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**PROSPECTIVE OBSERVATIONAL STUDY ON PRESCRIBING
PATTERN OF ANTI HYPERTENSIVES IN CARDIOVASCULAR
DISEASE PATIENTS AT TEACHING HOSPITAL, CARDIOLOGY
HOSPITALS IN KHAMMAM DISTRICT OF TELANGANA**

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*doi: 10.33472/AFJBS.6.11.2024.886-897***ABSTRACT:**

Hypertension is considered one of the major risk factors for various cardiovascular disorders, including coronary artery disease, congestive heart failure, atrial fibrillation, peripheral arterial disease, and aortic aneurysm. Chronically elevated blood pressure puts more strain on the heart, causing structural and functional changes that are referred to as hypertensive heart disease, these alterations affect the left ventricle, left atrium, and coronary arteries, this is prospective observational study conducted for 6 months; this study found some interesting facts about prescribing pattern of antihypertensives in cardiac patients. Mono therapy antihypertensives are prescribed for denovo hypertension and blood pressure within the targeted range, ACEi and ARBs are the first line drugs in mono therapy and along with these selective beta blockers like metoprolol has been mostly used to prevent cardiac problems, Dual drug therapy is used in uncontrolled hypertensive cases with other co morbidities like CAD, CKD, persistent elevated blood pressure, ARBs with diuretics are the initial choice of drugs later on ARBs with beta blockers, ARBS, CCBs. Triple drug regimen has been prescribed to the patients with uncontrolled persistent blood pressure with other comorbidities like CKD are suggested with clonidine to manage the blood pressure to less than 140mmHg, sacubitril with valsartan, diuretics gave the best results in heart failure cases, digoxine with ARBs, diuretics improved patient condition, these combinational drugs decreased the cardiac associated mortality.

Keywords: Antihypertensives, prescribing pattern, cardiac patients, efficacy, safety

1. INTRODUCTION

Hypertension is a chronic lifestyle disease marked by increased blood pressure. Over 1 billion adults worldwide have hypertension, with the condition affecting about 45% of the adult population. Hypertension affects 30% of adults in India on average, with 34% of urban adults and 28% of rural adults having the medical condition. [1]. The most fatal consequence of persistent or chronic high blood pressure is cardiovascular disease, which claimed 17.5 million lives in 2016 compared to 14.4 million in 1990. Most often as a result of coronary heart disease (CHD).

More than 80% of fatalities are occurring in developing and middle-income nations. Because of this, CVD is now thought to be the leading cause of mortality worldwide and is likely to stay that way in the future. [2]. In the third-world nation of India, where there are many low- and middle-income families, CVD risk is higher.

As the risk of CVD in young people rises daily as due to the effects of lifestyle and eating habits, alcohol and smoking play a significant part in the pathophysiology of blood pressure-related CVD, therefore controlling blood pressure in young patients at the earliest possible stage of diagnosis gives the best results.

According to the INTERHEART study, which involved participants from 52 countries with high, middle, and low income levels, modifiable risk factors, such as smoking, dyslipidemia, hypertension, diabetes, abdominal obesity, psychosocial factors, alcohol consumption, and sedentary lifestyles, accounted for 90% of CVDs. [3]

Hypertension effect on CVD: Hypertension is considered one of the major risk factors for various cardiovascular disorders, including coronary artery disease, congestive heart failure, atrial fibrillation, peripheral arterial disease, and aortic aneurysm. Chronically elevated blood pressure puts more strain on the heart, causing structural and functional changes that are referred to as hypertensive heart disease. These alterations affect the left ventricle, left atrium, and coronary arteries. [4]

Heart failure is characterized by fluid retention and congestion, which are linked to more severe symptoms and worse outcomes. Diuretics continue to be essential components of heart failure treatment despite the paucity of controlled studies. Due to its good bioavailability, torasemide is frequently used. A few studies have suggested that torasemide may lower the number of heart failure admissions, but there is limited evidence to support up this claim. Thiazides are the good drug of choice in some patients with hypocalcaemia, and very less number of adverse effects is seen in these patients, dehydration and hyperuricemia are the situations to be monitored. Sometimes diuretics may alter endocrine function also. [5,6]

Treatment of Hypertension: Hypertension is the most common modifiable risk factor for cardiovascular disease and death, and lowering blood pressure with antihypertensive drugs reduces target organ damage and prevents cardiovascular disease outcomes. The first and most important step in preventing hypertension, is making the appropriate lifestyle changes, many epidemiological studies have shown that reduced salt intake is directly related to decreased BP, according to epidemiological research, dietary n-3 PUFAs and fish oil had a marginally but significantly inverse relationship with blood pressure. [7,8] In Western nations, consuming even a small amount of fish (30–60 g/d) lowers the risk of CHD and sudden cardiac death [9,10]

There are about 15 different classes of antihypertensive medications available on the market to lower blood pressure and prevent heart and circulatory problems; each of these medications has a unique safety and toxicological profile that must be taken into account before therapy is started.

