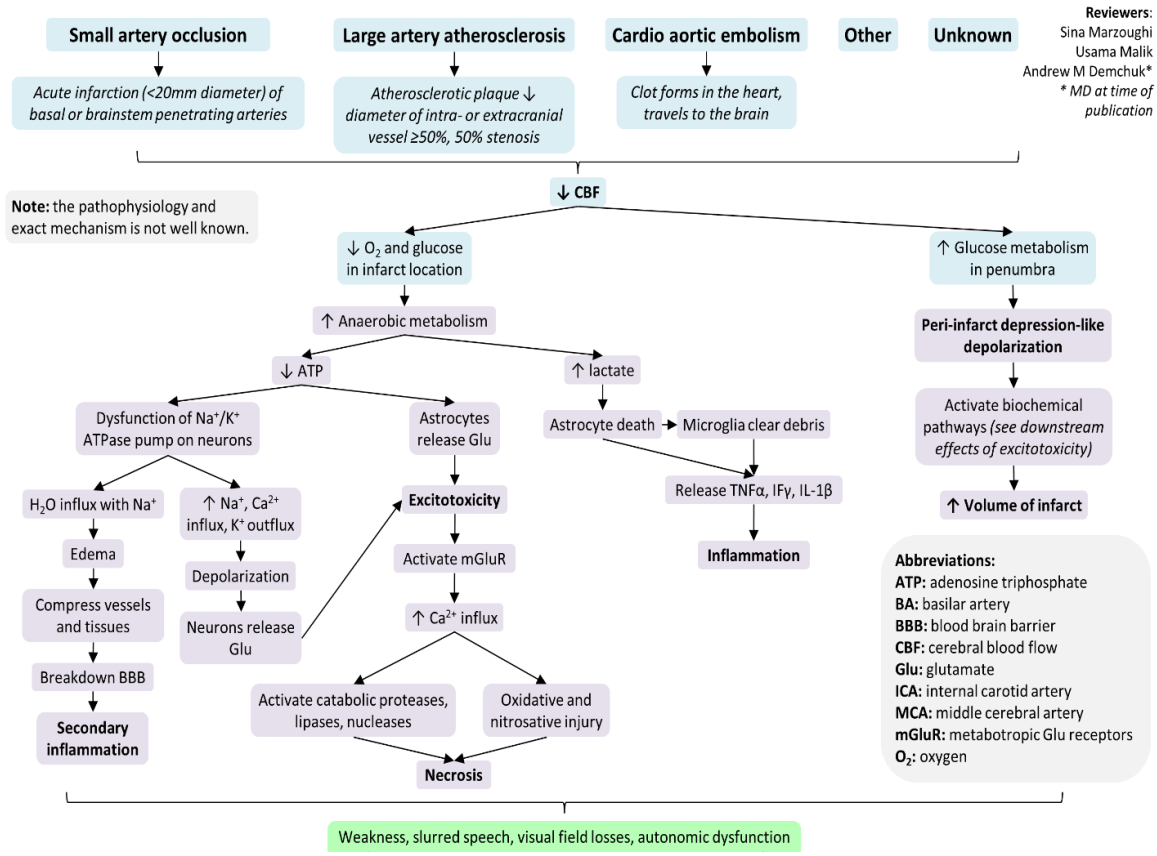
Table 2. TOAST classification of ischaemic stroke:

Stroke type	Causes	Percentage
Large artery thrombotic strokes	Atherosclerotic plaques in the large blood vessels of the brain lead to ischemia and infarction	20%
Small penetrating artery thrombotic stroke (Lacunar stroke)	One or more vessels in the brain are affected (microatheromatosis)	25%
Cardiogenic embolic stroke	Associated with cardiac dysrhythmias, valvular heart disease, and thrombi in the left ventricles	15%
Cryptogenic strokes	Cause is unknown	5-10%
Strokes associated with other causes	Such as illicit drug use	20-25%

Pathogenesis of acute ischemic stroke:

The figure below summarises the Pathogenesis of ischaemic stroke, (27)

Figure 9. Pathogenesis of ischaemic Stroke:



Managementof acute ischemic stroke:

Ancrod, anti-platelet medications, mechanical removal of the clot (thrombectomy), and thrombolysis using tPA are the main management options.(36)The selection criteria for mechanical thrombectomy recommended by the American Heart Association and American Stroke Association in acute ischemic stroke are shown in the following table. (37)

Table 3. Selection criteria for mechanical thrombectomy-acute ischemic stroke:

Functionally independent pre-stroke (mRS score of 0 to 1)
Acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset
Stroke caused by occlusion of the internal carotid artery or proximal (M1) middle cerebral artery on imaging (CT angiography)
Age ≥18 years old
NIHSS score of ≥6
CT brain without evidence of large infarct (ASPECTS score ≥6)
Treatment is able to be initiated (groin puncture) within 6 hours of symptom onset

Anti-platelet therapyin acute ischemic stroke:

Aspirin used within 48 hours after a stroke improves outcome by lowering the risk of recurrent stroke.(38,39)Aspirin offers less benefit than reperfusion treatments, although it is inexpensive and widely available. Alternative options include clopidogrel or aspirin-dipyridamole combinations, which are more expensive than aspirin but slightly more effective than aspirin in the early detection of stroke.(40)In individuals who are at high risk, the combination of aspirin and clopidogrel, when given continuously for around 3 weeks after the commencement of a small stroke or Transient Ischaemic Attack, reduced the incidence of subsequent strokes.(41,42)

Low NIHSS (CHANCE, POINT), or no acute stroke (ACTIVE A), as shown by the studies (SAMMPRIS), verified the benefit of DAPT. Stroke recurrence is decreased compared to historical controls with aggressive medical therapy following cerebral atherosclerotic stroke for 90 days (21 to 30 days after TIA or small stroke). The American Heart Association Guidelines take this into account and find it to be useful in secondary prevention of stroke.(43)

Role of statinsin acute ischemic stroke:

A cholesterol-independent lipid-lowering medication called a statin (3-hydroxy-3-methylglutaryl-coenzyme A reductase) also improves endothelial function, inhibits inflammation and thrombosis, encourages angiogenesis and neuroprotection, and stabilises atherosclerotic plaques.(44)

One can utilise statins like fluvastatin, simvastatin, rosuvastatin, atorvastatin, pravastatin, and rosuvastatin. Through a comprehensive review and meta-analysis, Irene **Tramacere et al**. examined the effect of statins for secondary prevention in ischemic

stroke patients or transient ischemic attack patients. They came to the conclusion that statins are associated with a reduction in the absolute risk of cardiovascular events and ischemic strokes.(45)

Role of Physiotherapyin acute ischemic stroke:

The main objectives of physical therapy and rehabilitation are to minimise deficits, prevent problems, and maximise function. Positioning, early mobilisation, modified constraint-induced movement therapy, strength training, and treatments that enhance balance, gait, and mobility are among the approaches.(46)

c. Fibrinogen:

The liver produces fibrinogen, a 340 kDahexameric plasma glycoprotein. On chromosome 4, there are three distinct genes that code for the production of fibrinogen. The plasma concentration ranges from 200 to 400 mg/dL. Of all the coagulation factors, it has the highest concentration. It is a clot's main structural element. Three to four days make up the plasma half-life. The bare minimum needed to keep hemostasis is 100mg/dL.(47–49)

Disorders of the fibrinogen:

Fibrinogen abnormalities that call for replacement therapy might be acquired or congenital. Circulating fibrinogen's quantity or functionality may be aberrant. These disorders are categorised as follows:

i. Lack of circulating fibrinogen is known as afibrinogenemia.

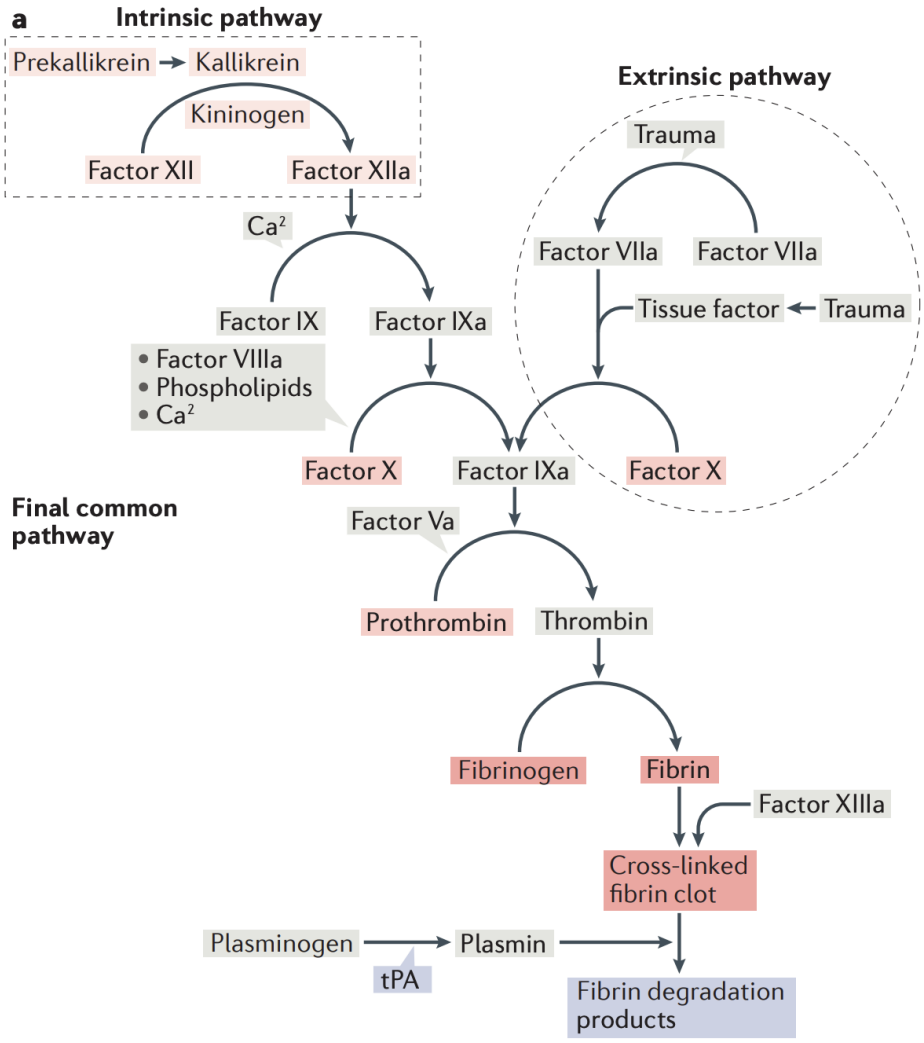
ii. Hypofibrinogenemia: Circulating fibrinogen levels below 150 mg/dL

iii. Dysfibrinogenemia: Fibrinogen in circulation is malfunctioning.

iv. Hypo dysfibrinogenemia: Low levels of abnormally functioning circulating fibrinogen. (49)

When the blood-brain barrier (BBB) is disrupted by a variety of neurological illnesses and traumatic accidents, the blood coagulation protein fibrinogen gets deposited in the brain. Recent studies have revealed that fibrinogen plays pleiotropic functions in the stimulation of CNS inflammation, the creation of brain scarring, the promotion of cognitive decline, and the inhibition of repair. The distinctive structure of fibrinogen, which has numerous binding sites for cellular receptors and proteins expressed in the nervous system, makes it possible for such a variety of activities. The following image represents the coagulation cascade, (50)

Figure 10.Coagulation cascade

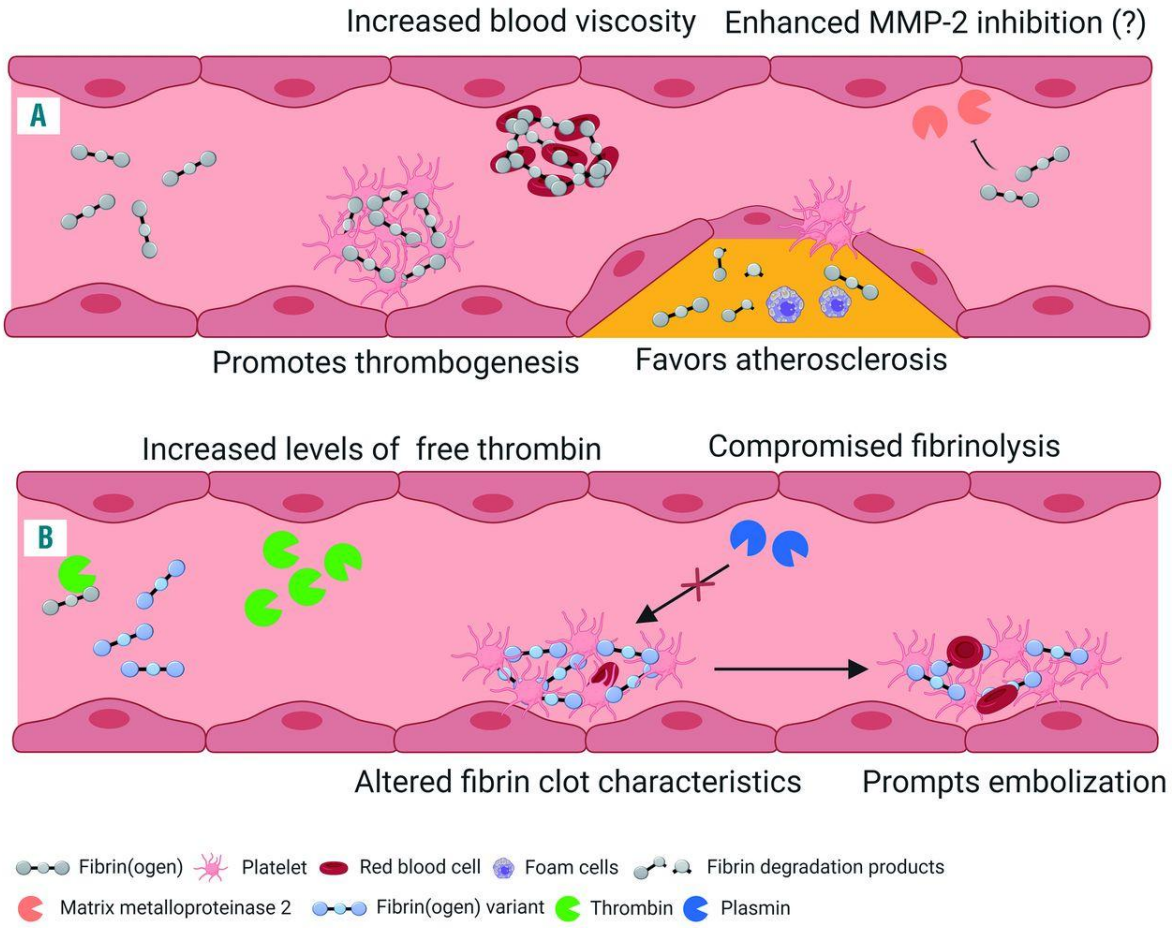


The three main cardiovascular disorders (CVD)—ischemic heart disease, stroke, and venous thromboembolism—all involve thrombosis. While venous thrombosis is connected to endothelial dysfunction and blood stasis, which cause the aggregation of

fibrin and red blood cells, arterial thrombosis is associated with the creation and rupture of an atherosclerotic plaque leading to the accumulation of platelets.(17,18)

The following image represents the Potential mechanisms of cardiovascular illnesses induced by fibrinogen. (A) represents the potential links between cardiovascular illnesses and plasma fibrinogen levels that are high. (B) represents the effects of fibrinogen structural variants.(51)

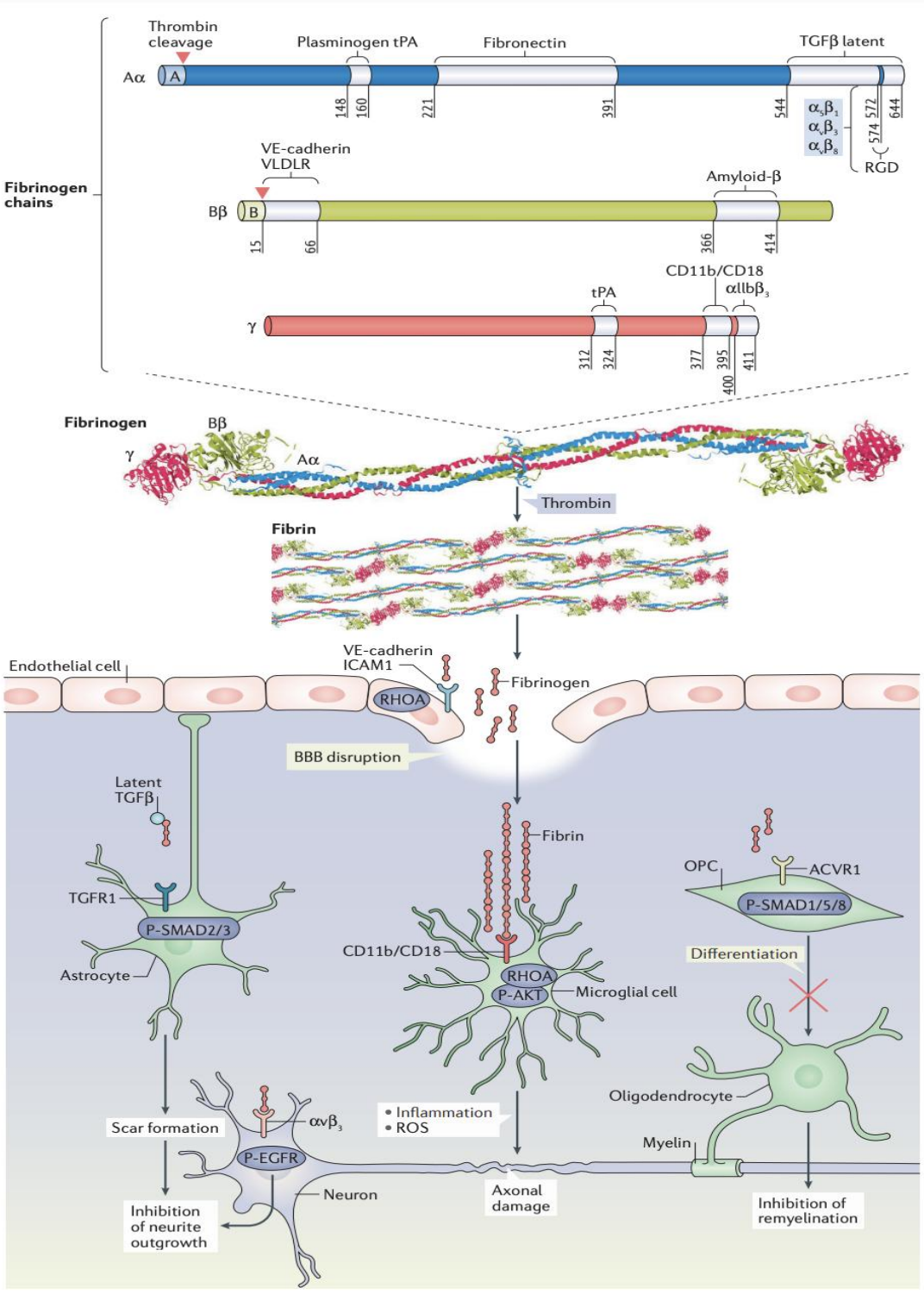
Figure 11.Potential mechanisms of cardiovascular illnesses induced by fibrinogen.



