EJPMR, 2026, 13(8), 659-674 **Review Article** **Impact Factor: 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

A STUDY ON ASSESSING COMORBIDITY PATTERNS, PHYSICAL AND COGNITIVE FUNCTION IN FIRST EVER ISCHEMIC STROKE

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DOI: https://doi.org/10.5281/zenodo.21886446

How to cite this Article: [1]Agna Rino, [1]Nalina S. Kaimal, [1]Sona Joseph, [2]*Mrs. Zuhara Mariyam. (2026). A Study on Assessing Comorbidity Patterns, Physical and Cognitive Function In First Ever Ischemic Stroke. European Journal of Pharmaceutical and Medical Research, 13(8), 659–674.

Article Received on 15/07/2026 **Article Revised on 05/08/2026** **Article Published on 10/08/2026**

ABSTRACT

Objectives: This study aims to assess association of comorbidities like hypertension, diabetes mellitus and dyslipidemia with outcomes of stroke such as functional independence and cognitive function. **Methods:** This cross-sectional study will be conducted in the Department of Neurology at a tertiary care hospital over six months. A total of 64 patients, aged 45-75 years who are newly diagnosed with acute ischemic stroke will be enrolled and divided into two groups- with at least one comorbidity and without any comorbidity. Patient demographic details, medical history, baseline BI and MoCA will be noted at the beginning of the study and during the follow- up. **Result:** The study revealed that ischemic stroke predominantly affected the older population with an average age of 63±8.7 years. In terms of gender, there was a slight male predominance (56.3%). Among the comorbidities, diabetes mellitus was the most common (42.2%. At baseline, the majority of patients showed moderate to high levels of independence. The follow-up indicated a reduction in severe disability among the patient population. The baseline mean MoCA score showed prevalent cognitive impairment. At follow- up, a notable improvement was observed. **Conclusion:** Our findings demonstrated that at baseline, the patients with comorbidities showed a higher percentage of severe dependence compared to those without. At follow- up, there was a notable improvement in both physical and cognitive function, owing to the impact of post-stroke rehabilitation and supportive care.

KEYWORDS: Acute ischemic stroke, comorbidity, hypertension, dyslipidaemia, diabetes mellitus, Barthel Index, Montreal cognitive assessment scale, physical dependence, cognitive impairment.

INTRODUCTION

Background: Stroke is one of the leading causes of morbidity and mortality worldwide. The cause and severity of stroke varies significantly and it depends upon various etiological factors. Comorbidity refers to the presence of at least one health condition or disease alongside a primary diagnosis.

Commonly seen comorbidities in stroke patients include: hypertension, diabetes mellitus and dyslipidaemia. Comorbidity plays a major role in the development of stroke and is in turn associated with increased mortality risk, poor quality of life, reduced physical function, increased healthcare utilization and cost among the patients. Post- stroke patients often manifest poor or decreased physical as well as cognitive function.

Functional symptoms include physical dependence and cognitive impairment. Physical dependence is characterized by difficulty in carrying out tasks like bathing, feeding, dressing, etc. whereas cognitive symptoms are manifested by loss of memory, difficulty in focusing, trouble in speaking, reading, etc. Analysis of prescription patterns helps in promoting and monitoring areas like rational use of medicine and evidence-based medicine. Stroke survivors require an integrative treatment approach which includes medications, rehabilitation, and lifestyle modification to prevent the future recurrence of stroke. They also examine individualized patient requirements and focus on better care for patients.

DEFINITION OF THE DISEASE

Stroke is a common neurological disorder associated with peripheral neuropathy, myopathy and dysautonomia. Stroke can be caused when the blood supply to the brain is either obstructed or reduced thereby depriving the brain of oxygen and nutrients. Accordingly, there are mainly two types of strokes; ischemic stroke and haemorrhagic stroke.

Ischemic stroke

This type of stroke occurs when there is inadequate blood supply to an area of the brain. It is the most commonly seen type of stroke which constitutes about 88% of the total stroke.

Haemorrhagic stroke

It accounts for about 12% of total stroke. It can be due to the presence of blood in brain parenchyma which causes damage to surrounding tissue which results in haemorrhages and in turn results in compression of neighbouring tissue and finally result in tissue damage.[2]

CLINICAL SYMPTOMS

Clinical manifestations of stroke can appear in various areas of the brain. Some of the main presentations in particular areas include:

❖ The Left hemisphere (most dominant presentation included)

- Left gaze preference: it refers to the individual's tendency to initially look towards the left visual field particularly while viewing the face while focusing on the right side of the face first.
- Right visual field deficit: loss of vision in the right half of the visual field of both eyes.
- Right hemiparesis: weakness on the right side of the body.
- Right hemi sensory loss: reduced sensation in the right side of the body.

❖ Right hemisphere(non-dominant)

- Right gaze preference: here the individuals tend to look forward but it deviates to the right side.
- Left visual field deficit: loss of vision in the left side of the visual field of both eyes.

❖ Left hemiparesis: weakness on the left side of the body.

❖ Left hemi sensory loss deficit: difficult to process the sensation on the left side even though the sensory system is not impaired.

❖ Brain stem

- Nausea and vomiting
- Diplopia: double vision
- Dysconjugated gaze: failure of the eye to move together in the same direction.
- Dysarthria: weakness in muscles engaged in speech. It manifests as slow and slurred speech.
- Dysphagia: difficulty in swallowing food
- Vertigo: sudden spinning sensation
- Tinnitus: ringing or buzzing noise in both ears
- Hemiparesis: muscle weakness or paralysis in any one side of the body.
- Quadriplegia: paralysis that affects the ability to voluntarily move the upper and lower body
- Sensory loss in the half body or all 4 limbs
- Decreased or reduced consciousness
- Hiccups
- Abnormal respiration

❖ **Cerebellum**

- Truncal/gait ataxia: difficulty in coordinating upper body.
- Limb ataxia: lack of coordination in both upper and lower limbs
- Neck stiffness.[2]

EPIDEMIOLOGY

Stroke is the leading cause of death, globally. Between 2009 and 2012 a prevalence of 2.6% was observed in the United States as it is the fifth leading cause of death. 85 % of total strokes constitute ischemic stroke of which 17.8% have experienced stroke symptoms at the age of 45.

The risk of recurrent stroke is about 20% at 5 years. Both stroke incidence and mortality have decreased over the past 30 years or more and the age - adjusted stroke death rate decreased about 33.7% from 2003-2013. About 7,95,000 experience new or recurrent strokes each year leaving 26 % of people with a disability in basic activity and 50% of people with reduced mobility due to hemiparesis. Stroke is more common in men than women and young and middle-aged women have a higher lifetime risk of stroke than men with poorer functional outcomes.