2. MATERIALS AND METHODS

This is a prospective observational study approved by institutional ethics committee (IEC) conducted in teaching and cardiology hospitals in khammam district of Telangana for a period of six months. This study aims to emphasize the safety and efficacy of antihypertensives in cardiovascular diseases.

Study Design: This is a prospective observational study

Inclusion criteria: Includes Patients using anti-hypertensive medication along with cardio vascular diseases who visited and admitted in study sites.

Exclusion criteria: Patients with psychiatric illness and patients not willing to participate in the study.

Sample size: A total of 100 cases were collected by using prepared data collection form.

Study period: The study was performed over a period of 6 months from January 2023 to June 2023

Study location: Teaching hospital and Cardiology hospitals in Khammam district.

Study Procedure: Patients were selected for the study by simple random sampling and the data captured is analyzed in terms of efficacy and safety of antihypertensives in cardio vascular diseases.

Source of data: Patient case sheets and patient interview about their antihypertensive medication, co-morbidities, lifestyle, and social habits, past medical history, present medical history, and lab investigation reports.

Assessing factors: Risk factors, adverse drug reactions, safety and efficacy of antihypertensives in CVD patients.

Statistical plan: Statistical analysis will be carried out by Microsoft Office Excel and Graph Pad Prism 8

Monitoring Parameters: Blood Pressure.

3. RESULTS AND DISCUSSION

The study coordinators collected the data of 100 CVD patients, 46 were male and 54 are female using various antihypertensives for blood pressure and to manage cardio vascular diseases with respect to the underlying pathological conditions.

Table 1: Details of age groups, gender, and residential status of study participants

Age group	Number of Cases			Percentage	Residential status			
	Male (M)	Female (F)	Total		Rural		Urban	
					(M)	(F)	(M)	(F)
30-40	7	7	14	14%	5	4	2	3
41-50	10	12	22	22%	6	8	4	4
51-60	8	14	22	22%	3	6	5	8
61-70	14	10	24	24%	9	6	5	4
71-80	7	11	18	18%	5	6	2	5
Total	46	54	100	100%	28	30	18	24

In our study, we found that patients over 61 years of age are more likely than patients in other age groups to experience serious cardiovascular diseases, and that middle-aged people are more susceptible to cardiovascular problems as a result of their alcohol and smoking habits. [11]

Table 2: Details of alcoholics and smokers of study participants

Age Group	Alcoholics		Smokers		Alcoholic + Smoker	
	(M)	(F)	(M)	(F)	(M)	(F)
30-40	7	01	15	00	3	00
41-50	10	00	3	00	2	00
51-60	8	00	3	00	4	00
61-70	14	00	4	00	2	00
71-80	7	00	2	00	1	00

Total	46	01	27	00	12	00
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Table 3: Family history of hypertension:

Family History of HTN	Number	Percentage
Yes	57	57%
No	43	43%
Total	100	100%

We found some intriguing data on the relationship between the duration of hypertension and the development of cardiovascular problems. Even six months of uncontrolled hypertension with poor medication adherence resulted in the diagnosis of CVD. Since heart problems affect patients regardless of the duration of their hypertension or their age, we would like to address how unrecognized hypertension and cardiovascular issues can cause sudden cardiovascular collapse in young people. Cardiovascular diseases will become more likely after an average of seven years with hypertension.

Table 4: Duration of HTN in study participants

Duration of HTN	Number of cases	Percentage
De-novo HTN	1	1%
6 months	1	1%
7 months	1	1%
8 months	2	2%
1 year	3	3%
2 years	9	9%
3 years	7	7%
4 years	10	10%
5 years	15	15%
6 years	4	4%
7 years	14	14%
8 years	4	4%
9 years	4	4%
10 years	11	11%
12 years	5	5%
14 years	2	2%
15 years	3	3%
20 years	4	4%
Total	100	100%

The majority of the patients in our study had coronary artery disease (CAD) and CAD with left ventricular dysfunction. During the patient history collection, we learned that the majority of CAD with myocardial infarction patients had hyperlipidemia, sedentary lifestyles, and stressful occupations.

