INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Research Article

Optimising Antihypertensive Therapy: Prescribing Patterns and Adherence

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ARTICLE INFO

Published: 14 April. 2025
Keywords:
Blood pressure, Hypertension, Antihypertensive drugs, Medication adherence.
DOI:
10.5281/zenodo.15208587

ABSTRACT

The purpose of this study is to assess prescription trends for antihypertensive and compliance to the prescription for the treatment of hypertension. In order to lower the morbidity, mortality and healthcare expenses associated with hypertension, it is crucial to audit antihypertensive prescriptions. The selection of antihypertensive medications is influenced by various factors. It's critical to evaluate prescription patterns over time in order to support the prudent use of medications. Globally, hypertension is the primary factor contributing to rising rates of morbidity and mortality. Maintaining strong adherence to antihypertensive drugs remained the most significant problem, even though therapy adherence is a key factor in treatment success to lower apparent resistant hypertension. The clinical course of hypertension is significantly influenced by adherence to antihypertensive medication. Therefore, the purpose of this study was to examine the antihypertensive medication prescription patterns of patients with concomitant conditions and hypertension alone and to evaluate hypertensive patient's adherence to antihypertensive drugs.

INTRODUCTION

The generalized definition of hypertension is the continuous elevation in systemic arterial pressure over a predetermined threshold.[1] Hypertension is defined as a ratio of systolic blood pressure of 140 mmHg or more to the diastolic pressure of 90 mmHg or more in the joint national committee's seventh report on the prevention, identification, evaluation and management of hypertension.[2]

Table No.1- Classification of Hypertension

Classification	Systolic BP (MMHG)	Diastolic BP (MMHG)
Normal	Less than 120	Less than 80
Prehypertension	120-139	80-89

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Stage 1 hypertension	140-159	90-99
Stage 2 hypertension	≥160	≥100

Etiology

Based on etiology HTN is classified as primary/essential and secondary hypertension. The term essential hypertension is used when the root cause of hypertension is unknown in about 90% of the cases though it is known in a few cases.it is a complex disease resulting from various genetic, environmental and behavioral factors.[3] The term secondary hypertension is used when the hypertension is linked to a specific root cause. Around10% of patients have secondary hyper tension due to illness or medications. Secondary HTN due to illness includes obstructive sleep apnea, CKD, renal parenchymal disease, systemic scleroderma etc. Drugs like glucocorticoid, caffeine, cyclosporine A, alkylating agents etc. are known to cause secondary hypertension. [4,5]

Signs And Symptoms

High blood pressure often does not exhibit any symptoms. however a hypertensive crisis which occurs when the BP reaches approximately 180/120 mmHg can be a medical emergency .these symptoms include severe headaches, chest pain, dizziness, difficulty in breathing, nausea, vomiting, vision impairment, vertigo, edema, sleep apnea, confusion, epistaxis, fatigue, abnormal heart rhythm, alternations in urinary frequency etc.[6]

Diagnosis

Arterial hypertension is diagnosed when a patient has numerous measures done in doctor's office and the results shows a reading of 140/90 mmHg or higher. Mercury sphygmomanometers are still regarded as the gold standard for blood pressure monitoring, but because of a widespread ban on their use, their use in hospital setting has declined. An increasing number of alternative methods such as automated electrical equipment are being used. [7,8]

Pathophysiology

The various pathological mechanisms involved in hypertension are:

1. Neural Mechanisms

SNS overactivity

High blood pressure baroreceptors in the aortic arch and the carotid sinus cause a reflex vagal bradycardia in response to abrupt elevations in blood pressure. This reflex is mediated by the parasympathetic nervous system and suppresses sympathetic output from CNS. The renal sympathetic nervous system, which influences blood pressure through the efferent and afferent pathways, is primarily responsible for the development and maintenance of hypertension. These signals cause the kidney to release more renin, activate the RAAS system and retain more salt and water. These effects increase circulation volume which in turn raise BP.

