SERUM FERRITIN,CRP,RDW IN CORRELATION WITH SEVERITY OF ACUTE ISCHAEMIC STROKE

A Dissertation submitted to

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY

in partial fulfilment of the Regulations

for the award of the degree of

M.D (GENERAL MEDICINE) BRANCH-I

I

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CERTIFICATE

This is to certify that this dissertation entitled, " **SERUM FERRITIN ,CRP AND RDW IN CORRELATION WITH SEVEARITY OF ACUTE ISCHAEMIC STROKE "-An observational cross section Study-** is the original Bonafide work done by **DR.S.GOPAL** Post graduate in General Medicine, under my overall supervision in the Department of General Medicine, Govt. Kilpauk Medical College in partial fulfillment of the regulations of The Tamilnadu Dr. M.G.R Medical University for the award of **M.D. DEGREE IN GENERAL MEDICINE.**

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I solemnly declare that this dissertation titled, " **SERUM FERRITIN ,CRP AND RDW IN CORRELATION WITH SEVERITY OF ACUTE ISCHAEMIC STROKE -An observational cross section Study** " is the original Bonafide work done by **DR.S.GOPAL** Post graduate in General Medicine, under my overall supervision in the Department of General Medicine, Govt. Kilpauk Medical College in partial fulfillment of the regulations of The Tamilnadu Dr. M.G.R Medical University for the award of **M.D. DEGREE IN GENERAL MEDICINE.** "

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ABSTRACT

ABSTRACT

Introduction:

Stroke is an abrupt onset of a neurological deficit attributable to a focal vascular cause. Globally, it is one of the leading causes of death and disability-adjusted life-years (DALYs) as per the estimates from the Global Burden of Diseases, Injuries, and Risk Factors Study. They are broadly classified as ischemic and haemorrhagic strokes. About 85% of all strokes are ischemic, and 15% are haemorrhagic. Ischemic strokes result from interruption of the blood supply to the brain, while haemorrhagic strokes result from the rupture of blood vessels. NIHSS,on the other hand, evaluates patients on 11 different parameters and has been found to be an excellent predictor of patient outcomes. Red cell distribution width (RDW) is a measure of the variation in red blood cell (RBC) sizes, based on the width of the mean corpuscular volume (MCV) and is easily and inexpensively determined by automated flow cytometer, as part of a complete blood counts. High RDW levels may be associated with elevated levels of inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and interleukin (IL) levels (6). High RDW levels have been found to be associated with a poor prognosis in acute myocardial infarction and peripheral artery disease. RDW has also been evaluated as a predictor of mortality in patients with cardiovascular disease, cancer, chronic lung disease, symptomatic chronic congestive cardiac insufficiency and acute

cardiac insufficiency. Utility of RDW in predicting stroke severity, is still being evaluated. In this study, we tried to correlate RDW With the severity of acute ischemic stroke and also tried to find out whether RDW can be used as a predictor of mortality in acute ischemic stroke.

Aims and Objectives:

To study the severity of acute ischemic stroke in correlation with serum ferritin ,CRP and RDW concentration.

Materials and methods:

All patients who presented within 48 hrs of onset of stroke and who gave informed consent to participate in the study were included As ferritin ,CRP,RDW is an Acute phase reactant samples are taken with in 48 hrs of onset.

Results:

The present study included 183 participants who presented with acute ischemic stroke and were evaluated with several markers. A high prevalence of acute ischemic stroke was reported in patients aged 61-70 (33.33%), followed by the age group of 41-50 (26.8%). In addition, a male predominance was reported in the current study, with a high incidence of hypertension (56.8%), diabetes mellitus (54.1%), the social habit of smoking (26.2%), and alcohol intake (17.5%). The NIHSS stroke severity assessment revealed that a majority of the

patients were in the mild scoring criteria (42.6%), followed by moderate (21.9%), moderate to severe (16.4%), and severe criteria (19.1%). The clinical outcome of the study reports a loss of life due to mortality among 36 participants, with acute ischemic stroke accounting for 19.7% of the total participants. The RDW elevated levels, compared with the NIHSS score, revealed a significant difference (p-value <0.0001). Our study also reported that patients with a high RDW level had an increased mortality risk compared with the NIHSS score. The study revealed that patients with high CRP levels were associated with stroke mortality in AIS. In addition, higher CRP levels were also associated with larger infarct volumes in patients with acute ischemic stroke. [73] The findings revealed that patients with elevated CRP levels are more prone to developing complications in acute ischemic stroke, and the levels of CRP can be used to reflect the severity of AIS among patients. The comparison of mortality (loss of life) and recovery also reported a statistical difference concerning elevated serum CRP levels and mortality.During admission, elevated ferritin levels were reported based on the severity of the NIHSS score, which was in an upward trend with increasing severity (p-value <0.0001), which signifies that with increased severity of a stroke, high levels of serum ferritin can be reported. Literature has suggested that elevated serum ferritin levels can be a prognostic marker in ischemic stroke and act as a risk factor for ischemic episodes by causing atherogenesis

. **Conclusion:** The study concludes with a linear relationship between the RDW, serum CRP, and serum ferritin levels in predicting the severity of stroke and mortality outcomes in patients with acute ischemic stroke.The study also reports a significant difference in clinical outcome and mortality (loss of life) when compared with all three markers (p-value <0.0001) respectively, which conclude that RDW, serum CRP levels, and serum ferritin levels can be used as a prognostic marker for assessing the severity of the stroke and formulating a therapeutic plan based on the severity.

Key words :acute ischaemic strike,RAW,CRP,FERRITIN ,NHISS SEVERITY SCORE

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ABBREVIATION

CVA	-	Cerebrovascular accident
AF	-	Atrial fibrillation
DALYs	-	Adjusted life-years
IS	-	Ischemic stroke
CRP	-	C-reactive protein
NIHSS	-	National Institutes of Health Stroke Scale
GCS	-	Glasgow Coma Scale
AIS	-	Actual ischemic stroke
RDW	-	Red cell distribution width
MCV	-	Mean corpuscular volume
RBC	-	Red blood cell
ESR	-	Erythrocyte sedimentation rate
IL	-	Interleukin levels
ICH	-	Intracerebral haemorrhage
GBD	-	Global Burden of Disease
LDL	-	Low-density lipoprotein
HDL	-	High-density lipoprotein
CBF	-	Embolism or situ thrombosis

INTRODUCTION

INTRODUCTION

A stroke or cerebrovascular accident (CVA) is an abrupt onset of neurological deficit attributable to the focal vascular cause. Ischemic stroke is one of the leading causes of mortality and disability in the world due to the nature of the disease; stroke can affect a spectrum of motor, sensory, and cognitive impairment in an individual, which can also decrease the quality of life. [1]

Developing countries like India are facing a burden on the healthcare sector with communicable and non-communicable diseases. In such circumstances, stroke remains the second leading cause of mortality in hospital admission and critical care. [3] According to WHO Fact Sheet, from 1990 to 2019, the stroke burden increased substantially, with a 70% rate accompanied by 43% of death and affecting 143% of disability-adjusted life-years (DALYs). [4] A majority of the patient suffering from stroke were seen in low- or middle-economic-income countries. [3] [4]

A recent report shows that the estimated global lifetime risk of stroke in 2016 for individuals over 25 years of age was 24.9%, including a lifetime risk of 18.3% for ischemic stroke and 8.2% for hemorrhagic stroke. [5]

Even with the recent medical advancement, Ischemic stroke remains the cause of mortality, morbidity, and disability in developed and developing countries. Early

identification of the disease, modification of risk factors, and institution of proper treatment can decrease the impact of the disease and improve the overall patient outcome. One such prognostic factor is the serum ferritin levels; alteration of ferritin levels is often correlated with the stress response to stroke. [6]

Literature has suggested that high serum ferritin levels influence the prognosis of ischemic stroke and act as a risk factor for ischemic episodes by atherogenesis. [7]

Another prognostic marker is the C-reactive protein (CRP), often raised during acute ischemic stroke onset. High CRP levels correlate with poor outcomes and prognosis, reflecting an inflammatory response or tissue damage. [8]

Various scoring systems, such as the Glasgow Coma Scale (GCS) and the National Institutes of Health Stroke Scale (NIHSS), have been used as a validated methods for predicting the severity of actual ischemic stroke (AIS). [9]

Red cell distribution width (RDW) is the measure of variation in the red blood cell (RBC) sizes based on the width of mean corpuscular volume (MCV). High RDW levels can be associated with elevated inflammatory markers such as CRP, erythrocyte sedimentation rate (ESR), and interleukin levels (IL). Several pieces of literature have reported a direct correlation with RDW as a predictor of mortality in patients with cardiovascular disease. One study has suggested that high RDW levels are related to a poor prognosis of acute myocardial infarction and AIS. [10]

As the research for direct correlation is still under investigation, the study aims to assess the association of high levels of RDW for predicting the severity of acute ischemic stroke. In addition, the study also aims to determine a significant correlation between inflammatory markers and RDW in patients with acute ischemic stroke.

REVIEW OF LITERATURE

LITERATURE REVIEW

Cerebrovascular accidents are also known as strokes. The condition is clinically characterized by a blocked artery or the leaking or rupture of a blood vessel which can increase the overall mortality and morbidity among the patients. Majorly stroke is subdivided into three types; Ischemic, hemorrhagic, and subarachnoid. [1]

The review focuses on acute ischemic stroke, epidemiology, risk factors, morbidity, clinical management, and classification.

Acute ischemic stroke is the acute onset of focal neurological findings in the vascular territory due to underlying cerebrovascular disease. Currently, stroke is the fifth leading cause of mortality and a first leading cause of disability. [12]

Ischemic stroke is a common type caused by an interruption of blood flow in a certain brain area. Clinically ischemic strokes account for 85% of all acute strokes, whereas 15% of acute strokes are hemorrhagic. The hemorrhagic strokes are divided into:

- **Intracerebral haemorrhage (ICH)**
- **Subarachnoid haemorrhage (5% of all strokes)**

According to the TOAST [13] classification, there are four main types of ischemic strokes.

- Large vessel atherosclerosis

- Small vessel diseases (lacunar infarcts)
- Cardioembolic strokes
- Cryptogenic strokes

Regardless of the type of stroke, each minute of large vessel ischemic stroke untreated results in the death of nearly two million neurons. [12] [13]

There are several etiological reasons for stroke, such as prolonged hypertension, arteriosclerosis, and the presence of emboli that develop in the heart due to atrial fibrillation or rheumatic heart disease. In the younger population, the aetiology can be due to clotting, cervical arterial dissection, and vasculitis. In the early event of a stroke, it is essential to conduct a precise history and physical examination alongside neurological imaging before providing any treatment to the patient. [12]

Ischemic stroke can be further classified as;

1. Thrombotic – accounting for 25% of strokes
    i. Lacunar stroke – 20-25%
    ii. Large vessel disease – 1-5%
2. Embolic – 75%
    i. Cardioembolic – 20%
    ii. Artery-Artery – 15%
    iii. Cryptogenic – 30%
    iv. Other – 10%

EPIDEMIOLOGY OF STROKE

The second leading cause of death worldwide is stroke. Each year, it affects 13.7 million people and kills about 5.5 million. The prevalence of ischemic infarctions, which account for about 87% of strokes, increased significantly between 1990 and 2016, which is attributed to lower mortality and better clinical interventions. Most strokes are caused by primary (first-time) haemorrhages, with secondary (second-time) haemorrhages accounting for approximately 10% to 25% of all strokes. [13] [14] [15] From 1990–2016, the incidence of stroke doubled in low- and middle-income countries, while it decreased by 42% in high-income nations. The Global Burden of Disease Study (GBD) reports that although the prevalence of stroke has decreased, the age, sex, and location of those affected have increased the socioeconomic burden of stroke over time. [15]

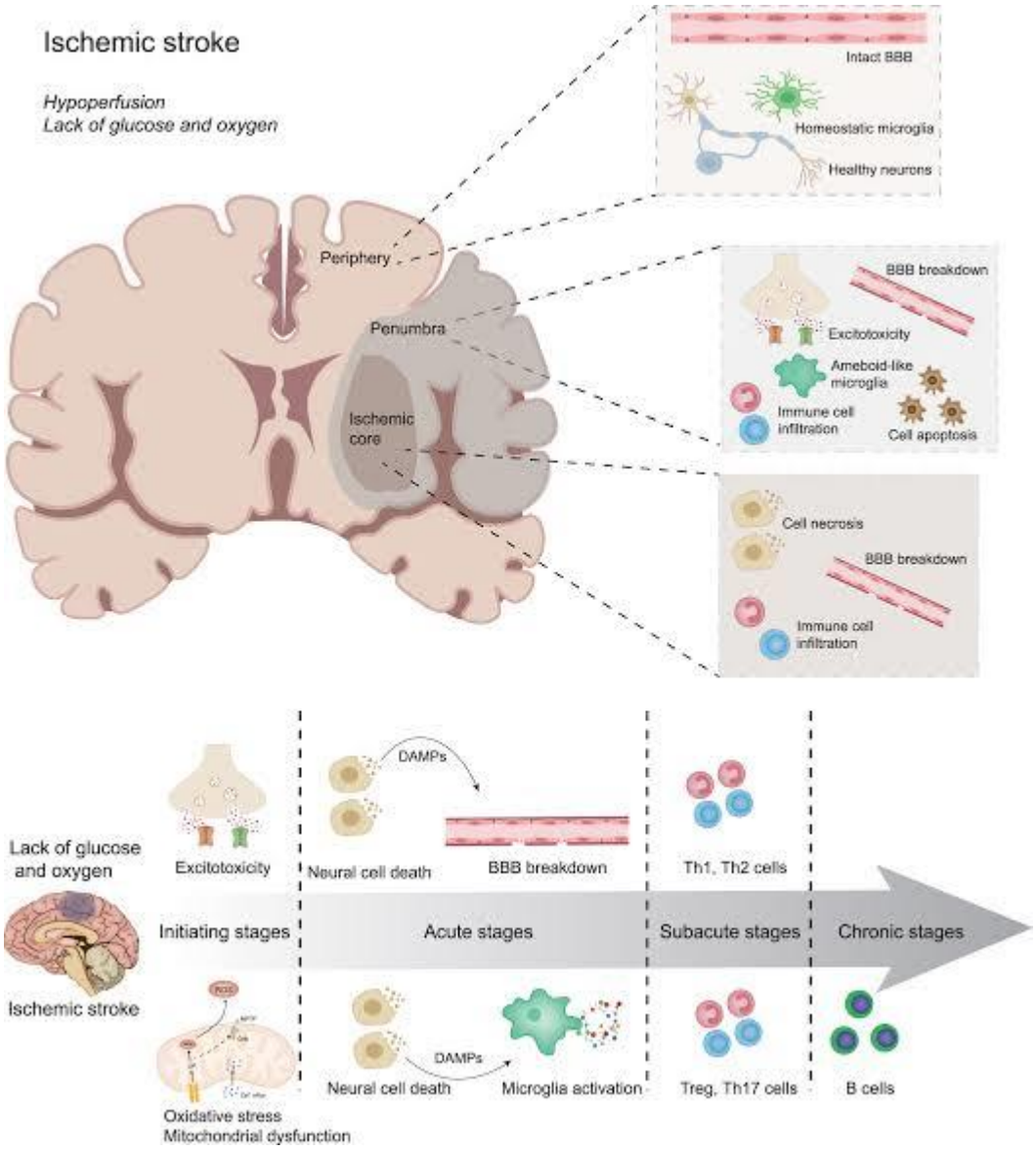
Age-specific stroke

As with increasing age, the risk for stroke increases. After the age of 55 years, a two-fold increase in the development of stroke has been reported by several studies. However, the recent trend shows that strokes are more prevalent in the age group of 20-54 years, increasing from 12.9% to 18.6% between 1990 and 2016. [15]

Gender-specific stroke

The prevalence of stroke differs in men and women based on their age, and literature has revealed that younger women are more prone to stroke, and men in their older age have a higher prevalence of stroke. In young women, the risk factors include; pregnancy, preeclampsia, contraceptives use, hormonal therapy, and migraine with aura. [16] [17] For men, the most common risk factors include; smoking, excessive alcohol intake, myocardial infarction, arterial disorders, and tobacco use. [18]