Between 1981 and 2013 a greater decline in age - adjusted death rate was seen in men than women. The difference in stroke risk was seen with race and ethnicity. Stroke incidence was higher in blacks than in whites with an incidence ratio of 4.02 in those 45-55 years of age and 0.86 in those over 85 years of age.

Between 1990 and 2005 a decline in incidence was observed among whites but stroke incidence remained the same in blacks. In high - income countries, the incidence and mortality of stroke have decreased between the years 1990-2010. X no significant changes were observed in the incidence in low- and middle-income countries and no number of stroke deaths increased over that time.[4]

ETIOLOGY

Usually occurs from blood vessel occlusion from thrombosis or embolism. Thrombosis refers to the formation of blood clots in a blood vessel, which blocks blood flow. An embolism is a clot that travels along the bloodstream. It can also be caused by atherosclerosis, which is the accumulation of fatty infiltrates in blood

vessels.

- ❖ There are certain risk factors associated with the development of stroke that can be modifiable as well as non-modifiable risk factors.
- ❖ Some of the non – modifiable risk factors include age, gender, race, family history and genetic predisposition.

- Age: greater than 55. stroke incidence increases with age
- Gender: among males and females occurrence of stroke tends to be higher in the women population.
- Race: while compared with whites, African – Americans have an increased risk of developing stroke.
- Family history: individuals have a high risk for the occurrence of stroke if they have a family history of stroke among first - degree relatives.
- Genetic predisposition: diseases like hereditary dyslipoproteinemia can progress the development of atherosclerosis. Also, deficiency of protein C and S or antithrombin can cause stroke.
- Metabolic disorders like mitochondrial encephalopathy, lactic acidosis, Fabry disease and homocystinuria can cause stroke risk.
- The Presence of the Apo lipoprotein epsilon – 2 allele in the elderly and the absence of angiotensin - converting enzyme may increase the risk of stroke.

❖ **Modifiable risk factors include**

- Diseases like hypertension, diabetes mellitus, and dyslipidaemia.
- Social habits like alcohol consumption and cigarette smoking.
- Sedentary lifestyle like lack of physical activity and obesity.
- Use of drugs like oral contraceptives.

❖ Hypertension can contribute to ischemic stroke by promoting atherosclerosis which further progresses to heart disease, thereby increasing the risk for stroke development.

❖ Diabetes mellitus can cause cerebrovascular atherosclerosis and cardiac embolism and hence increase the risk of stroke.

❖ An increase in total cholesterol and dyslipidaemia is associated with the development of atherosclerosis and hence increase the risk of stroke.

❖ While compared with non-smokers, smokers have a 2-3-fold time risk higher in the development of stroke. Cigarette smoking can cause decreased blood supply thereby reducing oxygen. Cardiac arrhythmia, increased blood coagulability and promoting arterial thrombosis can result from cigarette smoking.

❖ The use of tobacco leads to carotid artery plaque thickness.

❖ Heavy drinking of alcohol may cause cardiogenic brain embolism. Alcohol consumption is unrelated to the development of haemorrhagic stroke.

❖ Obesity increases the risk for cardiovascular disease in both men and women therefore regular physical activity may reduce the risk of stroke.

❖ Women who use high doses of oestrogen oral contraceptives have a lower risk when compared to the risk factors associated with the development of stroke.[5]

PATHOPHYSIOLOGY

Pathophysiology of ischemic stroke is largely dependent upon atherosclerosis, which can occur by the accumulation of lipids and inflammatory cells which combined with hypertrophy of arterial smooth muscle cells, results in plaque formation.

Due to stress, the plaque ruptures, collagen becomes exposed and platelet aggregation occurs finally resulting in clot formation. This can either result in thrombus or embolus formation. Finally, the formation of either a thrombus or embolus can contribute to arterial occlusion, which results in decreased or reduced cerebral blood flow thereby causing ischemia.

Ischemia deprives the brain of blood, oxygen and essential nutrients which are required for their proper functioning. As a result, there is a lack of high - energy phosphate, which is necessary for the maintenance of membrane integrity.

Potassium accumulates extracellularly whereas sodium and water accumulate intracellularly, which leads to cell swelling and subsequent lysis of the cell.

Due to electrolyte imbalance, depolarisation of cells takes place. There is an influx of calcium into the cell, causing an increase in intracellular calcium, resulting in the activation of enzymes like lipase, protease and releasing free fatty acids from membrane phospholipids. The accumulation of these free fatty acids results in the formation of prostaglandins, leukotrienes and free radicals. Free radicals are highly reactive and can attack and damage cell membranes, leading to intracellular acidosis. These events occur within 2-3 hours after the onset of ischemia.

The release of excitatory amino acids like glutamate and aspartate occurs from depolarisation of neurons and can cause neuronal damage when released excessively.[6]

DIAGNOSIS

Diagnosis of ischemic stroke can be carried out by:

❖ History and physical examination

- Time of onset of symptom
- Obtain circumstances that lead to the development of symptoms
- Identify risk factors
- Physical examination including vitals, pulse oximetry, etc...

❖ **Clinical stroke score**

- NIHSS scale (The National Institute of Health Stroke Scale): it aids in identifying neurological

deficits and their location.

❖ **Diagnostic tests**

- CT scan (Computed Tomography): helpful in distinguishing between types of strokes. It is mandatory to perform them before the commencement of the therapy.[2]

CURRENT TREATMENT OPTIONS

The management of acute ischemic stroke typically involves pharmacological and non-pharmacological treatments. Key treatment options include:

Non – pharmacological treatment

Smoking cessation: is a major risk factor. Individuals should avoid smoking and its passive exposure.

❖ **Lifestyle modification**

- Individuals should include diet - rich fruits and vegetables. Fruits such as blueberries, pomegranate, tomato, avocado, etc. and vegetables such as spinach, broccoli, cabbage, carrot, etc.
- Avoid heavy use of alcohol.
- Maintain adequate bodyweight.
- Exercise regularly.

❖ Rehabilitation and Supportive Care: Regardless of the treatment approach, rehabilitation plays a crucial role in the management of stroke. Supportive care in stroke includes:

- Provide adequate nutrition and hydration. Patients with swallowing problems should be administered with IV fluid.
- Dextrose - containing solutions should be avoided.
- Nasogastric feeding should be started when the patient is neurologically stable.
- Thickened liquids or semi-solids should be orally fed.
- Initially start with a mechanically soft blended diet then followed by a regular diet.

Rehabilitation in stroke is as follows

- All patients diagnosed with stroke should be assessed for rehabilitation.
- Present complications including swallowing problems, skin breakdown, DVT, bowel and bladder dysfunction and pain should be assessed.
- Assess impairments such as communication and motor impairments, cognitive deficits, visual and spatial deficiency, psychological deficits and sensory deficits.
- Individualized programs should be started when the patient is stabilized to prevent long - term complications.
- Prevention and management of comorbid illness.
- Training for maximum independence.
- Helping patients and families with psychological coping and adaptation.
- Promote community integration.
- Improve the quality of life if disabilities are present.
- Prevention of recurrent stroke or other vascular events.

