"PROGNOSTIC ROLE OF NEUTROPHIL LYMPHOCYTE RATIO IN ACUTE ISCHEMIC STROKE– A ONE YEAR PROSPECTIVE COHORT STUDY"

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LIST OF ABBREVIATIONS USED

AIS	Acute ischemic stroke
NLR	Neutrophil-Lymphocyte ratio
CNS	Central Nervous System
PNS	Peripheral Nervous System
MAP	Mean arterial pressure
mmHg	millimetre(s) of mercury
CBF	cerebral blood flow
mL	Milliliter
BCF	brachiocephalic fistula
TIA	Transient Ischemic Attack
ICU	intensive care unit
CVA	Cerebrovascular accident
DWI	Diffusion-weighted imaging
MRI	magnetic resonance imaging
BNP	Brain natriuretic peptide
MMX	Multimarkerindex
ROS	reactive oxygen species
RNS	reactive nitrogen species
ATP	adenosine triphosphate
AMPA	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
NMDA	N-methyl-D-aspartate
AMP	Adenosine monophosphate
XO	xanthine oxidase

XD	xanthine dehydrogenase
NADH	Nicotinamide adenine dinucleotide
NET	Neutrophil extracellular traps
ANC	Absolute neutrophil count
WBC	White Blood Cells
PMN	Polymorphonuclear
PMNL	Polymorphonuclear leukocytes
HOCl	Hypochlorous acid
MPO	myeloperoxidase
BPI	bacterial permeability–increasing protein
NK	natural killer
COPD	chronic obstructive pulmonary disease
hs-CRP	high sensitivity C-reactive protein
ACS	acute coronary syndrome
ICH	Intracerebral hemorrhage
MMP	Matrix metallopeptidases
TIMP	Tissue inhibitors of metalloproteinases
LMR	lymphocyte-monocyte ratio
NIHSS	National Institutes of Health Stroke Scale
MRS	modified Rankin Scale
HTN	hypertension
T2DM	Type 2 Diabetes mellitus
NL	Neutrophil Lymphocyte

ABSTRACT

Background and objectives: Stroke is the leading cause of mortality and disability. NLR and inflammatory marker can be used as simple and easy marker for prognosis and mortality. The study aims to investigate the role of NLR ratio in acute ischemic stroke

Materials and Methods: Patients withfeatures of acute ischemic stroke were subjected to detailed history, examination and thorough investigations.

The diagnosis was made by clinical history, neurologic examination and neuroimaging

The severity of stroke at the time of admission was classified based on NATIONAL INSTITUE OF HEALTH STROKE

The functional outcome at discharge have been determined using MODIFIED RANKIN SCALE

Results: Out of 68 patients enrolled in the study,13 patients (19.1%) had mild stroke, 45 patients (66%) were affected by moderate stroke, 6 patients (8.8%) had moderate to severe stroke, and 8 patients (5.9%) were severely affected.In the Chi-Square analysis for the association betweenNLR and MRS, the pearson chi square analysis shows significant results(p value =0.000<0.001)

Conclusion:This study found that NLR is a simple prognostic marker to predict the functional outcome ofthe patient during discharge using MRS. The duration ofhospital stay of patient depends on NLR.Lifestyle of patient and diet maintenance alsoaffects the neutrophil and lymphocyte count of the blood (NLR).

Keywords- Acute Ischemic Stroke, NLR, MRS, NIHSS

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF GRAPHS

INTRODUCTION

Stroke is the central nervous system related disease which can be ischemic or hemorrhagic. This is the third deadly disease in the world. Global Burden of diseases reported that the stroke is third most cause of disability and the second most reason for mortality. After the effective treatment many of them are surviving with better ability to carry out daily routine. In India80-85% of the patients are affected with ischemic stroke, showncerebral embolism lead to irreversible nerve impairment [1, 2].The inflammatory response has been reported to occur in all the stages of acute ischemic stroke (AIS) [3].

The major initial stage in stroke because of inhibition in the blood flow to the cranial region which causes brain insult [4]. Stroke was classified into many types, among all strokes, 80% of people affected by the ischemic stroke. Most recently medical researchers are exploring the effective treatment in low cost for the treatment of acute ischemic stroke include intravenous or intra-arterial recombinant tissue plasminogen activator (rt-PA) and mechanical endovascular therapies [5]. But therapeutic factors are affected by some unfavorable prognostic factor that trigger the immune response in all the affected stages of the acute ischemic stroke [6]. Many of the ischemic stroke are can be curbed in the earlier stage of the affection by the help of the anti-inflammatory factors.

Chemokines, cytokines, and recruited peripheral circulating leukocytes were the major factors in the Ischemic response [7, 8]. Among all the leukocytes, neutrophils are the most important mediator, which causes the ischemic brain injury. Larger infarct volumes and increased stroke severity is instigated by the neutrophils effects. As per the research reports the immune system plays a vital role in Acute

Ischemic Stroke (AIS). Neutrophil is the first cell, which enter into the brain after stroke [9, 10]. The inflammatory mediators has additive brain damage by releasing proteases in the ischemic brain region [11, 12].

Neutrophil-Lymphocyte ratio (NLR) is the most important risk factor in the latest treatment case studies. NLR is an inflammatory marker [13, 14]. Both are very simple and low in cost. Neutrophil-Lymphocyte ratio (NLR) being the prognostic marker have been reported with poor prognosis in patients who had carcinoma and ischemic cardiac disease. Several studies have found that lymphocytes count were correlated with the post AIS [15-17]. They play the prognostic role in the inflammatory response that should be watched based on the Neutrophil-Lymphocyte ratio (NLR). Importantly patients face higher hospital mortality and less improvement in the 90 days of ischemic stroke treatment when they were treated and had high NLR [18, 19]. As per the case studies NLR reflects post stroke immune response.

In this study association between NLR and other clinical factors related to stroke were analyzed with the functional outcomes of patients. Prognostic role of the NLR in acute ischemic stroke patients has been investigated with the Chi Square analysis. Analyzed report helps to understand the NLR association in the duration of hospital stay, lifestyle of the patient as well as functional outcome at the time of discharge.

OBJECTIVES

1. The main objective of this study is to find whether neutrophil lymphocyte ratio (NLR) can be used as short term prognostic marker in patients with acute ischemic stroke.

2. To find the association between NLR and various other clinical factors related to stroke.

REVIEW OF LITERATURE

INTRODUCTION

Central Nervous System collect the information from internal and external cell signalling of the body. During integration function, received signals are due processed in the brain and spine [20]. Then it imparts the signals to the muscles, glands, and organs to express various actions which called as Motor Function[21]. It plays vital role in the coordination of all the functions of body and maintaining the homeostasis balance. It have been classified as Central and Peripheral System [22]. In this study, the specifically focused problem called stroke, which modify the function of central nervous system.

CENTRAL NERVOUS SYSTEM (CNS)

The central nervous system (CNS) controls most functions of the body and mind. The brain and the spinal cord are the major parts of the central nervous system. The brain is the centre of our thoughts, it is the signal processer in the sensory system, and it is the origin of control for our body movement. Central nervous system can interpret the signals from the sensory organs such us eyes (sight), ears (sound), nose (smell), tongue (taste), and skin (touch)[23]. The spinal cord is the most important part in the communication system of the cental nerve system which connect the the body and the brain[24].

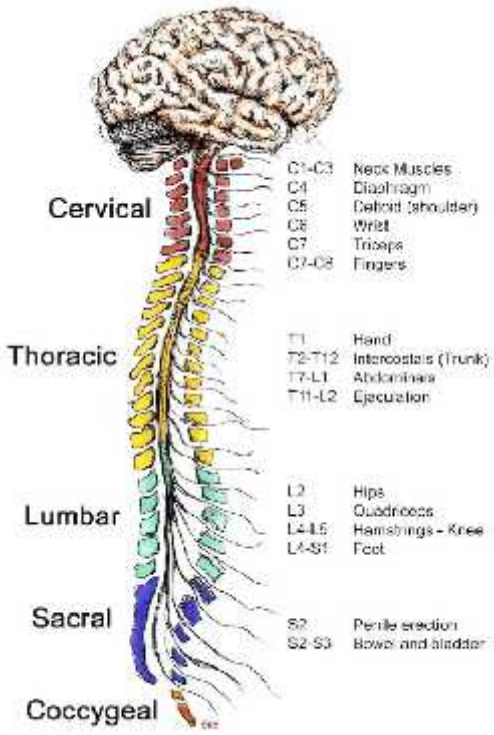

Fig 1. Major parts in Central Nerve System

The spinal cord is formed with extended cylinder of neuron cell bodies with group of axons and endangered with the connective tissue and bone. Medulla oblongata is present in the brain which connected with spinal cord and runs downcast the vertebral column, the hollow tunnel fenced inside the vertebrae of the spine. The brain has act as the central information collection and processing organ of the body. The blood supply to the brain is most important for survival and function of the brain cells, if interrupted , the cells apoptose causing the brain insult [25, 26].

ADEQUATE PERFUSION TO BRAIN

Ideal blood flow to the brain (CBF) rate for a normal human is within 45-50 milliliter per minute per hundred grams amid a mean arterial blood pressure (MAP) 130 mmHg and 60mmHg [27]. If the CBF rate is reduced below or equal the range of 20 to 30 ml/min/100g, that causes a shift in brain metabolism. Consequently the electrolyte and water transpose and perfusion within the zones of cortex. If the CBF

rate decline below to 10 millilitre per minute per hundred grams, that consequently affects neuron's depolarization and cause the loss of potassium within the cell which extravastes to the extracellular space. Using positron emission tomography, cerebral blood volume and cerebral energy metabolism were measured based on the cerebral metabolic rate of oxygen. The oxygen abstraction segment should be maintaining in the linear range. Gradual fall of cerebral blood flow, cerebral blood volume, glucose level and oxygen level are observed when the vessels are interrupted by thrombus or other causes. If blood flow to the cerebrum reduces equal or lesser than 20 millilitre per minute per hundred grams, an electric tranquility arises with a reduction within activity of synapse so that energy is provided[28]. If reperfusion happens erstwhile to substantial amount of cell death, that considered as the Transient Ischemic Attack (TIA).

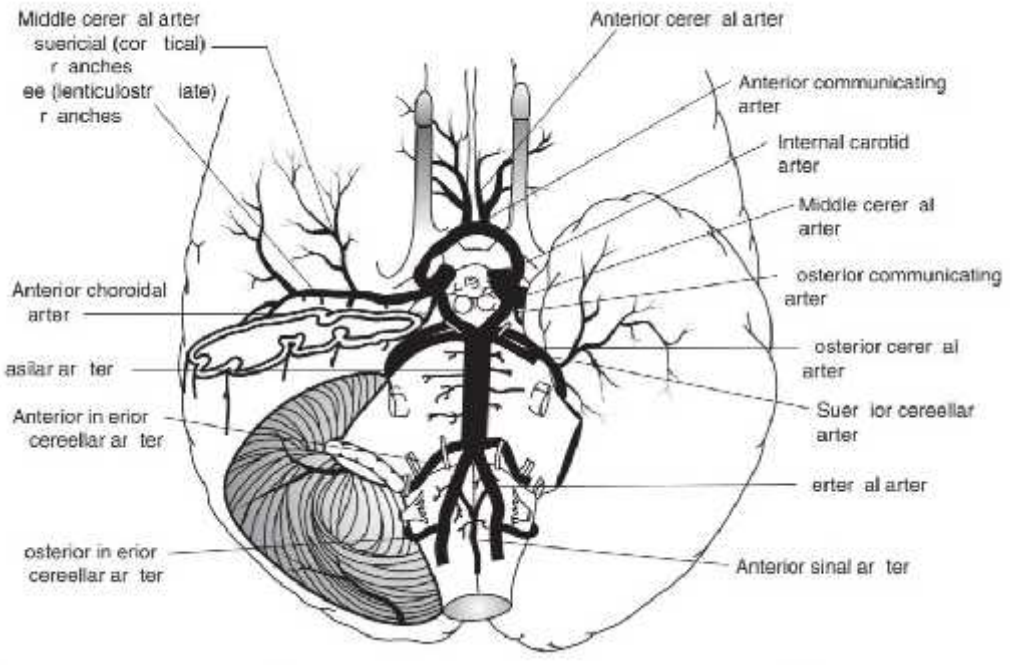

Fig 2. Blood flow paths in the central nervous system

The Mean Arterial Pressure (MAP) needs to be maintained for the cerebral viability and that should be above 40 mm Hg. MAP in the normal human should be in

45 to 50 mm Hg for the preserved cerebral viability [29]. A clinical evaluation of manual explained that out of fifteen only three who had acute cardiac asystole admitted in the ICU had MAPs above 40 mm Hg, this gives the better understanding of the arterial pressure[30].

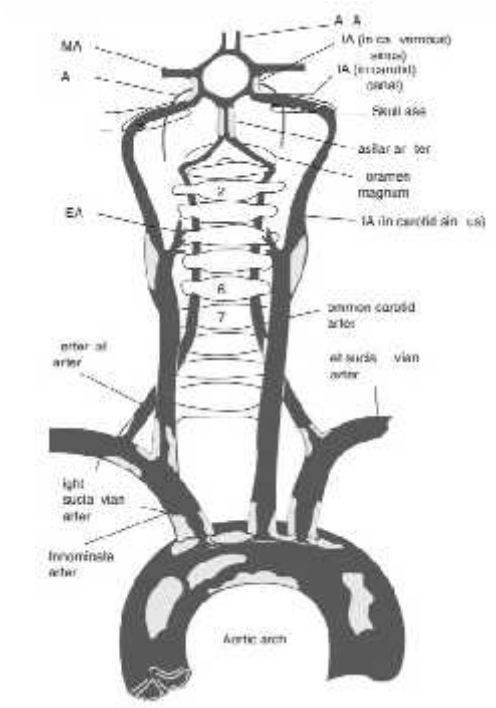

Fig 3. Arterials blood flow between brain and eye

STROKE

Second foremost reason of death in the global in known as the Stroke. Almost 56 million deaths that occur in every year, in that 10.8% of peoples were died due to stroke. One in five women and one in six men affected by this illness called stroke in their lifetime. World Health Organization reported that the fifteen lakh people in global had stroke yearly, among the affected people five lakh decease and five lakh will be eternally handicapped [31, 32]. Stroke also leading cause of adult disability. As per the research reports diability could have been prevented in 80 percent of affected population by proper medical practices.

Sudden inception of a focal neurological shortage being absent in for more than 24 hours is known as the Stroke. The very first 24 hr of the stroke is considered as the Cerebrovascular accident (CVA) or apoplexy. This kind of an acute stroke leads to the focal neurological shortage If lasting less than 24 hours (usually 5–20 minutes), it also called as the transient ischemic attack (TIA)[33]. Stroke is termed as the brain attack, which caused by an unexpected disruption within arterial supply in the encephalon. This happens if any zone of the functioning encephalon doesn't receive adequate blood flow. Due to the stroke approximately two million brain cells have died in every minute that increase the rate of brain damage, functional disturbance and inactivation. Affection rate of the stroke has been vary based on the brain attack and the size of area damaged by the blood flow disruption [34, 35]. When cells of the cerebrum perish in event of stroke, which promotes improper communication in the brain and that were reduce the functional process of the brain. Communication lacking in the central nervous system leads the inability of speaking, loss of movement and memory.

Causes

Two reasons were observed by researchers that cause the stroke, which are

A blocked artery (ischemic stroke) [36]

Leaking or bursting of a blood vessel (hemorrhagic stroke),

Temporary disruption of blood flow to the brain, known as a transient ischemic attack (TIA) [37, 38].

TYPES

Stroke is classified into 2 types based on the aetiology that are ischemic and hemorrhagic. 85 % of stroke diagnosed population has the ischemic stroke. This Ischemic stroke formed by the blocking of a cerebral artery, that includes various kind

of process such as thrombotic in 50%, embolic in 25% and lacunar stroke in 25%. 15% of the stroke population are affected by the Hemorrhagic stroke, which caused primarily by impulsive estrangement of blood vessels. Blood vessel rupture leads the secondary level trauma to brain.

