Evaluation On Prescription and Drug Utilization Pattern of Antihypertensive Agents in The Management of Acute Stroke in A Tertiary Care Hospital

[1]Muhammed Hashim kp, [2]Archa Manoj, [3]Athulya Jayakrishnan, [4]Praisy Mercy Joseph

Pharm D Intern
Pharmacology Department,
East Point College of

Abstract- **A Retrospective observational study was conducted on 150 stroke patients who were taking antihypertensives in a 650-bedded tertiary care multidisciplinary teaching hospital in Bangalore for a period of 6 months to evaluate the prescription pattern of antihypertensive agent in patient with acute stroke and to know which antihypertensive is normally prescribed**
A self-designed data collection form was used to record the patient specific information. A total of 150 patients who met our inclusion criteria were enrolled into the study, out of which 72% patients were male and remaining 28 were female. The most commonly prescribed antihypertensive were amlodipine 30.66% which belong to CCBs followed by ARBs among which telmisartan 40mg (26.66%). The investigation led us to the conclusion that monotherapy rather than combination therapy is more commonly employed.

Index Terms- **Drug utilization evaluation (DUE), prescription pattern,antihypertensives, stroke.**

I.   INTRODUCTION

Hypertension also known as high blood pressure, is a long-term medical condition in which the blood pressure in the arteries is persistently elevated. The systolic blood pressure (SBP) will be more than or equal to 140mmhg and diastolic blood pressure (DBP) will be more than or equal to 90mmhg. It increases the risk of renal failure, heart diseases, and stroke as well as early mortality and disability [1].12.8% of all deaths or 7.5 million, are thought to be caused by hypertension.
The Joint National Committee (JNC-8) consensus guidelines for the management of hypertension are regarded as the "gold standard" in the field which emphasizes that patient over the 60 years old should aim to have blood pressure that is less than 150/90mmhg[1].
Stroke also known as cerebrovascular accident (CVA), is a disorder brought on by inadequate blood flow to the brain that, if not identified and adequately treated, can ultimately result in death[4]. The most significant risk factor for stroke is hypertension. Over time, high blood pressure wears down arteries and organ and workload. Blood clot or plaque may form, rip arterial wall off, and block a brain artery as a result.
4 stroke victims out of every 10 could have been saved if their blood pressure had been controlled. A key theme for the immediate treatment and prevention of first and subsequent strokes is proper blood pressure management. The goal of the project is to examine the use of antihypertensive medication in acute stroke.

CLASSIFICATION OF HYPERTENSION

The Joint National Committee (JNC-8) consensus guidelines for the management of hypertension are regarded as the "gold standard" in the field. According to a 2014 recommendation from the Eighth Joint National Committee (JNC-8), patients over 60 years old should aim to have blood pressure that is less than 150/90 mmHg[1]

BLOOD PRESSURE SYSTOLICCATEGORY (mmHg)		DIASTOLIC (mmHg)
NORMAL	< 120	< 80
PREHYPERTENSION	120-139	80-89
HYPERTENSION STAGE 1	140-159	90-99
HYPERTENSION STAGE 2	160 Or Higher	100 Or Higher
HYPERTENSION CRISIS (EMERGENCY CARE NEEDED)	Higher than 180	Higher than 110

STROKE

A stroke is a serious medical condition that occurs when the blood supply to the brain is interrupted or reduced, it causes oxygen demand to the brain cells and it led to causing brain cells to die. A stroke can cause lasting damage, disability, or even death

➢ **CLINICAL PRESENTATION**
- Trouble speaking
- Numbness or weakness of face, arm or leg, especially on one side of the body.
- Severe headache
- Trouble walking dizziness, loss of balance or coordination
- Blurred or blackened vision in one or both eyes, or double vision.
- Fatigue, light-headedness, or vertigo
- Inability to understand, mental confusion, or rapid involuntary eye movement

➢ **RISK FACTORSMODIFIABLE**
- Hypertension
- Diabetes Mellitus
- Dyslipidemia
- Obesity and Physical Inactivity
- Tobacco use
- Atrial fibrillation
- Sickle cell disease
- Excessive alcohol consumption
- Unhealthy diet and nutrition
- Birth control pills (oral contraceptives)
- Abnormal heart rhythm
- Cardiac structural abnormalities
- Carotid stenosis

OTHER LESS COMMON MODIFIABLE RISK FACTORS
- Metabolic syndrome
- Drug abuse
- Obstructive sleep apnea
- Hypercoagulability
- Inflammation and infection
- Migraine

NON-MODIFIABLE RISK FACTORS
- Older age
- Low birth weight
- Race/ Ethnicity
- Male gender

➢ **TYPES OF STROKES**
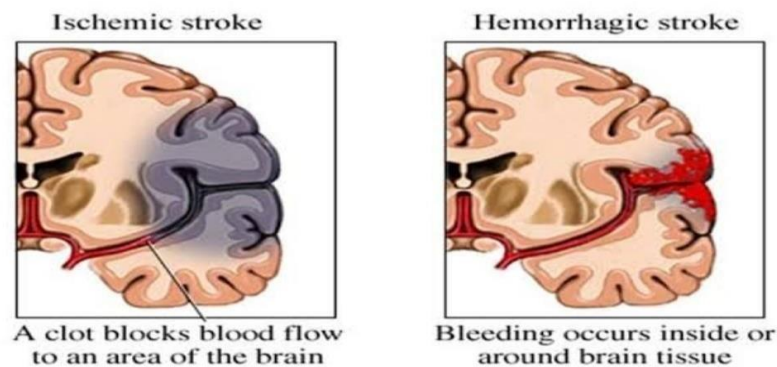
❖ **ISCHEMIC STROKE**