Table 5: List of cardiovascular diseases in study participants

CVS Comorbidities	Number of cases	Percentage %
Aortic Sclerosis	1	1
Arrhythmia	1	1
Coronary Artery Disease	13	13
CAD AWTMI	7	7
CAD IWMI	7	7
CAD AWTMI+IWMI	1	1
CAD evolved AWTMI	5	5
CAD acute AWTMI	2	2
CAD LVD	2	2
CAD mild LVD	11	11
CAD MI	9	9
CAD moderate LVD	5	5
Non-ST elevated Myocardial infraction (NSTEMI)	3	3
Unstable Angina	4	4
Cardiac Arrest	5	5
Congestive Cardiac Failure (CCF)	3	3
CHB	3	3
DCMP with LVD	4	4
Ischemic H(IH) ischemic heart disease	4	4
Left ventricular Hypertrophy(LVH)	2	2
Mild Heart Stroke	3	3
Severe LVD	4	4
Supraventricular Tachycardia	1	1
Total	100	100%

In our study, 28 patients were prescribed only one antihypertensive along with other medications such as antiplatelets and oral hypoglycemic agents, depending on their comorbidity, and 56 patients were prescribed two antihypertensives. Out of these, 4 patients had a risk of stroke due to high blood pressure and other comorbidities like chronic kidney disease and hypercoagulability, and these patients are prescribed multi-drug regimens such as more potent antiplatelet drugs and lipid-lowering therapies.

Over the years, there have been many developments and modifications to the use of β -adrenoceptor antagonists (β -blockers) in cardiovascular therapy. β -blockers are no longer the first-line treatment for essential hypertension due to the development of a large range of good antihypertensive medications, for heart failure, coronary artery disease, atrial fibrillation, and hypertension intensified by heart failure, angina pectoris, or past myocardial infarction, they continue to be the drug of first choice, according to recommendations from various medical associations. Patients with diabetes mellitus or chronic obstructive pulmonary disease should be prescribed cardio selective β -blockers as necessary. [12]

We examine the data that is currently available for the use of β -blockers in clinical situations where suggestions for standard practice can be made. Bradycardia is the major adverse effect of beta blockers, two diabetic patients who are on oral hypoglycemic agents experienced masking hypoglycemia effect, most of the physicians chose cardio selective beta blockers. Improvements in ventricular shape and function are made possible in HF patients by the action of beta-blockers against the negative effects of increased adrenergic activity caused by myocardial dysfunction. [13]

Angiotensin converting enzyme inhibitors (ACEi) use is very limited now a day because of side effects by these drugs. Angiotensin receptor blockers (ARBs) are the second most frequently prescribed antihypertensives with a better safety profile in CVD patients; they tend to develop only 14.8% of adverse drug reactions (ADRs), which are classified as mild ADRs after Naranjo's causality assessment. The majority of the population in India can afford the ARBs losartan and telmisartan because they are very inexpensive drugs in the market. [14]

Because of the high expense of medications, many people do not take medicines as prescribed. It is the duty of the healthcare professional to choose and prescribe the most appropriate medication for the individual case. ARBs provide the best results for patients with CVD and chronic renal disease and lower their death rate.

Calcium channel blockers (CCBs) are prescribed for heart failure and angina patients with combination with nitrates to decrease pre-load and after-load, but contraindicated in patients with decreased ejection fraction. CCBs are potent vasodilators to reduce the blood pressure; they are not dependent on any other external factor to show their effect. A combination of CCBs with ARBs gives an additive effect in many individuals. In our study, few patients were prescribed CCBs, like amlodipine, which is the preferred CCB in cardiac patients due to its potential effect on blood pressure and long half-life, which allows prescribing a once-daily dose. [15]

Table 6: Details of antihypertensives prescribed to study participants

Type of Therapy	Number of prescriptions
Monotherapy	28
Two drug therapy	56
Three drug therapy	16