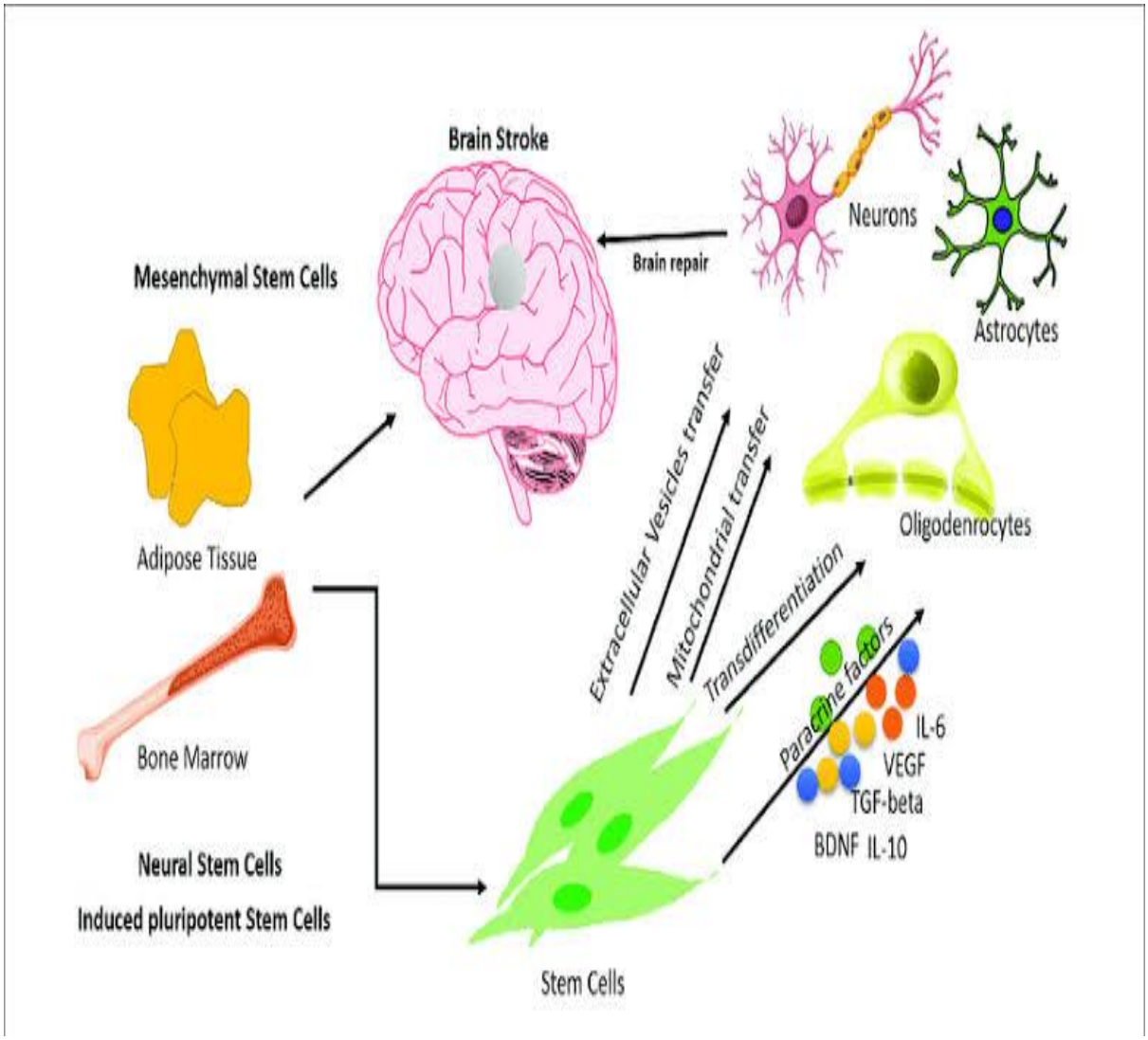
PATHOPHYSIOLOGY OF STROKE



A stroke is a neurologic event caused by the death of brain cells due to an insufficient supply of blood, which lasts> 24 hours. The thrombotic stroke events are similar to the pathogenesis of myocardial infarction, which initiates the development of atherosclerosis, plaque disruption, and subsequent thrombus formation followed by artery occlusion. The formed thrombosis can occlude the

local artery or moves in the bloodstream to form a thrombotic embolus. However, the carotid arteries are the common sites of thrombus formation. [19] [20] [21]

Cardioembolic stroke events originate mainly from the atria, ventricles, septum, or heart valves without clear pathogenesis of atherosclerosis. The embolus generally travels through the left side of the heart into the arterial system and blocks the intracranial artery to cause ischemia. About 50% of cardioembolic strokes are caused due to atrial fibrillation (AF). [22]



The uncoordinated contractions of the atrial appendage with decreased blood flow velocities and stasis are fundamental factors in forming atrial thrombi in AF. The other causes of cardioembolic strokes are caused by various aetiology, including infection and non-infective endocarditis, mitral/aortic stenosis, prosthetic heart valves, dilated cardiomyopathy, and myxoma. [23]

Hemorrhagic stroke comprises 10-15% of all strokes with high mortality rates. During intracerebral haemorrhage (ICH), the blood vessels rupture and cause an abnormal accumulation of blood within the brain, which results in stroke. Figure 1 denotes the molecular mechanism responsible for a stroke. [24]

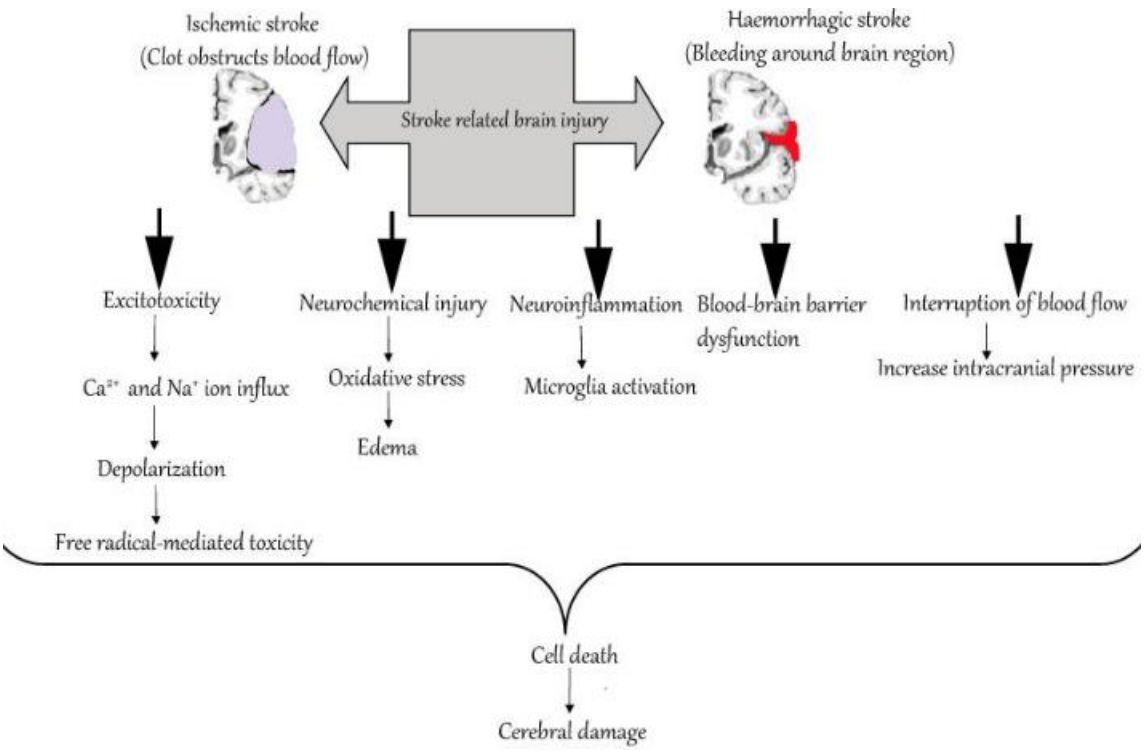


Figure 1- Molecular mechanism of stroke [24]

The most prevalent and significant underlying condition that results in the accumulation of low-density lipoprotein cholesterol (LDL) in the arteries feeding the brain is atherosclerosis. These plaques can cause distal ischemia of the brain if they obstruct or reduce the diameter of the intracranial or neck arteries. They may also, and more frequently, rupture. When a plaque ruptures, the hidden cholesterol crystals attracted to platelets and fibrin are exposed. Strokes are brought on by the release of fibrin-platelet-rich emboli that travel from artery to artery in the distal arterial regions. The underlying cardiac issue determines the kind of cardiac cause of emboli. Clots frequently occur in the left atrium in atrial fibrillation. These clots are enriched in red blood cells. [12]

The adjacent neurons lose their oxygen supply and nutrients in an arterial blockage. The Na+/K+ ATPase pumps malfunction due to the inability to undergo aerobic metabolism and produce ATP, causing an accumulation of Na+ inside and K+ outside the cells. Cells depolarization results in the accumulation of Na+ ions, which releases glutamate. Calcium ions can enter cells when glutamate activates NMDA and AMPA receptors. A continuous flow of calcium results in neuronal firing and eventually leads to cell death due to excitotoxicity. [25]

There are no significant macroscopic changes in the initial 12 hours of the disease. Cytotoxic oedema due to energy production failure results in neuronal cellular swelling. This early infarction state shows restricted diffusion due to neuronal

cellular swelling on diffusion-weighted MRI. Vasogenic oedema appears six to twelve hours after the stroke. FLAIR sequence MRI might be the most effective way to see this stage. Increased intracranial pressure and swelling of the infarcted area are two effects of cytotoxic and vasogenic oedema. Following these, phagocytic cells invade to remove the dead cells. The affected brain tissues soften and liquefy from extensive phagocytosis, reaching their peak six months after the stroke. After a stroke, astrocytes develop a dense network of connective tissue, capillaries, and glial fibres. [26] [27]

The two major mechanisms for ischemia include thromboembolism and hemodynamic failure. The former typically results in an abrupt decrease in regional cerebral blood flow due to embolism or situ thrombosis (CBF). In the latter case, collateral blood supply keeps CBF levels high enough to preserve brain function when arterial occlusion or stenosis occurs. In these situations, cerebral ischemia may be brought on by factors such as systemic hypotension or low cardiac output that reduce perfusion close to the arterial lesion and raise metabolic demands (fever, acidosis), as well as factors that cause "blood stealing"

from affected to unaffected areas of the brain. [28]

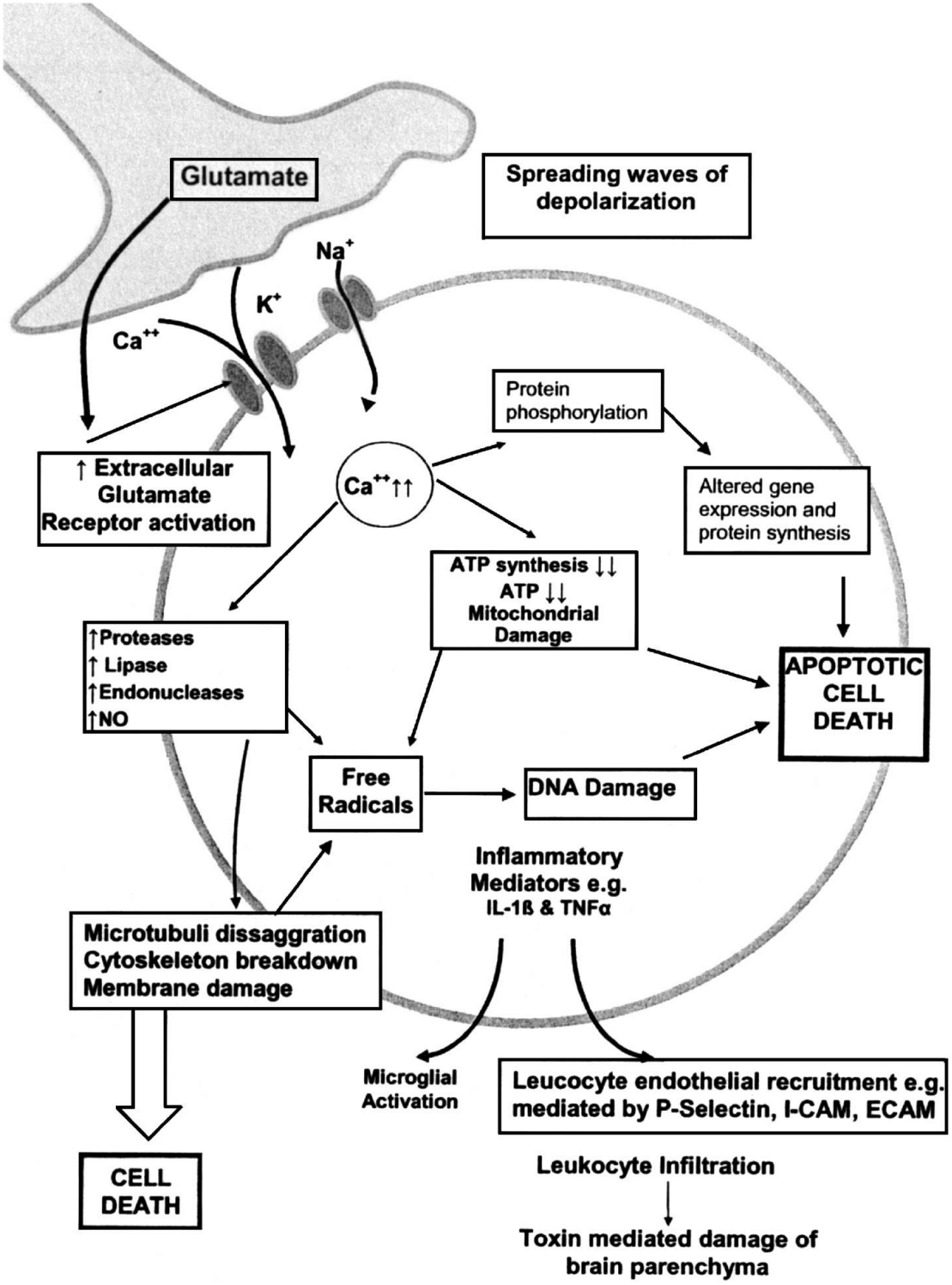


Figure 2 – Cellular mechanism of ischemic neuronal injury in acute stroke

[28]

RISK FACTORS FOR ACUTE ISCHEMIC STROKE

1. Unmodifiable risk factors
2. Modifiable risk factors
3. Weak modifiable factors
4. Predominant risk factors in the young population

Table 1 shows the summarisation of risk factors involved in ischemic stroke.

Table 1 – Risk factors associated with ischemic stroke [12] [13]

Unmodifiable risk factors	**Weak modifiable risk factors**	**Predominant risk factors**
Age Gender Race Family History Previous history of stroke	AIDS Alcohol Fibrinogen and platelets Lipids Sedentary lifestyle Haematocrit Dehydration Pregnancy Diet Socioeconomic status	Mitral valve leaflet prolapses Sickle cell disease Migraine Cocaine abuse Obstructive sleep apnea Intercurrent infection Atrial septal aneurysm Systemic lupus erythematosus

Major modifiable risk factors

These factors play an essential role in the prevention and timely management of the disease. Therefore, by the use of the proper precautionary measure, these factors can be managed and can prevent the occurrence of stroke.

1. Atrial fibrillation - According to research, the left atrium's reduced blood flow results in brain embolism and thrombolysis in AF. Recent studies, however, have refuted this conclusion, citing a lack of evidence for the sequential timing of AF and stroke incidence and pointing out that in some patients, the occurrence of AF is only recorded after a stroke. In other cases, people with AF-related genetic mutations may experience strokes years or even decades before they develop AF. [29] [30]

2. Hypertension - It is one of the main causes of stroke risk. One study found that 54% of stroke victims had blood pressure (BP) readings of at least 160/90 mmHg and a history of hypertension, both of which were important predispositions for stroke. [31]

3. Diabetes mellitus results in a 20% higher mortality rate and doubles the risk of ischemic stroke. Additionally, diabetic patients have a worse prognosis for recovery from a stroke than non-diabetic patients due to higher rates of severe disability. Strict glycemic control alone is ineffective; medical intervention

combined with behavioural changes may lessen stroke severity in people with diabetes. [32]

4. Smoking - Stroke risk is directly correlated with tobacco use. Compared to non-smokers, the average smoker has a twofold increased risk of stroke. 15% of deaths from stroke are caused by smoking. According to research, those who stop smoking have a lower relative risk of stroke, while prolonged exposure to secondhand smoke increases that risk by 30%. [32] [33]

5. Alcohol - The risk of stroke increases with daily alcohol consumption, according to a curvilinear relationship between the two variables. Stroke risk is decreased when alcohol consumption is low to moderate (2 standard drinks per day for men and 1 for women), whereas it is increased when intake is high. Contrarily, even moderate alcohol use increases the risk of hemorrhagic stroke. [34]

6. Low physical activity and poor diet - Lack of exercise increases a person's risk of having a stroke attack. High blood pressure, obesity, and diabetes—all conditions associated with a high incidence of stroke—are linked to insufficient physical activity and other health problems. Our diet affects our risk of stroke by causing high blood pressure, high cholesterol, obesity, and diabetes. It is well known that certain dietary elements increase risk; for

instance, consuming too much salt is associated with high blood pressure and stroke. [35] [36]

CLINICAL PRESENTATION OF STROKE

Ischemic stroke syndrome

Ischemic stroke is a pre-determined syndrome caused due t reduced blood to particular areas of the brain, which can be correlated with the examination findings.

The clinical findings allow clinicians to predict the area of the brain vasculature that is affected.

Middle cerebral artery (MCA) infarction

The middle cerebral artery is the most frequent artery involved in stroke. The artery supplies blood to a larger area of the lateral surface of the brain, the basal ganglia, and the internal capsule through the four segments (M1, M2, M3, and M4). The basal ganglia, which is involved in motor control, learning, executive function, and emotions, receive its energy from the M1 (horizontal) segment. The insula, superior temporal lobe, parietal lobe, and inferolateral frontal lobe are all supplied by the M2 (Sylvian) segment. [12] [13]

The lateral cerebral cortex is involved in the MCA distribution. The study of the somatosensory cortex, whose lateral section encompasses motor and sensory activities that affect the face and upper extremities, is the key to understanding

MCA syndrome. This is consistent with the usual symptoms of facial paralysis, contralateral hemiparesis, and sensory loss in the face and upper extremities. [37] Although the lower extremity may be affected, the symptoms often affect the upper extremity more. There may be a preference for looking in that direction. Additional signs comprise:

- Dysarthria is diagnosed by the difficulty of phonating words due to the weakness of the muscles, especially involved in phonation
- Neglect occurs when a patient appears to "ignore" a portion of their environment because they are unable to observe it
- Aphasia, or the inability to produce or recall words as a result of brain damage to the language centres

Anterior cerebral artery (ACA) infarction

The frontal, prefrontal, primary motor, primary sensory, and supplemental motor cortices are all supplied with blood by the anterior cerebral artery (ACA). Due to the substantial collateral blood flow provided by the anterior circulation artery, pure ACA infarcts are not common. The sensory and motor cortices control the contralateral lower extremity's movement, which also processes sensory data. The Broca area, which is involved in speech start, is part of the supplemental motor area. The prefrontal cortex is thought to impact personality and is utilized to organize and plan complex behaviour. [37]

The middle cerebral cortex is involved in the ACA distribution. The motor and sensory functions of the leg and foot are included in the somatosensory cortex in that region. Sensory and motor impairments in the lower extremity on the contralateral side are part of the clinical manifestation of an ACA infarction. The face and upper extremities are unharmed. Kumral et al. looked at the clinical spectrums of ACA in connection to MRI/MRA. They found that left-sided lesions showed increased transcortical motor aphasia, which affects patients' ability to respond spontaneously with speech while maintaining their ability to repeat. Lesions on the right side showed more severe disorientation and motor neglect (loss of one side's motor function). [37]

Posterior cerebral artery (PCA) infarction

The occipital lobe and the inferior part of the temporal lobe are supplied by the superficial posterior cerebral artery (PCA). In contrast, the deep PCA also supplies the thalamus, the posterior limb of the internal capsule, and other deep brain structures. The primary and secondary visual areas are found in the occipital lobe, which also processes sensory information from the eyes. The lateral and ventral corticospinal tracts' descending fibres are located in the internal capsule, while the thalamus is a relay for information between ascending and descending neurons.