Acute ischemic strokes happen when an intracranial or cervical artery is blocked, depriving a portion of the brain of blood and oxygen.
- Ischemic stroke can be of two major types:

THROMBOLIC STROKE also known as an atherosclerotic stroke, is brought on by a blood clot that develops in an artery that carries blood to the brain

EMBOLIC STROKE, this condition develops when a blood clot develops elsewhere in the body and moves via the blood vessels to the brain. It becomes caught there and prevents your blood from flowing

❖ **HEMORRHAGIC STROKE**

Between 5% and 21% of acute strokes are hemorrhagic strokes. A weakened blood vessel ruptures, which is how it happens. Hypertension is one of the most typical contributors of hemorrhagic strokes. It can also be caused by vascular abnormalities. Because hemorrhage is the most frequent presentation of acute hemorrhagic strokes, arteriovenous malformations (AVMS) should be taken into account in younger individuals.
- Aneurysm
- Trauma
- Cerebral amyloid angiopathy

Hemorrhagic strokes come in two different varieties depending on where the bleeding occurs.

- SUBARACHNOID HEMORRHAGE: This condition affects the region of the skull and brain.
- INTRACEREBRAL HEMORRHAGE: A brain hemorrhage is referred to as an intracerebral hemorrhage.
- TRANSIENT ISCHEMIC ATTACK (TIA) A mini stroke is another name for a transient ischemic attack. It is brought on by a severe transient clot, which can reduce blood flow for as little as five minutes to a portion of the brain. A TIA does not result in long-term harm. A clot or piece of debris restricts or obstructs blood flow to a portion of the nervous system, similar to how an ischemic stroke happens. The symptoms often only last a few minutes or disappear within 24 hours

➢ **DIAGNOSTIC TEST**
- MRI- Magnetic Resonance Imaging
- CT SCAN-Computerized Tomography
- NCCT- Non-contrast computed tomography

- Carotid Doppler Studies
- ECG- Electrocardiogram

➤ NON-PHARMACOLOGICAL TREATMENT

- Lean meat, fish, eggs, whole grains and milk are all important components of a healthy diet.
- Limit salt consumption: According to international recommendations, the daily salt intake for the average person should not exceed 5-6g. Higher salt intake is linked to an increased risk of ischemic and hemorrhagic stroke.
- Abstinence from smoking: Smoking increases the risk of other risk factors, such as hypertension, and is an independent risk factor for stroke. Reduced endogenous fibrinolysis and enhanced thrombocyte activity are the causes of the process.
- Physical exercise: Through positive effects on the vascular risk factors like hypertension, hyperlipidemia, and obesity, regular physical activity reduces stroke risk by 25-30%.
- Maintain a low BMI: It has been estimated that a 5% increase of stroke occurs for every unit higher in BMI.
- Limit alcohol consumption: While a daily intake of up to two drinks for males and one drink for women may reduce the risk of stroke by 30%, greater intakes are associated with a higher risk of stroke.[10]

➤ PHARMACOLOGICAL TREATMENT

The degree of BP increases and the presence of strong indications for the chosen medications determine the initial drug choice.

- Angiotensin II receptor blockers (ARB), Angiotensin converting enzyme inhibitors (ACEI), Thiazide diuretics and calcium channel blockers (CCBs) are acceptable first choices.
- Beta blockers are used singly or in combination to treat a particular compelling indication. Patients without a compelling reason should get treatment with a first-line antihypertensive drug.
- Most patients with stage 1 hypertension should be treated initially with a first-line antihypertensive drug or a two-drug combination.
- Combination therapy is recommended for patients with stage 2 hypertension
- Additional kinds of antihypertensive medications (alpha-1 blockers, directs renin inhibitors, central alpha 2 agonists, peripheral adrenergic antagonists, and direct arterial vasodilators) are alternatives to first line medications that could be used for some individuals

➤ GUIDANCE STATEMENT ON BP MANAGEMENT IN STROKE

According to the 2017 ACC/AHA BP Guideline, the definition of a BP treatment threshold of 140/90 mm Hg has been shifted downward to 130/80 mmHg.

❖ PRIMARY PROPHYLAXIS

Patients with hypertension should be treated with antihypertensive drugs to a target BP of <140/90mmHg

• ACUTE ISCHEMIC STROKE

Patient with elevated BP who are eligible for treatment with iv alteplase should have their carefully lowered to a systolic BP<185mmhg and diastolic BP<110mmhg before iv fibrinolytic therapy is initiated.

In patients not treated with iv thrombolytics therapy for whom intra-arterial therapy is planned, it is reasonable to maintaining BP≤185/110mmHg before the procedure

• ACUTE HEMORRHAGIC STROKE

In patients with systolic BP 150-220mmHg and without contraindication to acute BP treatment, acute lowering of systolic BP to 140mmHg is safe.

In patients presenting with systolic BP >220mmHg, it may be reasonable to consider aggressive reduction of BP with continuous IV infusion and frequent BP monitoring

❖ SECONDARY PROPHYLAXIS

Antihypertensives therapy is indicated for previously untreated patients with ischemic stroke or TIA who after the first several days, have an established BP≥140 mmHg systolic or ≥90 mmHg diastolic.

