# “COMPARATIVE CLINICAL STUDY ON HYPERTENSIVE PATIENT”

*Dissertation work submitted to*
*The TamilNadu Dr.M.G.R. Medical University Chennai*

*In Partial Fulfillment for the Award of Degree of*

**MASTER OF PHARMACY**

**IN**

**PHARMACY PRACTICE**


Submitted by
**RAMESH BABU.P**
**Reg No.261640711**

Under the guidance and supervision of
**Dr. ANISH N**
Assistant Professor
Department of Pharmacy Practice

**DEPARTMENT OF PHARMACY PRACTICE**

**PADMAVATHI COLLEGE OF PHARMACY & RESEARCH INSTITUTE**

**PERIYANAHALLI-635205,**

**DHARMAPURI DIST.**

**TAMILNADU.**


**OCT-2020**

## EVALUATION CERTIFICATE

This is to certify that this dissertation work entitled "**COMPARATIVE CLINICAL STUDY ON HYPERTENSIVE PATIENT"** is the bonafide work carried out by **Mr. P. RAMESH BABU** **Reg. No: 261640711** under guidance of **Dr. N. Anish, Pharm.D**., Assistant Professor, Department of Pharmacy Practice for the partial fulfillment of the requirement of award for Master of Pharmacy and this is forwarded to the **The Tamilnadu Dr.M.G.R Medical University, Chennai** during the academic year 2020-2021 has been evaluated on _____

Evaluators:

1. 2.

# CERTIFICATES

# CERTIFICATE

This is to certify that this dissertation work entitled "**COMPARATIVE CLINICAL STUDY ON HYPERTENSIVE PATIENT"'** is the bonafide work carried out by **Mr. P. RAMESH BABU Reg. No: 261640711** under guidance of **Dr. N. Anish, Pharm.D**., Assistant Professor, Department of Pharmacy Practice for the partial fulfillment of the requirement of award for Master of Pharmacy and this is forwarded to the **The Tamilnadu Dr.M.G.R Medical University**, **Chennai** during the academic year 2020-2021.

**Prof. Dr.D.C.PREM ANAND, M.Pharm. Ph.D. ,**
Principal
Padmavathi College of Pharmacy & Research Institute,
Periyanahalli,Dharmapuri-635205

**Place: Dharmapuri**

**Date:**

# CERTIFICATE

This is to certify that this dissertation work entitled "**COMPARATIVE CLINICAL STUDY ON HYPERTENSIVE PATIENT""'** is the bonafide work carried out by **Mr. P. RAMESH BABU Reg. No: 261640711** under guidance of **Dr. N. Anish, Pharm.D**., Assistant Professor, Department of Pharmacy Practice for the partial fulfillment of the requirement of award for Master of Pharmacy and this is forwarded to the **The Tamilnadu Dr.M.G.R Medical University, Chennai** during the academic year 2020-2021.

**GUIDE**
**Dr.N.ANISH, Pharm.D.,**
Department of Pharmacy Practices
Padmavathi College of Pharmacy & Research Institute
Periyanahalli
Dharmapuri-**635205**

## DECLARATION

I hereby I declare that this thesis work '"**COMPARATIVE CLINICAL STUDY ON HYPERTENSIVE PATIENT**"' has been originally carried out by myself under the guidance and supervision of **Dr. N. Anish, Pharm.D**., Assistant Professor, Department of Pharmacy Practice, Padmavathi College of Pharmacy and Research Institute, Periyanahalli, Dharmapuri. I also declare that the matter embodied in its original and the same has not previously performed on the basis for the award of any degree, diploma, associate ship or fellowship of any other university or institution.

**RAMESH BABU. P**

**REG. NO: 261640711**

**Place: Dharmapuri**

**Date:**

# ACKNOWLEDGEMENT

## ACKNOWLEDGEMENT

The task of preparing this distraction has been fascinating experience and it is really a moment of great pleasure for me to express my hearty gratitude to those who have supported help me in successful completion of this dissertation.

First and foremost, I would like to thank Almighty God for show showing his immense blessing upon me and granting me the courage, wisdom, healthy and strength to undertake this thesis work and enabling me to its completion

I would like to express my sincere thanks to **kalvi kodai vallal, Mr. M.G.SEKHAR, B.A., B.L., EX.M.L.A, Chairman,** Saptagiri, Padmavathi & Pee Gee group of institution for granting me permission to utilize all the facilities and amenities successful to achieve this task.

It is a difficult moment for me, to put into words all my deep sense gratitude to my beloved and esteemed guide **Dr. Anish N. Pharm.D., Assistant Professor,** Department of Pharmacy Practice, Padmavathi College of Pharmacy and Research Institute, for her unstinted guidance, innovating ideas, constructive criticism and continuous supervision, and also for making the requisite arrangement to enable me to complete my project.

I would like to express my sincere thanks to **Prof**. **Dr. D. C. PREMANAND, M.Pharm. Ph.D., Principal,** Padmavathi College of Pharmacy and Research Institute of permitting to carry out the work in college

I would like to express my sincere thanks to **Prof. M. Madeswaran, M.Pharm., Ph.D.,** Department of Pharmacology, Padmavathi College of Pharmacy and Research Institute.

I would like to thank **Prof. M. Raja**. **M.Pharm.,** Department of Pharmacognosy, **Prof. Rajesh Kumar, M.Pharm.,** Department of Pharmaceutics. **Ms. K. Hedie, M.Pharm.,** Asst. Professor, Department of Pharmacology, **Mrs. Kavitha Ramesh Babu, M.Pharm., M.B.A., Global Pharmaceutical Pvt. Ltd, Hosur,** gave me valuable suggestion and encouragement to my project.

