

**AN INVESTIGATION ON PREVALENCE OF ABNORMALITIES IN  
HYPERTENSIVE PATIENTS IN LABORATORY PARAMETERS UNDER  
VARIOUS CLASSES OF ANTIHYPERTENSIVE DRUGS**

A Dissertation submitted to

**THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY**  
Chennai-600032



*In partial fulfillment of the requirements for the award of degree of*

**MASTER OF PHARMACY  
IN  
PHARMACY PRACTICE**

Submitted by

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Under the Guidance of

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**MAY-2019**



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This is to certify that the dissertation entitled “**An Investigation on prevalence of abnormalities in hypertensive patients in laboratory parameters under various classes of antihypertensive drugs**” submitted to The Tamilnadu Dr. M.G.R Medical University, Chennai, is a bonafide project work of **JAYAPRAKASH K. (Reg No: 261740451)**, carried out in the Department of Pharmacy Practice, Swamy Vivekanandha College of Pharmacy, Tiruchengode in partial fulfillment for the degree of Master of Pharmacy under the guidance of **Mrs. RANGAPRIYA, M. Pharm.,Ph.D., Professor and Head, Department of Pharmacy Practice** during the academic year 2018-2019.

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This work is original and has not been submitted earlier for the award of any other degree or diploma in this or any other university.

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### DECLARATION BY THE CANDIDATE

I do hereby declare that the dissertation entitled “**An Investigation on prevalence of abnormalities in hypertensive patients in laboratory parameters under various classes of antihypertensive drugs**” submitted to The Tamilnadu Dr. M. G. R Medical university, Chennai, is a record of independent work carried out in the Department of Pharmacy Practice, Swamy Vivekanandha College of Pharmacy, Tiruchengode in partial fulfillment for the degree of Master of Pharmacy under the guidance and direct supervision of **Mrs.Dr.RANGAPRIYA,M.Pharm.,Ph.D., Professor and Head, Department of Pharmacy Practice** during the academic year 2018-2019.

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## ACKNOWLEDGEMENT

**“The act of thanks giving does not exhibit ones sense of gratitude, but the true tendency of leading a helping hand during emergency and the fact that every work has thousands of hands behind”**

This thesis is the result of one whole year of work whereby I have been accompanied and supported by many people .It is a pleasant aspect that i have now the opportunity to express my gratitude for all of them.

First and foremost I bow down before **Lord Almighty** for these splendid blessings and care in completing my project work and throughout my life till this very second.

I would like to express my profound gratitude my **beloved parents** who taught me hard work by their own example and rendered me enormous support during the whole tenure of life to achieve more.

I render my sincere thanks to our honourable Chairman and Secretary, **Vidhya Ratna, Rashtriya Ratna, Hind Ratna, Prof Dr. M. Karunanithi, B. Pharm., M.S., Ph.D., D.Litt.,** for providing all facilities for my study and rendering his noble hand in the upliftment of women education in all the disciplines.

I express my gratefulness to our Executive Director **Dr. S. Arthanareeswaran, MBBS., MD.,** for permitting me to carry out this project in his hospital, and for providing all facilities for my study.

I would like to express my very great respect and gratefulness to my guide and direct supervisor **Mrs.Dr. RANGAPRIYA, M. Pharm.,Ph.D., Professor and Head, Department of Pharmacy Practice** , Swamy Vivekananda College of pharmacy. I thank him for her willingness and dedication to offer continuous guidance, support and patience and for her valuable and constructive suggestions during the planning and development of this research work. Her willingness to give her time so generously has been very much appreciated.

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It is difficult to overstate my gratitude to **Dr. G. Muruganathan, M. Pharm., Ph.D.**, Principal of this institution. His enthusiasm and integral view on research and his mission for providing 'only high-quality work and not less', has made a deep impression on me. I owe him lots of gratitude for having me shown this way of research.

I am highly indebted to **Dr. Ragupathy, MBBS, MD., (Cardiology)**, Vivekanandha medical care hospital for providing guidance and necessary information regarding the project. I am also thankful to all the health care professionals especially nurses and pharmacists who supported me the whole length task. Also, my heartfelt gratitude to all patients and caregivers who co-operated with me throughout.

I will be failing in my duty, when I am not expressing my heartfelt thanks to **Dr. Palanisamy, M. Pharm., Ph.D., Mr. S. Anand Kumar, M. Pharm., Mrs. T. Kumutha, M. Pharm., Dr. Anu Philip, Pharm D., Mrs. P. Parkavi Rani, M. Pharm.**, Department of Pharmacy Practice, who had helped my project work.

I remain thankful to our lab assistant **Mrs. Poongodi** for her help during my project work.

Friends are treasures to me and it is very difficult to overstate my thanks to all my friends. It has been my happiest time to study, discuss, laugh and play with them all.

Also, I would like to thank **The Tamil Nadu Dr. M.G.R. Medical University** for providing a nice environment for learning.

I feel delighted to express my whole hearted gratitude to all those who gave their helping hands in completing my course and my project successfully.

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## ABBREVIATIONS

ACE	-	Angiotensin converting enzyme
ADR	-	Adverse drug reaction
HDL	-	High density lipoprotein
TC	-	Total Cholestrol
LDL	-	Low density lipoprotein
BP	-	Blood Presure
ARB	-	Angiotensin receptor blockers
CCB	-	Calcium Channel Blocker
DBP	-	Diastolic Blood Pressure
SBP	-	Systolic blood pressure
IP	-	In patient
OD	-	Once a day.
BD	-	Twice a day
MI	-	Myocardial infraction
HDFP	-	Hypertension Detection and Follow-up Program
EWPHE	-	European working party on high blood pressure
CO	-	Cardiac output
TPR	-	Total peripheral resistance.
JNB	-	Joint National Committee
STEMI	-	ST Elevated Myocardial Infraction
NSTEMI	-	Non ST Elevated Myocardial Infraction
RR	-	Respiratory Rate.

## 1. INTRODUCTION

Hypertension is blood pressure elevated enough to perfuse tissues and organs. Elevated systemic blood pressure is usually defined as a systolic reading greater than or equal to 140 mm hg and diastolic reading greater or equal to 90 mm hg ( $\geq 140/90$ ). The most recent recommendations of the seventh report of the joint national committee on detection, evaluations, and treatment of high blood pressure (JNC-7) has added a “Prehypertension“ category which includes individual with systolic blood pressure reading of 120-139 or diastolic blood pressure reading of 80-89 mm hg.<sup>1</sup>

Hypertension is the most common disease affect human beings, its high prevalence involving both sexes and extending to either industrialized and developing countries. Compared with Normotensives , individuals with a high blood pressure stand a much greater chance of having during their life a stroke, coronary heart disease, heart or renal failure and peripheral artery disease also they have a substantially higher risk of developing atrial fibrillation, deterioration of cognitive function and dementia. The high prevalence and the multifold important contribution of hypertension to cardiovascular and renal risk account for its position as the top contributor to the burden of disease worldwide.<sup>2</sup>

Blood pressure categories as per the new guidelines are:

Normal: less than 120/80 mmHg

Elevated: systolic between 120-129 and diastolic less than 80;

Stage 1: systolic between 130-139 or diastolic between 80-89;

Stage 2: systolic at least 140 or diastolic at least 90 mm Hg;

Systolic pressure over 180 and/ or diastolic over 120, with patients needing prompt changes in medication if there are no other indication of problems, or immediate hospitalization if there are signs of organ damage.

The guideline eliminates the category of prehypertension, categorizing patients as having either elevated (120-129 and less than 80) or stage 1 hypertension (130-139 or 80-90). While previous guidelines classified 140/90 mm Hg as stage one hypertension, this level is classified as stage 2 hypertension under the new guidelines. In addition, the guideline stress the importance of using proper technique to measure blood pressure; recommend use of home blood pressure monitoring using validated devices and highlight the value of appropriate training of health care provides to reveal “white coat hypertension.”<sup>3</sup>

## **EPIDEMIOLOGY:**

### **GLOBAL SCENARIO:**

Rates of systolic blood pressure  $\geq$  140 mm hg have increased globally in the past 25 years, as have the associated rates of death and disability. Hypertension remains a dominant risk factor for cardiovascular disease, around the world.

Among the key findings was that the number of people with systolic blood pressure (SBP) of 140 mm hg or higher was estimated to have increased from 442 million in 1990 to 874 million in 2015, where this SPB level was responsible for 14% of total deaths and 143 million disability associated life –years. The rate of hypertension increased from 17,307 per 100,000 in 1990 to 20,525 per 1,00,000 in 2015. Most of the deaths associated with hypertension were related to cardiovascular disease.<sup>4</sup>

### **IN INDIA:**

Hypertension is the most important risk factor for chronic disease burden in India. Studies from various parts of India have reported high prevalence of hypertension. These studies have also reported that hypertension is increasing and there is low awareness and control. Two recent studies have been conducted with inform tools and nationwide sampling to determine the true prevalence of hypertension in country. Fourth national family health survey evaluated

hypertension in a large population based sample ( n=799,228) and reported hypertension in 13.8% men vs. 8.8% women (over all 11.35) aged 15-49 and 15-54 respectively. More representative data ( age> 18 years, n=1,320,555) in fourth district level household survey reported hypertension in 25.3% with greater prevalence in men (27.4%) than women (20.0%). This translates into 207 million persons (men 112 million, women 95 million)with hypertension in India. Prevalence would be much higher using 2017 American guideline. Global burden of diseases study reported that hypertension led to 1.63 million deaths in India in 2016 as compared to 0.78 million in 1990 (+108%). The disease burden (DALY<sub>s</sub>) attributable to hypertension increased from 21 million in 1990 to 2016 (+89%). Social determinants of hypertension are important and Indian states with greater urbanization, human development and social development have more hypertension. There is poor association of hypertension prevalence with healthcare availability although there is positive association with healthcare access and quality. The health system in India focus on better hypertension screening and control to reduce cardio vascular morbidity and mortality<sup>5</sup>.

#### **PATHOPHYSIOLOGY:**

As the blood pressure equals cardiac output total peripheral vascular resistance (TPR), pathogenic mechanisms must involve

- Increased Cardiac output (CO)
- Both
- Increased TPR

In most patients cardiac output is normal or slightly increased and TPR is increased. This pattern is typical of primary hypertension and hypertension due to primary aldosteronism, pheochromocytoma, renovascular disease, and renal paranchymal disease.

In other patients, cardiac output is increased ( possibly because of venoconstriction in large veins), and TPR is inappropriately normal for the level of CO. Later in the disorder, TPR increase and CO returns to normal probably

because of auto regulation. Some disorders like increase CO ( thyrotoxicosis, arteriovenous fistula, aortic regurgitation). Particularly when stroke volume is increased, it cause isolated systolic hypertension. Some elderly patient have isolated systolic hypertension with normal or low CO, probably due to inelasticity of the aorta and its major branches. Patient with high, fixed diastolic pressure often have decreased CO.

Plasma volume tends to decrease as BP increase; rarely, plasma volume remains normal or increase. Plasma volume tends to be high in hypertension due to primary aldosteronism or renal parenchymal disease and may be quite low in hypertension due to pheochromocytoma. Renal blood flow gradually decrease as diastolic BP increases and arteriolar sclerosis begins. GFR remains normal until late in the disorder; as a result, the filtration is increased. Coronary, cerebral, and muscle blood flow is maintained unless severe atherosclerosis coexists in these conditions.

### **ABNORMAL SODIUM TRANSPORT**

In many cases of hypertension, sodium transport across the cell wall is abnormal, because the sodium potassium pump (  $\text{Na}^+$ ,  $\text{Cl}^-$  - ATPase) is defective or inhibited as the permeability to sodium ions is increased. This results in increased intracellular sodium, which make the cell more sensitive to sympathetic stimulation. Calcium follow sodium, So accumulation of intracellular calcium may be responsible for the increased sensitivity. Because  $\text{Na}^+$ ,  $\text{Cl}^-$  -ATPase may pump norepinephrine back into sympathetic neurons inhibition of this mechanism could also enhance the effect of norepinephrine, increasing BP. Defects in sodium transport may occur in normotensive children of hypertensive patients.

### **SYMPATHETIC NERVOUS SYSTEM**

Sympathetic stimulation increase blood pressure, usually more in patients with elevated BP and hypertension than in normotensive patients. Whether this hyper responsiveness resides in the sympathetic nervous system or in the myocardium and vascular smooth muscle is unknown. A high resting pulse rate which may



result from increased sympathetic nervous activity is a well-known predictor of hypertension. In some hypertensive patients, circulating plasma catecholamine levels during rest levels are higher than normal.

### **RENIN-ANGIOTENSION-ALDOSTERONE SYSTEM**

The rennin-angiotensin-aldosterone system helps regulate blood volume and therefore blood pressure. Rennin, an enzyme formed in the juxtaglomerular apparatus, catalyzes conversion of angiotensinogen to angiotensin I, that inactive is cleaved by ACE, mainly in the lungs but also in the kidneys and brain, to angiotensin II, a potent vasoconstrictor that also stimulates autonomic centers in the brain to increase sympathetic discharge and stimulates release of aldosterone and vasopressin. Aldosterone and vasopressin cause sodium and water retention, elevating BP. Aldosterone also enhance potassium excretion; low plasma potassium (<3.5 mEq/l) and increased vasoconstriction through closure of potassium channels. Angiotensin III, present in the circulation stimulates aldosterone release as actively as angiotensin II but has much less pressor activity. Because chymase enzymes also convert angiotensin I to angiotensin II, drugs that inhibit ACE do not fully suppress angiotensin II production.

Rennin secretion is controlled by at least 4 mechanisms which are not mutually exclusive:

- A renal vascular receptor respond to changes in tension in the afferent arteriolar wall
- A macula densa receptor detects changes in delivery rate of concentration of sodium chloride in the distal tubule
- Circulating angiotensin has a negative feedback affect on rennin secretion
- Sympathetic nervous system stimulates rennin secretion mediated by beta-receptors ( via the renal nerve)

Angiotensin is generally acknowledged to be responsible for renovascular hypertension, at least in the early phase, but the role of the rennin angiotensin aldosterone system in primary hypertension is not established. However, in black

and elderly patients with hypertension, rennin levels tend to be low. the elderly also tend to have low angiotensin II levels.

Hypertension due to chronic renal parenchymal disease (renoprival hypertension) result from the combination of a rennin dependent mechanism. In most cases, increased rennin activity is not evident in pheripheral blood. Hypertension is typically moderate and sensitive to sodium and water balance.

### **Vasodilator deficiency**

Deficiency of vasodilator (eg, bradykinin, nitric oxide) rather than excess of vasoconstrictor (eg, angiotensin, norepinephrine) may cause hypertension.