Prescribing pattern of mono therapy

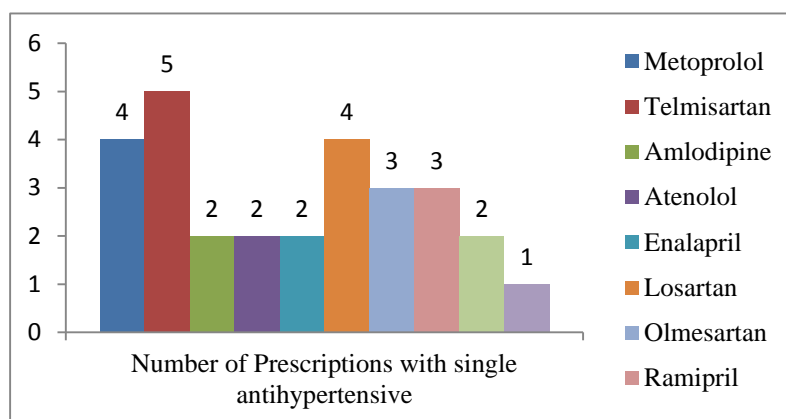
Telmisartan, losartan, metoprolol are most prescribed drugs from ARBs, Beta blockers these drugs are safe and good tolerability profile with less ADR profile, these drugs help the patients in various ways like prevent cardiac remodeling, left ventricular hypertrophy, peripheral vascular resistance and improve the blood pressure this decreases the cardiac work load further improve in the patient condition and quality of life. Medication adherence to these drugs will reduce the cardiac related mortality. Propranolol a non selective beta blocker used in the case of hyperthyroidism to prevent the thyroid storm and one of the patient experienced hypoglycemia effect, so physician and patient should aware of these effects to avoid further attacks.

Table 7: Prescribing pattern of mono therapy

Sl. No	Drug	Doses	No: of Cases
1	Metoprolol	12.5, 25,50 mg	4
2	Telmisartan	20,40 mg	5
3	Amlodipine	2.5, 5 mg	2

4	Atenolol	25, 50 mg	2
5	Enalapril	2.5, 5, 10 mg	2
6	Losartan	25, 50 mg	4
7	Olmesartan	10, 20, 40 mg	3
8	Ramipril	2.5, 5 mg	3
9	Propranolol	20 mg	2
10	Furosemide	40 mg	1

Figure 1: Prescribing pattern of mono therapy



Prescribing pattern of two drug therapy

It has been reported that combination tablets containing two classes of antihypertensive medications, such as thiazide diuretics or Ca-channel blockers, and renin-angiotensin system (RAS) inhibitors (ACEIs and ARBs), can be beneficial for lowering blood pressure (BP) and preventing cardiovascular disease. For a variety of problems, such as diabetes, chronic heart failure, and chronic renal disease, the use of RAS inhibitors is advised. It is therefore advised to use a RAS inhibitor with a diuretic or a calcium channel blocker to control hypertension. [16]

Table 8: Prescribing pattern of two drug therapy

Sl.No	Two Drug Combination	Dose	No:of Cases
1	Losartan + Hydrochlorothiazide	50 mg+ 12.5 mg	09
2	Amlodipine + Atenolol	5mg + 50mg	07
3	Clinidipine + Metoprolol	10mg + 50mg	03
4	Amlodipine + Hydrochlorothiazide	5mg + 12.5mg	05
5	Telmisartan + Hydrochlorothiazide	40mg + 12.5mg	11
6	Metoprolol + Telmisartan	50mg + 40mg	04
7	Atenolol + Chlorthalidone	25mg + 12.5mg	3
8	Telmisartan + Amlodipine	40mg + 5mg	6
9	Spiranolactone + Torasemide	50mg + 10mg	3
10	Olmesartan + Hydrochlorothiazide	20mg + 12.5mg	5

The fixed drug combinations of anti hypertensives are more effective and safe to treat the chronic uncontrolled hypertension with co morbidities and to prevent complications like stroke, heart failure, kidney failure. ARB's with diuretics will decrease the cardiac work load, further prevention of cardiac remodeling; this combination is more effective and safe which had reduced blood pressure by 10mmHg in the patients.

Clinidipine with metoprolol has been used to treat the patients with heart failure and stroke to improve the circulation to brain and heart simultaneously, this combination has improved the patient quality of life. Spiranolactone with torasemide is a long acting potent diuretic used to treat the complicated cases this combination had better effect when used along with other anti hypertensives like ARBs. [17]

Olmesartan, losartan and telmisartan with hydrochlorothiazide is the most essential combinational drug for patients to use in long term, ARBs are more effective than the ACEi in terms of safety and efficacy this combination has reduced the blood pressure by 8mmHg with in the short time and improved the patient symptoms like edema, shortness of breath associated with heart failure and kidney failure.

Amlodipine with hydrochlorothiazide are used in the cases of kidney failure with un controlled hypertension and had a risk of heart failure, but still the safety of this combination has to be established. Amlodipine with atenolol combination has been used in the patients of heart failure with risk of stroke, as it is a potent anti hypertensive combination this drug has caused a side effect of hypotension in patients so health care professionals and patients should be aware of this.