Pharmacological treatment

Management of stroke includes thrombolytics, antiplatelets and anticoagulants. The goal of the therapy is to prevent future stroke and management of complications.

❖ **Thrombolytics**

- Alteplase 0.9mg/kg IV infusion over 60 mins
- Streptokinase
- Urokinase
- Tenecteplase

❖ **Anticoagulants**

- Unfractionated heparin
- Low molecular weight heparin
- E.g.: enoxaparin 1.5mg/kg SC OD or 1mg/kg SC BD Dalteparin

❖ **Antiplatelets**

- Aspirin 150-325mg
- Clopidogrel 75mg

Thrombolytic therapy

These are recombinant tissue plasminogen activators which are selective fibrinolytic agents used in the management of acute ischemic stroke. Thrombolytic therapy is one of the most widely used therapy and is considered a first - line treatment in the management of acute ischemic stroke. It is administered as an IV infusion within 3 hours of symptom onset.

Pharmacological action

❖ Thrombolytic agents act by the following mechanisms:

- They lyse the thrombi/clot to recanalize occluded blood vessels.
- t-PA activates fibrin bound plasminogen within the thrombus and also plasmin that leaks its inactivated by circulating antiplasmin.
- Plasmin converts insoluble fibrin into soluble fibrin fragments.
- The fibrin fragments which are now soluble are then eliminated.

However, all patients cannot undergo thrombolytic therapy. Therefore, there are certain inclusion and exclusion criteria.

❖ **Inclusion criteria: these include**

- Age greater than or equal to 18 years.
- Diagnosis of ischemic stroke indicating neurologic deficit.
- The time of onset of symptoms should be less than 4.5 hours.

❖ **Exclusion criteria**

- Evidence of brain haemorrhages in CT scan.
- Rapidly improving stroke symptoms.

- Active bleeding in GIT etc.
- A patient who has been administered with heparin within 48 hours.
- Recent use of anticoagulants like warfarin.
- Any brain surgery, complicated head trauma, has a previous history of stroke within 3 months.
- History of intracranial haemorrhage, aneurysm, etc.
- Seizure at the onset of stroke.
- Recently diagnosed acute myocardial infarction.
- Blood pressure should be less than 185/110 mm Hg during the time of treatment.

❖ **Parameters to be monitored**
- Blood pressure
- Neurologic function
- Bleeding

❖ **Adverse reactions**
- Hematologic reactions: haemorrhage, internal bleeding
- GI effects: nausea, vomiting
- Miscellaneous effects: fever, chills, abdominal pain
- Reactions: allergy (rashes, anaphylaxis)
- Infusion may cause hypotension.

Anti-coagulants
Anti-coagulants are the drugs used to reduce coagulability of blood. They inhibit the development of new clots or prevent existing clots from growing larger. Anti-coagulants are used in post - stroke care management in order to prevent the risk of recurrent stroke.

The most commonly used agents in this category for the management of ischemic stroke include unfractionated heparin and low molecular weight heparin.

Unfractionated heparin
They are administered in the form of IV infusion or subcutaneous infusion because it is more preferred.

❖ **Pharmacological action**
- They indirectly activate plasma anti - thrombin III.
- The heparin – antithrombin III complex thus formed then binds to clotting factors Xa, IIa, IXa, XIa, XIIa and XIIIa and inactivates them.
- Thus, factor Xa is inhibited by the anti-coagulant action of heparin and also thrombin (II a) mediated conversion of fibrinogen to fibrin.

Heparin is given at a dose of 5,000-10,000 U followed by continuous infusion of 750-1000 U/hour.

Overdose of heparin therapy may lead to bleeding and also heparin therapy cannot be initiated in patients with bleeding disorders, severe hypertension and renal failure as it is contraindicated.

❖ **Adverse reactions**
- Bleeding
- Heparin - induced thrombocytopenia
- Alopecia
- Osteoporosis
- Hypersensitivity reactions

Low molecular weight heparin
LMW heparin is smaller heparin fragments formed by chemical or enzymatic depolymerization of unfractionated heparin.

❖ **Pharmacological action**
- Due to the smaller chain length of LMW heparin, they cannot bind simultaneously to thrombin and anti-thrombin. So, they inhibit only factor Xa and they are less effective in inhibiting thrombin when compared to unfractionated heparin.

When compared to UFH, LMW heparin is preferred as the initial anti-coagulant. They have a lower risk of heparin - induced thrombocytopenia.

❖ **Adverse reactions**
- Bleeding
- Thrombocytopenia
- Alopecia
- Hyperkalemia
- Osteoporosis
- Hypersensitivity reactions

Antiplatelets
They are the drugs that are used in the prophylaxis of thromboembolism disorders.

Aspirin
Aspirin is a drug that is used in the management of stroke and is administered at the dose of 150-325 mg within 48 hours after the onset of stroke symptoms.

In the secondary prevention of subsequent stroke, aspirin is given at a dose of 50-100mg per day.

❖ **Pharmacological action**
- Aspirin acts by inactivating the enzyme cyclooxygenase which is responsible for the production of prostaglandins and thromboxane from arachidonic acid.
- The thromboxane is mainly responsible for platelet aggregation which finally develops into a clot.
- As a result, aspirin blocks thromboxane A2 thus producing an inhibitory effect on platelet aggregation.

❖ **Adverse reactions**
- GI bleeding
- Peptic ulcer
- GI irritation
- Hypersensitivity reactions

Clopidogrel
Clopidogrel is an antiplatelet drug that is used in the

prevention of blood clots and reduces the risk of stroke recurrence.

They are also used in combination with aspirin as DAPT (dual antiplatelet therapy) which is effective in reducing stroke reoccurrence.

❖ **Pharmacological action**

- They act by indirectly blocking the P2Y12 type of purinergic receptor on the surface of the platelet.
- The GI - coupled GPCR mediates ADP - induced platelet aggregation therefore inhibiting adenyl cyclase and reducing c-AMP.
- Clopidogrel is safer and better tolerated.
- They also act as a prodrug in which 50% of ingested dose is absorbed.

❖ **Adverse reactions**

- Neutropenia
- Thrombocytopenia
- Bone marrow toxicity[8]

COMORBIDITY IN STROKE

Stroke and hypertension

Hypertension is a major modifiable risk factor associated with the development of ischemic stroke. People with hypertension are 3-4 times more likely to suffer a stroke than those without hypertension.