Reduction in nitric oxide due to stiff arteries is linked to salt-sensitive hypertension. An inordinate increase of > 10 to 20 mmHg systolic BP after large sodium load (eg, meal of Chinese food).

If the kidney do not produce adequate amounts of vasodilators (because of renal paranchymal disease or bilateral nephrectomy), blood pressure can increase.<sup>6</sup>

## **COMPLICATIONS OF HYPERTENSION**

### **Congestive heart failure**

Left ventricular hypertrophy and congestive heart failure are hypertensive complications due to the adaptation of the heart to the increased after load and are frequently (40-50%) percent in elderly patient Left ventricular hypertrophy is a substantial risk factor that increase the incidents of premature ventricular contraction to (40-50) times and the risk of sudden death and cardiovascular mortality by 5-6 times.

### **Renal insufficiency**

Treatment of hypertension can slow the progression of renal impairment in patient with renal disease. In patient with renal paranchymal disease ( creatinine >2/5 mg/dl) sodium retention become a major factor, and larger dose of

furosemide, bumetanide, or metolazone are needed because thiazide diuretics are ineffective. Other drugs that are effective in patients with renal disease are central anti-adrenergics.

### **Coronary artery disease**

Patients with angina pectoris or a previous myocardial infarction can be treated with  $\beta$  blockers or calcium blockers which reduce angina.  $\beta$  blockers are also shown to reduce mortality following myocardial infarction, at least in men. Because of increased arrhythmias, caution must be exercised to avoid diuretic-induced hypokalemia.

### **Cerebrovascular disease**

Anti-hypertensive therapy can reduce the risk of recurrent stroke and is an important component of therapy in patients with cerebrovascular disease. It is important to avoid orthostatic hypotension and drugs like guanethidine should not be used. Even diuretic therapy should be started cautiously because elderly patients with cerebrovascular disease are more likely to develop hypotension from these drugs.

### **Diabetes mellitus**

Patients with both diabetes mellitus and hypertension are at an increased risk of cardiovascular complications. The control of blood pressure is of particular importance in the diabetic patients. Many antihypertensive drugs can adversely affect glycemic control or serum lipids. Thiazide diuretics impair insulin release, probably by potassium depletion. Non-selective  $\beta$  blockers impair recovery from hypoglycemia and reduce the awareness of sympathetic-mediated hypoglycemic symptoms.  $\beta$  blockers may increase peripheral vasoconstriction and blood pressure during hypoglycemia.

### **Advanced age**

In elderly patients the systolic blood pressure is the most reliable predictor of cardiovascular disease. Because systolic blood pressure continues to increase with advancing age there is a high incidence of isolated systolic hypertension in the elderly. Hypertension patients have a threefold increase in cardiovascular mortality. Information from the HDFP Australian national trial, the EWPHE trial has suggested that the elderly will benefit from antihypertensive therapy.

### **Pregnancy**

Hypertension is a major cause of maternal and fetal morbidity and mortality. Pregnant women can have chronic hypertension that predated gestation or can develop preeclampsia. Hypertension associated with proteinuria and edema can progress to a convulsive phase termed eclampsia. Preeclampsia requires hospitalization and if severe hypertension develops near term parenteral therapy with hydralazine or low dose diazoxide is recommended. Most experience in the treatment of pregnant hypertensive women has been with hydralazine methyldopa and  $\beta$  blockers.<sup>7</sup>

## MANAGEMENT

Guideline	Population	Goal BP (mm Hg)	First-Line Treatment Options
2014 Hypertension Guideline <sup>8</sup>	Adults <60 y	<140/90	Nonblack: thiazide, ACEI, ARB, or CCB Black: thiazide or CCB
	Adults ≥60 y	<150/90	
	Adults with diabetes	<140/90	Thiazide, ACEI, ARB, or CCB
	Adults with CKD	<140/90	ACEI or ARB
JNC 7 <sup>9</sup>	Adults ≥18 y	<140/90	Thiazide, 2-drug combination for BP >20/10 mm Hg over target
	Adults with diabetes	<130/80	Thiazide, ACEI, b-blocker, CCB, or ARB
	Adults with CKD	<130/80	ACEI or ARB
ASH/ISH 2014 <sup>10</sup>	Adults <80 y	<140/90	Nonblack <60 y: ACEI or ARB
	Adults <80 y	<140/90	Nonblack <60 y: ACEI or ARB
	Adults ≥80 y	<150/90	Nonblack ≥60 y or black: CCB or thiazide
	Adults ≥80 y with CKD or diabetes	<140/90	ACEI or ARB
	Adults <80 y with CKD and albuminuria	<130/80	ACEI or ARB
CHEP 2014 <sup>11</sup>	Adults <80 y	<140/90	Thiazide, b-blocker (age <60 y), ACEI (nonblack), CCB, or ARB
	Adults ≥80 y	<150	Thiazide, ACEI (nonblack), CCB, or ARB
	Adults with diabetes	<130/80	ACEI or ARB (CVD or CKD), or ACEI, ARB, CCB, or thiazide
	Adults with CKD	<140/90	ACEI or ARB
ESH/ESC 2013 <sup>12</sup>	Nonfrail adults <80 y	<140/90	Diuretic, b-blocker, CCB, ACEI, or ARB
	Adults >80 y	<150/90	Diuretic, CCB
	Adults with diabetes	<140/85	ACEI or ARB
	Adults with CKD without proteinuria	<140/90	ACEI or ARB
	Adults with CKD with overt proteinuria	<130/90	ACEI or ARB
	Adults with CHD	<140/90	ACEI, ARB, or b-blocker
ADA 2015 <sup>13</sup>	Adults with diabetes	<140/90*	ACEI or ARB
KDIGO 2012 <sup>14</sup>	Adults with CKD and urine albumin ≥30 mg/24 h	<130/80	ARB or ACEI with urine albumin ≥300 mg/24 h

## **Pharmacological treatments for HTN:**

Choices of drugs for HTN are influenced by age, comorbidities, ethnicity, pregnancy and other parameters necessitating individual specific treatment regimens ACE inhibitors have a dual mode of action. They prevent the formation of angiotensin II, the active vasoconstrictor of RAAS and decrease the metabolism of the vasodilator bradykinin increasing its availability. These drugs are mostly well tolerated except for the occasional cases of non-dose dependent side effects of cough and angioedema seen sporadically in patients of Asian and African descent.

Although these drugs can be used as monotherapy or in combination with calcium channel blockers (CCB) and diuretics the former is more beneficial in Caucasians possibly since the RAAS is less pronounced in the black population. Several studies have identified the benefits of these drugs in clinical outcomes in patients with heart failure, chronic kidney disease, left ventricular systolic dysfunction and post myocardial infarction

Angiotensin receptor blockers (ARBs), similar to ACE inhibitors target the RAAS by blocking AT1 receptor responsible for downstream effects of angiotensin II. Owing to similar mechanisms of action, patients on these drugs share the same benefits as with ACE inhibitors mentioned earlier and as an added advantage these drugs do not cause the undesired cough. Potentially ACE inhibitors and ARB can be used together for more complete blockade of the RAAS if BP control is not achieved, although often other classes of agents will be considered for combination use first (i.e. thiazide diuretics).

Calcium channel blockers (CCB's) work by binding to the L- channels of vascular smooth muscle cells and disrupting influx of calcium into muscle cell preventing contraction of smooth muscle cells and cardiac myocytes. Dihydropyridine CCBs decrease blood pressures mainly via direct vasodilation and decreasing systemic

vascular resistance but non dihydropyridines function by decreasing both heart rate and force of myocardial contraction. There is significant evidence demonstrating that CCB's improve all-cause mortality plus reduce risk of stroke in patients with HTN<sup>15</sup>. Caution should be exercised when administering these drugs in combination with  $\beta$ -blockers and in patients with heart failure since non-dihydropyridines are not the treatment of choice in these groups. Overall CCBs in conjunction with ACE inhibitors or ARBs are important tools in achieving significant drops in blood pressures in patients with HTN.

Diuretics function by increasing renal sodium and water excretion. It has been well documented that diuretics improve cardiovascular outcomes and reduce risk of stroke. Heart failure is long term complication of HTN and studies have demonstrated that use of spironolactone decreases risk of morbidity and mortality in hypertensive patients with heart failure<sup>16</sup>. Albeit thiazide diuretics are favored in clinical practice, use of loop diuretics in association with Potassium sparing diuretics reduces the risk of hypokalemia and hypomagnesaemia both conditions known to thwart diuretic therapy. Finally, even small doses diuretics potentiate blood pressure lowering capacity of most antihypertensive drug regimes. However, studies have shown an increased risk of type II diabetes mellitus in patients taking thiazide diuretics. They aren't contraindicated in patients with preexisting type II diabetes mellitus, but in at risk patients, greater attention to lifestyle changes to reduce this risk should be considered.

Beta-blockers are the drug of choice when treating hypertensive patients with a history of myocardial infarction and heart failure. These drugs reduce cardiac output and decrease renal renin secretion, thus initial worsening of heart failure should be anticipated when commencing therapy in the presence of heart failure. Beta-blockers are known to alter glucose metabolism and mask hypoglycemia necessitating caution when used in patients at risk for diabetes. Patient compliance is a challenge with beta-blocker therapy due to its association with depression, fatigue and sexual dysfunction and therefore patient education is

warranted. Aldosterone antagonists in particular spironolactone deserves special mention due to its utility when used in combination with ACE inhibitors, ARBs, CCBs and diuretics especially in patients with heart failure. However, its use as an anti-hypertensive has been shown to be excellent in those patients that can tolerate its use. Common problems with its use include gynaecomastia and electrolyte disturbances such as hyperkalaemia and deteriorating renal function. The later two are more common in patients in whom renal function is already compromised, and in patients already on ACE inhibitors or ARBs.

Alpha-blocker use in treatment of HTN continues to evolve since its inception over a decade ago. This drug that inhibits vascular sympathetic tone by blocking postganglionic  $\alpha$ 1-receptors is usually used as add-on medication in patients with uncontrolled HTN or in those who have poor tolerance to other first line medications. Owing to its two main side effects namely first dose-syncope and vasovagal syncope, a measure of caution should be practiced during initiation of such therapy. Coupling of alpha-blockers with a diuretic can increase efficiency of therapy particularly since it could potentially off set adverse glucose and lipid imbalances caused by diuretic therapy. The drug is especially useful when treating HTN in older male patients with benign prostrate hypertrophy.

Other drugs in the armamentarium against HTN include direct vasodilators and centrally acting adrenergic inhibitors. However, their use in practice has diminished since their side effects outweigh benefits and are now utilised as add-on therapy in specific patient groups. Direct renin inhibitors, which target a different part of RAAS compared to ACE inhibitors and ARBs, is another option as add-on or monotherapy in patients intolerant to first line antihypertensive therapies<sup>17</sup>. However, further studies assessing the utility of the latter group is imperative considering the ambiguity of treatment efficacy and the potential side effects in specific patient subgroups. Other potential targets such as endothelin receptor antagonists and vasopeptidase inhibitors have been studied but no role has yet been identified for these therapies<sup>18</sup>



**Non-pharmacologic treatment of HTN:**

The importance of lifestyle changes like weight reduction, dietary salt reduction, regular aerobic exercise, smoking cessation and reduction in alcohol consumption cannot be stressed enough and has to be complemented along with drug therapy in all patients with HTN. The benefits of these changes are apparent in various studies revealing reductions in systolic blood pressures Table 3. In fact, in prehypertensive patients with SBP between 120-139 mmHg and DBP between 80-89 mmHg merely making lifestyle changes would delay and possibly halt progression to HTN. Similarly, even in patients with stage I HTN (SBP between 140 to 159 mmHg and DBP between 90-99 mmHg) life style changes for 6-12 months might preclude the necessity for drug therapies and should be encouraged in the absence of cardiovascular and renal risk factors<sup>19</sup>.

<b>Modification</b>	<b>Approximate SBP# reduction</b>
Weight: maintenance of normal body weight as defined by BMI of 18.5–24.9 kg/m <sup>2</sup>	5–20 mmHg/10kg reduction in weight <sup>18,20</sup>
Sodium consumption: reduction of dietary sodium to less than 100 m mol per day (2.4 g sodium or 6 g sodium chloride)	2–8 mmHg <sup>21,22</sup>
Physical activity: maintenance of healthy physical activity by including regular aerobic activity at least 30mins/day most days of the week	4–9 mmHg <sup>23,24</sup>
Healthy diet: consumption of recommended servings of fruits and vegetables along with reduced saturated and total fat content in die	8–14 mmHg <sup>21,22</sup>

Alcohol consumption: reduction of alcohol intake to less than 2 drinks in men and less than 1 drink in women	2–4 mmHg <sup>25</sup>
Smoking: Abstinence from smoking for a one week period in habitual smoker	3–5 mmHg <sup>26</sup>

## **VARIOUS CLASS OF HYPERTENSIVE DRUGS:**

### **1. DIURETICS:**

#### **a. Thiazide diuretics**

Antihypertensive effect are produced by directly dilating the arterioles and reducing the total fluid volume. Urinary excretion of sodium and water by inhibiting sodium sodium and chloride reabsorption in the distal convoluted tubules. Urinary excretion of potassium and to a lesser extent bicarbonate The effectiveness of other antihypertensive agents by preventing reexpansion of extracellular and plasma volumes.

- Bendroflumethiazide
- Chlorothiazide
- Hydrochlorthiazide
- Hydroflumethiazide
- Indapamide
- Methyclothiazide
- Metolazone
- Polythiazide
- Trichlormethiazide

#### **b. Loop diuretics**

primarily in the ascending loop of henle, there called loop diuretics. By acting within the loop of henle, the decrease sodium reabsorption. Their action is more

intens but of shorter duration (1-4 hour) than that of the thiazides and may also be more expensive.

- Bumetanide
- Ethacrynic acid
- Furosemide
- Torsemide

### **C. potassium sparing diuretics**

potassium sparing diuretics achieve their diuretic effect differently and less potentially than the thiazides and loop diuretics. Their most pertinent shared feature is that they promote potassium retention.

- amiloride
- spironolactone
- triamterene

## **2. VASODILATORS**

These drugs are used as second line agents in patients refractory to initial therapy with diuretics,  $\beta$ -blockers or supplemental agent such as ACE inhibitors or calcium channel blockers. Vasodilators directly relax peripheral vascular smooth muscle arterial venous or both. The direct vasodilators should not be used alone owing to increase in plasma rennin activity, cardiac output and heart rate.