PCA infarctions can be categorized as deep or superficial depending on the PCA supply. Hypersomnolence, cognitive deficits, ocular findings, hypoesthesia, and

ataxia are possible symptoms if the deep segments of the PCA are affected. Homonymous hemianopsia, in which patients experience visual field deficits in one-half of their visual field, is one possible ocular finding. Due to the involvement of the thalamus and internal capsule in larger infarcts that affect the deep structures, chemosensory loss and hemiparesis can result. Superficial infarcts present with visual and somatosensory deficits, including impaired stereognosis, tactile sensation, and proprioception. Rarely, bilateral PCA infarcts cause cortical blindness and amnesia. Cortical blindness is due to lesions in the optic radiation that causes vision loss. [38] [39]

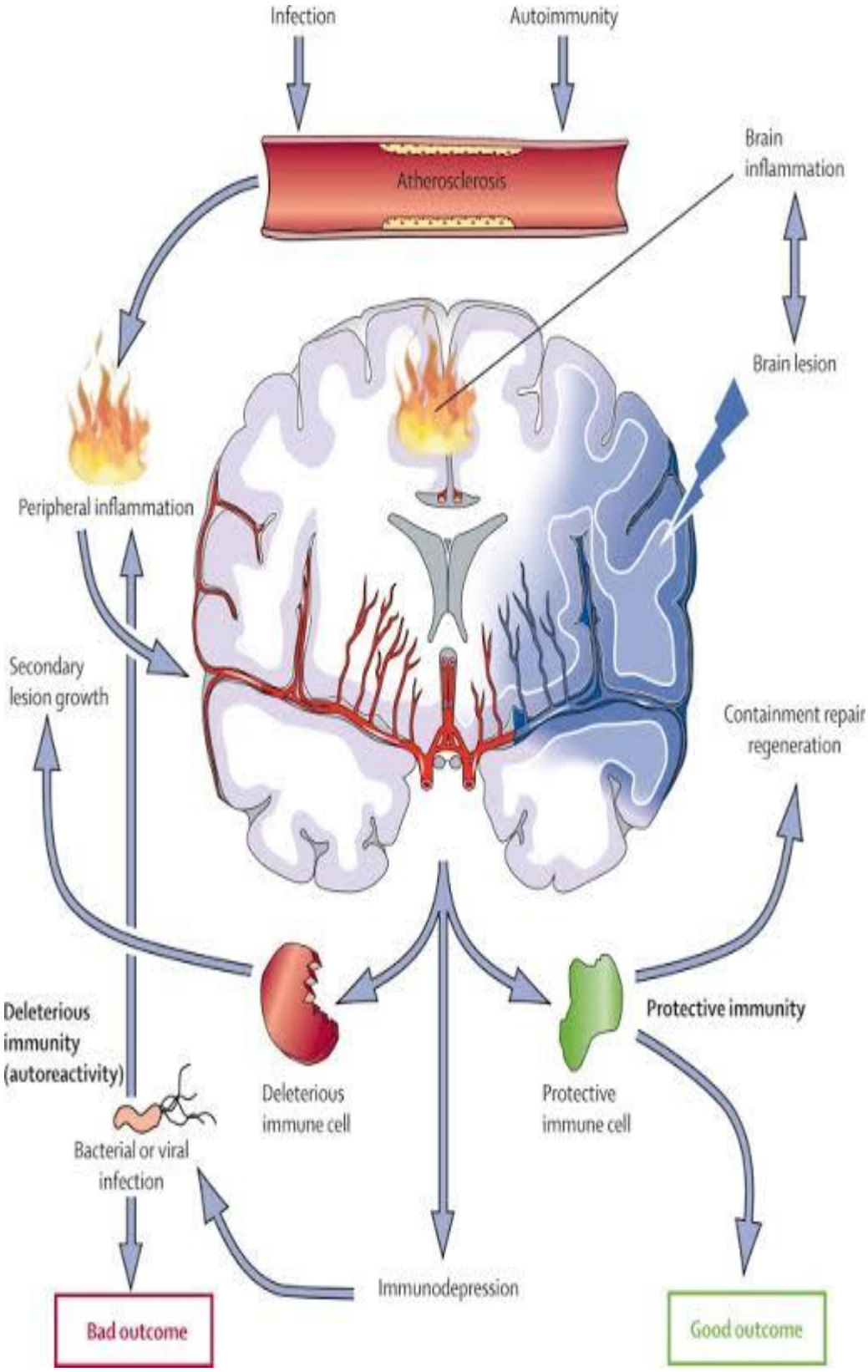
Vertebrobasilar infarction

The basilar and vertebral arteries, which start in the spinal column and end at the Circle of Willis, supply the vertebrobasilar region of the brain. These regions supply the brainstem and cerebellum. The clinical presentation includes ataxia, vertigo, headache, nausea, oropharyngeal dysfunction, visual-field deficits, and abnormal oculomotor findings. Different clinical presentation patterns exist depending on the site and the infarction pattern of an embolism or atherosclerosis. [40] [41]

Lacunar infarction

A small perforating artery is becoming blocked, leading to lacunar infarcts. The precise mechanism is unknown because an embolism or intrinsic vessel occlusion can cause an infarct, depending on its nature. Pure motor or sensory loss,

sensorimotor deficit, or ataxia with hemiparesis are all possible presentations of infarction in this region. [42] [43]



CLINICAL INVESTIGATIONS

A CT scan is one of the essential diagnostic tools used to confirm and rule out bleeding or the presence of a hemorrhagic stroke. A patient might be a candidate for fibrinolytic therapy depending on the CT scan results and the time since the onset of the symptoms. A diffusion-weighted MRI is the most accurate form of imaging for acute ischemic infarction. Confirming the diagnosis may also show the infarction's size and location. Due to the time required to obtain the images and the relative scarcity of availability, it is not thought of as first-line imaging. Other MRI protocols, particularly the diffusion-perfusion mismatch protocol, identify patients who benefit from reperfusion therapy after the first 4.5 to 6 hours of an acute ischemic stroke and describe the area of tissue at risk (the "penumbra") that can be saved with prompt treatment. [44] [45]

Initial evaluation

The first evaluation comprises checking the airway, breathing, circulation, and vital signs. Patients can be presented with respiratory abnormalities from elevated intracranial pressure, posing a risk of aspiration and asphyxiation. Patients with an emergent situation may require endotracheal intubation to provide adequate oxygenation and ventilation.

A finger stick glucose check should be conducted, as it is easy to rule out hypoglycemia due to neurological abnormalities.

Imaging studies

To rule out bleeding, a plain CT of the head or brain MRI is recommended for patients within 20 minutes of stroke presentation. In hospital centres for stroke care, vascular imaging should be used to intervene in possible endovascular involvement; however, imaging studies should not delay the administration of thrombolytic agents. [2] [13]

The clinical presentation of acute ischemic stroke can be seen by using the diffusion-weighted MR sequence. In addition, the FLAIR sequence also helps predict the onset of stroke, which is paramount in determining thrombolytic therapy. The DWI features with no changes in the FLAIR sequence can be identified as an ischemic stroke that occurred within 6 hours and can be managed to revert the neurological deficit using intravenous thrombolytics. [13]

Other diagnostic tests

An electrocardiogram (ECG), troponin, complete blood count, electrolytes, blood urea nitrogen (BUN), creatinine (Cr), and coagulation factors are examples of additional diagnostic tests. Because stroke frequently coexists with coronary artery disease, an ECG and troponin are advised. The results of a complete blood count may reveal infection or look for anaemia. Any abnormalities in the electrolyte should be treated. As contrast studies may worsen kidney function, BUN and Cr should be monitored. Additionally, coagulation factors like PTT,

PT, and INR should be assessed because elevated levels may indicate a hemorrhagic stroke cause. [13]

THE GLASGOW COMA SCALE [46]

The Glasgow Coma Scale is divided into three parameters;

Best eye response (E)

Best verbal response (V)

Best motor response (M)

The Glasgow Coma Scale's response levels are "scored" on a scale of 1 for no response to, 4 for eye-opening, 5 for a verbal response, and 6 for total response (Motor response).

The total Coma score is between 3 and 15, with three being the poorest diagnosis and 15 being the highest.

Best eye response (4)

- No eye opening
- Eye-opening to pain
- Eye-opening to sound
- Eyes open spontaneously

Best verbal response (5)

- No verbal response

- Incomprehensible sounds
- Inappropriate words
- Confused
- Orientated

Best motor response (6)

- No motor response.
- Abnormal extension to pain
- Abnormal flexion to pain
- Withdrawal from pain
- Localizing pain
- Obeys commands

GOALS OF TREATMENT AND THERAPEUTICS

After evaluating the airway, breathing, and circulation, the patient should be assessed for the criteria of alteplase administration. The American Heart Association/American Stroke Association's recommendations are the foundation for the exclusion criteria. Fibrinolytic therapy aims to break up the clot and get the blood flowing again in the affected areas. Depending on the exclusion criteria, the fibrinolytic must be given within 3 to 4.5 hours of the onset of the symptoms to be effective. The "time is brain" approach during a stroke is crucial and necessitates a quick and team-based treatment approach, just like with the

treatment of myocardial infarction and sepsis care. Telemedicine and mobile stroke units have been developed to shorten the time to treatment window. [47] [48] [49]

Criteria for thrombolytic therapy

- No recent head traumas
- Symptoms and clinical presentation suggest ischemic stroke
- No history of myocardial infarction in the past 3 months
- No history of GI bleeding within 21 days
- No presence of arterial puncture within 7 days
- No history of intracranial bleed
- No history of surgery within the past 2 weeks
- No recent trauma or bleeding
- Not prescribed with oral anticoagulants
- Blood glucose levels of more than 50 mg/dL and platelet count of more than 100000.

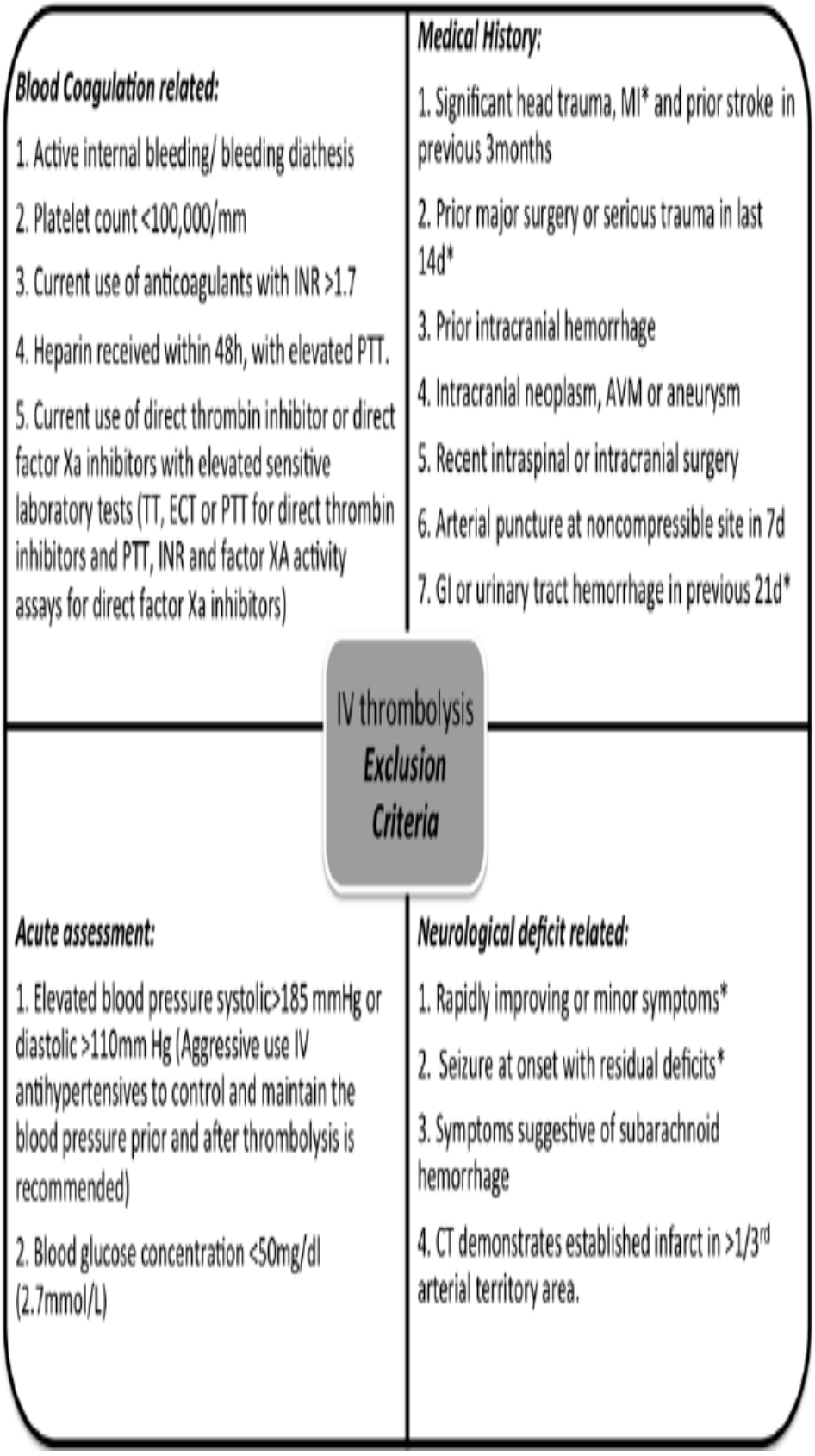


Figure 2 – Exclusion criteria for IV thrombolytics

Haemorrhage is a serious potential side effect following fibrinolytic therapy. Hemorrhagic infarction and parenchymal hematoma are the two subsets of hemorrhagic transformation. Parenchymal hematomas are less frequent than hemorrhagic infarctions. Predictive factors for the occurrence of this complication include increased infarction area, grey matter location, atrial fibrillation, cerebral embolism, acute hyperglycemia, low platelet count, and poor collateral circulation. [50]

Significant improvements in acute stroke care have been made in recent years. In patients with large vessel occlusion in the anterior circulation, endovascular thrombectomy in the first six hours is significantly superior to standard medical care, according to several trials published in 2015. These advantages continue regardless of patient characteristics and location. [51]

Another significant paradigm shift in stroke care took place in 2018. In patients with large vessel occlusion in the arteries of the proximal anterior circulation, the DAWN and DEFUSE 3 trials demonstrated the significant advantages of endovascular thrombectomy. This trial used perfusion imaging to increase the stroke window in a subset of patients from 16 to 24 hours. As a result, we can treat the patient in 16-24 hours. [52] [53]

Management of cerebral oedema

Cerebral oedema reaches a peak stage at 72-96 hours post-stroke, diagnosed mainly with a non-contrast CT. In addition, alteration in mental state, loss of consciousness, and pupil size can be clinical findings for cerebral oedema.

The management of oedema mainly includes the use of mannitol; however, the use of corticosteroids can be reflected in good outcomes, including side effects. Patients usually present with hypothermia, hyperventilation, and hyperosmolar therapy can be used in such patients. [1] [2] [13]

Management of seizures

2-25% of the patients are generally seen with seizures in the first few days after ischemic stroke. The treatment generally involves the use of antiepileptic medications. [1] [2] [13]

Medical care and support therapy

Patients with acute ischemic stroke with hypertension require specific thrombolytic therapy depending on their targeted blood pressure. The main goal is to limit the risk of bleeding and reduce elevated blood pressure.

The ideal goal is to maintain the blood pressure below 185 mm/ 110 mm Hg before initiating fibrinolytic therapy. In several stroke patients, extreme hypertension (> 220/120 mm Hg) can be managed after a 15% reduction in systolic blood pressure. [12] [13]

Because acute cerebral ischemia causes the release of interleukin-6 into the blood and cerebrospinal fluid, which is a key mediator of the acute phase reaction and induces the synthesis of acute phase proteins during ischemia, it is assumed that acute phase response proteins, such as ferritin, fibrinogen, or others, play a significant role in the pathogenesis of ischemic stroke. The primary substance in the body used to store iron is ferritin. As needed, it offers an elemental reserve that can synthesize molecules like haemoglobin, cytochromes, and iron-sulfur compounds. [54]

A reliable indicator of the number of cellular iron stores, plasma ferritin, may be connected to iron availability in the infarcted area. Most of the non-heme iron in brain tissue is in ferritin, which is concentrated in astrocytes and microglia. It is an acute-phase response protein, and inflammation causes an increase in its concentration. Blood viscosity and blood flow are significantly influenced by fibrinogen, which is a crucial part of the coagulation cascade. It is a biomarker of inflammation and a high molecular weight plasma adhesion protein. The complications in peripheral blood circulation during a stroke are worsened by changes in blood rheological properties brought on by elevated fibrinogen levels. [55]

Fibrinogen binds to its integrin receptor on the surface of leucocytes, facilitating chemotactic response, increasing phagocytosis, antibody-mediated leucocyte toxicity, and delaying apoptosis. These actions regulate NF-kappa B activation

and expression of inflammatory chemokines in endothelial cells. Fibrinogen is a protein up-regulated in the acute phase by cytokines like interleukin-6 and glucocorticoids. [56]

Levels of serum ferritin

The normal range of ferritin is 15-300 ng/mL, which is mainly lower in children than adults. The level decreases with blood donation and increases with alcohol intake.