2. Renal mechanisms

- **The Renin Angiotensin-Aldosterone Pathway**

Renin transforms angiotensinogen into angiotensin I. Angiotensin converting enzyme breaks down angiotensin I to form angiotensin II, the most vasoactive peptide and a potent blood artery constrictor.[9]

- **Aldosterone**

When exposed to aldosterone the renal tubular cells in the collecting tubules, distal tubules, and collecting ducts release more K^+ and absorbs more salt. Aldosterone therefore preserves extracellular Na^+ and promotes the K^+ in the urine.[10]

3. Local endothelium derived factor

Increased release of endothelium derived growth, constricting, pro inflammatory and pro-thrombotic factor as well as release of endothelial-derived relaxing factors (NO, endothelial derived hyperpolarizing factor) are characteristics of endothelial dysfunction which is associate with hypertension.[11]Other hormones or systems involved in bp control include natriuretic peptides, the tissue kallilrein-kinin system, adipose tissue and adipokines, leptins, insulin resistance and hypertension metabolic syndrome.[12]

Treatment

Non pharmacological treatment of hypertension involves dietary salt restriction, weight loss, to increase physical activity, high-fibre and low fat diet and withdrawl of interfering medications.[13,14]

Pharmacological treatment for hypertension involves various drug classes as follows

Diuretics

Diuretic antihypertensive drugs function by altering the kidney's epithelial cells ability to transport water and salt which raises the body's excretion of these minerals.

- **Thiazide diuretics**

By inhibiting the apical sodium/chloride transporter in epithelial cells in the distal convoluted tubules, thiazide diuretics reduce cardiac output and extracellular fluid.[15] alkalosis, hyponatremia and hypokalemia and volume depletion are known adverse effects of thiazide diuretics.

- **Loop diuretics**

These are the strongest diuretics that function by obstructing the transporter of sodium, potassium and chloride located at the tip of loop of henle. hypokalemia, hyponatremia, alkalosis and hypocalcaemia are the side effects of loop diuretics.

- **Potassium sparing diuretics**

These diuretics preserve potassium by preventing its secretion into the urine. two sodium channel inhibitors that operate as potassium sparing diuretics are amiloride and triamterene. these drugs work by increasing the excretion of sodium and decreasing the excretion of potassium. aldosterone blockers including spironolactone and eplerenone function by blocking aldosterone's activation of mineralocorticoid receptors in collecting ducts, which modifies gene expression and inhibits the synthesis of proteins required for the transport of electrolytes.

Raas Inhibitors

Renin angiotensin aldosterone system inhibitors acts by preventing or lowering the activities of angiotensin II.

- **Angiotensin converting enzyme inhibitors**

ACE inhibitors i.e. captopril, enalapril, lisinopril etc. acts by decreasing the action of angiotensin converting enzyme, preventing conversion of angiotensin II from angiotensin I. bradykinin

elevation is linked to the pathophysiology of cough and angioedema caused by ACE inhibitors.

- **Angiotensin receptor blockers**

ARBs displace angiotensin II from angiotensin I receptor, causing dropped BP by blocking angiotensin II induced vasoconstriction, aldosterone release, catecholamine release, arginine vasopressin release, water intake and hypertrophic response.[16]

Calcium Channel Blockers

CCBs block the L-type calcium channels which results in peripheral and coronary vasodilation. the dihydropyride (DHP) type which includes nifedipine, amlodipine and non dihydropyridine (non- DHP) type which includes verapamil and diltiazem are two main subgroups of CCBs. compared to DHPs non-DHPs have lower vasodilatory potency. Edema flushing, headache, dizziness, constipation etc. are typical side effects of CCBs. [17,18]

Beta Blockers

The effects of sympathetic nerve stimulation or catecholamines in circulation are countered by β-blockers at β- adrenoceptors which are found throughout the body's system. β-1 receptors are more prevalent in heart while β-2 receptors are more prevelant in other organs such as lungs, peripheral blood vessels and skeletal muscle. [19,20]