Goals for target are uncertain and should be individualized, but it is reasonable to achieve a systolic pressure <90mmHg. For patients with a recent lacunar stroke, a systolic BP of 130mmHg might be reasonable to target[11]

II. AIM AND OBJECTIVE

AIM
To Evaluate the prescription and drug utilization pattern of antihypertensive agents in the management of Acute stroke.
OBJECTIVE
Primary Objective:

- To examine the antihypertensive medication prescribing trends in patients with acute stroke.

Secondary Objective:

- To determine the age group most impacted.

- To carry out a pharmacoeconomic analysis for cost estimation.
- To determine the typical antihypertensives used in acute stroke.

III.   METHODOLOGY

The study was a hospital based Retrospective observational study design carried out in East Point College of medical sciences and research Centre, a 650- bedded tertiary care multidisciplinary teaching hospital in Bangalore. The study was conducted for a period of 6 months (January 2022- June 2022) and the sample size about 150
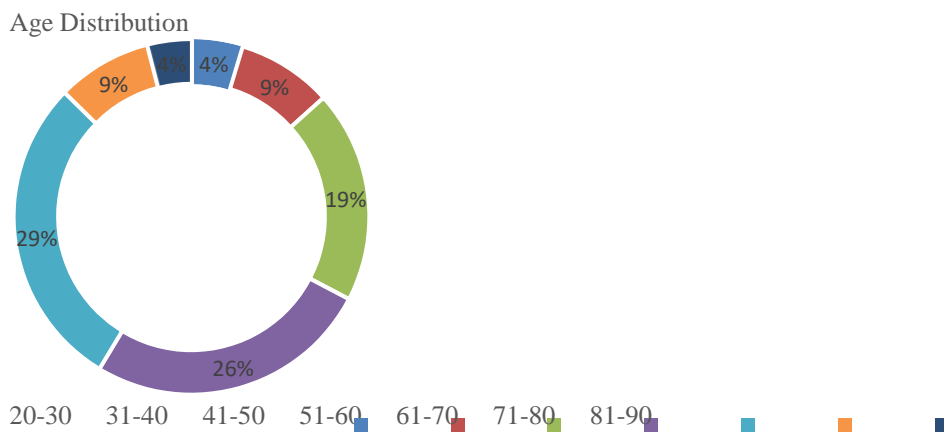
STUDY CRITERIA

Inclusion Criteria:

- Patients with Hypertension and Acute stroke
- Patients of both genders are included
- Patients above the age of 18 yearsExclusion Criteria:
- Pregnant women and children are excluded
- Case reports having incomplete information.

IV.   RESULTS

❖   <u>**AGE DISTRIBUTION OF THE PATIENTS**</u>

Age Distribution

Among the 150 patients studied, majority were under the age group of 61-70 (28.66%) followed by 51-60 (26%) and least were of age group 81-90 (4%), p value is 0.0103.
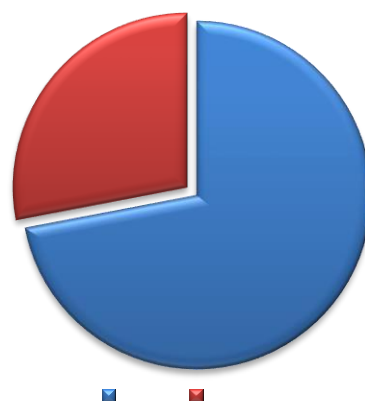
❖   <u>**GENDER DISTRIBUTION OF THE PATIENTS**</u>

GENDER DISTRIBUTION

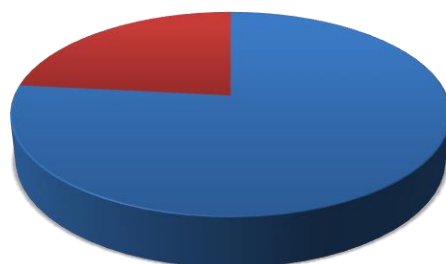Female 28%

Male 72%

Male   Female

Based on gender distribution of the patients, 108 patients were male (72%) and 42 patients were female (28%), p value is 0.026.