Literature has suggested that iron overload results in the development of vascular disease by promoting thrombosis after an arterial injury. Studies have found that high serum ferritin levels at admission were the poor prognosis of acute stroke in patients, especially within 24-48 h of onset. The data signifies that a higher iron level in stroke patients can aggravate the cytotoxicity of brain ischemia. Hence, it has been quoted that serum ferritin levels influence the prognosis of ischemic stroke and can act as a risk factor for ischemic episodes due to atherogenesis. [57] [58]

SERUM CRP AS A PROGNOSTIC FACTOR FOR ACUTE ISCHEMIC STROKE

C-reactive protein is the trace protein found in blood circulation with a concentration of 1mg/L. The concentration of CRP increases significantly during a response to injury, infection, or inflammation. The use of CRP has been seen

majorly in monitoring the response to antibiotics in patients with bacterial infections and intrauterine infections, differentiating factors between active disease and infections, measuring the activity of the disease and disease-modifying drugs in rheumatoid arthritis, and detecting the presence of complications in postoperative patients. [2]

CRP & RISK OF VASCULAR DISEASE

Elevated levels of serum CRP are prevalent in three-quarters of patients with ischemic stroke. These high levels are often associated with atherosclerosis in carotid, coronary, or lower limb arteries. The amount of cerebral infarction brought on by an incident stroke and the presence of secondary stroke complications like infection, underlying malignancy, or deep vein thrombosis at the time of sampling are correlated with CRP concentration. These all can raise CRP and other inflammatory mediators. High CRP may be an inflammatory marker for underlying processes that lead to more severe strokes. [59] [60]

Multiple studies have shown that a single, non-fasting CRP measurement in individuals who appear to be in good health can predict future fatal and non-fatal cerebrovascular events. Numerous studies consistently show a connection between a patient's CRP baseline concentration and future cerebrovascular risk. This has generally been shown to be unrelated to the major risk factors of age, smoking, high blood pressure, and diabetes. Numerous studies revealed that the

effectiveness of secondary prevention treatments like statins and aspirin depends on the patient's baseline CRP. [61]

Numerous studies show that independent of age, stroke severity, and other traditional prognostic factors, CRP concentrations in stroke patients predict outcomes or new vascular events. Large infarcts have been linked to higher CRP levels. Additionally, understanding the level of inflammation aids in choosing an aggressive or conservative management strategy. For the in-hospital prognostic stratification, the data are less reliable. Following a spontaneous intracerebral haemorrhage, plasma CRP production increases noticeably over 48 to 72 hours which also plays an important role in the outcome of the disease. [62]

Plasma CRP concentrations in patients with acute stroke are elevated early and stay elevated above control values for a few months after the index stroke. Following a stroke, the CRP concentration is persistently elevated. It is unknown whether the inflammatory response to a stroke or underlying atherosclerosis causes the degree of elevation. Concentrations after discharge closely mirror initial inflammatory activity. A case can be made for assessment of CRP concentration at admission, discharge, 1 to 3 months, and again at further intervals. This is because the highest risk of future events is present in patients with persistently elevated CRP. [61] [62]

RDW ROLE AS A PROGNOSTIC MARKER IN ACUTE ISCHEMIC STROKE

Since the last few decades, limited evidence has been suggested supporting RDW and arterial cardiovascular diseases.

A connection between RDW and carotid atherosclerosis has been noted in patients with hypertension. In the cross-sectional study, 156 hypertensive patients between 60 and 85 underwent carotid ultrasonography with carotid atherosclerotic plaque detection and IMT measurements. Subjects with higher RDW values had significantly higher rates of IMT and carotid plaque prevalence. In a cross-sectional study of 193 non-anaemic patients undergoing coronary

angiography for stable angina pectoris, 188 RDW was associated with both the presence and complexity of CAD, as measured by the SYNTAX score. [62] [63]

In a post hoc analysis of 4111 patients who had previously experienced a MI, Tonelli et al. discussed the connection between RDW and MI. They discovered a graded, independent relationship between RDW and the risk of recurrent non-fatal and fatal MI throughout a median follow-up of 59.7 months. [64] The risk of a negative cardiac outcome was inversely correlated with RDW quartiles when Lee et al. examined the 12-month risk of a major cardiac event in patients with a prior MI. [65]

There is only a small amount of current research on the connection between RDW and arterial CVD. Studies on the subject have been published in a surprisingly small number. Additionally, the published data is constrained by the study design, particular study populations, and reverse causation. Three cross-sectional studies on RDW and atherosclerosis were conducted, with two of them focusing on patients with stable angina or high blood pressure. There are few participants in the RDW and stroke studies, and those who participate have heart failure or an MI. Reverse causation is a problem because participants in most studies on RDW and MI also have a history of MI. Only the prospective cohort study by Chen et al. found no association. [66]

AIM AND OBJECTIVES

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Aim

To study the severity of acute ischaemic stroke in correlation with the serum ferritin, CRP and RDW concentration.

Objective

In this study, we tried to correlate the serum ferritin, CRP, and RDW with the severity of acute ischemic stroke.

MATERIALS AND METHODOLOGY

METHODOLOGY

STUDY DESIGN:

Hospital-based observational cross-sectional analytical study

STUDY POPULATION:

All patients who presented within 48 hrs of the onset of stroke and gave informed consent to participate in the study were included and admitted to Government Kilpauk medical college and hospital – tertiary centre.

STUDY PERIOD

Six months from the date of approval of the ethical committee.

INCLUSION CRITERIA

- Rapidly developing clinical signs of focal or global (coma) neurological deficit lasting more than 24 hrs or leading to death with no apparent cause other than Vascular origin.
- All patients who presented within 48 hrs of the onset of stroke and gave informed consent to participate in the study were included.

EXCLUSION CRITERIA

- Patients with hemorrhagic stroke
- Ferritin, CRP, and RDW is an Acute phase reactant, and samples are taken within 48 hrs of onset.

SAMPLE SIZE:

The sample size is determined based on a similar study authored by Adv J Emerg Med, the prognostic significance of serum ferritin in acute stroke.

Sample Size calculated based on the formula

$N=(Z\alpha)\ ^2 * PQ * /d2$

p=Prevalence

q=1-p

d was taken as 6.9

$Z\alpha=1.96$

$N= (1.96)\ ^2 * 34.5*65.5/ 6.8^2$

$= 3.84*2259.75/47.61$

$=183$

The minimum sample size required for the study= 183.

METHODS

HISTORY TAKING

- Detailed history has been taken from patients
- Sex (male and female)

- Old medical records (history of diabetes/hypertension/coronary artery disease/dyslipidemia)
- Drug intake history (anti-hypertensives, anti-diabetes, drugs for ischemic heart disease, drugs for hypercholesterolemia)
- Smoking and alcohol history

CLINICAL EXAMINATION:

- Level of consciousness
- Orientation to time, place and person GCS SCALE
- CNS EXAMINATION

LABORATORY ASSESSMENT:

- Serum ferritin
- Serum CRP Level
- RDW

STATISTICAL ANALYSIS:

All data were analysed using IBM SPSS ver.20 software.

Data were expressed as percentages if and otherwise explained. Analysis to be performed using Two-way ANOVA and Independent Sample Student t-test.

RESULTS

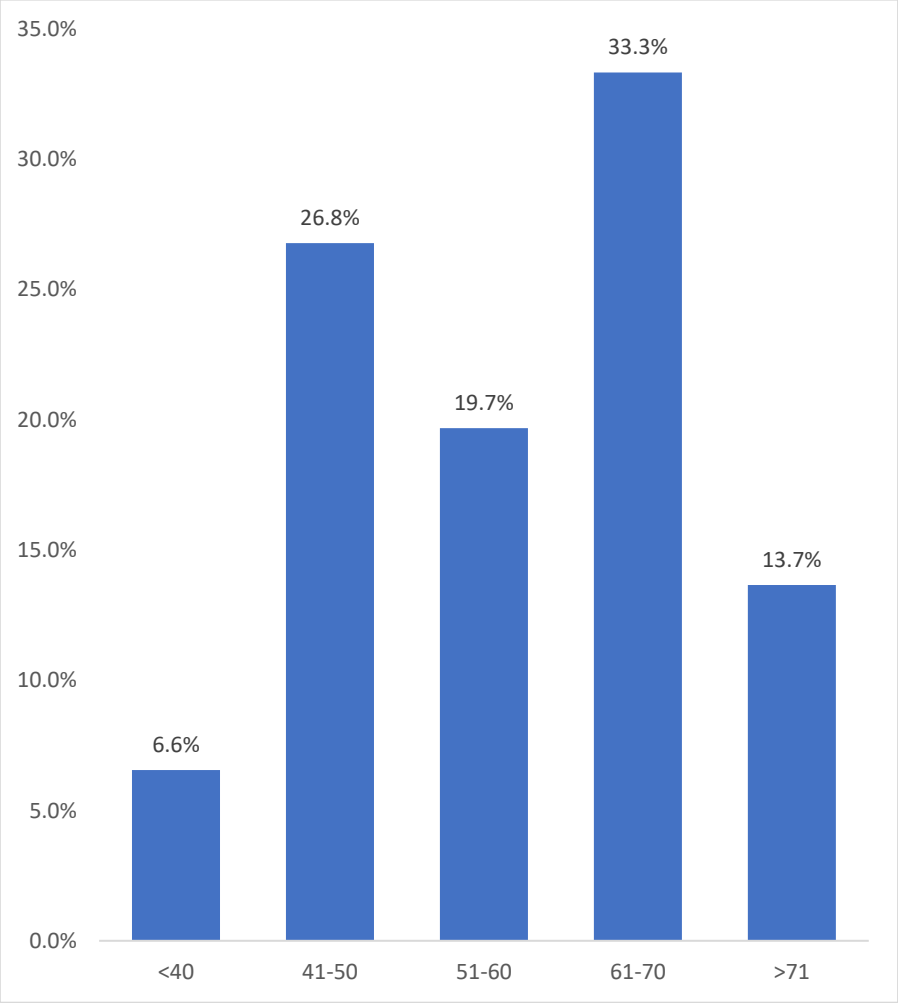
1. Age distribution

A majority of the participants were in the age group of 61-70 (33.3%), followed by the age group 41-50 (26.8%) and the age group of 51-60 (19.7%). On the other hand, the incidence was low in the age group of >71 years (13.7%) and the age group of <40 years (6.6%).

Table 1 -Age distribution among participants

Age group	Frequency	Percent
<40	12	6.6%
41-50	49	26.8%
51-60	36	19.7%
61-70	61	33.3%
>71	25	13.7%
Total	183	100.0%

Figure 1 - % Age distribution



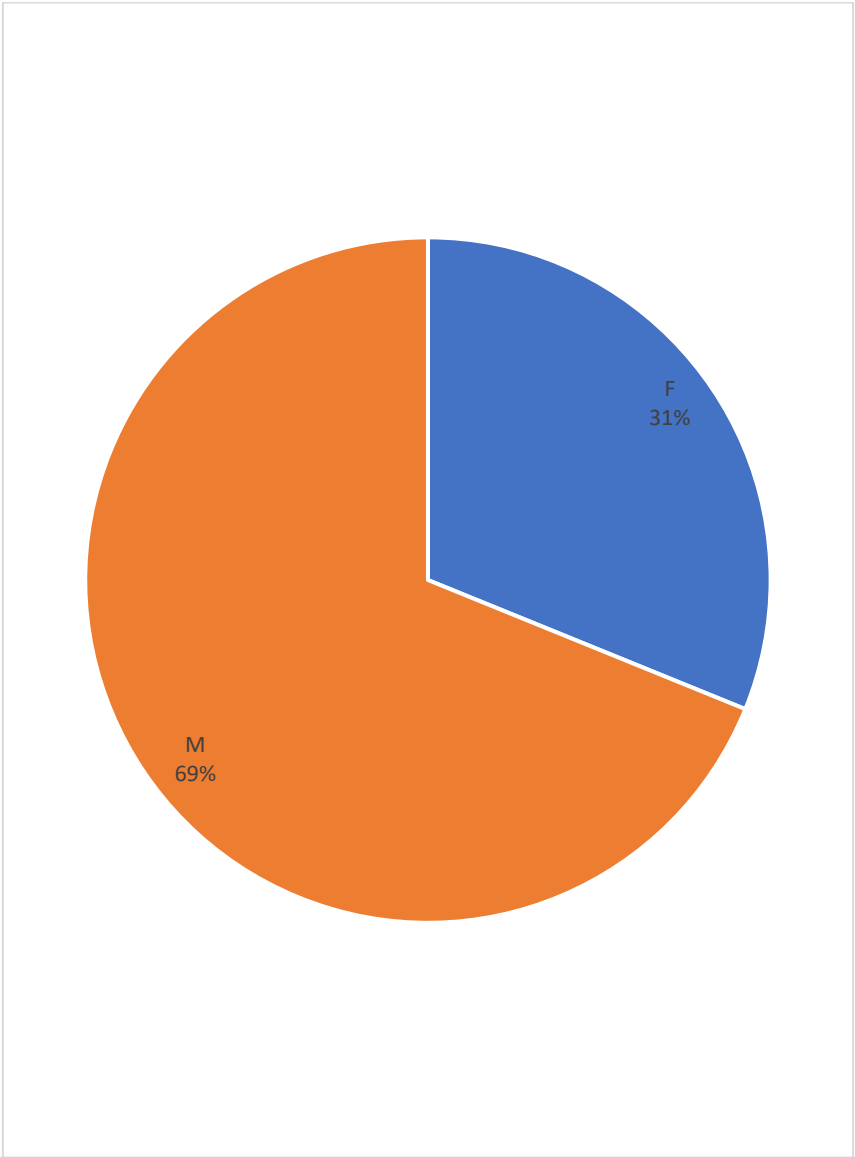
2. Gender distribution

A male predominance was reported in the current study, with 126 patients out of 183 comprising 68.9% of the overall participants.

Table 2 – Gender distribution in patients

Sex	Frequency	Percent
F	57	31.1%
M	126	68.9%
Total	183	100.0%

Figure 2 - % Gender distribution



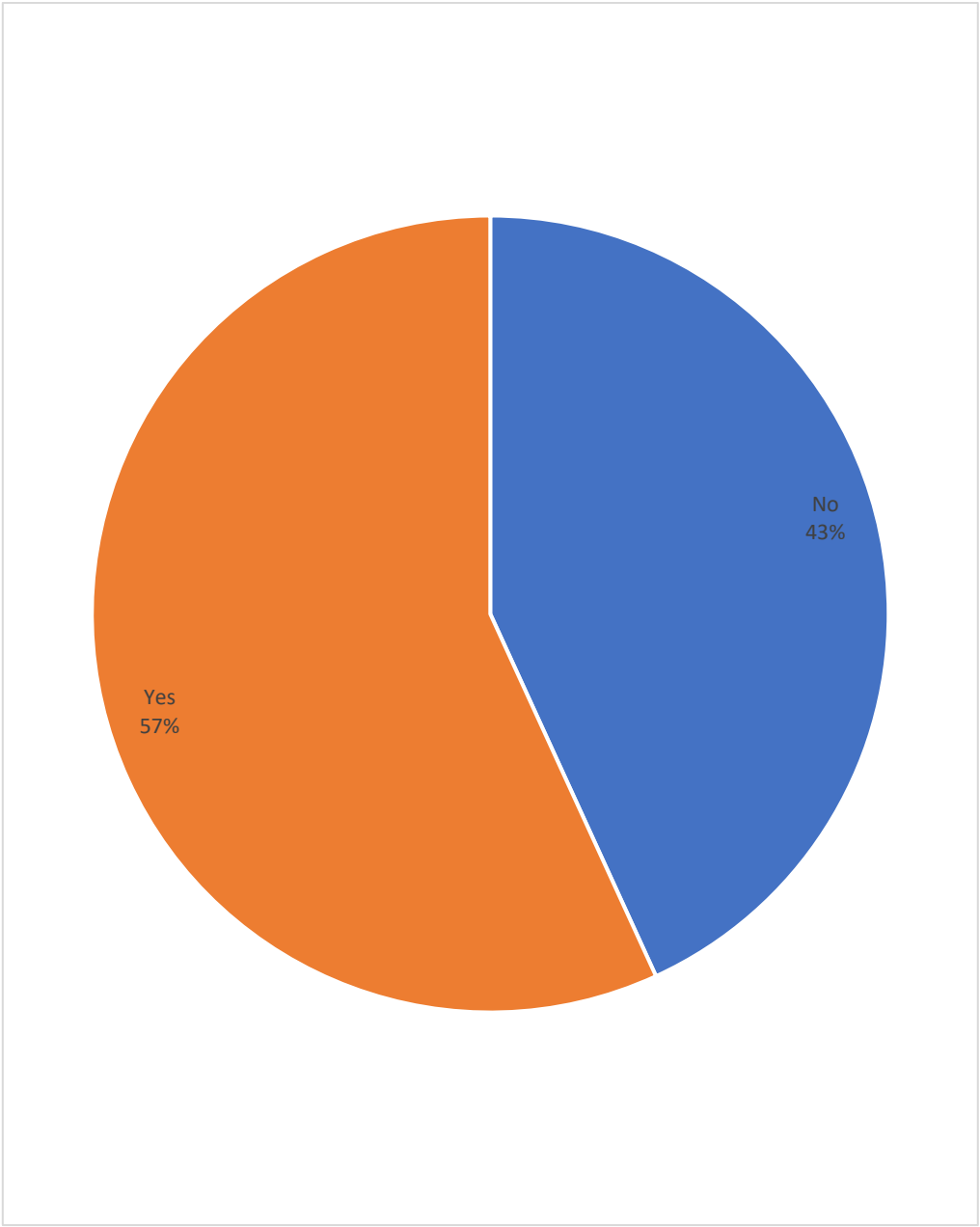
3. Incidence of hypertension

Of 183 patients, 104 participants (56.8%) presented with hypertension, and 79 patients (43.2%) were not.