I would like to thank Mr. Gandhi,. Chief Librarian, Padmavathi College of Pharmacy and research institute. I place on record sincere acknowledgement to whole teaching and non-teaching staff of College of Pharmacy.

I would like to thank **Mr. Ramesh**, M.C.A., office in charge, **Mrs. J. Sangeetha, M.A.,** Office Asst. in Charge, **Ms. Meenakshi, M.Com.,** Accountant, Padmavathi College of Pharmacy, Dharmapuri.

I would like to express my thanks to our Iron lady Aaya **Mrs. Muniyammal.**

I take this opportunity to express gratitude to my dearest classmates for all their help and support when I needed them. Words have no power to pay regards to my most beloved parents and siblings of for their Prayers, love and inspiration bestowed upon me without which I would not have accomplished the completion of my thesis work. I greatly acknowledge my friends and my juniors for generous help during project work.

**RAMESH BABU.P.**

**Reg No: 261640711**

DEDICATED TO
MY BELOVED FAMILY,
TEACHERS AND
FRIENDS

## Contents

# PLAN OF WORK

# INTRODUCTION

# 1. INTRODUCTION

## HYPERTENSION

Hypertension easier silent killer currently affects approximately one billion adult globally. Hypertension is an important risk factor for cardiovascular diseases and stroke and is associated with metabolic systems including insulin resistance and abnormalities. At a defining cutoff 140/90 mmHg, 28-44% of world population has hypertension[1]. Estimated hypertension is about 25% among urban adult and 10% in the rural areas[2]. The lifetime risk for developing hypertension is estimated to be up to 90% it is condition the blood pressure is related to an exempt where clinical benefit can be obtained from blood pressure lowering. Components used for determination for systolic and diastolic blood pressure there is no clear cut off point between hypertensive and normotensive subject.

The blood pressure is a product of cardiac output and the total resistance of peripheral vascular resistance system, of the high blood pressure arises as a result of increased resistance of peripheral system due to constriction of small arterioles. Hypertension is a condition the pressure that is put on the walls of the arteries as blood is pumped through the circulatory system. The circulation of blood through the veins and arteries is at certain pressure. In natural limit it is not harmful. But with this pressure increase, heart is over worked and an abnormal interior tissue growth can be developed in arteries. This cause further blocked in passage of blood, leading to increased blood pressure.

In many cases, genetic susceptibility to hypertension is observed. Hypertension is twice common in subject with hypertensive parents. Essential hypertension occurs four times more frequently in blacks than whites. And in middle aged population males are more frequently with hypertension than the females.

Many drugs which are commonly using can cause high blood pressure as side effects. Some of the drugs belongs to the above category includes non-steroidal anti-inflammatory drugs, contraceptive, steroids. Obesity causes high blood pressure due to increased body weight and additional pressure that it exerts on the heart and arterial system. A healthy diet which is rich with salt and fact lack of dietary fibers along with secondary life style devoid of proper exercise, excessive use of alcohol, cigarette smoking is an another culprit of hypertension.

Advanced medical research service for developing new methods to lower the high blood pressure and it has gone two great lengths. Even the arterial hypertension is almost never serious health treat; doctors attempt to lower high blood pressure because it can have serious long term consequences.

It was also shown that more than 64 % of patients with hypertension also have dyslipidemia and 47 % of patients with dyslipidemia have hypertension[3]. Highly elevated TGL levels are found in hypertensive on comparing with normotesives[4] patients with hypertension frequently have additional cardiovascular risk[5]. Conversely hypertension is a significant risk factor in patient with elevated cholesterol and diabetes[6].

Strategies that reduce BP and lipid levels simultaneously are likely to lead to a greater reduction in the incidence of CVD related events then treating either factor in isolation

## A.1 DEFINITION

Hypertension is defined as a sustained diastolic blood pressure greater than 90 mmHg accompanied by an elevated systolic blood pressure greater than 140 mmHg, blood pressure is the force by which blood drives through blood vessels to supply Oxygen and nutrients to the body organs and carry away metabolites and waste materials. The blood pressure is optimal if it is less than 120/ 80 mmHg

## A.2 ETIOLOGY

More than 90 % of the patients having essential hypertension, it is a disorder of unknown or can affect the BP regulation mechanism. A subject with family history of hypertension is likelihood to develop hypertensive disease. Primary hypertension is four times more frequently in blacks than in whites. Likely it observed more often in middle aged male subjects than middle aged females. Many environmental factors like stressful lifestyle unhealthy diet obesity, smoking and alcoholism, lack of proper exercise and usage of drugs such as NASID are predisposing factors to develop hypertension[8]

## A.3 CAUSES OF HYPERTENSION

90-95% of hypertension is essential hypertension and 5-10% of Hypertension belongs to secondary hypertension. Cases of primary hypertension are not clearly unknown. Secondary hypertension is renal or endocrine diseases, vascular diseases and the same may be arising due to the drugs.

Endocrine diseases which can produce secondary hypertension are Acromegaly, Cyonn's syndrome, Cushing's syndrome, phaeochromocytoma, pre eclampsia. Vascular cases includes fibro muscular hyperplasia renal artery

Atheroma etc. Mini drugs can also be leading factors for secondary hypertension. Adrenal steroids, antidepressants appetite suppressants, cocaine, cyclosporine, Erythropoietin, nasal decongestants, NSAIDs, oral contraceptives, sympathomimetics are there in the category of drugs which can induce hypertension[9].