The cellular and molecular mechanisms underlying fibrinogen's effects are just now starting to be understood, giving information about how it affects neurological

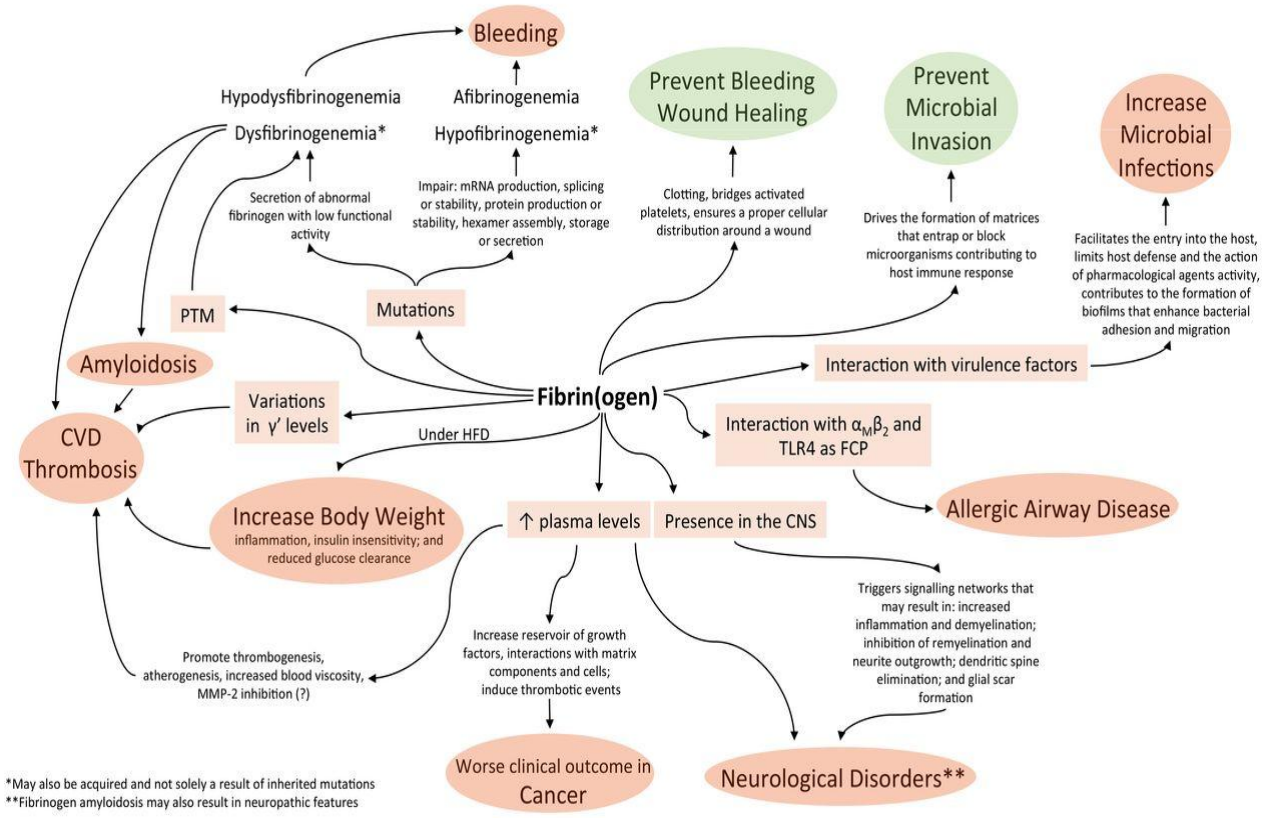
conditions such multiple sclerosis, Alzheimer's disease, and traumatic CNS injury. A new fibrinogen therapies pipeline for neurological disorder is opened by selective drug targeting to reduce the harmful functions of fibrinogen in the nervous system without impacting its helpful effects in haemostasis. The following image represents the structure, cellular targets and signalling networks of fibrinogen in the nervous system, (50)

Figure 12.Structure, cellular targets and signalling networks of fibrinogen in the nervous system



The following figure summarises the mechanisms of fibrin(ogen) involved in the diseases in human, (52)

Figure 13.Mechanisms of fibrin(ogen) involved in the diseases


Bleeding
Hypodysfibrinogenemia
Afibrinogenemia
Dysfibrinogenemia*
Hypofibrinogenemia*
Secretion of abnormal fibrinogen with low functional activity
Impair: mRNA production, splicing or stability, protein production or stability, hexamer assembly, storage or secretion
Prevent Bleeding Wound Healing
Clotting, bridges activated platelets, ensures a proper cellular distribution around a wound
Prevent Microbial Invasion
Drives the formation of matrices that entrap or block microorganisms contributing to host immune response
Increase Microbial Infections
Facilitates the entry into the host, limits host defense and the action of pharmacological agents activity, contributes to the formation of biofilms that enhance bacterial adhesion and migration
PTM
Mutations
Amyloidosis
Fibrin(ogen)
Interaction with virulence factors
Variations in γ' levels
CVD Thrombosis
Under HFD
Interaction with $\alpha_M\beta_2$ and TLR4 as FCP
Allergic Airway Disease
Increase Body Weight
inflammation, insulin insensitivity; and reduced glucose clearance
↑ plasma levels
Presence in the CNS
Triggers signalling networks that may result in: increased inflammation and demyelination; inhibition of remyelination and neurite outgrowth; dendritic spine elimination; and glial scar formation
Promote thrombogenesis, atherogenesis, increased blood viscosity, MMP-2 inhibition (?)
Increase reservoir of growth factors, interactions with matrix components and cells; induce thrombotic events
Worse clinical outcome in Cancer
Neurological Disorders**
*May also be acquired and not solely a result of inherited mutations
**Fibrinogen amyloidosis may also result in neuropathic features

d. Similar studies on prognostic role of serum fibrinogen in patients affected with acute ischemic stroke:

Ghada Samir et al, from Egypt, studied the relationship between level of fibrinogen and the outcomes in 64 acute ischemic stroke patients. They observed that the With an area under the curve of 0.97, a cutoff value of 557 mg/dL demonstrated sensitivity of 85.71%, specificity of 96%, and accuracy of 93.75% for mortality in this population. The in-hospital outcome was only affected by diabetes mellitus (P =.04). High serum fibrinogen levels can be used to predict the development of acute ischemic stroke and stroke death in high-risk people, particularly diabetics.(53)

Dina M Abdelgawad et al, from Egypt, studied the relationship between level of fibrinogen and the outcomes in 35 acute ischemic stroke patients. They observed that the Patients with ischemic stroke had high plasma fibrinogen levels, which ranged from 1.8 to 8.2 g/l with a mean of 5.33 g/l (S.D. 1.77). Ten patients (29%) and twenty-five patients (71%) had plasma fibrinogen levels below 4.5 g/l, respectively. Three months after a stroke, high fibrinogen levels were linked to poor outcomes, with hypertension being the most common risk factor. Plasma fibrinogen levels and ischemic stroke are associated. Increased fibrinogen levels were a sign of poor results.(54)

VinodKhandaitet al, did a prospective observational study of two years duration, studied the relationship between level of fibrinogen and the outcomes in 50 acute ischemic stroke patients. They observed that the In both ischemic and haemorrhagic stroke, they reported much higher than normal mean fibrinogen levels, with ischemic stroke showing a strong association between infarct volume and fibrinogen levels.(55)

Jae Hyuk Kimet al, from Korea, studied the relationship between level of fibrinogen and the outcomes in 619 acute ischemic stroke patients. They observed that

theA worse clinical outcome and an elevated plasma fibrinogen level appeared to be related with Large artery atherosclerosis in acute ischemic stroke.(56)

MarietaPeychevaet al, from Bulgaria, studied the relationship between level of fibrinogen and the outcomes in 153 acute ischemic stroke patients. They observed that theThe mean amount of fibrinogen was substantially higher in ischemic stroke patients (> 4g/l). Patients with strokes of unknown cause and those with atherosclerotic stroke had considerably higher median levels of fibrinogen than those with several other forms of stroke, according to an analysis of stroke subtypes. Neurological impairment and fibrinogen level did not significantly correlate. The period between blood samples and fibrinogen was shown to be positively linear. The progression of a patient's clinical condition after an ischemic stroke and the level of fibrinogen were found to be negatively correlated. On cerebral CT, there was a strong correlation between fibrinogen level and the presence of ischemic lesions: patients with a fibrinogen level > 3.41g/l had a 3.29-times higher chance of developing ischemia lesions.(57)

WojciechTurajet al, from Poland, studied the relationship between level of fibrinogen and the mortality rates at 1, 3, 6, and 12 months in 600 acute ischemic stroke patients. They observed that theIn comparison to patients with normal plasma fibrinogen, those with hyperfibrinogenaemia had higher mortality rates at 1, 3, 6, and 12 months (21.1% vs. 15.6%, 36.4% vs. 24.6%, 42.6% vs. 27.3%, and 45.7% vs. 31.2%, respectively; P 0.001 for the final three differences). Hyperfibrinogenaemia did not predict case fatalities in the short term, although an increase in plasma fibrinogen concentration did (P = 0.013; Odds Ratio: 1.69 (95% CI 1.12-2.55)).(58)

İ İyigünet al, from Turkey, studied the relationship between level of C-Reactive Protein and fibrinogen with the outcomes in 83 acute ischemic stroke patients. They

observed that theIn comparison to conscious hemiplegic patients, the fibrinogen and CRP levels in unconscious patients with hemiparesis or hemiplegia were higher. Additionally, there was a statistically significant difference in GOS scores between the aware and unconscious patients with hemiparesis or hemiplegia. Large infarcts in the median cerebral artery and anterior cerebral artery in patients were associated with greater levels of fibrinogen and CRP compared to the control group. In conclusion, fibrinogen and CRP may be crucial indicators of prognosis and outcome in patients who have suffered acute ischemic stroke.(58)

5 RESEARCH QUESTION OR HYPOTHESIS

5.1 **RESEARCH QUESTION:**

What is the prognostic role of serum fibrinogen in patients affected with acute ischemic stroke?

5.2 **NULL HYPOTHESIS:**

There is no significant associationbetween the serum fibrinogen and the outcomes of acute ischemic stroke.

5.3 **ALTERNATE HYPOTHESIS:**

There is a significant association between the serum fibrinogen and the outcomes of acute ischemic stroke.

6 METHODOLOGY

6.1 **STUDY SUBJECTS:**

70 patients both male and female presenting as Acute Stroke, admitted under the Department of Internal Medicine, Thanjavur Medical College and Hospital, Thanjavur.

6.2 **STUDY DESIGN:**

Prospective cross-sectional study

6.3 STUDY PERIOD:

Data collection –1 year (2021February to 2022March).

6.4 **STUDY SETTING:**

The study was conducted in the inpatient wards, Department of Internal Medicine, Thanjavur Medical College and Hospital, Thanjavur.

6.5 STUDY PARAMETERS:

- A detailed medical history including present, past, family and personal history were asked.
- General examination.
- Vitals monitoring including blood pressure, pulse rate.
- Detailed neurologic examination.
- Examination of other systems.
- Severity score using National Institute of Health Sciences Scale at admission.
- Serum cholesterol.
- Serum fibrinogen.
- CT brain plain.
- Reassessment of morbidity and mortality using Modified Rankin's scale scores at one month follow-up

6.6 **SAMPLING PROCEDURE:**

Convenient Sampling.

6.7 **INCLUSION CRITERIA:**

- ✓ All Patients with acute ischemic stroke having following criteria were selected.
- ✓ All patients presenting with new onset focal neurological deficit following ischemic stroke, within 48 hours of onset of stroke are taken into study.
- ✓ Patients with new onset stroke with risk factors of hypertension, diabetes mellitus, dyslipidaemia, smoking, alcohol were included.

6.8 **EXCLUSION CRITERIA:**

- ☒ Elderly Patients (> 80 years) were excluded.
- ☒ Patients with infective, malignant aetiology for stroke were excluded.
- ☒ Individuals with associated Connective Tissue disorders and Rheumatic heart disease, Coronary Artery disease were excluded.
- ☒ Haemorrhagic Stroke Patients (ICH, SDH) were excluded with the aid of CT scan.
- ☒ Patients with history of Transient ischemic attacks (TIA) or Reversible ischemic neurological deficit (RIND), cerebrovascular accidents (CVA) were excluded
- ☒ Patients with chronic kidney disease, uraemia were excluded.
- ☒ Patients with liver diseases like cirrhosis were excluded.
- ☒ History of recent surgery and trauma.

6.9 **SAMPLE SIZE:**

According to **Ghada Samir et al** study,(53) considering the sensitivity of serum fibrinogen cut-off value ≥557 mg/dL as 85.71% for the prediction of mortality among acute ischaemic stroke patients, with a precision of 19% and 95% confidence interval, the sample size is calculated as

$N = Z21\text{-}\alpha/2*Sn*(1\text{-}Sn)/p* d2$

$Z1\text{-}\alpha/2$ – two-tailed proabability for 95% confidence interval = 1.96

Sn (%) - sensitivity of serum fibrinogen cut-off value ≥557 mg/dL = 0.86

d (%) - precision or allowable error for the sensitivity of serum fibrinogen cut-off value ≥557 mg/dL = 0.19

p (%) - prevalence of the mortality in acute ischaemic stroke = 0.19

N = 1.96^2 * 0.8571 * (1 - 0.8571) / 0.19 * 19^2

N = 68.6

Thus the total sample size required for the study is 68.6, and rounded off to 70.

6.10 **ETHICAL CONSIDERATION:**

Institutional Ethical Committee approval, from Thanjavur Medical College and Hospital, Thanjavur, was obtained before the start of the study. Informed written consent was obtained.

Source of Funding: None declared

Conflict of Interest: None declared

6.11 **STUDY PROCEDURE:**

70 consecutive patients admitted with acute ischemic stroke under the Department of Internal Medicine, Thanjavur Medical College and hospital, Thanjavur, who fulfilled the eligibility criteria (inclusion and exclusion criteria) were included in the study.

After explaining the study purpose, procedure and rationale, informed written consent was obtained from all the participants. Relevant clinical history, clinical examinations, biochemical parameters especially the serum fibrinogen levels were compared with the outcomes of the study population. Prognostic value of the serum fibrinogen levels were analysed.

6.12 BUDGET:

Self. (No added investigation or intervention)

6.13 STATISTICAL METHODS:

I. Descriptive Statistics:

1. Data was entered in MS excel sheet and analysed using SPSS software version 16.

2. Numerical variables like systolic and diastolic blood pressure, Age, Random blood sugar, fibrinogen, cholesterol, SSSetc., are represented in mean, SD,median, and mode. Histograms are used wherever necessary.

3. Categorical variables like smoking and alcohol status, gender,type of stroke, outcomes etc., are represented in frequencies and percentages. Pie-charts and bar diagrams are used as appropriate.

II. Inferential Statistics:

1. When a Numerical variable like systolic and diastolic blood pressure, Age, Random blood sugar, cholesterol, SSS is compared with the fibrinogen,Pearson's correlation test is used.
2. When a Categorical Variable like smoking and alcohol status, gender,type of stroke, outcomes iscompared with a fibrinogen, the test of significance, t test/ANOVA test is used.
3. P-values less than 0.05 were considered statistically significant.

7 RESULTS

Results of the study, on prognostic role of serum fibrinogen in patients affected with acute stroke, is discussed under the following headings:

I.Age (years)

II.Age group

III.Gender

IV.Smoker

V.Alcoholic

VI.Blood Pressure

VII.Hypertension

VIII.Diabetes Mellitus

IX.Blood Sugar (mg/dl)

X.Serum Fibrinogen (mg/dl)

XI.Serum Cholesterol (mg/dl)

XII.Stroke Scale

XIII.Modified Ranking Score at Admission

XIV.Modified Ranking Score at Discharge

XV.Etiology of Stroke

XVI.Outcome

XVII.Serum Fibrinogen (mg/dl) with Outcome

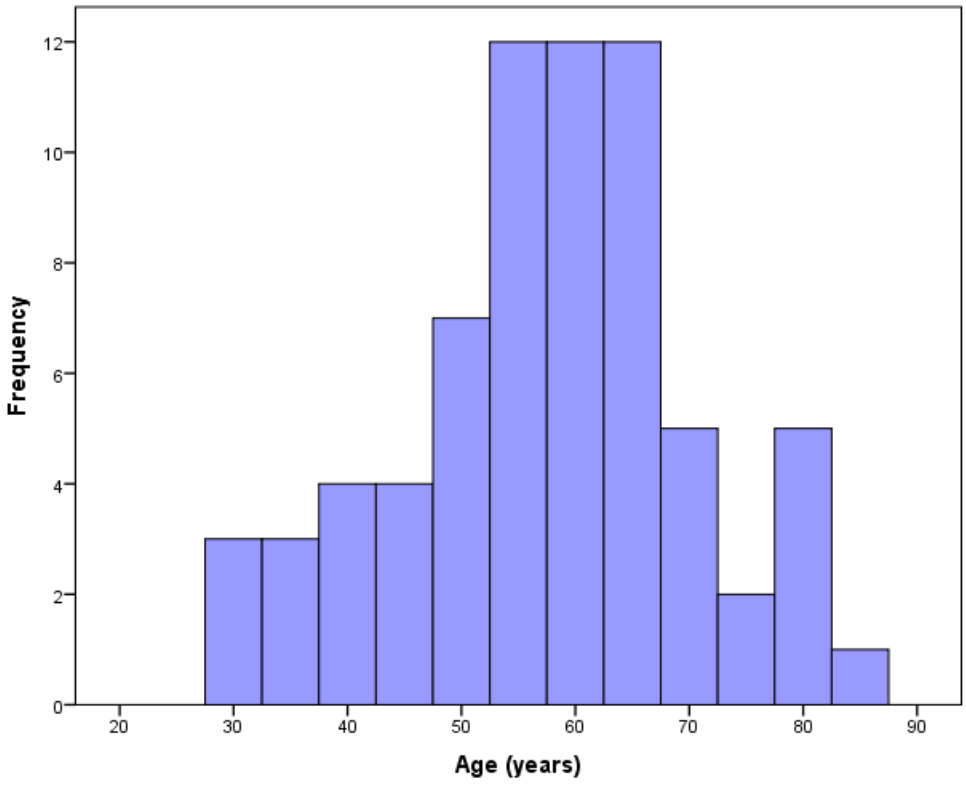
I.Age (years)

The mean Age (years) among the subjects was 57.37 (± 12.82) ranging from 30 to 85 years.