Mechanisms involved in hypertension - induced stroke include:

1) Vascular remodelling
2) Inflammation
3) Oxidative stress

❖ **Vascular remodelling**

- Hypertension has a deep effect on the composition of cerebrovasculature.
- Hypertension accelerates the development of atherosclerotic plaques in the cerebral artery and arterioles, which may lead to arterial obstruction thereby leading to ischemia.
- When there is increased intraluminal pressure, hypertrophy, hyperplasia or remodelling of smooth muscle cells occur and grow inside which intrudes into the lumen of the artery. This in turn results in the narrowing of vessels with an increase in thickness of the wall.
- HTN can cause stiffness of vasculature, resulting in an increase in pulse pressure, which is a good indicator of stroke.

❖ **Inflammation**

- It is a vital process that involves changes in vascular integrity and involves common mechanisms like cerebral aneurysms and atherosclerosis.
- Biomarkers of inflammation can predict the risk of primary ischemic stroke like C - reactive protein, IL-6, leukocyte elastase, lipoprotein, E -selectin, etc.
- These biomarkers are higher in people who are at risk of developing stroke when compared to those who are not.

❖ **Oxidative stress**

❖ It is a condition where reactive oxygen species (ROS) overrun the capacity of antioxidant defence system.

It can occur when

- There is an increased production of ROS
- There is a decreased anti-oxidant capacity.
- Or a combination of both

❖ Oxidative stress in cerebral blood vessels can cause HTN.

ROS is an important intermediate for cerebrovascular dysfunction which is induced by angiotensin II. This occurs through the activation of NADPH oxidase in vasculature.

❖ HTN alone can cause oxidative stress in cerebrovasculature, thereby causing functional and structural remodelling in cerebral blood vessels.[38]

Stroke and diabetes

Diabetes is one of the risk factors that can contribute to ischemic stroke. Mechanisms involved include:

1) Hyperglycemia
2) Metabolic memory
3) Insulin resistance

❖ **Hyperglycemia**

- It can increase oxidative stress leading to several complications in the microvasculature.
- There is an increased ROS production, which inhibits the action of GADPH (glyceraldehyde 3 phosphate dehydrogenase), which is an enzyme in glycolysis. This leads to endothelial dysfunction and complications associated with diabetes.
- Chronic hyperglycemia stimulates atherosclerosis leading to complications.

❖ **Metabolic memory**

- ROS production stimulates epigenetic changes in nuclear factor – KB within endothelial cells and returns to normal blood glucose levels.
- Epigenetic changes cause chromatin remodelling and changes in gene expression and lead to endothelial dysfunction.

❖ **Insulin resistance**

- Due to excess adipose tissue, insulin is unable to inhibit lipolysis activity which leads to mobilization of free fatty acids.
- Insulin - stimulated peripheral glucose uptake in the liver and various other organs is inhibited by the entry of FFA.
- Increased generation of FFA causes an increase in TG, LDL and a decrease in HDL and it accumulates in the arterial wall.
- Necrotic breakdown of lipid - rich plaques

leads to stimulation of atherosclerotic lesions.[39]

Stroke and dyslipidemia

- Elevated cholesterol levels are linked to increased risk of stroke development and act as a prevalent risk factor.
- Patients with elevated cholesterol have reduced white matter hyperintensity volume, which is a predictor of infarct progression of stroke, leading to poor clinical outcomes.
- White matter abnormalities occur due to elevated levels of LDL and decreased levels of HDL in obese individuals with abnormal cholesterol profiles.
- Therefore, long - term mortality after stroke is associated with LDL levels.[40]

FUNCTIONAL OUTCOMES

Physical dependence

- Evaluation of physical function will be carried out by Barthel Index score.
- Barthel Index constitutes ten daily activities of living which include bowel and bladder control, personal hygiene, toilet transfer, feeding, dressing, etc.
- The score ranges from 0 – 100 in which a high score, i.e., greater than 75 indicates a high degree of independence.
- If the score is less than or equal to 75, moderate to severe dependence is indicated.

Cognitive impairment

- The cognitive impairment post - stroke can be carried out by the Montreal Cognitive Assessment Scheme.
- MOCA is a thirty - point test that measures language, memory, attention, abstraction, orientation and executive function.
- A score of 26 or more indicates normal cognitive function.
- A score ranging from 18 – 25 indicates mild cognitive impairment.
- A score of 10 – 17 indicates moderate cognitive impairment, whereas a score less than 10 shows cognitive impairment.[1]

MATERIALS AND METHODS

STUDY DESIGN

The study was conducted as a cross-sectional study.

STUDY SITE

Department of Neurology in Tertiary Care Teaching Hospital, Mukkam, Kozhikode.

STUDY DURATION

The study was conducted for a duration of 6 months.

STUDY POPULATION

Acute ischemic stroke patients who visited the hospital during the study period Sample size is calculated by the following equation.

$$n = \frac{(Z_{\alpha/2}+Z_{\beta})^2 \times 2pq}{d^2}$$

Where,

- n= required sample size
- Zα= is the Z value at an α error
- Zβ = is the Z value at a β error.
- SD = Standard deviation.
- d = clinically relevant effect size.

$$n = \frac{(1.96+0.84)^2 \times 2(57.5\times42.5)}{35^2} = 32$$

Sample size of each group = 32

A minimum of 32 patients with acute ischemic stroke in each group, who consulted the Neurology department during the study period were included in the study.

PLAN OF WORK

The entire study was designed to be conducted in three phases.

PHASE 1

- A detailed literature review was done extensively using tertiary resources, secondary resources and primary resources.
- Designing of the data entry form, informed consent document and patient information sheet.
- Sample size calculation.
- Ethical committee approval: Ethical clearance was obtained from the Institutional Ethics Committee of the National College of Pharmacy.

PHASE 2

- Samples were allocated into groups, considering the inclusion and exclusion criteria.
- Data including patient demographic details, past medical and medication history and relevant laboratory values were collected using the data entry form after explaining the patient information sheet and signing an informed consent document.
- The physical and cognitive function were analysed using the Barthel index and MoCA score.

PHASE 3

- Data were analyzed by a combination of descriptive and inferential technique. Descriptive statistics including frequencies and percentages, mean, median and standard deviation .Inferential techniques including chi-square and paired sample t-test was used.
- Documentation and presentation of data.

STUDY CRITERIA

Patients were selected based on the following inclusion and exclusion criteria.

INCLUSION CRITERIA

- Patients aged 45 to 75 years.
- Newly diagnosed acute ischemic stroke patients.
- Willingness to participate and provide informed consent.

EXCLUSION CRITERIA

- Severely ill, bedridden patients.
- A patient diagnosed with transient ischemic attack and haemorrhagic stroke.
- Previous history of physical and cognitive impairment.