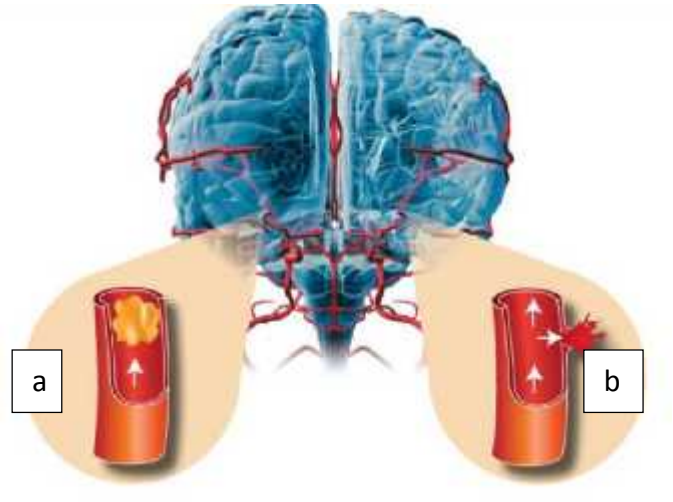

Fig 4. Types of stroke. a) Ischaemic stroke, b) Hemorrhagic stroke

CAUSES

- Hypertension
- Trauma
- Amyloid angiopathy
- Amphetamines and cocaine addicts (common in younger)
- Coagulopathies
- Arterio-venous malformation
- Metastatic carcinoma in brain

RISK FACTORS FOR STROKE

For stroke affection risk factors have been divided as controllable and uncontrollable [39, 40]. Lifestyle risk factors and medical risk factors are the controllable risk factors. Uncontrollable risk factors are gender, age, ethnicity (Hispanic or Asian/Pacific Islander, being African American), and having a family history of stroke.

Some common risk factors:

Gender

Male gender has an increased rate for risk of stroke. Males have 1.3 times more likelihood of stroke. But it may have some exclusion in the uppermost ages. The probability in subarachnoid haemorrhage where the menace increases in females[41].

Age

Occurrence of stroke higher in the upper age group in both men and women. People over the 65 age were majorly affected by the stroke. In the whole affected population 28 percent of people were below the age 65[42].

Ethnicity

African origin people have the poor management of treatable risk factors, so the risk is higher than other countries. Caucasians peoples also has the risk of stroke. Patients who has the intracerebralhemorrhage rate is more in Chinese. In ischemic stroke, the affection frequency is lesser in Caucasians [31].

Genetics

- "MELAS (mitochondrial myopathy encephalopathy, lactic acidosis, and stroke like episodes)"
- Pseudoxanthomaelasticum
- "Homocystinuria"

- "Cerebral autosomal dominant arteriopathy with subcortical infarcts and leuko encephalopathy (CADASIL-notch-3 gene)"
- "Cerebral autosomal recessive arteriopathy and leuko encephalopathy (CARASIL-HTRA gene)"
- "Ehlers Danlos syndrome type IV"
- "HANAC (hereditary angiopathy, nephropathy, aneurysm, and muscle cramps syndrome;COL4A/ mutation)"
- Fabry disease (alpha galactosidase gene)
- Marfan syndrome

These above-mentioned syndromes are considered as the leading causes for the stroke. Sickle cell anemia patients hasan increased risk for stroke associated brain injury between the age of 6 to 12. Transcranial ultrasound showed velocities input is higher quantity in the middle cerebral, which increases the likelihood in children having sickle cell disease[43].

Diabetes

Hyperglycemia has a saviour impact on flow in the arterial blood vessels and its an highly affecting peril in stroke. Prevalence of repeated stroke is more common in diabetic patients. Stroke having patients with diabetes mellitus has been monitored through the glucose level, that should be >126 mg/dL in preprandial and >200 mg/dL in postprandial[44].

Hypertension

In case of the stroke patients it can be controlled. Its usually noticed in stroke population with 55 years of age or less. An increase of 20 mmHg of systolic or a diastolic BP increase of 10 mmHg more than duos the menace of stroke death[45].

White matter disease

Stroke causes severe damage to white matter, a risk factor for higher frequency of strokes and adverse neurological outcomes. The bulk of stroke-induced damage is in subcortical regions and, surprisingly, white matter comprises about half of the total amount of infarction. White matter is in general highly vulnerable to ischemia and is sometimes more seriously injured than gray matter. Clinical effects associated with white matter injury include cognitive dysfunction, mental disturbances, sensorimotor impairments, urinary incontinence and discomfort, all closely linked to the disruption and remodeling of white matter connectivity [72].

Dyslipidemia

High levels of cholesterol leads to the risk of atherosclerosis within carotids. Acute fall in cholesterol parameters, who has stroke has higher chance of ICH. Total cholesterol concentration should be >200 mg/dL and/ and the triglyceride concentration should be >140 mg/dL for initiating lipid lowering therapy.

Coagulation disorders

Anti-phospholipid antibody and lupus anticoagulant have the direct relation with the ischemic stroke. There are numerous numbers of coagulation-based disorder are in the human system, which are all were caused by the venous thrombosis. Paradoxical embolism through patent foramen ovale is the major risk factor for the stroke.

Obstructive sleep apnea

Obstructive sleep apnea causes the blood pressure increment and lead to deficit in blood supply to brain. Hypercoagulability, decreased cerebral blood flow, atherosclerosis were the major predicted symptoms. Wake up stroke also linked with the obstructive sleep apnea(20)

Renal disease

Renal disease also play the risk factor oriented process in stroke that has to be considered in the atherothrombotic disease. Micro albuminuria also act as the independently associated stroke causing risk factor.

Lifestyle risk factors

Cigarette smoking is one of the major risk factor for ischemic stroke. Passive and active smoking leads to the stroke in the younger age . In a person who have quit smoking, that itself decreases the likelihood in stroke by almost fifty percent. Excessive liquor or booze has an higher risk of stroke. Fruit and vegetables may have an anti oxidant role.Omega-3 fatty acids that are found in certain types of fish can promote heart health and lower your risk of stroke. Physical activity also shown the effective reduction the risk of stroke. 30 min of daily exercise is one of the main reasons for reduction in the relative risk of stroke. Body mass index has the important role in the risk management in the stroke, For women more than 30kg/m2 and men more than 25kg/m2 are the risk of ischaemic stroke accuracy[46, 47].

DIAGNOSIS

Primary observations about the stroke like ischemic injury is based on the biochemical and physiological changes within encephalon. Changes like

- lactate accumulation
- Deprivation in adenosine triphosphate and other energy providing compounds
- Swollen astrocytes which compact capillaries consequenly leading to disruption in flow

After some time period the researchers have found the major biomarkers for the diagnosis.

BNP, D-Dimers, MMP-9, S and 100β were tested with a Stroke patient, which has the correlation with mortality at 120 days. Conferring the significant role of the markers of inflammation, thrombosis and cellular death were done by the immunoassay. This kind of the assays has the better reliability of the clinical diagnosis of stroke reports. DWI-MRI is well-known method to identify acute cerebral ischemia in high quality manner. Prognostic implications are helps to avoid the imperfect result. MMX value had not shown perfect diagnostic result in the 120 days of analysis. S100β, which is a marker of astrocyte initiation, the biomarkers in this stroke panel are not precise to central nervous system tissues. When they used the biomarkers in conjunction, they deliver corresponding info in the prognosis of stroke. High levels of BNP are related with congestive heart failure and High level of D-dimer in clinical circumstance may lead the blood clot formation and subsequent fibrinolysis. Stroke Diagnosis process has various methods in the medical research. That are all given below.

Neurological Examination

A through examination (including neurological signs, history and other systems)For some emergency cases the neurologist, the brain specialist, prescribes using various techniques to determine the cause of the cerebral attack and to locate the affected area[48, 49].

CT-Scan

An X-ray based imaging of the brain, which helps to confirm the presence of a stroke. Also it specifies the type of stroke if its an ischemic stroke began by a blood

clot or a hemorrhagic stroke (cerebral hemorrhage) began by bleeding. The extention of this is CT where one can identify its it's a stenosis or occlusion. [50].

MRI (Magnetic Resonance Imaging)

A magnetic field system had used to produce cross-sectional images of brain. It takes approximately 45min for test to be done. The sensitivity for detecting vasogenicedema is high. For detecting ischemia DWI is used.

ACUTE ISCHEMIC STROKE (AIS)

AIS is insufficient arterial supply for cerebral perfusion, because of attenuated or occluded vessels flowing into or inside brain. It have two types thrombotic and embolic strokes. The blood vessel becomes narrowed and the blood flow to the area beyond is less. Damaged areas of an atherosclerotic plaque lead the blood clot - a thrombotic stroke. In an embolic stroke, blood clots or debris generated from any other part of the body may block and lead to narrower blood vessels[51, 52]. AIS also has subtype

Subtypes

Acute ischemic stroke has the five subtypes, which are

Large-artery atherosclerosis,

Cardioembolic,

Small vessel occlusion (lacunar),

Stroke of other determined cause, and

Stroke of undetermined cause.

Excitotoxicity, oxidative, ionic imbalance, and nitrative stresses, and apoptotic-like mechanisms are the major pathways in the AIS. After ischemic inception, loss of energy substrates leads to mitochondrial dysfunction and generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS). Downstream

pathways eventually comprise direct free radical damage to membrane lipids, as well as calcium-activated proteases cellular proteins, and DNA, plus caspase cascades that dismantle a wide range of homeostatic, reparative, and cytoskeletal proteins[53, 54].

Mechanism of Acute Ischemic Stroke

Mechanism of the AIS development has 4 different process, which are explained in the table 1 [55, 56]

Table 1: Mechanism of the Acute Ischemic Stroke

Mechanisms	Events
Excitotoxicity	Membrane depolarization in response to disrupted cellular oxidative and energy production processes leading to damaging activity of secondary messengers
Depolarization	Local depolarization caused by focal hypoxia decompensates already threatened metabolism in penumbra and propagates ischemic damage
Inflammation	Injury mediated by enzymic (proteases and collagenases), cellular (neutrophils and macrophages) and vascular processes
Apoptosis	Programed or ordered cell death mediated by caspase enzymes

1. Blocking of required blood supply to brain, deficit in o2 , so cell drops its capability to generate fuel for normal cell function.

2. Cells present in the afflicted zone modify themselves by switching to oxygen free metabolism that causes decreased production of compounds required for energy genration. Instead of ATP brain cells producing the by-product called lactic acid.

3. Lactic acid is the kind of an irritant, harmful to neuronal cells, that have ability to apoptose cells by the effecting the ion balance within brain.

4. ATP is related to the ion transport pumps, hence decreased ATP concentration might lead to cellular dysfunction. It leads to depolarization of the cell membrane. As a result large influx of ions, including calcium (Ca++), and an efflux of potassium ions occurs in the cell.

5. Due to ion unbalancing intracellular calcium levels become too high, which prompt the release of the excitatory amino acid neurotransmitter glutamate.

6. Glutamate excites AMPA receptors and Ca++-permeable NMDA receptors, which helps to allow more calcium influx into cells.

7. More calcium entry excites cells and triggers proteases, lipases and free radicals formed as a result of the ischemic cascade in a development called excitotoxicity.

8. Phospholipase lyse cell's membrane. Cell wall become more permeable, and that make the entry of more ions and harmful chemicals in to cell.

9. Improper signalingoccur in the cell which break down the Mitochondria, liberating harmful compounds within cell that cause it to lyse.

10. Cell death releases the glutamate and toxic chemicals into the brain environment.

11. Unwanted chemical entry makes changes within the vascular structural integrity and it affects the blood brain barrier and contributes to cerebral oedema, which can cause secondary progression of the brain injury

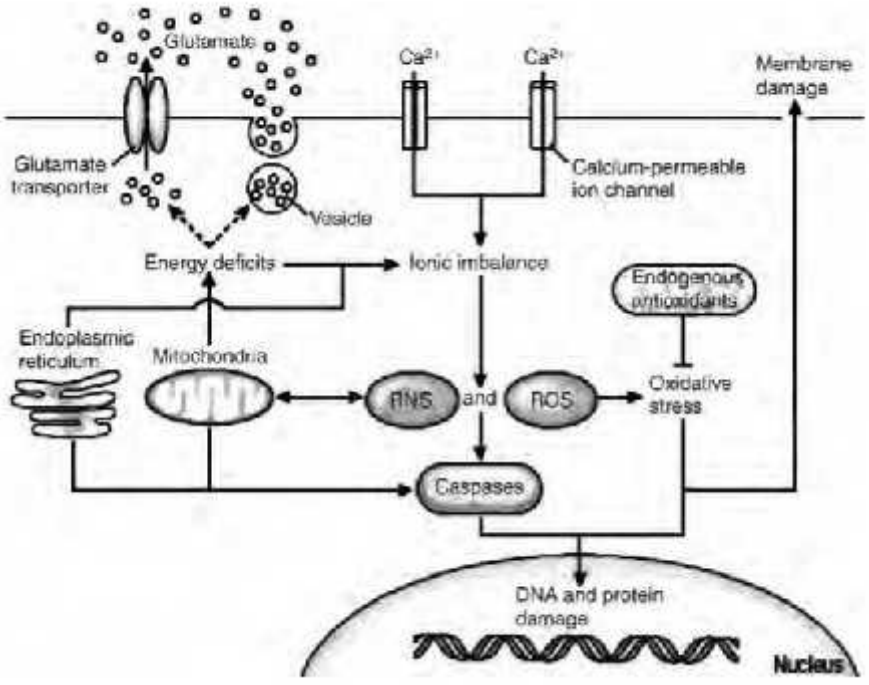

Fig 5. Mechanism of the AIS

CAUSES

Biochemical Events

The failure of high-energy metabolism occurs in 0.333 minutes in intrusion of arterial blood supply to the encephalon. In no less than three hundred seconds, the adenosine tri phosphate have been disappeared (ATP depletion) and ion imbalances within cell begin to appear[57].

Calcium

Extracellular concentration of the calcium is 10,000 times greater than the intracellular concentration [57]. Four mechanisms are involved in the cellular functions:

(1) Active extrusion of calcium from the cell by an ATP-driven membrane pump

(2) Interchange of calcium for sodium at the cell membrane obsessed by the intracellular to extracellular disparity in the concentration of Na+, that shown the cell membrane's Na+ -- K+ pump activation.

(3) Impounding of intracellular calcium in the endoplasmic reticulum by an ATP-driven process

(4) Accrual of intracellular calcium by oxidation-dependent calcium appropriation inside the mitochondria.

Free Radical

In an ongoing ischemic episode, the adenosine triphosphate lysis by adenosine monophosphate is the main step that causes accrual in “hypoxanthine”. Elevated level of the calcium within cell boost transformation of “xanthine dehydrogenase (XD) to xanthine oxidase (XO)”. During reperfusion and re-oxygenation, suggestively higher levels of several free-radical species that damage cell and capillary membranes. Re-oxygenation also returns ATP levels, and it promotes uptake of calcium by the

mitochondria, resulting in massive calcium overload and destruction of the mitochondria [57].

Mitochondrial Dysfunction

Structural alterations in the mitochondria lead the biochemical derangements . The accumulation of long-chain acyl-CoA is perchance most important, since intramitochondrial accretion of long-chain acyl-CoA is the first step to several different mitochondrial reactions [57].

Other Factors

The one more contributing insult is lactic acid accumulation resulting in neuronal injury. Lactic acid degradation of NADH has the interference of ATP recovery. “NMDA receptor inhibitors have proved effective in preventing global cerebral ischemic injury”.

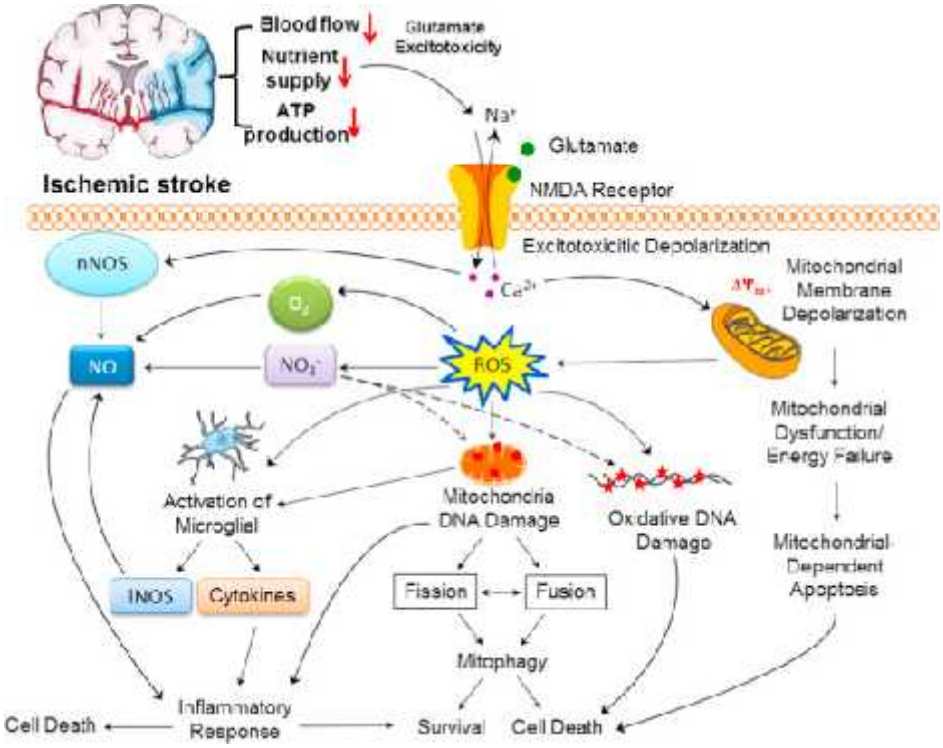

Fig 6: Factors involved in the Ischemic stroke

CLASSIFICATION

Ischemic stroke classified based on its aetiology.