Table 4.Age (years)

Age (years)	
Mean	57.37
Median	58
Std. Deviation	12.82
Range	55
Minimum	30
Maximum	85

Figure 14.Age (years)



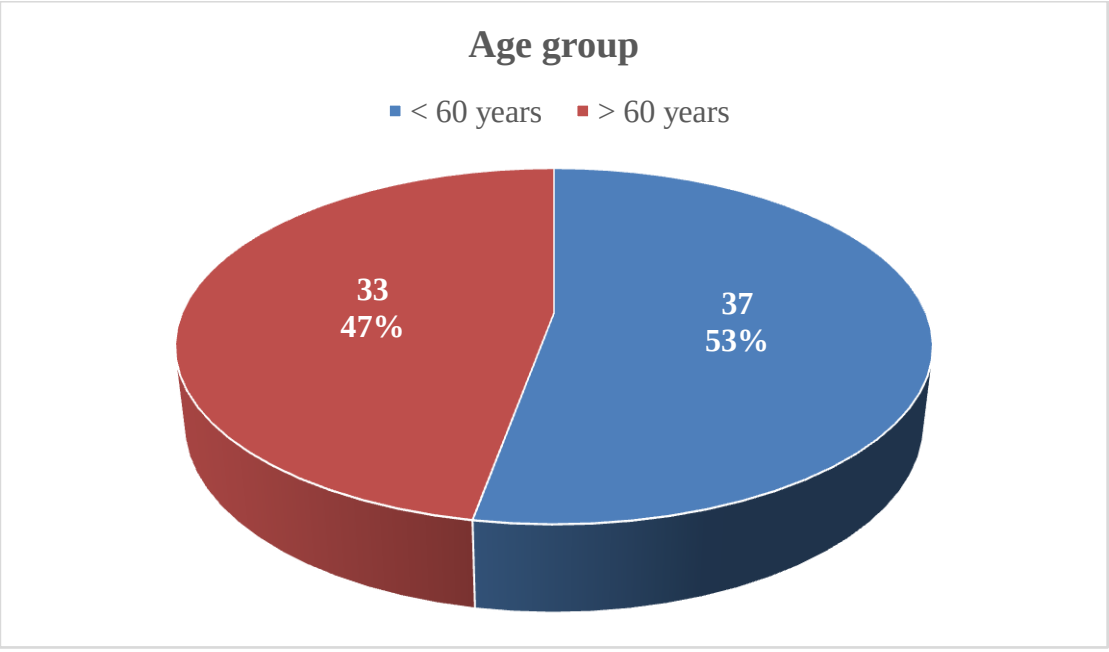
II.Age group

Among the subjects, 37 (52.86%) were in< 60 years and 33 (47.14%) were in> 60 years

Table 5.Age group

Age group	Frequency	Percent
< 60 years	37	52.86
> 60 years	33	47.14
Total	70	100.00

Figure 15.Age group



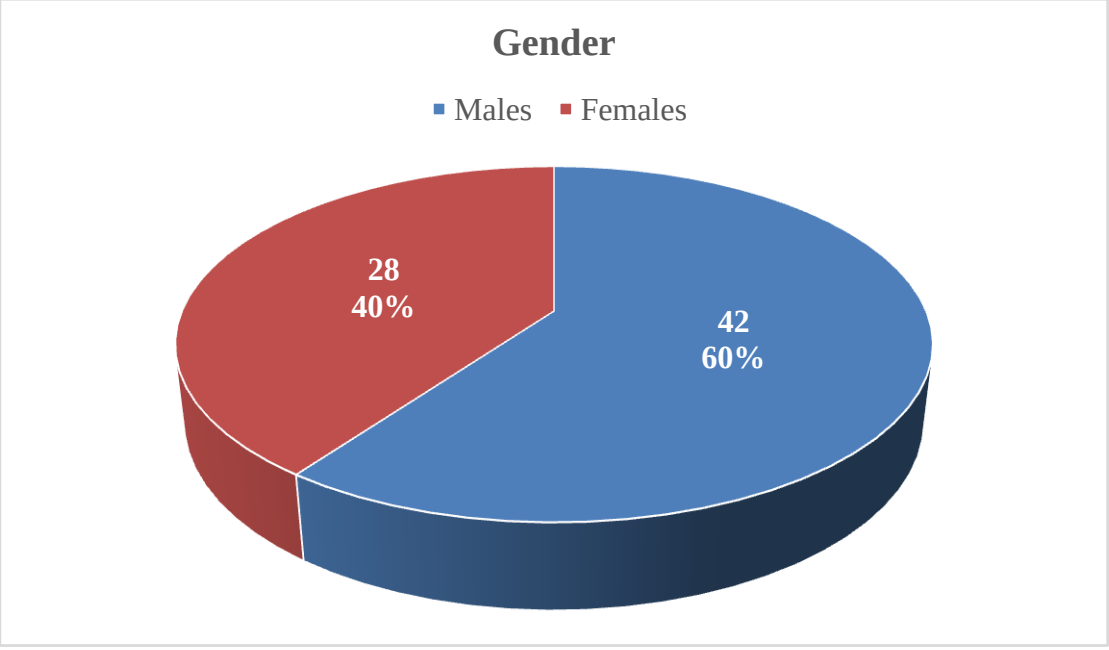
III.Gender

Among the subjects, 42 (60%) had Males and 28 (40%) had Females

Table 6.Gender

Gender	Frequency	Percent
Males	42	60.00
Females	28	40.00
Total	70	100.00

Figure 16.Gender



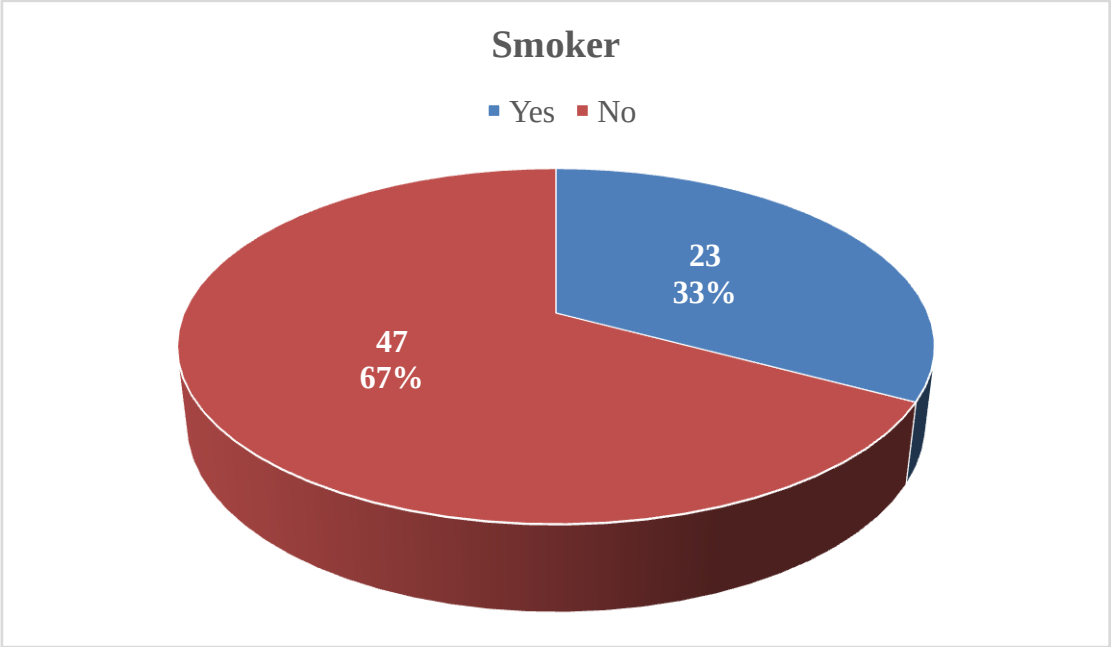
IV.Smoker

Among the subjects, 23 (32.86%) were Smoker

Table 7.Smoker

Smoker	Frequency	Percent
Yes	23	32.86
No	47	67.14
Total	70	100.00

Figure 17.Smoker



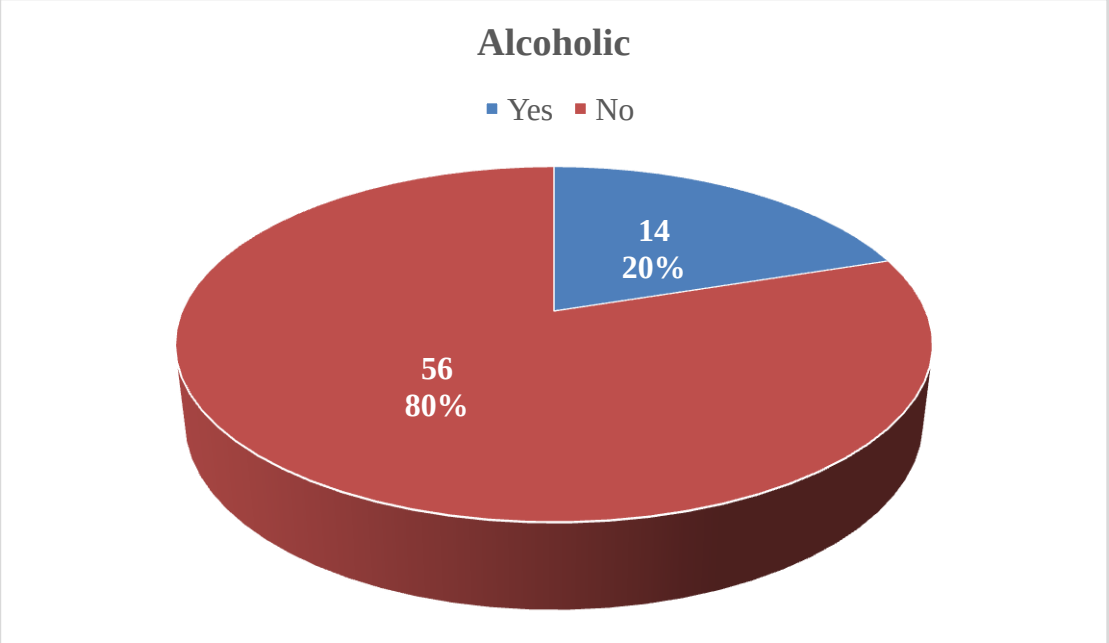
V.Alcoholic

Among the subjects, 14 (20%) were Alcoholic

Table 8.Alcoholic

Alcoholic	Frequency	Percent
Yes	14	20.00
No	56	80.00
Total	70	100.00

Figure 18.Alcoholic



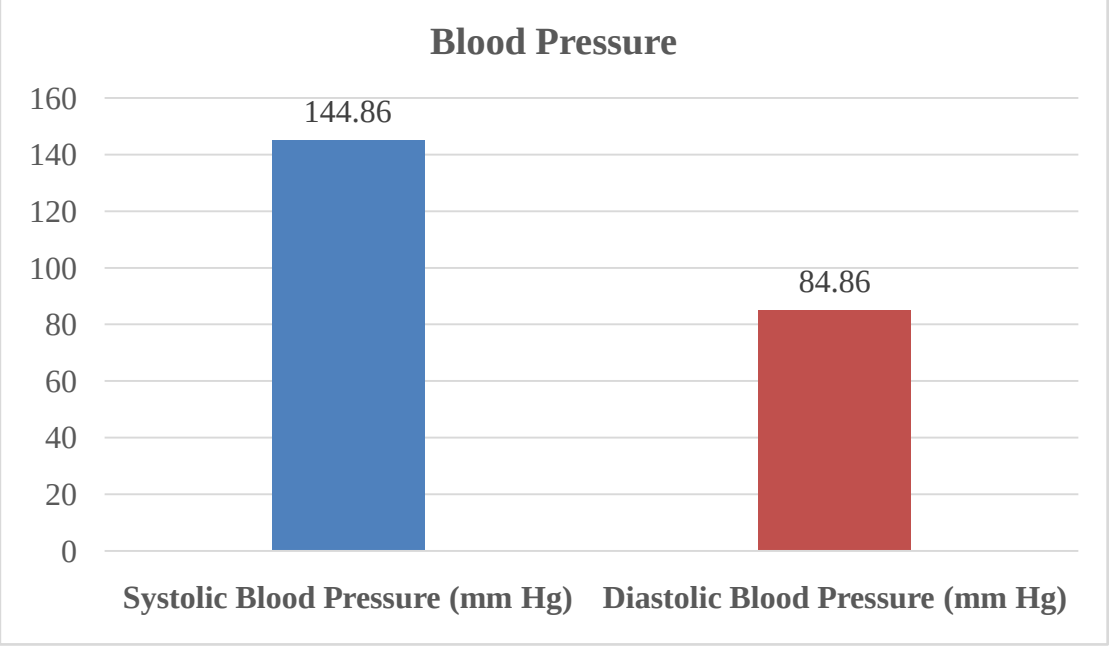
VI.Blood Pressure

The mean Systolic Blood Pressure (mm Hg) among the subjects was 144.86 (± 21.52) ranging from 110 to 200 mm Hg. The mean Diastolic Blood Pressure (mm Hg) among the subjects was 84.86 (± 11.13) ranging from 60 to 110mm Hg.

Table 9.Blood Pressure

	N	Mean	S.D.	Minimum	Maximum
Systolic Blood Pressure (mm Hg)	70	144.86	21.52	110.0	200.0
Diastolic Blood Pressure (mm Hg)	70	84.86	11.13	60.0	110.0