SOURCES OF DATA

- Patient Case Records
- Patient or patient representative interview

STUDY MATERIALS

1. INFORMED CONSENT FORM AND PATIENT INFORMATION SHEET

To enroll patients in the study, an informed consent and patient information sheet in the local language (Malayalam) was prepared.

2. PATIENT DATA ENTRY FORM

For collecting the necessary data obtained from the sources, a separate data entry form was designed by including the demography of patients, past medical history, diagnosis, and current medication and laboratory investigations.

3. BARTHEL INDEX

It is a tool used to assess a person's ability to perform activities of daily living independently. It contains 10 basic self-care activities like bowel and bladder control, dressing, feeding, etc.

4. MoCA SCORE

It is a tool designed to evaluate a range of cognitive abilities such as memory, language, attention, abstraction, etc.

STUDY PROCEDURE

In this cross-sectional study titled **"A STUDY ON ASSESSING COMORBIDITY PATTERNS, P HYS IC AL AND COGNITIVE FUNCTION IN FIRST EVER**

ISCHEMIC STROKE" we aimed to determine the prevalence, comorbidity patterns associated with ischemic stroke and prescription patterns in the management of stroke. Patients were diagnosed with acute ischemic stroke by CT brain with MR diffusion. Patients were categorized into two groups based on the presence or absence of comorbid conditions: newly diagnosed ischemic stroke patients having at least one comorbid condition and newly diagnosed stroke patients without any comorbid conditions.

Demographic information, medical history and relevant laboratory values were collected at the time of admission in the data entry form.

Barthel index and Montreal cognitive assessment scale were noted at the beginning of the study in order to analyse the physical and cognitive function, when the patient's clinical condition became stable. The same parameters were analysed again after a follow – up period of two weeks.

STATISTICS

To evaluate changes in functional and cognitive status, from baseline to follow-up, paired sample t test was applied. Chi - square test was used to assess the association between the presence of comorbidities and various categorical factors including age groups, gender and the baseline and follow- up, BI and MoCA score. Data analysis was performed using open-source statistical software Jamovi 2.6.26.

RESULTS

The study entitled "A STUDY ON ASSESSING COMORBIDITY PATTERNS, PHYSICAL AND COGNITIVE FUNCTION IN FIRST EVER ISCHEMIC STROKE" will be conducted in the department of neurology in a tertiary care hospital for a period of 6 months. A total number of 64 patients were selected based on inclusion criteria. Prevalence of comorbidity pattern, physical and cognitive function were assessed.

CATEGORIZATION OF STUDY POPULATION

1. BASED ON AGE DISTRIBUTION

The results are as follows

Table 1: Age Distribution of Participants.

Age in years	Frequency	Percent
≤50	7	10.9
51 - 60	14	21.9
61 - 70	25	39.1
>70	18	28.1
Total	64	100

Average age of the study population was 63.7±8.7 years and age ranges from 45 to 75 years.

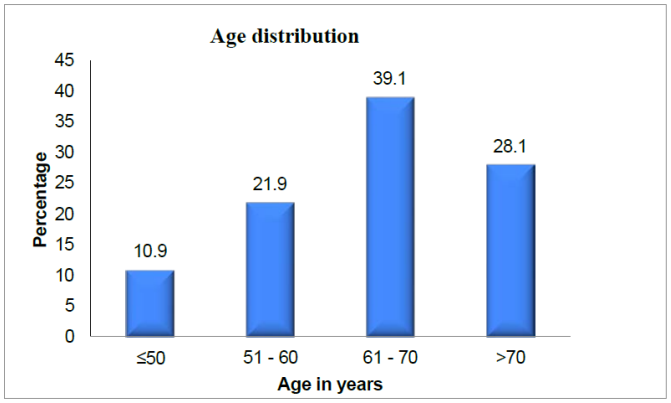

Figure No. 1: Age distribution.

2. GENDER DISTRIBUTION

The results are as follows:

Table 2: Gender distribution.

SEX	Frequency	Percent
Male	36	56.3
Female	28	43.8
Total	64	100

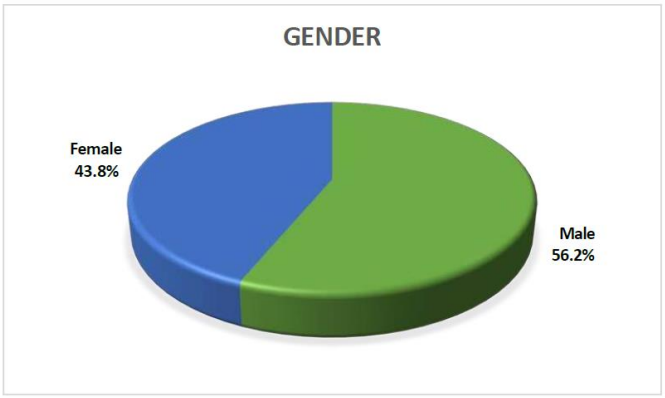

Figure No. 2: Gender distribution.

3. PREVALENCE AND COMORBIDITY PATTERN IN ISCHEMIC STROKE

Table 3: Prevalence and Comorbidity Pattern.

Comorbidities	Frequency	Percent
Diabetes	27	42.2
Hypertension,	22	34.4
Dyslipidaemia	3	4.7

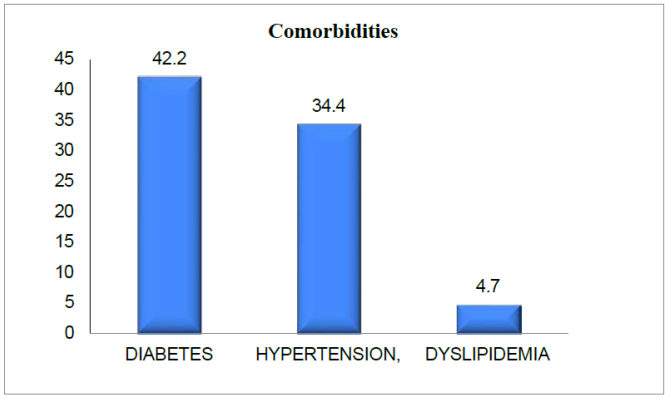

Figure no. 3: Prevalence and comorbidity pattern.

Barthel Index Score

	Barthel index score	
	mean ± SD	P
Baseline	81.98 ± 21.199	0.004
FOLLOW UP	84.53 ± 19.206	

The **Barthel Index Score** table illustrates the functional status of 64 patients with first-ever ischemic stroke at baseline and follow-up. At baseline, the mean score was 81.98 with a standard deviation of 21.20, indicating that the majority of patients exhibited moderate to high levels of independence in performing daily activities.

At follow-up, there was a measurable improvement in functional independence. The mean Barthel Index score increased to 84.53 (SD = 19.21). The improvement in scores was statistically significant (p = 0.004), emphasizing the impact of post-stroke rehabilitation and supportive care.