Table 9: Prescribing pattern of three drug therapy

Sl.No	Two Drug Combination	Dose	No:of Cases
1	Sacubitril + Valsartan + Hydrochlorothiazide	24mg + 26mg+ 12.5mg	5
2	Clonidine + clinidipine + prazosin	75 mcg+ 10mg + 5mg	3
3	Clinidipine + Metoprolol + Clonidine	10mg + 50mg + 75mcg	3
4	Digoxin + Losartan + Furosemide	0.25mg + 50mg+ 40mg	5

In our study 5 patients are with heart failure and prescribed with sacubitril with valsartan, the first drug approved in a new family of medications known as angiotensin receptor neprilysin inhibitors (ARNI) is sacubitril-valsartan. Patients with decreased ejection fraction (HFrEF) and chronic heart failure are prescribed by this medicine, The renin-angiotensin-aldosterone system (RAAS) is triggered as part of a maladaptive response that contributes to the pathophysiology of heart failure. Vasoconstriction, hypertension, elevated aldosterone, elevated sympathetic tone, and ultimately cardiac remodeling are all consequences of RAAS activation that are harmful to the disease's progression. By preventing the maladaptive components of heart failure, ACEi or ARBs significantly lower the morbidity and death associated with the condition. Heart failure exacerbations are characterized by high BNP and NT-pro BNP due to simultaneous activation of the natriuretic peptide system. Natriuresis, diuresis, and vasodilation are the results of this compensatory mechanism. As a result, the natriuretic peptide system lowers sympathetic tone, aldosterone levels, and blood pressure (BP). The natriuretic peptide system has beneficial effects on the pathophysiology of heart failure and acts in opposition to RAAS. Neprilysin is the enzyme that breaks down natriuretic peptides. [18]

Valsartan-sacubitril is a combination medicine. Sacubitril is a prodrug that functions as an inhibitor of neprilysin when it is activated. The medication prolongs the beneficial effects of natriuretic peptides by inhibiting the function of neprilysin, which stops the peptides from breaking down. Valsartan is an ARB that works by blocking the RAAS system. However,

because neprilysin breaks down angiotensin II, inhibiting neprilysin will accumulate angiotensin II. For this reason, a neprilysin inhibitor cannot be used alone; it should be combined with an ARB to block the effect of the excess angiotensin. Another substance broken down by neprilysin is bradykinin; neprilysin inhibition will also cause a build-up of bradykinin. Therefore, sacubitril cannot be used with an ACEi due to an increased risk of angioedema if ACEi and ARNI are used together or dosed in a short timeframe. When switching between ACEi and sacubitril-valsartan, the patient must undergo a 36-hour washout to lower the angioedema risk. This drug aims to prevent the heart failure complications like cardiac remodelling, mortality and it improved the patient condition significantly. [19]

Clonidine is added to regimen of prazosin and clonidine in the patients of cardiac problems with chronic kidney disease experiencing uncontrolled hypertension with persistent elevated blood pressure more than 180mmHg SBP, clonidine is a safe drug in a kidney failure cases but few patients will experience the orthostatic hypotension during the treatment, so it is advised to monitor the patients for the symptoms of hypotension. Clonidine, metoprolol with clonidine is used to treat patients with tachycardia, uncontrolled hypertension in CAD with CKD, this fixed regimen gave best results in the short time by mitigating the blood pressure, improved the tachycardia significantly and decreased risk of stroke.

Digoxin with ARBs and diuretics give the best result in heart failure patients with low ejection fraction, digoxin improves the cardiac contractility and heart rate which further improve the circulation, ARBs will prevent the angiotensin which is compensatory effect of heart failure, diuretics like furosemide and spironolactone will decrease the volume overload, pre load and after load this combinational medicine will prevent the left ventricular hypertrophy and cardiac remodeling, this will also decrease the mortality rate and enhance the quality of life of cardiac patients. [20]

4. CONCLUSION

Prescribing antihypertensives to patients with cardiovascular diseases is complex; choosing the appropriate drug depends on the patient's clinical condition. Antihypertensives not only control the blood pressure but also manage the underlying pathology like peripheral vascular resistance, pre-load, after-load, cardiac remodeling, and complications of heart failure. Antihypertensives will prevent mortality and improve patient quality of life with increased life expectancy.

Conflict of interest: Author declares no conflict of interest

Ethical clearance: Consent was obtained or waived by all participants in this study. Institute Ethics Committee of Anurag Pharmacy College issued approval to the study.

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