Figure 19.Blood Pressure



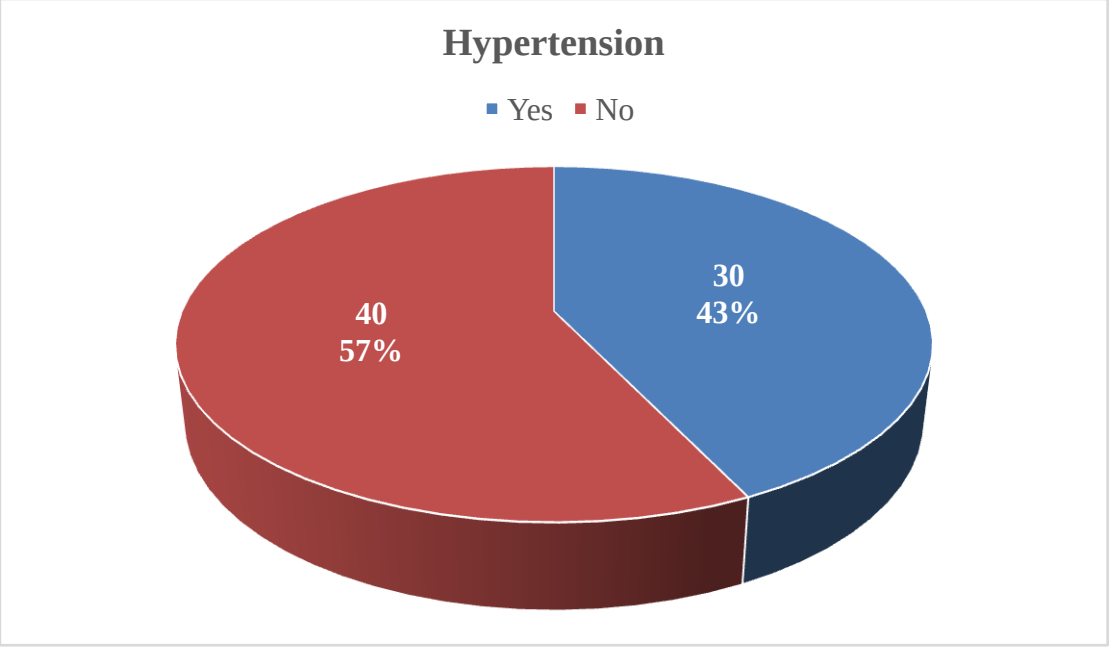
VII.Hypertension

Among the subjects, 30 (42.86%) had Hypertension

Table 10.Hypertension

Hypertension	Frequency	Percent
Yes	30	42.86
No	40	57.14
Total	70	100.00

Figure 20.Hypertension



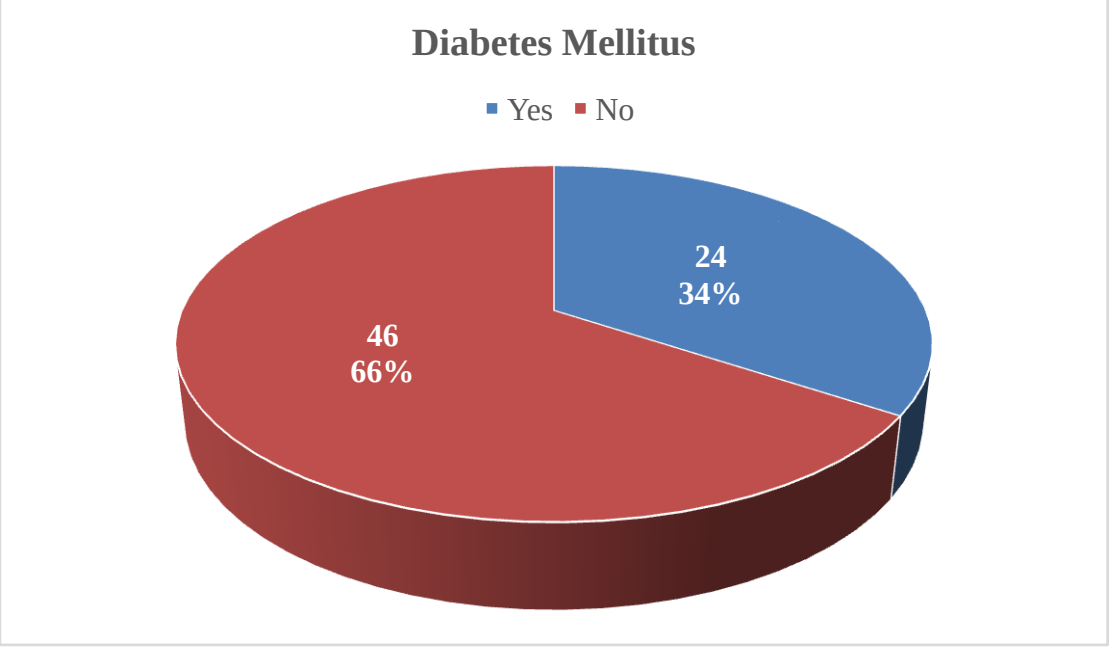
VIII.Diabetes Mellitus

Among the subjects, 24 (34.29%) had Diabetes Mellitus

Table 11.Diabetes Mellitus

Diabetes Mellitus	Frequency	Percent
Yes	24	34.29
No	46	65.71
Total	70	100.00

Figure 21.Diabetes Mellitus



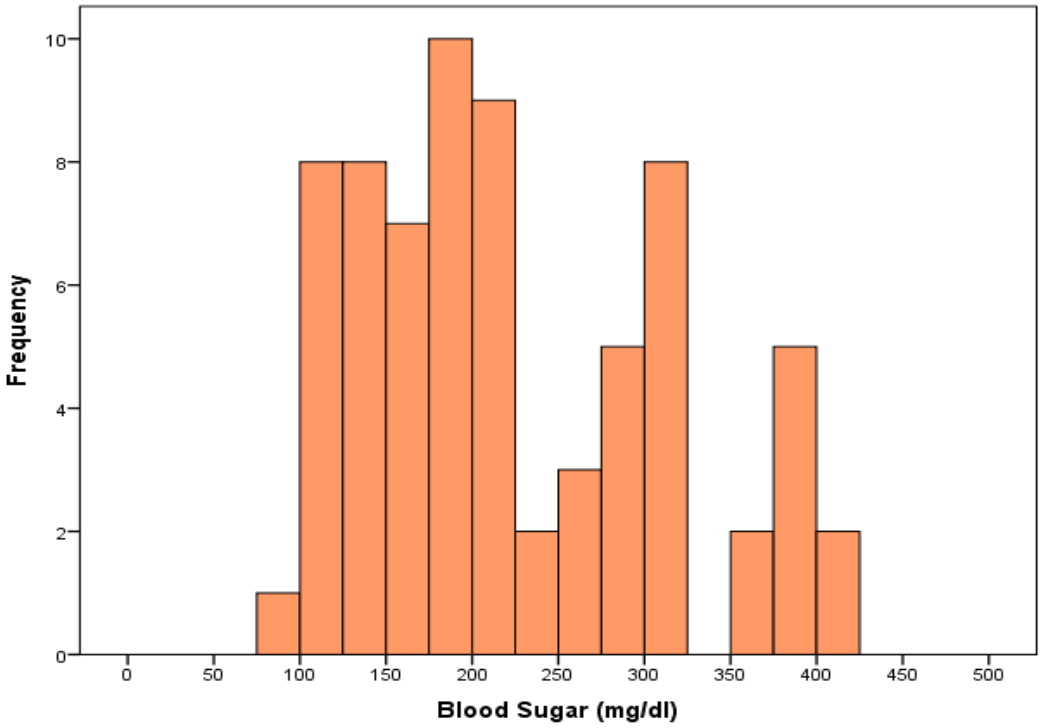
IX.Blood Sugar (mg/dl)

The mean Blood Sugar (mg/dl) among the subjects was 220.09 (± 88.07) mg/dl ranging from 82 to 402 mg/dl

Table 12.Blood Sugar (mg/dl)

Blood Sugar (mg/dl)	
Mean	220.09
Median	200
Std. Deviation	88.07
Range	320
Minimum	82
Maximum	402

Figure 22.Blood Sugar (mg/dl)



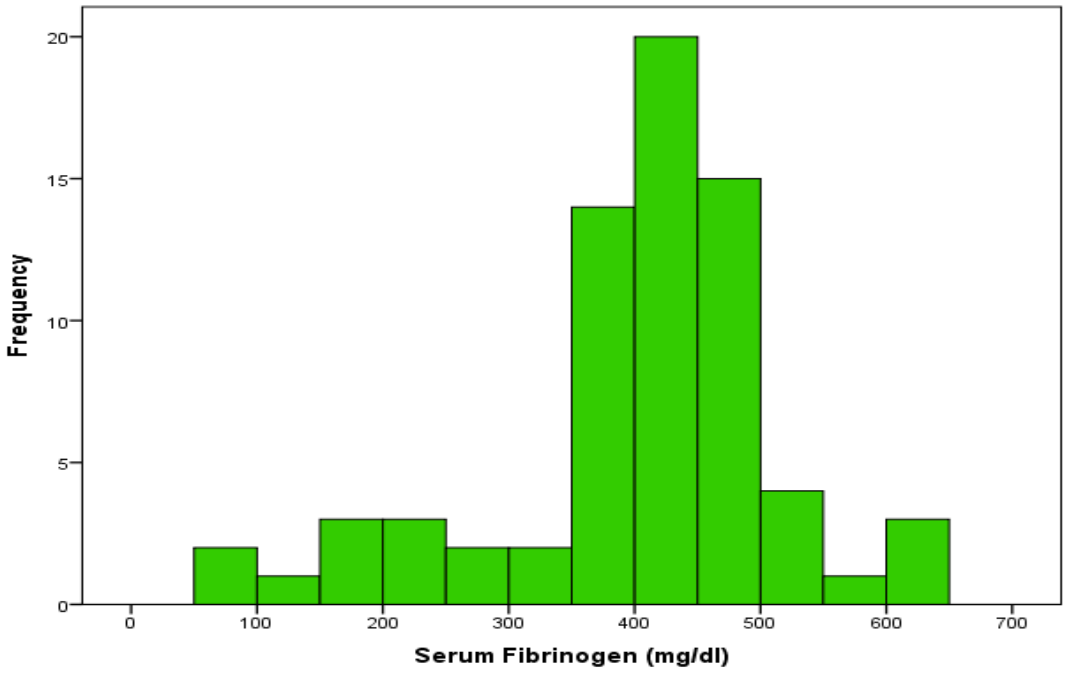
X.Serum Fibrinogen (mg/dl)

The mean Serum Fibrinogen (mg/dl) among the subjects was 396.36 (± 114.68) mg/dl ranging from 60 to 649 mg/dl

Table 13.Serum Fibrinogen (mg/dl)

Serum Fibrinogen (mg/dl)	
Mean	396.36
Median	417
Std. Deviation	114.68
Range	589
Minimum	60
Maximum	649

Figure 23.Serum Fibrinogen (mg/dl)



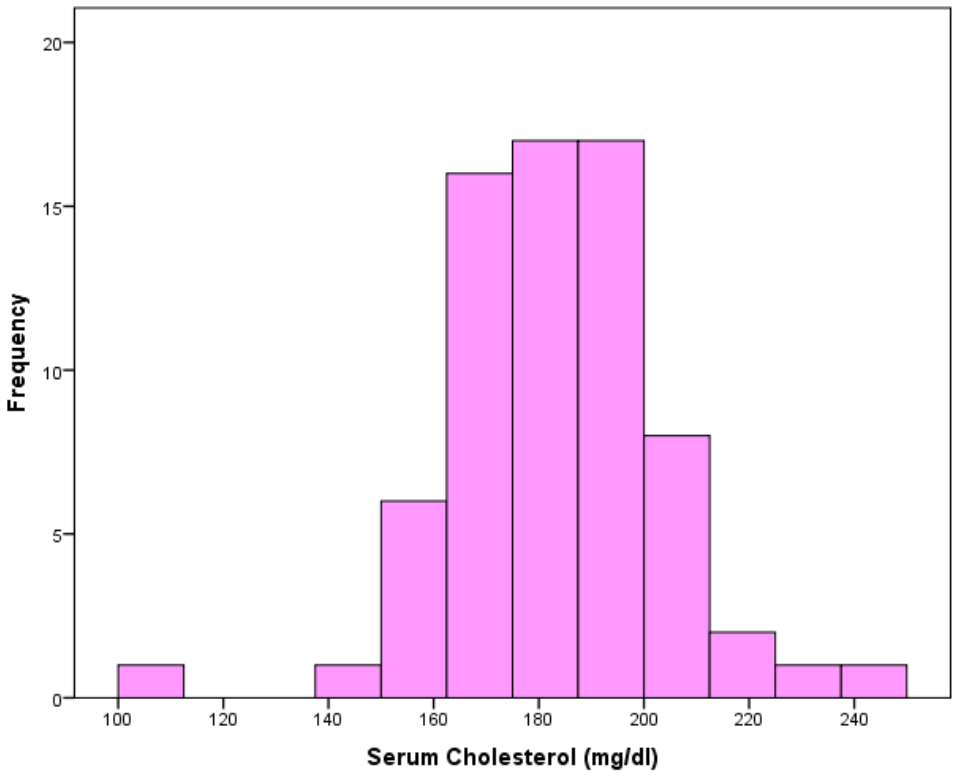
XI.Serum Cholesterol (mg/dl)

The mean Serum Cholesterol (mg/dl) among the subjects was 183.19 (± 20.88) mg/dl ranging from 101 to 240 mg/dl

Table 14.Serum Cholesterol (mg/dl)

Serum Cholesterol (mg/dl)	
Mean	183.19
Median	184.5
Std. Deviation	20.88
Range	139
Minimum	101
Maximum	240

Figure 24.Serum Cholesterol (mg/dl)



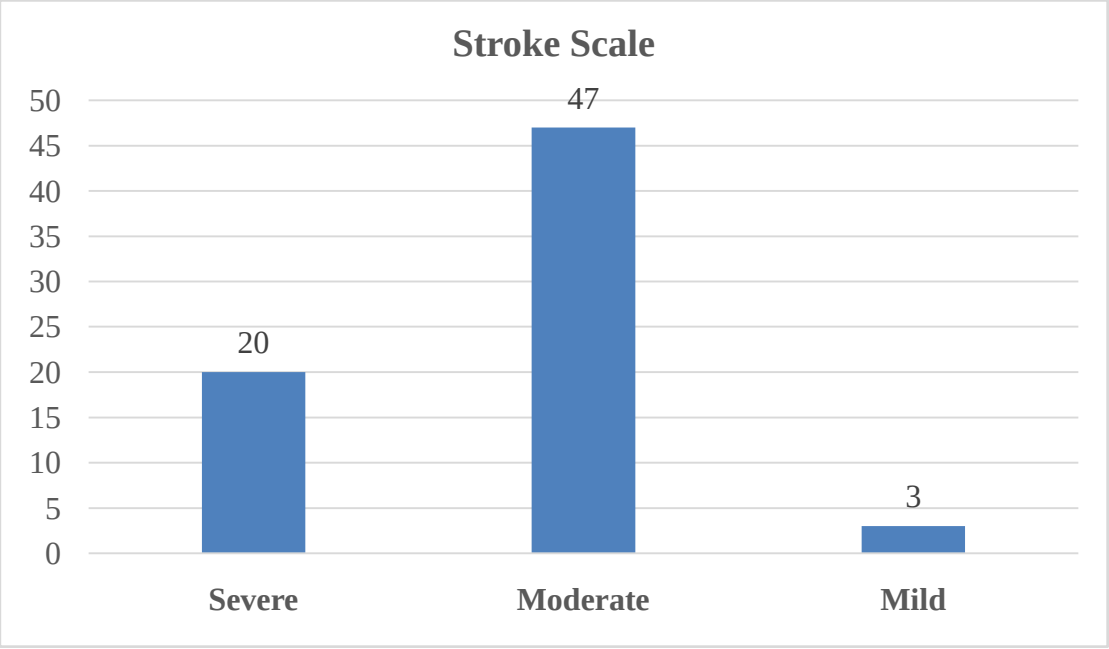
XII.Stroke Scale

Among the subjects, 47 (67.14%) had Moderate, 20 (28.57%) had Severe and 3 (4.29%) had Mild stroke according to Scandinavian Stroke Scale

Table 15.Stroke Scale

Stroke Scale	Frequency	Percent
Severe	20	28.57
Moderate	47	67.14
Mild	3	4.29
Total	70	100.00

Figure 25.Stroke Scale



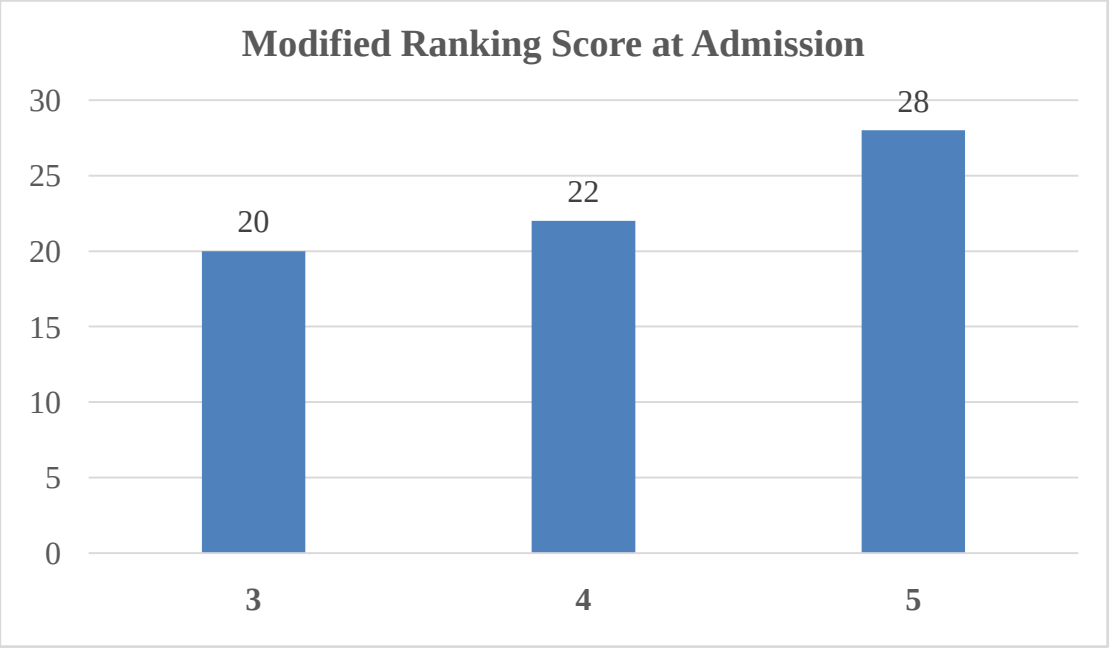
XIII.Modified Ranking Score at Admission

Among the subjects, 28 (40%) had score 5 followed by 22 (31.43%) had score 4 and 20 (28.57%) had score 3.

Table 16.Modified Ranking Score at Admission

Modified Ranking Score at Admission	Frequency	Percent
3	20	28.57
4	22	31.43
5	28	40.00
Total	70	100.00

Figure 26.Modified Ranking Score at Admission



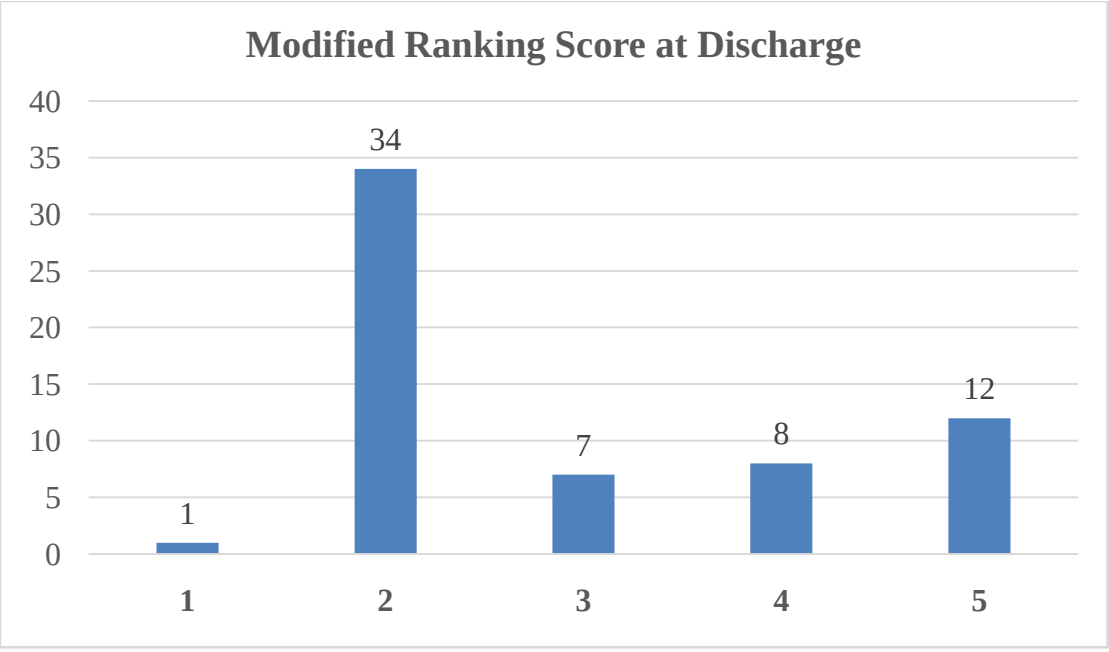
XIV.Modified Ranking Score at Discharge

Among the subjects, 34 (54.84%) had score 2, 12 (19.35%) had score 5, 8 (12.9%) had score 4, 7 (11.29%) had score 3 and 1 (1.6%) had score 1

Table 17.Modified Ranking Score at Discharge

Modified Ranking Score at Discharge	Frequency	Percent
1	1	1.61
2	34	54.84
3	7	11.29
4	8	12.90
5	12	19.35
Total	62	100.00