Alpha Blockers

When treating hypertension that is difficult to control or when other drugs are not well tolerated ,α-blockers are often taken as supplements. Doxazosin, indoramin, prazosin and terazosin are few examples. Most α-blockers selectively act on Gq protein coupled post ganglionic α-1 receptors. Hence, reducing vasodilation and SVR. Phentolamine and phenoxybenzamine are examples of non-selective α-blockers that function at α1 and α2 receptors.[21]

Vasodilators

Vasodilators include nitrates (nitroglycerine, isosorbide dinitrate) hydralazine, minoxidil and other arteriolar vasodilators as well as venous dilators (sodium nitroprusside).[22]

Centrally Acting Agents

Centrally acting agents include methyldopa which is a precursor of alpha 2 adrenoceptors agonist, moxonidine which is an agonist at imidazole binding sites. Methyldopa's immunological side effects include pyrexia hemolytic anemia and hepatitis.[23]

Medication Adherence

The WHO defines medication adherence as the extent to which an individual's behavior aligns with the established recommendations from a health care provider.

Barriers for medication adherence:

- Complexity: due to the large number of medications, it is not convenient to go over each one.
- Expensive: unaffordability to purchase the medicine
- Difficulties recalling schedules
- Ignorance: what makes it necessary for me
- Side effects
- Stigma/embarrassment
- Depression
- Belief system

Methods to improve medication adherence

1. Levels of prescribing: begin a collaborative process with the patient when writing a prescription.

- Include patients in the decision making process regarding their prescription.
- Make taking medications simpler

2. Communicating with the patient: discuss the fundamentals of the pharmacology: what, why, when, how and for how long.

- Inform patients about side effects that are common and those that they should be cautious of.
- Use tools for medication adherence like drug cards, medication charts, pill boxes, dose indicating containers etc.
- Provide behavioral support.

3. During follow ups:

- Plan an appropriate follow up
- Assess adherence in the subsequent check ins
- Be aware of the difficulties and challenges related to adherence
- Address the problems
- Inform the patients of the issues resolved. [24,25]

Aim And Objectives:

- To classify the prescription pattern and determine which antihypertensive medications are more frequently administered as To enhance the appropriate drug prescription patterns
- To evaluate the patient's adherence to the anti-hypertensive drugs as directed so to increase the prescription adherence by the patient.

MATERIALS AND METHODS:

All information was obtained using patient data entry form and Morisky Medication Adherence scale – 8.

RESULTS AND DISCUSSION:

In this study total of 100 subjects were taken into consideration and accordingly their prescription pertaining to anti-hypertensive medications were thoroughly studied and their adherence to the medication was also noted.

Table no. 2 – Frequency and percentage of the subjects according to the age

Age group	Frequency (n)	Percentage (%)
<45 years	7	7
45-60 years	33	33
>60 years	60	60
Total	100	100
Mean	62.81 (10.51)	

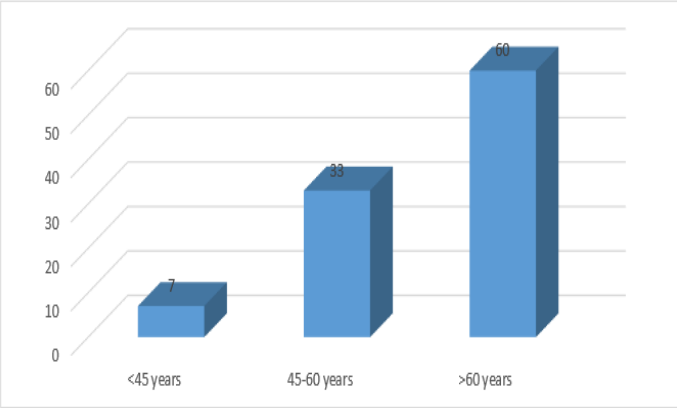

Figure No.1 – Bar Diagram Representing Frequency and Percentage of Subjects According to The Age.

Our study results shows that there was a gradual increase in the prevelance of hypertension with the age group of greater than 45 years. The mean age of hypertension observed in this study was 62.81 years.