Table 4: Barthel Index – Baseline and Follow Up Functional Status.

	Barthel index			
	Baseline		Follow up	
	Frequency	%	Frequency	%
Total dependence	1	1.6	0	0
Severe dependence	11	17.2	10	15.6
Moderate dependence	24	37.5	25	39.1
Slight dependence	3	4.7	3	4.7
Full independence	25	39.1	26	40.6

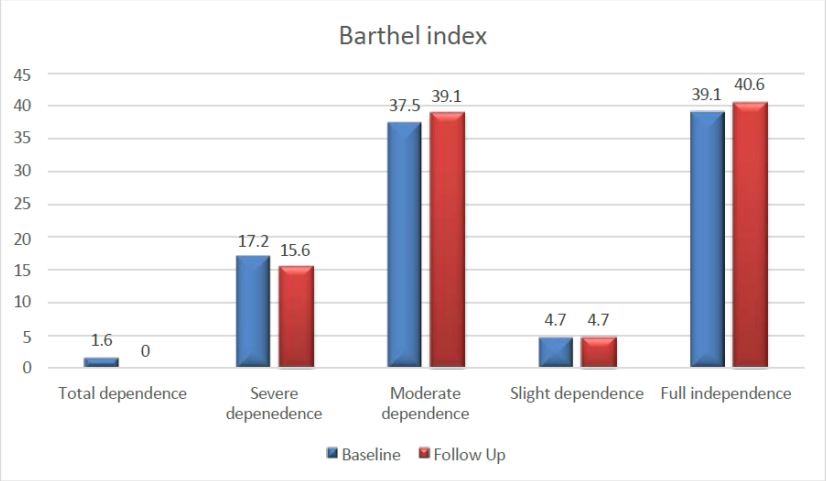

Figure no. 4: Barthel Index Baseline and Follow up Functional Status.

MoCA- Score

	MoCA	
	mean ± SD	P
Baseline	20.02 ± 5.272	0.001
FOLLOW UP	23.59 ± 5.185	

The Montreal Cognitive Assessment (MoCA) scores presented in the table reflect cognitive function at baseline and follow-up among 64 participants with first-ever ischemic stroke. At baseline, the mean MoCA score was 20.02 with a standard deviation of 5.27, indicating prevalent cognitive impairment among patients.

At follow-up, a notable improvement in cognitive function was observed. The mean MoCA score increased to 23.59 (SD = 5.19). The observed improvement was statistically significant (p = 0.001), demonstrating the effectiveness of interventions or rehabilitation efforts over time.

Table 5: MOCA – Baseline and Follow Up Cognitive Function.

Cognitive impairment	MoCA			
	Baseline		Follow up	
	Frequency	%	Frequency	%
Severe	3	4.7	1	1.6
Moderate	14	21.9	8	12.5
Mild	38	59.4	26	40.6
Normal	9	14	29	45.3
Total	64	100	64	100

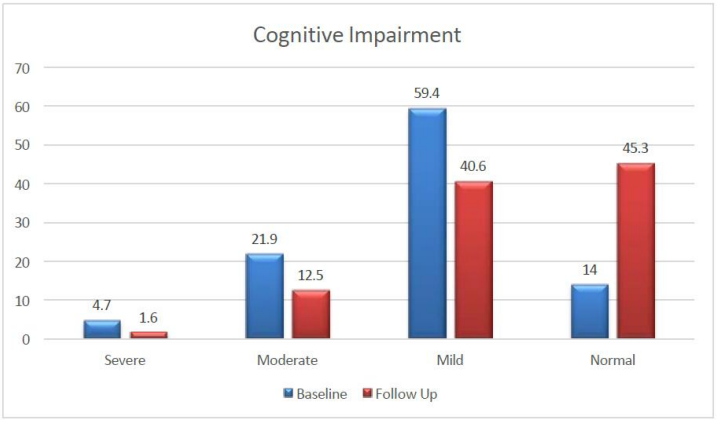

Figure No. 5: MoCA – Baseline and Follow up Cognitive Function.

Table 6: Age Group and Comorbidity Association.

Age in years	Comorbidities (%)		χ^2	p
	No	Yes		
≤50	9.4	12.5	1.01	0.799
51 - 60	25	18.8		
61 - 70	34.4	43.8		
>70	31.3	25		
Total	100.0	100.0		

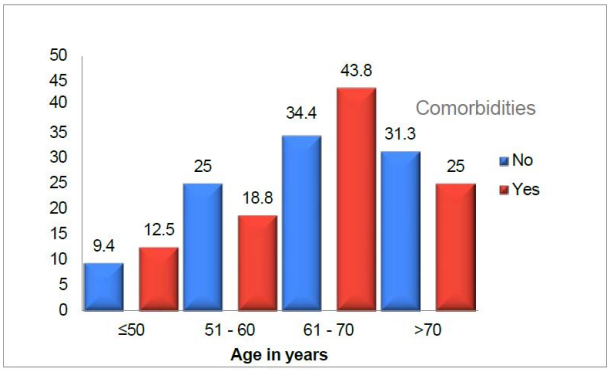

Figure No. 6: Age Group And Comorbidity Association.

Table 7: Gender and Comorbidity Association.

Sex	Comorbidities (%)		χ^2	p
	No	Yes		
Male	59.4	53.1	0.25	0.614
Female	40.6	46.9		
Total	100.0	100.0		

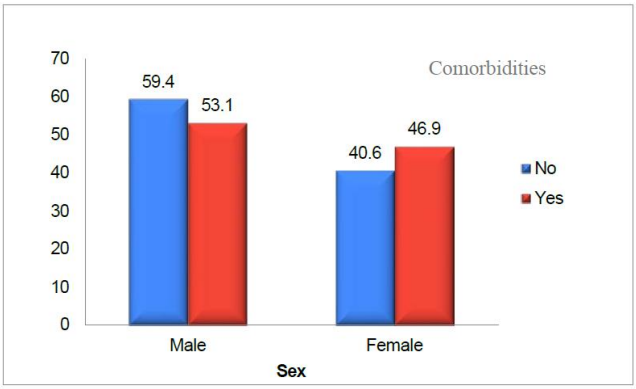

Figure No. 7: Gender and Comorbidity Association.

Table 8: Baseline Barthel Index and Comorbidities.