Figure 27.Modified Ranking Score at Discharge



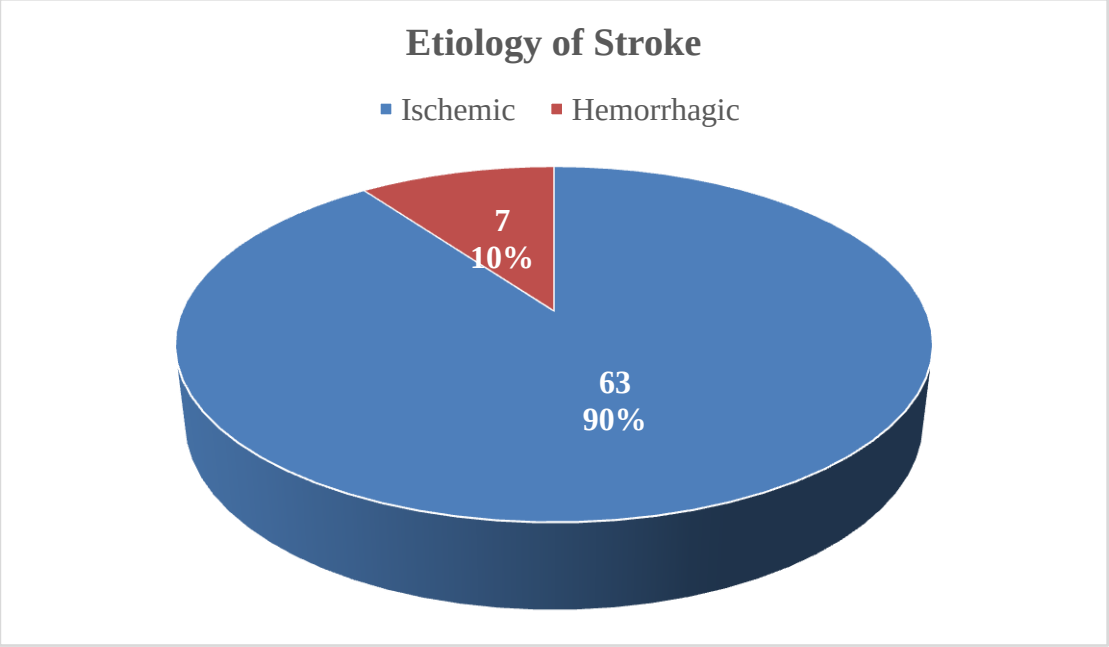
XV.Etiology of Stroke

Among the subjects, 63 (90%) had Ischemic and 7 (10%) had Hemorrhagic stroke

Table 18.Etiology of Stroke

Etiology of Stroke	Frequency	Percent
Ischemic	63	90.00
Hemorrhagic	7	10.00
Total	70	100.00

Figure 28.Etiology of Stroke



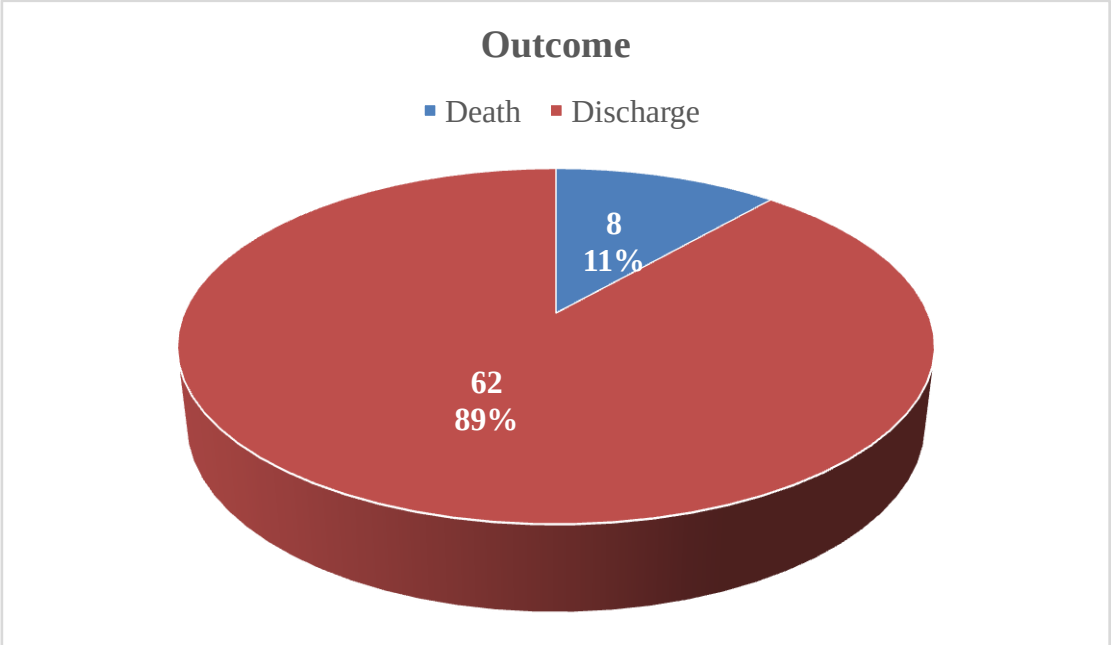
XVI.Outcome

Among the subjects, 62 (88.57%) had Discharge and 8 (11.43%) had Death

Table 19.Outcome

Outcome	Frequency	Percent
Death	8	11.43
Discharge	62	88.57
Total	70	100.00

Figure 29.Outcome



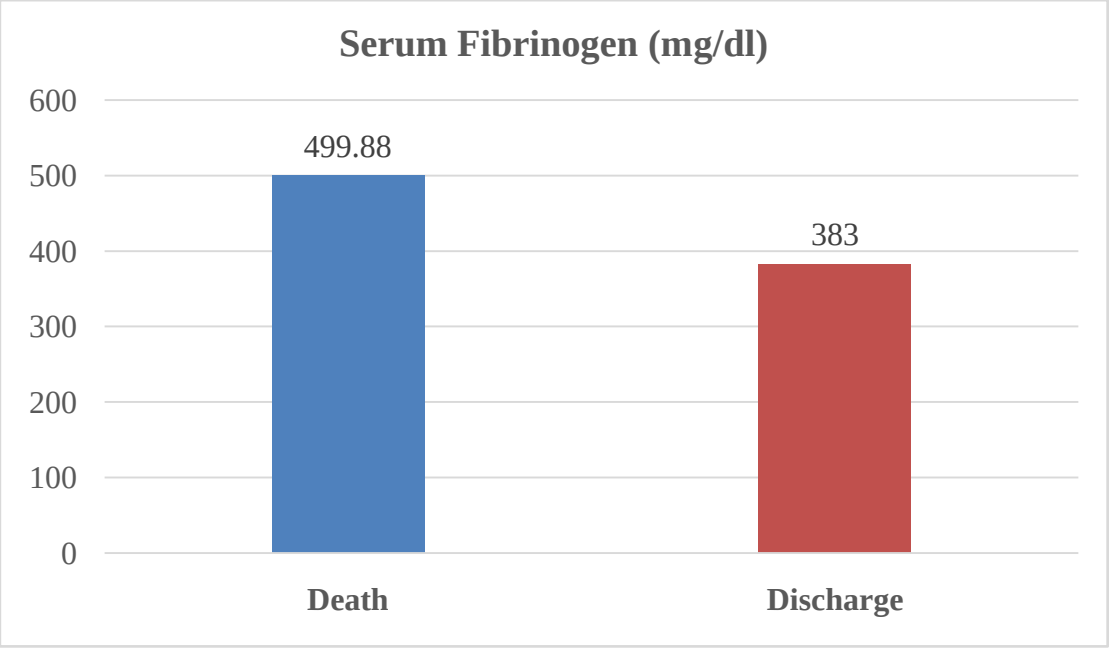
XVII.Serum Fibrinogen (mg/dl) with Outcome

The mean Serum Fibrinogen (mg/dl) among Death was 499.88 (± 186.97) which is higher by 116.88 and statistically significant compared to 383 (± 96.32) in Discharge

Table 20.Serum Fibrinogen (mg/dl) with Outcome

	Outcome	N	Mean	Std. dev.	Mean diff.	p value by 't' test
Serum Fibrinogen (mg/dl)	**Death**	8	499.88	186.97	116.875	0.006
	Discharge	62	383.00	96.32		

Figure 30.Serum Fibrinogen (mg/dl) with Outcome



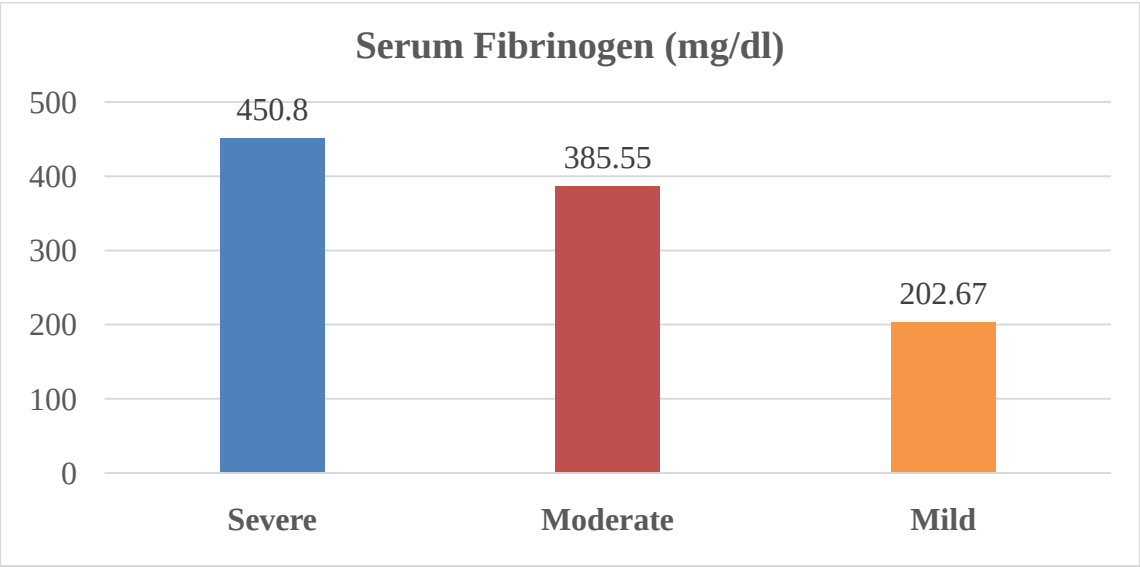
XVIII.Serum Fibrinogen (mg/dl) with Stroke Scale

The mean Serum Fibrinogen (mg/dl) among Severe was 450.8 which is higher than mean among Moderate which was 385.55 followed by Mild with a mean of 202.67 and the difference was statistically significant ($p < 0.05$).The difference in mean Serum Fibrinogen (mg/dl) was statistically significant among Severe vs Moderate and Severe vs Mild and Moderate vs Mild.

Table 21.Serum Fibrinogen (mg/dl) with Stroke Scale

Stroke Scale	Serum Fibrinogen (mg/dl)			ANOVA p value
	N	Mean	S.D.	
Severe	20	450.80	138.99	0.001
Moderate	47	385.55	88.67	
Mild	3	202.67	25.72	
	N	**Mean diff**	**S.D.**	**p value**
Severe vs Moderate	67	65.25	27.87	0.022
Severe vs Mild	23	248.13	64.63	0.001
Moderate vs Mild	50	182.89	62.16	0.004

Figure 31.Serum Fibrinogen (mg/dl) with Stroke Scale



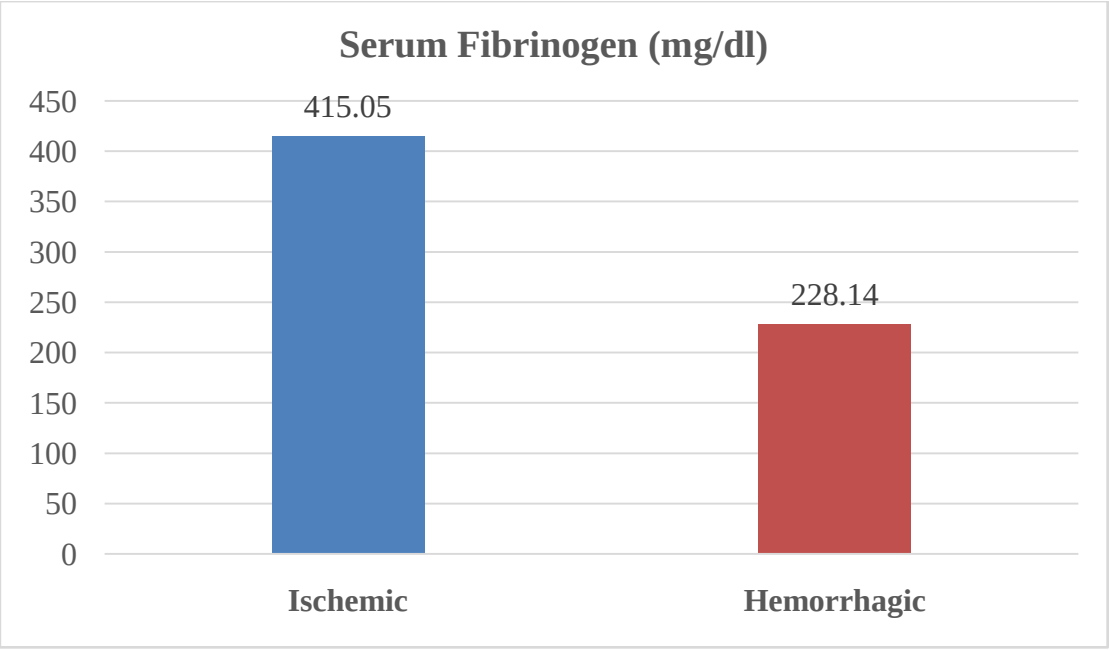
XIX.Serum Fibrinogen (mg/dl) with Etiology of Stroke

The mean Serum Fibrinogen (mg/dl) among Ischemic was 415.05 (± 89.13) which is higher by 186.9 and statistically significant compared to 228.14 (± 180.17) in Hemorrhagic stroke.

Table 22.Serum Fibrinogen (mg/dl) with Etiology of Stroke

	Etiology of Stroke	N	Mean	Std. dev.	Mean diff.	p value by 't' test
Serum Fibrinogen (mg/dl)	**Ischemic**	63	415.05	89.13	186.905	0.033
	Hemorrhagic	7	228.14	180.17		

Figure 32.Serum Fibrinogen (mg/dl) with Etiology of Stroke



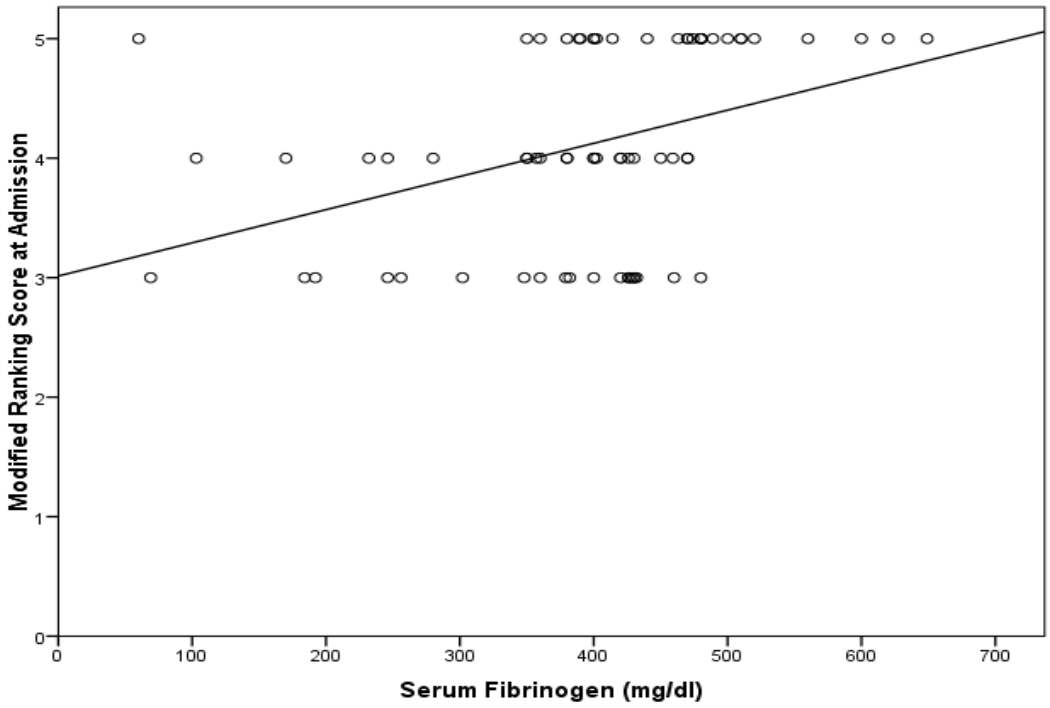
XX.Correlation between Serum Fibrinogen (mg/dl) and Modified Ranking Score at admission

Serum Fibrinogen (mg/dl) has a positive correlation with Modified Ranking Score at admission with a correlation coefficient of 0.436 and was statistically significant indicating that increase in fibrinogen level leads to more disability among stroke patients at admission.