**A.4 COMPLICATIONS OF HYPERTENSION**

MI

Stroke

Malignant hypertension dissecting aortic aneurysm hypertensive nephrosclerosis peripheral vascular diseases [10].

**A.4 a) MYOCARDIAL INFARCTION[11]**

A heart attack occurs when blood flow to a part of heart is blocked for a long enough time that part of the earth muscles is damage or dies. The medical term for this is myocardial infarction. Most heart attack are caused by a blood clot that blocks one of the coronary arteries. The coronary arteries bring blood and oxygen to the heart. If the blood flow is blocked, the heart is starved of oxygen and heart cells die. A hard substance called plaque can build up in the walls of coronary arteries. This plaque is made up of cholesterol and other cells. Chest pain is the most common symptoms of heart attack. One man feel the pain in only one part of your body, or it may move from your chest to arms, shoulder, neck, teeth, jaw, belly area or back. Other symptoms of heart attack can include anxiety, cough fainting light headedness, dizziness, nausea, vomiting, and shortness of breath, sweating, palpitation [12].

**A.4 b) STROKE**

A stroke happen when blood float to a part of the brain stops. A stroke is sometimes called as a "brain attack the blood flow is stopped for longer than a few seconds, the brain cannot get blood and oxygen. Brain cells can die, causing permanent damage. There are two major type of stroke, ischemic stroke and hemorrhagic stroke. Ischemic stroke occurs when a blood vessels that supplies blood to the brain is blocked by blood clot. This may happens in two ways, thrombotic stroke or embolic stocks. Ischemic stroke may be clogged arteries. Fat, cholesterol, and other substance collect on the artery walls, forming in sticky substance called plaque. A hemorrhagic stroke occurs when a blood vessels in part of the brain becomes weak and bursts open, causing blood to leak into the brain. Some people have defects in the blood vessels of the brain that makes this more likely.

**A.4 c) MALIGNANT HYPERTENSION**

Malignant hypertension is very high blood pressure that comes on suddenly and quickly. The lower (diastolic) blood pressure reading, which is normally around 80 mm Hg, is often the above 130 mm Hg.The disorders effect about 1% of people with high blood pressure, including both children and adults. It is more common in youngster adults. It also occurs in people with collagen vascular disorders, kidney problems, toxemia of pregnancy. High risk for malignant hypertension includes kidney failure, renal hypertension

**A.4 d) DISSECTING AORTIC ANEURYSM**

Aortic dissection occurs when a year in the inner wall of the the aorta causes blood to flow between the layers of the wall of the aorta, forcing the layers apart. In

most cases this is associated with severe characteristics chest or abdominal pain described as "tearing" in character, and often with other symptoms that result from decreased blood supply to other organs. Aortic dissection is a medical emergency and can quickly lead to death, even with optimal treatment, as a result of decreased blood supply to other organs, cardiac failure, and sometimes rupture of the aorta. Aortic dissection is more common in those with a history of high blood pressure, a known thoracic aortic aneurysm, and in a number of condition that affect blood vessel wall integrity such as Marfan syndrome and the vascular subtype of Ehlers-Danlos Syndrome. The treatment of aortic dissection depends on the part of the aorta involved. Surgery is usually required for dissections that involve the aortic arch, while dissection of the part further away from the heart may be treated with blood pressure lowering only. Aortic dissection is relatively rare, occurring at an estimated rate of 2-3.5 per 100,000 people every year. It is more common in males. Mean age at diagnosis is 63, although all age may be affected. Many cases of aortic dissection (40%) lead to death so rapidly that the person doesn't make it to hospital in time

**A.4 e) HYPERTENSIVE NEPHROSCLEROSIS**

Hypertensive nephropathy for hypertensive nephrosclerosis, or Hypertensive renal diseases is a medical condition referring to damage to the kidney due to chronic high blood pressure. It should be distinguished from renovascular hypertension disease a form of secondary hypertension in the kidneys, as a result of benign arterial hypertension. Hyaline (pink, amorphous, homogeneous material) accumulates in the wall of small arteries and arterioles, producing the thickening of their walls and the narrowing of the lumina hyaline arteriolosclerosis. Consequent

Ischemia will produce tubular atrophy, interstitial fibrosis, glomerular alterations and per glomerular fibrosis. In advanced stages, renal failure will occur. Functional nephrons have dilated tubules, often with hyaline casts in the lumens. Additional complications of associated with hypertension nephropathy include glomerular damage resulting in proteinuria and hematuria[12].

**A.4 f) PERIPHERAL VASCULAR DISEASE**

Peripheral vascular disease is a narrowing of blood vessels that restricts blood flow. It mostly occurs in the legs, but is sometimes seen in the arms. Peripheral vascular disease include a group of diseases in which blood vessels become restricts or blocked. Typically, the patients has peripheral vascular disease from atherosclerosis. Atherosclerosis is a disease in which fatty plaque from in the inside walls of blood vessels. Other process such as blood clots, further restrict blood flow in the blood vessels. Both veins and arteries may be affected, but the disease is usually arterial. All the symptoms and consequences of peripheral vascular disease are related to restrict blood flow. Peripheral vascular disease is a progressive disease that can lead to gangrene of the affected area. Peripheral vascular disease may also occur suddenly if an embolism occurs or when a blot clot rapidly develops in a blood vessels already restricted by an arthroscopic plaque, and the blood flow is quickly cut off. There are many causes of peripheral vascular disease, one major risk factor is smoking cigarettes. Other diseases predispose patient to develop a peripheral vascular diseases. These include diabetes, Burger's, disease, hypertension, and Reynaud's disease. The main symptom is pain in the affected area. Early symptoms include an achy, tired sensation in the affected muscles. Since this disease is seen mainly in the legs, these sensations usually occur

