A PROSPECTIVE OBSERVATIONAL STUDY ON PRESCRIBING PATTERN AND RATE OF MEDICATION ADHERENCE IN STROKE PATIENTS

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ABSTRACT

Cerebrovascular accident (CVA) is the medical term for stroke in which blood flow to a part of the brain is stopped either by blockage or rupture of blood vessels. Worldwide, stroke is the second leading cause of mortality and the third leading cause of disability. The main objective of our study is to assess the prescribing pattern and rate of medication adherence in stroke patients. A prospective observational study was conducted for a period of 6 months at various departments of a Tertiary Care Hospital. Patients of both sex, above the age of 18 years, with a history of stroke and its associated comorbidities, and those who are diagnosed with stroke are included in the study. Written informed consent, Demographic details, clinical and medication details were collected in a specially designed form. A total of 77 patients were included in the study. This disease is mostly observed within the age group of 61-70 years, out of which 51 were male and 26 were female. Majority of the patient suffered from Ischemic stroke (87.01%). Dysarthria (41.55%) was the predominant symptom. Hypertension (62.23%), Diabetes mellitus (55.84%), and cardiovascular diseases (32.46%) were found to be the major comorbidities of stroke. The most commonly prescribed drug category was Antiplatelets (76.62%). The most commonly prescribed monotherapy drug was Atorvastatin (14.17%) and frequent combination therapy was Aspirin+clopidogrel (49.33%). The rate of medication adherence is measured using MARS (Medication Adherence Rating Scale) and the scored value of MARS showed that high adherence was reported in males and with patients less than 60 years of age. Based on comorbidities, patients with CVD were highly

adherent. Regular investigations are therefore required to ascertain the prescribing pattern, increase adherence, stop recurring hospital admissions, and boost quality of life.

KEYWORDS: Prescribing pattern, Stroke, Comorbidities, Medication adherence.

INTRODUCTION

Definition

WHO has defined stroke as "rapidly developing clinical signs of focal or global disturbance of cerebral function, lasting for more than twenty-four hours or leading to death, with no apparent cause other than vascular origin.[1] Stroke is a major cause of mortality worldwide and commonly occurs in elderly patients. It is the second leading cause of both disability and death which affect the quality of life of the patients negatively, causing depressive symptoms.[2]

Types

1) **Ischemic stroke** is caused by sudden occlusion of arteries supplying the brain, either due to a thrombus at the site of occlusion or formed in another part of the circulation. It accounts for 50%−85% of all stroke worldwide.

2) **Hemorrhagic stroke** is an acute episode of focal or global cerebral or spinal dysfunction caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage and accounts for 15% of strokes. Hemorrhagic stroke is further subdivided into:
   - Intracranial hemorrhages [ICH]
   - Subarachnoid hemorrhages [SAH].[3],[4]

3) **Transient ischemic attack (TIA)** also called a ("mini-stroke," caused by a temporary blood clot), it is a transient event, where arterial blockage in brain resolves on its own without causing any tissue death.[5]

Epidemiology

In 2010, the estimated number of incident ischemic stroke and hemorrhagic stroke across the globe was 11.6 million and 5.3 million respectively. In 2016 the number of incident new strokes increased to 13.7 million. In the same year, 5.5 million deaths worldwide were attributed to stroke and the prevalence was 80.1 million. Stroke is the second leading cause of disability and accounted for approximately 116 million global Disability adjusted life years

(DALYs) lost in 2016. Recent data from 2010 to 2017 continue to show alarming increase in stroke incidence and mortality by 5.3% each, prevalence by 19.3% and DALYs lost by 2.7%.[6] In India the estimated adjusted prevalence rate of stroke range, 84-262/100,000 in rural and 334-424/100,000 in urban areas. The incidence rate is 119-145/100,000 based on the recent population-based studies.[5]

Risk factors

According to AMERICAN STROKE ASSOCIATION (ASA) Guidelines, There are two types of risk factors in Stroke:

a) Risk Factors you can control treat and improve. (Modifiable risk factors)

b) Risk Factors not within your control. (Non-modifiable risk factors)

a. Risk factors you can control treat and improve.

1. **Hypertension:** The most major and modifiable risk factor for stroke is hypertension. Uncontrolled high blood pressure damages and weakens brain blood vessels, which can rupture or leak.

2. **Diabetes:** Diabetes mellitus, whether type 1 or type 2, is an independent risk factor for stroke. While diabetes is treatable, the presence of the disease increase the risk of stroke.

3. **Smoking:** The cardiovascular system is harmed by nicotine and carbon monoxide in cigarette smoke, which also increases the risk of a stroke.

4. **Alcohol consumption:** Excessive alcohol drinking can increase the blood pressure, which can cause atrial fibrillation that leads to the formation of blood clots in the heart, and significantly raises risk of stroke.

5. **Diet:** Blood cholesterol levels can increase with diets heavy in cholesterol, Trans fat, and saturated fat. Salt-rich diets can raise blood pressure. Diets with high calories can lead to obesity.

6. **High blood cholesterol:** High blood cholesterol levels can accumulate and lead to blood clots, which can result in a stroke.

7. **Obesity:** Obesity and excess body weight are associated with a higher risk of diabetes, high blood pressure, heart disease, and stroke.

8. **Physical inactivity:** Physical inactivity can increase risk of stroke, heart disease, overweight/obesity, high blood pressure, high blood cholesterol and diabetes.

9. **Carotid artery disease:** The neck's carotid arteries carry blood to the brain. A blood clot may block a carotid artery that has been constricted by fatty deposits from atherosclerosis (plaque build-up in arterial walls), which can result in a stroke.

10. **Other heart diseases:** Stroke risk is higher in those with coronary heart disease or heart failure than in those with healthy hearts. Stroke risk can also be increased by conditions including heart valve disease, dilated cardiomyopathy (an enlarged heart), and some congenital heart problems.

b. **Risk factors not within control**

1. **Age:** Both males and females who are older have an increased risk of getting a stroke. Even though stroke are more common in the elderly, many people under 65 also experience stroke. A stroke can occur in babies and children.

2. **Family history:** If any of the family members had a past history of stroke, especially before reaching age 65, then a person may be at greater risk. Sometimes genetic conditions like CADASIL, which can obstruct blood flow to the brain, can cause strokes.

3. **Prior stroke, TIA or heart attack:** A stroke survivor is far more likely to experience another one than someone who has never experienced one. A stroke is nearly 10 times more likely to occur in someone who has had one or more transient ischemic attacks (TIAs) compared to someone of the same age and sex who hasn't.

4. **Race:** Compared to Caucasians, African-Americans have a significantly higher risk of dying from a stroke. This is partially due to the increased prevalence of diabetes, high blood pressure, and obesity among the black population.[7]

Pathophysiology

Vascular risk factors and other general predisposing variables like coagulation cascade activation and vascular inflammation can act as a trigger for stroke. Coagulopathies and vascular abnormalities will cooperate with other risk variables to accelerate the development of stroke (either hemorrhagic or ischemic).[8]

Ischemic stroke: An ischemic stroke occurs when a blood clot prevents blood from flowing to the brain. Atherosclerosis, a buildup of fatty deposits on the inner lining of a blood vessel, is frequently the cause of the blood clot. Some of these fatty deposits may break off andobstruct blood flow to the brain. It can be an embolic stroke, is one in which a blood clot moves from another part of the body to the brain. The atrial fibrillation causes 15% of embolic stroke.

Hemorrhagic stroke: It can be caused by the rupturing or breaking of the blood vessel in the brain. This can result in spilling blood into the surrounding tissues.

It consist of three main types

- **Aneurysm**, which can force a part of the weakened blood vessel to expand outward and burst.
- **Arterio-Venous malformation**, which consist of abnormally formed blood vessels and the rupturing of these blood vessels can result in hemorrhagic stroke.
- **High blood pressure** can weaken the small blood vessels in the brain and leads to bleeding into the brain.