• Large artery disease –

atherosclerosis of large vessels,

including the internal carotid artery,

vertebral artery,

basilar artery, and

other major branches of the Circle of Willis.

• Small vessel disease –

changes due to chronic disease, such as

diabetes,

hypertension,

hyperlipidaemia, and

smoking.

• Embolic stroke –

the most common cause of an embolic stroke is atrial fibrillation.

• Stroke of determined etiology –

Inherited diseases,

metabolic disorders, and

coagulopathies.

COAGULATION NECROSIS

Blood clots in the arteries may increase stroke risk. One of the leading causes of acute ischemic stroke in adults is local hypercoagulability. Accumulating research has shown patients with thrombosis to have a hypercoagulable condition before

symptoms start. Therefore it is very critical that patients at risk may be diagnosed before the onset of the stroke.Fibrinogen – a component in thrombin enzymatic procoagulant, which lyses to fibrin. It develops into bifurcated, spatial structure thats interlinked in the last step of the coagulation cascade by triggered factor XIII (FXIIIa). Cross-linked fibrin forms a network that provides the blood clots with chemical and physical hold up. Decreased or consequential diminishment of fibrinogen is linked with hemorrhage in patients with AIS who had thrombolysis [58, 59].

NEUTROPHILS

In patients with ischemic stroke, the number of neutrophils in circulation increases within the first few hours of the onset of the stroke. This increase is linked to severity of the stroke, volume of the infarction and worse functional outcomes. In comparison to neutrophils, lymphocytes decrease after ischemic stroke. This increases neutrophil-lymphocyte ratio after stroke and is correlated with mortality and the size of the infarction.The upsurge in neutrophils after stroke occurs as a result of increased production, enhanced release from the bone marrow and spleen, and possibly from a reduction in neutrophil apoptosis. [60].

STRUCTURE

Neutrophil granulocytes are in the diameter of 12–15 micrometers (µm) in peripheral blood smears. Normal human neutrophils have an average diameter of 8.85 µm in suspension mode. The nucleolus is not therein the mature neutrophil. Within cell ribosomes, mitochondria are few and Golgi stucture is tiny, RER is absent. They display sexual dimorphism. Females have a mini extra chromosome called "neutrophil drumstick". They has the higher dichotomisation and typical one has 3–5 segments [60].

It has the intricated structure, which promotes the phagocytosis, chemotaxis, and exocytosis. 45% of the neutrophil cytosolic protein is serene of migration inhibitory factor such as the MRP-8 and MRP-14 Protein. Neutrophils build biomolecules in three types of granules, this phenomenon known as “degranulation” [61].

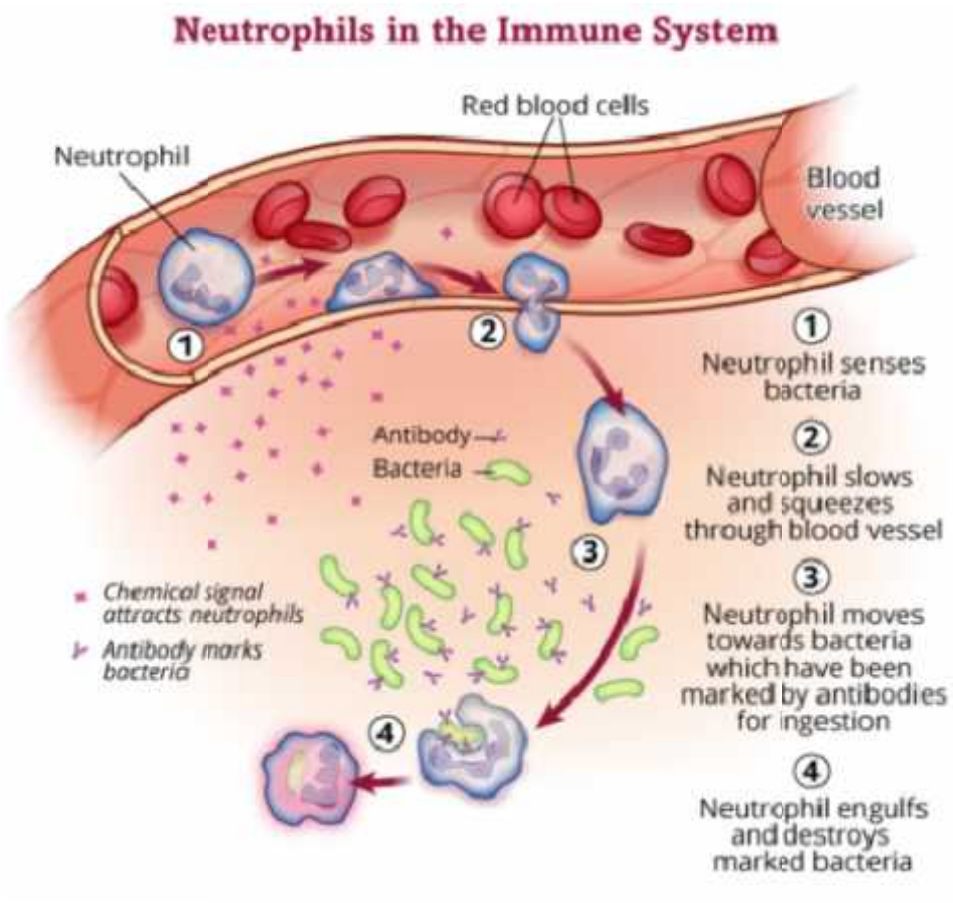

Fig 7. Mechanism of Neutrophil in the blood stream

NEUTROCYTES AND HYPERGLYCEMIA

Elevated glucose in blood condition reduce the functioning of neutrophil, leading to higher probability in ailment in population afflicted with diabetes. Effective control of plasma glucose inhibits neutrophil degranulation, this process called as the opsonization. Previous reports explained that the hyperglycemia badly afflicts neutrophil function when infected.

NEUTROCYTE'S EXTRACELLULAR TRAPS

Neutrophils origins the release of web-like structures of DNA, for apoptizing or neutralizing microorganisms. "Neutrophil extracellular traps (NETs)" composed of intricatednetwork of fibres containing serine proteases & chromatin that helps to shut in and apoptose microorganisms. Researchers reported , traps composed of antimicrobial compounds, excess in proportion that cohere and causes apoptosis in infection causing bacteria. Additionally NETs act as the physical barrier to prevent the attachment of pathogens. Many recent research studies reported that the NETs play the important role in inflammatory diseases such as preeclampsia, a pregnancy-related inflammatory disorder [61].

CLINICAL SIGNIFIANCE

In the clinical testing aspects the Absolute neutrophil count (ANC) is the major link for depicting aggregate of neutrocytes in blood. In Adults fifteen hundred to eight thousand cells/µL is the normal value of absolute neutrophil count, if a person has below or equal to fifteen hundred cells/µL, the condition is termed neutropenia wherein the possibility of bacterial invasion escalates.

ANC = WBC (cells/µL) X percent (PMNs + bands) ÷ 100

DEVELOPMENT

Morphologic stages are classified into 3 stages that aids in neutrophil maturation, which have the ability to multiply. Myeloblasts, promyelocytes, and myelocytes are the major representative molecules in the development. Polymorphonuclear leukocytes (PMNLs) and monocytes/macrophages had been reported from the year of 1960, it promotes consequential physiology in ischemia

within brain. In past ten years there were numerous research reports explained the mechanism of PMNL in reperfusion injury. When PMNLs are activated in the blood stream that promotes the release of hydrogen peroxide. This hydrogen peroxide-myeloperoxidase system possibly produces Cl- in the form of HOCl. Product is well known household bleach and that damage the wide range of organic molecules. The amounts of HOCl produced by the neutrophil are higher in stress or infectious states. 106 neutrophils were generated with the two hundred and fourteen mol of HOCl, this is sufficient to kill the 15 crores of infectious microbes [62, 63].

COMPOSITION OF NEUTROPHILS

Neutrophils are composed with four different granular compounds that are specific, functioning as bactericidal. They are divided further into -the secretory vesicle, primary also called azurophil, secondary granules which are also labelled specific and lastly tertiary or the gelatinase

Primary granular compounds contain defensins, enzymes myeloperoxidase-MPO, azurocidin, lysozymes, microorganism's cell membrane permeability–increasing protein labelled as "BPI", cathepsin G, elastases , proteinases & esterase. Secondary granular compounds have been unconfined outside cell membrane and contains, cobalamin–bounding compound apolactoferrin, lysozyme, plasminogen activator & collagenases. Tertiary or gelatinase granules composed of acetyltransferase, gelatinase, and lysozyme. Tertiary granules playing the vital role in the upregulation of surface molecules with stimulation.

LYMPHOCYTE

It has been demonstrated that they have principal effects in AIS and the prognosis later. The inflammation occurring post the disruption of arterial supply, it has been observed altering the extent of inflammation has a significant therapeutic

role .Post occurrence of stroke lymphocytes travel from blood vessels into cerebral parenchyma. T lymphocytes, as part of the adaptive arm of the immune response, are present bordering the infarct region within days after stroke in post-mortem human samples. More specifically, CD8+ T cells, CD4+ T cells, and NK T cells are recruited within 24 hours after ischemic attack and accumulation of these cells in the early inflammatory phase peaks 3 to 4 days after injury. The presence of T cells persists as late as 7 weeks post-stroke [62].

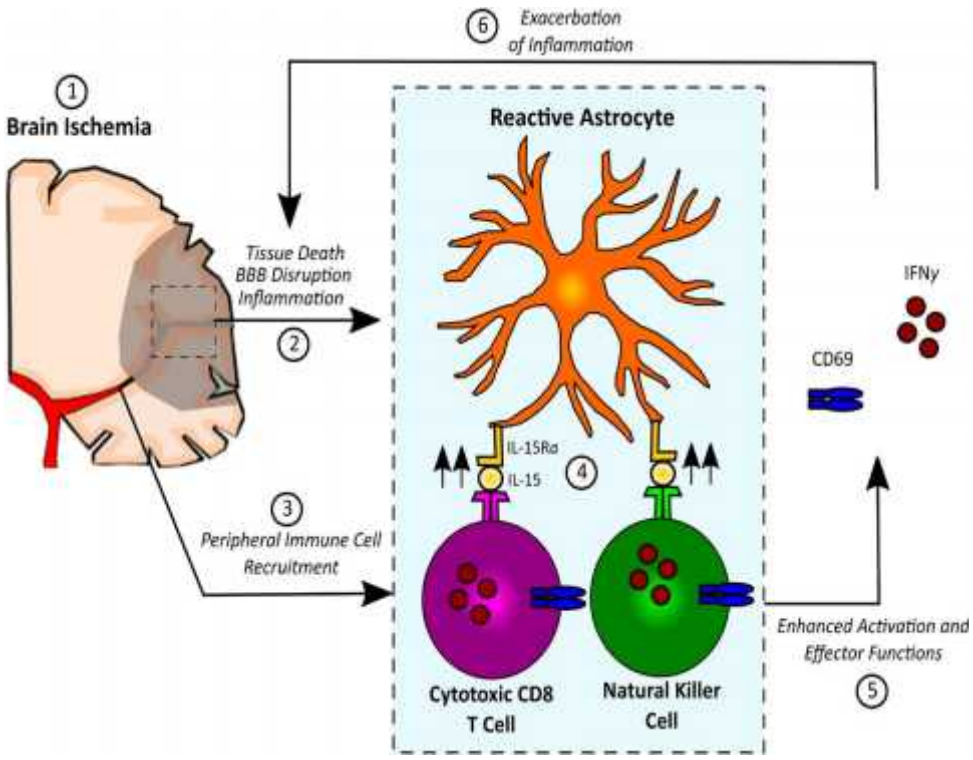

Fig 8. Mechanism of Lymphocytes in Brain

LYMPHOCYTE CELL MATURATION

Stem cells which are pluri-potent give raise to lymphocytes .Intitially they develop from yolk sac, then within liver and lastly bone marrow. In normal human in the age of 18 to 30 the stem cells found within marrow of bone which are pluripotent give rise to multiple heredities of different blood components. The myeloid and lymphoid progenitor cell is the first differentiated cells in the development.

Myelocytic cells consequently produce cells which are precursor to thrombocytes, red blood cells, neutrophils & monocytes. [64, 65].

NEUTROPHIL TO LYMPHOCYTE RATIO

The "neutrophil to lymphocyte ratio (NLR)", is well known prognostic marker for the identification of Acute Ischemic Stroke. This has been calculated from the complete blood count of patient with the absolute neutrophil count per absolute lymphocyte count as the denominator. If the people with any small amount of change in the any condition, which change the value of ratio that can increase or decrease. Inflammatory status can be monitored by the NLR calculation, which may be the inflammation reaction triggered by cells. Higher ratio of NLR translates that the inflammation triggered in the body[66]. NLR ratio is the predominant marker for the diabetes, renal failure, malnutritional status (mostly chronic), cerebro-vascular events, COPD, alzheimer's, and psychiatric illness, metabolic syndrome. Higher blood inflammatory effect on markers like "highly sensitive C-reactive protein (hs-CRP)" is noted as possible risk for AIS/IHD independently[64, 67].

Recent research reports explained that the leukocytes having an alike activity in ischemic stroke. Inflammatory cascade in stroke has a significant pathologic influence on cell death within brain. Cytokines and chemokineshas the major role in inflammatory process of AIS. In the blood circulation leukocytes, and neutrophils causes the ischemic injury. Gathered neutrophils leads to the production and release of free oxygen radicals, neurotoxic substances, and various inflammatory cytokines. These processes are the major reason for the necrotic cell death within tissue that developed ischemia. Low level lymphocyte counts in blood promotes the sympathetic activity and baseline cortisol levels that cause activation of inflammatory cytokines and introduce the ischemic injury. Some of the research reports suggested that only

the right ratio, or a certain level of balance between neutrophils to lymphocytes maintaining is most important in the mechanism of delirium formation.

Ischemia within brain stroke aids the production inflammatory granules and recruitment of white blood cells, this is the mechanism of secondary progression of brain lesion. Every WBC subtype are having the diverse prognostic role. Neutrophils are the foremost cells in the WBC subtype which enlisted to the injured brain area. Neutrophils in the active mode will promote the entry of proteolytic compounds like phosphatases, free oxygen radicals that readily react which exaggerate pre existing ischemic injury in brain. The role of lymphocytes in AIS also the influential in very active manner. Lymphocyte counts decreased after ischemic insult to brain tissue, indicating bad outcome. NLR has significant correlation with ACS infarct volume, which can be used independently for determining risk of death within three months [68].

Factors involved in NLR

Various clinical research reports mentioned that the Age, previous stroke history, atrial fibrillation, initial National Institutes of Health Stroke Scale score, and high-sensitivity C-reactive protein has significant role in the monitoring of NLR. The NLR was higher in the unadorned pneumonia group when it was evaluated by Pneumonia Severity Index. The NLR evaluation helps to identify high-risk patients in the initial and throughout time of treatment. 116 affected people in the age of 67 shown the significant relationship between NLR and mRS ($p=0.02$). In that case report many of them noted with the age-based variation in NLR controlling. NLR, is the gladly available biomarker, it is clinically suitable tool for risk stratification when assessing AIS patients [71, 69].

Another study reported with 293 large vessel occlusion patients, they observed higher median admission NLR values was noted in symptomatic intracranial hemorrhage. Higher admission NLR is a sovereign predictor of symptomatic intracranial hemorrhage and it may recognize a target group for testing adjunctive anti-inflammatory therapies. Major research reports explained that the elevated NL ratio values has been related to higher incidence of hemorrhagic transformation or SICH in AIS patients getting intravenous thrombolysis.