Table no.3- Frequency and percentage according to gender

Gender	Frequency (n)	Percentage (%)
Male	65	65
Female	35	35
Total	100	100

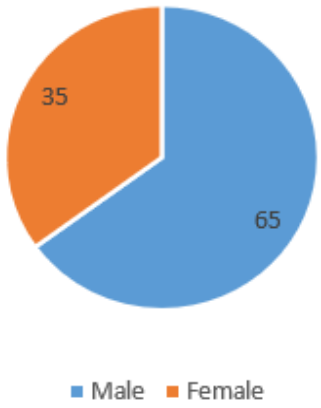

Figure no.2 - Pie diagram representing frequency and percentage according to the gender

Male population was found to be more vulnerable to sustained hypertension, leading the table with 65% when compared to the female population.

Table no.4- Frequency and percentage according to the type of drug therapy

Type of drug therapy	Frequency	Percentage
Mono therapy	23	23
Dual therapy	37	37

Triple therapy	25	25
Quadruple therapy	11	11
Quintuple therapy	4	4
Total	100	100

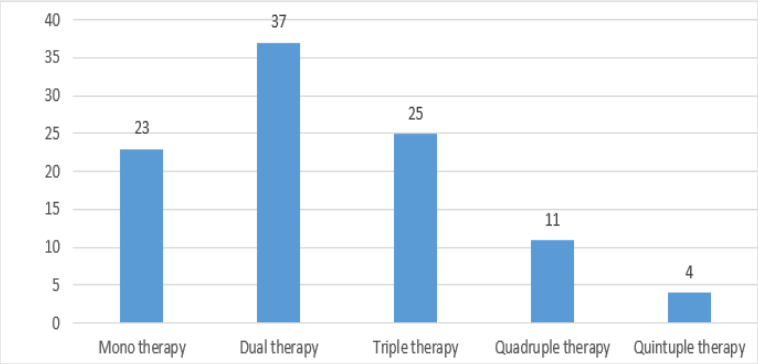

Figure no.3- Bar diagram representing frequency and percentage based on type of drug therapy

37% of the subject population was prescribed with dual therapy followed by triple therapy prescribed by 25% then monotherapy i.e 23% followed by quadruple therapy and quintuple therapy i.e 11% and 4% respectively.

Table no.5 – Frequency and distribution based on monotherapy

Type of drug therapy		**Frequency (n=23)**	**Percent (%)**
Monotherapy	ARB	8	34.8
	BB	12	52.2
	DHP CCB	3	13.0
	Total	23	100.0

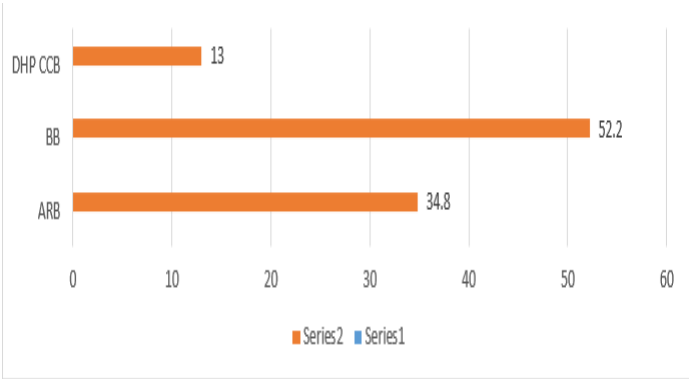

Figure No.4- Bar Diagram Representing Frequency and Percentage Based on Monotherapy

In patients prescribed with monotherapy, beta blockers were found to be the m;ost prescribed(52.2%) among various other antihypertensive drug classes, followed by angiotensin receptor blockers(34.8).