Table 23. Correlation between Serum Fibrinogen (mg/dl) and Modified Ranking Score at admission

Predictor for Modified Ranking Score at	Spearman Correlation coefficient "r"	B (95% C.I.)	p value
Serum Fibrinogen (mg/dl)	0.436	0.003 (0.001–0.004)	0.001

Figure 33. Correlation between Serum Fibrinogen (mg/dl) and Modified Ranking Score at admission



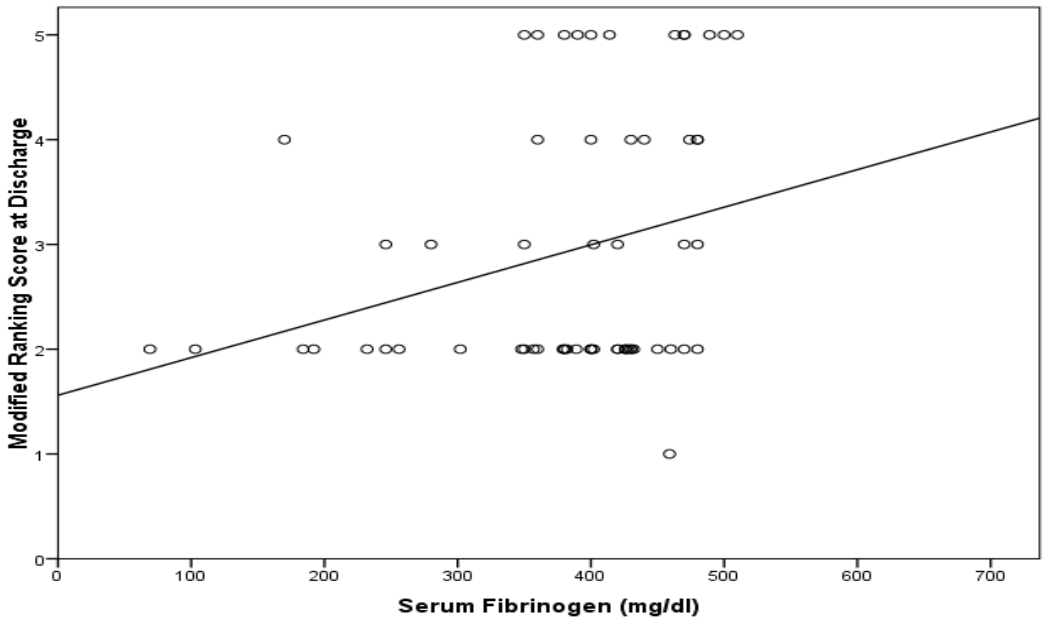
XXI.Correlation between Serum Fibrinogen (mg/dl) and Modified Ranking Score at discharge

Serum Fibrinogen (mg/dl) has a positive correlation with Modified Ranking Score at with a correlation coefficient of 0.28 and was statistically significant indicating that increase in fibrinogen level leads to more disability and poor prognosis among stroke patients

Table 24. Correlation between Serum Fibrinogen (mg/dl) and Modified Ranking Score at discharge

Predictor for Modified Ranking Score at	Spearman Correlation coefficient "r"	B (95% C.I.)	p value
Serum Fibrinogen (mg/dl)	0.279	0.004 (0 - 0.01)	0.028

Figure 34. Correlation between Serum Fibrinogen (mg/dl) and Modified Ranking Score at discharge



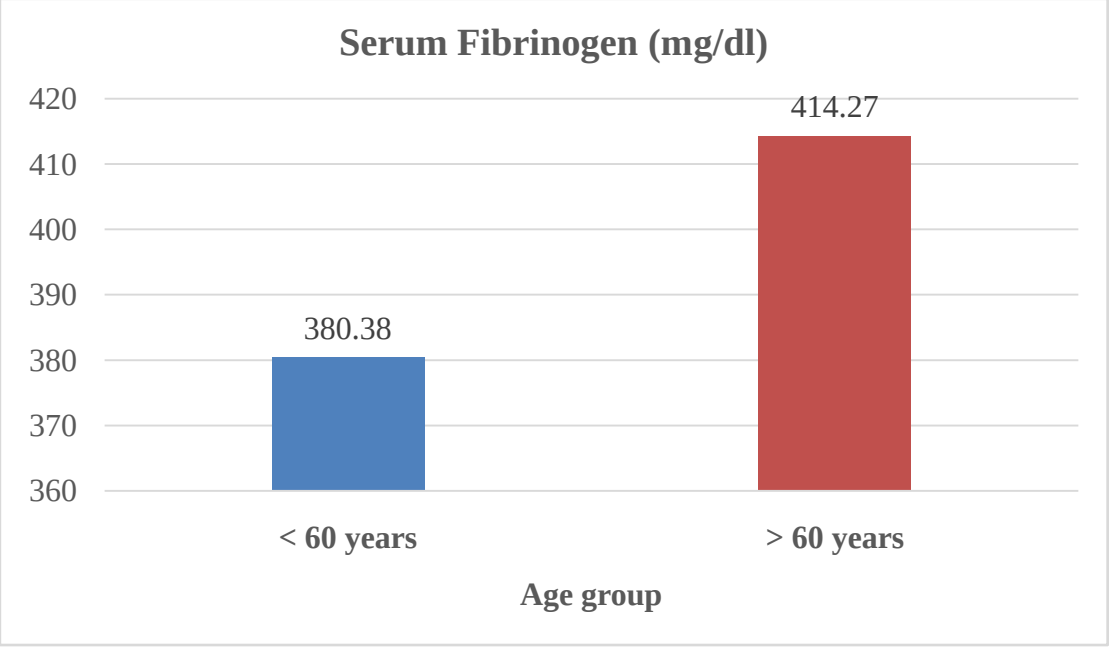
XXII.Serum Fibrinogen (mg/dl) with Age group

The mean Serum Fibrinogen (mg/dl) among < 60 years was 380.38 (± 125.44) which is lower by 33.89 but not statistically significant compared to 414.27 (± 100.14) in > 60 years

Table 25.Serum Fibrinogen (mg/dl) with Age group

	Age group	N	Mean	Std. dev.	Mean diff.	p value by 't' test
Serum Fibrinogen (mg/dl)	**< 60 years**	37	380.38	125.44	33.894	0.220
	> 60 years	33	414.27	100.14		

Figure 35.Serum Fibrinogen (mg/dl) with Age group



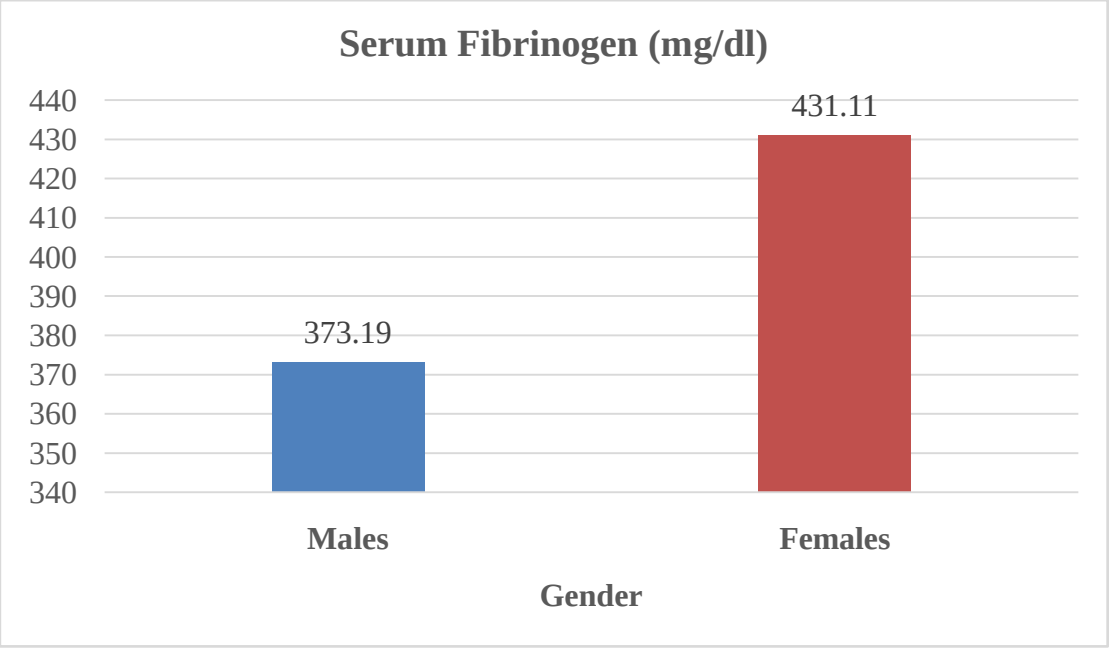
XXIII.Serum Fibrinogen (mg/dl) with Gender

The mean Serum Fibrinogen (mg/dl) among Males was 373.19 (± 125.06) which is lower by 57.92 and statistically significant compared to 431.11 (± 88.14) in Females

Table 26.Serum Fibrinogen (mg/dl) with Gender

	Gender	N	Mean	Std. dev.	Mean diff.	p value by 't' test
Serum Fibrinogen (mg/dl)	**Males**	42	373.19	125.06	57.917	0.037
	Females	28	431.11	88.14		

Figure 36.Serum Fibrinogen (mg/dl) with Gender



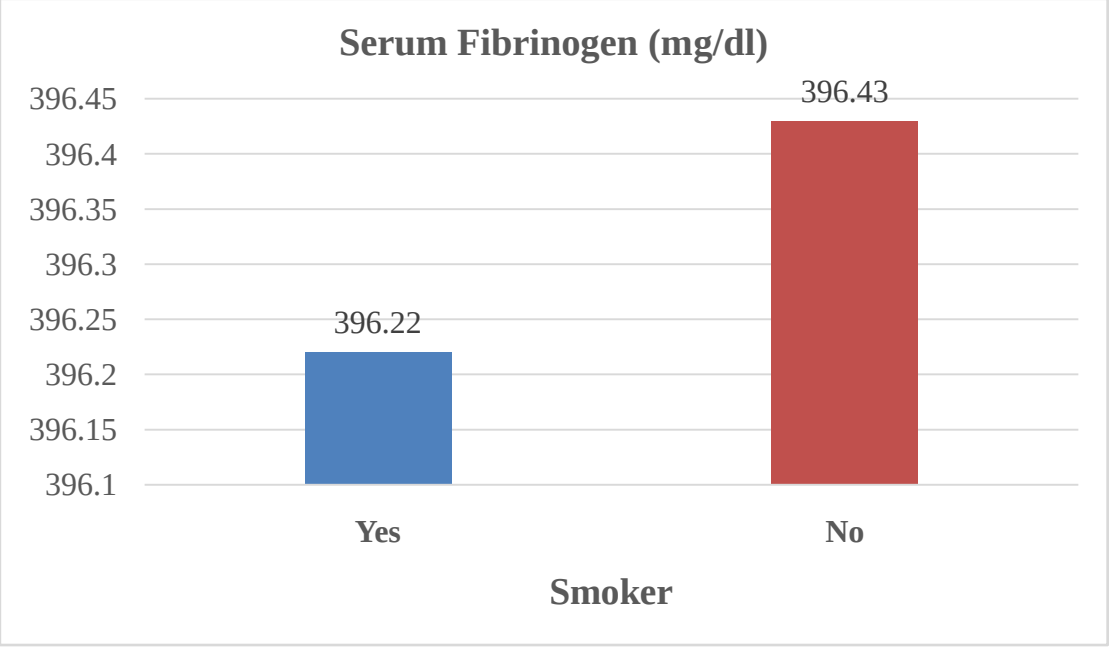
XXIV.Serum Fibrinogen (mg/dl) with Smoker

The mean Serum Fibrinogen (mg/dl) among those with Smoker was 396.22 (± 102.91) which is lower by 0.21 but not statistically significant compared to 396.43 (± 121.08) in those without Smoker

Table 27.Serum Fibrinogen (mg/dl) with Smoker

	Smoker	N	Mean	Std. dev.	Mean diff.	p value by 't' test
Serum Fibrinogen (mg/dl)	**Yes**	23	396.22	102.91	0.208	0.994
	No	47	396.43	121.08		

Figure 37.Serum Fibrinogen (mg/dl) with Smoker



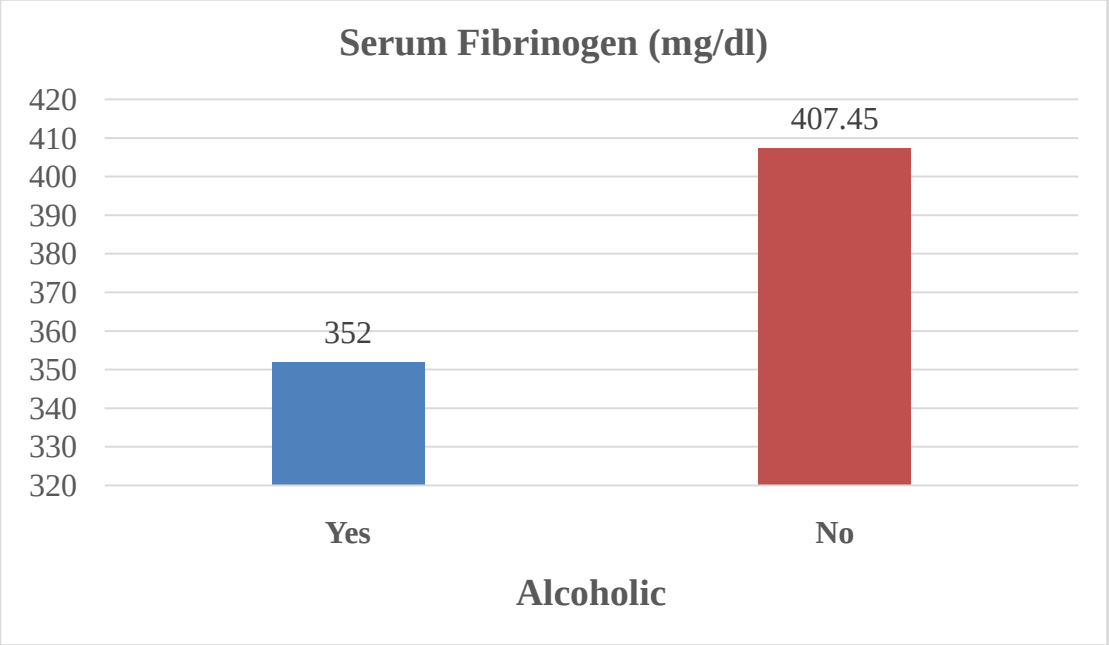
XXV.Serum Fibrinogen (mg/dl) with Alcoholic

The mean Serum Fibrinogen (mg/dl) among those with Alcoholic was 352 (± 159.98) which is lower by 55.45 but not statistically significant compared to 407.45 (± 99.11) in those without Alcoholic

Table 28.Serum Fibrinogen (mg/dl) with Alcoholic

	Alcoholic	N	Mean	Std. dev.	Mean diff.	p value by 't' test
Serum Fibrinogen (mg/dl)	**Yes**	14	352.00	159.98	55.446	0.106
	No	56	407.45	99.11		

Figure 38.Serum Fibrinogen (mg/dl) with Alcoholic



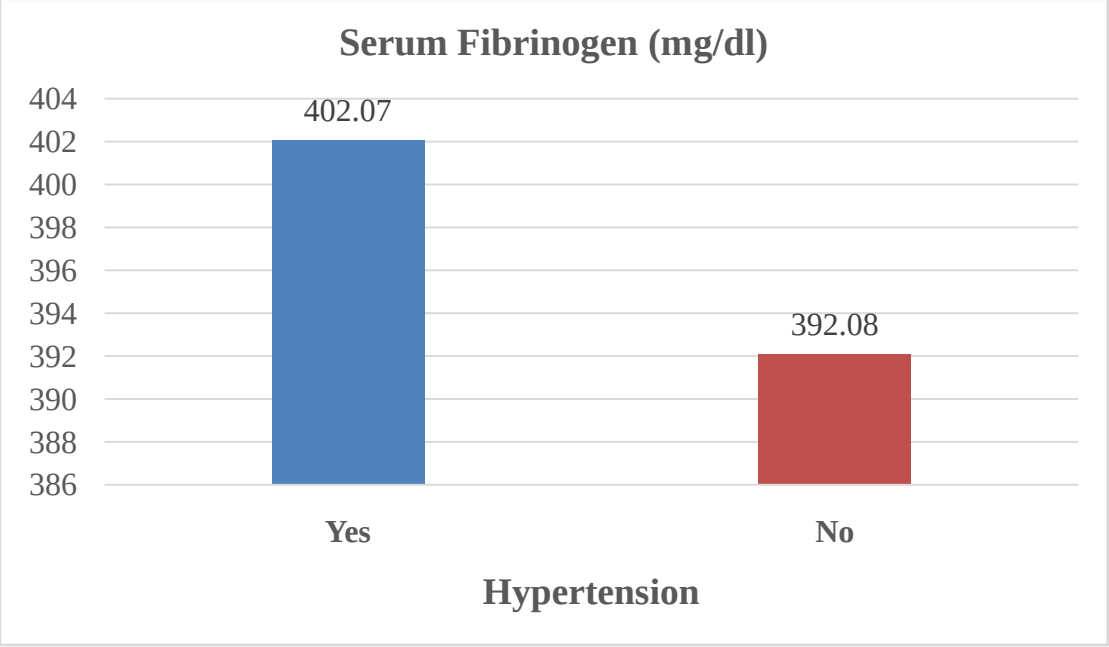
XXVI.Serum Fibrinogen (mg/dl) with Hypertension

The mean Serum Fibrinogen (mg/dl) among those with Hypertension was 402.07 (± 123.79) which is higher by 9.99 but not statistically significant compared to 392.08 (± 108.76) in those without Hypertension

Table 29.Serum Fibrinogen (mg/dl) with Hypertension

	Hypertension	N	Mean	Std. dev.	Mean diff.	p value by 't' test
Serum Fibrinogen (mg/dl)	**Yes**	30	402.07	123.79	9.992	0.721
	No	40	392.08	108.76		

Figure 39.Serum Fibrinogen (mg/dl) with Hypertension



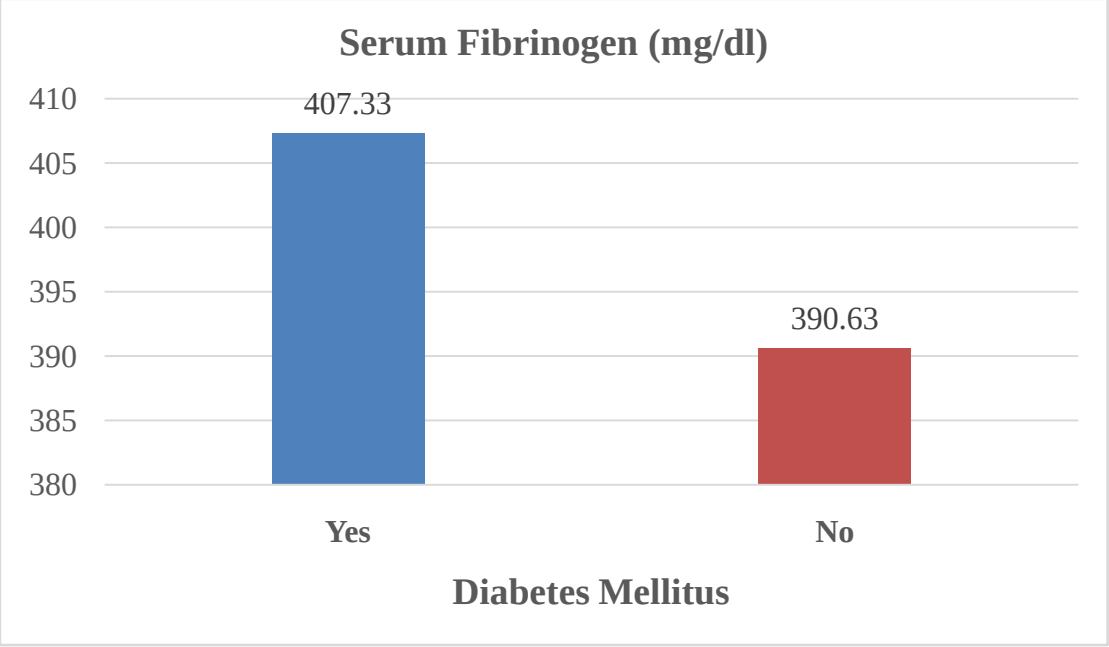
XXVII.Serum Fibrinogen (mg/dl) with Diabetes Mellitus