AIS use the healthy immune system in animal models of middle cerebral artery for the migration of neutrophils in the brain. One of the individual components of PREDICT scale is admission NLR is the most widely used in the treatment [64].

Limitation

- The uncertain sample size and retrospective study of prospectively collected data are the most significant methodological shortcomings.
- Outcomes required central settlement.
- Not able to collect the perfect NLR variability data from all the patients.
- The prospect of an indefinite perplexing factor disturbing the results cannot be ruled out completely.
- The imaging modalities used for diagnosis of AIS
- The askew spreading of admission NLR is not stable.

Post-stroke inflammation has a dual role in ischemic stroke. Peripheral immune cells are getting stimulated post stroke can in turn effect fate of brain tissue that has undergone ischemia. Neutrophils expressed early after stroke to promote active inflammatory reaction, while lymphocytes also having the regulatory function in inflammation persuading neuroprotection. If there is any reduction of neutrophils

and induction of lymphocyte after stroke, that can progress functional outcome of AIS [71, 64, 69].

Lymphopenia is another inflammatory marker, which trigger the response to higher production of secondary to stress. Inflammatory process carried out with the lymphopenia to promote the lymphocyte apoptosis. Lymphopenia has strong correlation with the mortality in patients. The neutrophil count, lymphocyte count, and NLR, were obtained from the WBC count, and that values are useable in the prediction of mortality and prognosis of stroke patients and also the markers of systemic inflammation. NLR will be useful in the evaluation of the risk of stroke in asymptomatic patients with plaques causing intermediate carotid artery stenosis. This patient group, with an higher NLR have the higher chance of stroke[64, 69].

Studies have reported operating outcome is decreased in patients having higher NL ratio. Disability/Mortality was observed in patients with uninterruptedly elevated NL ratio level at forty eight hours or more post ischemic injury in brain started. Elevated NL ratio is related to both initial and long-term mortality. Elevated NLR levels have increased possibility of ICH post thrombolysis. In one hundred fifty one population having primary insult of ischemic brain injury were observed for a month, observations exhibits that the neutrophil lymphocyte ratio and infarct size correlated[64, 69].

Inflammatory biomarkers and association:

"Fibrinogen, TNF-α, IL 1β, IL-6, IL-10, anticytomegalovirusIgG antibody titer, high-sensitivity C-reactive protein (hsCRP), serum levels of vascular cell adhesion molecule-1 (sVCAM-1), S100A8, S100A9, S100A12, the apolipoprotein B/A1 ratio, oxidized low-density lipoprotein (OxLDL), homeostatic model assessment (HOMA) insulin resistance, baseline conjugated dienes-low density

lipoprotein (BCD-LDL), L-selectin, E-selectin, neopterin, matrix metalloproteinase-1 (MMP-1), MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, tissue inhibitor of metalloproteinase-1 (TIMP-1), TIMP-2, CD19 + CD40 + and CD19 + CD86 + B cell counts", etc.

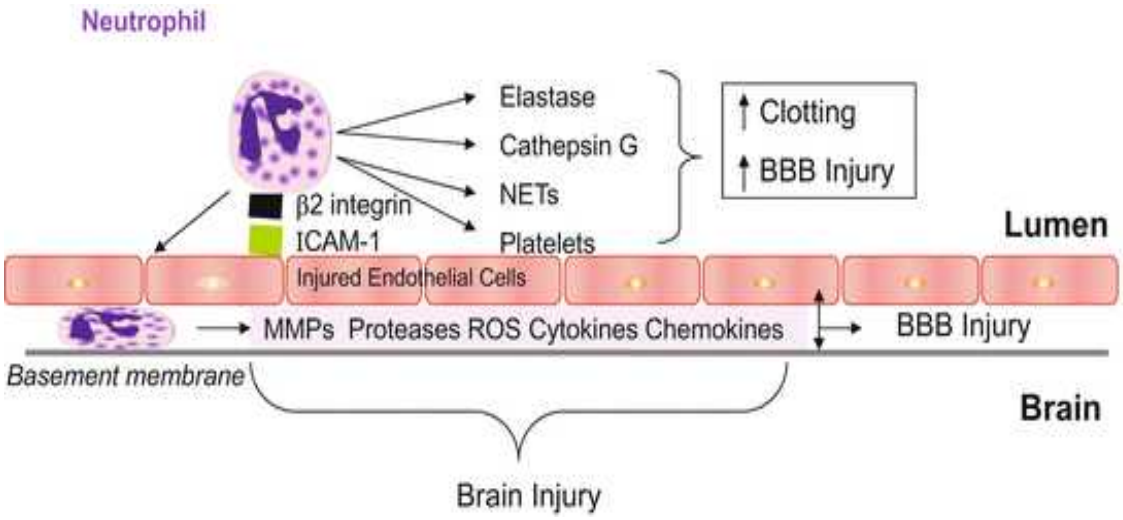

Fig 9. Inflammatory factors associated in ischemic injury of brain

Post ischemia apoptised brain cells and the tissue release profound inflammatory reaction, leading to accumulation of biomarkers of inflammation like neutrophils, lymphocytes, cytokines. The normal value of NLR in healthy populations was 1.65 (mean), ranging from 0.78 to 3.53. Milena et al considered the relation between NLR and LMR (Lymphocyte to Monocyte ratio) with Ischemic Stroke. 58 adult patients were involved in the study, followed by the analysing the blood sample their NLR and LMR were observed. There if no influence of LMR found in the stoke patients. But they found that patients with higher NLR have the possibility of getting severe stroke[70].

A study with the large number of patients (1001 patients) carried out for delirium and AIS and its prospective data collection of NLR monitoring. C-reactive protein can control the inflammation, that promotes the neutrophil activation and

maintain the NLR value. Patients with higher NLR value involved in the 30 day mortality of AIS patients[63].

In this Study, we are focusing to find out the prognostic role in NLR ratio role in population having AIS.

METHODOLOGY

SOURCE OF THE STUDY

The primary data collected directly from the patients who were admitted in the wards at KLES Dr. Prabhakar Kore Hospital serves also as Medical Research Centre, situated at Belgaum. Informed consent was taken and the database was collected specifically from acute ischemic stroke patients who were admitted in the hospital, within 72 hours of onset of symptoms, aged above 18 years.

Study Design: Prospective study

Period of study: One year (1st January 2019 to 31st December 2019)

DATA COLLECTION

Data from the patients who are enrolled in this study includes their demographic factors, co morbidities, duration of hospital stay, day-to-day life activities such as food habits and lifestyle of the patient. Blood samples were collected once the patient was admitted to find the neutrophills and lymphocyte counts in their blood. Patients with features of acute ischemic stroke will be subjected to detailed history, examination and thorough investigations.

Clinical history of the patient such as severity of stroke during admission and the outcome of their health was collected in the database. Neurological examination and Neuro-imaging method used to diagnose the stage of severity of AIS. Based on the NIHSS, the intensity of stroke is classified and functional outcome at the time of discharge is determined using MRS. Patients are followed up in the hospital to retrieve clinical data from the time of admission until they discharge from the

hospital. Information collected from the patients are maintained securely as per the informed consent.

The defined co-morbidities includes hypertension, type 2 diabetes mellitus, history of CVA, seizure disorder, history of preeclampsia, Ischemic heart disease, depression, hypothyroidism, and rheumatic heart disease. Patients with acute infarction, sub-acute infarction, as well as focal hyper acute infarction were identified and their infracted site was collected to analyses their severity of stroke. During the discharge day of the patient, the number days patient got admitted and stayed in the hospital for treatment was collected in database.

INCLUSION CRITERIA

In this study, patients with following categories was included

- Only the patients who has post-acute ischemic stroke were selected
- Patients who got admitted before 72 hrs of onset of symptoms.
- All acute ischemic stroke patients above 18 years of age,

EXCLUSION CRITERIA

In this study, people who comes under the following category was excluded

- Patient with history of more than 3 days of onset of symptoms
- Patients with history of infection within 1 week of stroke or within 72 hours of onset of symptoms
- Patient with malignancies or hematological symptoms

- Patients who are taking immune suppressant drugs
- Patients having history of recent stroke (for past 6 months) or with previous stroke diability
- Patients with severe pulmonary disorder or chronic renal failure undergoing treatment i.e. Dialysis,
- Patients with intra-cerebral hemorrhage.

Data collected by following up of the patient during the hospital stay

SAMPLING TECHNIQUE

To collect the data from patient, prospective sampling technique is used. The sample data was collected from the patients who are admitted in hospital from the period of 1st January 2019 to 31st December 2019, specifically who were admitted for acute ischemic stroke. Out 112 patients admitted at Karnataka Lingayat Education Society's Dr. Prabhakar Kore Hospital & Medical research cente for acute ischemic stroke, 68 samples were enrolled and the patients, who have chronic renal failure, hemorrhage, malignancies etc. were excluded. Almost 60% of the samples were selected from the average admission cases in previous year.

RESULTS AND INTERPRETATION

DEMOGRAPHIC ANALYSIS

In this section, the distribution of demographic details of the patients who were admitted in the hospital with acute ischemic disorder is interpreted along with graphical representation

Gender Distribution

Among the 68 patients admitted in the hospital, 47 (69.1%) were male and 21 (30.9%) were female. The table 5.1 shows the distribution of gender and the corresponding graphical representation is shown in fig 5.1

Distribution of gender		
Gender	**Frequency**	**Percentage**
Male	47	69.1
Female	21	30.9

Table 1: Distribution of gender

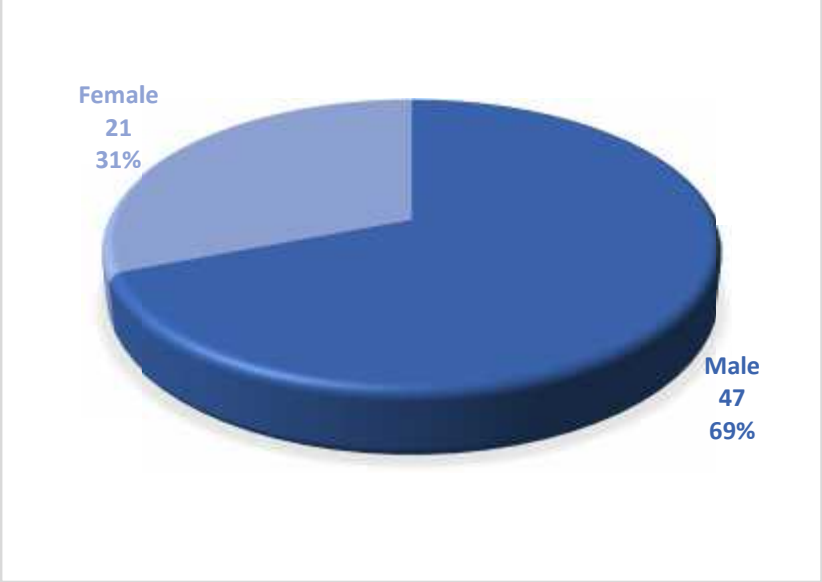

Fig 5.1 Pie-chart representing distribution of gender

Age Distribution

On analysing the 68 patients, 4 patients (5.9) were in the age group of 18-30, 9 patients are in the age group of 31-45, 25 patients were in the age group of 46-60, 26 patients were in the age group of 46-60, and 4 patients were in the age group of 76-90. The table 5.2 shows the distribution of age group and the corresponding graphical representation shown in fig 5.2.

Distribution of age groups		
Age Groups	**Frequency**	**Percentage**
15-30	4	5.9
31-45	9	13.2
46-60	25	36.8
61-75	26	38.2
76-90	4	5.9

Table 5.2 Distribution of age group

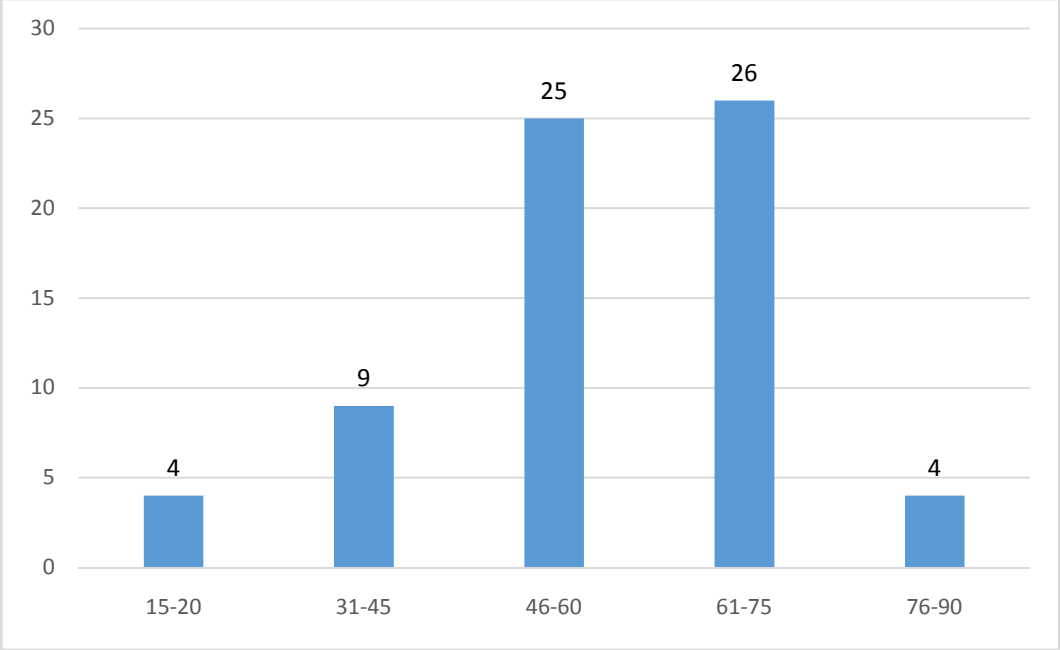

Fig 5.2 Graphical representation of age group distribution

Distribution of lifestyle habits of the patients

Among 68 patients with acute ischemic stroke, 50 patients were without any habits of drinking, smoking or tobacco chewing, 3 patients were alcoholic, 3 patients were smokers, 7 patients had the habit of tobacco chewing, 2 patients have habits in the past, and remaining patients have 2 or more habits. Table 5.3 shown below is the distribution of lifestyle habits and the corresponding graphical representation is shown in fig 5.3

Lifestyle Habits of patients		
Habits	**Frequency**	**Percentage**
Without any habits	50	73.5
Alcoholic	3	4.4
Smoking	3	4.4
Tobacco Chewing	7	10.3
Both Alcoholic and Smoking/Tobacco Chewing	2	2.9
Habits in the past or occasional	2	2.9
Smoking, Alcoholic, and Tobacco Chewing	1	1.5

Table 5.3 Table showing distribution of lifestyle habits

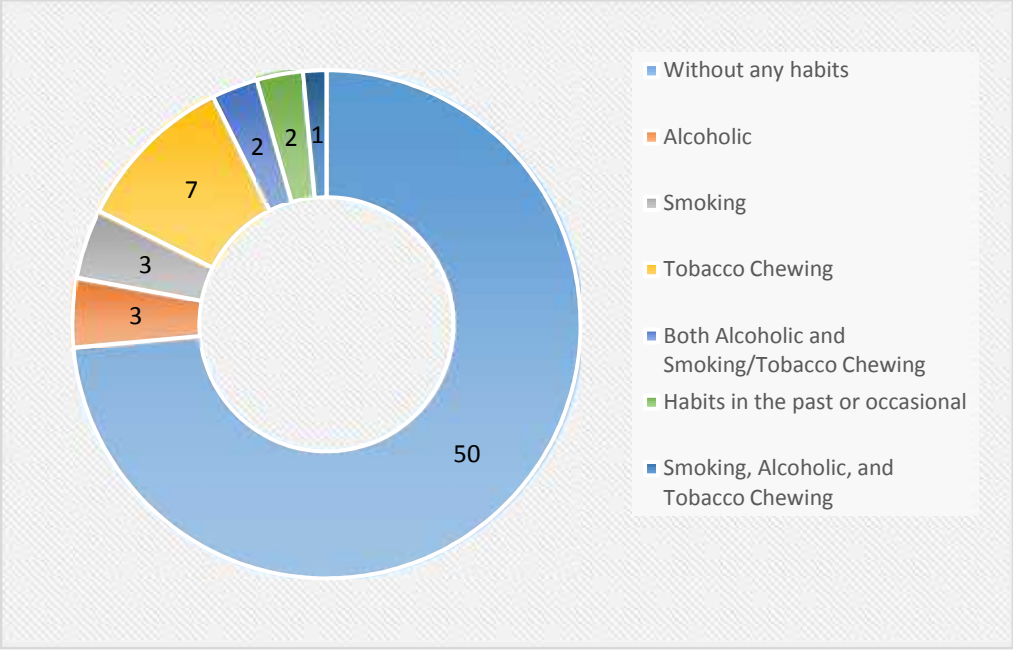

Fig 5.3 Graphical representation of lifestyle habit distribution

Distribution of Eating habits of patients

In analysing the distribution of eating routines of patient, 22 patients have the routine of eating only vegetarian foods, and 46 patients have mixed routine in their eating habits. The table 5.4 showing the distribution of eating habits of the patients and the corresponding graphical representation is shown in fig 5.4