- Diazoxide
- Hydralazine
- Minoxidil
- Nitroprusside

## **3. ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITORS**

These agents inhibit the conversion of angiotensin I to an angiotensin II which decrease the availability of angiotensin II. ACE inhibitors indirectly inhibit fluid volume increase when interfering with angiotensin II by inhibiting angiotensin II-stimulated release of aldosterone, which promotes sodium and water retention. The

net effect appears to be a decrease in fluid volume, along with peripheral vasodilation.

- Benzepril
- Captopril
- Enalapril
- Enalaprilat
- Fosinopril
- Lisinopril
- Moexipril
- Perindopril
- Quinapril
- Ramipril
- Trandolapril

#### **4. ANGIOTENSIN II RECEPTOR ANTAGONIST (ARB)**

This class of drug works by blocking and binding of angiotensin II receptor. By blocking the receptor site, these agents inhibit the vasoconstrictor effect of angiotensin II as well as prevent the release the aldosterone due to angiotensin II from the adrenal gland. These two properties of angiotensin II have been shown to be important causes for developing hypertension. Clinically angiotensin receptor blockers appear to be equally effective for the treatment of hypertension and ACE inhibitors.

- Candestartan
- Eprosartan
- Irbesartan
- Losartan
- Olmesartan
- Telmesartan
- Valsartan

## **5. SYMPATHOLYTICS**

### **A. $\beta$ - adrenergic blocking agent:**

Stimulation of rennin secretion is blocked and cardiac contractility is decreased, thus diminishing cardiac output. Sympathetic output is decreased centrally and reduction in heart rate decreases cardiac output.

- Acebutolol
- Atenolol
- Betaxolol
- Bisoprolol
- Carteolol
- Carvedilol
- Labetalol
- Metoprolol
- Nadolol
- Penbutolol
- Pindolol
- Propranolol
- Timolol

### **B. CENTRALLY ACTING $\alpha$ - AGONIST**

They act primarily within the CNS on  $\alpha_2$  receptors to decrease sympathetic outflow to the cardiovascular system.

- Clonidine
- Guanabenz
- Guanfacine.
- Methyldopa

### **C. $\alpha$ - ADRENERGIC BLOCKING AGENT**

The  $\alpha$  blockers block the peripheral postsynaptic  $\alpha$  adrenergic receptors causing vasodilation of both arteries and veins. Also the incidence of reflex tachycardia is

lower with these agents than with the vasodilator hydralazine. These hemodynamic changes reverse the abnormalities in hypertension and preserve organ perfusion. Recent studies have also shown that these agents have no adverse effect on serum lipids and other cardiac risk factors.

- Doxazosin
- Prazosin
- Terazosin

#### **D. POSTGANGLIONIC ADRENERGIC NEURON BLOCKER**

- Reserpine

Reserpine acts centrally as well as peripherally by depleting catecholamine stores in the brain and in the peripheral adrenergic receptors.

#### **E. CALCIUM CHANNEL BLOCKERS**

Calcium-channel blockers inhibit the influx of calcium through slow channels in vascular smooth muscle and cause relaxation. Low renin hypertensive black and elderly patients respond well to these agents. Although the calcium-channel blockers share a similar mechanism of action each sino atrial and artio ventricular nodal depression and a decrease in myocardial contractility.

- Benzothiazepine derivatives :  
Diltiazem
- Diphenylalkylamine derivatives :  
Verapamil
- Dihydropyridines:  
Amlodipine  
Felodipine  
Isradipine  
Nicardipine  
Nifedipine  
Nisoldipine.<sup>27</sup>

## 2. REVIEW OF LITERATURE

- ❖ In The Year 2017, Aslam Mand His Colleagues Performed A Comparative Study On Efficacy And Tolerability Of Antihypertensive Drugs In Diabetic And Non Diabetic Patients. The Study Was Conducted On 200 Hypertensive Patients With Diabetes And 230 Hypertensive Patients Without (Three Hospitals) Diabetes. The Study Was Conducted For 4 Months. After 4 Months; Patients Were Assessed For Efficacy By Monitoring Blood Pressure (BP) And Tolerability By Assessing Safety Profile On Renal Function, Liver Function As Well As Lipid Profile. Adverse Effects Observed Were Dry Cough, Pedal Edema, Dizziness, Muscular Cramps, Constipation, Palpitations, Sweating, Vertigo, Tinnitus, Paresthesia, And Sexual Dysfunction. All Classes Of Antihypertensives Were Found To Control Blood Pressure Significantly In Both Groups Of Patients That Is Diabetic Patients With Hypertension And Non-Diabetic Patients With Hypertension.<sup>28</sup>
- ❖ **Christina Sommerauer et al., (2017)** carried out a systemic review on thiazides in the management of hypertension in older adults. To identify the evidence on the risks and benefits of use of thiazides among adults aged  $\geq 65$  years and to develop recommendations to reduce potentially inappropriate use was the objective of this study. The study suggested three recommendations that in preventing cardiovascular events for the population thiazides were efficacious, low-dose regimens of thiazides may be safer than high dose and a history of gout may increase the risk of adverse events. The study concluded that in adults aged  $\geq 65$  the use of low dose treatment with thiazides for the management of hypertension seems justified, unless a history of gout is present. Characteristics of the participants such as polypharmacy and frailty were rarely described.<sup>29</sup>
- ❖ **Hedong Han et al., (2017)** carried out a systematic review and meta-analysis of prospective cohort studies on dose-response relationship

between dietary magnesium intake, serum magnesium concentration and risk of hypertension. This study found an inverse association between dietary magnesium intake and the risk of hypertension comparing the highest intake group with the lowest. A 100 mg/day increment in magnesium intake was associated with a 5% reduction in the risk of hypertension. The association of serum magnesium concentration with the risk of hypertension was marginally significant. The study concluded that the inverse dose-response relationship between dietary magnesium intake and the risk of hypertension was supported by the current evidence.<sup>30</sup>

- ❖ **Chao Ji et al., (2018)** estimated handgrip strength is positively related to blood pressure and hypertension risk: results from the National Health and nutrition examination survey. In this study Pearson correlation test and multivariable linear regression was used to analyze relationship of systolic blood pressure and diastolic blood pressure, and binary logistic regression was used to analyze the association between handgrip strength and prevalence of hypertension. This study concluded that with higher risk of hypertension strong handgrip strength may be associated especially in overweight and obese men.<sup>31</sup>
- ❖ **Peter L. Evans et al., (2018)** carried out a systemic review and meta-analysis of cohort studies on obesity, hypertension and diuretic use as risk factors for incident gout. The study aimed to assess the risk of incident gout associated with obesity, hypertension or diuretic use and with incident gout as their outcome. The study found that in individuals with body mass index  $\geq 30$  kg/m<sup>2</sup> gout was 2.24 times more likely to occur. Hypertensive individuals were 1.64 and 2.11 times more likely to develop gout as normotensive individuals. Almost 2.5 times the risk of developing gout was associated with diuretic use compared to no diuretic use. So from this study a conclusion was made that for incident gout obesity, hypertension and use of diuretics are risk factors.<sup>32</sup>



- ❖ **Kehui Huang et al., (2016)** reviewed about health system strengthening and hypertension management in China. 11 articles were left according to the inclusion and exclusion criteria among 572 publications identified. Period of study ranged from 2010 to 2015 in which all about 11 researches linked health system factors to the outcome of hypertension management. In this study outcomes were just focused on the awareness, treatment and control of hypertension but not hypertension incidence. This review concluded that in China hypertension prevalence has been rising rapidly and the management of hypertension in China is a detection problem rather than treatment problem.<sup>33</sup>
- ❖ **Lina Su et al., (2018)** carried out a review on the prevalence, risk factors and disease management of hypertension among floating population in China during 1990–2016. The study objective was to have a basic and comprehensive understanding among floating population in China about the prevalence, risk factors and disease management situation of hypertension. The study found that in floating population prevalence of hypertension, is lower than that of both general population and local residents, it is higher in males than in females and it also increases with age. From this study the conclusion was that their unhealthy lifestyle (drinking) and deficient disease management was the major problem of the floating population.<sup>34</sup>
- ❖ **Manjula Sudeep Sarkar et al., (2018)** reviewed pulmonary hypertension and cardiac anesthesia through an anesthesiologist's perspective. During cardiac surgery perioperative management of pulmonary hypertension is one of the most challenging scenarios associated with high morbidity and mortality due to right ventricular failure, arrhythmias, myocardial ischemia, and intractable hypoxia. The study concluded that perioperative management has become more effective due to deeper understanding of the disease and newer therapeutic interventions.<sup>35</sup>
- ❖ **Sarah-Jo Sinnott et al., (2017)** studied a population based cohort study in UK 1995-2015 on trends for prevalence and incidence of resistant

hypertension. 1 317 290 users of antihypertensive drugs with a diagnosis of hypertension participated in this study. The study showed that throughout the study period, those aged 80 or more years were more likely to have prevalent resistant hypertension compared with patients aged 65-69 years. The study concluded that consistent with a decrease in incidence from 2004 onwards, prevalent resistant hypertension has plateaued and decreased in recent years. It was also concluded that resistant hypertension is common in UK hypertensive population and hypertension is a modifiable risk factor for cardiovascular disease, reducing uncontrolled hypertension should remain a population health focus.<sup>36</sup>

❖ **Wiysonge CS et al., (2017)** reviewed beta-blockers for hypertension. In adults with hypertension assessing the effects of beta-blockers and mortality endpoints was the objective of the study. A randomized controlled trial was carried out for atleast one year duration of time. From the study it was found that there was no difference in all-cause mortality between beta-blockers and placebo, diuretics or RAS inhibitors, but it was higher for beta-blockers compared to CCBs and Total CVD was lower for beta-blockers compared to placebo since there was no difference in coronary heart disease. The study concluded that there was high risk of bias for most outcome RCTs on beta-blockers as initial therapy for hypertension. Beta-blocker most used was atenolol. The study also concluded that initiating treatment of hypertension with beta-blockers leads to modest CVD reductions and little or no effects on mortality from current evidences.<sup>37</sup>

❖ **Jens Jordan et al., (2018)** reviewed about arterial hypertension diagnosis and treatment. Based on pertinent publications retrieved by a selective literature search in PubMed he reviewed the study. The study resulted that long-acting dihydropyridine calcium channel blockers, angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers, and thiazide-like diuretics are the first-line drugs for arterial hypertension. The study thus concluded that through a combination of lifestyle interventions

and first-line antihypertensive drugs the blood pressure can be well controlled and the cardiovascular risk reduced In most patients with essential hypertension.<sup>38</sup>

- ❖ **Vishnu K. Gupta et al., (2018)** carried out a study on an epidemiological study of prevalence of hypertension and its risk factors among non migratory tribal population of Mawai block of Mandla district of central India. The study was a cross sectional study among adults aged 20-65 years who were non migratory residents of Mawai block of Mandla districts, and they were selected through multi stage random sampling method. The study resulted that among study population hypertension prevalence was 27.1% and 82.2% study subjects had never undergone for blood pressure check-up. Prevalence was associated with high age group, study subjects taking mixed diet and study subjects with smoking and alcohol intake. The study concluded that every fourth study individual is Hypertensive, where smoking (in any form) and obesity was found as commonest risk factor for it.<sup>39</sup>
- ❖ **Louise M. Webster et al., (2017)** carried out a systemic review and meta-analysis on impact of antihypertensive treatment on maternal and perinatal outcomes in pregnancy complicated by chronic hypertension. With antihypertensive treatment a clinically important reduction in the incidence of severe hypertension was seen compared to no antihypertensive treatment/placebo The study concluded that in pregnant women with chronic hypertension antihypertensive treatment reduces the risk of severe hypertension.<sup>40</sup>
- ❖ **Sushil K. Bansal et al., ()** studied a prospective door-to-door study on prevalence of hypertension and hypertension risk factors in a rural Indian community. Data relating to the demographics of the individuals, dietary habits, alcohol consumption, tobacco use, psychosocial stress, past medical history and drug history were interviewed and collected. Blood pressure (BP) and anthropometric data was recorded and blood samples taken. Rates of hypertension in the rural community under study are

similar to those seen in high-income countries and in urban India. With the exception of age, all the risk factors identified were potentially modifiable were the conclusions made from the study.<sup>41</sup>

❖ **Rabia Naseem et al., (2017)** studied prevalence and characteristics of resistant hypertensive patients in an Asian population. To evaluate the prevalence and determinants of resistant hypertension in an Asian cohort of hypertensive patients was the objective of the study. The study method was cross-sectional study. Using a pre-coded questionnaire patient data and characteristics were recorded. A total of 515 patients were included in the study in which overall, 12% of the total patients were resistant hypertensive and 25% had pseudo-resistant hypertension. Resistant patients were more often females, older and had a higher body mass index. The study concluded that nearly one in ten hypertensive patients had true resistant hypertension, and twenty-five percent of patients had pseudo-resistance. Resistance hypertension is significantly associated with female gender, older age, obesity, dietary noncompliance and increased use of NSAIDs.<sup>42</sup>

❖ **Marta Walczak-Gale et al., (2018)** studied the effect of nebivolol and ramipril on selected biochemical parameters, arterial stiffness, and circadian profile of blood pressure in young men with primary hypertension. The study aimed to evaluate the effect of nebivolol and ramipril on biochemical parameters, arterial stiffness, and circadian profile of blood pressure (BP) in young men undergoing treatment for hypertension (HT). The study conducted was the prospective randomized, open label trial. 80 patients aged 16 to 28 years of age with grade 1 HT were enrolled in the study. Arterial stiffness index (SI), the circadian profile of BP registered in ambulatory blood pressure monitoring (ABPM), and biochemical parameters—including lipid profile, insulinemia, glycemia, and high sensitivity C-reactive protein (hsCRP) levels—were evaluated before and after the twelve-week period. The study concluded that ramipril seems to possess better clinical potential in

reducing cardiovascular risk in young men with HT despite the similar hypotensive effect of nebivolol and ramipril.<sup>43</sup>