when walking. When the symptoms may disappear when resting. As the disease becomes worse, symptoms occur even during light exertion and, eventually, occur all the time, even at rest. In the severe stage of the disease the leg and foot may be cold to the touch and will feel numb. The skin may become dry and scaly. If the leg is even slightly injury ulcers may form because, without a good blood supply, proper healing cannot take place. At the most severe stage of the disease, when the blood flow is greatly restricted. Gangrene can develop in those areas lacking blood supply. in some cases, peripheral vascular diseases occur suddenly. This happens when an embolism rapidly blocks blood flow to the blood vessels. That patients will experience a sharp pain, followed by a loss of sensation in the affected area. The limb will become cold and numb and loose color or turn bluish.

The most common and important CV complication associated with hypertension are stock and myocardial infarction, Increase of 5 mmHg diastolic pressure from usual range shows 35 - 45% increased risk of stroke and similar but less steep association for coronary heart disease. According to Framingham heart study subjects with BP value between 130 to 139 and 85 to 89 mmHg are associated with more than two fold increase in relative risk from CVD when comparing subjects with a BP level lesson 120/80 mm Hg.

**A.5 RISK FACTOR OF CVD**

- Hypertension
- Elevated LDL or low HDL
- Age
- Diabetes mellitus
- Renal disease

. Family history

. Obesity

. Life style [13].

Management of hypertension and other risk factor is essential to reduce the morbidity and mortality risk arise due to hypertension

**A.6 classification of blood pressure**

1. Heart failure

2. High coronary artery disease risk

3. H/O MI in the past

4. H/O stroke in the past

5. Diabetes

6. Chronic renal disease

**Table 1 Compelling indications for use of antihypertensive drugs**

| Classification | Systolic (mm Hg) | Diastolic (mm Hg) |
|---|---|---|
| Normal | <120 | <80 |
| Prehypertension | 120-139 | 80-89 |
| Stage 1 hypertension | 140-159 | 90-99 |
| Stage 2 hypertension | >160 | >100 |

People with stage 1 and 2 are to be treated. The goal of treatment in individuals without compelling indications for use of antihypertensive drugs is

>140/90 mmHg, and the same in subjects with prehypertension is to lower the BP with life style changes to prevent it's further progression [15]

## A.7 PREVENTION OF HYPERTENSION

By preventing the rise in BP hypertensive risk like cardiovascular diseases, renal diseases stroke, and the hypertension itself can be reduce or minimize. For that preventive measures to minimize or avoid the causing factors or risk factors of hypertension should be introduced to the specific population. The causing factors that are to be avoided or minimized for attaining the aim of prevention of hypertension includes smoking, intake of sodium rich and fatty diets, excess of alcohol intake excess of bodyweight etc. A diet which is rich in fruits and vegetables with sufficient potassium is suggested with an improved Physical activity to minimize the rise in BP. It is mainly meant for the population who belong to prehypertension. It is observed and estimated from studies that it can be attain a reduction of 8% in mortality rates with stroke. 5% reduction in mortality due to CAD, by reducing 3 mmHg of systolic BP[16].

1. Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)

2. Maintain normal body weight for adult (body mass index 18.5 -24.9 $kg/m^2$)

3. Limit alcohol consumption to no more than 1 Oz[ 30ml ] ethanol (e.g., 24 Oz[ 720 ml ] of beer 10 Oz [ 30 ml ] of wine or 2 Oz [ 60ml] 100-proof whisky per day in most Men and to no more than 0.4 15 ml of ethanol per day in women and lighter weight persons**.**

4. Reduce dietary sodium intake to no more than 100 m mol per day (approximately 2.4 g of sodium or 6 g of sodium chloride)
5. Maintain adequate intake of dietary potassium (more than 90 m mol [3,500 mg] per day).
6. Consume a diet that is rich in fruits and vegetables and in low fat dairy products with reduced the content of saturated and total fat (Dietary approaches to stop Hypertension [DASH] eating plan).

## A.8. DIAGNOSTIC PRODUCERS AND LABORATORY TESTS

The primary parameter for diagnosing of primary hypertension is physical examination of BP. The arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, and retinal hemorrhage exudates and infracts are examined for hypertensive emergency. Cardiopulmonary examination or done for identifying the abnormality in heart rate of rhythm, left ventricular (LV) hypertrophy, Pericardial heave, third and fourth heart sound. Peripheral vascular examination are performed to evidence of atherosclerosis, aortic or abdominal bruits distended Veins and edema17. Renal artery stenosis can be indicated by abdominal systolic-diastolic bruit. Hypokalemia suggested mineralocorticoid-induced hypertension. The pressure of protein in blood cells and casts in the urine for examined for presence of renovascular disease.

Laboratory test recommended Prior to initiating drugs therapy include urinalysis, Serum chemistries (sodium potassium creatinine, fasting glucose, fasting lipid panel), and 12-lead electrocardiogram (ECG)

These laboratory test or recommended to identify the risk factors and the metabolic changes that are produced due to treatment more extensive testing for identifiable cause is not generally indicated unless BP control is not achieved or the clinical and routine laboratory evaluation strongly suggests an identifiable secondary cause.