Distribution of Eating habits of patients		
Veg / Mixed	**Frequency**	**Percentage**
Only vegetarian	22	32.4
Mixed	46	67.6

Table 5.4 Table showing distribution of Diet

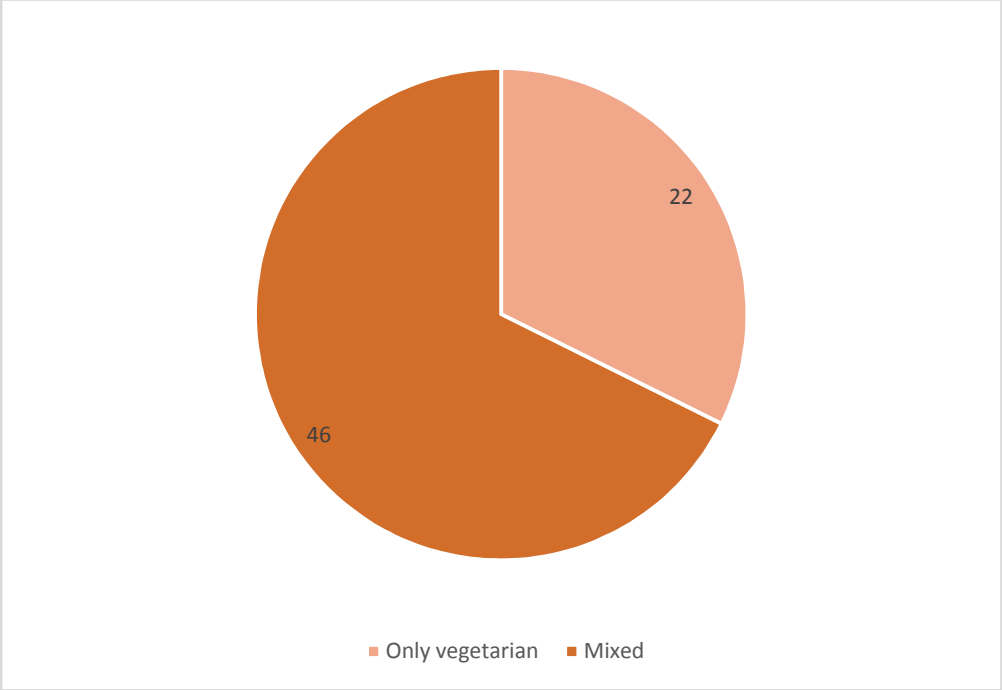

Fig 5.4 Graphical representation of diet distribution

CLINICAL DATA ANALYSIS

Distribution of Comorbidities along with Stroke

Analysing the co-morbidities, 13 patients has only hypertension (HTN), 5 patients has only Type 2 Diabetes mellitus (T2DM), 12 patients have both HTN as well as T2DM, 8 patients have other comorbities such as preeclampsia, mitral stenosis, hypothyroidism, etc., major of the patients were observed without any comorbidities and counted as 21. Table 5.5 shown below is the distribution of comorbidities and the corresponding graphical representation is shown in fig 5.5

Distribution of Comorbidities along with Stroke		
Comorbidities	**Frequency**	**Percentage**
Only HTN	13	19.1
Only T2DM	5	7.4
HTN with T2DM	12	17.6
HTN with other comorbidity	8	11.8
Other comorbidities	7	10.3
Presence of more than 2 comorbidities	2	2.9
Without any Comorbidities	21	30.9

Table 5.5 Table showing distribution of comorbidities

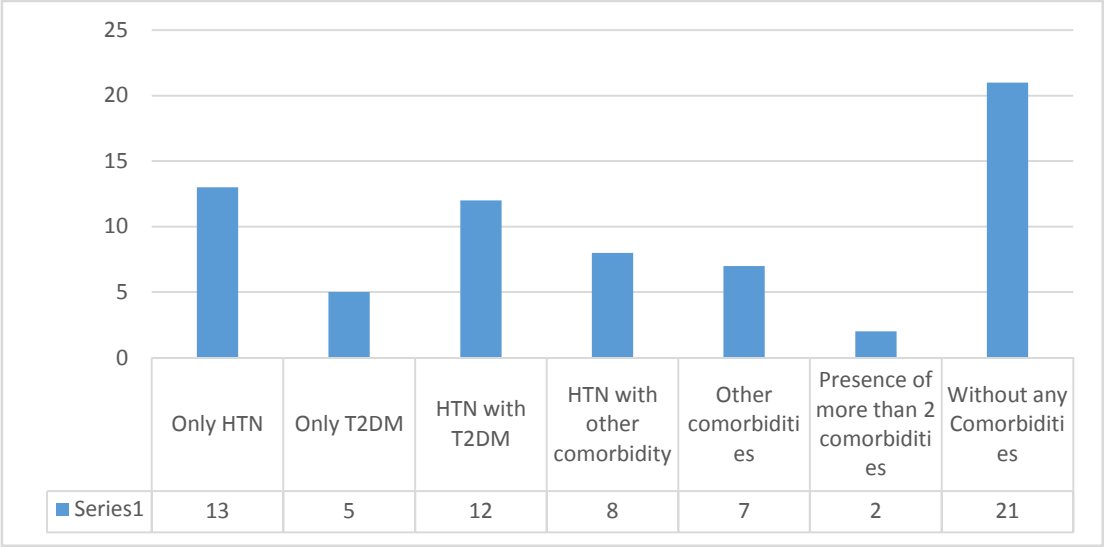

Fig 5.5 Graphical representation of co morbidities

Distribution of Neutrophil Lymphocyte ratio

The blood sample of 68 enrolled patients was taken to calculate NLR. On analysing the NLR data, 12 people admitted in hospital have normal NLR of range 1-3, 29 people (42.6%) admitted in hospital have NLR of range 3 to 6, 16 patients (23.5%) have NLR ranging from 6-9 NLR, 8 patients (11.8%) have NLR ranging from 9-18, and 3 people (4.4) have NLR ranged above 18. Table 5.6 shown below is the distribution of NLR and the corresponding graphical representation is shown in fig 5.6

Distribution of Neutrophill-Lymphocyte Ratio		
NLR	**Frequency**	**Percentage**
1-3 (Normal NLR)	12	17.6
3-6 (Mild Stroke)	29	42.6
6-9 (Mild to moderate Stroke)	16	23.5
9-18 (Moderate Stroke)	8	11.8
>18 (Severe Stroke)	3	4.4

Table 5.6 Table showing distribution of NLR

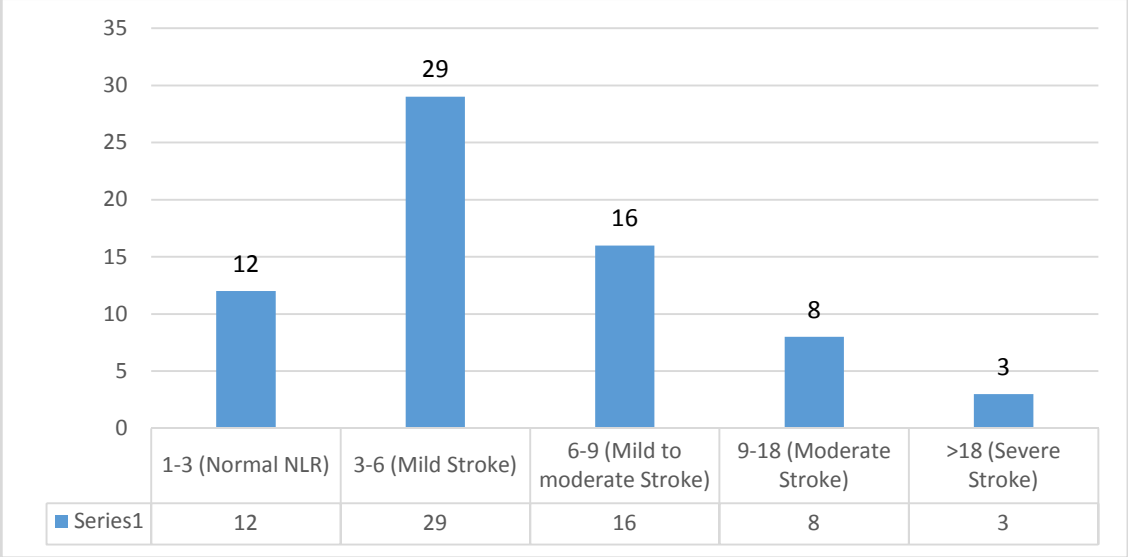

Table 5.6 Graphical representation of distribution of NLR

Distribution of NIHSS

NIHSS was taken on the admission of AIS patient and was found that almost 13 patients (19.1%) were affected by minor stroke, 45 patients (66%) were affected by moderate stroke, 6 patients (8.8%) were found to be in the stroke scale of moderate to severe, and only 8 patients (5.9%) were severely affected. Table 5.7 shown below is the distribution of NIHSS and the corresponding graphical representation is shown in fig 5.7

Distribution of NIHSS		
NLR	**Frequency**	**Percentage**
Minor Stroke	13	19.1
Moderate Stroke	45	66.2
Moderate to Severe Stroke	6	8.8
Severe Stroke	4	5.9

Table 5.7 Table showing distribution of NIHSS

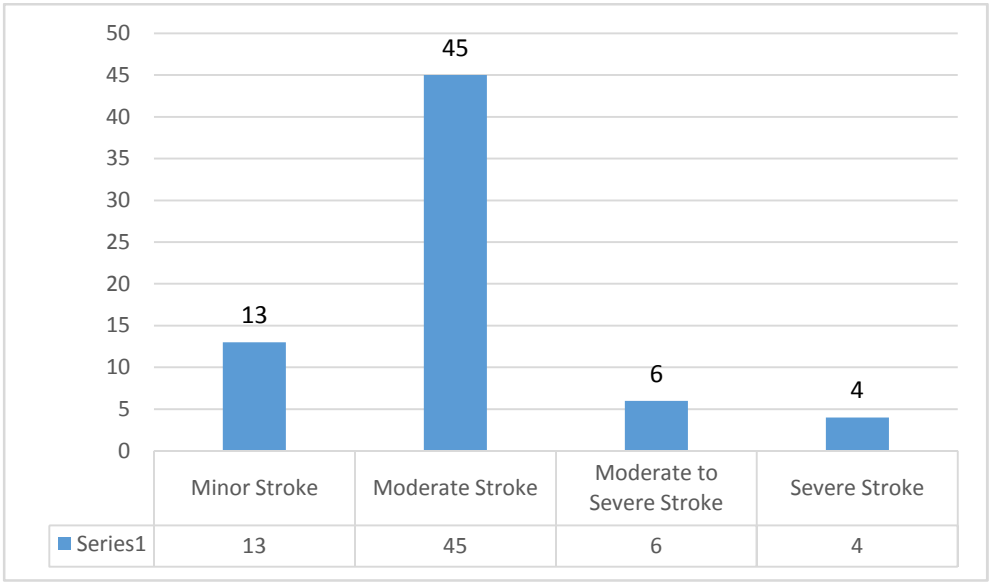

Fig 5.7 Graphical representation of distribution of NIHSS

Distribution of MRS

Among the enrolled patients, 12 patients (17.6%) shows no significant disability, 15 patient (22.1%) shows slight disability, 14 patients (20.6%) shows moderate disability, 13 patients (19.1%) shows moderately severe disability, 8 patients (11.8%) shows severe disability and one patient (1.5%) was passed away. Table 5.8 shown below is the distribution of MRS and the corresponding graphical representation is shown in fig 5.8

Distribution of MRS (Modified Rankin Scale)		
MRS	**Frequency**	**Percentage**
No symptoms	5	7.4
No significant disability	12	17.6
Slight disability	15	22.1
Moderate disability	14	20.6
Moderately Severe Disability	13	19.1
Severe disability	8	11.8
Dead	1	1.5

Table 5.8 Table showing distribution of MRS

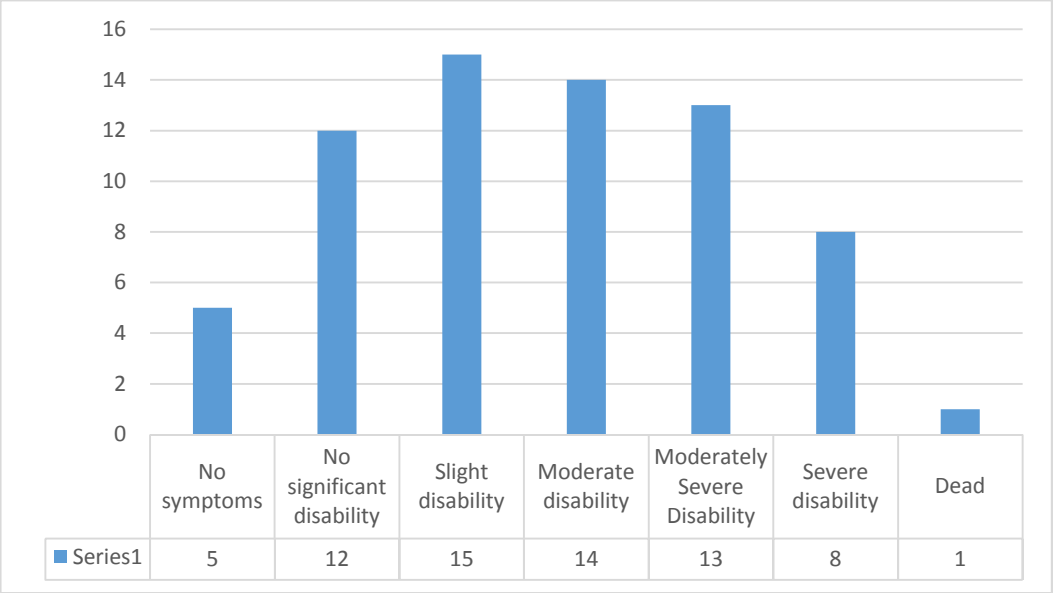

Fig 5.8 Graphical representation distribution of MRS

Distribution of no. of days patients admitted in hospital

From the analysis, 7 patients stayed less than 4 days, 41 patients stayed in the range of 5-8 days, 17 patients stayed 9-12 days, 2 patients stayed 13-16 days and only one stayed for 18 days. Table 5.9 shown below is the distribution of no. of days the patient was admitted and the corresponding graphical representation is shown in fig 5.9

Distribution of No. of days Patients admitted in Hospital		
Duration	**Frequency**	**Percentage**
<= 4 days	7	10.3
5-8 days	41	60.3
9-12 days	17	25.0
13-16 days	2	2.9
17-20 days	1	1.5