Barthel Index	Comorbidities (%)		χ^2	P
	No	Yes		
Total dependence	0.0	3.1	6.98	0.137
Severe dependence	9.4	25.0		
Moderate dependence	43.8	31.3		
Slight dependence	9.4	0.0		
Full independence	37.5	40.6		
Total	100.0	100.0		

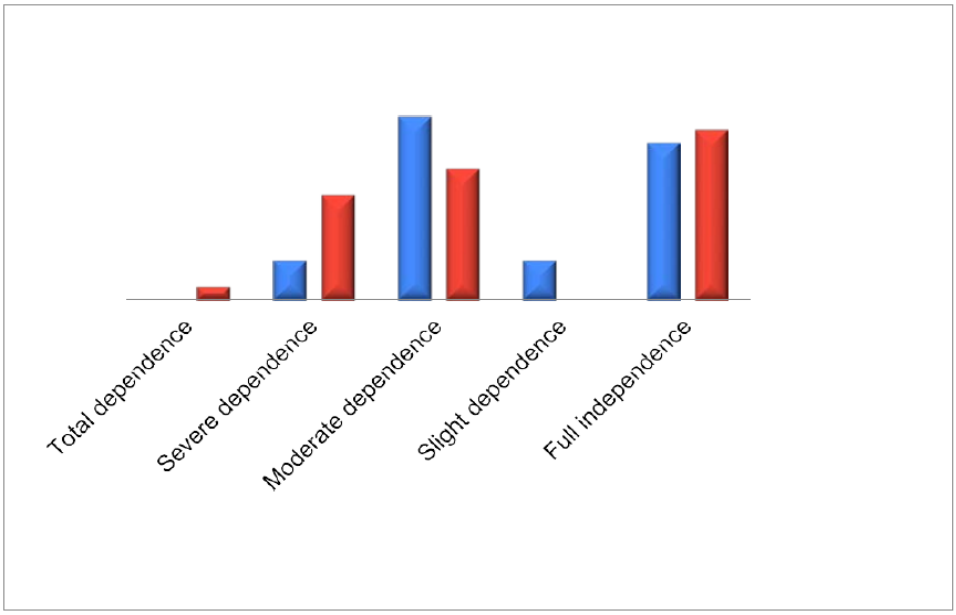

Figure No: 8 Baseline Barthel Index and Comorbiditie.

Table 9: Follow-Up Barthel Index and Comorbidities.

Barthel Index (Follow up)	Comorbidities (%)		χ^2	p
	No	Yes		
Severe dependence	6.3	25	7.75	0.051
Moderate dependence	46.9	31.3		
Slight dependence	9.4	0		
Full independence	37.5	43.8		
Total	100.0	100.0		

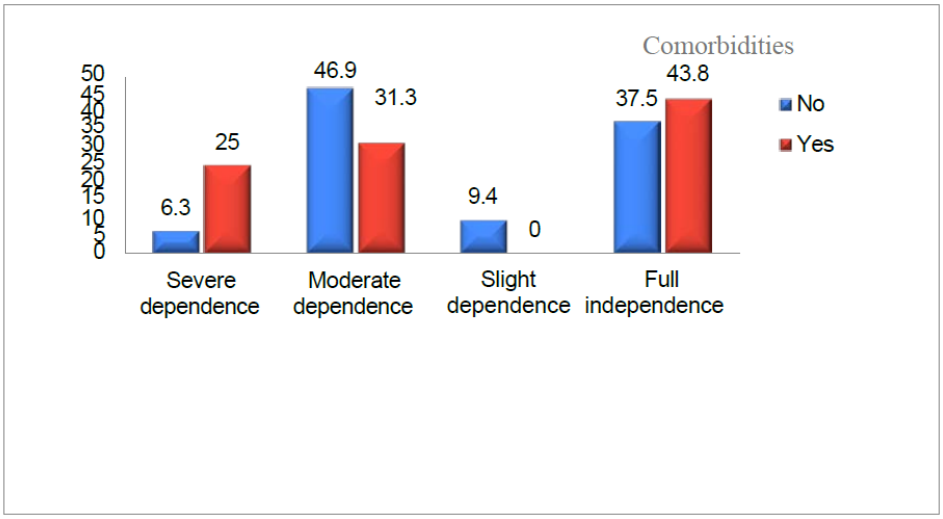

Figure No. 9: Follow-Up Barthel Index and Comorbidities.

Table 10: Baseline Cognitive Impairment and Comorbidities.

Cognitive impairment	Comorbidities (%)		χ^2	p
	No	Yes		
Severe	3.1	6.3	10.2	0.017
Moderate	6.3	37.5		
Mild	71.9	46.9		
Normal	18.8	9.4		
Total	100.0	100.0		

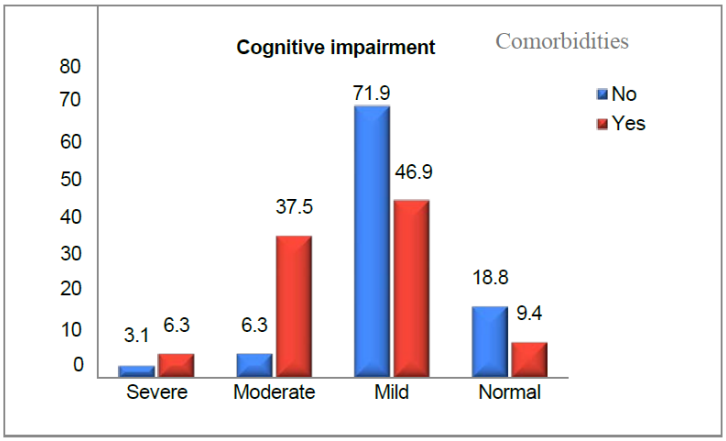

Figure No. 10: Baseline Cognitive Impairment and Comorbidities.

Table 11: Follow-up cognitive impairment and comorbidities.

Cognitive impairment (follow up)	Comorbidities (%)		X_2	P
	No	Yes		
Severe	0.0	3.1	8.56	0.036
Moderate	6.3	18.8		
Mild	31.3	50.0		
Normal	62.5	28.1		
Total	100.0	100.0		

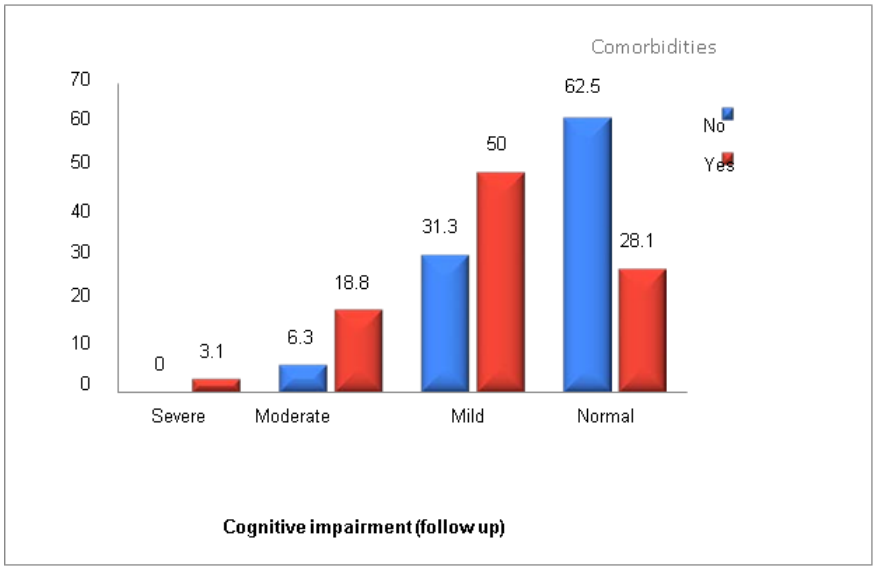

Figure No: 11 Follow-Up Cognitive Impairment and Comorbidities.