**A.9 Pathophysiology of Hypertension**

Hypertension is a heterogeneous disorder the underlying mechanism for the hypertension that may have specific case which is known as secondary hypertension and maybe other physiology mechanism of unknown etiology which is known as primary or essential hypertension 10 percentage of total hypertension cases belong to the secondary hypertension renovascular disease are come kidney diseases is the major causing factor for secondary hypertension The other underlying conditions are Cushing's Syndrome pheochromocytoma, hyperthyroidism hyperparathyroidism, pregnancy primary aldosterone's, obstructive sleep apnea, and contraction of the aorta etc. Manydrugs can also be a leading factor for secondary hypertension Adrenal steroid, Antidepressant, Appetite Suppressants, Cocaine, Cyclosporine, Erythropoietin, Nasal decongestants. NSAIDs, Oral Contraceptive, Sympatho-mimetic are some drugs in above class.

**A. 10 primary hypertension can result from multiple factors which includes**

1. Abnormalities in Rennin-Angiotensin-Aldosterone-System, natriuretic hormone
2. Pathological disturbance in nervous system (in CNS, nerve fibers of autonomic nerve system, adrenergic or baroreceptors)

3. Abnormalities in renal system or auto regulatory process for sodium excretion, plasma volume, arteriolar constriction.

4. Either because of increased production of angiotensin II and endothelin Ⅰ (vasoconstrictors) or a decrease in synthesis of vasodilators like -prostacyclin, bradykinin, and nitric oxide.

5. Sodium intake: increased vascular reactivity and a rise in BP can be resulted from excessive sodium intake and inhibition of sodium transport.

6. Intracellular calcium concentration: a rise in intracellular calcium concentration may results in alteration of vascular smooth muscle function and elevation in peripheral vascular resistance.

The life threatening events in hypertensive patients is mainly associated with cerebrovascular events, CV events and renal failure.

**A. 11 TREATMENT**

The overall winner of antihypertensive therapy is to reduce morbidity and mortality associated with elevated blood pressure[18]. A disproportionate rise in systolic blood pressure with respect to diastolic blood pressure is founded in elderly patients due to decreased compliance of blood vessels associated with aging and atherosclerosis. So it was founded that more difficulty is there with systolic pressure reduction than diastolic blood pressure reduction. Systolic blood pressure is used as primary clinical marker in hypertension, and the same is there a better predictor of CV complication. In most of the population and achievement of blood pressure <140/90 mmHg is considered as desirable. It is preferred to be<130/80 mm Hg in subjects with diabetes mellitus, chronic kidney disease, coronary artery disease (MI, angina)

etc. And for patients with LV dysfunction blood pressure lower than120/80 mmHg is advised.

The primary focus is given to SBP reduction. Life style modifications, pharmacological treatment with single drug or combination are required to reduce reduce blood pressure. And that must be prescribed according to patient condition and the other comorbidities present.

## A. 12 NON PHARMACOLOGICAL THERAPY

Lifestyle modification are advisable as initial approach to pharmacological treatment. Epidemiological data supports its importance in hypertensive population. Minor alteration in normal physical activity and diet control can reduce blood pressure. Non pharmacological method helps the patient to participate actively in management of disease.

Body weight reduction[19], sodium restriction, increased physical activity, smoking cessation, moderate consumption of alcohol is the major consideration in Life style modification.

### A. 12 a) Body Weight Reduction

Obesity and hypertension closely associated and have positive degree of correlation[20]. Even the exact mechanism is not known with lowering of BP. Body can be attain regardless of salt consumption. Secretion of insulin is high in obese population that may cause an increase in insulin mediated renal tubular reabsorption of Na+ and extra cellular volume expansion[21]. A combination of aerobic exercise with good dietary consideration is advised in hypertension.

**A.12 (b) SODIUM RESTRICTION**

Restriction of salt intake up to 5g/day offers a significant reduction in pressure (12/6mm Hg), the better response is observed in subjects with high blood pressure. When it come to the age consideration subjects over 40 years are more responsive to the moderate restriction of salt[22]. Improved responsiveness to some antihypertensive drug is an additional benefit of moderate salt intake. Reduced sodium intake to approximately 100mmol/day can prevent hypertension. Lower intake of sodium approximately 60 mmo1/day further reduced pressure in both hypertensive and normotensive subjects [24].

**A.12 (c) INCREASED PHYSICAL ACTIVITY**

Lack of physical activity is highly correlated with hypertension. The cardiovascular diseases is decreased with increased physical activity [25]. A regular isotonic exercise reduces the blood volume and plasma catecholamine's, with this atrial natriuretic peptide concentration in plasma is increased[26]. Regular isotonic exercise offers reductions of 10 mmHg of blood pressure. It also reduced plasma renin activity, norepinephrine levels in plasma.

**A. 12(d) SMOKING CESSATION**

Cigarette smoking is one of the strongest contributors to the risks of cardiovascular disease, including coronary heart disease, stroke, sudden death, peripheral artery disease, and aortic aneurysm[27]. Considerable reductions in the risk of cardiovascular disease occur immediately after the discontinuation of cigarette smoking [28]. Alterations in blood pressure (BP) heart rate (HR) and autonomic nervous function are thought to be at least in part responsible for the rapid reduction

In the risk of cardiovascular diseases after quitting.

**A.12 (e) MODERATE CONSUMPTION OF ALCOHOL**

Consumption of alcohol is restricted in hypertensive population as it can lead to elevations in blood pressure. High alcohol consumption leads to increased risk for cerebrovascular accidents. Not more than 30 ml of alcohol per day is advised to hypertensive subjects.