Table 5.9 Table showing distribution of admission days of patient

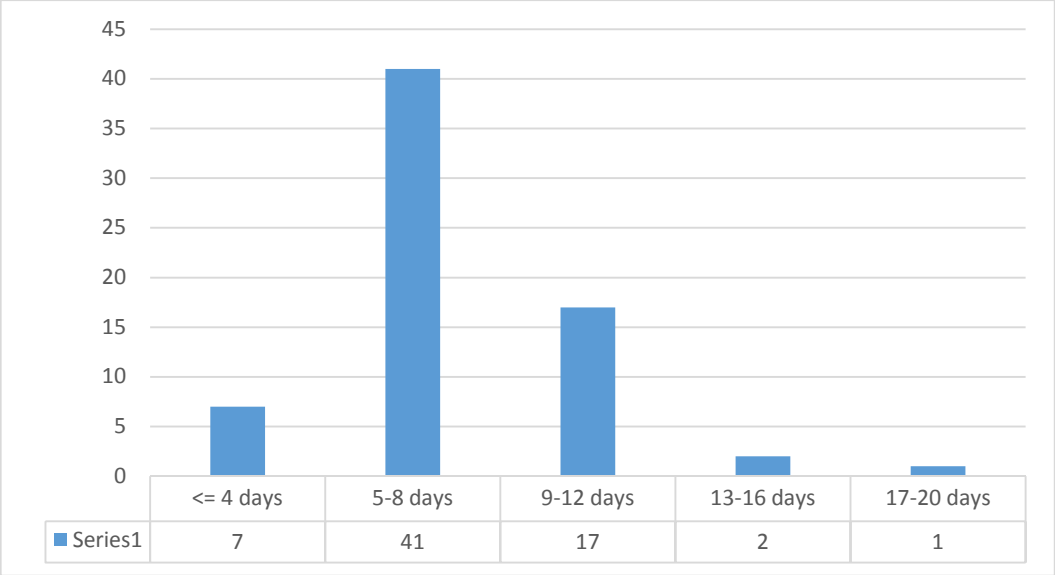

Fig 5.9 Graphical representation showing distribution of admission days

Chi-Square Analysis

Association between Lifestyle Habits and Duration of Hospital Stay

On finding the association between the lifestyle of the patients and their duration of hospital stay, the pearson chi square analysis shows significant results (p value =0.016 <0.05). Table 5.10 shown below is the statistical crosstab between lifestyleHabits and Duration of Hospital Stay and the corresponding Chi square table is shown in fig 5.11

		Duration of Hospital stay				
		<= 4 days	5-8 days	9-12 days	13-16 days	17-20 days
Lifestyle habits of patient	WIthout smoking/drinking/TC	6	31	11	1	1
	Alcoholic	0	2	1	0	0
	Smoker	0	2	1	0	0
	Tobacco Chewer	0	4	3	0	0
	Alcoholic with TC/Smoker	0	1	1	0	0
	Habits in the past or occasional	1	1	0	0	0
	Smoker, Alcoholic and TC	0	0	0	1	0

Table 5.10 Crosstab of association between Lifestyle Habits and Duration of Hospital Stay

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	41.130[a]	24	.016
Likelihood Ratio	16.211	24	.880
Linear-by-Linear Association	1.075	1	.300

Table 5.11 Chi square table of Association between Lifestyle Habits and Duration of Hospital Stay

Association between Lifestyle habits of Patient and NLR

From the analysis, lifestyle habits of the patients are significantly associated with NLR ratio. The pearson chi square analysis shows significant results (p value =0.049 <0.05). Table 5.12 shown below is the statistical crosstab between Lifestyle habits of Patient and NLA and the corresponding Chi square table is shown in fig 5.13

		NLR Ratio				
		Normal	**Possible Stroke**	**Mild Stroke**	**Moderate Stroke**	**Severe Stroke**
Lifestyle habits of Patient	**Without Drinking/smoking**	10	23	11	4	2
	Alcoholic	0	1	1	1	0
	Smoker	0	1	1	1	0
	Tobacco Chewer	0	3	3	1	0
	Alcoholic with TC / Smoker	1	0	0	1	0
	Habits in the past or occasional	1	1	0	0	0
	Smoker, Alcoholic and TC	0	0	0	0	1

Table 5.12 Crosstab of association between Lifestyle Habits and Duration of NLR

Chi-Square Tests			
	Value	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	36.472[a]	24	.049
Likelihood Ratio	23.237	24	.506
Linear-by-Linear Association	1.893	1	.169

Table 5.13 Chi square table of Association between Lifestyle Habits and Duration of Hospital Stay

Association between Diet Methods and Duration of Hospital Stay

Analysing the data, there is a significant association between diet methods and duration of hospital stay. The pearson chi square analysis shows significant results (p value =0.024 <0.05). Table 5.14 shown below is the statistical crosstab between Diet Methods and Duration of Hospital Stay and the corresponding Chi square table is shown in fig 5.15

		Duration of Hospital Stay				
		<=4 days	**5-8 days**	**9-12 days**	**13-16 days**	**17-20 days**
Diet Methods	**Vegetarian**	5	14	2	0	1
	Mixed	2	27	15	2	0

Table 5.14 Crosstab of association between Diet Methods and Duration of Hospital Stay

Chi-Square Tests			
	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	11.284[a]	4	.024
Likelihood Ratio	12.277	4	.015
Linear-by-Linear Association	3.706	1	.054

Table 5.15 Chi square table of association between Diet Methods and Duration of Hospital Stay

Association between Comorbidities and NIHSS

Pearson chi square analysis of comorbidities present in patient along with stroke and NIHSS observed during admission shows statistically significant association with pvalue<0.05 as shown in Table 5.16. The corresponding Chi square table is shown in fig 5.17

	NIH Stroke Scale				
Comorbities an Old CVA present in patient along with Stroke		Minor	Moderate	Moderate to Severe	Severe Stroke
	Only HTN	5	8	0	0
	Only T2DM	0	5	0	0
	HTN with T2DM	2	4	6	0
	HTN with other comorbidity	0	6	2	0
	Other comorbidities	0	7	0	0
	Presence of more than 2 comorbidities	1	1	0	0
	Without any Comorbidities	4	7	9	1

Table 5.16 Crosstab of Association between Comorbidities and NIHSS

Chi-Square Tests			
	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	30.396[a]	18	.034
Likelihood Ratio	38.076	18	.004
Linear-by-Linear Association	4.865	1	.027

Table 5.17 Chi square table of Association between Comorbidities and NIHSS

Association between NLR and Duration of Hospital Stay

To find the association between NLR and duration of hospital stay, chi square analysis was carried out. This results in significant association between NLR and duration of hospital stay (p value < 0.001) as shown in table 5.18. The corresponding Chi square table is shown in fig 5.19

		Duration of Hospital stay				
		<=4 days	**5-8 days**	**9-12 days**	**13-16 days**	**17-20 days**
NLR	**Normal NLR**	3	7	2	0	0
	Possibility of Stroke	4	21	4	0	0
	Mild Stroke	0	8	7	1	0
	Moderate Stroke	0	5	3	0	0
	Severe Stroke	0	0	1	1	1

Table 5.18 Crosstab of Association between NLR and Duration of Hospital Stay

Chi-Square Tests			
	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	46.205[a]	16	.000
Likelihood Ratio	29.327	16	.022
Linear-by-Linear Association	17.480	1	.000

Table 5.19 Chi square table of Association between NLR and Duration of Hospital Stay

Association between NLR and MRS

Table 5.20 also shows the association between NLR of patient's blood and MRS (Modified ranking scale) observed at the discharge time. This association shows statistically significant p value < 0.001. The corresponding Chi square table is shown in fig 5.21

		Modified Ranking Scale						
		No Symptoms	**No Significant Disability**	**Slight Disability**	**Moderate Disability**	**Moderately to Severe Disability**	**Severe Disability**	**Dead**
NLR	**Normal NLR**	5	7	0	0	0	0	0
	Possibility of Stroke	0	5	15	8	1	0	0
	Mild Stroke	0	0	0	6	9	1	0
	Moderate Stroke	0	0	0	0	3	5	0
	Severe Stroke	0	0	0	0	0	2	1

Table 5.20 Crosstab of Association between NLR and MRS

Chi-Square Tests			
	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	138.817[a]	24	.000
Likelihood Ratio	119.953	24	.000
Linear-by-Linear Association	53.844	1	.000

Table 5.21 Chi square table of Association between NLR and MRS

Association between NLR and NIHSS

There is no significant association between NLR and NIHSS (p value >0.05, p=0.561) as shown in table 5.22. The chi square table is shown in table 5.23

		NIHSS			
		Minor	**Moderate**	**Moderate to Severe**	**Severe Stroke**
NLR	**Normal NLR**	4	8	0	0
	Possibility of Stroke	6	20	2	1
	Mild Stroke	2	10	2	2
	Moderate Stroke	0	5	2	1
	Severe Stroke	1	2	0	0

Table 5.22 Crosstab of Association between NLR and MRS

Chi-Square Tests			
	Value	**Df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	10.627[a]	12	.561
Likelihood Ratio	12.920	12	.375
Linear-by-Linear Association	4.057	1	.044

Table 5.23 Chi square table of Association between NLR and MRS

Association between MRS and NIHSS

There is no significant association between NIHSS and Modified ranking scale (p value >0.05, p=0.474) as shown in table 5.24. The chi square table is shown in table 5.25

		NIHSS			
		Minor Stroke	**Moderate Stroke**	**Moderate to Severe**	**Severe Stroke**
MRS	**No symptoms**	2	3	0	0
	No significant Disability	3	8	0	1
	Slight disability	4	10	1	0
	Moderate disability	2	9	3	0
	Severe disability	0	6	1	1
	Dead	1	0	0	0

Table 5.24 Crosstab of Association between MRS and NIHSS

Chi-Square Tests			
	Value	**Df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	17.729[a]	18	.474
Likelihood Ratio	20.253	18	.319
Linear-by-Linear Association	4.152	1	.042

Table 5.25 Chi square table of Association between MRS and NIHSS

Association between Duration of hospital stay and NIHSS

There is no significant association between NIHSS and duration of hospital stay (p value > 0.05, p = 0.561) as shown in table 5.26. The chi square table is shown in table 5.26

		Duration of Hospital stay				
		<= 4 days	**5-8 days**	**9-12 days**	**13-16 days**	**17-20 days**
NIHSS	**Minor Stroke**	1	7	5	0	0
	Moderate Stroke	**6**	29	7	2	1
	Moderate to Severe	0	4	2	0	0
	Severe Stroke	0	1	3	0	0

Table 5.26 Crosstab of Association between duration of hospital stay and NIHSS

Chi-Square Tests			
	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	10.852[a]	12	.542
Likelihood Ratio	11.727	12	.468
Linear-by-Linear Association	.733	1	.392

Table 5.27 Chi square table of Association between duration of hospital stay and NIHSS

The results and its interpretation are discussed in this chapter. Demographic and clinical data are analysed and their frequency and percentage were calculated and shown in respective table. Using Pearson chi square analysis, the association between various factors has been analysed and associated statistical significance are interpreted in this chapter.

DISCUSSION

Stroke affects the central nervous system due to acute injury which stops the cerebral flow to the brain leads to damage in tissues of brain. According to Global Burden of diseases, stroke is ranked as the second most reason for mortality and third most cause of disability (2) and it is also found that most of the survivors of the stroke suffer from disability. So it is most important to find the factors affecting ischemic stroke at the earlier stage in order to control the risk factors.

The main objective of this study is to find whether NLR ratio can be used as short term prognostic marker in patients with acute ischemic stroke. To collect the data from patient, convenience sampling technique is used where the details of the patients were collected from K.L.E.S Dr. Prabhakar Kore Hospital and Medical Research Centre, situated in Belagavi, Karnataka, India. The blood sample of 68 enrolled patients was taken to calculate NLR. During admission, severity of stroke was calculated using NIHSS.

At the time of discharge, the functional outcome was calculated using MRS. Results of chi square analysis inferred the association between NLR and various other clinical factors related to stroke. Analyzing the data showed significant association between NLR and duration of hospital stay, lifestyle of the patient as well as functional outcome at the time of discharge.

CONCLUSION

The present study inferred that NLR is a simple prognostic marker to predict the functional outcome of the patient during discharge using MRS (Modified ranking scale). And also the duration of hospital stay of patient depends on NLR. Lifestyle of patient and diet maintenance also affects the neutrophil and lymphocyte count of the blood (NLR). This study is limited to only 68 samples. Further investigation is needed with large number of samples to confirm the results analyzed.

SUMMARY

- Among the 68 patients admitted in the hospital, 47 were male and 21 were female.

- Among the 68 patients, 4 patients were in the age group of 18-30, 9 patients are in the age group of 31-45, 25 patients were in the age group of 46-60, 26 patients were in the age group of 46-60, and 4 patients were in the age group of 76-90.

- Among 68 patients with acute ischemic stroke, 50 patients were without any habits of drinking, smoking or tobacco chewing, 3 patients were alcoholic, 3 patients were smokers, 7 patients had the habit of tobacco chewing, 2 patients have habits in the past, and remaining patients have 2 or more habits.

- In the distribution of eating routines of patient, 22 patients have the routine of eating only vegetarian foods, and 46 patients have mixed routine in their eating habits.

- In the co-morbidities, 13 patients has only hypertension (HTN), 5 patients has only Type 2 Diabetes mellitus (T2DM), 12 patients have both HTN as well as T2DM, 8 patients have other comorbities such as preeclampsia, mitral stenosis, hypothyroidism, etc., major of the patients were observed without any comorbidities and counted as 21.

- Among the NLR data, 12 people admitted in hospital have normal NLR of range 1-3, 29 people admitted in hospital have NLR of range 3 to 6, 16 patients have NLR ranging from 6-9 NLR, 8 patients have NLR ranging from 9-18, and 3 people have NLR ranged above 18.

- NIHSS obtained on the admission of AIS patient showed that almost 13 patients were affected by minor stroke, 45 patients were affected by moderate stroke, 6 patients were found to be in the stroke scale of moderate to severe, and only 8 patients were severely affected.

- In distribution of MRS,among the enrolled patients, 12 patients shows no significant disability, 15 patient shows slight disability, 14 patients shows moderate disability, 13 patients shows moderately severe disability, 8 patients shows severe disability and one patient was passed away.

- Distribution of no. of days patients admitted in hospital results showed that 7 patients were stayed less than 4 days, 41 patients stayed in the range of 5-8 days, 17 patients stayed 9-12 days, 2 patients stayed 13-16 days and only one stayed for 18 days.

- In the Chi-Square analysis of the association between the lifestyle of the patients and their duration of hospital stay, the pearson chi square analysis shows significant results (p value =0.016 <0.05).

- In the Chi-Square analysis of the associationbetween Lifestyle habits of Patient and NLA, the pearson chi square analysis shows significant results (p value =0.049 <0.05).

- In the Chi-Square analysis of the associationbetween diet methods and duration of hospital stay, the pearson chi square analysis shows significant results (p value =0.024 <0.05).

- In the Chi-Square analysis of the associationbetween Comorbidities and NIHSS, the pearson chi square analysis shows significant results(p value =0.034<0.05).

- In the Chi-Square analysis of the association betweenNLR and Duration of Hospital Stay, the pearson chi square analysis shows significant results(p value =0.000<0.001).

- In the Chi-Square analysis for the association betweenNLR and MRS, the pearson chi square analysis shows significant results(p value =0.000<0.001).

- In the Chi-Square analysis of the association betweenNLR and NIHSS, the pearson chi square analysis shows that there is no significant association between NLR and NIHSS (p value >0.05, p=0.561).

- In the Chi-Square analysis of the association betweenMRS and NIHSS, the pearson chi square analysis shows that there is no significant association between NIHSS and Modified ranking scale (p value >0.05, p=0.474).

- In the Chi-Square analysis of the association between duration of hospital stay and NIHSS, the pearson chi square analysis shows that there is no significant association between NIHSS and duration of hospital stay (p value > 0.05, p = 0.561).

BIBLIOGRAPHY

1. Carr, J.H., et al., Investigation of a new motor assessment scale for stroke patients. Physical therapy, 1985. 65(2): p. 175-180.

2. Overgaard, K., The effects of citicoline on acute ischemic stroke: a review. Journal of Stroke and Cerebrovascular Diseases, 2014. 23(7): p. 1764-1769.

3. Kim, J.-T., et al., Aspirin resistance in the acute stages of acute ischemic stroke is associated with the development of new ischemic lesions. PLoS One, 2015. 10(4): p. e0120743.

4. INGVAR, B.D.H. and N.A. LASSEN, Regional blood flow of the cerebral cortex determined by Krypton85. Acta physiologica scandinavica, 1962. 54(3-4): p. 325-338.

5. Epstein, C., Recombinant tissue plasminogen activator (rt-PA). The Australian nurses' journal. Royal Australian Nursing Federation, 1992. 21(8): p. 29.

6. Malone, K., et al., The immune system and stroke: from current targets to future therapy. Immunology and cell biology, 2019. 97(1): p. 5-16.

7. Ramesh, G., A.G. MacLean, and M.T. Philipp, Cytokines and chemokines at the crossroads of neuroinflammation, neurodegeneration, and neuropathic pain. Mediators of inflammation, 2013. 2013.

8. Chen, Y., et al., Recruitment of endogenous bone marrow mesenchymal stem cells towards injured liver. Journal of cellular and molecular medicine, 2010. 14(6b): p. 1494-1508.