❖ **TYPE OF STROKE**
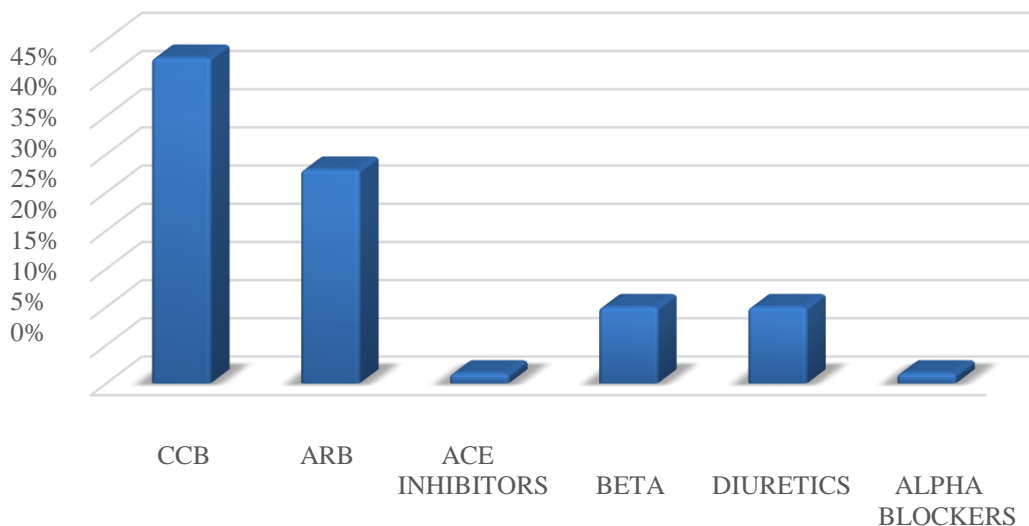
STROKE TYPE

HAEMORRHAGIC

ISCHEMIC

ISCHEMIC   HAEMORRHAGIC

Out of 150 patients studied, Ischemic stroke patients was found to 115 (76.66%) which was higher than the haemorrhagic patients 35 (23.33%), p value is 0.031.
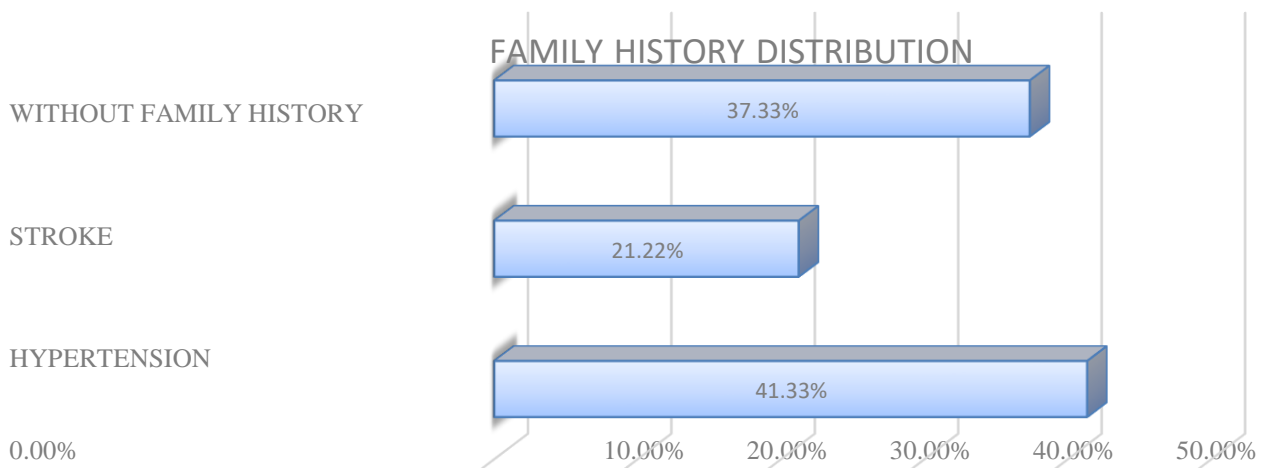
❖ **CLASS OF ANTIHYPERTENSIVE PRESCRIBED**

CLASS OF ANTIHYPERTENSIVE PRESCRIBED

The most prescribed class of antihypertensives was found to be calcium channel blocker 64 (42.66%) followed by ARBs 42(28%) and the least prescribed was ACE Inhibitors 2(1.33%) and alpha blockers 2(1.33%), p value is 0.0686.
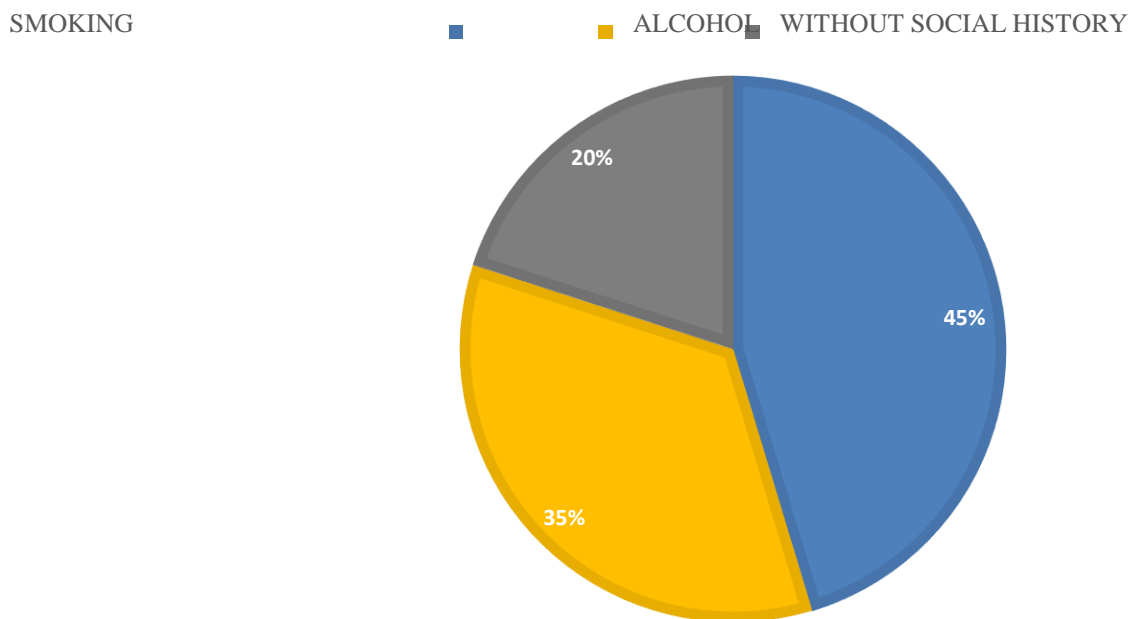
❖   **FAMILY HISTORY DISTRIBUTION**