**A.12 (f) DIET**

Diet with increased usage of fruits, vegetables and low-fat dairy products and includes whole grains, nuts, poultry and fish. It has low quantities of fats, red meat, sweets and sugar containing beverages. It is thus rich in potassium, magnesium, calcium and fiber and has low amount of total fat saturated fat and cholesterol is advised in hypertension. Some example for the above includes vegan's diet – dash diet, Mediterranean diet1. Animal products meat and it's products have been shown to rise in BP, were fish has shown to reduce BP because of Omega -3 fatty acid.

**A. 13 ORAL ANTIHYPERTENSIVE DRUGS**

Drugs that are used to treat Hypertension are called as antihypertensive drugs. Antihypertensive therapy is meant to prevent the complications of high blood pressure, such as stroke, myocardial infarction. Reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34% of ischemic heart disease by 21%, and reduce the likelihood of dementia, heart failure, and mortality from cardiovascular disease.

## A.13 (a) DIURETICS

These classes of drugs are very important in hypertensive treatment. The diuretics are also known as water pills-as they help body get rid of water and salt through urine. Diuretics bringing out an alterations in Na+ balance and decrease in extra cellular volume. They are used either alone or in combination with other antihypertensive drugs. Diuretics are used in treatment of several pathological conditions like high blood pressure heart failure, kidney and liver problems and glaucoma etc.

The exact mechanism of arterial blood pressure reduction by diuretics is not certain. Initially the interaction with thiazide- sensitive Na-Cl co transporter rate in kidney decreases the extra cellular volume which can produce fall in cardiac output. Reduction in blood pressure is produced and maintained in long term therapy because of reduced vascular resistance

Diuretics are widely used to treat hypertension. Thiazide diuretics having additive effect with other antihypertensive drugs, this reason sounds for its combination regimen with other antihypertensive drugs. Diuretics show an advantage of minimizing the salt and water retention that is commonly produced by vasodilators and some sympatholytic drugs.

The most commonly used diuretics are hydrochlorothiazide, furosemide, and torsemide. The combination of triamterene and hydrochlorothiazide and metolazone are also used in antihypertensive therapy. Thiazide diuretics are used in indication like hypertension and to treat edema in heart failure. Loop diuretics are used in subjects with congestive heart failure symptoms and in emergency symptoms. Potassium sparing diuretics are mainly suggested in CHF**.**

Omitting or underutilization of diuretics lead to "resistant hypertension"

**A.13 b) SYMPATHOLYTIC AGENTS**

Both α and β adrenergic receptor antagonist drugs shows antihypertensive action. Early invented sympathetic drugs were poorly tolerated and advice side effects. Many of new sympathetic drugs are currently used in antihypertensive therapy. They primarily used in treatment of angina pectoris and their arterial blood pressure lowering activity is laterally investigated.

Reduction of blood pressure by β adrenergic agents are achieved through different mechanisms including, reductions in myocardial contractility, heart rate, and cardiac output. On general considerations blood pressure reduction is produced by a blocking action of adrenaline receptor. Beta blockers or prescribed in populations with heart diseases, angina, or history and heart attack. Examples: Propranolol, Metoprolol, Atenolol.

Alpha1 adrenergic antagonist drugs are used in therapy of Hypertension. They reduce arteriolar resistance and increase venous capacitance; hence the reduction in blood pressure is obtained. The α1 adrenergic receptor blockers are not recommended as monotherapy for hypertensive patients but suggested to use in combination with diuretics and β blockers. Enhanced effect of α1 adrenergic receptor blocker is observed on combining with β receptor antagonist. Since all adrenergic receptor blocker improves urinary symptoms they are attractive drug for hypertensive patient with benign prostatic hyperplasia. Examples Prazosin, Terazosin, Doxazosin.

## A. 13 (C) COMBINED AI AND P ADRENERGIC RECEPTOR ANTAGONISTS

The drugs with combined α and β adrenergic receptor antagonist action are also there in anti-hypertensive category; they include labetalol, carvedilol etc. In that labetalol is given intravenously to reduce the blood pressure rapidly so used in treatment of hypertensive emergencies. Another drug carvedilol reduces the mortality in patients with systolic dysfunction and heart failure when used with diuretics and ACE inhibitors.

Centrally acting antihypertensive agents like Methyldopa, Clonidine, Guanfacine and adrenergic neuron blockers are also comes under the sympatholytic agents.

## A.13 d) CALCIUM CHANNEL BLOCKERS

Calcium channel blockers (CCBs) are a group of drugs used in treatment of hypertension. The antihypertensive action is quick and long acting preparations are available for once a day administration. The CCBs monotherapy is effective in-50% hypertensive subjects. CCBs voltage sensitive calcium channel blocking action reduces the entry of extracellular calcium into cells cause cardiac and smooth muscles relaxation. These above change leads to vasodilation and a corresponding reduction in BP.CCBs blood pressure regulation is independent of patients renin status. CCBs are effective in lowering of blood pressure and decreasing cardiovascular event in the elderly with isolated systolic hypertension. Examples: Nifedipine, Diltiazem, Nicardipine, Amlodipine, Foelodipine.