9. Strecker, J.-K., et al., Neutrophil granulocytes in cerebral ischemia–evolution from killers to key players. Neurochemistry international, 2017. 107: p. 117-126.

10. García-Culebras, A., et al., Myeloid cells as therapeutic targets in neuroinflammation after stroke: Specific roles of neutrophils and neutrophil–platelet interactions. Journal of Cerebral Blood Flow & Metabolism, 2018. 38(12): p. 2150-2164.

11. Jickling, G.C., et al., Targeting neutrophils in ischemic stroke: translational insights from experimental studies. Journal of Cerebral Blood Flow & Metabolism, 2015. 35(6): p. 888-901.

12. Yamashima, T., Implication of cysteine proteases calpain, cathepsin and caspase in ischemic neuronal death of primates. Progress in neurobiology, 2000. 62(3): p. 273-295.

13. Qin, B., et al., Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. Modern rheumatology, 2016. 26(3): p. 372-376.

14. Gasparyan, A.Y., et al., The platelet-to-lymphocyte ratio as an inflammatory marker in rheumatic diseases. Annals of laboratory medicine, 2019. 39(4): p. 345-357.

15. Petrone, A.B., et al., The role of arginase 1 in post-stroke immunosuppression and ischemic stroke severity. Translational stroke research, 2016. 7(2): p. 103-110.

16. Huang, G., et al., High platelet-to-lymphocyte ratio are associated with post-stroke depression. Journal of Affective Disorders, 2019. 246: p. 105-111.

17. Gong, P., et al., Neutrophil–lymphocyte ratio predicts post-thrombolysis early neurological deterioration in acute ischemic stroke patients. Brain and Behavior, 2019. 9(10): p. e01426.

18. Campbell, B.C., et al., Endovascular therapy for ischemic stroke with perfusion-imaging selection. New England Journal of Medicine, 2015. 372(11): p. 1009-1018.

19. Jovin, T.G., et al., Thrombectomy within 8 hours after symptom onset in ischemic stroke. New England Journal of Medicine, 2015. 372(24): p. 2296-2306.

20. Tønnesen, J. and U.V. Nägerl, Dendritic spines as tunable regulators of synaptic signals. Frontiers in psychiatry, 2016. 7: p. 101.

21. Pavlov, P.I., Conditioned reflexes: an investigation of the physiological activity of the cerebral cortex. Annals of neurosciences, 2010. 17(3): p. 136.

22. Mietto, B.S., K. Mostacada, and A.M.B. Martinez, Neurotrauma and inflammation: CNS and PNS responses. Mediators of inflammation, 2015. 2015.

23. Matic, A.I., Introduction to the Nervous System, Part 2: The Autonomic Nervous System and the Central Nervous System. AMWA Journal: American Medical Writers Association Journal, 2014. 29(2).

24. Furness, J. and M. Stebbing, The first brain: species comparisons and evolutionary implications for the enteric and central nervous systems. Neurogastroenterology & motility, 2018. 30(2): p. e13234.

25. Fielder, E., T. Von Zglinicki, and D. Jurk, The DNA damage response in neurons: die by apoptosis or survive in a senescence-like state? Journal of Alzheimer's Disease, 2017. 60(s1): p. S107-S131.

26. van Velthoven, C.T., A. Kavelaars, and C.J. Heijnen, Mesenchymal stem cells as a treatment for neonatal ischemic brain damage. Pediatric research, 2012. 71(2): p. 474-481.

27. Warland, J., H. McCutcheon, and P. Baghurst, Maternal blood pressure in pregnancy and stillbirth: a case-control study of third-trimester stillbirth. American journal of perinatology, 2008. 25(05): p. 311-317.

28. Sawicki, M., et al., Reply to Letter to the Editor "Neuroimaging of Intracranial Perfusion and the Clinical Diagnosis of Brain Death: Setting the Gold Standard in Humans". Clinical neuroradiology, 2019. 29(3): p. 579-580.

29. Munro, M.J., A.M. Walker, and C.P. Barfield, Hypotensive extremely low birth weight infants have reduced cerebral blood flow. Pediatrics, 2004. 114(6): p. 1591-1596.

30. Sharpey-Schafer, E., Effects of coughing on intra-thoracic pressure, arterial pressure and peripheral blood flow. The Journal of Physiology, 1953. 122(2): p. 351.

31. Feigin, V.L., et al., Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet Neurology, 2016. 15(9): p. 913-924.

32. STROKE, M.I.A.I., Serum calcium as a severity marker in acute ischemic stroke. 2018.

33. Johnston, S.C., et al., Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. The Lancet, 2007. 369(9558): p. 283-292.

34. Li, X., et al., RF-assisted gadofullerene nanoparticles induces rapid tumor vascular disruption by down-expression of tumor vascular endothelial cadherin. Biomaterials, 2018. 163: p. 142-153.

35. Siegel, J.S., et al., Disruptions of network connectivity predict impairment in multiple behavioral domains after stroke. Proceedings of the National Academy of Sciences, 2016. 113(30): p. E4367-E4376.

36. Sifat, A.E., B. Vaidya, and T.J. Abbruscato, Blood-brain barrier protection as a therapeutic strategy for acute ischemic stroke. The AAPS Journal, 2017. 19(4): p. 957-972.

37. Chowdhury, R. and S.K. Bandyopadhyay, Detection of Stroke: A Proposed Method. IJAR, 2017. 3(4): p. 593-599.

38. Lapchak, P.A. and D.M. Araujo, Advances in ischemic stroke treatment: neuroprotective and combination therapies. Expert Opinion on Emerging Drugs, 2007. 12(1): p. 97-112.

39. Aboyans, V., et al., 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS) Document covering atherosclerotic disease of

extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries Endorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). European heart journal, 2018. 39(9): p. 763-816.

40. Abascal, J.V., et al., Modifiable risk factors in uncontrolled high blood pressure patients of Banjul, Gambia. Correo Científico Médico, 2016. 20(3).

41. Boehme, A.K., C. Esenwa, and M.S. Elkind, Stroke risk factors, genetics, and prevention. Circulation research, 2017. 120(3): p. 472-495.

42. Sacco, R.L., Risk factors and outcomes for ischemic stroke. Neurology, 1995. 45(2 Suppl 1): p. S10.

43. Della-Morte, D., et al., Genetics of ischemic stroke, stroke-related risk factors, stroke precursors and treatments. Pharmacogenomics, 2012. 13(5): p. 595-613.

44. Lindsberg, P.J. and A.J. Grau, Inflammation and infections as risk factors for ischemic stroke. Stroke, 2003. 34(10): p. 2518-2532.

45. Leffert, L.R., et al., Hypertensive disorders and pregnancy-related stroke: frequency, trends, risk factors, and outcomes. Obstetrics and gynecology, 2015. 125(1): p. 124.

46. von Sarnowski, B., et al., Lifestyle risk factors for ischemic stroke and transient ischemic attack in young adults in the Stroke in Young Fabry Patients study. Stroke, 2013. 44(1): p. 119-125.

47. Amen, M.R., Assessment of hypertensive patients' knowledge about lifestyle risk factors and warning signs of stroke. Journal of Contemporary Medical Sciences, 2016. 2(5): p. 28-32.

48. Herzberg, M., et al., Prehospital stroke diagnostics based on neurological examination and transcranial ultrasound. Critical ultrasound journal, 2014. 6(1): p. 3.

49. Walter, S., et al., Diagnosis and treatment of patients with stroke in a mobile stroke unit versus in hospital: a randomised controlled trial. The Lancet Neurology, 2012. 11(5): p. 397-404.

50. John, S., et al., Performance of CT angiography on a mobile stroke treatment unit: implications for triage. Journal of Neuroimaging, 2016. 26(4): p. 391-394.

51. Heit, J.J., E.S. Sussman, and M. Wintermark, Perfusion computed tomography in acute ischemic stroke. Radiologic Clinics, 2019. 57(6): p. 1109-1116.

52. Leigh, R., et al., Imaging the physiological evolution of the ischemic penumbra in acute ischemic stroke. Journal of Cerebral Blood Flow & Metabolism, 2018. 38(9): p. 1500-1516.

53. Doyle, K.P., R.P. Simon, and M.P. Stenzel-Poore, Mechanisms of ischemic brain damage. Neuropharmacology, 2008. 55(3): p. 310-318.

54. Chelluboina, B. and R. Vemuganti, Chronic kidney disease in the pathogenesis of acute ischemic stroke. Journal of Cerebral Blood Flow & Metabolism, 2019. 39(10): p. 1893-1905.

55. Siepmann, T., et al., Selective serotonin reuptake inhibitors to improve outcome in acute ischemic stroke: possible mechanisms and clinical evidence. Brain and Behavior, 2015. 5(10): p. e00373.

56. Deb, P., S. Sharma, and K. Hassan, Pathophysiologic mechanisms of acute ischemic stroke: An overview with emphasis on therapeutic significance beyond thrombolysis. Pathophysiology, 2010. 17(3): p. 197-218.

57. Reiche, E.M.V., et al., Immune-inflammatory, oxidative stress and biochemical biomarkers predict short-term acute ischemic stroke death. Metabolic brain disease, 2019. 34(3): p. 789-804.

58. Mărgăritescu, O., et al., Histopathological changes in acute ischemic stroke. Rom J Morphol Embryol, 2009. 50(3): p. 327-39.

59. Nguyen, T.-V.V., et al., Multiplex immunoassay characterization and species comparison of inflammation in acute and non-acute ischemic infarcts in human and mouse brain tissue. Acta neuropathologica communications, 2016. 4(1): p. 100.

60. Xue, J., et al., Neutrophil-to-lymphocyte ratio is a prognostic marker in acute ischemic stroke. Journal of Stroke and Cerebrovascular Diseases, 2017. 26(3): p. 650-657.

61. Sollberger, G., D.O. Tilley, and A. Zychlinsky, Neutrophil extracellular traps: the biology of chromatin externalization. Developmental cell, 2018. 44(5): p. 542-553.

62. Pikija, S., et al., Neutrophil to lymphocyte ratio predicts intracranial hemorrhage after endovascular thrombectomy in acute ischemic stroke. Journal of neuroinflammation, 2018. 15(1): p. 319.

63. Kotfis, K., et al., Could Neutrophil-to-Lymphocyte Ratio (NLR) serve as a potential marker for delirium prediction in patients with acute ischemic stroke? A Prospective Observational Study. Journal of Clinical Medicine, 2019. 8(7): p. 1075.

64. Nam, K.-W., et al., High neutrophil-to-lymphocyte ratio predicts stroke-associated pneumonia. Stroke, 2018. 49(8): p. 1886-1892.

65. Zhang, W.-B., et al., A high neutrophil-to-lymphocyte ratio predicts hemorrhagic transformation of large atherosclerotic infarction in patients with acute ischemic stroke. Aging (Albany NY), 2020. 12(3): p. 2428.

66. Song, Q., et al., Increased neutrophil-to-lymphocyte ratios are associated with greater risk of hemorrhagic transformation in patients with acute ischemic stroke. Current Neurovascular Research, 2018. 15(4): p. 326-335.

67. Lee, J.-H., et al., Characteristics of platelet indices, neutrophil-to-lymphocyte ratio and erythrocyte sedimentation rate compared with C reactive protein in patients with cerebral infarction: a retrospective analysis of comparing haematological parameters and C reactive protein. BMJ open, 2014. 4(11).

68. Kocaturk, O., et al., The relationship among neutrophil to lymphocyte ratio, stroke territory, and 3-month mortality in patients with acute ischemic stroke. Neurological Sciences, 2019. 40(1): p. 139-146.

69. Yu, S., et al., Neutrophil to lymphocyte ratio and early clinical outcomes in patients with acute ischemic stroke. Journal of the neurological sciences, 2018. 387: p. 115-118.

70. Segatore, M., Understanding central post-stroke pain. Journal of Neuroscience Nursing, 1996. 28(1): p. 28-35.

71. Zhang, J., Ren, Q., Song, Y., He, M., Zeng, Y., Liu, Z., & Xu, J. Prognostic role of neutrophil-lymphocyte ratio in patients with acute ischemic stroke. Medicine, 2017. 96(45), e8624.

72. Wang, Y., Liu, G., Hong, D., Chen, F., Ji, X., & Cao, G. White matter injury in ischemic stroke. Progress in neurobiology, 2016. 141, 45–60.

ANNEXURE I

ETHICAL COMMITTEE CERTIFICATE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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Ref: MDC/DOME/ 59 **Date: 24/11/2018**

To,

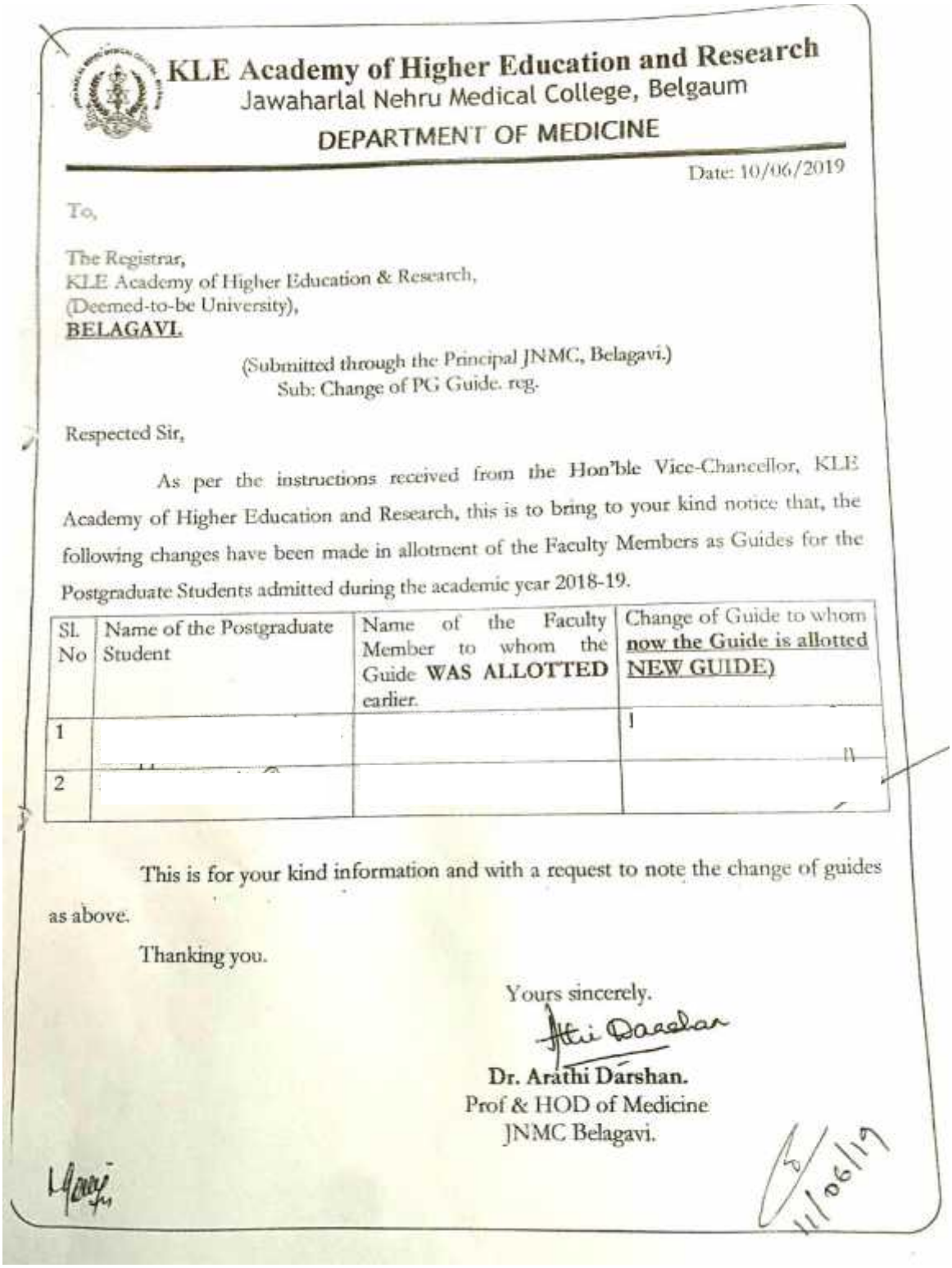
PG student in Medicine,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"PROGNOSTIC ROLE OF NEUTROPHIL –LYMPHOCYTE RATIO IN PATIENTS WITH ACUTE ISCHAEMIC STROKE – ONE YEAR CROSS- SECTIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.