Among 150 patients, 62 (41.33%) patients had a family history of hypertension and 32 (21.22%) patients had a history of stroke. Most of the patients, 56 (37.33%) were without family history, p value is 0.032.
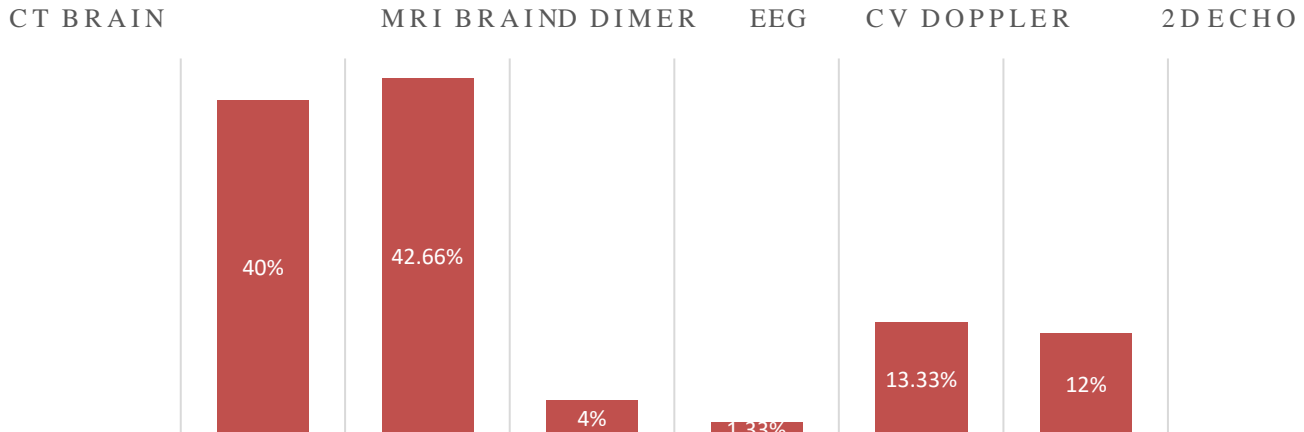
❖   **SOCIAL HISTORY**

SOCIAL HISTORY

SMOKING

Out of 150 patients, 68 patients (45.33%) were smokers and about 52 patients (34.66%) were alcoholic and only 30 patients (20%) were without any social history, p value is 0.0453.
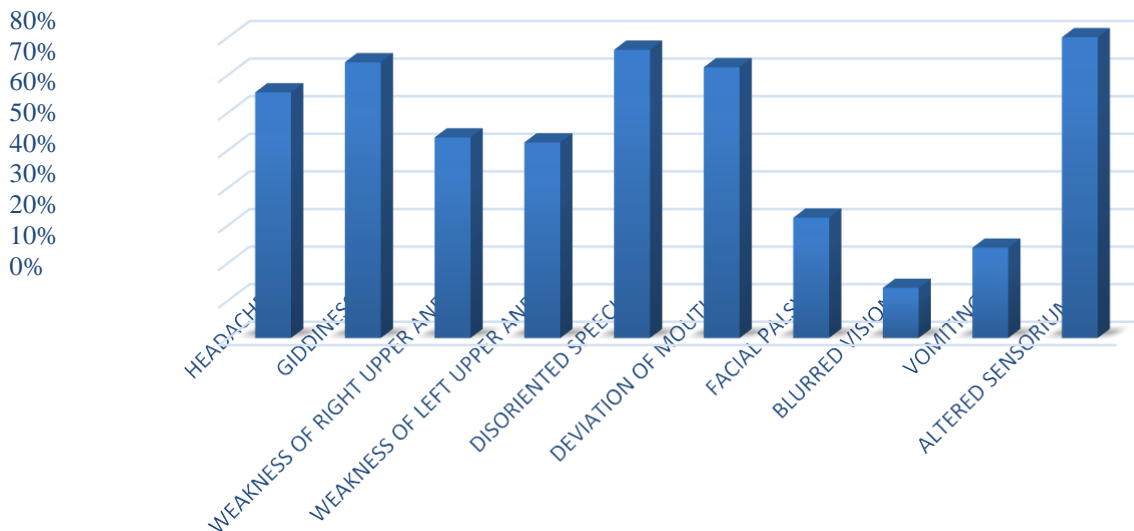
❖   **DIAGNOSTIC METHOD**

DIAGNOSTIC METHOD
CT BRAIN   MRI BRAI ND DIMER   EEG   CV DOPPLER   2 D ECHO

Among 150 patients studied, the most commonly used diagnostic criteria done for stroke were MRI done in 64 (42.66%) patients, followed by CT Brain 60 (40%) patients, p value is 0.05.