Transient ischemic attack: TIA is a warning or mini stroke. It can be caused by anything that temporarily prevents blood flow to brain. The blood clot and TIA symptoms only persist for a short time period.[7]

Signs and Symptoms

- Slurred Speech
- Hemiplegia
- Change in Speech
- Vomiting
- Deviation of Mouth
- Giddiness,
- Headache
- Numbness & tingling sensation
- Weakness in right side
- Weakness in left side
- Drowsiness.[9]

Diagnosis

i. CT scan

- Help to distinguish between the types of stroke.
- To rule out alternate differential diagnoses and forecast stroke outcomes

ii. **Brain MRI:** Helps in evaluation of vascular blood flow, evaluation of brain tissue perfusion, and the detection of carotid artery stenosis, distinguishing between old and new lesions, identifying stroke anatomy.[4]

iii. **Fast examination:** Which adopts facial, arm and speech weakness.

iv. **Electrocardiogram (ECG):** Determines whether the patient has arterial fibrillation, a potent risk factor for stroke.

v.   **Identifying the underlying inflammatory or clotting disorders or other** diseases like hyperlipidemia, hypertension, heart failure, myocardial infarction, ischemic heart disease, diabetes mellitus and angina.[9]

vi. **Diffusion weighted imaging:** it will reveal an evolving infarct within minutes.

vii. **Carotid Doppler:** determines the degree of stenosis in the carotid arteries which supplies the blood to the brain in patients.[10]

Complication

- Paralysis or loss of muscles movement
- Difficulty talking or swallowing.
- Memory loss or thinking difficulties.
- Emotional problems.
- Changes in behavior and self-care ability.
- Dangerous blood clots.
- Seizures.
- Swelling in the brain.
- Loss of bone density.

Management of stroke

Goals of treatment

- To minimize the signs and symptoms of stroke.
- To reduce the ongoing neurologic injury and decrease mortality and long-term disability.
- Prevent complications secondary to immobility and neurologic dysfunction.
- Prevent stroke recurrence.
- To improve quality of life.

General approach to treatment

- The first step in treating a patient who has a suspected acute stroke is to make sure they are receiving respiratory and cardiac care.

- Using the results of a CT scan, quickly evaluate if the lesion is ischemic or hemorrhagic.

- Patients who have suffered from an ischemic stroke and present within hours of the onset of their symptoms should be assessed for reperfusion therapy.

- Patients with elevated blood pressure should remain untreated unless their blood pressure exceeds 220/120 mm Hg or they have evidence of aortic dissection, acute myocardial infarction (AMI), pulmonary edema, or hypertensive encephalopathy.

- When treating high blood pressure, short-acting parenteral medications including labetalol, nicardipine, and nitroprusside are preferred.

- Hemorrhagic stroke patients should be evaluated to see if they qualify for surgical intervention using an endovascular or craniotomy method.

- After the hyper acute phase has passed, attention is directed toward:

- Preventing progressive deficits.

- Minimising complications.

- Implementing the required secondary preventative measures.[11]

Non-pharmacological treatment

a. Ischemic stroke

- A craniectomy has been tried in some cases of ischemic cerebral edema caused by a significant infarction to relieve some of the increasing pressure.

- Surgical decompression can be lifesaving, in cases of significant swelling associated with a cerebellar infarction.

- In secondary prevention, carotid endarterectomy of an ulcerated or stenotic carotid artery is a very effective way to reduce stroke incidence and recurrence in appropriate patients.

- Carotid stenting may be useful in lowering the risk of recurrent stroke in patients in whom the endarterectomy risk is deemed to be excessive yet is less invasive.

b. Hemorrhagic stroke: In patients with subarachnoid hemorrhage owing to a ruptured intracranial aneurysm or an AVM, surgical intervention to either clip or ablate the offending vascular abnormality substantially reduces mortality owing to rebleeding.[10]

c. Rehabilitation

- Physiotherapy and speech therapy has particular value in the first few weeks after stroke. It relieves spasticity, prevents contractures and teaches patients to use walking aids. Baclofen (a GABA agonist) is sometimes helpful in the management of severe spasticity following stroke.

- In aphasia, the speech therapist has a vital understanding of the patient's problems and frustration. Spontaneous return of speech is hastened by normal conversation with a help of a therapist. If the patient cannot swallow safely without the risk of aspiration, either nasogastric feeding or percutaneous gastrostomy will be needed.

- Following early recovery, aids and modifications may be necessary at home. For example: stair rails, portable lavatories, bath rails, hoists, sliding boards, wheelchairs, tripods, altering doorways and sleeping arrangements, stair lifts and kitchen modifications. Liaison between a hospital-based neurology community care team, locally based therapists and primary care physician is valuable.[11]

Pharmacological treatment

Ischemic stroke

- The american stroke association has created and published guidelines that address the management of acute ischemic stroke.

- In general, the only two pharmacologic agents recommended with a grade A recommendation are:

- Intravenous tissue plasminogen activator (tPA) within 3 hours of onset

- Aspirin within 48 hours of onset.

I. IV Tissue plaminogen activator

- Early reperfusion (<3 hours from onset) with intravenous tPA has been shown to reduce the ultimate disability due to ischemic stroke. Caution must be exercised when using this therapy, and adherence to a strict protocol is essential to achieving positive outcomes.

- The essentials of the treatment protocol can be summarized as

(1) Stroke team activation.

(2) Onset of symptoms within 3 hours.

(3) CT scan to rule out hemorrhage.

(4) Meet inclusion and exclusion criteria.

(5) Administer tPA 0.9 mg/kg over 1 hour, with 10% given as initial bolus over 1 min.

(6) Avoid antithrombotic (anticoagulant or antiplatelet) therapy for 24 hours.

(7) Monitor the patient closely for response and hemorrhage.

II. Antiplatelets/Anticoagulants

- Early aspirin therapy also has been shown to reduce long-term death and disability but should never be given within 24 hours of the administration of tPA because it can increase the risk of bleeding in such patients.

- The AHA/ASA guidelines recommend that:

- Antiplatelet therapy as the corner stone of antithrombotic therapy for the secondary prevention of ischemic stroke.

- Should be used in non cardioembolic stroke.

- Aspirin, clopidogrel and extended release dipyridamole plus aspirin are all considered first line antiplatelet agents.

- The combination of aspirin and clopidogrel can only be recommended in patient with Ischemic stroke and a recent history of myocardial infarction or coronary stent placement only with ultra-low dose aspirin to minimize bleeding risk.

- WARFARIN: the antithrombotic agent is the first choice for the secondary prevention in patients with atrial fibrillation and a presumed cardiac source of embolism.

III. Blood pressure control

- Elevated blood pressure is common after ischaemic stroke.

- Its treatment is associated with a decreased risk of stroke recurrence.

- The JNC and AHA/ASA guidelines recommend an ACEI and a diuretics for the reduction of blood pressure in patients with stroke or TIA after the acute period (first 7 days).

- ARB"S used in patients unable to tolerate ACEI"S.

- THE NATIONAL CHOLESTROL EDUCATION PROGRAM considered ischaemic stroke or TIA to be a CORONARY RISK EQUIVALENT and recommends the use of statins on ischemic patients to achieve an LDL<100mg/dl.

- LMWH or LOW-DOSE SUBCUTANEOUS UH (5000 units twice daily) is recommended for prevention of DVT in hospitalized patients with decreased mobility due to stroke and should be used in all but the most minor strokes.[12]

Table 1.1: Pharmacotheraphy of ischemic stroke.

DRUG	MOA	DOSE
THROMBOLYTICS STREPTOKINASE ALTEPLASE (rt-PA)	Promotes the conversion of plasminogen to plasmin, which in turn degrades fibrin into fibrin degradation products and thus rapidly dissolves blood clot.	7.5-15 lac IU infused over 1hr. 15mg IV bolus injection followed by 50mg over 30 min, then 35mg over the next 1 hr.
ANTIPLATELET THERAPY ASPIRIN	Irreversibly inhibits COX which in platelets prevent conversion of arachidonic acid to thromboxane.	75-325mg OD.
DIPYRADAMOLE (200mg) +ASPIRIN(25 mg)	Inhibits platelet aggregation by inhibiting PDE.	200mg+25mg (1 capsule) BID.
CLOPIDOGREL TICLOPIDINE	Inhibits ADP pathway. Inhibits activation of ADP receptors on platelets.	75mg OD. 250mg BID.
ORAL ANTICOAGULANTS WARFARIN	Acts as an anticoagulant by interfering with the synthesis of vitamin K dependent clotting factor in the liver.	5mg daily. Maintenance dose: 2-10mg for 2 days.
HMG CoA REDUCTASE INHIBITORS ATORVASTATIN ROSUVASTATIN SIMVASTATIN	Reduces the risk of stroke in patients with coronary artery disease and elevated plasma lipids.	10-20mg OD. 10mg OD 40mg OD

Hemorrhagic stroke

- There are no standard pharmacologic strategies for treating intracerebral hemorrhage.