Table 3 – Incidence of hypertension

HTN	Frequency	Percent
No	79	43.2%
Yes	104	56.8%
Total	183	100.0%

Figure 3 - % distribution of hypertension



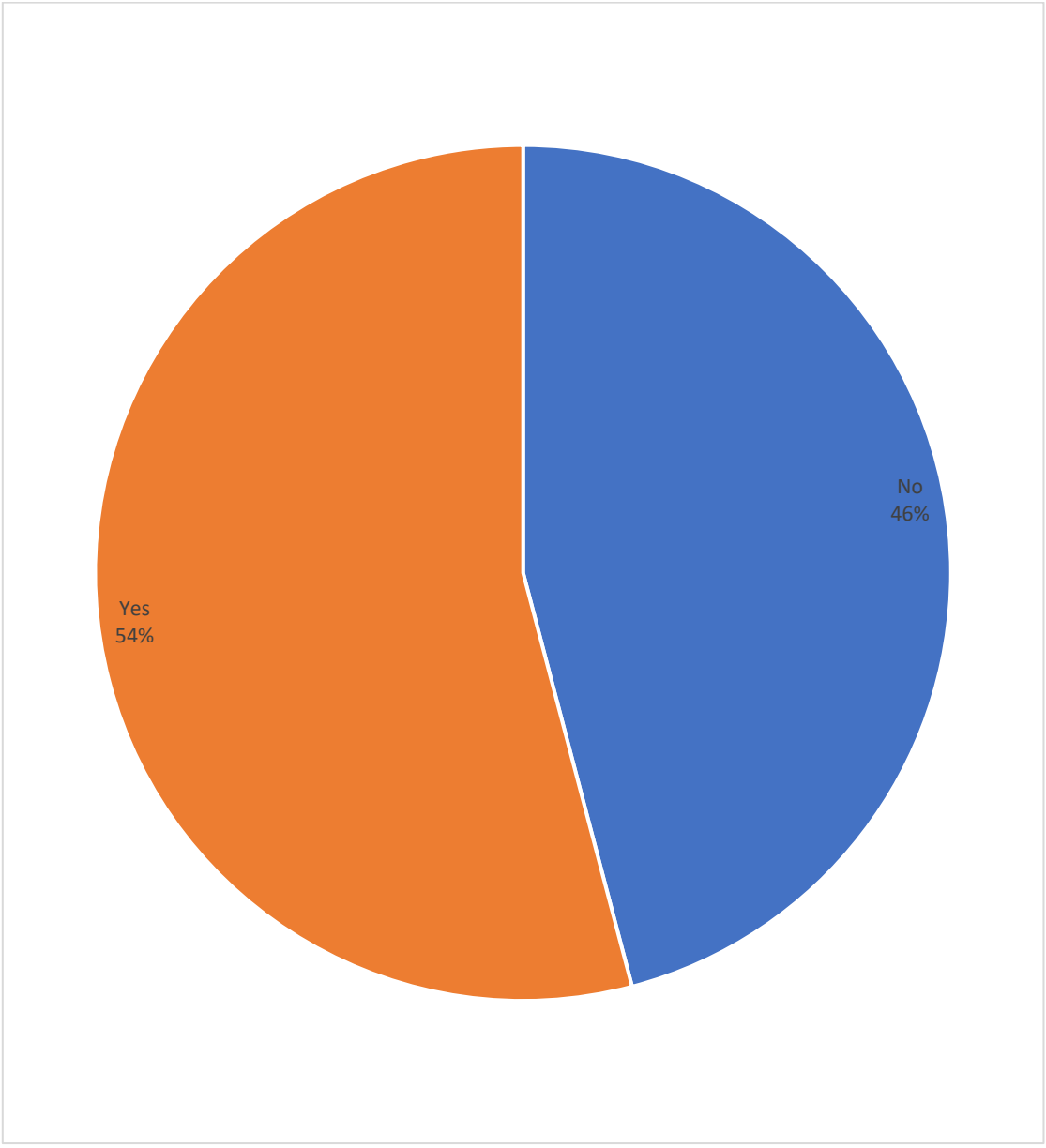
4. Incidence of Diabetes mellitus

A total of 99 patients (54.1%) were reported to have diabetes mellitus, and 84 patients did not have diabetes.

Table 4 – Incidence of Diabetes mellitus

DM	Frequency	Percent
No	84	45.9%
Yes	99	54.1%
Total	183	100.0%

Figure 4 - % Distribution of diabetes in patients



5. Social History

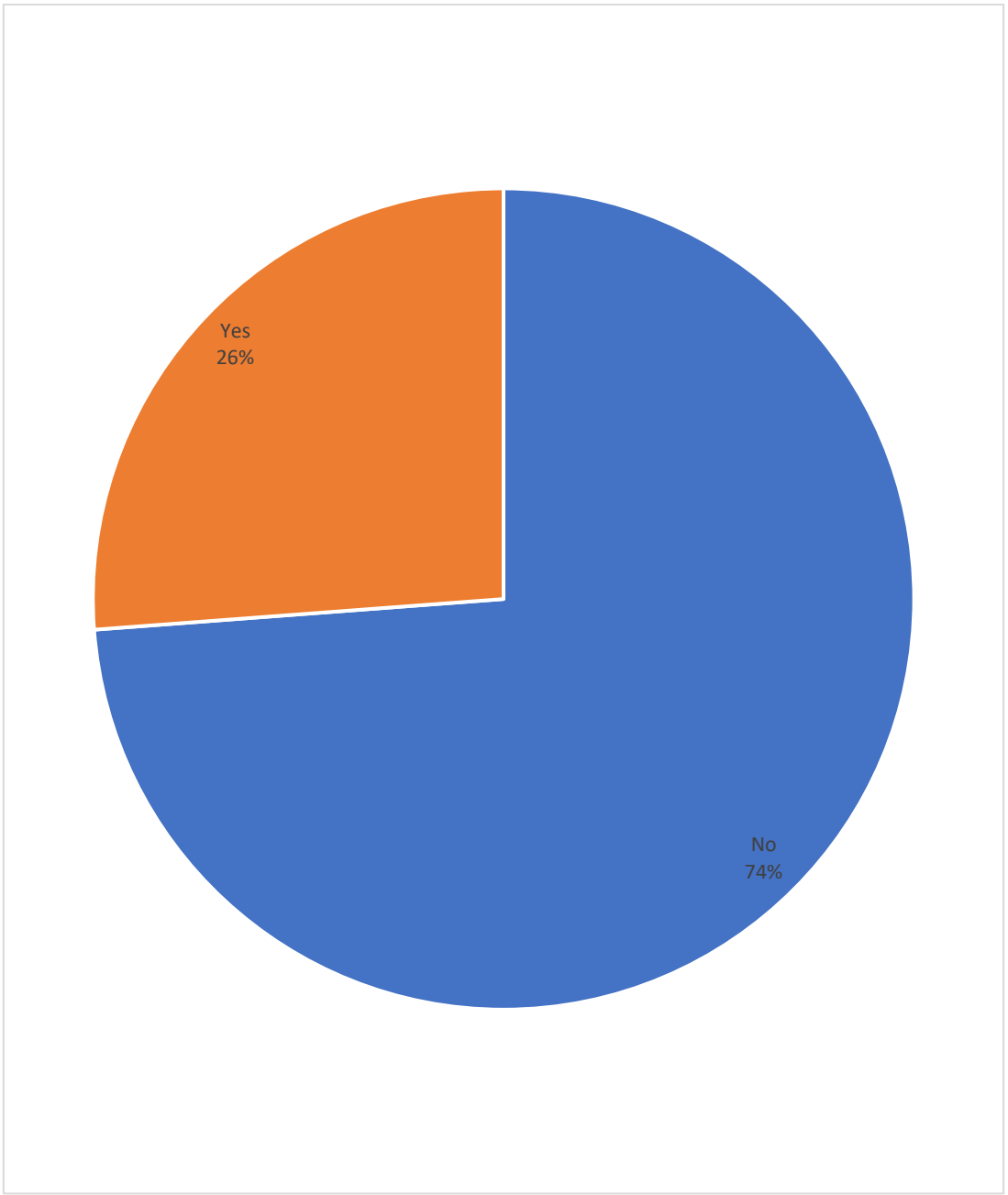
a. Smoking

Smoking was reported in 33 patients (26.2%) of the overall participants.

Table 5 – Smoking habit in patients

SMOKING	Frequency	Percent
No	93	73.8%
Yes	33	26.2%
Total	126	100.0%

Figure 5 - % distribution of smoking in patients



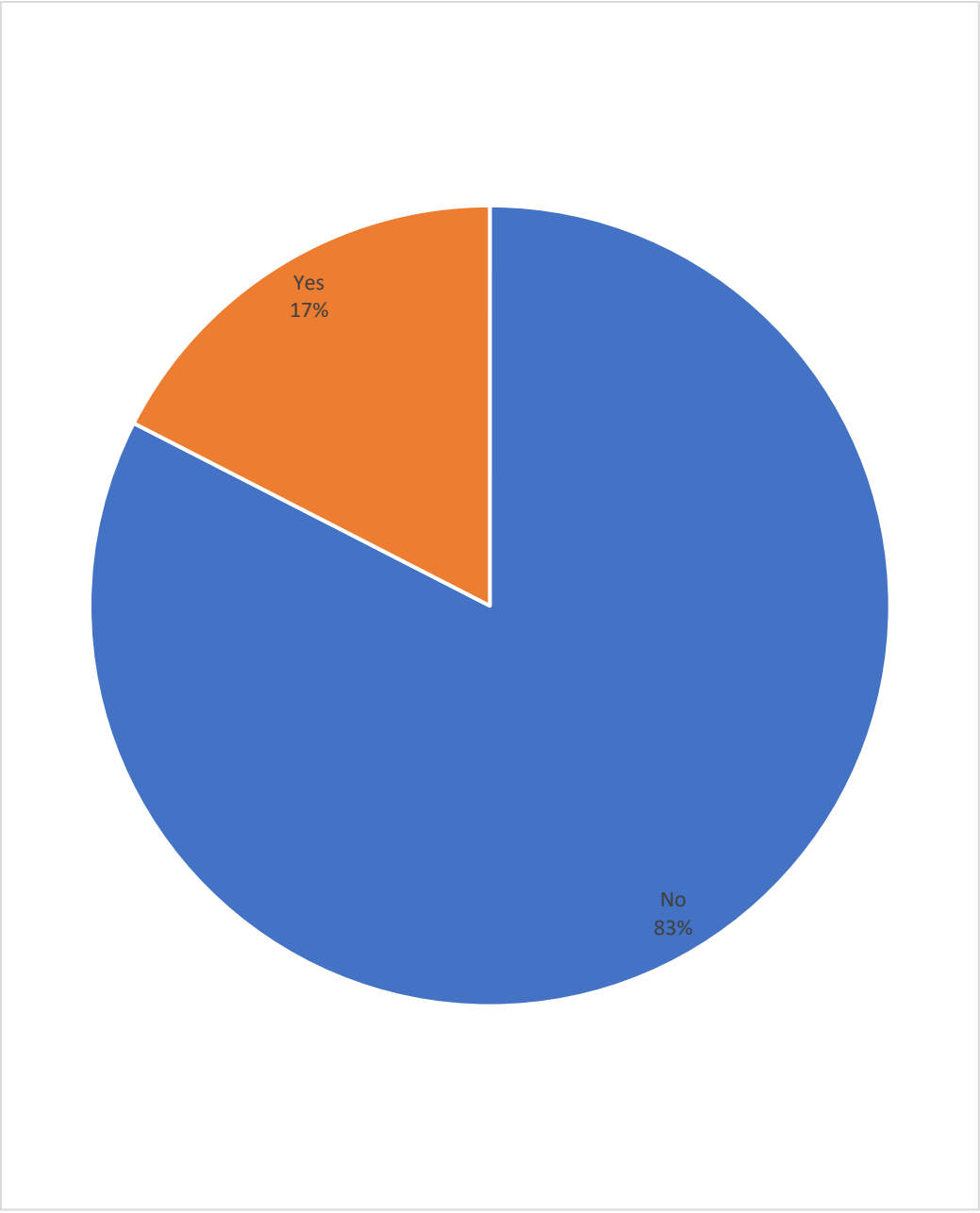
b. Alcohol intake in patients

A total of 22 patients were reported with a history of alcohol intake, comprising 17.5% of the overall participants.

Table 6 – Alcohol intake in patients

ALCOHOL	Frequency	Percent
No	104	82.5%
Yes	22	17.5%
Total	126	100.0%

Figure 6 – Alcohol intake % incidence



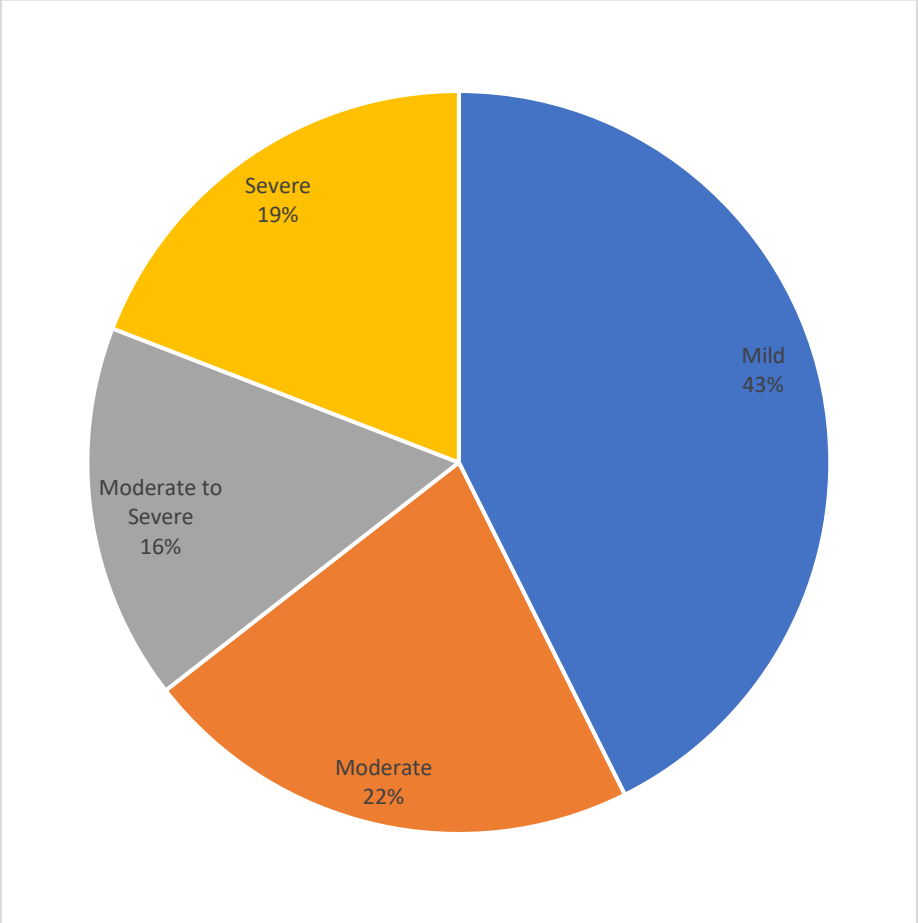
6. NIHSS stroke severity score

The study finds a high incidence of mild stroke score in 78 participants accounting for 42.6%, followed by moderate severity in 40 patients (21.9%) and moderate to severity score in patients (16.4%). A total of 35 patients (19.1%) were presented with NIHSS severity stroke scores.