- ❖ **David A. Calhoun et al., (2014)** determined prevalence, risk factors and co-morbidities of refractory hypertension. In this study population-based cohort were evaluated to determine the prevalence of refractory hypertension and associated cardiovascular risk factors and co-morbidities. According to this study the prevalence of refractory hypertension was 3.6% among participants with resistant hypertension and 41.7% among participants on 5 or more antihypertensive drug classes. African American race, male gender, living in the stroke belt or buckle, higher body mass index, lower heart rate, reduced estimated glomerular filtration rate, albuminuria, diabetes and history of stroke and coronary heart disease were associated with refractory hypertension among all hypertensive participants. The study concluded that compared to resistant hypertension, prevalence ratios for refractory hypertension were increased for African Americans and those with albuminuria and diabetes.<sup>44</sup>
- ❖ **Katherine T. Mills et al., (2016)** carried out a systematic analysis of population-based studies from 90 countries on global disparities of hypertension prevalence and control. Global disparities of hypertension prevalence, awareness, treatment, and control in 2010 were examined and secular changes from 2000 to 2010 were compared. 135 population-based studies of 968,419 adults from 90 countries were included in the study. To calculate regional and global numbers of hypertensive adults sex-age-specific hypertension prevalence from each country were applied to population data. The study concluded that global hypertension disparities were large and increasing. To combat the emerging hypertension burden in low- and middle-income countries collaborative efforts were urgently needed.<sup>45</sup>
- ❖ **Dan Qi et al., (2017)** carried out a study to determine the link between vitamin D concentrations and incident hypertension in prospective study and meta-analysis. 2,456 men and women free of prevalent hypertension,

age 21 to 67 at baseline were studied. Using ELISA Serum 25-hydroxyvitamin D was measured from previously frozen baseline samples. The study concluded that lower serum 25-hydroxyvitamin D concentrations were not associated with a greater risk of incident hypertension.<sup>46</sup>

- ❖ **Isabel C Pinto et al., (2017)** carried out a literature review which aimed to assess the prevalence of arterial hypertension and its risk factors. 14 articles and 3 websites/reports were identified that corresponded to inclusion criteria of the study. It was found that arterial hypertension was more prevalent in female gender, with the highest incidence in adults and the elderly, African-native peoples and lower education. It was also found that is positively associated to other diseases and genetic and environmental factors, such as: obesity, high sodium ingestion, sedentary lifestyle, stress, alcohol consumption and smoking. The study concluded that development of several studies is important to contribute to the public health policies and actions, by providing indications to combat the increasing prevalence of Arterial Hypertension and risk factors, in order to better control this disease.<sup>47</sup>
- ❖ **Hyungseon et al., (2018)** evaluated the prospective association between the TG/HDL-C ratio in adolescents and hypertension in early adulthood. 272 participants who completed health examinations at the age of 16 and 35 years were followed and 27 participants with adolescent hypertension were excluded, finally 245 participants were analysed. To evaluate the association between adolescent TG/HDL-C logistic regression analysis was performed. The study result showed that during 20-year follow-up, 18.3% developed hypertension in the high TG/HDL-C ratio group and 5.4% developed hypertension in the low TG/HDL-C ratio group. The adjusted odds ratio for incident hypertension in the high TG/HDL-C ratio group, compared with the low TG/HDL-C ratio group, was 3.40. The study concluded that high TG/HDL-C ratio in adolescence is associated with hypertension in early adulthood.<sup>48</sup>

- ❖ **Rebecca et al., (2018)** carried out a study on national patterns of physician management of sleep apnea and treatment among patients with hypertension. Data from the National Ambulatory Medical Care Survey/National Hospital Ambulatory Medical Care Survey (NAMCS/NHAMCS), 2005±2012, were analyzed for this study. Multivariate logistic regression was used to examine treatment by demographic/clinical factors. The study result showed that among patients with hypertension, sleep apnea was identified in 11.2-per-1,000 visits. Overall, patients with hypertension and a sleep disorder were referred for sleep study in 14.4% of visits, prescribed sleep medication in 11.2% of visits, and offered behavioral therapy in 34.8% of visits. Adjusted analyses show behavioral therapy more likely to be provided to obese patients than normal/overweight, but less likely to be provided to smokers than nonsmokers. Non-Hispanic blacks were less likely to receive medications than non-Hispanic whites. The study concluded that in U.S., sleep apnea was observed in a small proportion of hypertension visits. Behavioral therapy was underutilized, and non-Hispanic Blacks were less likely to receive medications than non-Hispanic Whites.<sup>49</sup>
- ❖ **Tomasz et al., (2018)** aimed to evaluate clinical and biochemical differences between patients with low renin and high-renin primary arterial hypertension (AH), mainly in reference to serum lipids, and to identify factors determining lipid concentrations. In untreated patients with AH stage 1, plasma renin activity (PRA) was measured and the group was subdivided into low-renin (PRA < 0.65 ng/mL/h) and high-renin (PRA ≥ 0.65 ng/mL/h) AH. Office and 24-h ambulatory blood pressure, serum aldosterone, lipids and selected biochemical parameters between subgroups were compared. In regression analysis factors determining lipid concentration in both subgroups were assessed. The study result showed that patients with high-renin hypertension were characterized by higher heart rate, lower serum sodium and aldosterone-to-renin ratio, and significantly higher serum aldosterone, albumin, total protein, total

cholesterol and low-density lipoprotein cholesterol (LDL-C) than low-renin subjects. In univariate linear regression, only PRA in the low-renin group was in a positive relationship with LDL-C; this association remained significant after adjustment for age, sex, and serum albumin and aldosterone concentrations. The study concluded that higher serum levels of total and LDL-C characterized high-renin subjects, but the association between LDL-C level and PRA existed only in low-renin primary AH.<sup>50</sup>

- ❖ **Suo et al., (2018)** examined whether the use of a renin-angiotensin-aldosterone system (RAS) inhibitor plays a role in protecting against left atrial appendage thrombus (LAAT) in patients with hypertension complicated by atrial fibrillation (AF). In this study two observational studies were conducted on patients with diagnoses of hypertension and AF, who were categorized into RAS inhibitor user or nonuser groups and demographic characteristics, clinical characteristics, echocardiographic parameters and hemostatic markers were examined and the occurrence of LAAT during follow-up were recorded. The study result showed that in the first study, LA peak systolic strain and LAA emptying flow velocity (LAA eV) were significantly increased in patients on RAS inhibitors compared with the nonuser group. Lower D-dimer and fibrinogen levels were observed in patients on RAS inhibitors. In the second study, 25.9% of patients on RAS inhibitors developed LAAT, compared with 46.7% in the nonuser group. After controlling for risk factors related to LAAT, use of RAS inhibitors remained associated with a significantly lower risk of developing LAAT. The study concluded that RAS inhibitors use was associated with a significant reduction in the risk of LAAT in patients with hypertension and AF.<sup>51</sup>
- ❖ **Lee et al., (2019)** carried out a study on retinal micro-vascular change in hypertension as measured by optical coherence tomography angiography. The study compared OCTA parameters between chronic hypertension, relieved hypertensive retinopathy, and normal controls. A 3 × 3 mm macular scan was performed in each group by OCTA. The study result



showed that in vessel density of 3 mm full, group A and B were significantly decreased compared to normal control group. In foveal avascular zone, group A and B were significantly increased compared to normal control group. The study concluded that OCTA is useful for examining retinal microcirculatory changes in hypertension and it was confirmed that hypertension affects the OCTA parameters.<sup>52</sup>

- ❖ **Tseng et al., (2018)** carried out a study on metformin and risk of hypertension in Taiwanese patients with type 2 diabetes mellitus. From the reimbursement database of the Taiwan's National Health Insurance newly diagnosed patients with type 2 diabetes mellitus during 1999–2005 were enrolled and followed to December 31, 2011. Analyses were conducted in a propensity score matched-pair cohort of 4810 ever users and 4810 never users. Cox proportional hazards regression model was used to estimate the hazard ratios. Results showed that 2261 never users and 1908 ever users developed hypertension. The overall hazard ratio was 0.724 and the hazard ratios for the first, second and third months tertiles of cumulative duration were 0.820, 0.692, and 0.687, respectively. When cumulative duration of metformin therapy was treated as a continuous variable, the hazard ratio was 0.991 for every 1-month increment of metformin use. When hypertension was defined by a diagnosis plus the use of antihypertensive drugs, the overall hazard ratio was 0.831, the hazard ratios for the respective tertiles were 0.868, 0.852, and 0.787, and the hazard ratio was 0.994 for every 1-month increment of metformin use. The study concluded that a reduced risk of hypertension was observed in metformin users in a dose-response pattern.<sup>53</sup>
- ❖ **Alex et al., (2016)** evaluated the association between baseline antihypertensive medications that may affect potassium levels and hyperkalemia, defined by potassium, over a 3-year time period in 194,456 outpatients in the Geisinger Health System, as well as actions taken after an episode of hyperkalemia. The study result showed that proportions of patients with 0, <2, 2–4, and  $\geq 4$  potassium measurements per year were

20%, 58%, 16%, and 6%. Potassium levels  $>5$  mEq/L and  $>5.5$  mEq/L occurred in 10.8% and 2.3% of all patients over the 3-year period; among patients with  $\geq 4$  measurements per year, corresponding values were 39.4% and 14.6%. It was found that antihypertensive medication class most strongly associated with hyperkalemia was ACEIs. Among patients with a measurement of potassium  $>5.5$  mEq/L, only 24% were seen by a nephrologist and 5.2% were seen by a dietician during the 3-year period. The most common medication changes were discontinuation/dose reduction of an ACEI/ARB or potassium-sparing diuretic, which occurred in 29.1% and 49.6% of persons taking these medications, respectively. The study concluded that hyperkalemia was common and future research may enable optimal RAAS inhibitor use with improved management of hyperkalemia.<sup>54</sup>

- ❖ **Kyvelou et al., (2006)** carried out a study to evaluate blood pressure control and the plasma lipid profile in hypertensive patients after six months' treatment with ARB. In the study 2438 consecutive, untreated patients with uncomplicated essential hypertension were studied. All patients underwent full lab and echo examination at drug-free baseline, which was repeated after at least 6 months of ARB monotherapy. The study result showed that overall, ARB treatment reduced BP levels significantly. Evaluating lipid profile changes, a significant reduction was noted in total cholesterol, low density lipoprotein cholesterol, ratio of TC to high density lipoprotein cholesterol (HDL), apolipoprotein (Apo) B, and triglyceride levels, while ApoA1 and lipoprotein(a) levels were not significantly affected. Additionally, HDL levels increased from  $48.2 \pm 12.2$  to  $48.8 \pm 11.9$  mg/dL,  $p < 0.0001$ . According to the individual agent used, a different effect on lipid indices was observed. The study concluded that ARB antihypertensive therapy may have a uniquely beneficial metabolic effect in addition to blood pressure lowering.<sup>55</sup>

### **3. AIM AND OBJECTIVES**

#### **2.1 Aim**

The aim of the study was to An investigation on prevalence of abnormalities in hypertensive patients in laboratory parameters under various classes of antihypertensive drugs.

#### **2.2 Objectives**

The objectives of the study were

- To assess the prevalence of cardiac events in patients with under various classes of anti hypertensive drugs.
- To assess the investigation on abnormalities of lab parameters in patients with under various classes of anti hypertensive drugs.

## **4.PLAN OF WORK**

The proposed study entitled “An investigation on prevalence of abnormalities in hypertensive patients in laboratory parameters under various classes of antihypertensive drugs.” was planned and carried out in a tertiary care hospital as given below.

### **Phase I**

- Identification of research problem and scope of the study
- Literature survey
- Preparation of study protocol
- Obtaining ethical clearance from the hospital authorities

### **Phase II**

- Design of structured pro-forma
- Patient selection
- Obtaining patient consent
- Data retrieval from the cardiology and general medicine department.

### **Phase III**

- Data analysis
- Report submission

## **5.METHODOLOGY**

### **5.1 STUDY DESIGN**

Prospective observational study

### **5.2 STUDY CENTRE**

Department of General medicine and cardiology in Vivekananda Medical Care Hospital, Tiruchengodu.

### **5.3 STUDY DURATION**

DEC 2018 – APRIL 2019 (6months)

### **5.4 ETHICAL COMMITTEE APPROVAL**

The study protocol was approved by the institutional ethics committee of Vivekanandha Medical Care Hospital (Ref.No:VMCH/IEC/DEC/2018/01) (Annexure – 1)

### **5.5 SAMPLE POPULATION**

Total 230 patients who are having hypertension and under ARB inhibitor therapy were screened and 112 records were selected based on the following inclusion and exclusion criteria for further study.

### **5.6 INCLUSION CRITERIA**

- Patients with hypertensive disease
- Patients under any classes of anti hypertensive drug
- Patients with co morbidities like cardiac disease.
- Patients under age of 40-80.
- Both male and female patients are included.

### **5.7 EXCLUSION CRITERIA**

- Patients with renal disorder.

- patients with hepatic disorder.
- Patient under psychiatric medication.
- Pregnancy and lactation.

## **5.8 DATA COLLECTION**

Consent was obtained from each subject in Patient Consent form before initiating the study. Structured pro-forma was used to collect various clinical and demographic details of the patients such as age, gender, reason for admission, past medical history, past medication history, vital signs, lab investigations, primary diagnosis and treatment chart. Treatment data including prescribed drugs, doses, frequency and route of administration were also recorded.

## **5.9 METHOD**

Patients were assessed at baseline with respect to age, gender, BMI, co-morbidity conditions, ARB inhibitors prescribed and duration of therapy. Patient was followed up for 3 months. The Prevalence of cardiac events were identified and investigation on abnormalities of lab parameters were analyzed.

## **5.10 STATISTICS**

The statistical analysis was done using Microsoft excel. All the datas were expressed in percentage. Collected data's were entered in Microsoft excel spreadsheet for further interpretations.

## 6. RESULTS

A total of 230 patients who are having hypertension and taking ARB inhibitors in cardiology and general medicine department were screened and 112 records were selected based on the inclusion and exclusion criteria.