- Follow medical guidelines for managing BP, increased intracranial pressure and other medical complications in acutely ill patient in neurointensive care units.

- SAH due to aneurysm rupture is often associated with delayed cerebral ischemia, 2 weeks after the bleeding episodes.

- Vasospasm of the cerebral vasculature is thought to be responsible for the delayed ischemia and occurs between 4 and 21 days after the bleed. The calcium channel blocker nimodipine 60mg every 4hrs for 21 days, along with maintenance of intravascular volume with pressor therapy, is recommended to reduce the incidence and severity of neurologic deficits resulting from delayed ischemia.[12]

AIMS AND OBJECTIVES

The main aim of the study is to assess the prescribing pattern and rate of medication adherence in stroke patients.

Primary objectives

- To assess the prescribing pattern of drugs in stroke patients and associated comorbidities.
- To know the proportion of adherence and non-adherence in stroke patients using the MEDICATION ADHERENCE RATING SCALE (MARS).

MATERIALS AND METHODOLOGY

Study design: A Prospective Observational Study.

Study site: The study will be conducted in various departments of Indiana Hospital And Heart Institute, Pump well, Mangalore.

Study duration: The study will be carried out for a period of 6 months.

Study criteria: The study will be carried out by considering the following criteria:

Inclusion criteria

- Inpatient.
- Male and female patients of age 18 years and above.
- Patients with a history of stroke.
- Patients willing to participate in the study.
- Patients diagnosed with ischaemic and hemorrhagic stroke.
- Patients with identified and unidentified risk factors.
- Patients diagnosed with stroke and having other comorbidities.

Exclusion criteria

- Patients refusing the consent.
- Age group less than 18 years.
- Patients with intracranial abnormalities like subdural hematoma, brain tumor, and dementia.
- Patients unable to respond to verbal questions with no caretaker.
- Pregnant or lactating women.

Ethical approval: This study was approved by Indiana Hospital And Heart Institute, Pumpwell, Mangalore.

Source of data

a) Patient case sheet.

b) Prescriptions.

c) Patient Interview.

d) Questionnaires.

e) Data collection form.

Study procedure: The study will be conducted in the neurology department of Indiana Hospital And Heart Institute, Mangalore. Considering the inclusion and exclusion criteria, patients will be enrolled after taking written consent from each patient for the study. A suitably designed data collection form will be used to collect all the necessary information. The data collection includes the following details: demographics of the patient, laboratory findings, comorbidities, if any, medication prescribed, doses, route of administration, frequency, and total duration of treatment. Pharmacological therapy prescribed was analyzed to determine the pattern of prescription of drugs. Medication adherence of the patient will be observed using MEDICATION ADHERENCE RATING SCALE (MARS).

Sample size: Based on the study conducted by Isaac BS et al.,[17] assuming p= 26.1% with 95% Confidence interval and 10% absolute allowable error (L) the sample size estimated for the study is 77.

Sampling technique: Convenient sampling.

Statistical analysis: Baseline data will be entered in Microsoft Excel. Categorical data will be expressed as percentages. Quantitative data will be expressed as mean and standard deviation. Non-Parametric test was assessed using the chi-square test. The p-value of <0.05 was considered significant. Appropriate diagrams and graphs will be used to represent the data.

RESULT

A prospective observational study was conducted for 6 months at Indiana Hospital and Heart Institute, Pumpwell, Mangalore. A total of 77 patients having stroke were included in the study.
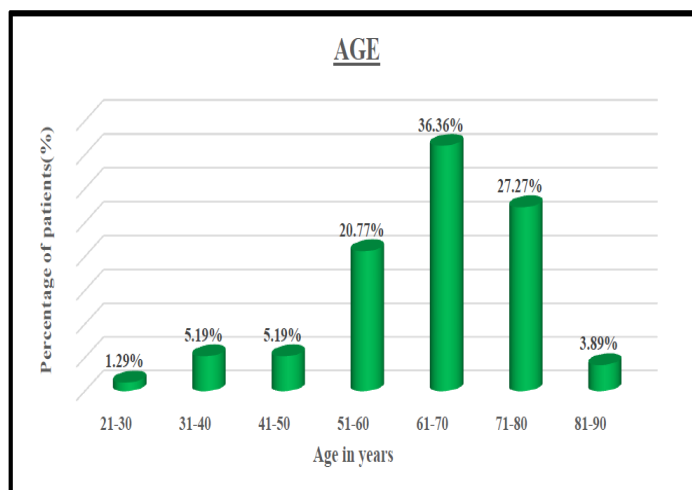
Age-wise distribution of patients

Out of 77 patients, most of the patients were in the range of 61-70 years (36.36%). The age range was from 21-90 years with a mean age of 64.09 years (SD=11.45).

Table 5.1: Frequency and Percentage distribution of patients according to age in years. N=77

Age in years	Frequency	Percentage
21-30	1	1.29%
31-40	4	5.19%
41-50	4	5.19%
51-60	16	20.77%
61-70	28	36.36%
71-80	21	27.27%
81-90	3	3.89%
Mean ± SD		64.09 ± 11.54

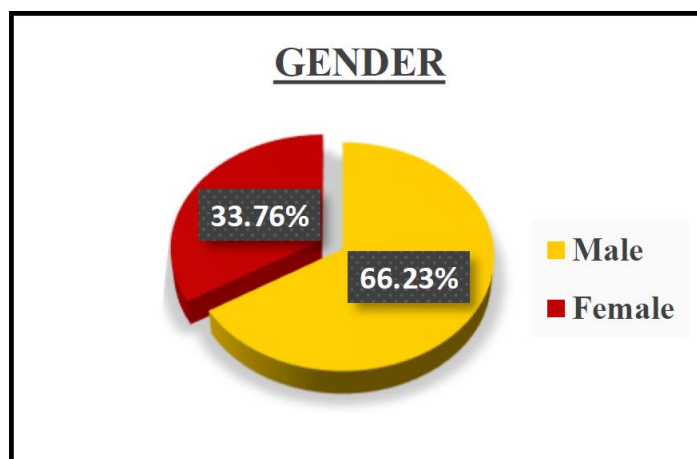**Figure 5.1: Percentage distribution of patients according to age in years.**

Gender distribution of patients

Out of 77 patients, 51 (66.23%) were males and 26 (33.76%) were females.

Table 5.2: Frequency and Percentage distribution of patients based on gender. N=77

Gender	Frequency	Percentage
Male	51	66.23%
Female	26	33.76%

**Figure 5.2: Pie chart of percentage distribution of patients based on gender.**

Patient based on types of stroke

Out of total study population (77), number of patients who experienced Ischemic stroke were 67 (87.01%), Hemorrhagic stroke were 9 (11.68%) and Transient Ischemic Attack were 1 (1.29%).

Table 5.3: Frequency and Percentage distribution of patients based on types of stroke. N=77

Types of stroke	Frequency	Percentage
Ischemic stroke	67	87.01%
Hemorrhagic stroke	9	11.68%
TIA	1	1.29%
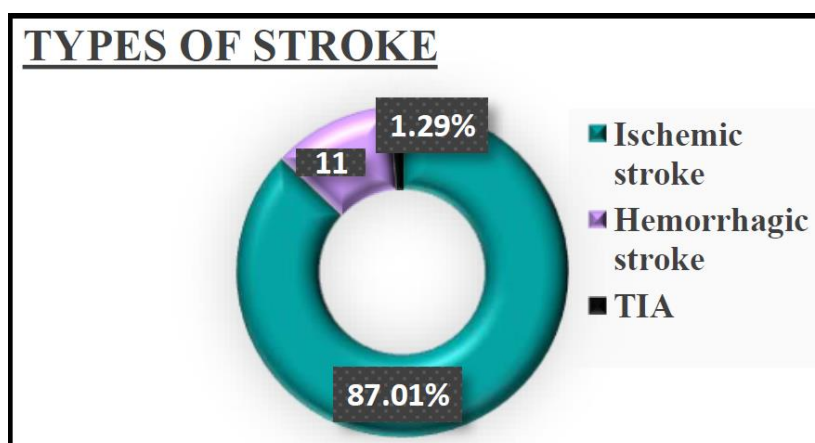
**Social habits of study participants**

In our studies social habits of patients with cigarette smoking and alcohol consumption were evaluated and smoking (20.77%) indicated a higher rate of incidence than either alcoholic use (2.59%) or both (11.68%).