DISCUSSION

Stroke is a common neurological disorder associated with peripheral neuropathy, myopathy and dysautonomia. The causes and severity of stroke vary significantly and are dependent upon various etiological factors. One such factor for the development of stroke includes comorbidities. They are associated with increased mortality risk, poor quality of life, decreased physical function, increased healthcare utilization and cost among patients.

Our study aimed to investigate the intricate relationships between comorbidity patterns, physical function and cognitive function in patients with a first ever - ischemic stroke which included 64 patients revealed that ischemic stroke predominantly affected the older population with an average age of 63.7 + 8.7 years and an age range spanning from 45-75 years. Our study is consistent with (Nikunj Koradiya et.al) who found that the age group between 60-79 years was most affected by stroke, with a higher risk of developing stroke after the age of 60.

In terms of gender, there was a slight male predominance with males accounting for 56.3% and females 43.8%. This observation is consistent with (Nikunj Koradiya et.al) who revealed that the proportion of male patients (60%) with stroke was higher than that of female patients (40%)

Comorbidities were highly prevalent in this cohort. Analysis of specific conditions revealed that diabetes mellitus was the most common affecting 42.2% of patients. Hypertension was also very frequent (34.4%) and dyslipidaemia was reported in smaller. A cross-sectional study in the Chinese population (She et. al) identified that the most common comorbidities in stroke patients were hypertension (74.7%), diabetes mellitus (28.5%), dyslipidaemia (23.3%). A study (Nikunj Koradiya et.al) also identified hypertension and diabetes mellitus as the most common comorbidity found in stroke patients.

Functional status and cognitive function were assessed using the Barthel Index and MoCA in which BI showed a considerable burden of disability at baseline, with significant variability. Whereas, MoCA revealed substantial impairment at baseline. The mean baseline BI score was 81.98 ± 21.19 and the mean baseline MoCA was 20.0±5.27. At follow - up, using BI there was a statistically significant improvement in functional status and at follow - up using MoCA the population of patients with normal cognitive functions increased substantially. In a similar study by She et. Al the increasing number of comorbidities were associated with increased physical dependence and cognitive impairment using BI and MoCA.

This study further explored the association between comorbidity and demographic factors as well as functional and cognitive outcomes. There is no statistically significant association between age group and comorbidity as well as comorbidities and baseline functional status. In contrast, the association between comorbidity and cognitive function was statistically significant both at baseline and follow - up (She et al).

Our study is consistent with (She et al), who depicted the prevalence of comorbidity in first - ever ischemic stroke and their associated outcomes like physical and cognitive function and Nikunj Koradiya et al who demonstrated the prescription pattern involved in the management of ischemic stroke and comorbidities.

CONCLUSION

This study compared the post–stroke outcomes between patients having comorbid conditions like HTN, DM and DLP with those not having any of the comorbidities. The outcomes assessed were physical and cognitive functions. Our findings demonstrated that at baseline, the patients with comorbidities showed a higher percentage of severe dependence compared to those without comorbidities. Also, among patients with comorbidities, there was a high prevalence of moderate cognitive impairment when compared to non-comorbid patients. At follow - up, there was a notable improvement in both physical and cognitive function in the patient population owing to the impact of post-stroke rehabilitation and supportive care. This study emphasized that comorbidities were fairly distributed across age brackets in this population, rather than being more concentrated in the elderly and the likelihood of having a comorbid condition among ischemic stroke is not influenced by gender. The study also shows a diverse range of neurologic presentations, a high prevalence of comorbidities like diabetes and hypertension and management of these conditions.

ACKNOWLEDGEMENT

All praise, honour, and glory to ***Almighty*** for blessing us with the opportunity and perseverance for the accomplishment of this thesis.

This work bears the imprint of many people who have inspired, guided, accompanied and contributed for the successful completion of this thesis.

First and foremost, we wish to express our sincere thanks to our dear ***Parents, Grandparents*** for their prayers, blessings, and support throughout the journey.

We would like to sincerely and gratefully thank our respected teacher and guide ***Mrs. Zuhara Mariyam*** (*M. Pharm, Assistant Professor, Department of Pharmacy Practice, National College of Pharmacy,)* for her valuable guidance, encouragement, and support laid by her during all stages of our work. Her encouragement and valuable suggestions have enabled us to make our work worthy of presentation.

Words are not enough to express our deep gratitude to ***Dr. Anoop K,*** *Department of Neurology, KMCT Medical College,* for his keen interest, timely help and valuable suggestions for our study.

We humbly owe our gratitude and sincere regards to our respected HOD***, Mr. Rajeev P Thomas*** Department of Pharmacy Practice, National College of Pharmacy, for his constant inspiration and encouragement to conduct the study.

We express our sincere gratitude to our beloved

Principal (***Prof).*** ***Dr. Sujith Varma K*** for supporting us to complete our study successfully.

We are highly obliged to record our respectful thanks to ***Dr. Biju George*** *Assistant Professor, Department of community medicine, Govt. Medical College, Kozhikode and* ***Mr. Babu P K****, Assistant Professor, Department of research, biostatistics and epidemiology.* In spite of their busy time schedule, they provided us with all statistical facilities and encouragement for the successful completion of our study.

We are extremely grateful to all other teachers of National College of Pharmacy who shared their knowledge, time, patience, valuable support and suggestions given us throughout this study.

We express our gratitude to all the ***Nursing Staff*** and **nonclinical staff** of KMCT Medical College, for their co-operation during our study.

We express our sincere thanks to ***Ms. Hyfoona****, Librarian, National College of Pharmacy* for her sincere cooperation in our study.

We extend our heartfelt thanks to ***Mr. Shiju****, Nirag Printers, Manassery*, who provided us with technical support in editing and printing our dissertation.

We feel deeply indebted to our ***Seniors*** for giving appropriate help, valuable suggestions and encouragement throughout our work.

We would like to extend our heartfelt thanks to all our ***Batchmates*** for their affection and concern throughout the course of study. We wish to thank all patients and their caregivers who so willingly co-operated with us to complete this study. Once again, our sincere thanks to all.

AGNA RINO NALINA S KAIMAL SONA JOSEPH

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