## A.13 (e) ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITORS

The ACE inhibitors are one of the first choice drugs in all grade of essentials

as well as renovascular hypertension. Most patients require relatively lower doses. Used alone they control hypertension in patients, and addition of diuretics / β blocker extends efficacy to 90%. The ACE facilitates production of angiotensin II, which as a major role in regulating arterial BP. ACE is distributed in many several different cell types including endothelial cells. The major site for angiotensin II production is the blood vessels. ACE inhibitors block the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor and stimulator of aldosterone secretion. ACE inhibitors also block the degradation of bradykinin and stimulate the synthesis of other vasodilating substances including prostagladilin and prostacyclin. The fact that ACE inhibitors lower BP in patients with normal plasma renin activity suggests that bradykinin and perhaps tissue production of ACE are important in hypertension.

ACE inhibitors widen or dilate blood vessels to improve the amount of blood heart pump and lower blood pressure. ACE inhibitors also increase blood flow, which helps to decrease the amount of work heart has to do and can help protect the Kidneys from the effects of hypertension and diabetes. ACE inhibitors are used in many indications including high blood pressure, heart failure, Heart Attack, and preventing kidney damage associated with high blood pressure and diabetes. Examples: Captoril, Enalapril, Lisinopril, Quinapril, Ramipril, Fosinopril.

**A. 13 f) ANGIOTENSIN II RECEPTOR ANTAGONISTS (ARBs)**

ARBs produce blood pressure reduction by antagonizing the effects of angiotensin II, thus relaxation of smooth muscle is produced which leads to vasodilation, increase renal salt and water excretion, reduce plasma volume and decrease Cellular hypertrophy. The ARBs have the same effects as ACE inhibitors

but work by different mechanism.ARBs also overcomes some disadvantages of ACE inhibitors, which not only prevents the conversion of angiotensin I to angiotensin II but also prevent the ACE-mediated degradation of bradykinin.

Clinical Trials comparing ARBs with active controls have reported significant reductions in stroke in ARB treated patients. Data on ARBs and other drugs that activate the RAS support a potential role for RAS in protecting against stroke [32].

Clinical trials have also demonstrated that ARBs is effecting against in reducing the risk of CV mortality, stroke HF, and a new onset atrial fibrillation[33].Ongoing trials are expected to confirm and may be extend the place of such agents for improving CV outcomes[34].

The addition of thiazide diuretic can increase the efficacy significantly. ARB therapy offers a significant reduction in progression of nephropathy in hypertensive patients with diabetes and a reduction in risk of CV events in patients with LV dysfunction. ARB therapy is an alternative to ACE inhibitor therapy in intolerant patients. ARBs show the lowest incidence of side effects compared with other antihypertensive drugs. The ARBs have advantage over ACE inhibitors since they didn't produce dry cough. Examples: Losartan, Candesartan, Irbesartan, Valsartan, Telmisartan.

**A. 13 g) VASODILATORS:**

The vasodilators directly act on arteries and with little action on Veins. Vasodilators produce better reduction in diastolic blood pressure than systolic blood pressure. Vasodilators are combined with diuretics and sympatholytic agents for

Achieving better therapeutic response. Vasodilators are used in hypertensive Crisis and are administered intravenously to rapid lowering of blood pressure.

Examples

Arterial: Hydralyzine,Minoxidil, Diazoxide, Fenoldopam.

Arterial and venous: Nitroprusside.

**2. DIABETES MELLITU S**

The Diabetes Mellitus is a commonest endocrine disorder. This is a chronic condition and is characterized by hyperglycemia due to impaired insulin secretion with or without insulin resistance. Diabetes is developed in people when the pancreas does not produce enough insulin or when the cells in the muscles, liver and fat do not use insulin properly or due to combination of both of the above reasons. Due to this the amount of glucose in the blood increases while the cells are starved of energy. High blood glucose, also called hyperglycemia. The most common forms of diabetes are type 1(10%), which is an autoimmune disorder and type 2 (90%), which is associated with obesity. Gestational diabetes is the form of diabetes occurring during pregnancy. Other forms of diabetes are rare and are caused by a single gene mutation.

It is a metabolic disorder which is characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism resulting due to defects in insulin secretion, insulin action or both.

**2.1 DEFINITION**

Diabetes mellitus (DM) a group of metabolic disorders characterized by

Hyperglycemia and abnormalities in carbohydrate, fat, and protein metabolism. It results from defects in insulin secretion, insulin sensitivity, or both. Chronic micro vascular, macro vascular, and neuropathic complicating issue.

## 2.2 CLASSIFICATION OF DIABETES MELLITUS

Out of many types, the most common ones are[35]

1. Type 1 Diabetes Mellitus

   Immune mediated

   Idiopathic

2. Type 2 Diabetes Mellitus

3. Other specific types of diabetes

   Genetic defects of islet β-cell function

   Genetic defects of insulin action

   Diseases of the exocrine pancreas

   Endocrinopathies.

   Drug-or chemical-induced diabetes

   Other genetic syndromes

## 2.3 EPIDEMIOLOGY

In 2000, according to the WHO, at least 171 million people worldwide suffer from Diabetes which is about 2.8 % of the population. The incidence of diabetes is increasing rapidly. By 2030 it is estimated that this number will almost double. Diabetes mellitus occurs throughout the world, but it is more common

(Especially type 2) in the developed countries. The greatest increase in incidence is expected to occur in Asia and in Africa, where most patients will probably be found by 2030. The increase in incidence of diabetes in developing countries is due to the trend of urbanization and lifestyle changes, perhaps most importantly due to their 'Western -style' diet.

Diabetes mellitus prevalence is expected to increase with age and the number of older persons with diabetes is expected to increase as the number of elderly population increases. Type 1 diabetes accounts for 5-10% of cases that affects 1 of 400 children and adolescents. Type 2 diabetes accounts for about 90-95 % of all cases of diabetes and is relatively common. It can go undiagnosed for many years. But the number of cases that are being diagnosed is also rising rapidly and that leads to reports of a diabetes epidemic.