Table 5.4: Frequency and Percentage distribution of social habits in stroke patients.
N=77

Social habits	Frequency	Percentage
Smoker	16	20.77%
Alcoholic	2	2.59%
Both	9	11.68%
None	50	64.93%
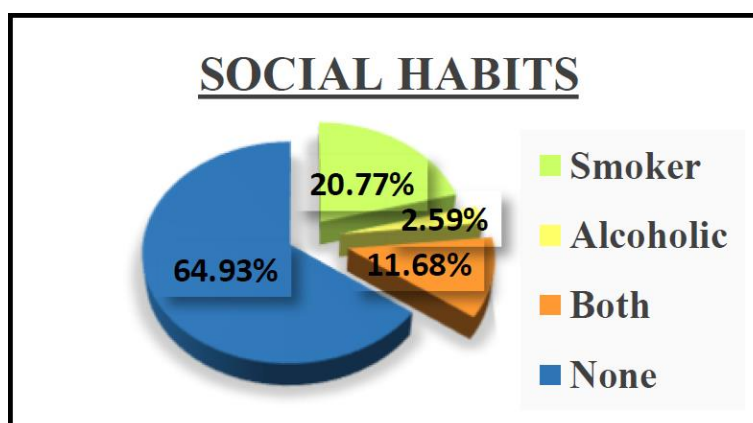
Figure 5.4: Percentage distribution of social habits in stroke patients.

Patient distribution based on symptoms

Symptom-wise distribution of stroke was analyzed in which dysarthria (41.55%) was predominant followed by right hemiparesis (32.46%), left hemiparesis (27.27%), generalized weakness (22.07%), vomiting and giddiness (11.68%), altered sensorium (10.38%), headache (9.09%), facial palsy (7.79%), ataxia and loss of consciousness (6.49%) and aphasia (2.59%) was observed in study participants.

Table 5.5 Frequency and Percentage distribution of symptoms in stroke patients (N=77)

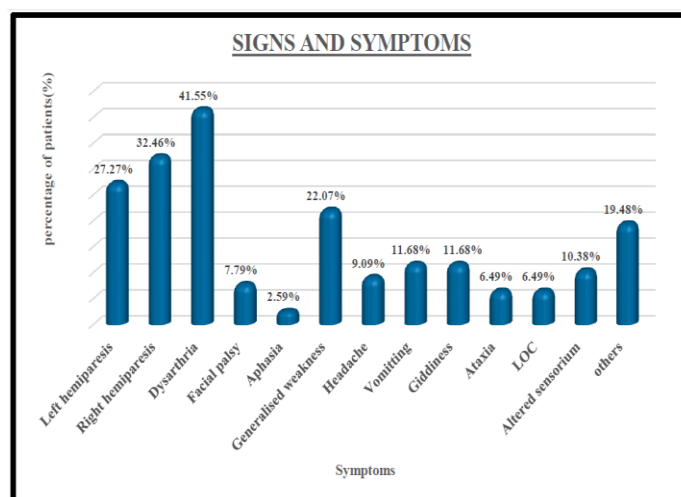| Signs and Symptoms	Frequency	Percentage
Left hemiparesis	21	27.27%
Right hemiparesis	25	32.46%
Dysarthria	32	41.55%
Facial palsy	6	7.79%
Aphasia	2	2.59%
Generalized weakness	17	22.07%
Headache	7	9.09%
Vomiting	9	11.68%
Giddiness	9	11.68%
Ataxia	5	6.49%
LOC	5	6.49%
Altered sensorium	8	10.38%
Others	15	19.48%

Figure 5.5: Percentage distribution of symptoms in stroke patients.

Patient distribution based on comorbidities

Out of 77 patients, HTN (62.33%) was the most prevalent comorbidity followed by diabetes mellitus (55.84%), CVD (32.46%), CKD (10.38%) and seizures (3.89%).

Table 5.6: Frequency and Percentage distribution of patients according to comorbidities N=77.

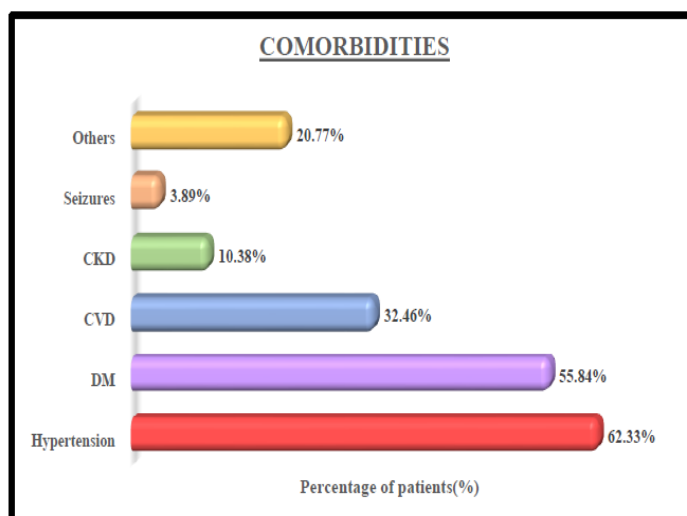| Comorbidities	Frequency	Percentage
Hypertension	48	62.33%
DM	43	55.84%
CVD	25	32.46%
CKD	8	10.38%
Seizures	3	3.89%
Others	16	20.77%

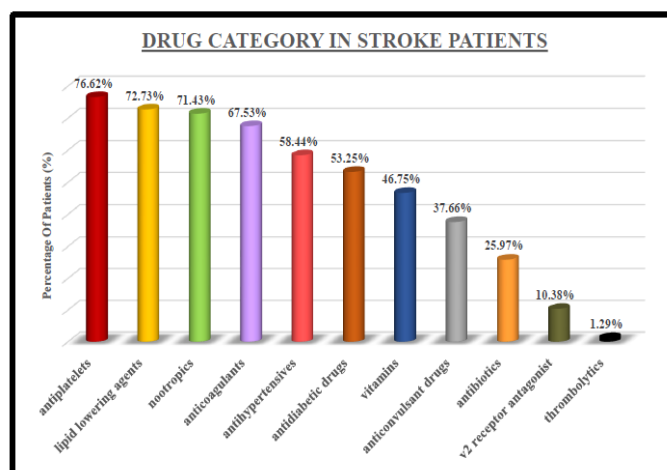**Figure 5.6: Percentage distribution of patients according to comorbidities.**

Percentage distribution of stroke patients based on drug categories

Among the drug categories prescribed for hospitalized stroke patients, Antiplatelets (76.62%) was the most commonly prescribed drug followed by lipid lowering agents (72.73%), nootropics (71.43%), anticoagulants (67.53%), antihypertensives (58.44%), antidiabetic (53.25%), vitamins (46.75%), anticonvulsants (37.66%), antibiotics (25.97%), V2 receptor antagonist (10.38%) and thrombolytics (1.29%).

Table 5.7: Frequency and Percentage distribution stroke patients based on drug categories N=77.

| Drug category	Frequency	Percentage
Antiplatelets	59	76.62%
Lipid Lowering Agents	56	72.73%
Nootropics	55	71.43%
Anticoagulants	52	67.53%
Antihypertensives	45	58.44%
Antidiabetic Drugs	41	53.25%
Vitamins	36	46.75%
Anticonvulsant Drugs	29	37.66%
Antibiotics	20	25.97%
V2 Receptor Antagonist	8	10.38%
Thrombolytics	1	1.29%

Figure 5.7: Percentage distribution of drug categories in stroke patients.

Monotherapy vs Combination therapy

A total 463 drugs were prescribed for stroke treatment, out of which 388 (83.80) were monotherapy and 75 (15.85) were combination therapy.

Table 5.8: Frequency and Percentage distribution of Monotherapy Vs. Combination therapy.