KLE Academy of Higher Education and Research
Jawaharlal Nehru Medical College, Belgaum
DEPARTMENT OF MEDICINE

Date: 10/06/2019

To,

The Registrar,
KLE Academy of Higher Education & Research,
(Deemed-to-be University),
BELAGAVI.

(Submitted through the Principal JNMC, Belagavi.)
Sub: Change of PG Guide. reg.

Respected Sir,

As per the instructions received from the Hon'ble Vice-Chancellor, KLE Academy of Higher Education and Research, this is to bring to your kind notice that, the following changes have been made in allotment of the Faculty Members as Guides for the Postgraduate Students admitted during the academic year 2018-19.

Sl. No	Name of the Postgraduate Student	Name of the Faculty Member to whom the Guide **WAS ALLOTTED** earlier.	Change of Guide to whom **now the Guide is allotted NEW GUIDE)**
1			
2			

This is for your kind information and with a request to note the change of guides as above.

Thanking you.

Yours sincerely.

Dr. Arathi Dárshan.
Prof & HOD of Medicine
JNMC Belagavi.

11/06/19

ANNEXURE II

INFORMED CONSENT

TITLE OF RESEARCH AND STUDY:LYMPHOCYE NEUTROPHIL RATIO AS A PROGNOSTIC FACTOR IN ACUTE ISCHEMIC STROKE

Principal Investigator:-

Dr. _____

Post Graduate Student,

Department Of General Medicine,

JNMC, Belgaum**.**

Guide:-

Dr. _____

Professor

Department of General Medicine,

JNMC, Belgaum.

Introduction and Purpose:-

This research is intended to study if NLR can be used as prognostic factor in acute ischemic stroke. The principal investigator of the study is Dr. _____ under the guidance of Dr. _____ This study is aimed to investigate Prognostic role of Lymphocyte Neutrophil ratio in acute ischemic stroke

Procedure:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood samples for the necessary investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while doing venipuncture for investigations. It may cause pain or slight discomfortyou may/may not be benefitted by these investigations but you will be part of this study which is going to be useful to others in the future.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study. If you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy:

Does not apply to this research

Financial incentives for participation:

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

In case of the queries during study or in future you may contact following persons,

1 **DR. Roopa M Bellad** $_{MD}$
Professor of Paediatrics
J.N. Medical College,
K.A.H.E.R, Belagavi – 10

2. **Dr. _____**
Professor,
Dept of General Medicine,
JNMC, Belagavi-10

3. **Dr. _____**
PG Department of general medicine
JNMC,Belagavi-10

CONSENT FORM

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this consent form, or it has been read to me and has been explained to me in my vernacular language and all my questions have been answered. I will be given a copy of this consent form.

Signature / Left Thumb print of the Participant or legally authorized representative

Participant's name:…….....

Signature / Left thumb impression:……...

of the participant

Name of the legally authorized

representative / guardian:……..

Signature / Left thumb impression:…….....

Witness' name:…….....

Signature / Left thumb impression: …….....

Investigator's name and signature:…….....

Date:

Place:

ANNEXURE III

CASE PROFORMA

NAME: IP NO:

AGE/SEX: DOA:

ADDRESS: DOD:

PRESENTING COMPLAINTS WITH DURATION:

HISTORY OF PRESENTING ILLNESS:

PAST HISTORY:

Any other neurological illness:

Hypertension:

Diabetes:

Cardiac illness:

Any other illness

FAMILY HISTORY:

PERSONAL HISTORY:

Diet

Smoking

Alcohol

Tobacco

High risk behavior

GENERAL EXAMINATION:

Pulse: Weight Temperature:

B.P:

Skin

Icterus Neuro-cutaneous markers

Pallor

Cyanosis Pedal edema

Lymphadenopathy

Clubbing

Cardiovascular System

Heart sounds

Murmurs

Respiratory System

Breath sounds

Added sounds

Per Abdomen

Neurological Examination

(Handedness-)

Cranial Nerves examination:

Olfactory:

Optic:

Oculomotor Trochlear & Abducent nerve:

Pupils:

Eye movements:

Trigeminal nerve

Facial nerve

Vestibulocochlear nerve

Glossopharyngeal nerve

Vagus nerve

Spinal accessory nerve

Hypoglossal nerve

Motor system

Nutrition and bulk

Deformity

Involuntary movements

		Right	Left
Tone			
Power:			
Shoulder	Flexion		
	Extension		
	Adduction		
	Abduction		
Elbow	Flexion		
	Extension		
	Adduction		
	Abduction		
Wrist	Flexion		
	Extension		
Fingers	Flexion		
	Extension		
Small Muscles of hand			
Hand grip			
Hip	Flexion		
	Extension		
	Adduction		
	Abduction		
Knee	Flexion		
	Extension		
Ankle	Plantar Flexion		
	Dorsiflexion		
Toes	Flexion		
	Extension		

Cerebellar signs

Sensory system:

Pain
Touch
Temperature
Vibration
Joint and position

Reflexes

	Biceps	Supinator	Knee	Ankle
Right				
Left				

Corneal
Conjunctival
Abdominal

Cremasteric
Plantar

Gait
Signs of meningeal irritation:

Neck stiffness

Kernig's sign

Brudznski's sign

Diagnosis

ANNEXURE IV

KEY TO MASTERCHART

1. IP NUMBER : In patient number
2. MRI (or) CT of brain
3. NLR Ratio : Neutrophil Lymphocyte ratio
4. NIHSS : National Institute of Health Stroke Scale

	IP NUMBER	AGE	SEX	MRI REPORT/CT REPORT	Comormidities	Habits	Diet	Neutrophils	Lymphocytes	NLR ratio	NIHSS	Modified Rankin Scale	Duration of hospital stay
1	953545	57	M	Left temporal,occipital,lentiform nucleus,caudate infarct	HTN,T2DM	NILL	Vegetarian	66	25	2.64	11	1	6
2	953723	72	M	Acute infarct in left parietal region	HTN,OLD CVA	NILL	Mixed	83	15	5.53	4	2	7
3	953388	72	M	Sabcute infarct in right mca and pca territories	HTN,T2DM	Tobacco chewer	Vegetarian	77	12	6.41	10	4	7
4	953676	78	F	Subacute infarct in right thalamus	HTN	NILL	Veg	70	18	3.88	3	2	5
5	953739	18	F	Subacute infarct in right fronto-parieto-occipital region	NILL	NILL	Mixed	66	24	2.75	7	1	5
6	954018	72	M	Acute infarct in left MCA territory	HTN,OLD CVA	NILL	Mixed	81	10	8.1	22	4	6
7	954059	45	F	Acute infarct in bilateral medial thalami	NILL	NILL	Vegetarian	71	18	3.94	9	2	4
8	954746	56	F	Acute infarct in rt fronto-parieto-occipital,coronaregion	HTN,T2DM	NILL	Mixed	80	14	5.71	5	3	8
9	954800	63	M	Subacute infarct in b/l occipital,post.parietal,b/l cerebellar	HTN,T2DM,SEIZURE DISORI	NILL	Vegetarian	59	36	1.55	4	0	6
10	954722	26	F	Acute infarct in left MCA	H/O PREECCLAMPSIA	NILL	Mixed	92	7	13.14	15	5	5
11	953382	75	M	Subacute infarct in right caudate,right corona radiata	HTN,T2DM	Smoker	Mixed	84	8	10.5	18	4	9
12	954996	67	M	Subacute infarct in right frontal region	HTN,T2DM	NILL	Vegetarian	61	29	2.1	2	0	4
13	949356	56	M	Subacute infarct in right MCA artery	HTN,IHD	Tobacco chewer	Mixed	82	12	6.83	10	5	10
14	954999	57	M	Acute infarct in right MCA	HTN	Tobacco chewer	Vegetarian	72	20	3.6	1	1	6
15	955771	59	M	Subacute infarct in right fronto-parieto-temporal,temporal occipital,body and tail of caudate nucle	HTN,T2DM	NILL	Mixed	68	22	3.09	11	1	8
16	955883	70	F	Hyperacute infarct in posterior limb of internal capsule	T2DM	NILL	Mixed	68	22	3.09	5	1	8
17	955643	55	M	Left MCA territory infarct	NILL	Tobacco chewer	Mixed	71	18	3.94	12	2	5
18	956296	69	F	Subacute infarct in right MCA	HTN,T2DM	NILL	Mixed	82	12	6.83	12	4	10
19	956509	79	M	Acute infarct in corona radiata and lentiform nucleus	HTN	NILL	Mixed	87	11	7.9	9	4	14
20	956792	27	F	Subacute infarct in bilateral MCA territories	NILL	NILL	Mixed	78	16	4.87	16	3	8
21	957757	79	M	Subacute infarct in medulla	NILL	Smoker	Mixed	80	16	5	6	3	5
22	956103	75	M	Subacute infarct in right cerebellum and b/l occipital	HTN	NILL	Mixed	91	5	18.2	3	6	9
23	959165	48	M	Subacute infarct in right MCA & PCA territories	HTN	NILL	Vegetarian	78	22	3.54	5	2	4
24	959730	47	M	Subacute infarct in rt corona radiata,posterior limb of right internal capsule and cortical regions o	HTN,DEPRESSION	NILL	Vegetarian	69	21	2.55	6	1	3
25	959925	42	F	Subacute infarct in perirolandic,left frontal,parietal & occipital regions	NILL	NILL	Vegetarian	65	24	2.7	9	1	5
26	960284	60	M	Subacute infarct in left thalamus	HTN,T2DM	NILL	Vegetarian	81	14	5.78	4	3	10
27	952620	68	F	Acute infarct in left temporal tegion	HTN,OLD CVA	NILL	Mixed	78	12	6.5	10	3	7
28	960097	43	F	Subacute infarct-b/l cerebellar lobes,b/l occipital lobes,left posterior temporal,left thalamus	HTN	NILL	Mixed	87	10	8.7	13	3	8
29	961623	48	M	Subacute infarct in medulla on left side	HTN,OLD CVA,T2DM	OCCASIONAL ALCO	Mixed	65	35	1.85	8	0	6
30	961562	78	F	Focal hyper acute infarcts in right frontal and right insular cortex	NILL	NILL	Mixed	68	27	2.51	3	1	12
31	961505	67	M	Focal hyperacute infarcts in midbrain on left side,right frontal region and right centrum ovale	HTN,OLD CVA	NILL	Vegetarian	94	5	18.8	8	5	18
32	961636	70	F	Acute infarct in right fronto-parietal region,insular cortex,basal ganglia & corona radiata	NILL	NILL	Mixed	84	12	7	7	4	9
33	966007	73	M	Subacute infarct in right corona radiata and posterior limb of right internal capsule	HTN	Smoker,Alcoholic	Vegetarian	89	8	11.12	6	4	11
34	962754	48	M	Subacute infarct in right middle cerebral artery	NILL	Alcoholic	Mixed	91	6	15.16	8	5	7
35	964279	41	M	Acute infarct in head,body,tail of right-caudate nucleus,lentiform nucleus,posterior limb of right i	T2DM	Alcoholic	Mixed	85	13	6.53	8	3	9
36	961830	63	M	Subacute infarct in left MCA and PCA territories	HTN,T2DM	NILL	Vegetarian	72	20	3.6	11	2	4
37	965581	63	M	Hyperacute infarct in posterior limb of internal capsule,left thalamus & left temporal lobe	T2DM	NILL	Mixed	81	16	5.06	6	3	5
38	965601	70	M	Subacute infarct in left-temporal,occipital & left thalamus	NILL	NILL	Mixed	67	19	3.52	5	3	10
39	962476	52	M	Hyperacute infarct in left MCA	NILL	NILL	Vegetarian	92	8	11.5	15	5	8
40	966035	50	M	Subacute infarct in left MCA and PCA territories	OLD CVA	Alcoholic,Tobacco chewer	Vegetarian	67	27	2.48	8	1	5

	IP NUMBER	AGE	SEX	MRI REPORT/CT REPORT	Comormidities	Habits	Diet	Neutrophils	Lymphocytes	NLR ratio	NIHSS	Modified Rankin Scale	Duration of hospital stay
41	967888	68	M	Acute lacunar infarct in left posterior parietal lobe	HTN	Smoker,Alcoholic,Tobacco chewer	Mixed	72	4	18	7	5	13
42	968158	58	M	Subacute infarct in the medulla on left side	HTN,T2DM	NILL	Mixed	61	33	1.84	5	0	4
43	967723	25	F	Subacute infarct in posterior limb of right internal capsule and right thalamus	NILL	NILL	Mixed	83	14	5.92	2	2	5
44	967680	47	M	Subacute infarct in left frontal,parietal and occipital regions	NILL	NILL	Mixed	64	28	2.28	2	1	9
45	970106	36	F	Subacute infarct in posterior limb of internal capsule	T2DM	NILL	Mixed	74	21	3.52	10	3	6
46	970132	50	F	Subacute infarct in left fronto-temporal,left insular cortex & left external capsule	HTN	NILL	Mixed	80	15	5.33	4	2	7
47	971057	69	M	Acute ACA territory infarct	HTN	NILL	Mixed	84	13	6.46	4	3	7
48	970709	73	M	Subacute infarct in left thalamus	NILL	NILL	Mixed	84	11	7.63	2	4	10
49	970398	40	M	Subacute infarct in left MCA & ACA-MCA-PCA watershed territory	NILL	NILL	Vegetarian	88	10	8.8	9	4	6
50	970114	60	M	Subacute infarct in right MCA territory with mass effect	HTN	ALcoholic	Mixed	77	14	5.5	12	2	8
51	972180	41	F	Hyperacute infarct in right MCA territory	HYPOTHYROIDISM	NILL	Vegetarian	70	21	3.33	8	2	5
52	972678	52	F	Subacute infarct in right ACA territory	OLD CVA,HYPOTHYROIDISI	NILL	Mixed	73	20	3.65	5	2	5
53	974067	65	F	Acute infarct in right corona radiata,right putamen and right basal ganglia	T2DM	NILL	Vegetarian	60	18	3.33	10	2	8
54	974055	48	M	Subacute infarct in right lentiform nucleus,body of right caudate nucleus & corona radiata	HTN	NILL	Mixed	84	13	6.46	9	4	6
55	972515	65	M	Subacute infarct in b/l thalami,midbrain,left hippocampus & b/l cerebellar lobe	HTN	NILL	Mixed	83	10	8.3	21	4	10
56	974245	65	M	Right MCA infarct	HTN,OLD CVA	NILL	Vegetarian	54	36	1.5	5	0	5
57	974247	33	M	Right middle cerebral artery infarct	NILL	Tobacco chewer	Mixed	79	12	6.58	16	3	9
58	974741	41	M	Right middle cerebral artery infarct with hyperdense MCA	IHD	Tobacco chewer	Mixed	77	14	5.5	7	2	5
59	974772	57	M	Subacute infarct in left MCA	RHD WITH MR,TR	NILL	Mixed	72	18	4	11	4	12
60	974970	59	M	Subacute infarct in right MCA,MCA-PCA watershed territory	NILL	NILL	Mixed	85	20	4.25	14	2	6
61	975001	65	M	Subacute infarct in right MCA,MCA-PCA watershed territory,Left fronto-parietal occipital regior	NILL	NILL	Mixed	61	12	5.08	16	2	7
62	954339	56	M	s,rt cerebellar lobe,vermis,occipital	HTN,T2DM	NILL	Vegetarian	92	6	15.3	20	5	7
63	952575	69	M	Subacute infarct in right MCA territory	NILL	Smoker	Mixed	79	10	7.9	20	3	5
64	959885	72	F	Subacute infarct in right centrum ovale,corona radiata,posterior temporal region,insular cortex	HTN,T2DM	NILL	Mixed	72	22	3.27	8	1	6
65	975730	55	M	Subacute infarct in left MCA and PCA territories	CA ESOPHAGUS (2007)	EX TOBACCO CHEWER	Mixed	76	15	5.06	8	3	4
66	976411	60	M	Subacute infarct in right cortical,subcortical,frontal parietal region,right insular cortex,caudate nu	HTN,MITRAL STENOSIS	NILL	Vegetarian	88	8	11	7	4	8
67	975668	65	M	Acute infacrt in left MCA,right ACA and b/l PCA territories	NILL	NILL	Mixed	72	22	3.27	24	1	9
68	977333	50	F	Subacute infarct in right-thalamus,subcortical parietal,occipital regions&left centrum semiovale	NILL	Tobacco chewer	Mixed	90	7	12.8	28	5	12