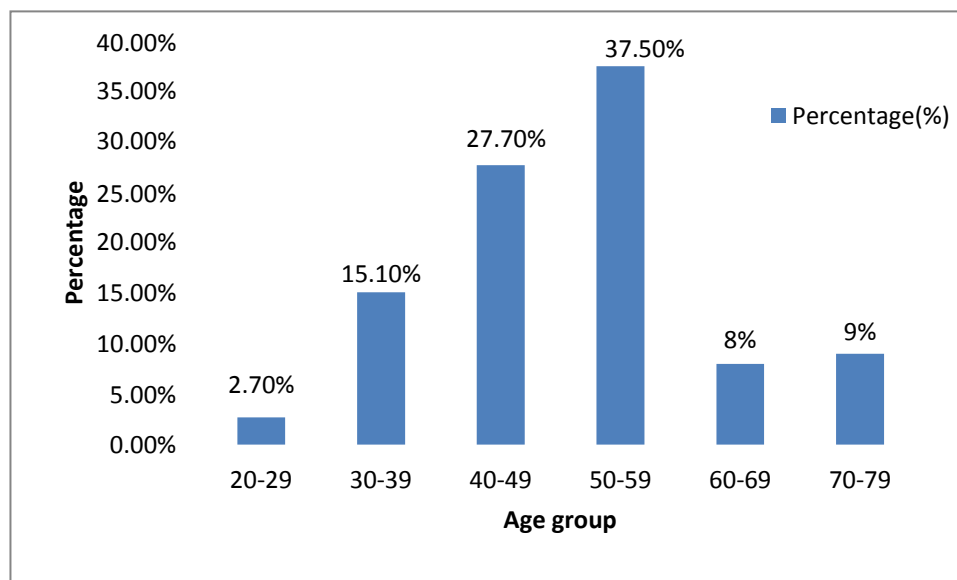
### 6.1. AGE WISE DISTRIBUTION OF THE STUDY POPULATION

Out of 112 cases, 2.7% (3) were in the age group of 20-29 years, 15.1% (17) were in the age group of 30-39 years, 27.7% (31) were in the age group of 40-49 years, 37.5% (42) were in the age group of 50-59 years, 8% (9) were in the age group of 60-69 years and 9% (10) were in the age group of 70-79 years. Mean age of the study population was  $55.7 \pm 6$  years. (Table 1, Figure 1)

**Table 1. Age wise distribution of the study population (n=112)**

S.No.	Age (years)	No of Patients	Percentage(%)
1.	20-29	3	2.7 %
2.	30-39	17	15.1%
3.	40-49	31	27.7%
4.	50-59	42	37.5%
5.	60-69	9	8%
6.	70-79	10	9%

**Figure 1. Age Wise distribution of the study population (n=112)**



## **6.2 GENDER WISE DISTRIBUTION AMONG THE STUDY POPULATION**

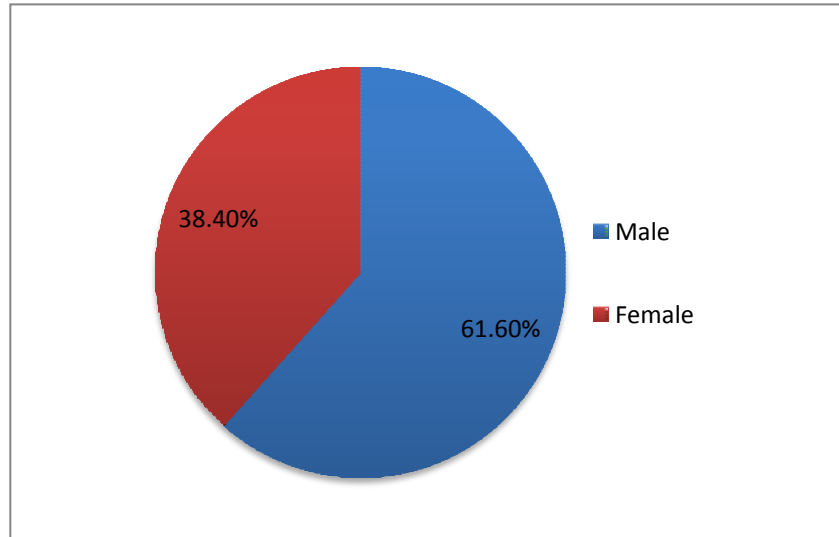
A total of 112 hypertensive patients, males were 61.6% (69) and females were 38.39% (43). (Table 2, Figure 2)

**Table 2. Gender wise distribution of the study population (n=112)**

<b>Gender</b>	<b>Number of Patients</b>	<b>Percentage</b>
Male	69	61.6 %
Female	43	38.4 %



**Figure 2. Gender wise distribution among the study population (n=112)**



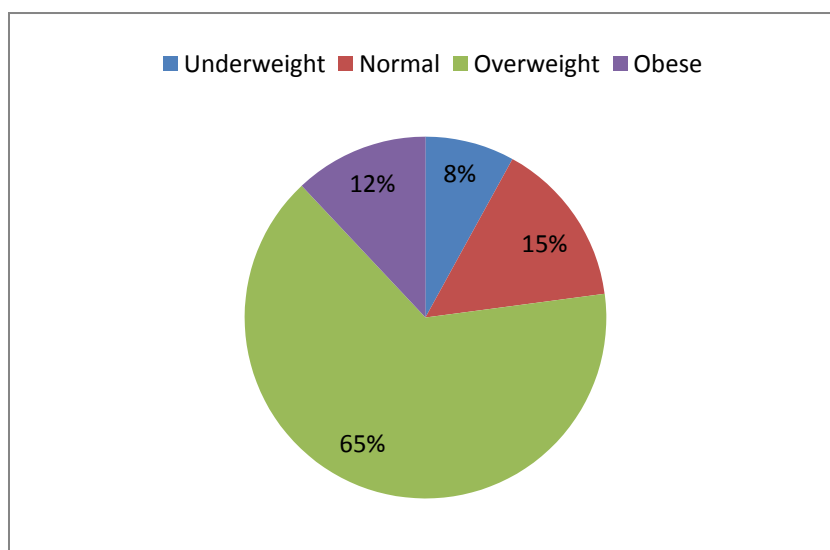
### **6.3 BODY MASS INDEX OF THE STUDY POPULATION**

A total of 112 patients, 8% (9) were in normal body weight, 14.9% (16) were Under Weight, 65.1% (74) were overweight and 12% (13) were Obese. (Table 3, Figure 3)

**Table 3. BMI among the study population (n=112)**

<b>BMI</b>	<b>Number of Patients</b>	<b>Percentage</b>
Underweight	9	8%
Normal	16	14.9%
Overweight	74	65.1%
Obese	13	12%

**Figure 3. BMI among the study population(n=112)**



#### **6.4 SOCIAL HABITS OF THE STUDY POPULATION**

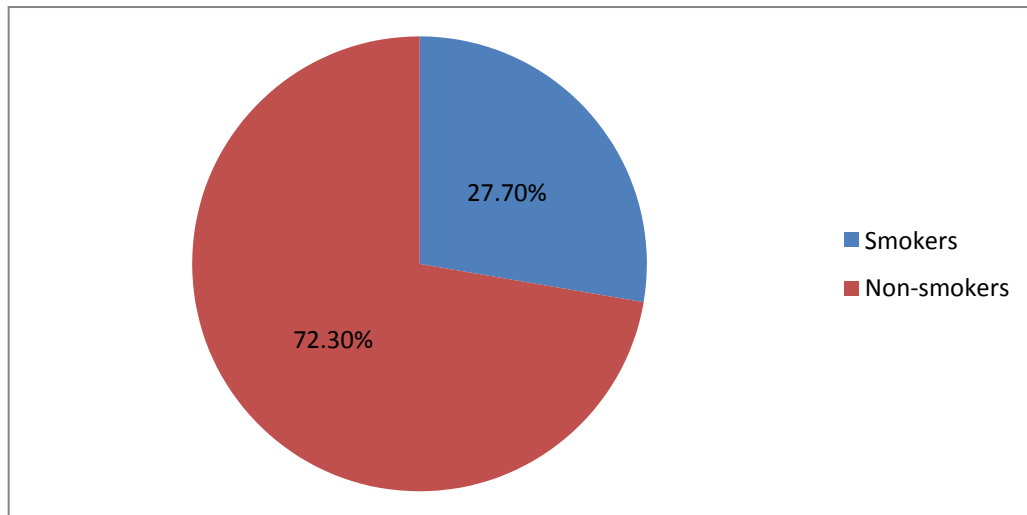
Out of 112 patients, 27.7% (31) were smokers and 72.3% (81) were non smokers.

(Table 4, Figure 4)

**Table 4. History of smoking among the study population (n=112)**

<b>Smoking habits</b>	<b>Number of Patients</b>	<b>Percentage</b>
Smokers	31	27.7%
Non-smokers	81	72.3%

**Figure 4. History of smoking among the study population (n=112)**

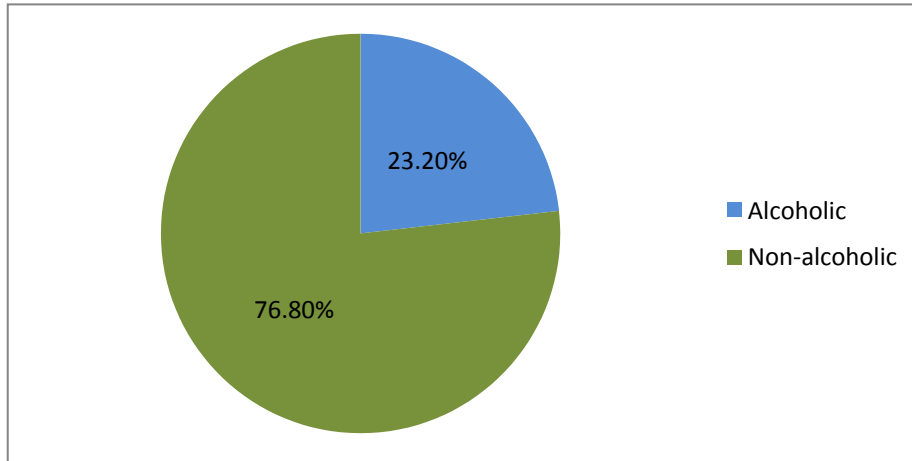


Out of 112 patients, 23.2% (26) were alcoholic and 76.8% (86) were non alcoholic, (Table 5, Figure 5)

**Table 5. History of alcoholism among the study population (n=112)**

<b>Alcoholic habits</b>	<b>Number of Patients</b>	<b>Percentage</b>
Alcoholic	26	23.2%
Non-alcoholic	86	76.8%

**Figure 5. History of alcoholism among the study population (n=112)**



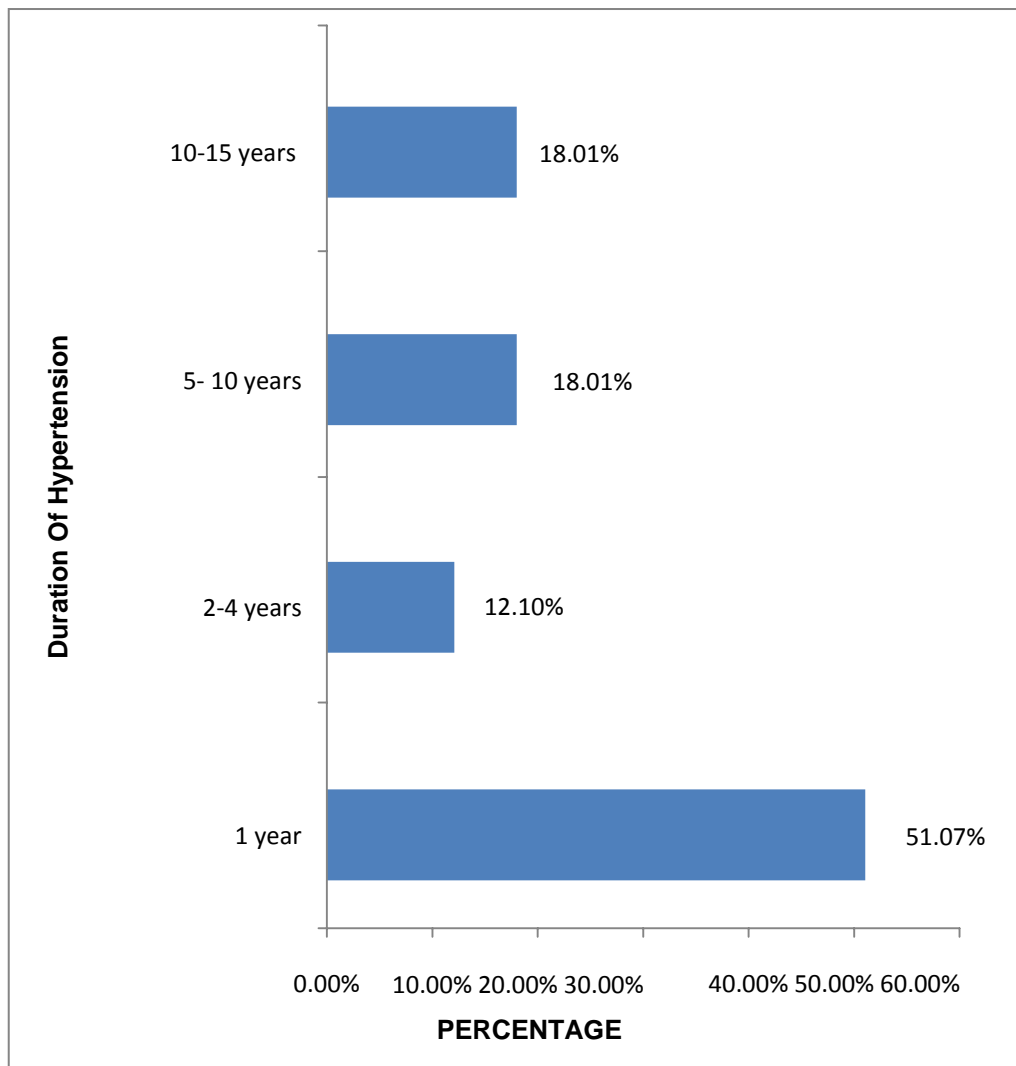
#### **6.6 DURATION OF HYPERTENSION AMONG THE STUDY POPULATION**

A total of 112 patients, 51.07% (59) were having 1 year duration of Hypertension, 12.1% (13 ) were having 2-4 years duration of Hypertension, 18.01% (20) were having 5-10 years duration of hypertension, 18.01% (20) were having 10-15 years duration of Hypertension (Table 6,figure 6)

**Table 6. Duration of hypertension among the study population (n=112)**

<b>Duration of Hypertension</b>	<b>Number of Patients</b>	<b>Percentage</b>
1 year	59	51.07%
2-4 years	13	12.1%
5- 10 years	20	18.01%
10-15 years	20	18.01%