Type of therapy	Frequency	Percentage
Monotherapy	388	83.80%
Combination therapy	75	15.85%
Total	463	
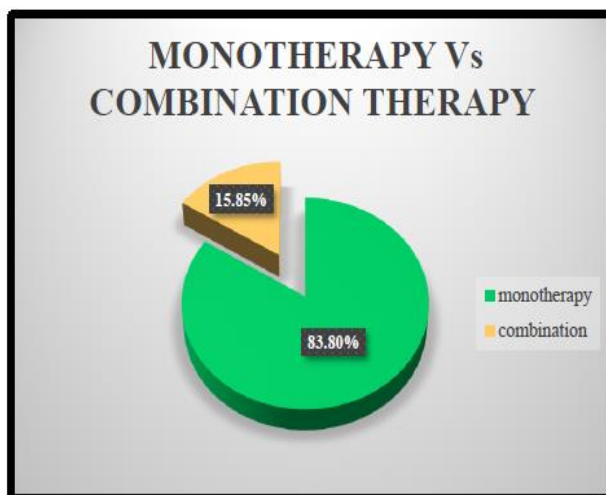
Figure 5.8: Monotherapy Vs Combination therapy.

Commonly prescribed monotherapy

Table 5.9: Shows most commonly prescribed monotherapy in patients. Atorvastatin (14.17%), Piracetam (13.40%), Enoxaparin (11.08%) were the most frequently used drugs in patients.

Drug name	Frequency	Percentage
Atorvastatin	55	14.17%
Piracetam	52	13.40%
Enoxaparin	43	11.08%
Vitamin E	23	5.92%
Clopidogrel	18	4.63%
Calcium Channel Blockers	14	3.60%
Aspirin	13	3.35%
Diuretics	12	3.09%
Levetiracetam	12	3.09%
ARB"s	10	2.57%
Beta Blockers	10	2.57%
Vitamin B1	10	2.57%
Insulin	9	2.31%
Cephalosporins	9	2.31%
Heparin	8	2.06%
Citicoline	8	2.06%
Central Alpha Agonist	8	2.06%
Sulfonylureas	8	2.06%

Tolvaptan	8	2.06%
DPP-4	6	1.54%
Fosphenytoin	6	1.54%
Pregabalin	6	1.54%
Biguanides	5	1.28%
Rivaroxaban	4	1.03%
SGLT-2 Inhibitors	4	1.03%
Phenytoin	4	1.03%
Clonazepam	3	0.77%
Vitamin K	3	0.77%
Vitamin D	3	0.77%
Rosuvastatin	2	0.51%
Alpha+Beta Blockers	2	0.51%
Lacosamide	2	0.51%
Vitamin B12	2	0.51%
Apixaban	1	0.25%
Tenecteplase	1	0.25%
ACE Inhibitors	1	0.25%
Alpha Blockers	1	0.25%
Brivaracetam	1	0.25%
Carbamazepine	1	0.25%
Total	388	

Commonly prescribed combination therapies

Table 5.10: Shows commonly prescribed combination therapies. Aspirin + Clopidogrel (49.33%) was the most commonly prescribed combination therapy followed by Glimepiride + Metformin (10.66%) and Sitagliptin + Metformin (6.66%).

Drug name	Frequency	Percentage
Aspirin + clopidogrel	37	49.33%
Glimepiride + metformin	8	10.66%
Sitagliptin + metformin	5	6.66%
Cefoperazone + sulbactam	5	6.66%
Piperacillin + tazobactam	5	6.66%
Glimeieride + metformin +voglibose	4	5.33%
Dapagliflozin + metformin	3	4%
Amoxicillin + clavulanic acid	3	4%
Telmisartan + metoprolol	2	2.66%
Atenolol + nifedipine	1	1.33%
Telmisartan + hydrochlorothiazide	1	1.33%
Amlodipine + telmisartan	1	1.33%
Total	75	

Distribution of drugs prescribed in a prescription

In the present study, majority of patients were prescribed with 5 drugs (31.19%) followed by 4 drugs (23.38%), 6 drugs (22.08%), 3 drugs (9.09%), 7 drugs (6.49%), 2 drugs (3.89%), 8 drugs (2.59%) and 1 drug (1.29%).

Table 5.11: Frequency and Percentage distribution of drugs prescribed in a prescription N=77.

No. of drugs	No. of Prescription	Percentage (%)
1	1	1.29%
2	3	3.89%
3	7	9.09%
4	18	23.38%
5	24	31.19%
6	17	22.08%
7	5	6.49%
8	2	2.59%

Who prescribing indicators

Based on the result of the study, 10.1 medication were typically prescribed for each prescription, which was more than the optimal value (1.6-1.8). Only 3.89% of prescription were written in generic names which was much lower than the standard range (100%). 25.97% of prescription were prescribed with antibiotics which was within the optimal range (20-26.8%). The total percentage of encounter with injections prescribed was 96.1%, which was much higher than the ideal value (13.4-24.1%). The percentage of drug prescribed from EDL of WHO was 40.85%, which is lesser than the standard value (100%).

Table 5.12: Who prescribing indicator.

Indicator	Value	Optimal Value
Average number of drugs per prescription	10.01	1.6-1.8
Percentage of drugs prescribed by generic name	3.89%	100%
Percentage of encounters with antibiotic prescribed	25.97%	20-26.8%
Percentage of encounters with an injection prescribed	96.1%	13.4-24.1%
Percentage of drugs prescribed from essential drug list	40.85%	100%

Measurement of medication adherence in stroke patients using medication adherence rating scale (mars)

a) By using Medication Adherence Rating Scale (MARS), high, medium, and low adherence was reported in 54.55%, 33.77%, and 11.68% respectively.

Table 5.13: Medication adherence rating scale.

Variables	Frequency	Percentage (%)
Low	9	11.68%
Medium	26	33.77%
High	42	54.55%
Total	77	100%
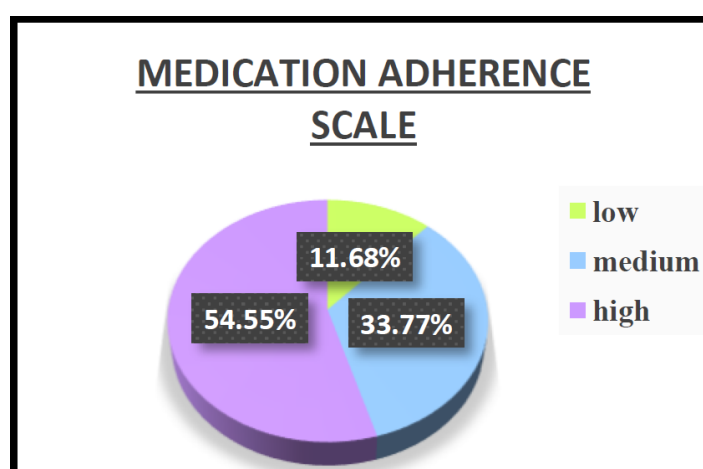
Figure 5.13: Percentage distribution of stroke patients based on medication adherence using MARS.

Characteristics of patients based on medication adherence rating scale (mars)

a) Based on age

Among patients with age < 60 years, high, medium, and low adherence was reported in 56%, 36%, and 8% respectively, and in >60 years of age, it was reported at 53.84%, 36.53% and 9.61% respectively. From the chi-square test, we analyzed that our result has no statistically significant relationship between age and adherence **(p-value 0.05< 0.9684)**.

Table 5.14(a) Medication adherence rating scale based on age.

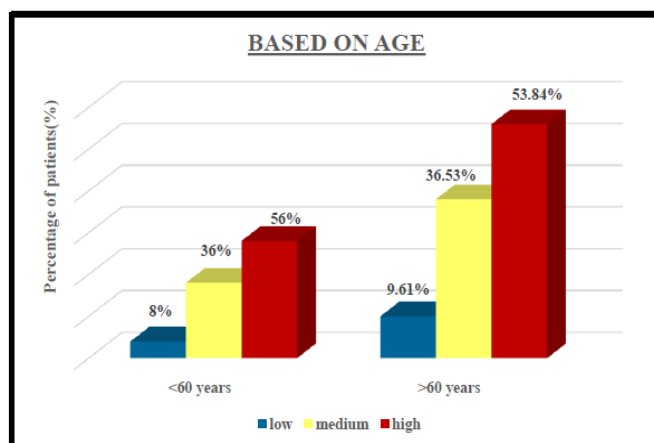| Variables	<60 Years	>60 Years	p-value
Low	2	5	**0.968426**
Percentage (%)	8%	9.61%	
Medium	9	19	
Percentage (%)	36%	36.53%	
High	14	28	
Percentage (%)	56%	53.84%	

Figure 5.14(a) Medication adherence rating scale based on age.

b) Based on gender

In the present study, majority of males (58.82%) and females (46.16%) were highly adherent to the treatment. From the chi-square test, we analyzed that our result has no statistically significant relationship between gender and adherence **(p-value 0.05< 0.54248)**.