Table No.6 - Frequency And Percentage Based On Dual Therapy

Type of drug therapy		Frequency (n=37)	Percent (%)
Dual therapy	ARB+DHP CCB	3	8.1
	ARB+Thiazide diuretics	1	2.7
	ARB+Thiazide diuretics	1	2.7
	BB+ Centrally acting alpha agonist	1	2.7
	BB+ARB	17	45.9
	BB+BB	1	2.7
	BB+DHP CCB	3	8.1
	BB+Loop diuretics	2	5.4
	BB+Potassium sparing diuretics	2	5.4
	BB+Vasodilator	1	2.7
	CCB+Diuretic	1	2.7
	DHP CCB+ NDHP CCB	1	2.7
	DHP CCB+ARB	1	2.7
	Loop diuretic +ARB	1	2.7
	Loop diuretic +Potassium sparing diuretic	1	2.7
	Total	37	100.0

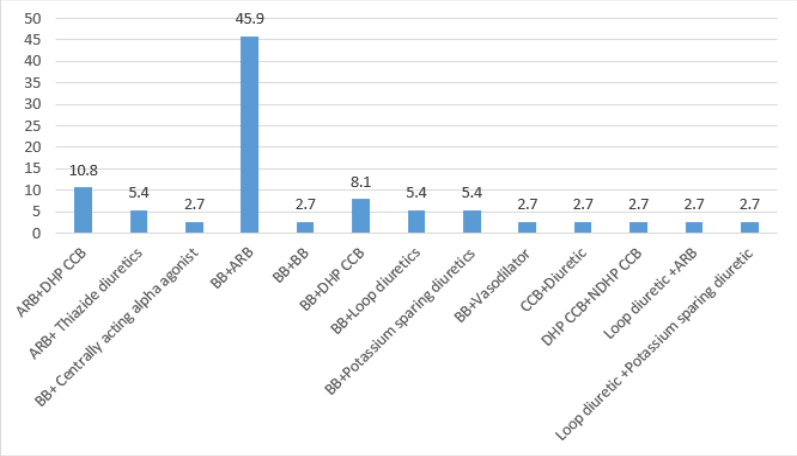

Figure No.5 – Bar Diagram Representing Frequency and Percentage Based on Dual Therapy

In subjects prescribed with dual therapy, a combination of BB and ARB was found to be predominantly prescribed i.e 45.9% followed by combination of ARB+ dhp CCB and BB+dhp CCB i.e 10.8 and 8.1 followed by others.

Table no.7- Frequency and percentage based on triple therapy

Type of drug therapy		Frequency(n=25)	Percent
Triple therapy	ARB+DHP CCB+Alpha 2 adrenergic agonist	1	4.0
	ARB+DHP CCB+BB	3	12.0
	ARB+Thiazide diuretic+BB	1	4.0
	BB+DHP CCB+Thiazide diuretic	1	4.0

	BB+Angiotensin II receptor antagonists and Thiazide diuretic	1	4.0
	BB+ARB+DHP CCB	1	4.0
	BB+ARB+Potassium sparing diuretics	2	8.0
	BB+CCB+ Potassium sparing diuretics	1	4.0
	BB+Potassium sparing diuretics+Loop diuretic	8	32.0
	BB+Potassium sparing diuretics+ARB	1	4.0
	DHP CCB+ARB+nDHP CCB	1	4.0
	DHP CCB+CCB+ARB	1	4.0
	Loop diuretic+Potassium sparing diuretic+ nDHP CCB	1	4.0
	Selective BB agents+Thiazide diuretics +ARB	1	4.0
	Valsartan+Loop diuretic+Potassium sparing diuretics	1	4.0
	Total	25	100.0

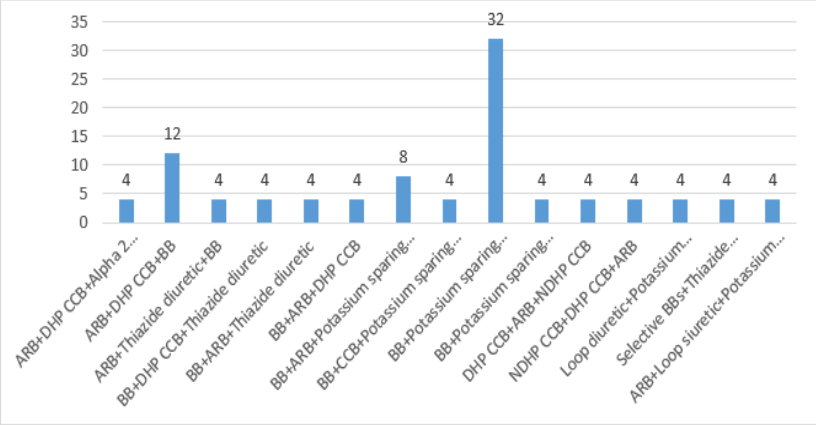

Figure no.6-Bar diagram representing frequency and percentage based on triple therapy

In subjects prescribed with triple therapy, a combination of BB+ potassium sparing diuretics+ loop diuretics was found to be commonly prescribed i.e 32% followed by other combinations.