**Figure 6. Duration of hypertension among the study population (n=112)**



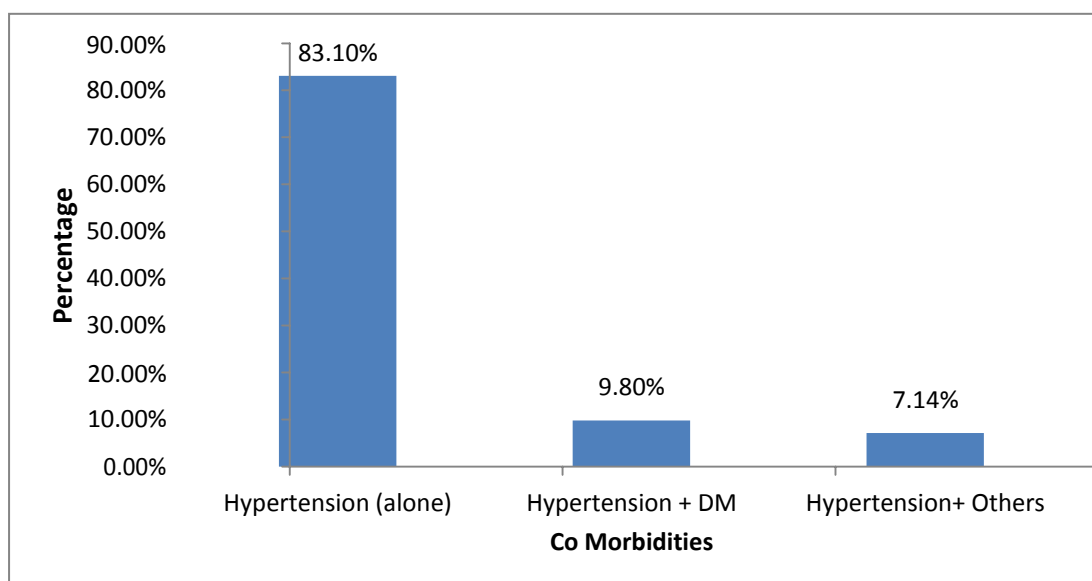
### **6.7 PATTERN OF PREVALENCE OF CO-MORBIDITIES AMONG THE STUDY POPULATION**

A total of 112 patients, 83.1% (93) were having hypertension alone, 9.8% (11) were hypertension with diabetes mellitus, and 7.14% (8) have hypertension with other complications. (Table 7, figure 7)

**Table 7. Pattern of co-morbidities prevalence among the study population (n=112)**

<b>Co-Morbidities</b>	<b>Number of Patients</b>	<b>Percentage</b>
Hypertension (alone)	93	83.1%
Hypertension + DM	11	9.8%
Hypertension+ Others	8	7.14%

**Figure 7. Pattern of co-morbidities prevalence among the study population (n=112)**



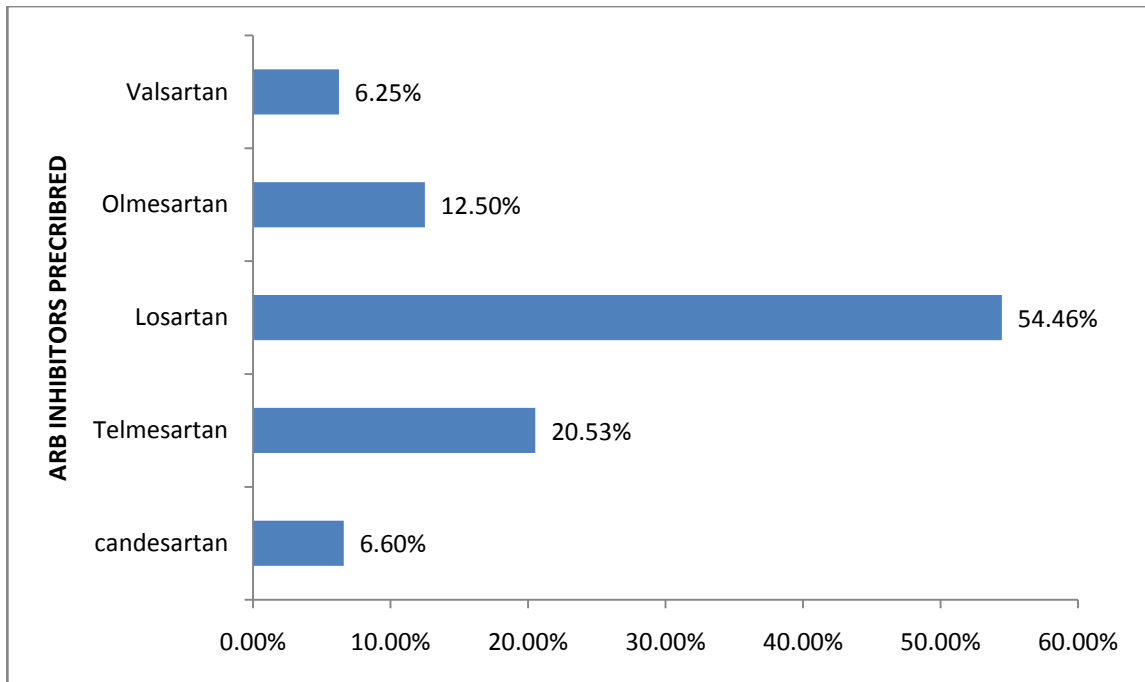
## 6.8 ARB INHIBITORS PRESCRIBED IN THE STUDY POPULATION

A total of 112 patients, 6.6% (7) prescribed with candesartan, 20.53% (23 patients) prescribed with telmesartan, 54.46 % ( 61) prescribed with losartan, 12.5% prescribed with (14) prescribed with olmesartan and 6.25% (7) prescribed with Valsartan. (Table 8, Figure 8)

**Table 8. ARB inhibitors prescribed in the study population (n=112)**

S. No	ARB Inhibitors prescribed	Dose	Frequency	Number of Patients	Percentage
1.	candesartan	4mg	BD	7	6.6%
2.	telmesartan	20mg	OD	23	20.53%
3.	losartan	25mg	BD	61	54.46%
		50mg			
4.	olmesartan	10mg	OD	14	12.5%
5.	Valsartan	40mg	OD	7	6.25%

**Figure no :8 ARB inhibitors prescribed in the study population (n=112)**





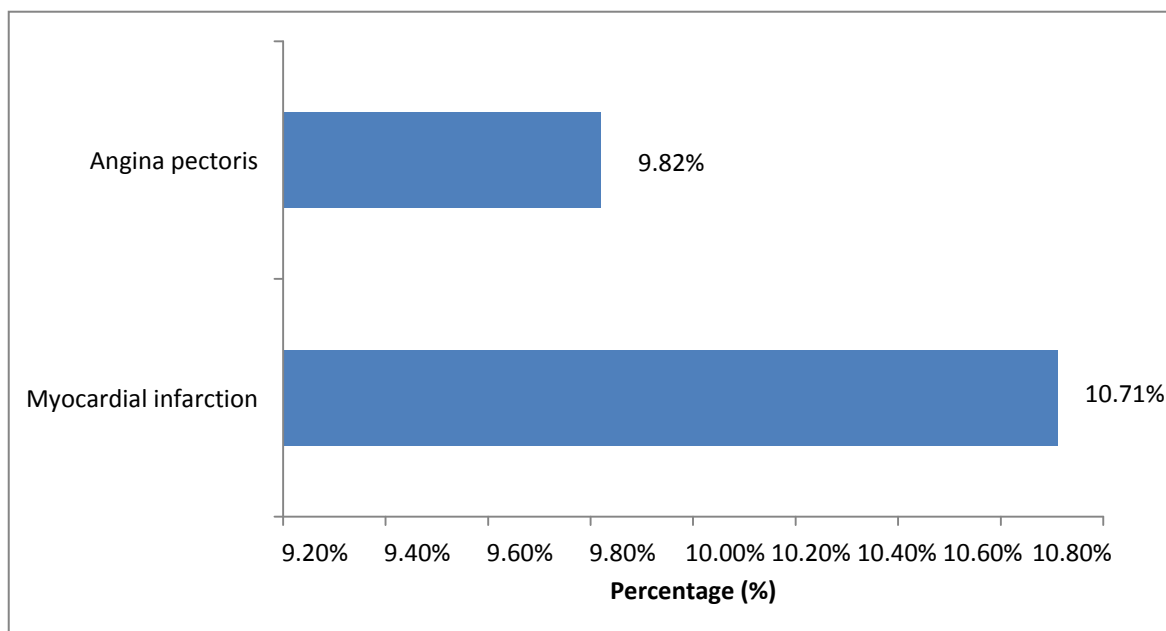
## 6.9 ASSESSMENT OF PREVALANCE OF CARDIAC EVENTS IN THE STUDY POPULATION

Out of 112 patients incidence of cardiac events found in Hypertensive patients who are under ARB inhibitors were 23, in which 10.71% (12) had myocardial infarction and 9.82% (11) had Angina pectoris. (Table 9, Figure 9)

**Table 9. prevalence of cardiac events in the study population (n=112)**

Cardiac events	No. of patients	Percentage (%)
Myocardial infarction	12	10.71%
Angina pectoris	11	9.82%
<b>Total</b>	23	100 %

**Figure 9. prevalence of cardiac events in the study population (n=112)**



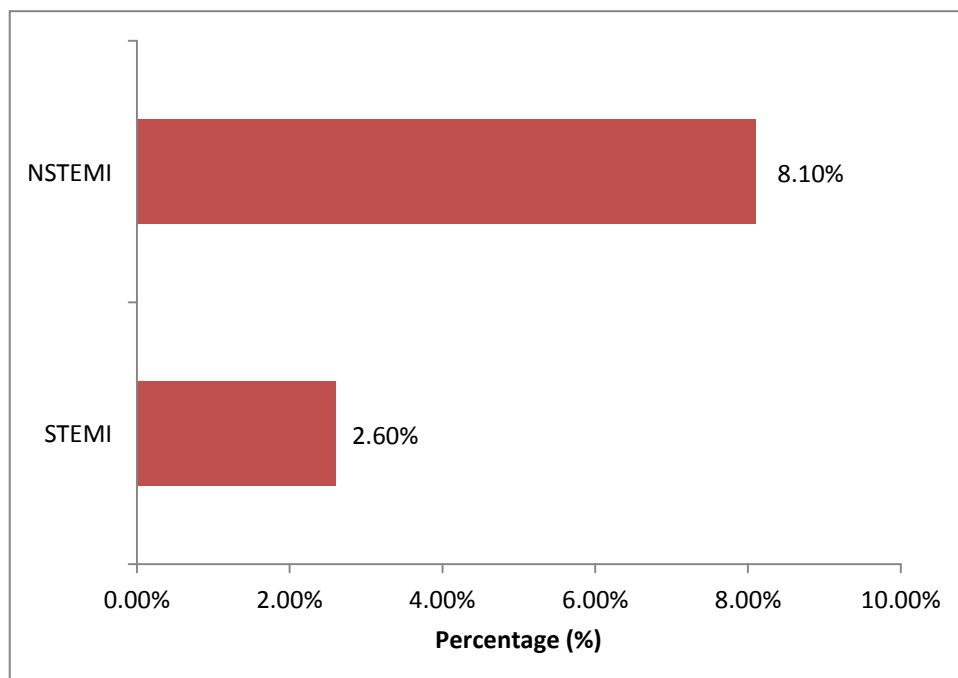
### 6.10 PREVALANCE OF MYOCARDIAL INFARCTION

Among 12 patients with incidence of myocardial infarction 2.6% (3) were having STEMI and 8.1 % (9) were having NSTEMI. (Table 10, Figure 10)

**Table 10. prevalence of myocardial infarction based on type (n=112)**

Myocardial infarction	No. of patients	Percentage (%)
STEMI	3	2.6%
NSTEMI	9	8.1%

**Figure 10. Prevalence of myocardial infarction based on type (n=112)**



## 6.11 PREVALANCE OF MYOCARDIAL INFARCTION IN PATIENTS ON ARB INHIBITORS

Out of 12 patients with incidence of MI with ACE inhibitors 1.8% (2) prescribed with candesartan , 4.4% (5) with telmesartan , 0.9% (1) with losartan, 1.8% (2) with olmesartan and 1.8% (2) prescribed with valsartan.

(Table 11, Figure 11)

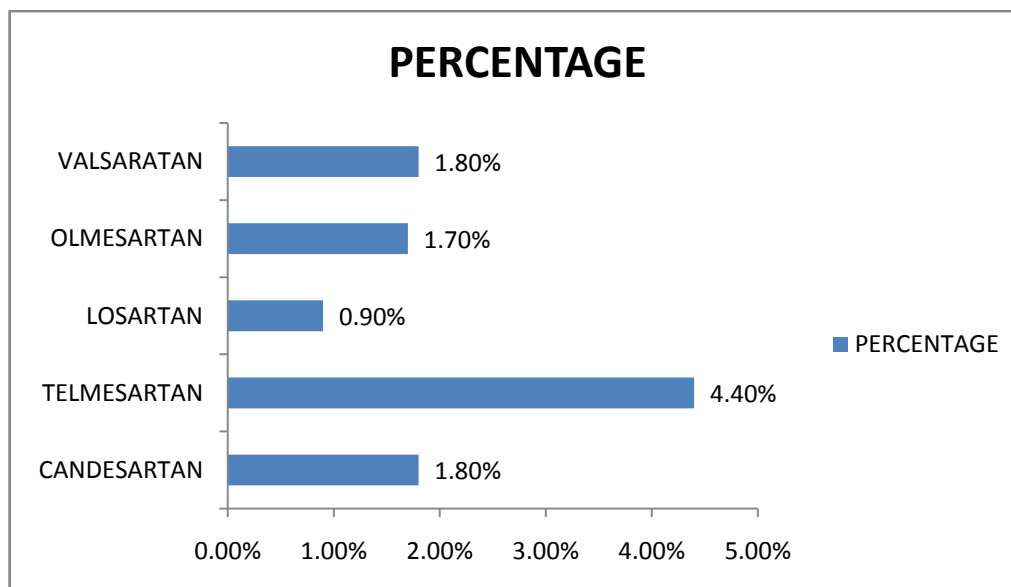
**Table 11. Prevalence of Myocardial Infarction in Patients on ARB Inhibitors**

(n=112)

S. no.	ARB Inhibitors prescribed	Dose	Frequency	Number of Patients	Percentage
1	candesartan	4mg	BD	2	1.8%
2	telmesartan,	20mg	OD	5	4.5%
3	Losartan	25mg	BD	1	0.8%
		50 mg		0	0%
4	olmesartan	10mg	OD	2	1.8%
5	Valsartan	40mg	OD	2	1.8%

**Figure 11. prevalence of Myocardial Infarction in patients on ARB inhibitors**

(n=112)