Table 7 -NIHSS severity score

NIHSS	Frequency	Percent
Mild	78	42.6%
Moderate	40	21.9%
Moderate to Severe	30	16.4%
Severe	35	19.1%
Total	183	100.0%

Figure 7 - % incidence of NIHSS severity score



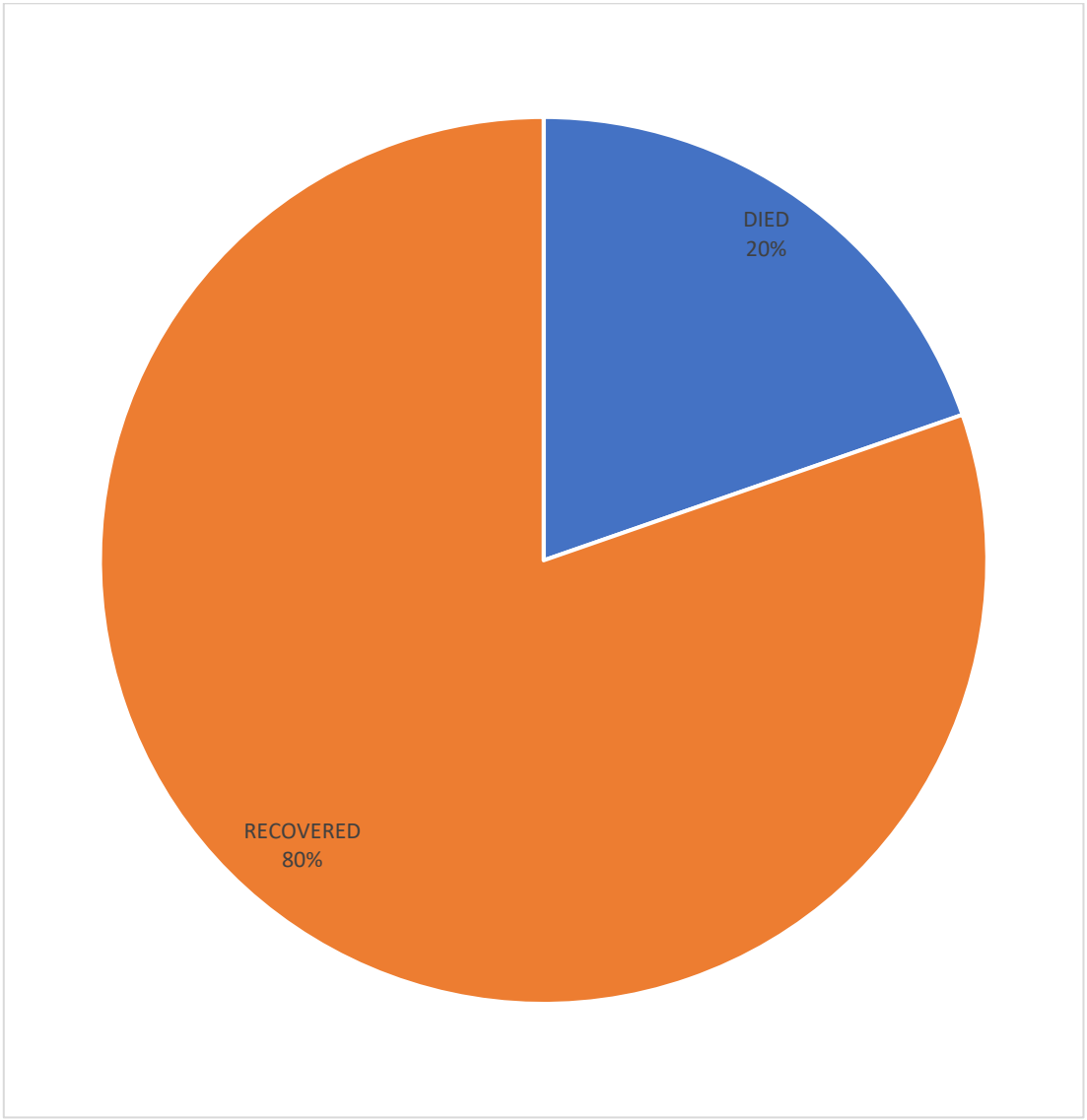
7. Clinical outcome of the study

From a total of 183 participants, 36 patients were lost due to severity accounting for 19.7% loss due to mortality. However, 147 patients (80.3%) recovered in the current study.

Table 8 – Outcome of the patients

OUTCOME	Frequency	Percent
DIED	36	19.7%
RECOVERED	147	80.3%
Total	183	100.0%

Figure 8 - % distribution of outcome



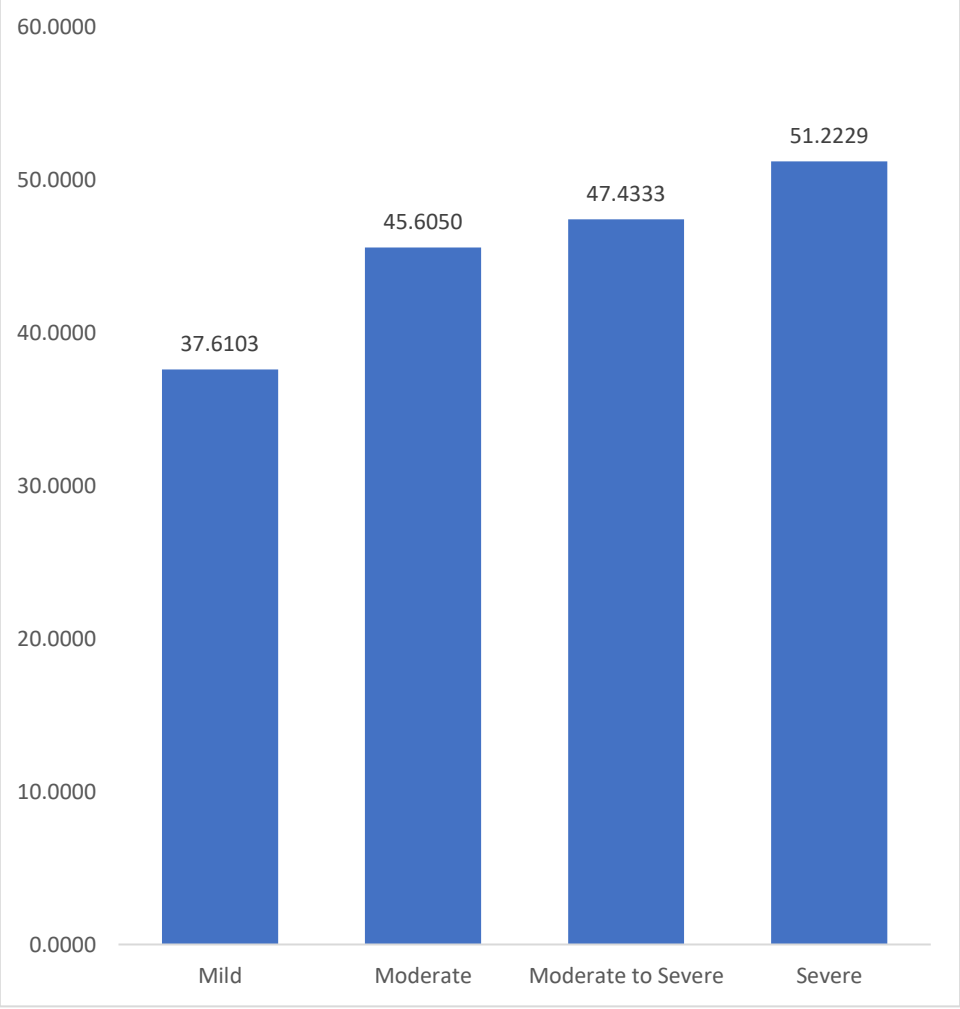
8. RDW coefficient comparison in participants

The study reports a statistical difference (p-value <0.0001) in the RDW findings in participants. The difference was observed in comparison with the severity of the NIHSS score.

Table 9 – RDW comparison in patients

		Mean	Std. Deviation	P value
RDW	Mild	37.6103	8.11779	<0.0001
	Moderate	45.6050	5.83987	
	Moderate to Severe	47.4333	3.63814	
	Severe	51.2229	6.35587	
	Total	43.5716	8.64288	

Figure 9 – RDW comparison in patients



9. RDW dependent variable comparison with severity

In the overall comparison of severity, the study observed a significant difference in the dependent variable of severity. A significant difference was reported in the RDW comparison with the NIHSS score (p-value <0.0001); the mild elevation of RDW was also seen with a statistical difference in the NIHSS scoring system of moderate, mild to severe, and severe. In moderate alteration of RDW, a significant difference was observed in the mild scoring system with a p-value <0.0001. In addition, the moderate elevation reported a significant difference in the mild scoring group (p-value <0.0001), and a similar finding was reported in the severe mortality group concerning to mild scoring system (p-value <0.0001).

Table 10 – Dependent variable comparison of RDW with NIHSS score

Dependent Variable			Mean Difference	P value
RDW	Mild	Moderate	-7.99474*	<0.0001
		Moderate to Severe	-9.82308*	<0.0001
		Severe	-13.61260*	<0.0001
	Moderate	Mild	7.99474*	<0.0001
		Moderate to Severe	-1.82833	1.000
		Severe	-5.61786*	0.003
	Moderate to Severe	Mild	9.82308*	<0.0001
		Moderate	1.82833	1.000
		Severe	-3.78952	0.152
	Severe	Mild	13.61260*	<0.0001
		Moderate	5.61786*	0.003
		Moderate to Severe	3.78952	0.152

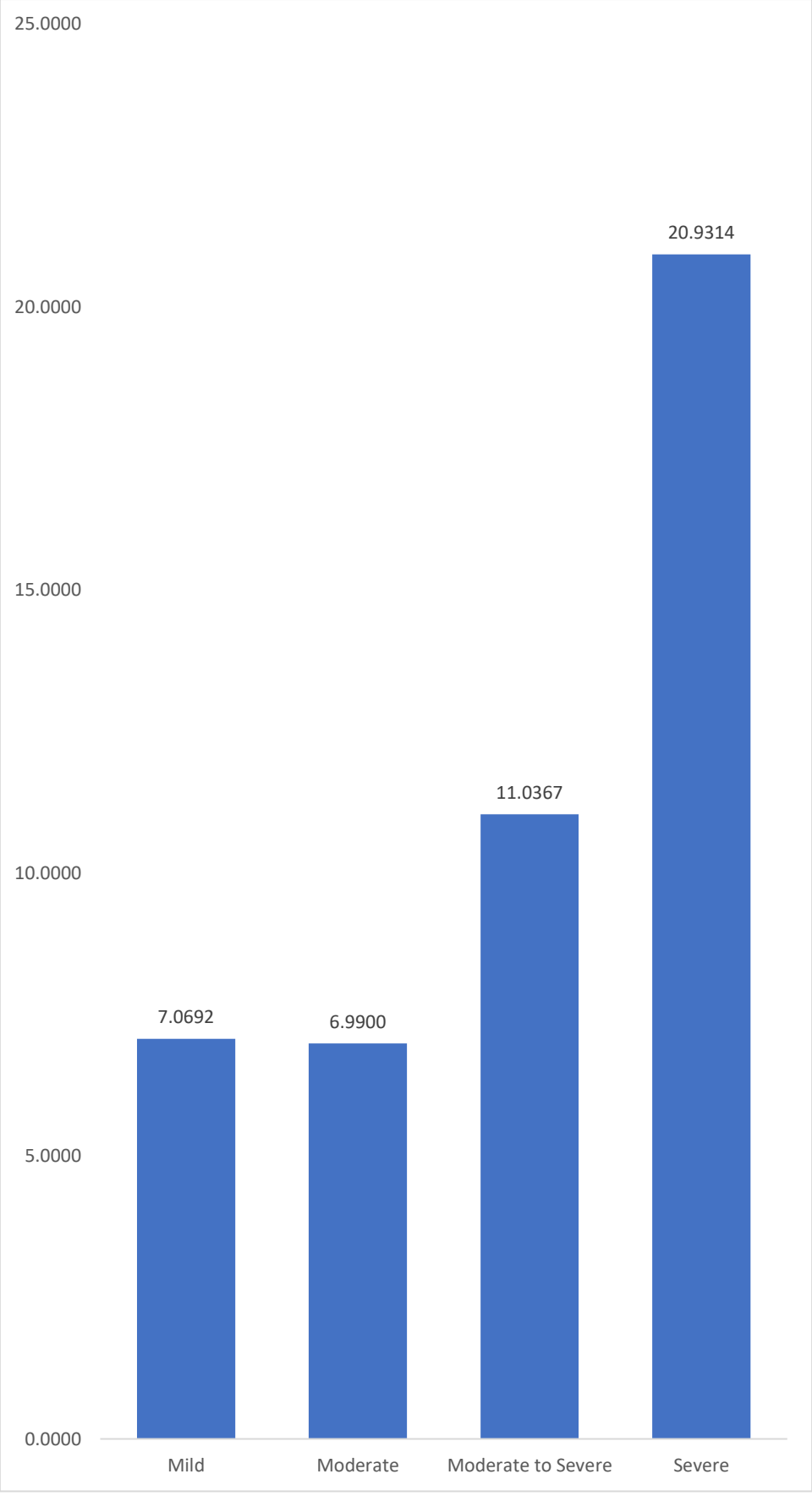
10.Serum CRP levels in patients

The study reports a significant difference between the mild (mean 7.069 [SD = 2.547]), moderate (mean 6.990 [SD = 2.827]), moderate to severe (mean 11.036 [SD = 6.754]), and severe (mean 20.931 [SD = 5.909]) scoring system with a p-value <0.0001. This interprets that depending on the severity of the stroke, CRP levels are altered.

Table 11 – CRP levels in patients

		Mean	Std. Deviation	P value
CRP	Mild	7.0692	2.54703	<0.0001
	Moderate	6.9900	2.82714	
	Moderate to Severe	11.0367	6.75469	
	Severe	20.9314	5.90985	
	Total	10.3536	6.85245	

Figure 10 – CRP level comparison with severity



11.Serum CRP comparison with severity NIHSS

The study reports a significant difference between mild, moderate, severe, and severe groups. In addition, for each dependent variable of serum CRP, the mild CRP group reported a significant difference in the NIHSS score of moderate to severe and severe with a p-value <0.0001. Further to this, a statistical difference was also reported in the moderate to severe group of serum CRP when correlated with the NIHSS mild score (p-value <0.0001) and NIHSS severe score (p-value <0.0001). The severe levels of the serum CRP group, when correlated with the NIHSS score, and the mild, moderate, and severe scores, reported a significant difference (p-value <0.0001), respectively.

Table 12 – Mean difference of Serum CRP

Dependent Variable			Mean Difference	P value
CRP	Mild	Moderate	0.07923	1.000
		Moderate to Severe	-3.96744*	<0.0001
		Severe	-13.86220*	<0.0001
	Moderate	Mild	-0.07923	1.000
		Moderate to Severe	-4.04667*	0.001
		Severe	-13.94143*	<0.0001
	Moderate to Severe	Mild	3.96744*	<0.0001
		Moderate	4.04667*	0.001
		Severe	-9.89476*	<0.0001
	Severe	Mild	13.86220*	<0.0001
		Moderate	13.94143*	<0.0001
		Moderate to Severe	9.89476*	<0.0001

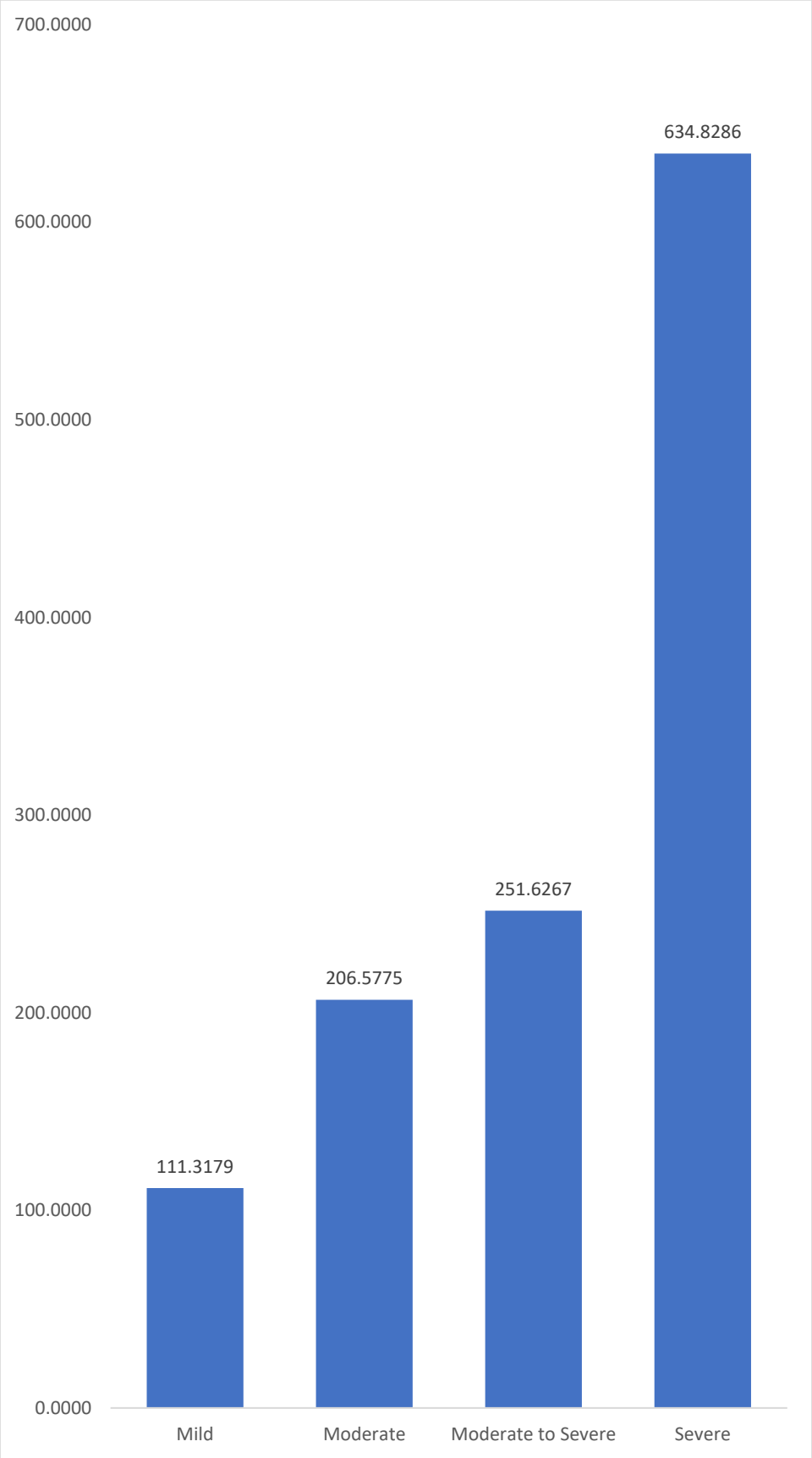
12.Serum ferritin levels

The current study reports a significant difference in levels of serum ferritin level in all 4 categories (p-value <0.0001). In addition, the study finds mild serum ferritin levels (mean - 111.31 [SD = 63.594], followed by moderate (mean – 206.57 [SD = 121.064], moderate to severe (mean 251.626 [SD = 108.560], and severe (mean 634.828 [SD = 316.509].