Table 5.14(b) Medication adherence rating scale based on gender.

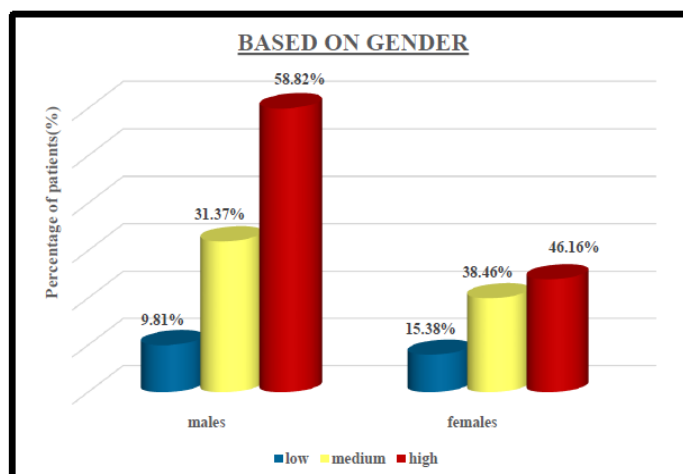| Ariables	Males	Females	p-value
Low	5	4	
Percentage (%)	9.81%	15.38%	
Medium	16	10	0.542824
Percentage (%)	31.37%	38.46%	
High	30	12	
Percentage (%)	58.82%	46.16%	

Figure 5.14(b) Medication adherence rating scale based on gender.

c) Based on comorbidities

Patients with cardiovascular diseases (62.50%) showed high adherence when compared to hypertension (46.94%) and diabetes mellitus (46.51%). From the chi-square test, we analyzed that our result has no statistically significant relationship between comorbidities and adherence **(p-value 0.05< 0.67053)**.

Table 5.14(c) Medication adherence rating scale based on comorbidities.

Variables	Hypertension	Diabetes Mellitus	CVD	p-value
Low	9	6	3	
Percentage (%)	18.37%	13.95%	12.50%	
Medium	17	17	6	**0.670531**
Percentage (%)	34.69%	39.53%	25%	
High	23	20	15	
Percentage (%)	46.94%	46.51%	62.50%	
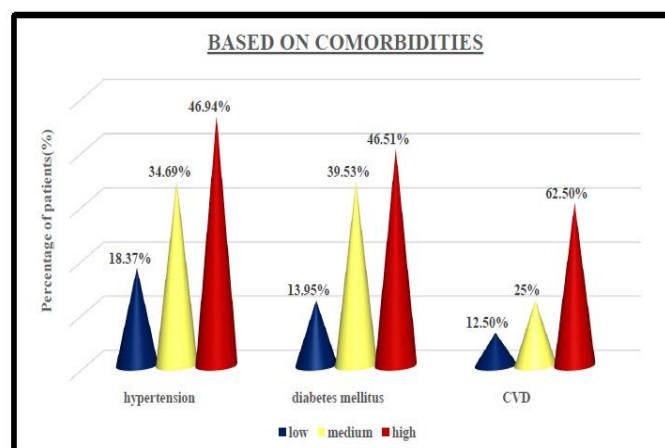
Figure 5.14(c): Medication adherence rating scale based on comorbidities.

DISCUSSION

Stroke is a cerebrovascular disorder in which cerebral blood vessels gradually deteriorate.[20] It is recognized as one of the neurological disease that affect a large number of people worldwide. Consequently, it is the second most common cause of death.[2]

This prospective observational study was conducted for a period of 6 months at the Indian Hospital and Heart Institute, Pumpwell Mangalore, to evaluate the prescribing pattern and rate of medication adherence in stroke patients.77 patients were identified and included for further study as they fulfil the study criteria. According to the current study, stroke incidence was greater in patients aged 61-70 years (36.36%) followed by 71-80 years (27.27%), whichis in accordance with the outcomes of the study conducted by **Jose MM *et.al,***[3] **Sk K *et.al.***[7] This indicates that as age advances there is a significant chance to have a neurological

illness due to decreased physical activity, and an increased rate of lack of educational status in the elderly compared to younger people. Age being one of the non-modifiable risk factors of stroke increases the rate of stroke occurrence even more. The mean age of patients who developed stroke in our study was found to be 64.09 years (SD=11.54). This can be correlated to the study conducted by **Jose MM *et.al,***[3] **Waegl *et.al***[34] and **Po HL *et.al***[16] was 60.4 years (SD=12.8), 61.52 years (SD=16.2).65.2 years (SD=12.3) respectively. Out of 77 patients, 51 (66.23%) were males and 26 (33.76%) were females. This study revealed that males were more prone to develop a stroke than females which was in compliance with the result of the study conducted by **Jose MM *et.al,***[3] **Sk K *et.al,***[7] and **Dungavath S *et.al.***[9] This may be due to an increased risk of hypertension and diabetes mellitus in males than in females. Thus it has been observed that age and sex-related increase in stroke have made neurological disorders a common complaint in many types of research including our study.

Amid the 77 patients reported with stroke, ischemic stroke (87.01%) occurred more frequently than hemorrhagic stroke (11.68%). This result coincides with the study conducted by **Sk K *et.al,***[7] in which ischemic stroke (86.09%) and hemorrhagic stroke (13.9%). A higher rate of ischemic stroke over hemorrhagic stroke was observed in almost all the studies, this stipulated a higher prevalence of clinical factors such as older age, lifestyle, risk factors, family history of stroke, or any other cardiovascular disease. Certain pathophysiological changes in brain vessels can also be the reason for the increase of ischemic stroke over hemorrhagic stroke.

Social histories of 77 patients were observed, in which smoking (20.77%) indicated a higher rate of incidence than either alcoholic use (2.59%) or both (11.68%). This result was similar to the study conducted by **Dungavath S *et.al.***[9] In our study, the symptom-wise distribution of patients was analyzed, in which dysarthria (41.55%) was predominant followed by right hemiparesis (32.46%), left hemiparesis (27.27%), generalized weakness (22.07%), vomiting and giddiness (11.68%), altered sensorium (10.38%), headache (9.09%), facial palsy (7.79%), ataxia and loss of consciousness (6.49%) and aphasia (2.59%). This study result corresponded to the research conducted by **Dungavath S *et.al.***[9] **Sangram vurumadla *et.al,***[27] and **Konduru SS *et.al.***[29] This suggests that participants were likely to report all the symptoms, indicating that doctors should pay close attention to these symptoms in patients while also being aware of the potential symptoms that may be underreported in somepopulations. Considering the high prevalence of symptoms listed in the current study,

documenting individual stroke symptoms is necessary for academic research and even therapeutic practice.

Major comorbidities associated with stroke were assessed, in which Hypertension (62.33%) was the most prevalent followed by diabetes mellitus (55.84%), CVD (32.46%), CKD (10.38%), and seizures (3.89%). This was in concordance to the outcomes conducted by **Jose MM *et.al,*** [3] **Swetha K *et.al,*** [1] and **Sangram vurumadla *et.al.*** [27]

Prescribing pattern studies are drug utilization studies with the main focus on the rational use of drugs in populations. By conducting a periodic prescription audit, one can assess the rational prescribing skill of the clinicians. [23] In the present study, we observed that the most commonly prescribed category of drugs in stroke patients was Antiplatelets (76.62%) followed by lipid-lowering agents (72.73%), nootropics (71.43%), anticoagulants (67.53%), antihypertensives (58.44%), antidiabetic (53.25%), vitamins (46.75%), anticonvulsants (37.66%), antibiotics (25.97%), V2 receptor antagonist (10.38%) and thrombolytics (1.29%). This result was similar to the study conducted by **Konduru SS *et.al.*** [29] In **Sk K *et.al.*** [7] article, based on etiology stroke prevention was classified into two types:

A) **Primary prevention:** Included treatment with antiplatelets, lipid-lowering agents, and antihypertensives. Our study too proved that for the primary prevention of stroke, patients were treated with Antiplatelets (76.62%), Lipid-Lowering Agents (72.73%), and Antihypertensives (58.44%).

B) **Secondary prevention:** This included Warfarin, Heparin, Carotid Endarterectomy, and Carotid Angioplasty. Our study prioritized the use of Anticoagulants (67.53%).