❖   **PATTERN OF SYMPTOMS AMONG STROKE PATIENTS**

PATTERN OF SYMPTOMS AMONG STROKEPATIENTS

Out of 10 presenting symptoms, most commonly seen were altered sensorium 120 patients (80%), disoriented speech 115 patients (76.66%), giddiness 110 patients (73.33%), deviation of mouth 108 patients (72%), headache 98 patients (65.33%), weakness of right upper and lower limb 80 patients (53.33%), weakness of left upper and lower limb 78 patients (52%), p value is 0.04.
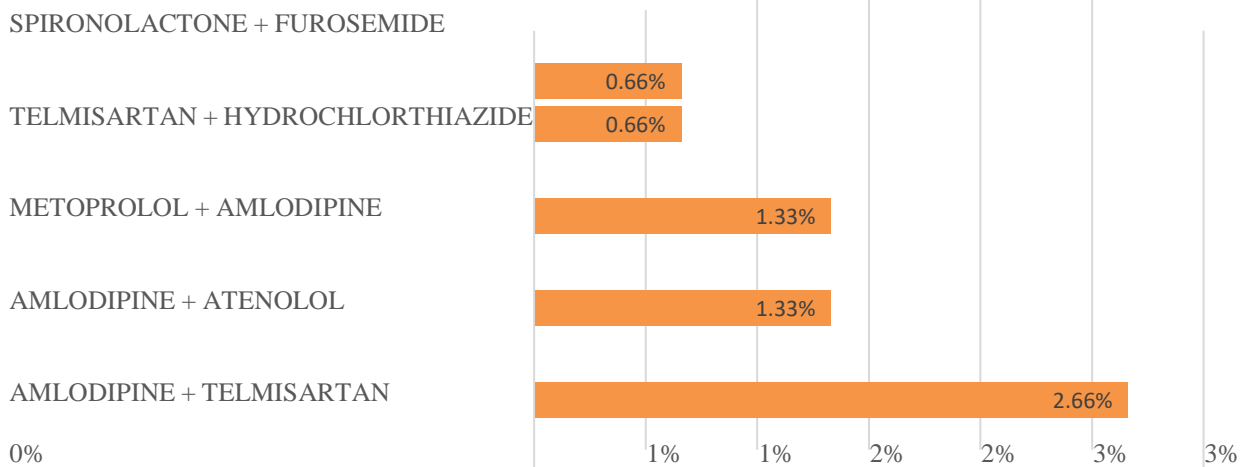
❖ **CO MORBIDITIES DISTRIBUTION**

CO MORBIDITIES DISTRIBUTION

HYPERLIPIDEMIA	6.66%
CADDM	9.33%
HTN	57.33%
	(100%)

0%   50%   100%   150%
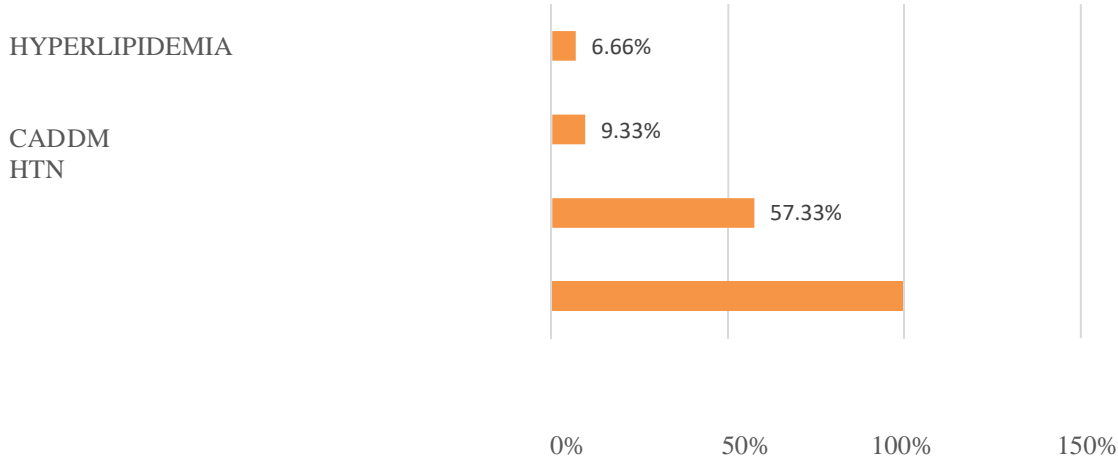
Out of 150 patients studied, the main co morbidities seen were hypertension 150 patients (100%), diabetes mellitus 86 (57.33%), CAD 14 (9.33%), hyperlipidemia 10 (6.66%), p value is 0.014

❖ **COMBINATION THERAPY**

COMBINATION THERAPY

SPIRONOLACTONE + FUROSEMIDE	0.66%
TELMISARTAN + HYDROCHLORTHIAZIDE	0.66%
METOPROLOL + AMLODIPINE	1.33%
AMLODIPINE + ATENOLOL	1.33%
AMLODIPINE + TELMISARTAN	2.66%