Table No.8- Frequency And Percentage Based on Quadruple Therapy

Type of drug therapy		**Frequency (n=11)**	**Percent (%)**
Quadruple therapy	ARNI+BB+ Potassium sparing diuretics+Loop diuretics	3	27.3
	BB+ARB+Loop diuretics+Potassium sparing diuretics	4	36.4
	BB+Loop diuretic +Potassium sparing diuretics+DHP CCB	1	9.1
	BB+Loop diuretics+ARNI+Potassium sparing diuretics	1	9.1

	Potassium sparing diuretics+Loop diuretics+Vasodilator+BB	1	9.1
	Vasodilator+BB+ARB	1	9.1
	Total	11	100.0

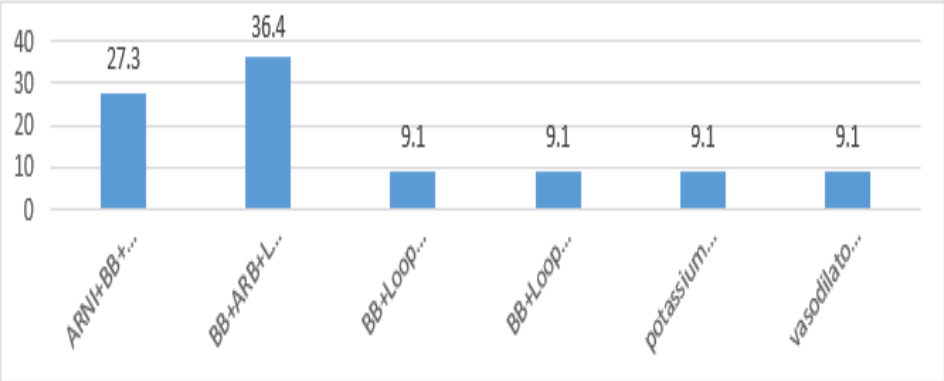

Figure No.7- Bar Diagram Representing Frequency and Percentage Based on Quadruple Therapy

In subjects prescribed with quadruple therapy a combination of BB+ ARB+ loop diuretics+ potassium sparing diuretics was commonly prescribed with percentage of 36.4 followed by others.

Table no.9- Frequency and distribution based on quintuple therapy

Type of drug therapy		Frequency (n=4)	Percent
Quintuple therapy	BB+ACEi+ARB+Thiazide diuretic+Loop diuretic+Potassium sparing diuretic	1	25.0
	BB+ARB+DHP CCB+ARB	1	25.0
	BB+ARNI+Loop diuretics+ Potassium sparing diuretics +ARB	1	25.0
	BB+Potassium sparing diuretics+ARB+Loop diuretic+BB	1	25.0
	Total	4	100.0

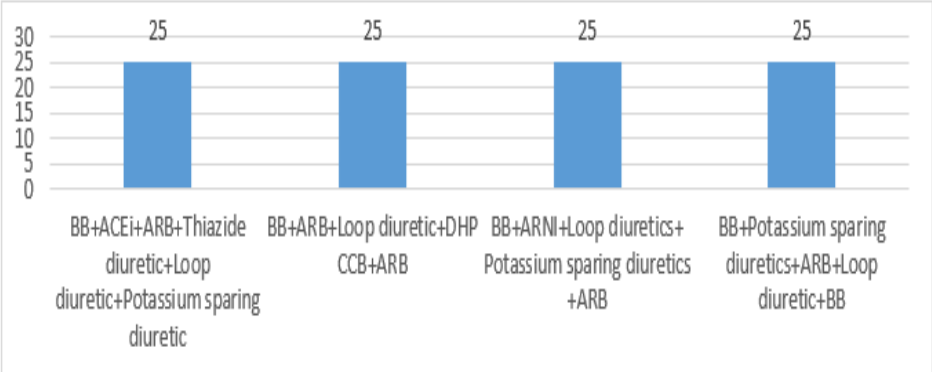

Figure no.8- Bar diagram representing frequency and percentage based on quintuple therapy