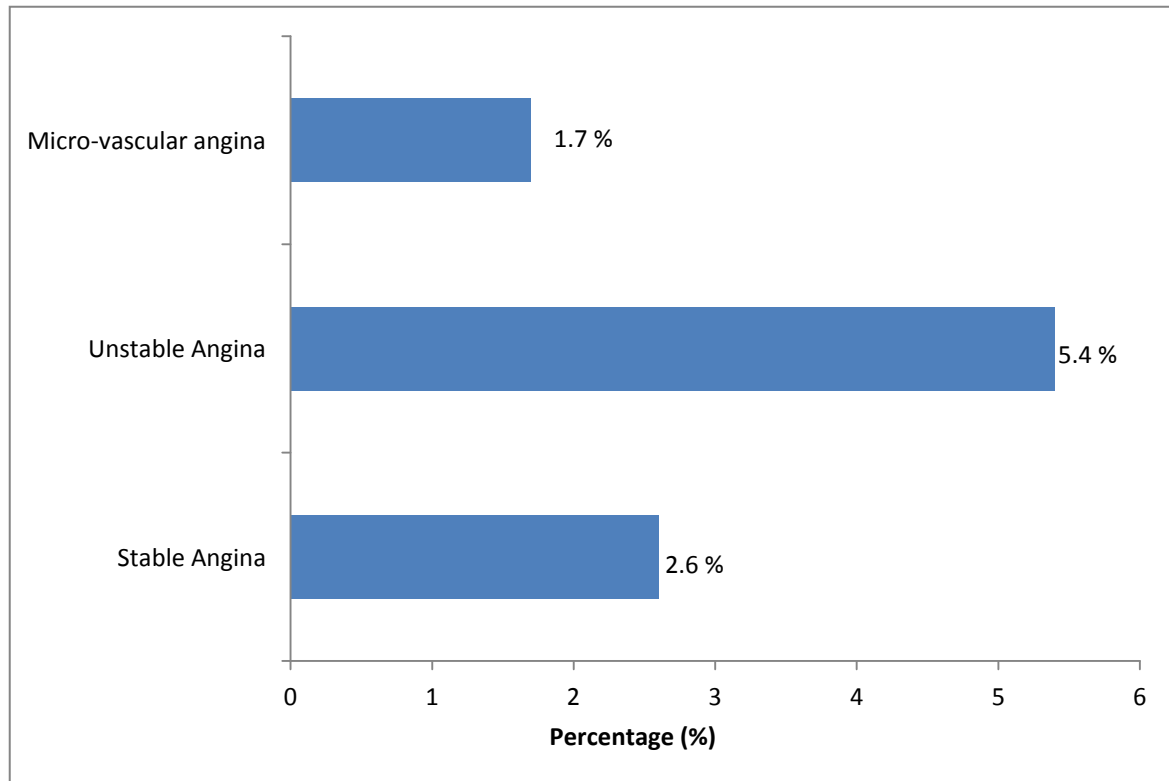
### 6.12 PREVALANCE OF ANGINA PECTORIS BASED ON TYPE

Among 112 patients in the study population 11 patients were having Angina pectoris in which 2.6% (3) are having stable angina, 5.4% (6) were having unstable Angina, 1.7% (2) having micro vascular angina. (Table12, Figure12)

**Table 12. prevalence of Angina Pectoris based on Type (n=112)**

Cardiac events	No. of patients	Percentage (%)
Stable Angina	3	2.6 %
Unstable Angina	6	5.4%
Micro-vascular angina	2	1.7%

**Figure 12. prevalence of Angina pectoris based on Type (n=112)**



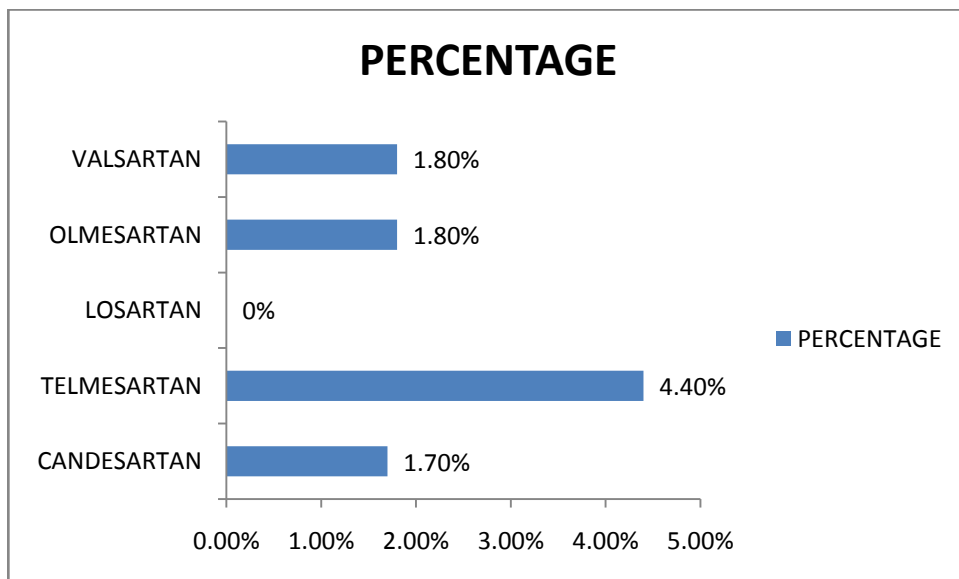
### **6.13 PREVALENCE OF ANGINA PECTORIS IN PATIENTS ON ARB INHIBITORS**

Among 11 patients, Incidence of Angina pectoris on ARB inhibitors 1.7% (2patients) prescribed with candesartan , 4.4% (5) with telmesartan , 0% (0) with losartan , 1.8% (2) with olmesartan and 1.8% (2) with Valsartan . (Table 13, Figure 13)

**Table 13. prevalence of Angina Pectoris in patients on ARB inhibitors (n=112)**

S. No.	ARB Inhibitors prescribed	Dose	Frequency	Number of Patients	Percentage (%)
1.	candesartan	4mg	BD	2	1.7%
2.	telmesartan	20mg	OD	5	4.4%
3.	losartan	25mg	BD	0	0%
		50 mg		0	0%
4.	olmesartan	10mg	OD	2	1.8%
5.	Valsartan	40mg	OD	2	1.8%

**Figure 13. prevalence of angina pectoris in patients on ARB inhibitors (n=112)**



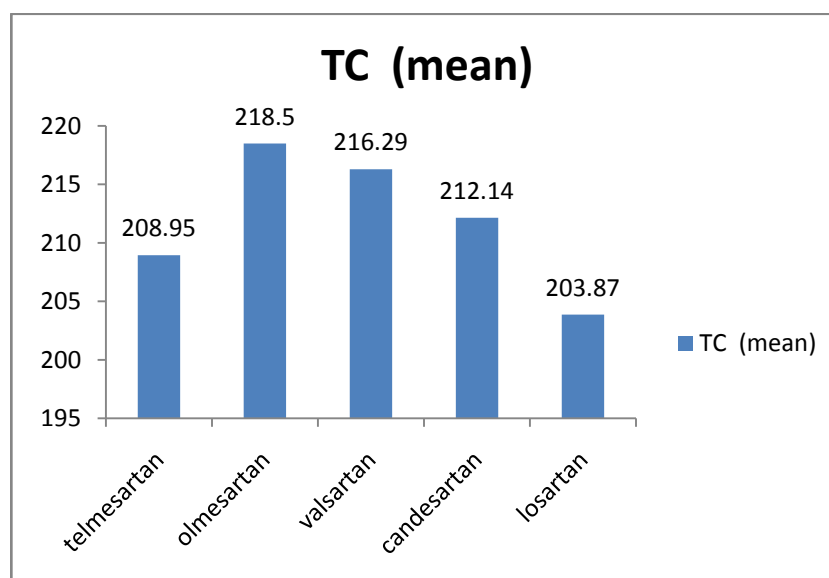
## 6.14 Investigation of lipid profile changes among the study population

**Table no:14 Investigation Of total cholesterol Changes Among The Study Populations n=(112)**

In this study investigation of abnormalities in total cholesterol among the various Drug like telmesartan ( $208.95 \pm 7.12$ ), olmesartan ( $218.3 \pm 8.12$ ), valsartan ( $216.29 \pm 4.47$ ), Candesartan ( $212.14 \pm 8.78$ ) and losartan ( $203.87 \pm 14.78$ ) ( Table:13, Figure :13)

S.No	ARB Drugs	TC Level Mean $\pm$ Sd
1	Telmesartan	$208.95 \pm 7.13$
2	Olmesartan	$218.5 \pm 8.12$
3	Valsartan	$216.29 \pm 4.47$
4	Candesartan	$212.14 \pm 8.78$
5	Losartan	$203.87 \pm 14.78$

**Figure no:14 Investigation Of total cholesterol Changes Among The Study Populations (n=112)**



**Table no: 15 Investigation Of low density lipoprotein Changes Among The Study Populations (n=112)**

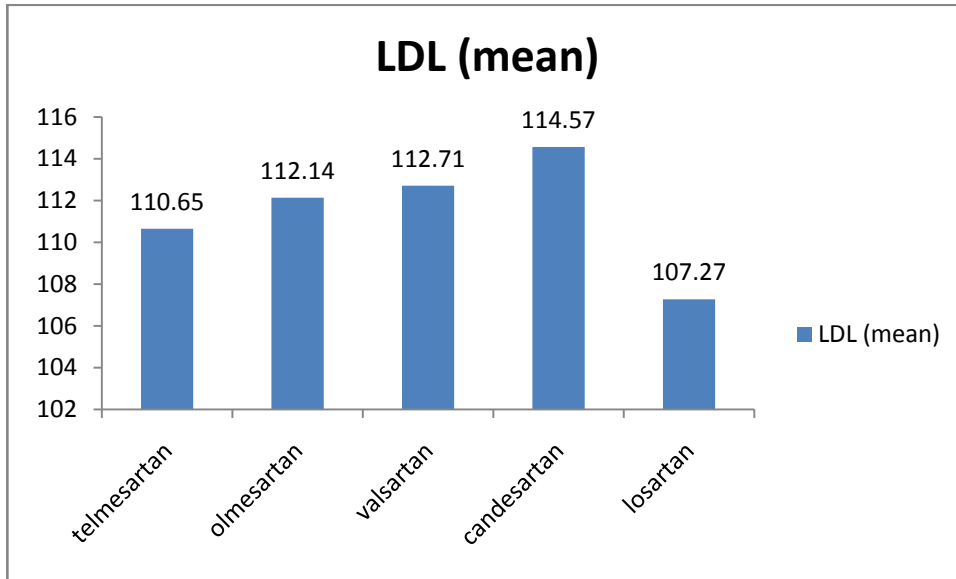
In this study investigation of abnormalities on low density lipoprotein among various drugs of various drugs of ARB like, telmesartan ( $110.65 \pm 7.33$ ), olmesartan ( $112.14 \pm 6.02$ ), valsartan ( $112.71 \pm 4.34$ ), candesartan ( $114.57 \pm 6.13$ ) and losartan ( $107.27 \pm 8.01$ ).

(Table no:15, Figure no:15)

S.No	ARB drugs	LDL Level Mean $\pm$ SD
1	Telmesartan	$110.65 \pm 7.33$
2	Olmesartan	$112.14 \pm 6.02$
3	Valsartan	$112.71 \pm 4.34$
4	Candesartan	$114.57 \pm 6.13$
5	Losartan	$107.27 \pm 8.01$



**Figure no: 15 Investigation Of low density lipoprotein Changes Among the Study Populations (n=112)**

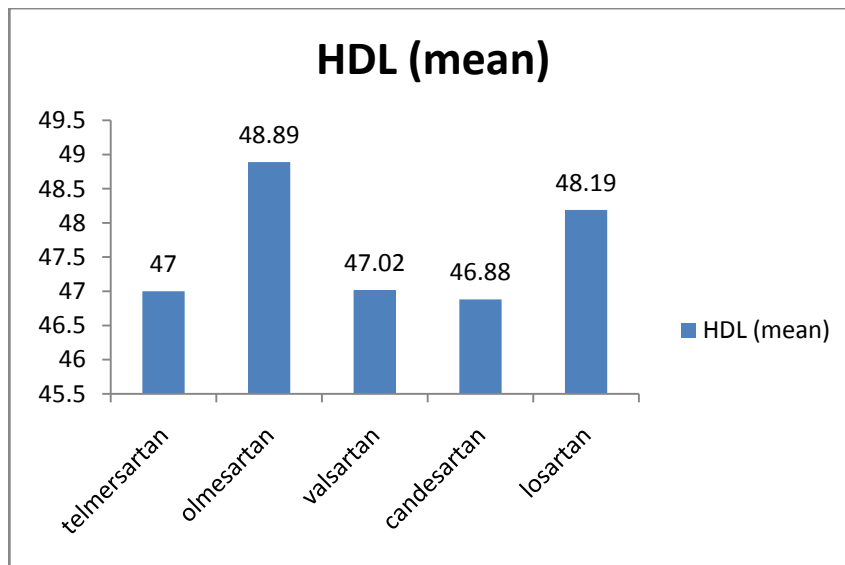


**Table no:16 Investigation Of high density lipoprotein Changes Among The Study Populations (n=112)**

in this study investigation of abnormalities on low density lipoprotein among various drugs of ARB like, telmesartan ( $47.00 \pm 4.72$ ), olmesartan ( $48.89 \pm 2.70$ ), valsartan ( $47.02 \pm 3.42$ ), candesartan ( $46.88 \pm 3.03$ ) and losartan ( $48.19 \pm 4.50$ ). (Table no:16, Figure no:16)

S.No	ARB Drugs	HDL Level Mean $\pm$ SD
1	Telmesartan	$47.0 \pm 4.27$
2	Olmesartan	$48.89 \pm 2.70$
3	Valsartan	$47.02 \pm 3.42$
4	Candesartan	$46.88 \pm 3.03$
5	Losartan	$48.19 \pm 4.50$

**Figure no:16 Investigation Of high density lipoprotein Changes Among The Study Populations (n=112)**



## 7.DISCUSSION

Hypertension is a leading risk factor affecting mortality and disability-adjusted life years worldwide.<sup>55</sup> It is considered to be the third major cause of disease burden, globally.<sup>56</sup> Regardless of the advancement in medical science, reports have shown a rising trend in hypertension prevalence among Indians.<sup>57,58</sup>

It is a chronic disorder, so long term intake of medicine is necessary to control elevated blood pressure. Long term usage of drugs may have adverse impacts on patients health and quality of life. This study specifically tried to find out the prevalence of Cardiac Events and investigation of abnormalities in ARB inhibitors.

The total outcome of the study was clear and demonstrative. This study comprised of 112 patients, out of which, most patients were in the age group of 50-59 years Mean age of the study population was  $55.7 \pm 6$  years. In this study, the male patients 61% were more predominant in number than the female patients 39%. A study conducted by Aslam et al.<sup>28</sup> showed that the patients were in the age group of 50-59 years with regard to gender distribution, 59.7% were males. In this study shows majority of the patients were overweight.

Out of 112 patients, non smokers and non alcoholic were more exposed to drug related outcomes than smokers and alcoholics.

A total of 112 patients, 51.07% (59) were having 1 year duration of Hypertension, 12.1% (13) were having 2-4 years duration of Hypertension, 18.01% (20) were having 5-10 years duration of hypertension, and 18.01% (20) were having 10-15 years duration of Hypertension. (Table 6, Figure 6).