The mean Serum Fibrinogen (mg/dl) among those with Diabetes Mellitus was 407.33 (± 100.62) which is higher by 16.7 but not statistically significant compared to 390.63 (± 122.03) in those without Diabetes Mellitus

Table 30.Serum Fibrinogen (mg/dl) with Diabetes Mellitus

	Diabetes Mellitus	N	Mean	Std. dev.	Mean diff.	p value by 't' test
Serum Fibrinogen (mg/dl)	**Yes**	24	407.33	100.62	16.703	0.567
	No	46	390.63	122.03		

Figure 40.Serum Fibrinogen (mg/dl) with Diabetes Mellitus



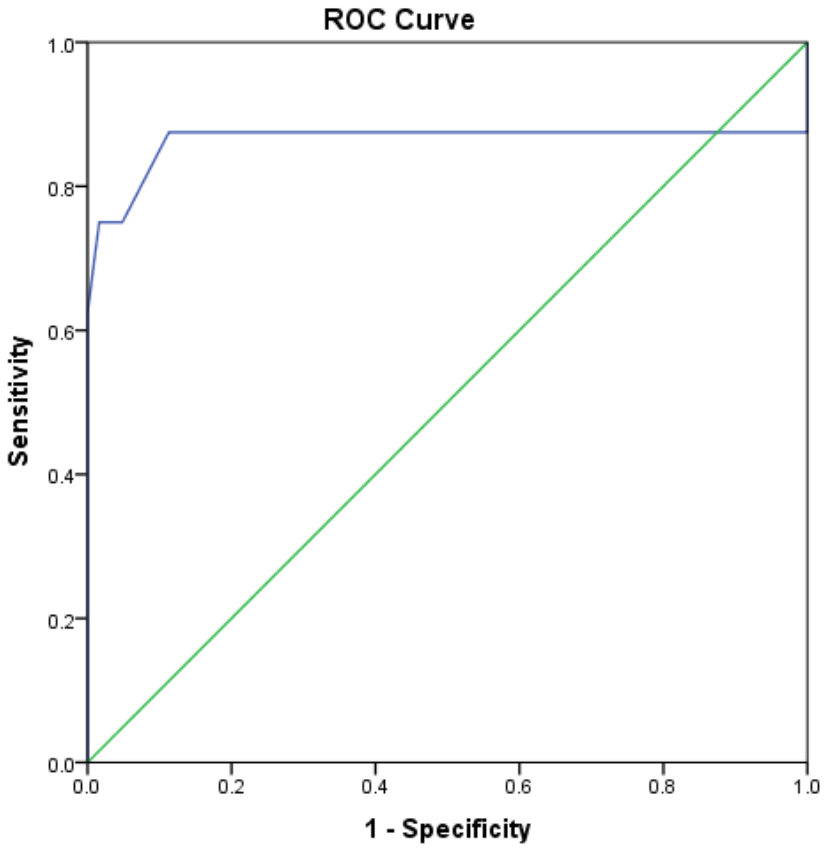
XXVIII. ROC for predicting outcome among stroke using Serum Fibrinogen

The area under the curve for Serum Fibrinogen (mg/dl) in predicting Outcome is 0.864 (0.637 - 1).The cut off of for predicting Outcome is 505 which had a sensitivity of 75%, specificity of 98.39%, positive predictive value of 85.71%, negative predictive value of 96.83% and a diagnostic accuracy of 95.71%.

Table 31.ROC for predicting outcome among stroke using Serum Fibrinogen

Test Result Variable(s)	Area under the curve	95% Confidence Interval		p value
		Lower Bound	Upper Bound	
Serum Fibrinogen (mg/dl)	0.864	0.637	1.000	0.001

Figure 41.ROC for predicting outcome among stroke using Serum Fibrinogen



Cut off	Sensitivity	Specificity	PPV	NPV	Accuracy
59.00	100.00%	0.00%	11.43%	0.00%	11.43%
64.50	87.50%	0.00%	10.14%	0.00%	10.00%
86.00	87.50%	1.61%	10.29%	50.00%	11.43%
136.50	87.50%	3.23%	10.45%	66.67%	12.86%
177.00	87.50%	4.84%	10.61%	75.00%	14.29%
188.00	87.50%	6.45%	10.77%	80.00%	15.71%
212.00	87.50%	8.06%	10.94%	83.33%	17.14%
239.00	87.50%	9.68%	11.11%	85.71%	18.57%
251.00	87.50%	12.90%	11.48%	88.89%	21.43%
268.00	87.50%	14.52%	11.67%	90.00%	22.86%
291.00	87.50%	16.13%	11.86%	90.91%	24.29%
325.00	87.50%	17.74%	12.07%	91.67%	25.71%
349.00	87.50%	19.35%	12.28%	92.31%	27.14%
353.50	87.50%	24.19%	12.96%	93.75%	31.43%
358.50	87.50%	25.81%	13.21%	94.12%	32.86%
369.50	87.50%	30.65%	14.00%	95.00%	37.14%
379.50	87.50%	32.26%	14.29%	95.24%	38.57%
381.00	87.50%	37.10%	15.22%	95.83%	42.86%
385.50	87.50%	38.71%	15.56%	96.00%	44.29%
389.50	87.50%	40.32%	15.91%	96.15%	45.71%
395.00	87.50%	41.94%	16.28%	96.30%	47.14%
401.00	87.50%	50.00%	18.42%	96.88%	54.29%
408.00	87.50%	53.23%	19.44%	97.06%	57.14%
417.00	87.50%	54.84%	20.00%	97.14%	58.57%
423.00	87.50%	59.68%	21.88%	97.37%	62.86%
427.00	87.50%	64.52%	24.14%	97.56%	67.14%
429.00	87.50%	66.13%	25.00%	97.62%	68.57%
431.00	87.50%	70.97%	28.00%	97.78%	72.86%
436.00	87.50%	72.58%	29.17%	97.83%	74.29%
445.00	87.50%	74.19%	30.43%	97.87%	75.71%
454.50	87.50%	75.81%	31.82%	97.92%	77.14%
459.50	87.50%	77.42%	33.33%	97.96%	78.57%
461.50	87.50%	79.03%	35.00%	98.00%	80.00%
466.50	87.50%	80.65%	36.84%	98.04%	81.43%
472.00	87.50%	87.10%	46.67%	98.18%	87.14%
477.00	87.50%	88.71%	50.00%	98.21%	88.57%
484.50	75.00%	95.16%	66.67%	96.72%	92.86%
494.50	75.00%	96.77%	75.00%	96.77%	94.29%
505.00	**75.00%**	**98.39%**	**85.71%**	**96.83%**	**95.71%**
515.00	62.50%	100.00%	100.00%	95.38%	95.71%
540.00	50.00%	100.00%	100.00%	93.94%	94.29%
580.00	37.50%	100.00%	100.00%	92.54%	92.86%
610.00	25.00%	100.00%	100.00%	91.18%	91.43%
634.50	12.50%	100.00%	100.00%	89.86%	90.00%
650.00	0.00%	100.00%	#DIV/0!	88.57%	88.57%

XXIX. Binomial Logistic Regression for predicting outcome among stroke patients

Serum fibrinogen had an odds of 1.02 times of getting death among stroke patients which indicates for each unit increase in serum fibrinogen level, the risk of getting death in stroke patients increases by 1.02 times.

Table 32.Binomial Logistic Regression for predicting outcome among stroke patients

Variables	**B**	**Std. Error**	**Adjusted Odds Ratio (95% C.I.)**	**p value**
Serum Fibrinogen	0.015	0.006	1.02 (1 - 1.03)	0.007

8 DISCUSSION

One of the leading causes of illness and mortality worldwide is acute ischemic stroke. The incidence seems to always be on the rise due to changing lifestyles. The patient must receive prompt attention and the proper care to survive. Serum fibrinogen level is a prognostic biomarker for acute ischemic stroke patients because they had a higher mortality rate when they admitted with high levels of fibrinogen. Plasma fibrinogen level is a simple marker which can be used to identify patients who are at risk.

The main objective of the study is to study the prognostic importance of serum fibrinogen in acute stroke in a series of 70 cases. This is a Prospective cross-sectional study, among 70 patients both male and female presenting as Acute Stroke, admitted under the Department of Internal Medicine, Thanjavur Medical College and Hospital, Thanjavur.Relevant clinical history, clinical examinations, biochemical parameters especially the serum fibrinogen levels were compared with the outcomes of the study population. Prognostic value of the serum fibrinogen levels wasanalysed.

Age:

The mean Age (years) among the subjects was 57.37 (± 12.82) ranging from 30 to 85 years.In a research by **MansourehTogha et al**., individuals with ischemic stroke had a mean and SD of 66.7 10.3, which is a little lower than this.(59)Among the subjects, 37 (52.86%) were in < 60 years and 33 (47.14%) were in > 60 years. The mean Serum Fibrinogen (mg/dl) among < 60 years was 380.38 (± 125.44) which is lower by 33.89 but not statistically significant compared to 414.27 (± 100.14) in > 60 years.

Gender:

Stroke incidences vary by gender as well, displaying the well-known "female paradox" phenomena. Men are more likely to have a stroke, but women do worse when one occurs.. (60)Among the subjects, 42 (60%) had Males and 28 (40%) had Females. The mean Serum Fibrinogen (mg/dl) among Males was 373.19 (± 125.06) which is lower by 57.92 and statistically significant compared to 431.11 (± 88.14) in Females.

Smoking and alcoholism:

Smoking was most likely to increase the risk of stroke.(61)Among the subjects, 23 (32.86%) were Smoker.Among the subjects, 14 (20%) were Alcoholic. The mean Serum Fibrinogen (mg/dl) among those with Smoker and alcoholics werenot significantly different. Alcohol consumption and fibrinogen concentration were closely related, with higher levels found in nondrinkers or those who consumed more than 60 g of alcohol per day. Men had a stronger relationship with this U-shaped pattern than did women.(62–64)

Hypertension and Diabetes Mellitus:

Diabetes and hypertension were regarded as important stroke risk factors. (61) Numerous studies have demonstrated that diabetes is a major risk factor for ischemic stroke, and meta analyses have demonstrated that people who have had an ischemic stroke are at higher risk of dying.(65)Among the subjects, 24 (34.29%) had Diabetes Mellitus.The mean Serum Fibrinogen (mg/dl) among those with Hypertension and diabetes werenot significantly different.

Serum Fibrinogen (mg/dl):

In this study, the mean Serum Fibrinogen (mg/dl) among the subjects was 396.36 (± 114.68) mg/dl ranging from 60 to 649 mg/dl.The mean Serum Fibrinogen (mg/dl)

among Death was 499.88 (± 186.97) which is higher by 116.88 and statistically significant compared to 383 (± 96.32) in Discharge.

Dina M Abdelgawad et al, observed that the Patients with ischemic stroke had high plasma fibrinogen levels, which ranged from 1.8 to 8.2 g/l with a mean of 5.33 g/l (S.D. 1.77). Ten patients (29%) and twenty-five patients (71%) had plasma fibrinogen levels below 4.5 g/l, respectively. Three months after a stroke, high fibrinogen levels were linked to poor outcomes, with hypertension being the most common risk factor. Plasma fibrinogen levels and ischemic stroke are associated. Increased fibrinogen levels were a sign of poor results.(54) In this study we did not observe the long-term outcomes of the study population and its relationship between the fibrinogen levels.

WojciechTurajet al, observed that theIn comparison to patients with normal plasma fibrinogen, those with hyperfibrinogenaemia had higher mortality rates at 1, 3, 6, and 12 months (21.1% vs. 15.6%, 36.4% vs. 24.6%, 42.6% vs. 27.3%, and 45.7% vs. 31.2%, respectively; P 0.001 for the final three differences). Hyperfibrinogenaemia did not predict case fatalities in the short term, although an increase in plasma fibrinogen concentration did (P = 0.013; Odds Ratio: 1.69 (95% CI 1.12-2.55)).(58)

Stroke Scale:

Among the subjects, 47 (67.14%) had Moderate, 20 (28.57%) had Severe and 3 (4.29%) had Mild stroke according to Scandinavian Stroke Scale.The mean Serum Fibrinogen (mg/dl) among Severe was 450.8 which is higher than mean among Moderate which was 385.55 followed by Mild with a mean of 202.67 and the difference was statistically significant ($p < 0.05$). The difference in mean Serum Fibrinogen (mg/dl) was statistically significant among Severe vs Moderate and Severe vs Mild and Moderate vs Mild.

VinodKhandaitet al, observed that the In both ischemic and haemorrhagic stroke, they reported much higher than normal mean fibrinogen levels, with ischemic stroke showing a strong association between infarct volume and fibrinogen levels.(55)**Jae Hyuk Kimet al**, observed that the A worse clinical outcome and an elevated plasma fibrinogen level appeared to be related with Large artery atherosclerosis in acute ischemic stroke.(56)

Modified Ranking Score:

Among the subjects, 28 (40%) had score 5 followed by 22 (31.43%) had score 4 and 20 (28.57%) had score 3Modified Ranking Score at admission.Serum Fibrinogen (mg/dl) has a positive correlation with Modified Ranking Score at admission with a correlation coefficient of 0.436 and was statistically significant indicating that increase in fibrinogen level leads to more disability among stroke patients at admission.

MarietaPeychevaet al, observed that theThe mean amount of fibrinogen was substantially higher in ischemic stroke patients (> 4g/l). Patients with strokes of unknown cause and those with atherosclerotic stroke had considerably higher median levels of fibrinogen than those with several other forms of stroke, according to an analysis of stroke subtypes. Neurological impairment and fibrinogen level did not significantly correlate. (57)

Among the subjects, 34 (54.84%) had score 2, 12 (19.35%) had score 5, 8 (12.9%) had score 4, 7 (11.29%) had score 3 and 1 (1.6%) had score 1Modified Ranking Score at discharge. Serum Fibrinogen (mg/dl) has a positive correlation with Modified Ranking Score at discharge with a correlation coefficient of 0.28 and was statistically significant indicating that increase in fibrinogen level leads to more disability and poor prognosis among stroke patients

Outcome

Among the subjects, 62 (88.57%) had Discharge and 8 (11.43%) had Death. The area under the curve for Serum Fibrinogen (mg/dl) in predicting Outcome is 0.864 (0.637 - 1). The cut off of for predicting Outcome is 505 which had a sensitivity of 75%, specificity of 98.39%, positive predictive value of 85.71%, negative predictive value of 96.83% and a diagnostic accuracy of 95.71%.

With a similar cut-offs, similar accuracy were predicted in **Ghada Samir et al**, where thay observed that the With an area under the curve of 0.97, a cutoff value of 557 mg/dL demonstrated sensitivity of 85.71%, specificity of 96%, and accuracy of 93.75% for mortality in this population. The in-hospital outcome was only affected by diabetes mellitus (P =.04). High serum fibrinogen levels can be used to predict the development of acute ischemic stroke and stroke death in high-risk people, particularly diabetics.(53)

Serum fibrinogen had an odds of 1.02 times of getting death among stroke patients which indicates for each unit increase in serum fibrinogen level, the risk of getting death in stroke patients increases by 1.02 times.

İ İyigünet al, observed that theIn comparison to conscious hemiplegic patients, the fibrinogen and CRP levels in unconscious patients with hemiparesis or hemiplegia were higher. Additionally, there was a statistically significant difference in GOS scores between the aware and unconscious patients with hemiparesis or hemiplegia. Large infarcts in the median cerebral artery and anterior cerebral artery in patients were associated with greater levels of fibrinogen and CRP compared to the control group. In conclusion, fibrinogen and CRP may be crucial indicators of prognosis and outcome in patients who have suffered acute ischemic stroke.(58) This indicates that the severity of the stroke is significantly associated with the fibrinogen level, indicating a dose-response relationship.

9 LIMITATIONS

In this study we did not observe the long-term outcomes of the study population and its relationship between the fibrinogen levels.

Female gender, ischemic stroke, severe cases in Scandinavian Stroke Scale, higher Modified Ranking Score at discharge and admission, had significantly higher levels of Serum Fibrinogen level.Hence the role of confounding by these factors, in the association, cannot be ruled out.

The role of unknown Confounding factors infusing bias cannot be ruled out.

The sample size was calculated based on the accuracy values of the fibrinogen in predicting the outcomes. The sample size was not sufficient to study many other associations.

Long-term outcomes were not studied.

The study design is a cross sectional one. Hence the temporal relationship and other causality points were not cleared.

This study was conducted in a tertiary care setting, hence the study results may not be readily generalised to the other health care settings.

10 STRENGTHS

Age, smoking, alcoholism, blood pressure, hypertension status, blood sugar, Diabetic status were not associated with Serum Fibrinogen level. Hence the role of confounding by these factors, in the association, can be ruled out.

Short-term outcomes such as mortality was studied.

Serum fibrinogen level is a prognostic biomarker for acute ischemic stroke patients because they had a higher mortality rate when they admitted with high levels of fibrinogen.

Plasma fibrinogen level is a simple marker which can be used to identify patients who are at risk.

11 RECOMMENDATIONS

Fibrinogen levels can be used to predict the prognosis in patients affected with acute ischemic stroke with good accuracy parameters.

This indicates that the severity of the stroke is significantly associated with the fibrinogen level, indicating a dose-response relationship.

Further studies with slightly increased sample size done also in other settings such as primary and secondary care will represent the true prognostic utility of the serum fibrinogen among stroke patients.

By taking steps like quitting smoking, losing weight, increasing physical activity, and managing blood pressure, serum fibrinogen can be reduced and hence the high-risk people are less likely to suffer a stroke in the future.

12 SUMMARY OF RESULTS

Study population:

- 70 patients both male and female presenting as Acute Stroke, admitted under the Department of Internal Medicine, Thanjavur Medical College and Hospital, Thanjavur.

Age:

- The mean Age (years) among the subjects was 57.37 (± 12.82) ranging from 30 to 85 years.
- Among the subjects, 37 (52.86%) were in < 60 years and 33 (47.14%) were in > 60 years.
- The mean Serum Fibrinogen (mg/dl) among < 60 years was 380.38 (± 125.44) which is lower by 33.89 but not statistically significant compared to 414.27 (± 100.14) in > 60 years.

Gender:

- Among the subjects, 42 (60%) had Males and 28 (40%) had Females.
- The mean Serum Fibrinogen (mg/dl) among Males was 373.19 (± 125.06) which is lower by 57.92 and statistically significant compared to 431.11 (± 88.14) in Females.