Treatment pattern of stroke along with its comorbidities involved following specific pharmacological agents

1. In this study, the most commonly prescribed drug category was Antiplatelet. We observed the use of combination Aspirin+Clopidogrel (54.41%) dominated the use of monotherapy Clopidogrel (26.47%) and Aspirin (19.12%) in stroke patients. This study was in compliance with the study conducted by **Waegl *et.al.*** [34] Antiplatelets were used to prevent clot formation in stroke patients. [5]

2. Lipid-lowering agents were the 2nd most prescribed drug category in our study. The most commonly prescribed drug in this category was Atorvastatin (96.49%). Statins effectively

reduce the risk of coronary heart disease, myocardial infarction, and stroke. It decreases LDL cholesterol levels in the blood and increases HDL levels effectively.[9]

3. The 3rd most commonly prescribed drug class was nootropics. In our study, Piracetam (86.67%) was the most commonly prescribed drug followed by Citicoline (13.33%). These agents have antithrombotic and neuroprotective effects. This reduces the rate of death and disability in patients with acute stroke. It mostly helps to restore language functions.[7]

4. Anticoagulant are often prescribed to patients with recent stroke to prevent early recurrent stroke and to improve neurological outcomes. in our study Enoxaparin (76.78%) was the most commonly prescribed anticoagulant followed by Heparin(14.29%), similar to the study by **Dasegowda G *et.al,***[33] **Waegl *et.al.***[34]

5. Antihypertensives are one of the major classes of drugs in stroke patients to lower blood pressure and prevent the recurrence of stroke.[5] In our study, we observed that B-blockers, diuretics, and calcium channel blockers were used to reduce target BP in patients. This was as per the study conducted by **Waegl *et.al.***[34] Calcium channel blockers and beta blockers were used for primary and secondary prevention of myocardial infarction and coronary heart disease[9] whereas, diuretics were considered rational for stroke treatment. In our study and the study conducted by **Dungavath S *et.al,***[9] **Preethi Prathyusha B *et.al***[21] furosemide and mannitol were the commonly prescribed diuretics. Mannitol has an antiodema effect and was used to reduce intracranial pressure.[9]

6. Antidiabetic drugs were used to treat diabetes mellitus which is an associated comorbidity as well as a risk factor for stroke. The use of these drugs coincides with the study conducted by **Dasegowda G *et.al.***[33]

7. Anticonvulsant drugs were used to treat seizures in stroke patients. Seizures are more likely observed in ischemic stroke than hemorrhagic stroke.[33] Levetiracetam (34.38%) is the most commonly prescribed drug in our study but other researches showed the predominance of Phenytoin, which was prescribed for 11.42% of patients in our study.

8. The risk of hospital-acquired infection in stroke patients is very high, thus they were prescribed with antibiotics. In our study, Cephalosporins (40.90%) were more commonly prescribed followed by combination therapy of Cefoperazone+Sulbactam (22.72%),

Piperacillin+Tazobactam (22.72%), and Amoxicillin+Clavulanic acid (13.66%). These results are similar to the study conducted by **Dungavath S *et.al.***[9]

9. Thrombolytic agents are recommended for the treatment of ischemic stroke. It was observed that only 3% of the population receive this agent**.** Thrombolytics therapy must be used within 3 hrs of onset of symptoms but improved clinical results are seen after 4.5 hours.[33] **Dasegowda G *et.al***[33] study shows a similar outcome as our study in which only one patient was prescribed with a thrombolytic agent due to delay in hospitalization.

In the present study, majority of the drugs were prescribed as monotherapy (83.80%), followed by combination therapies (15.85%). **Jose MM *et.al***[3] also concluded similar results in their study. The most frequently used drugs were Atorvastatin (14.17%), Piracetam (13.40%), and Enoxaparin (11.08%) and the most common combination therapy was Aspirin+ Clopidogrel (49.33%) which showed uniform results as that of the study by **Waegl *et.al.***[34]

In the present study, a total of 463 stroke drugs were prescribed in 77 prescriptions and most of the patients were prescribed with 5 drugs. Similar findings were found by **Jose MM *et.al.***[3] **and Chachu Kuriakose *et.al.***[13]

As per the results of this study, the average number of drugs prescribed per prescription was 10.1, which was higher than the standard value (1.6–1.8). Polypharmacy was quite evident in our study. If the treatment is based on the diagnosis rather than the clinical symptoms, polypharmacy can be avoided.[5] Drugs were prescribed by generic names in only 3.89 % of prescriptions, which was much lower than the standard value (100%). Medical representatives of pharmaceutical firms frequently influence doctors' prescribing practices, which may promote the use of brand-name drugs. The use of generic prescription medications might rationalize drug usage and lower healthcare costs.[5] WHO estimates that between 20.0% and 26.8% of prescriptions will include an antibiotic since infectious disorders are more widespread. In the present study, the total number of encounters with an antibiotic was 25.97%, which is optimal for the standard value. Antibiotic overuse increases the risk of adverse medication reactions, antimicrobial resistance, and health care costs.[5] The total number of encounters with injectables was 96.1%, which is higher than the standard value (13.4%–24.1%). The use of injectables must be reduced to prevent blood-borne diseases and hospital-acquired infections. The percentage of drugs prescribed from the EDL

by WHO was 40.85%, which is much lower than the standard value (100%). This can be due to a lack of knowledge, understanding, and awareness of the list of essential medications. This indicator result was almost similar to the study conducted by **Hussainy SA *et.al.*** [5]

Adherence to the treatment regimen is defined as the degree to which a person follows the recommended dosage and intervals for taking medications. [28] In our study, it was observed that stroke survivors reported good adherence to their medications. Medication adherence rating scale (MARS) was used to assess the adherence rate in our patients. Out of 77 patients, it was reported that 54.55% were highly adherent followed by, 33.77% were moderately adherent, and 11.68% were low adherent. The scale was referred from the study of **O'Carroll R *et.al.*** [14] Certain characteristics were used to assess adherence in patients. Age was the primary characteristic in which we observed that people aged above 60 years had a chance of low adherence (9.61%) when compared to people below 60 years (8%). Gender was the second characteristic in which we noticed that females were comparatively less adherent than males. The data showed no statistically significant relationship ($P \geq 0.05$) and thus there was no association between adherence and participants" sociodemographic data (age and gender). This finding was in concordance with the study conducted by **Han YK *et.al.*** [25] When adherence was assessed based on comorbidities, we observed that people with hypertension (46.94%) have a chance of being less adherent when compared to diabetes mellitus (46.51%) and CVD patients (62.50%). Thus, statistical test concluded that there was no statistically significant association between comorbidities and adherence ($P \geq 0.05$). This was similar to the conclusion of the study conducted by **Han YK *et.al.*** [25] Most of the patients in our study reported high adherence but an ample amount of patients were low adherent. The reason forlow adherence was: Old age patients cannot effectively participate in activities by themselves, personal belief in the effectiveness of the treatment, polypharmacy, forgetfulness, not finding it necessary to continue the drug, feeling better, and life stress.

CONCLUSION

Our study involved 77 participants with stroke disease and showed that majority of the patients were diagnosed with ischemic stroke attacks (87.01%). This disease is mostly observed within age group of 61-70 years, mean age being 64.09 years (SD 11.45). Most of the patients found were males compared to females (66.23% - males and 33.76% females). Dysarthria (41.55%), right hemiparesis (32.46%), left hemiparesis (27.27%) and generalised weakness (22.07%) were the symptoms that generally observed in the study population. The

study findings suggest that hypertension was the most prevalent comorbidity among the stroke patients.

Our study analysed the prescription pattern of stroke patients and revealed that Anti-platelets were the most usually prescribed drug among the study population followed by lipid loweringagents, nootropics, anticoagulants, anti-hypertensives, antidiabetic, vitamins, anticonvulsants, antibiotics, V2 receptor antagonist and thrombolytics. Atorvastatin, Piracetam, Enoxaparin were the most frequently used monotherapy drugs in patients and Aspirin + Clopidogrel was the most typically prescribed combination therapy in our study.

The rate of medication adherence among stroke patients in our study is measured using MARS (Medication Adherence Rating Scale) and the scored value of MARS showed that high adherence was reported in males and with patients less than 60 years of age. Based on comorbidities, patients with CVD were highly adherent. From the chi-square test, we concluded that our result has no statistically significant association between age/gender/comorbidities with medication adherence.

Limitations

A few shortcomings of this prospective observational study can be considered.