All the above quintuple combination of drugs hold equivalent percentage. this can be attributed to the difference in the individual subject conditions i.e their disease stage, its progression, complications, comorbid conditions etc.

Table no.10- Frequency and percentage based on adherence status

Adherence status	Frequency	Percentage
Low	29	29
Medium	65	65
High	6	6
Total	100	100

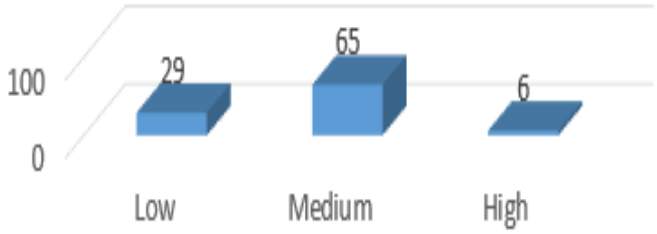

Figure No.9- Bar Diagram Representing Frequency and Percentage Based on Adherence Status

Table No.11 – Descriptive Statistics Based on Morisky Medication Adherence Scale

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
MMAS	100	1.50	8.00	5.4425	1.86943

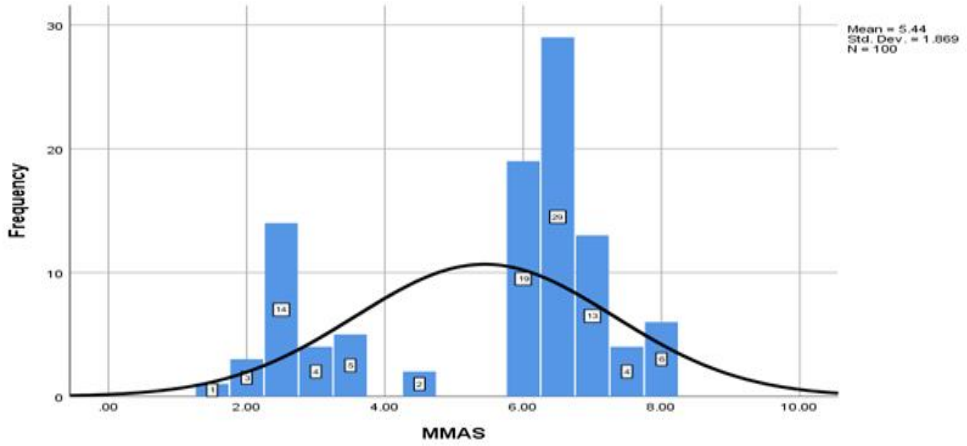

Figure no.10- Graphical representation of frequency vs MMAS Scoring

Among 100 subjects enrolled into the study, 65% of subjects were moderately adherent to the prescription and only 6% being highly adherent, with mean MMAS scoring 5.4425.

Hypertension prevalence increases with age, with the highest rate in those over 60 years old. Men are more prone to HTN as compared to women. Dual and triple therapy are more effective and preferred over monotherapy for achieving desired blood

CONCLUSION:

pressure control. Beta blockers and angiotensin receptor blockers are most frequently prescribed drug classes. Medication adherence remains a challenge with only a small percentage of subjects being highly adherent.

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HOW TO CITE: Kibriya Kulsum*, Asra Jabeen, Aneesh Bageliker, J. Om Prasad Reddy, Raghu Kishore Galla, Optimising Antihypertensive Therapy: Prescribing Patterns and Adherence, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 4, 1665-1677 https://doi.org/10.5281/zenodo.15208587