0%   1%   1%   2%   2%   3%   3%
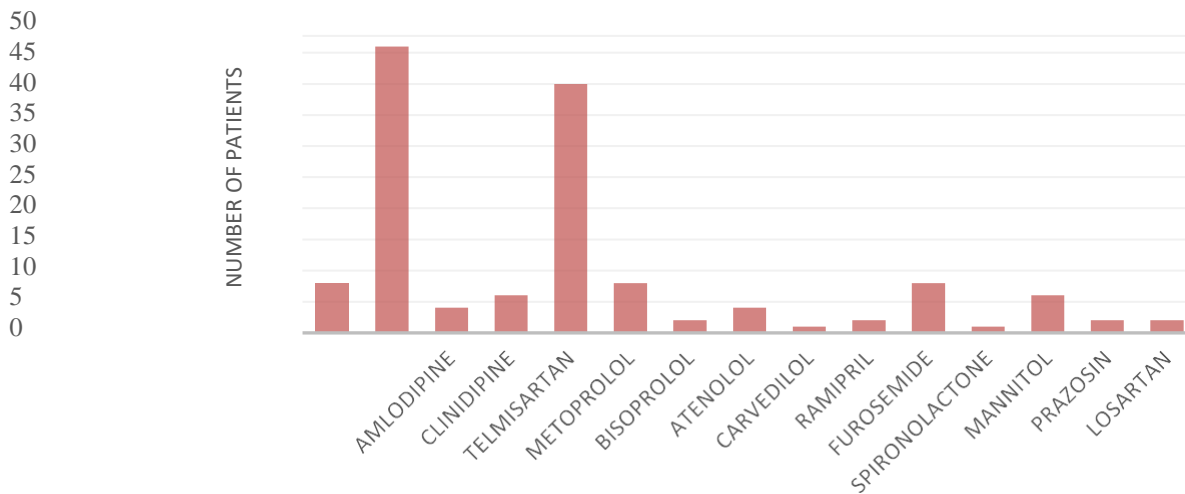
Among 150 patients studied, the most commonly given combination therapy was found to be amlodipine and telmisartan 4 (2.66%) were given as combination therapy more for ischemic stroke, p value is 0.0217.

❖   **ANTI HYPERTENSIVE DOSE DISTRIBUTION**

ANTI HYPERTENSIVE DOSEDISTRIBUTION

DRUG USED

Among 150 patients studied, amlodipine 5mg (30.66%) once daily was most commonly prescribed drug in the management of hypertension. Other amlodipine doses are 2.5mg (2.66%), 10mg (5.33%). Other drugs mostly prescribed were telmisartan 40mg (26.66%), cilnidipine 10mg (4%), p value is 0.0213.

V.   DISCUSSION

A retrospective observational study on prescribing pattern and drug utilization of antihypertensives in the management of stroke was conducted in East Point Hospital, Bangalore over a period of 6 months. A total of 150 patients were included in the study. Majority of patients were under the age group of 61-70 (28.66%) followed by 51-60 (26%) and least were of age group 81-90 (4%) and out of 150 patients, 108were male (72%) and 42 were female (28%).

Ischemic stroke patients were found to 115 (76.66%) which was higher than the haemorrhagic patients 35 (23.33%) .

The most prescribed class of antihypertensive agent was calcium channel blocker 64 (42.66%) followed by ARBs 42(28%) and the least prescribed was ACE Inhibitors 2(1.33%) and alpha blockers 2(1.33%).

On taking the family history into consideration, 62 (41.33%) patients had a family history of hypertension and 32 (21.33%) patients had a history of stroke but most of the patients, 56 (37.33%) were without family history.

Social history distribution such as smoking and alcoholism were also evaluated which lead to a conclusion that out of 150 patients, 68 patients (44.33%) were smokers and about 52 patients (34.66%) were alcoholic and only 30 patients (20%) were without any social history.

The important diagnostic criteria done for stroke were MRI done in 64 (4266%) patients, D Dimer done in 6(4%) patients. A study by Pedro Vilela et al. found that CT scan and MRI brain are more commonly used in ischemic stroke to exclude stroke mimics and haemorrhage to determine the cause and mechanism of stroke

Distribution of different types of symptoms were taken into consideration Out of 10 presenting symptoms, most commonly seen were altered sensorium 120 patients (80%), disoriented speech 115 patients (76.66%), giddiness 110 patients (73.33%), deviation of mouth 108 patients (72%), headache 98 patients (65.33%), weakness of right upper and lower limb 80 patients (53.33%), weakness of left upper and lower limb 78 patients (52%).

Distribution as done on the basis of comorbidities present in patients and it was found that the main comorbidities seen were hypertension 150 patients (100%), diabetes mellitus 86 (57.33%), CAD 14(9.33%), hyperlipidemia 10 (6.66%). The most preferred combination therapy was that of Amlodipine and telmisartan 4 (2.66%) given for ischemic stroke.

Antihypertensive dose distribution in stroke condition was evaluated and it showed that amlodipine 5mg (30.66%) once daily was most commonly prescribed drug in the management of hypertension. Other amlodipine doses are 2.5mg (2.66%), 10mg (5.33%). Other amlodipine doses are 2.5mg (2.66%), 10mg (5.33%). Other drugs mostly prescribed were telmisartan 40mg (26.66%), cilnidipine 10mg (4%).

VI.   CONCLUSSION

This study was conducted to know the prescription and drug utilization pattern of hypertensives in management of acute stroke.

A total of 150 patients that met out inclusion criteria were enrolled into the study, out of which 108 (72%) patients were male and 42 (28%) patients were females. Ischemic stroke was found in 115 (76.66%) patients while hemorrhagic stroke was seen in 35 (23.33%) patients. The age group between 51-70 years old had the highest number of cases.

The antihypertensive drug class with the highest prescription rate was calcium channel blockers (42.66%) among wherein amlodipine 5mg (30.66%) was used most frequently followed by ARBs (28%) among which telmisartan 40mg (26.66%) was commonly prescribed.

The investigation led us to the conclusion that monotherapy rather than combination therapy is more commonly employed.