- Patients were not chosen at random; instead, they were included in the study since they participated in the relevant departments and agreed to provide signed informed consent.
- Our study population was enrolled from a single study center that is limited to a hospital-based evaluation.
- We excluded patients with intracranial abnormalities like subdural hematoma, brain tumor, and dementia, Patient unable to respond to verbal questions with no caretaker, and Pregnant or lactating women.

The small sample size, short study duration, and lack of follow-up have limited our study's effectiveness.

Future perspectives

- Knowledge about the complications of underlying diseases like hypertension, DM and lifestyle modification can helps to reduce the recurrent stroke.

- The study can be extended to many centre, that is multicentre study instead of a single centre study, that can includes more participants and lasts longer can produce more accurate results.

REFERENCE

1. Swetha K, Singh S. A retrospective study of prescription pattern of drugs in the management of stroke, at BRIMS teaching hospital, Bidar, India. International Journal Basic Clinical Pharmacology, 2018; 7: 1929-33.

2. Fırat O, Arsava EM, Togay-Isıkay C, Basol M, Topcuoglu MA, Demirkan K. Clinical Pharmacist's Contribution on Treatment Adherence and Quality of Life in Patients with Stroke: A prospective, controlled, clinical pharmacist led-educational study. Authorea Preprints, 2021.

3. Jose MM, Shaji N, Varghese SA, Biju AS. Study on assessing the prescribing pattern of drugs, risk factors and symptoms in ischemic stroke patients in a tertiary care teaching hospital, 2019; 12(8): 1173-1185.

4. Keith W Muir. Medical management of stroke. Journal Neural Neurosurgery Psychiatry, 2001; 70(1): 12–16.

5. Hussainy SA, Habeeb M, Jeelani A, Sultana S, Meeran MM. A Prospective Observational Study on Risk Factors and Prescribing Patterns of Drugs used in Stroke Patients at a Tertiary Care Teaching Hospital. Journal of Drug Delivery and Therapeutics, 2020; 10(5-s): 71-5.

6. Saini V, Guada L, Yavagal DR. Global epidemiology of stroke and access to acute ischemic stroke interventions. Neurology, 2021; 97(20, 2): S6-16.

7. Sk K, Kumar N, Sneha S. Assessment of risk factors and drug utilization pattern of stroke patients in the neurology department. World Journal of Current Medical and Pharmaceutical Research, 2020; 2(1): 53-62.

8. Alrabghi L, Alnemari R, Aloteebi R, Alshammari H, Ayyad M, Al Ibrahim M, et.al. Stroke types and management. International Journal Community Medicine Public Health, 2018; 5(9): 1-5.

9. Dungavath S, Mudhaliar RM, Venkataramana B, Yiragamreddy PR. Drug use evaluation and appropriateness of medication used in stroke patients. World Journal, 2016; 2(5): 168-174.

10. Wells B.G, Dipiro C. Pharmacotherapy Graw Hill Professional Handbook 7th edition New York USA: Mc GrawHill Professional publishing, 2009; 13: 156-161.

11. Tolcha Regasa. Pharmacotherapy of Stroke slide share, 2021; 1-50.

12. S.Bibi Habiba. Stroke slide share, 2021; 1-55.

13. Wolfe CD The impact of stroke. British medical bulletin, 2000; 56(2): 275-86.

14. Kuriakose C, Shifafiya MN, Tharakan NS, Sattanathan K, Kumar RS. A prospective study of clinical profile of stroke in a tertiary care hospital. Asian Journal Pharmaceutical Clinical Research, 2016; 9(3): 1-4.

15. 15.O'carroll R, Whittaker J, Hamilton B, Johnston M, Sudlow C, Dennis M. Predictors of adherence to secondary preventive medication in stroke patients. Annals of Behavioral Medicine, 2011; 41(3): 383-90.

16. Cheiloudaki E, Alexopoulos EC. Adherence to treatment in stroke patients. International journal of environmental research and public health, 2019; 16(2): 196.

17. Po HL, Lin YJ, Hseuh IH. The prescribing patterns of antithrombotic agents for prevention of recurrent ischemic stroke. Acta Neurol Taiwan, 2009; 18(2): 98-103.

18. Yeo SH, Toh MP, Lee SH, Seet RC, Wong LY, Yau WP. Impact of medication nonadherence on stroke recurrence and mortality in patients after first-ever ischemic stroke: Insights from registry data in Singapore. Pharmacoepidemiology and drug safety, 2020; 29(5): 538-49.

19. Crayton E, Wright AJ, Ashworth M. Improving medication adherence in stroke survivors: the intervention development process. BMC health services research, 2018; 18(1): 1-3.

20. Mathew E, Chandrika C, Karanath PM, Srinivasa R. A prospective observational study on prescribing trends and adverse reaction in stroke patients. International Journal Pharmaceutical Science, 2017; 9: 25-30.

21. Pishkhani MK, Dalvandi A, Ebadi A, Hosseini M. Factor''s affecting adherence to rehabilitation in Iranian stroke patients: A qualitative study. Journal of Vascular Nursing, 2019; 37(4): 264-71.

22. Preethi Prathyusha B, Naveed A, Shreya S, Sri Lakshmi G, Rao V. Prescribing pattern of drugs in stroke patients admitted to a multi-specialty hospital, India. Indo-American Journal Pharmaceutical Research, 2014; 4(2): 1015-1020.

23. Abbasi MY, Ali MA. Prescribing pattern of drugs in stroke patients: A prospective study. Archives of Pharmacy Practice, 2012; 3(4): 283-288.

24. Hussain S, Yadav SS, Sawlani KK, Khattri S. Assessment of drug prescribing pattern using world health organization indicators in a tertiary care teaching hospital. Indian Journal of Public Health, 2018; 62(2): 156.

25. Bellamkonda Harsshene, Shaik Tanisha Bibi, Sreenu Thalla, N. Prathibha and Padmalatha Kantamaneni. A review study on prescribing patterns of drugs in stroke patients. World Journal of Pharmaceutical Research, 2020; 9(3): 775-790.

26. Han YK, Rajabalaya R, Binti Pg Hj Mohammad Yassin DH, David SR. Medication adherence in stroke patients in Brunei Darussalam Public Hospital: the cross-sectional study associated with chronic diseases, lifestyle and potential barriers. Journal of Pharmaceutical Health Services Research, 2020; 11(2): 127-132.

27. Chapman B, Bogle V. Adherence to medication and self-management in stroke patients. British Journal of Nursing, 2014; 23(3): 158-166.

28. Nair AV, Sylaja PN, Raj LS. Adherence to Drug Treatment after Stroke and its Association with Patients" Beliefs about Medicines among Stroke Survivors. Innovation Journal Nursing Healthcare, 2021; 7(1): 28-31.

29. Konduru SS, Ranjan A, Nallajerla JS, Gonuguntala S. Study of symptoms, risk factors and prescribing patterns in cerebral stroke patients. Indian Journal of Pharmacy Practice, 2017; 10(1).

30. Khan SN, Vohra EA. Risk factors for stroke: A hospital based study. Pakistan Journal Medical Science, 2007; 23(1): 17-22.

31. Kilkenny MF, Olaiya MT, Dalli LL, Kim J, Andrew NE, Sanfilippo FM et al. Treatment with Multiple Therapeutic Classes of Medication is Associated with Survival after Stroke. Neuroepidemiology, 2022; 56(1): 66-74.

32. Bini Susan Isaac, Bharathi.D. R, Priyanka.N, Joshni John. A Study on Management of Stroke in a Tertiary Care Hospital. International Journal of Scientific Research, 2019; 5(1): 26-41.

33. Dasegowda G, Bengalorkar GM, Sadaf S, Kumar Belaguthi PP, Mirmire S, Suresh R. Drug utilization pattern and risk elements of stroke patients in a tertiary care hospital: A cross-sectional study. INDIAN JOURNAL OF APPLIED RESEARCH, 2021; 20–23.

34. Wagle L, Thomas AA, Shrestha S. Drug utilisation study of stroke and other patients admitted to general ward of neurology unit at Quaternary care private hospital. International Journal Current Pharmaceutical Research, 2017; 9(4): 23.

35. Battula P, Pandey N, Sarojini NY, Reddy CB, Kumar KA, Ugandar RE. A study on prescribing patterns and assessing the functional outcomes in cerebral stroke patients. Journal Pharmaceutical Research International, 2022; 35–42.