Smoker:

- Among the subjects, 23 (32.86%) were Smoker.

- The mean Serum Fibrinogen (mg/dl) among those with Smoker was 396.22 (± 102.91) which is lower by 0.21 but not statistically significant compared to 396.43 (± 121.08) in those without Smoker.

Alcoholism:

- Among the subjects, 14 (20%) were Alcoholic.
- The mean Serum Fibrinogen (mg/dl) among those with Alcoholic was 352 (± 159.98) which is lower by 55.45 but not statistically significant compared to 407.45 (± 99.11) in those without Alcoholic.

Blood Pressure:

- The mean Systolic Blood Pressure (mm Hg) among the subjects was 144.86 (± 21.52) ranging from 110 to 200 mm Hg.
- The mean Diastolic Blood Pressure (mm Hg) among the subjects was 84.86 (± 11.13) ranging from 60 to 110 mm Hg.Among the subjects, 30 (42.86%) had Hypertension.
- The mean Serum Fibrinogen (mg/dl) among those with Hypertension was 402.07 (± 123.79) which is higher by 9.99 but not statistically significant compared to 392.08 (± 108.76) in those without Hypertension.

Diabetes Mellitus:

- Among the subjects, 24 (34.29%) had Diabetes Mellitus.
- The mean Blood Sugar (mg/dl) among the subjects was 220.09 (± 88.07) mg/dl ranging from 82 to 402 mg/dl.

- The mean Serum Fibrinogen (mg/dl) among those with Diabetes Mellitus was 407.33 (± 100.62) which is higher by 16.7 but not statistically significant compared to 390.63 (± 122.03) in those without Diabetes Mellitus.

Serum Fibrinogen (mg/dl):

- The mean Serum Fibrinogen (mg/dl) among the subjects was 396.36 (± 114.68) mg/dl ranging from 60 to 649 mg/dl.
- The mean Serum Fibrinogen (mg/dl) among Death was 499.88 (± 186.97) which is higher by 116.88 and statistically significant compared to 383 (± 96.32) in Discharge.

Serum Cholesterol (mg/dl):

- The mean Serum Cholesterol (mg/dl) among the subjects was 183.19 (± 20.88) mg/dl ranging from 101 to 240 mg/dl.

Etiology of Stroke:

- Among the subjects, 63 (90%) had Ischemic and 7 (10%) had Hemorrhagic stroke.
- The mean Serum Fibrinogen (mg/dl) among Ischemic was 415.05 (± 89.13) which is higher by 186.9 and statistically significant compared to 228.14 (± 180.17) in Hemorrhagic stroke.

Stroke Scale:

- Among the subjects, 47 (67.14%) had Moderate, 20 (28.57%) had Severe and 3 (4.29%) had Mild stroke according to Scandinavian Stroke Scale.
- The mean Serum Fibrinogen (mg/dl) among Severe was 450.8 which is higher than mean among Moderate which was 385.55 followed by Mild with a mean of 202.67

and the difference was statistically significant ($p < 0.05$). The difference in mean Serum Fibrinogen (mg/dl) was statistically significant among Severe vs Moderate and Severe vs Mild and Moderate vs Mild.

Modified Ranking Score:

- Among the subjects, 28 (40%) had score 5 followed by 22 (31.43%) had score 4 and 20 (28.57%) had score 3 Modified Ranking Score at admission.
- Serum Fibrinogen (mg/dl) has a positive correlation with Modified Ranking Score at admission with a correlation coefficient of 0.436 and was statistically significant indicating that increase in fibrinogen level leads to more disability among stroke patients at admission.
- Among the subjects, 34 (54.84%) had score 2, 12 (19.35%) had score 5, 8 (12.9%) had score 4, 7 (11.29%) had score 3 and 1 (1.6%) had score 1 Modified Ranking Score at discharge.
- Serum Fibrinogen (mg/dl) has a positive correlation with Modified Ranking Score at discharge with a correlation coefficient of 0.28 and was statistically significant indicating that increase in fibrinogen level leads to more disability and poor prognosis among stroke patients

Outcome

- Among the subjects, 62 (88.57%) had Discharge and 8 (11.43%) had Death.
- The area under the curve for Serum Fibrinogen (mg/dl) in predicting Outcome is 0.864 (0.637 - 1). The cut off of for predicting Outcome is 505 which had a sensitivity of 75%, specificity of 98.39%, positive predictive value of 85.71%, negative predictive value of 96.83% and a diagnostic accuracy of 95.71%.

- Serum fibrinogen had an odds of 1.02 times of getting death among stroke patients which indicates for each unit increase in serum fibrinogen level, the risk of getting death in stroke patients increases by 1.02 times.

13 CONCLUSION

The mean Serum Fibrinogen (mg/dl) among the subjects was 396.36 (± 114.68) mg/dl ranging from 60 to 649 mg/dl. The mean Serum Fibrinogen (mg/dl) among Death was significantly higher compared to the subjects who Discharged. Age, smoking, alcoholism, blood pressure, hypertension status, blood sugar, Diabetic status were not associated with Serum Fibrinogen level. Female gender, ischemic stroke, severe cases in Scandinavian Stroke Scale, higher Modified Ranking Score at discharge and admission, had significantly higher levels of Serum Fibrinogen level.The cut off for predicting Outcome is 505 which had a sensitivity of 75%, specificity of 98.39%, positive predictive value of 85.71%, negative predictive value of 96.83% and a diagnostic accuracy of 95.71%.The area under the curve for Serum Fibrinogen (mg/dl) in predicting Outcome is 0.864 (0.637 - 1). Hence fibrinogen levels can be used to predict the prognosis in patients affected with acute ischemic stroke.

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15 ANNEXURES

15.1.1 QUESTIONNAIRE

Name:

Age&Sex

IP No DOA: Address; Ph;

Time duration:

Presenting complaints:

LOC: Seizures: Fever: Others:

Past History

HTN DM PT BA IHD CVA Seizures

Personal history

Smoking Alcoholism

General Examination

BP: pulse RR JVP: Temperature:

CVS

RS

GIT

CNS

INVESTIGATIONS:

CBC:

Blood
  Sugar:
  Urea:
Creatinine:
  Electrolytes:

Urine
  Sugar
  Albumin
  Deposits

ECG

CXR

Lipid profile

Serum cortisol

CT Brain:

SSS

1. Consciousness
2. Orientation
3. Speech

4. Eye movements

5. Facial palsy

6. Gait

7. Arm power

8. Hand power

9. Leg power

ADMISSION	
DISCHARGE	

MRS (0-6)

Patient's outcome : discharged / death

15.1.2 CONSENT FORM

PATIENT INFORMATION SHEET

I ,Dr.S.KUMAR (Mobile:8220865608) am conducting

‘ A STUDY OF SERUM FIBRINOGEN LEVEL AND ITS PROGNOSTIC SIGNIFICANCE IN PATIENTS WITH ACUTE ISCHEMIC STROKE IN TERTIARY CARE CENTER’ to assess the prognostic predictor of serum fibrinogen level in acute ischemic stroke patients and how to reducing the morbidity and mortality in them. In this study after obtaining consent your blood sample is taken for analysis and non invasive painless procedures were to be done. You are expected to participate in the study from the time of admission at GOVERNMENT THANJAVUR MEDICAL COLLEGE until the day of discharge/expiry. You may benefit from decreasing the morbidity and mortality in ACUTE STEMI. At any given point of time during the study the confidentiality of the patient is assured.In participants who suffer direct physical,psychological , social ,legal or economic harm as a result of their participation are entitled, after due assessment to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability. In case of injury caused due to the research you are entitled to the utmost care and free treatment. You are free to withdraw from the study by refusing for the procedures to be done without the loss of benefits that the participant would otherwise be entitled. The data generated from the study maybe used to assess the significance and prognostic importance of serum fibrinogen level in ACUTE ISCHEMIC STROKE

Dr.S.KUMAR (8220865608)

Thanjavur Medical college,

Thanjavu

INFORMED CONSENT DEPARTMENT OF GENERAL MEDICINE

Thanjavur Medical College, thanjavur

Principal investigator :Dr. KUMAR S.

Research guide :Dr.S.Vetrivel, M.D.

Organisation : Department of General Medicine

Informed consent :

I have been invited to participate in research Project Titled

"**A STUDY OF SERUM FIBRINOGEN LEVEL AND ITS PROGNOSTIC SIGNIFICANCE IN ACUTE ISCHEMIC STROKE**"

I understand, it will be answering a set of questionnaire, undergo physical examination, investigations and appropriate treatment.

I also give consent to utilise my personal details for study purpose and can be contacted if necessary.

I am aware that I have the right to withdraw at any time which will not affect my medical care.

Signature of the participant : Date :

Signature of the witness : Date :

Signature of the investigator : Date :

நோயாளியின்ஒப்புதல்படிவம்

நோயாளியின்பெயர் :

முகவரி :

1 .மேற்கூறியஆய்வினைபற்றிஎழுத்துமூலமாகவும் ,
என்சொந்தமொழியிலும்முழுவிவரம்அறிந்துகொண்டேன்.

2 இந்தஆய்வில்நான்பங்கேற்பதற்கானதேவையைபற்றியும்,
எந்தசமயத்திலும்ஆய்வில்இருந்துவெளியேறமுடியும்என்றும்தெரிந்துகொண்டேன்.

3.ஆய்வின்போதுபெறப்படும்எனதுதகவல்கள்மற்றும்மருத்துவக்குறிப்புகள்அனைத்தையும்எ
ந்தவிததடையும்இன்றிஆராய்ச்சிக்குபயன்படுத்திகொள்ளலாம்.

4. மேற்கூறியஆய்விற்குஎனதுமுழுசம்மந்தம்தெரிவிக்கிறேன்.

நோயாளியின்கையொப்பம்: தேதி :

சாட்சியின்கையொப்பம் : தேதி:

ஆராய்ச்சியாளரின்கையொப்பம் : தேதி

15.1.3 DATA SHEET

1	NAME	AGE>60	AGE<60	SEX	SMOKER	ALCOHOLIC	SBP	DBP	SHTN	DM	SUGAR	FIBRINOGEN	CHOLESTEROL	SSS	MRS-ADMISSION	MRS-DISCHARGE	ISCHEMIC	HMRG	OUTCOME
2	SELVAM	38		M	YES	NO	150	90	NO	NO	193	560	235	11	5		YES		DEATH
3	SUBRAMANI	33		M	YES	YES	120	70	NO	NO	280	426	193	40	3	2	YES		DIS
4	MURUGAN	40		M	YES	NO	130	80	NO	NO	146	400	180	28	4	2	YES		DIS
5	SAMINATHAN	34		M	YES	YES	160	100	YES	YES	163	400	165	28	4	2	YES		DIS
6	MURUGAIYAN		65	M	YES	YES	180	100	YES	YES	237	428	240	30	3	2	YES		DIS
7	SELVARAJ		80	M	YES	YES	180	110	YES	NO	105	60	180	4	5			YES	DEATH
8	SELVAM		65	M	YES	NO	130	70	NO	NO	283	348	169	40	3	2	YES		DIS
9	PARVATHY		78	F	NO	NO	110	70	NO	NO	163	232	168	34	3	2	YES		DIS
10	NAGARAJAN	46		M	YES	NO	170	90	YES	NO	82	302	189	36	3	2	YES		DIS
11	ARUMUGAM		62	M	NO	NO	140	90	YES	NO	231	246	190	28	4	3		YES	DIS
12	RAVI	40		M	NO	NO	150	90	NO	NO	153	360	159	28	5	4	YES		DIS
13	VEERAMMAL		65	F	NO	NO	180	100	NO	NO	189	440	200	18	5	4	YES		DIS
14	MUNIYAN	43		M	NO	NO	130	90	NO	NO	143	192	169	36	3	2	YES		DIS
15	SRIVALLI		65	F	NO	NO	170	90	YES	NO	183	480	210	17	5		YES		DEATH
16	VASANTHA		70	F	NO	NO	190	100	YES	NO	202	520	190	11	5		YES		DEATH
17	AYESHA BEEVI		65	F	NO	NO	140	80	NO	YES	306	390	170	26	5	5	YES		DIS
18	AMBIKAVATHY		65	F	NO	NO	130	90	NO	YES	400	474	167	26	5	4	YES		DIS
19	PONNUSAMY	36		M	YES	NO	180	90	YES	NO	187	402	190	27	5	3	YES		DIS
20	GAJAPATHY	50		M	NO	YES	200	100	YES	NO	180	380	210	33	4	2	YES		DIS
21	DEVENDIRAN	47		M	NO	YES	130	90	NO	NO	183	600	220	12	5		YES		DEATH
22	VIRUMAN		68	M	NO	NO	130	80	NO	YES	180	480	200	22	5	3	YES		DIS
23	VENKATESAN	58		M	YES	NO	160	100	YES	NO	120	450	189	36	4	2	YES		DIS
24	VIJAYA		68	F	NO	NO	130	90	NO	YES	320	489	160	26	5	5		YES	DIS
25	RAMASAMY	55		M	NO	NO	130	70	YES	NO	124	500	174	14	5	5	YES		DIS
26	MARIYA	55		F	NO	NO	180	100	YES	NO	263	510	186	30	5	5	YES		DIS
27	SELVARAJ		65	M	NO	NO	130	80	NO	NO	153	470	150	33	4	2	YES		DIS
28	ABDUL SHERIF	58		M	NO	YES	130	70	NO	NO	301	103	167	39	4	2		YES	DIS
29	NADESAN		66	M	YES	NO	130	80	NO	YES	211	420	149	34	4	2	YES		DIS
30	ESAKKI	51		M	NO	YES	140	80	NO	NO	252	69	186	41	3	2		YES	DIS
31	GOVINDASAMY	50		M	NO	NO	130	70	NO	YES	383	246	168	30	3	2	YES		DIS
32	KOKILA		80	F	NO	NO	130	80	NO	NO	280	402	180	32	4	2	YES		DIS
33	FATHIMA BEEVI	54		F	NO	NO	160	90	YES	NO	213	379	170	40	3	2	YES		DIS
34	PANJALAI		65	F	NO	NO	200	100	YES	NO	280	620	210	4	5		YES		DEATH
35	PADMANABAN		65	M	YES	YES	120	70	NO	YES	390	470	194	18	5	5	YES		DIS
36	THANGARAJ		78	M	YES	NO	130	80	NO	YES	283	414	182	24	5	5	YES		DIS

37	SRINIVASAN	51		M	YES	NO	170	90	NO	NO	180	463	175	16	5	5	YES		DIS
38	DHANAM	53		F	NO	NO	130	90	NO	NO	141	430	188	35	4	4	YES		DIS
39	GUNASEELAN	48		M	NO	NO	130	70	NO	YES	180	170	194	24	4	4		YES	DIS
40	SUBBURAJ	55		M	NO	NO	130	60	NO	NO	143	420	198	37	4	3	YES		DIS
41	ASHMA BEGAM	41		F	NO	NO	130	70	NO	NO	200	360	190	33	4	2	YES		DIS
42	CHELLAMMAL	55		F	YES	NO	160	90	YES	NO	103	184	170	33	3	2	YES		DIS
43	KADLIDAS	64		M	YES	NO	160	80	YES	YES	180	420	169	44	3	2	YES		DIS
44	VADIVU	55		F	YES	NO	160	100	YES	NO	174	426	164	42	3	2	YES		DIS
45	NARAYANAN	58		M	NO	YES	130	80	NO	YES	302	350	150	42	5	5	YES		DIS
46	PADMA	58		F	NO	NO	120	70	NO	YES	356	470	187	24	5	5	YES		DIS
47	SARAVANAN		68	M	YES	NO	130	80	NO	YES	102	350	174	22	4	2	YES		DIS
48	SELVAM		85	M	NO	NO	160	100	YES	NO	120	382	208	30	3	2	YES		DIS
49	KANDAN	50		M	NO	NO	130	80	NO	NO	126	357	187	41	4	2	YES		DIS
50	POOMARI	31		F	NO	NO	120	80	NO	NO	200	256	180	30	3	2	YES		DIS
51	KUMARESAN		76	M	YES	NO	140	90	YES	NO	210	480	192	30	5	4	YES		DIS
52	VARALAKSHMI	31		F	NO	NO	160	100	YES	YES	380	649	208	12	5		YES		DEATH
53	RATHINAM		62	F	NO	NO	130	80	YES	YES	200	350	177	31	4	3	YES		DIS
54	SUBBULAKSHMI	55		F	NO	NO	170	100	YES	NO	160	480	184	24	5	4	YES		DIS
55	THANGAPANDI	45		M	NO	NO	130	70	YES	NO	130	400	191	44	3	2	YES		DIS
56	ANJALAI	55		F	NO	NO	130	80	NO	YES	380	470	190	31	4	3	YES		DIS
57	PARAMASIVAM	60		M	YES	NO	120	70	YES	NO	310	510	220	10	5		YES		DEATH
58	FATHIMA BEEVI	30		F	NO	NO	120	80	NO	NO	120	430	198	44	4	2	YES		DIS
59	MURALI	55		M	NO	NO	150	90	YES	NO	200	280	185	33	4	3	YES		DIS
60	PARIMALA	60		F	NO	NO	170	90	YES	NO	128	400	190	24	5	5	YES		DIS
61	VIJAYAN	61		M	YES	YES	130	80	YES	NO	200	380	200	18	5	5	YES		DIS
62	PETCHAYEE	60		F	NO	NO	130	80	NO	YES	250	426	182	33	4	2	YES		DIS
63	RENGASAMY	50		M	NO	YES	150	80	NO	YES	300	430	101	40	3	2	YES		DIS
64	POOMANI	75		M	NO	NO	160	90	YES	YES	360	460	174	37	3	2		YES	DIS
65	JEYARAM	60		M	NO	NO	160	100	NO	NO	380	480	185	35	3	2	YES		DIS
66	MUTHAMMAL		80	F	NO	NO	140	80	NO	YES	320	459	174	40	4	1	YES		DIS
67	KANI	53		F	NO	NO	160	90	YES	NO	153	380	181	30	4	2	YES		DIS
68	THANGARASI	62		F	NO	NO	130	80	NO	YES	320	389	160	28	5	2	YES		DIS
69	MUTHUKRISHNAN	65		M	YES	YES	130	70	NO	YES	402	400	179	26	5	4	YES		DIS
70	KAMATCHI	56		F	NO	NO	120	70	NO	NO	126	360	160	33	3	5	YES		DIS
71	KUMARAVEL		70	M	YES	YES	150	100	YES	NO	108	432	199	37	3	2	YES		DIS