REFERENCES:
1. Rakesh Romday, Ajay Kumar Gupta, Pawan Bhambani. An assessment of antihypertensive drug prescription patterns and adherence to joint national committee-8 hypertension treatment guidelines among hypertensive patients attending a tertiary care teaching hospital. International journal of research in medical sciences. 2016;4(12): 5125-5133.
2. Shakeel Ahmad Mir. Cost variation analysis of different brands of commonly prescribed antihypertensive drugs, available in Indian market: a pharmacoeconomic study. International Journal of basic and clinical pharmacology. 2018;7(3): 556-560.
3. Roger Walker text book 5th edition: 295 – 296
4. Subhransu Sekhar Jena, Monalisa Jena, Swati Mishra, Bikash Ranjan Meher. Utilization pattern of different drugs in different types of stroke in a tertiary care teaching hospital. International journal of pharmaceutical sciences review and research. 2018;49(2):85-90
5. Dariusz Gasecki, Mariusz Kwarciany, Kamil Kowalczyk, Krzysztof Narkiewicz, Bartosz Karaszewski. Blood pressure management in acute ischemic stroke. Journal of springer. 2020;23(3): 1-11
6. Sridhar Srimath Tirumala Konduru, Amit Ranjan, Jyothi Sri Nallajerla, Sravya Gonuguntala. Study of symptoms, risk factors and prescribing patterns in cerebral stroke patients. Indian journal of pharmacy practice. 2017;10(1): 20- 26
7. K. Soumya Lakshmi, Dr. Siddarama. Study of symptoms, risk factors and prescribing patterns in stroke patients. Indo Americanjournal of pharmaceutical research. 2018;8(7): 1453-1461.
8. Ashley Knight-Greenfield, MD, Joel Jose Quitlong Nario, BS, Ajay Gupta, MD, MS. Causes of acute stroke. Journal of HSS public access. 2019;57(6): 1-32.
9. Smita Patil, Rosanna Rossi, Duaa Jabrah, Karen Doyle. Detection, diagnosis and treatment of acute ischemic stroke: current andfuture perspectives. Journal of frontiers in medical technology. 2022;4: 1-12.
10. Kyung Bok Lee, Jeong-Yoon Lee, Nari Choi, Jee-Eun Yoon, DongWon Shin, Ji-Sun Kim, Hakjae Roh, Moo-Young Ahn, Hye- Won Hwang and Min-Su Hyon. Association between insufficient medication of antihypertensives and the severity of acute ischemicstroke. Journal of biomed central. 2016;22(11) 1-5.
11. Mauricio Wajngarten, Gisele Sampaio Silva. Hypertension and stroke: Update on treatment. Journal of European cardiology. 2019;14(2): 11-115.
12. Haken Sarikaya, Jose Ferro, Marcel Arnold. Stroke prevention-Medical and lifestyle measures. Journal of European Neurology.2015;73: 150-157.
13. Jithin KC, Arya G, Lekshmi P Nair, Lakshmi R. A study on pattern of prescribing medications used in secondary prevention ofstroke. Asian Journal of pharmaceutical and clinical research. 2016;9(3): 328-330.
14. Swetha K., Shailander Singh. A retrospective study of prescription pattern of drugs in the management of stroke, at BRIMS teaching hospital, Bidar, India. International journal of basic and clinical pharmacology. 2018;7(10): 19291933.
15. Harish Govind Naik, Harshitha C S. Study on antihypertensive drug utilization in a tertiary care hospital. National journal of physiology, pharmacy and pharmacology. 2019;9(11): 1063-1067.
16. Mohit N, Nalini G.K, Deepak P., Sahana G.N., Jayashree V. Nagaral, Rakshitha B.V., Divyashree C.R. Analysis of cost between branded medicines and generic medicines in a tertiary teaching hospital. International journal of basic and clinical pharmacology. 2019;8(5): 1074-1077.
17. Preethi Prathyusha B, Abdul Naveed, Shreya S, Sri Lakshmi G, Vinay Rao. Prescribing pattern of drugs in stroke patients admitted to a multispeciality hospital, India. Indo American journal of pharmaceutical research. 2014;4(2): 1015-1020. 18. Smitha V.K, Sharad Chand, Nandakumar U.P, Juno J Joel, Raghav Sharma. Pharmacoeconomic evaluation of anti- hypertensive therapy. Journal of bioscience biotechnology research communications. 2021;14(2): 489-492.
19. Kalyani Sonawane PhD, Yenan Zhu MS, Rajesh Balkrishnan PhD, Ryan Suk MS, Anjali Sharrief MD, MPH, Ashish A. Deshmukh PhD, MPH, David Aguilar MD. Antihypertensive drug use and blood pressure control among stroke survivors in the United States: NHANES 2003-3004. Wileyonline library journal. 2019;21: 766-773.
20. Hussainy Syed Areefulla, Habeeb Madiha, Jeelani Ayesha, Sultana Sumaiya, Meeran Mohd Mohiuddin. A prospective observational study on risk factors and prescribing patterns of drugs used in stroke patients at a tertiary care teaching hospital. Journal of delivery and therapeutics. 2020;10(5): 71-75.
21. Philip B. Gorlick, Shakaib Qureshi, Muhammad U. Farooq. Management of blood pressure in stroke. International journal of cardiology hypertension.2019;1-6.
22. Jalpa Suthar, Amishi Pathak, Bhavik Shelat. Comparison of safety and efficacy of different class of anti-hypertensive drugs prescribed in patients with hypertension. Indian journal of pharmacy practice. 2019;12(4): 256-261.