The co-morbidities like diabetes mellitus and other complications co-exist with hypertension. But patients with no co-morbidity other than hypertension are more predominant

in this study. (Table 7, figure 7)

A total of 112 patients, 6.6% (7) prescribed with candesartan , 20.53% (23) prescribed with telmesartan, 54.46% (61) prescribed with losartan, 12.5% prescribed with (14) prescribed with olmesartan and 6.25% (7) prescribed with valsartan. (Table 8, Figure 8) This shows that losartan is the most prescribed drug in the study population. This shows that losartan is the most prescribed drug in the study population

### **PREVALENCE OF CARDIAC EVENTS**

The prevalence of cardiac events in hypertensive patients with ARB inhibitors were found to be 20.53%. Our study also shows that the Prevalence of Angina pectoris and Myocardial infarction were predominant among cardiac events which were 10.71 % and 9.8% respectively. Males were more prone to the incidences of Angina and myocardial infarction.

### **INVESTIGATION OF LIPID PROFILE CHANGES AMONG THE STUDY POPULATIONS**

In this study we evaluated the ARB using patient on lipids level like TC, LDL, and HDL. We noted a positive effect of ARB on most lipids indices. As well as different alterations in lipid level according to the individual agent used. More precisely, TC and LDL level were mostly decreased in Losartan subgroup. (Table 14,15 and Figure 14, 15 ). While the reduction in HDL level was best in the Olmesartan as well as Losartan. (Figure16)

Compared to all ARB drugs losartan was controlled the lipid level in hypertension patients. Similarly another study conducted by Kyvelou et al.<sup>55</sup> reported that TC and LDL levels were mostly decreased in the candesartan. while the reduction in ApoB levels and TC/HDL ratio was best in the valsartan. TGL levels were decreased only by the valsartan and losartan drugs.

## 8.CONCLUSION

The prevalence of Cardiac events like Angina pectoris and myocardial infarction in males were much higher than in females. This indicates that hospitalization of cardiac events for males has increased who were in the age group of 50-59.

Patients who are overweight according to BMI are having the highest risk of cardiac events. Moderate exercises can be recommended to the patients so that the prevalence of cardiac events can be possibly reduced.

Patients prescribed with Telmesartan are having higher Prevalence of cardiac events among all the ARB inhibitors prescribed. So the pharmacist should actively participate and intervene to reduce the Prevalence and recommend alternate drug therapy to the physician.

The Investigation of Lipid Profile Changes like TC, LDL and HDL levels were more in male population and also predominant with alcoholics . Compared to all ARB drugs, the drug losartan was controlled the lipid level in hypertension patients.

Further studies may be carried out with other classes of drugs.

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# VIVEKANANDHA MEDICAL CARE HOSPITAL

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Website : www.vivekanandha.ac.in email : vivekanandhamedicalcare@gmail.com



Ref.No.:VMCH/IEC/DEC/2018/01

Date: 12.11.2018

To

Jayaprakash. K  
II-M.Pharm,  
Department of Pharmacy Practice,  
Swamy Vivekanandha College of Pharmacy,  
Elayampalayam, Tiruchengode - 637205.

Sub: Approval of the study Protocol-Reg

The Institutional Ethical Committee reviewed and discussed your application to conduct the study entitled "An Investigation on Prevalence of Abnormalities in Hypertensive Patients in Laboratory Parameters under Various Classes of Antihypertensive Drugs" Under The Guidance Of Mr. JOSEPH STALIN .D, M.Pharm.,(Ph.D)., on 7.11.2018.

The following documents were reviewed:

- Study protocol
- Patient Information sheet and Informed consent Form
- Study data collection form
- Principle Investigator's/CO-PI current CV.
- Investigator's undertaking

The following members of the ethics committee were present at the meeting held at Vivekanandha Medical Care Hospital.

- |                         |                      |
|-------------------------|----------------------|
| 1. Dr.Sathcesh K M      | - Chairperson        |
| 2. Dr.K.Jayaprakash     | - Member Secretary   |
| 3. Dr.S.Arthanreeswaran | - Physician (Member) |
| 4. Dr.T.Tamilselvan     | - Scientist (Member) |
| 5. Dr.Sachu Philip      | - Scientist (Member) |

We approve the study to be conducted in its presented form.

The Institutional Ethical Committee to be informed about the progress of the study, any serious adverse events occurring in this course of the study, any changes in the protocol and patient information/informed consent and to provide a copy of the final report on completion.

**MEMBER SECRETARY,**  
Institutional Ethics Committee,  
VIVEKANANDHA MEDICAL CARE HOSPITAL,  
ELAYAMPALAYAM-637 205,  
Tiruchengode Tk, Namakkal Dt, T. N.

**Swamy Vivekanandha College of Pharmacy, Elayampalayam**

**Institutional Ethics Committee**

**INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS**

*(Strike off items that are not applicable)*

I / We (write name of the investigator(s) here), \_\_\_\_\_ am / are carrying  
out a study on the topic: \_\_\_\_\_ as part of my / our research

project being carried out under the aegis of the Department of:

*(Applicable to students only):* My / our research guide is:

The justification for this study is:

**The objectives of this study are:**

Primary Objective:

Secondary Objective:

**Sample size:**

**Study volunteers / participants** are (specify population group & age group):

**Location:**

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:

**Initial interview** (specify approximate duration):

Data collected will be stored for a period of \_\_\_\_\_ years. We will / will not use the data as part of another study.

**Health education sessions:** Number of sessions: 1. Approximate **duration** of each session:

**Clinical examination** (Specify details and purpose):

**Blood sample collection:** Specify quantity of blood being drawn: No. of times it will be collected:

Whether blood sample collection is part of routine procedure or for research (study) purpose:

1. Routine procedure
2. Research purpose

Specify **purpose**, discomfort likely to be felt and side effects, if any:

Whether blood sample collected will be stored after study period: Yes / No, it will be destroyed

Whether blood sample collected will be sold: Yes / No

Whether blood sample collected will be shared with persons from another institution: Yes / No

**Medication** given, if any, duration, side effects, purpose, benefits:

Whether medication given is part of routine procedure: Yes / No (If not, state reasons for giving this medication)

Whether alternatives are available for medication given: Yes / No (If not, state reasons for giving this particular medication)

**Final interview** (specify approximate duration): NA If **photograph** is taken, purpose:

**Benefits** from this study:

**Risks** involved by participating in this study:

How the **results** will be used:

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

**Consent:** The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date:

Witness:

## ஓப்புதல் படிவம்

தேதி:

----- ஆகிய நான், VMCH மருத்துவமனையில் --  
----- துறையின் கீழ், -----  
-----

என்ற தலைப்பில் ஆய்வு மேற்கொள்ள உள்ளேன்.

என் ஆய்வு வழிகாட்டி:

ஆய்வு மேற்கொள்வதற்கான அடிப்படை:

ஆய்வின் நோக்கம்:

ஆய்வு மேற்கொள்ளும் இடம்:

ஆய்வின் பலன்கள்:

இந்தஆய்வில் கிடைக்கும் தகவல்கள் ----- வருடங்கள் பாதுகாக்கப்படும். இவை வேறுஎந்தஆய்விற்கும் பயன்படுத்தப் படமாட்டாது. எந்தநிலையிலும் உங்களைப் பற்றியதகவல்கள் யாருக்கும் தெரிவிக்கப்படமாட்டாது. அவை இரகசியமாகவைக்கப்படும்.

இந்தஆய்வில் பங்கேற்கஒப்புக்கொள்ளுவதால் எந்தவிதமானபலனும் உங்களுக்குக்கிடைக்காது. எந்தநேரத்தில் வேண்டுமானாலும் ஆய்விலிருந்துவிலகிக் கொள்ளும் உரிமைஉங்களுக்குஉண்டு.



ஆய்விலிருந்துவிலகிக்கொள்வதால் உங்களுக்கு அளிக்கப்படும் சிகிச்சையில் எந்தவிதமாற்றமும் இருக்காது.

இந்த ஆராய்ச்சிக்காக உங்களிடம் சில கேள்விகள் கேட்கப்படும் / சில இரத்தமாதிரிகள் அல்லது திசுமாதிரிகள் எடுக்கப்படும்.

மேலும், இந்த ஆய்வில் பங்குகொள்வது உங்கள் சொந்த விருப்பம். இதில் எந்தவிதக் கட்டாயமும் இல்லை. நீங்கள் விருப்பப்பட்டால், இந்த ஆய்வின் முடிவுகள் உங்களுக்குத் தெரியப்படுத்தப்படும்.

ஆய்வாளரின் கையொப்பம் :

தேதி :

ஆய்வுக்குட்படுவரின் ஒப்புதல்:

நான் இந்த ஆராய்ச்சியின் நோக்கம் மற்றும் அதன் பயன்பாட்டினைப் பற்றி தெளிவாகவும், விளக்கமாகவும் தெரியப்படுத்தப் பட்டுள்ளேன். இந்த ஆராய்ச்சியில் பங்குகொள்ளவும், இந்த ஆராய்ச்சியின் மருத்துவரீதியான குறிப்புகளைவரும் காலத்திலும் உபயோகப்படுத்திக் கொள்ளவும் முழு மனதுடன் சம்மதிக்கிறேன்.

ஆய்வுக்குட்படுவரின் பெயர், முகவரி :

கையொப்பம் :

தேதி :

## DATA ENTRY FORM

NAME OF PATIENT:				IP NO.	DEPARTMENT	DOA	DOD
AGE/SEX	HEIGHT (cm)	WEIGHT (kg)	BMI	FAMILY HISTORY:			OCCUPATION
COMPLAINTS ON ADMISSION:							
MEDICAL HISTORY:				MEDICATION HISTORY:			
SOCIAL HISTORY				KNOWN ALLERGIES:			
ALCOHOLIC	SMOKER	TOBACCO	OTHERS				

### VITAL SIGNS (PROGRESS CHART)

PARAMETERS	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8	DAY 9	DAY 10
BP(mmHg)										
Temp										
PR(beats/min)										
RR(breaths/min)										

BLOOD SUGAR	ELECTROLYTES	
FBS(70-110 mgs/dl)	SODIUM(135-145 mmol/l)	CALCIUM(0.8-2.0 mmol/l)
PPS(80-140 mgs/dl)	POTASSIUM(3.5-5.1mmol/l)	BICARABONATES
RBS(70-170 gm/dl)	CHLORIDE(97-106 mmol/l)	

### HAEMATOLOGY

Sl.No.	Parameters	Patient value	Normal value
1.	Hb		F: 11-16 gms/dl M: 11.5-18 gms/dl
2.	RBC'S COUNT		4.0-6.0 million/cu.mm
3.	HCT		35-60%
4.	MCV		80-100 cu.micron
5.	MCH		27-31 pg
6.	MCHC		33-37%
7.	RDW		11.6-13.7 %
8.	MPV		7.8-11 cu.micron
9.	WBC'S COUNT		4500-10500 cells/cu.mm
10.	ESR		M:< 10 F:< 20
11.	CLOTTING TIME		5-10 min
12.	BLEEDING TIME		1-6 min
13.	PROTHROMBIN TIME		
14.	PLT		1.5-4.5 lakhs/cu.mm
15.	PLATELETCRIT		0.17-0.35 %
16.	PDW		9-4 cu.micron
<b>DIFFERENTIAL LEUKOCYTE COUNT</b>			
17.	POLYMORPHS		42-75 %
18.	LYMPHOCYTES		21-51 %
19.	EOSINOPHILS		1-6 %
20.	MONOCYTES		1-4 %

### LIVER FUNCTION TEST

TOTAL BILIRUBIN (0.4-1 mg/dl):	S.TOTALCHOLESTEROL(<240mgs/dl):	SGOT(0-40lu/l):
DIRECT BILIRUBIN (0.1-0.4 mg/dl):	S.TRIGLYCERIDE (70-170mgs/dl):	SGPT(0-65 lu/l):
INDIRECT BILIRUBIN (0.2-0.8 mg/dl):	S.HDL(40-60mgs/dl):	GGTP(11-45lu/l):
TOTAL PROTEIN (6-8 gms/dl):	S.LDL(0-140mgs/dl):	ALKP(0-258lu/l):
ALBUMIN (3.5-5.5 gms/dl):	S.VLDL(0-38mgs/dl):	GLOBULIN (2-3.5 gms/dl):



3												
4												
5												
6												
7												
8												
9												
10												

**DRUG INTERACTION/ADVERSE DRUG REACTIONS**

DRUGS	EFFECTS	INFERENCE

**DISCHARGE MEDICATION**

	DRUGS		DOSE	FREQ	DURATION OF THERAPY
	T.Name	G.Name			
1					
2					
3					
4					
5					
7					
8					
9					
10					



**J.K.K.NATTRAJA COLLEGE OF PHARMACY**  
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*Certificate*  
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This Certificate is awarded to

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ELAYAMPALAYAM - 637 205, TIRUCHENGODE,  
NAMAKKAL Dt., TAMILNADU, INDIA.

## 2<sup>nd</sup> National Level Seminar on CLINICAL PHARMA PRACTICE - INDIAN AND GLOBAL SCENARIO (CPP-IGS 2018)

*Certificate*

This is to certify that Mr / Ms / Prof / Dr. ....**R...JAYAPRAKASH.H.**

has participated as delegate in the 2<sup>nd</sup> National Level Seminar

“CLINICAL PHARMA PRACTICE - INDIAN AND GLOBAL SCENARIO” (CPP-IGS 2018) on

30<sup>th</sup> June 2018, organized by the Department of Pharmacy Practice, sponsored by

The Tamilnadu Dr. M.G.R Medical University, Chennai.

Mr. S. Anandkumar  
Organizing Secretary

Dr. G. Muruganathan  
Convener

Prof. Dr. M. Karunanithi  
Chairman & Secretary





Department of Pharmacology  
**PSG COLLEGE OF PHARMACY**

Coimbatore

**National Seminar on Future Aspects of Pharmacotherapeutic  
 Approaches in Disease Management**

5<sup>th</sup> & 6<sup>th</sup> October 2018

*Certificate*

This is to certify that Prof./Dr./Mr./Ms./Mrs.....**K.JAYAPRAKASH**.....  
 has actively participated as delegate and presented a paper titled...**Clinical investigation  
 of iron supplements response for anaemia in chronic kidney disease**.....  
**patients**..... in **Orat**/ Poster session of the said seminar

Organised by Department of Pharmacology, PSG College of Pharmacy, Coimbatore

**Dr. G. Venkatesh**  
 Organising Secretary

**Dr. M. Ramanathan**  
 Principal / Chairman