Table 13 – Ferritin levels in patients

		Mean	Std. Deviation	P value
FERRITIN	Mild	111.3179	63.59459	<0.0001
	Moderate	206.5775	121.06454	
	Moderate to Severe	251.6267	108.56013	
	Severe	634.8286	316.50917	
	Total	255.2661	250.10632	

Figure 11 – Ferritin levels in patients



12.Serum Ferritin levels correlation with NIHSS severity score

The correlation of NIHSS score with serum ferritin level revealed a significant difference between the mild levels with moderate to severe NIHSS score (p-value <0.0001), followed by moderate levels of serum ferritin and severe NIHSS score (p-value <0.0001), and the severe comparison with the mild, moderate, and moderate to severe score (p-value <.0001) respectively.

Table 14 – Ferritin levels dependent variable comparison

Dependent Variable			Mean Difference	P value
FERRITIN	Mild	Moderate	-95.25955*	0.016
		Moderate to Severe	-140.30872*	<0.0001
		Severe	-523.51062*	<0.0001
	Moderate	Mild	95.25955*	0.016
		Moderate to Severe	-45.04917	1.000
		Severe	-428.25107*	<0.0001
	Moderate to Severe	Mild	140.30872*	<0.0001
		Moderate	45.04917	1.000
		Severe	-383.20190*	<0.0001
	Severe	Mild	523.51062*	<0.0001
		Moderate	428.25107*	<0.0001
		Moderate to Severe	383.20190*	<0.0001

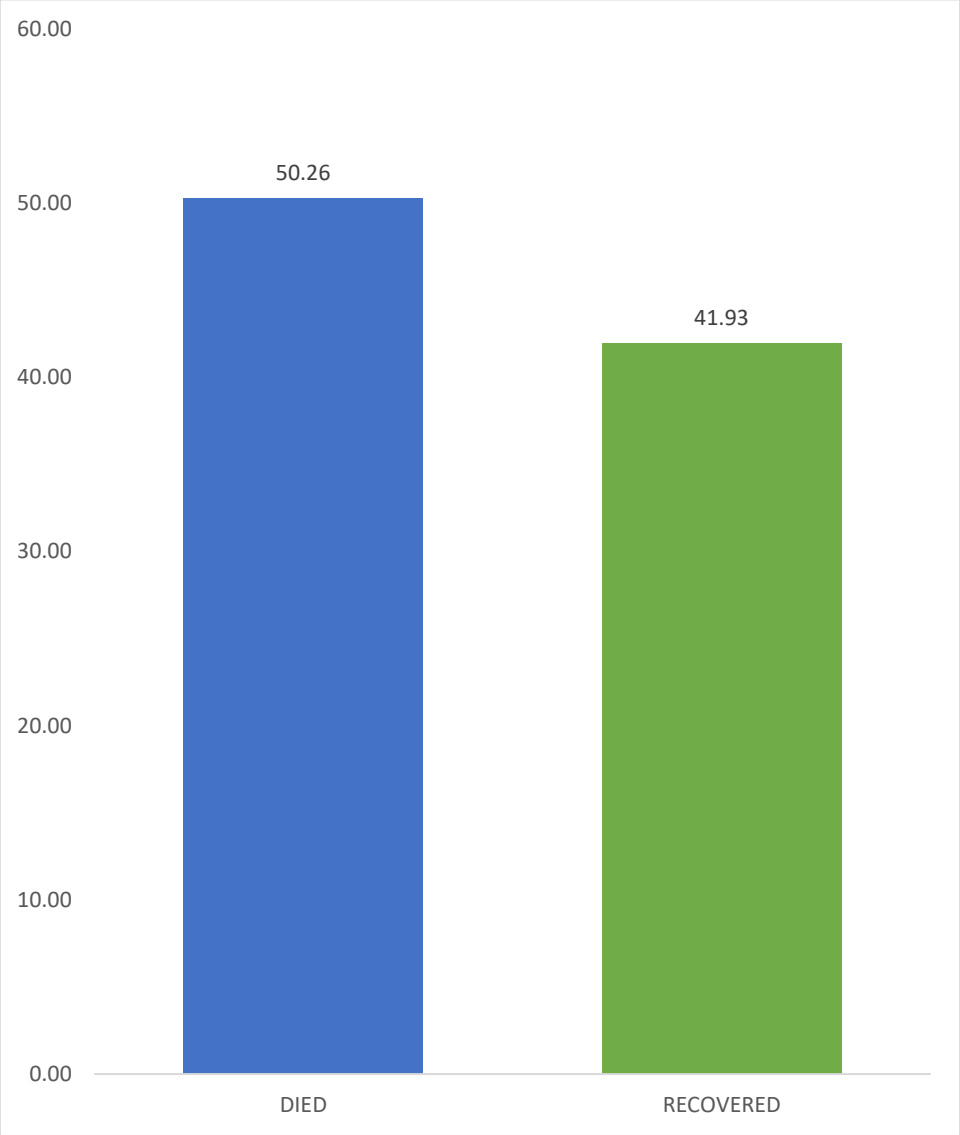
13.Study outcome of RDW, Serum CRP, and Serum Ferritin Levels

The current study depicts a significant correlation between RDW levels and mortality among patients [Table 15]. Furthermore, the table demonstrates a loss of life due to mortality with a mean of 50.25 (SD = 6.23) and a significant p-value <0.0001.

Table 15 – Mortality and RDW

		RDW		P value
		Mean	Standard Deviation	
OUTCOME	DIED	50.26	6.23	<0.0001
	RECOVERED	41.93	8.37	

Figure 12 – Correlation of RDW with the outcome

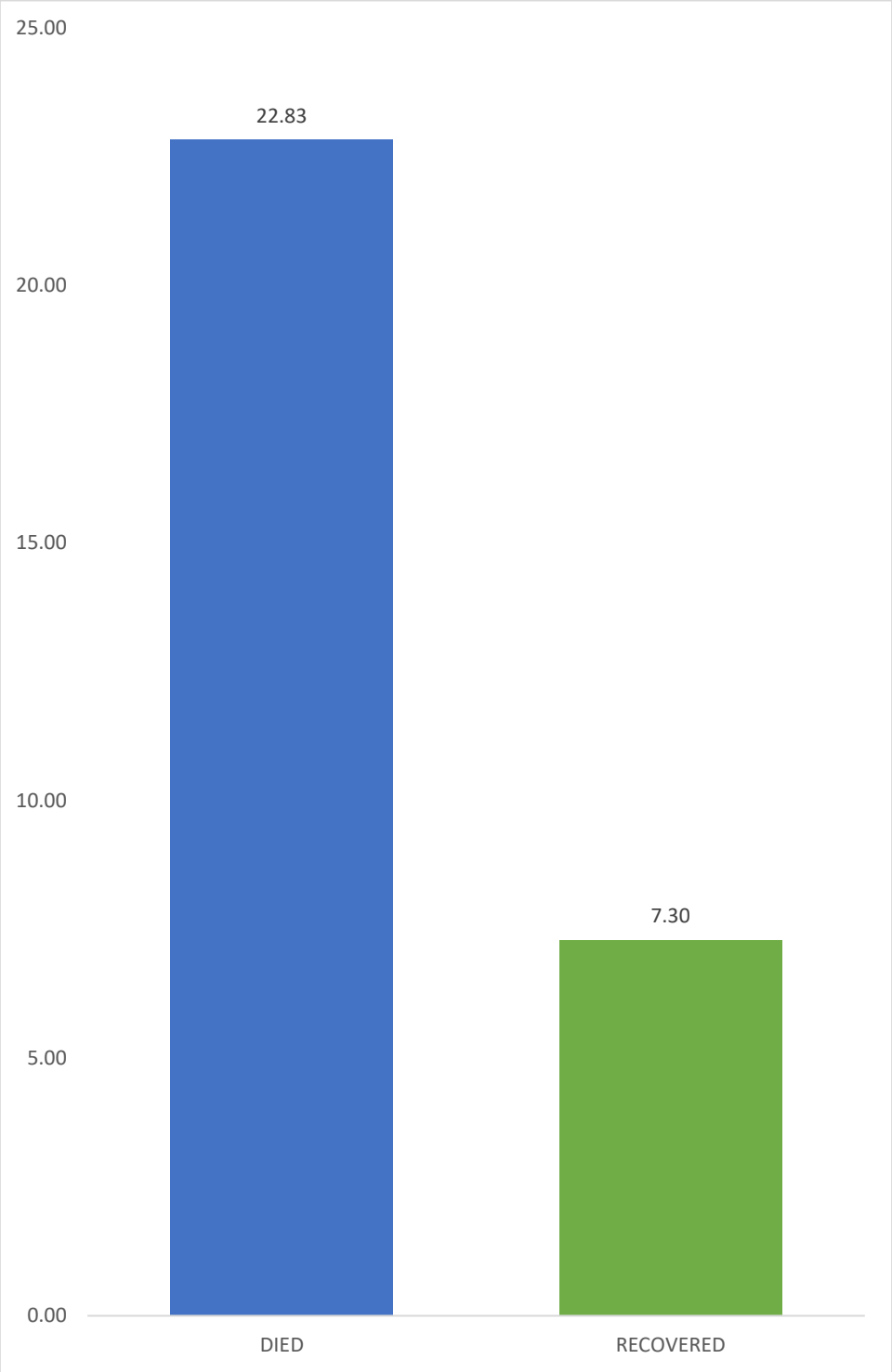


The CRP levels and outcome correlation also reported a statistical difference (p-value <0.0001 with a mean mortality of 22.83 (SD – 3.60) and a mean recovery of 7.30 (SD = 2.77) [Table 16].

Table 16 – Study outcome correlation with serum CRP

		CRP		P value
		Mean	Standard Deviation	
OUTCOME	DIED	22.83	3.60	<0.0001
	RECOVERED	7.30	2.77	

Figure 13 – Comparison of serum CRP levels with mortality

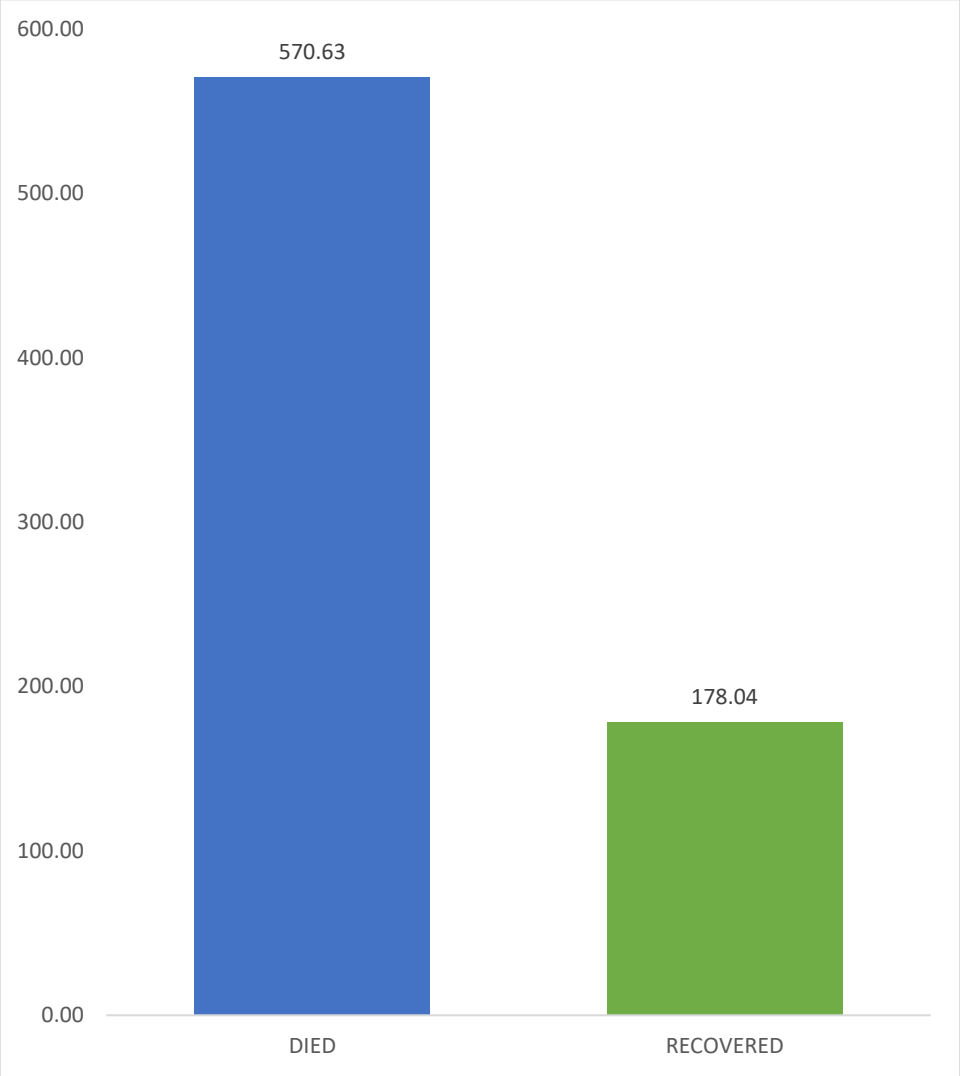


The mortality comparison of serum ferritin levels with the outcome of the study revealed a statistical difference p-value <0.0001, which reported a mean mortality of 570.63 (SD = 321.45) and a mean recovery of 178.04 (SD = 150.59) [Table 17].

Table 17 – Outcome comparison with serum ferritin level

		FERRITIN		P value
		Mean	Standard Deviation	
OUTCOME	DIED	570.63	321.45	<0.0001
	RECOVERED	178.04	150.59	

Figure 14 – Comparison of outcome with serum ferritin levels



DISCUSSION

DISCUSSION

A stroke is a focal vascular injury of the nervous system that is non-traumatic and can cause permanent nerve damage by cerebral infarction or intracerebral haemorrhage. The physiology of stroke includes the cessation of blood flow due to extracranial or intracranial thrombosis formation, embolism, and hypoperfusion.

Literature has suggested that an iron overload in patients can contribute to the progression of vascular disease mainly due to thrombosis formation after an arterial injury. The current study demonstrates the correlation of laboratories' test applicability as a prognostic marker in patients with acute ischemic stroke.

The present study included 183 participants who presented with acute ischemic stroke and were evaluated with several markers. A high prevalence of acute ischemic stroke was reported in patients aged 61-70 (33.33%), followed by the age group of 41-50 (26.8%). In addition, a male predominance was reported in the current study, with a high incidence of hypertension (56.8%), diabetes mellitus (54.1%), the social habit of smoking (26.2%), and alcohol intake (17.5%).

The NIHSS stroke severity assessment revealed that a majority of the patients were in the mild scoring criteria (42.6%), followed by moderate (21.9%),

moderate to severe (16.4%), and severe criteria (19.1%). The clinical outcome of the study reports a loss of life due to mortality among 36 participants, with acute ischemic stroke accounting for 19.7% of the total participants.

The RDW elevated levels, compared with the NIHSS score, revealed a significant difference (p-value <0.0001). This finding was similar to the study by Kara et al. and Ntaios et al. [67] [68]. A significant difference was also reported in the study conducted by Gianni et al., who reported that RDW (14% versus 13.6%; p-value <0.001) and NIHSS score (12 versus 4; p-value <0.001) was increased in patients with acute ischemic stroke during the admission, and resulted in an unfavourable outcome. [69] RDW has always been associated with a vital prognostic marker in elderly patients, and a high RDW can increase overall mortality. A similar finding was reported in our study, with high levels of RDW and a prevalence of elderly patients with acute ischemic stroke (Table 1). [70] In addition, Mohindra et al. also revealed significant findings in the mean age of 60 + 11.9 years presented with hypertension. [10] Our study also reported that patients with a high RDW level had an increased mortality risk compared with the NIHSS score (p-value < 0.0001) in a mild mod. In addition, the mortality rates were also found to be significant in the current comparison of RDW with NIHSS score and clinical outcome (p-value <0.001), which was similar to the finding of Mohindra et al., who reported high RDW levels (15.12 vs 14.23, p = 0.48) in patients with loss of life. [10] Another

study by Ani et al. also depicted that baseline RDW levels were higher in patients with stroke who died later when compared with the patients who recovered. [71]

In line with the current finding, the study also reported a significant difference in an elevated level of serum CRP in patients with the NIHSS score and clinical outcomes of the patients. The study reported a statistical difference in the NIHSS to score severity levels and serum CRP concentration in patients with acute ischemic stroke with criteria including; mild score, moderate to severe, and severe scoring system with a p-value <0.0001, respectively. Studies have reported that increased CRP is associated with patients' short-term or long-term prognosis. The study conducted by Luo et al. revealed a high incidence of elevated CRP levels in patients with AIS when compared with the control group. [72] Similar observations were reported by Chun Song Youn et al. in the retrospective analysis conducted among 96 patients. The study revealed that patients with high CRP levels were associated with stroke mortality in AIS. In addition, higher CRP levels were also associated with larger infarct volumes in patients with acute ischemic stroke. [73] The findings revealed that patients with elevated CRP levels are more prone to developing complications in acute ischemic stroke, and the levels of CRP can be used to reflect the severity of AIS among patients. The comparison of mortality (loss of life) and recovery also reported a statistical difference concerning elevated serum CRP levels and mortality (p-value <0.0001) [Table 16].

The study also reported a significant difference in the serum ferritin levels and mortality of patients with AIS. During admission, elevated ferritin levels were reported based on the severity of the NIHSS score, which was in an upward trend with increasing severity (p-value <0.0001), which signifies that with increased severity of a stroke, high levels of serum ferritin can be reported. Literature has suggested that elevated serum ferritin levels can be a prognostic marker in ischemic stroke and act as a risk factor for ischemic episodes by causing atherogenesis. [57] [58]

The study conducted by Aravind et al. in 50 patients also reported a high level of serum ferritin levels, 245.50 ± 121.36 and 259.58 ± 112.25 ng/mL, respectively, which was similar to our finding of serum ferritin levels of 255.26 (SD = 250.10). [6] The study also reported a statistical difference between serum ferritin levels and NIHSS scores. A similar study by Egovindarajulu et al. in 60 patients with AIS revealed high serum ferritin levels at admission. Of these patients, 22 had a severe stroke (based on NIHSS), and 13 had a moderate stroke. In addition, patients with low ferritin levels did not report any stroke, and the study reported a positive correlation between the serum ferritin levels and NIHSS score (p-value = 0.000). [74] Similarly, Koul et al. also reported a statistical correlation between the serum ferritin levels and NIHSS score (p-value <0.001) for assessing stroke severity. [75]

The study findings revealed a significant correlation between the RDW, serum CRP, and serum ferritin as the prognostic marker for assessing stroke severity and mortality in acute ischemic patients. Using such prognostic markers in adjuvant of the NIHSS scale can predict the mortality and severity of stroke.

SUMMARY

SUMMARY

A majority of the participants were in the age group of 61-70 (33.3%), followed by the age group 41-50 (26.8%) and the age group of 51-60 (19.7%).

A male predominance was reported in the current study, with 126 patients out of 183 comprising 68.9% of the overall participants.

The study finds a high incidence of mild stroke score in 78 participants accounting for 42.6%, followed by moderate severity in 40 patients (21.9%) and moderate to severity score in patients (16.4%).

The study reports a statistical difference (p-value <0.0001) in the RDW findings in participants. The difference was observed in comparison with the severity of the NIHSS score.

The study reports a significant difference between the mild (mean 7.069 [SD = 2.547]), moderate (mean 6.990 [SD = 2.827]), moderate to severe (mean 11.036 [SD = 6.754]), and severe (mean 20.931 [SD = 5.909]) scoring system with a p-

value <0.0001. This interprets that depending on the severity of the stroke, CRP levels are altered.

The severe levels of the serum CRP group, when correlated with the NIHSS score and the mild, moderate, and severe scores, reported a significant difference (p-value <0.0001).

The current study reports a significant difference in levels of serum ferritin level in all 4 categories (p-value <0.0001).

The current study depicts a significant correlation between RDW levels and patient mortality.

The CRP levels and outcome correlation also reported a statistical difference (p-value <0.0001 with a mean mortality of 22.83 (SD – 3.60) and a mean recovery of 7.30 (SD = 2.77).

The mortality comparison of serum ferritin levels with the study's outcome revealed a statistical difference p-value <0.0001.

CONCLUSION

CONCLUSION

The study concludes with a linear relationship between the RDW, serum CRP, and serum ferritin levels in predicting the severity of stroke and mortality outcomes in patients with acute ischemic stroke. Our study observed a high incidence of stroke in the patient's age group 61-70 years of age (33.3%) with a male predominance (68.9%). In addition, comorbid conditions such as hypertension (56.8%) and diabetes (54.1%) were seen in patients with AIS, including a low prevalence of smoking (26.2%) and alcohol consumption (17.5%) was reported. Based on the NIHSS severity finding, mild (42.6%) was the most prevalent, followed by moderate severity (21.9%) and severe stroke (19.1%) were seen. However, 36 patients (19.7%) died during the study, and 147 (80.3%) had a positive recovery.

The elevated levels of RDW reported a statistical difference based on the severity of stroke (p-value <0.0001), and the dependent variable comparison with NIHSS

also revealed a statistical difference in mild, moderate to severe, moderate to severe, and severe scores (p-value <0.0001) respectively. This portrays that patients with AIS can be assessed using the RDW levels to assess stroke severity.

An increased level of serum CRP has been observed in acute ischemic stroke patients with a statistical difference across various severity scales when compared with the NIHSS scale (p-value <0.0001). Elevated serum levels directly correlate with stroke severity with a p-value <0.0001. This signifies that higher serum CRP levels are associated with higher stroke severity.

Serum ferritin levels were increased based on the stroke severity from mild serum ferritin levels (mean - 111.31 [SD = 63.594], followed by moderate (mean – 206.57 [SD = 121.064], moderate to severe (mean 251.626 [SD = 108.560], and severe (mean 634.828 [SD = 316.509] with a statistical difference in severity scales (p-value <0.0001). In addition, the comparison of the NIHSS scale with serum ferritin levels also revealed a significant correlation which was increased based on the clinical condition (p-value <0.0001).

The study also reports a significant difference in clinical outcome and mortality (loss of life) when compared with all three markers (p-value <0.0001) respectively, which conclude that RDW, serum CRP levels, and serum ferritin levels can be used as a prognostic marker for assessing the severity of the stroke and formulating a therapeutic plan based on the severity.

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<u>சுய ஒப்புதல் படிவம்</u>

ஆய்வு செய்யப்படும் தலைப்பு: சீரம் ஃபெரிடின், சிஆர்பி, ஆர்டிடபிள்யூ கடுமையான இஸ்கிமிக் பக்கவாதத்துடன் தொடர்புடையது

இடம் : அரசு கீழ்பாக்கம் மருத்துவகல்லூரி மற்றும் மருத்துவமனை, சென்னை

பங்குபெறுபவரின் பெயர்:

பங்குபெறுபவரின் வயது:

பங்குபெறுபவரின் எண்:

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த சட்டச் சிக்கலுக்கும் உட்பட்டால் நாண் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெரும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவை இல்லை என அறிந்து கொள்கிறேன். இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ முடிவையோ பயன்படுத்திக்கொள்ள மறுக்க மாட்டேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உன்மையுடன் இருப்பேன் என்று உறுதி அளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம்:

ஆய்வாளரின் கையொப்பம்:

இடம்:

தேதி:

STUDY PROFORMA (attached)

NAME :

Age:

Sex:

I.P.No: Date of admission : Serial No. :

Diabetes :

Hypertension :

Smoking :

Alcohol :

Blood RDW :

Blood CRP :

Time of Blood sample

after stroke onset :

C.T. Scan Brain :

Serum Ferritin : GCS:

NIHSS SCORE :

S.No	Age		Sex	HTN	DM	SMOKING	ALCOHOL	RDW	CRP	FE
50	38	1	F	No	No			41.3	7.7	
66	38	1	M	Yes	Yes	No	No	57.3	9.4	
130	38	1	F	No	No			41.3	8.5	
180	38	1	F	No	No			41.3	3.9	
33	39	1	M	Yes	No	No	No	50.2	6.4	
57	39	1	M	Yes	No	No	No	50.2	3.2	
83	39	1	M	Yes	No	No	No	50.2	2.1	
133	39	1	M	Yes	No	No	Yes	50.2	9.9	
183	39	1	M	Yes	No	No	No	50.2	10.4	
102	40	1	M	Yes	No	No	No	52.9	12.2	
140	40	1	M	Yes	No	Yes	No	52.9	4.8	
152	40	1	M	Yes	No	Yes	No	52.9	16.2	
17	41	2	M	No	No	Yes	Yes	38.9	7.3	
34	41	2	M	No	No	No	No	38.9	4.5	
67	41	2	M	No	No	No	Yes	38.9	6.0	
104	41	2	M	No	No	No	No	38.9	3.0	
117	41	2	M	No	No	No	No	38.9	8.4	
167	41	2	M	No	No	No	No	38.9	6.1	
1	42	2	M	Yes	No	No	Yes	42.3	8.1	
51	42	2	M	Yes	No	Yes	No	42.3	8.4	
80	42	2	M	Yes	No	No	No	42.3	4.7	
101	42	2	M	Yes	No	No	Yes	42.3	4.0	
151	42	2	M	Yes	No	No	No	42.3	9.8	
7	43	2	M	No	Yes	No	No	37.8	6.2	
18	43	2	M	No	Yes	No	No	37.8	11.0	
78	43	2	M	No	Yes	No	No	37.8	9.6	
107	43	2	M	No	Yes	No	No	37.8	8.5	
157	43	2	M	No	Yes	No	No	37.8	5.7	
122	45	2	M	Yes	Yes	Yes	No	49	12	
132	45	2	M	Yes	Yes	No	No	49	11	
182	45	2	M	Yes	Yes	No	No	49	7	
48	47	2	M	Yes	Yes	No	No	46.3	7.8	
56	47	2	F	Yes	No			41.1	2.5	
75	47	2	M	Yes	Yes	No	No	46.3	6.5	
98	47	2	M	Yes	Yes	No	No	46.3	6.8	
136	47	2	F	Yes	No			41.1	6.8	
148	47	2	M	Yes	Yes	No	No	46.3	6.8	
5	48	2	F	No	No			39.4	5.7	
55	48	2	F	No	No			39.4	7.5	
79	48	2	M	Yes	No	Yes	Yes	51.3	9.1	
84	48	2	F	No	No			39.4	9.6	
103	48	2	M	No	Yes	Yes	No	48.4	10.5	
105	48	2	F	No	No			39.4	5.2	
118	48	2	M	No	Yes	Yes	No	48.4	5.5	
155	48	2	F	No	No			39.4	4.7	
168	48	2	M	No	Yes	No	No	48.4	8.0	

6	49	2	M	Yes	No	No	No	46.2	5.5	
19	49	2	M	Yes	No	No	No	46.2	0.4	
32	49	2	M	Yes	No	No	No	46.2	7.7	
119	49	2	M	Yes	No	Yes	No	46.2	5.7	
169	49	2	M	Yes	No	No	No	46.2	5.4	
20	50	2	F	No	Yes			43.1	6.7	
21	50	2	M	No	Yes	Yes	Yes	35.3	8.3	
36	50	2	F	No	Yes			43.1	9.4	
38	50	2	M	No	Yes	No	No	35.3	5.0	
70	50	2	F	No	Yes			43.1	3.1	
71	50	2	M	No	Yes	Yes	No	35.3	8.6	
120	50	2	F	No	Yes			43.1	6.2	
121	50	2	M	No	Yes	Yes	No	35.3	6.1	
170	50	2	F	No	Yes			43.1	9.4	
171	50	2	M	No	Yes	No	No	35.3	7.2	
106	52	3	M	Yes	No	No	No	49.3	8.2	
156	52	3	M	Yes	No	Yes	Yes	49.3	12.1	
8	55	3	F	Yes	No			37.3	5.3	
46	55	3	F	No	No			57.6	12.2	
58	55	3	F	Yes	No			37.3	6.2	
81	55	3	M	Yes	No	Yes	No	57.3	10.6	
86	55	3	F	Yes	No			37.3	5.9	
108	55	3	F	Yes	No			37.3	11.5	
131	55	3	M	Yes	No	No	No	40.7	8.9	
150	55	3	M	Yes	No	Yes	No	40.7	8.0	
158	55	3	F	Yes	No			37.3	6.8	
16	58	3	M	Yes	Yes	No	No	57.3	18.4	
37	58	3	M	Yes	Yes	No	No	52	6	
125	58	3	M	Yes	Yes	No	Yes	52	8	
175	58	3	M	Yes	Yes	Yes	No	52	12	
24	59	3	M	No	Yes	No	Yes	35.3	12.5	
45	59	3	M	No	Yes	No	No	35.3	4.9	
74	59	3	M	No	Yes	No	No	35.3	8.3	
87	59	3	F	Yes	Yes			47.1	21.5	
124	59	3	M	No	Yes	Yes	Yes	35.3	5.3	
129	59	3	F	Yes	Yes			47.1	9.1	
137	59	3	F	Yes	Yes			47.1	10.9	
174	59	3	M	No	Yes	Yes	No	35.3	8.1	
9	60	3	M	Yes	Yes	No	No	42.8	10.0	
23	60	3	M	Yes	Yes	No	No	42.8	7.3	
27	60	3	F	No	Yes			35.7	4.9	
49	60	3	M	No	No	No	No	48.7	24.9	
54	60	3	F	No	Yes			35.7	14.5	
77	60	3	F	No	Yes			35.7	6.8	
97	60	3	M	Yes	No	No	No	52.9	24.1	
109	60	3	M	Yes	Yes	Yes	No	42.8	11.0	
127	60	3	F	No	Yes			35.7	8.1	
149	60	3	M	No	No	No	No	48.7	27.3	

159	60	3	M	Yes	Yes	Yes	Yes	42.8	3.2	
160	60	3	M	Yes	No	No	No	53.7	19.1	
177	60	3	F	No	Yes			35.7	8.6	
15	61	4	F	No	Yes			37.3	9.5	
30	61	4	F	No	Yes			37.3	3.8	
44	61	4	M	Yes	No	Yes	No	38.7	21.6	
65	61	4	F	No	Yes			37.3	8.5	
68	61	4	M	No	No	Yes	Yes	40.1	6.3	
94	61	4	M	Yes	No	Yes	No	38.7	22.8	
95	61	4	F	No	Yes			37.3	5.7	
113	61	4	F	No	Yes			48	9	
115	61	4	F	No	Yes			37.3	6.3	
126	61	4	F	No	Yes			48	3	
138	61	4	M	No	No	No	No	40.1	5.3	
144	61	4	M	Yes	No	No	No	38.7	24.0	
165	61	4	F	No	Yes			37.3	13.1	
176	61	4	F	No	Yes			48	3	
10	62	4	M	Yes	No	No	No	53.7	25.5	
47	62	4	F	No	No			51.3	23.8	
52	62	4	M	No	Yes	No	No	43.4	1.1	
99	62	4	M	Yes	No	No	Yes	49.3	22.4	
134	62	4	M	No	Yes	Yes	No	43.4	12.0	
181	62	4	M	Yes	No	No	No	57.3	20.3	
11	63	4	M	Yes	No	Yes	No	57.3	6.0	
22	63	4	M	Yes	Yes	No	No	40.2	27.5	
26	63	4	M	Yes	No	No	No	57.3	4.4	
72	63	4	M	Yes	Yes	No	No	40.2	8.5	
111	63	4	M	Yes	No	No	No	57.3	8.7	
161	63	4	M	Yes	No	No	Yes	57.3	11.3	
172	63	4	M	Yes	Yes	Yes	No	40.2	25.2	
31	64	4	M	Yes	No	No	Yes	57.3	27.5	
41	64	4	M	Yes	No	No	No	37.3	13.5	
64	64	4	M	Yes	No	Yes	No	37.3	6.7	
73	64	4	M	No	Yes	No	No	40.8	9.6	
91	64	4	M	Yes	No	No	No	37.3	4.6	
116	64	4	M	No	Yes	No	No	43.1	4.1	
128	64	4	M	No	Yes	No	Yes	43.1	5.5	
141	64	4	M	Yes	No	No	No	37.3	3.0	
145	64	4	M	No	Yes	No	No	40.8	7.8	
178	64	4	M	No	Yes	No	No	43.1	3.7	
3	65	4	M	No	Yes	No	No	57.3	26.2	
53	65	4	M	No	Yes	No	No	57.3	12.7	
82	65	4	M	Yes	Yes	No	Yes	49	25	
146	65	4	F	No	No			57.6	20.2	
153	65	4	M	No	Yes	No	No	57.3	22.5	
39	66	4	M	Yes	No	No	No	36.3	7.7	
60	66	4	M	Yes	No	No	No	53.7	25.5	
61	66	4	M	Yes	No	No	No	36.3	8.0	

89	66	4	M	Yes	No	Yes	Yes	36.3	4.9	
139	66	4	M	Yes	No	Yes	No	36.3	5.7	
96	67	4	M	Yes	No	No	No	40.7	20.3	
29	68	4	M	Yes	No	No	No	51.3	23.1	
40	68	4	M	Yes	Yes	No	No	57.2	27.4	
90	68	4	M	Yes	Yes	Yes	Yes	57.2	10.5	
100	68	4	M	Yes	No	No	No	40.7	23.9	
166	68	4	M	Yes	Yes	No	No	57.3	19.8	
179	68	4	M	Yes	No	No	No	51.3	23.5	
13	70	4	M	No	Yes	Yes	No	49.3	19.2	
35	70	4	F	No	Yes			40.3	7.1	
59	70	4	F	No	Yes			40.3	9.2	
63	70	4	M	No	Yes	Yes	Yes	49.3	23.4	
85	70	4	F	No	Yes			40.3	5.0	
135	70	4	F	No	Yes			40.3	6.8	
163	70	4	M	No	Yes	No	No	49.3	22.0	
2	71	5	F	Yes	No			50	8	
14	71	5	F	Yes	No			50	4	
28	71	5	F	Yes	No			50	10	
43	71	5	F	Yes	Yes			40.7	4.7	
69	71	5	F	Yes	Yes			40.7	1.8	
93	71	5	F	Yes	Yes			40.7	10.6	
114	71	5	F	Yes	No			50	6	
143	71	5	F	Yes	Yes			40.7	4.5	
164	71	5	F	Yes	No			50	4	
4	72	5	M	Yes	Yes	No	No	47.7	9.0	
12	72	5	M	Yes	Yes	No	No	13.3	7.4	
25	72	5	M	Yes	Yes	No	No	13.3	8.3	
62	72	5	M	Yes	Yes	No	No	13.3	7.7	
76	72	5	M	Yes	Yes	No	No	47.7	7.7	
88	72	5	M	Yes	Yes	No	No	13.3	8.6	
110	72	5	M	No	Yes	No	No	48.3	7.2	
112	72	5	M	Yes	Yes	No	No	13.3	9.9	
123	72	5	M	No	Yes	No	No	48.3	5.7	
147	72	5	F	No	No			51.3	23.3	
154	72	5	M	Yes	Yes	Yes	Yes	47.7	5.8	
162	72	5	M	Yes	Yes	No	No	13.3	8.2	
173	72	5	M	No	Yes	No	No	48.3	8.3	
42	73	5	F	Yes	Yes			49.3	24.3	
92	73	5	F	Yes	Yes			49.3	27.8	
142	73	5	F	Yes	Yes			49.3	23.5	