**2.4 DIAGNOSIS OF DIABETES MELLITUS**

- Fasting plasma glucose (FPG).
- Oral Glucose Tolerance Test (OGTT).
- 2 Hour Post Prandial Glucose Level (2HPPG).
- Glycosylated Hemoglobin (HbA1C):

**2.4 PATHOPHYSIOLOGY**

**2.4 (A) PATHOPHYSIOLOGY OF TYPE 1 DIABETES/IDDM:**

It is characterized by absolute insulin deficiency either through autoimmune attack on pancreas, a viral infection or is idiopathic. As a result cells in the Islets of Langerhans in the pancreas are destroyed resulting in hypoinsulinaemia. The cause

of type - 1 Diabetes is still not fully understood but it is believed to be of immunological origin.

### 2.4 b) PATHOPHYSIOLOGY OF TYPE 2 DIABETES

The two metabolic defects that characterize type 2 diabetes are

1. The derangement in β-cell secretion of insulin
2. The inability of the peripheral tissues to respond to insulin.

### 2.5 TREATMENT:

The two main goals of treatment are[37]:

1. Reduction of mortality and concomitant morbidity due to assorted diabetic complications.
2. Preservation of quality of life.

### 2.5 (a) NON PHARMACOLOGICAL TREATMENT

Lifestyle modifications are the cornerstone of management of diabetes mellitus and include the prescription of a healthy diet, regular exercise, the management of stress, and avoidance of tobacco.

### 2.5 (b) PHARMACOLOGICAL TREATMENT

1. **BIGUANIDES**: **Metformin.**

2. **THIAZOLIDINEDIONES:** Pioglitazone, Rosiglitazone.

**3. SULFONYLUREAS:**

First generation Tolbutamide,Chlolrpropamide.

Second-generation: Glipizide,Glibenclamide,Glimerpiride,Glicazide

4. **MEGLITINIDE**S: Repaginate and Nateglinide [38].

5. **ALPHA GLUCOSIDASE INHIBITORS:** Acarbose, Miglitol and Voglibose

# REVIEW OF LITERATURE

## 2. REVIEW OF LITERATURE

**P.R Anand vijayakumar et al.,[39](2013)** conducted a study on the pleiotropic effects of Telmisartan and Olmesartan in hypertensive patient with metabolic syndrome. Telmisartan 20mg/day and Olmesartan 10mg/day were administered to group A&B dictation CM respectively for 2 months. The blood pressure lipid profile TC,TGL,LDL, HDL &VLDL)&FBS were measured on baseline and at end of study. Both of the study drugs demonstrate the significant reduction in blood pressure, FBS, LDL and VLDL. And Telmisartan is considered as an ideal agent in patients with elevated lipid profile because of its significant increase ($p<0.05$) in the level of HDL after two months of treatment. The pleiotropic effects of Telmisartan showed with two months of study recommended the use of the drugs in metabolic syndrome patients

**Yuji shimizu et ai.,[40](2020)** has studied the metabolic effect of combined Telmisartan and Nifedipine therapy in patients with essential hypertension. The patients were initiated on telmisartan (40 mg/day). If their office BP was not reduced to 140/90 mmHg after 6 weeks, Nifedipine (20-40mg per day) was added for 18 weeks. In the study Telmisertan showed a reduction in blood pressure and (HOMA-IR), but didn't reduced the adiponection or leptin levels. Telmisartan sounds for favorable metabolic effect in hypertensive patients without pre-existing metabolic disorders.

**Naziayasmeen et al.,[41](2011)** has conducted a study on efficacy and tolerability of different antihypertensive drugs in patients with essential Hypertension. Drugs used were Atenolol (A) 50mg, Enalapril(E) 5mg, Nifedipine (N) 10mg and

Furosemide (F) 40 mg in monotherapy (n=86) and in second and third drugs combination (n=166). After 8 weeks of therapy patients were assessed for efficacy and tolerability. In the study highest decrease in SBP was seen in A+E+N combination (29.2%) and in DBP with N+F combination (17.7%). all the drugs group from mono therapy and combination therapy BP effectively. Most effective group were A+E+N and N+F combination. Enalapril was effective and most frequently used drug.

**SE KJeldsen et al:[42] (2010)** has studied the effects of losartan vs candesartan in reducing cardiovascular event in the primary treatment of hypertension. There was no difference in blood pressure reduction when comparing the losartan and Candesartan group during follow up. Compared with the losartan group, the candesartan group had a lower adjusted hazard ratio for total CVD, heart failure, Cardiac arrhythmias, and peripheral artery disease. The observation of study suggesting that, since there is no difference in blood pressure reduction then the divergent clinical outcomes are due to difference in the pharmacological of the drugs.

**R.M Nixon et al.,[43] (2009)** Conducted a study on valsartan Vs other angiotensin II receptor blocker in the treatment of hypertension. Six studies include trail arm with Candesartan, six Irbesartan, and 13 Losartan, two Olmesartan, five Telmisartan and 12 valsartan. The study reported change in systolic and diastolic blood pressure from base line to follow upping 12 weeks The weighted-average reduction in means SBP and DBP for Valsartan 160 mg 15.32 / 11.3 mm Hg and for Valsartan 320 mg was 15.85/11.97 mmHg: these are statistical significantly greater protection compared with Losartan 100 mg, which was 12.01 mmHg and

9.37mmHg for SBP and DBP respectively. This paper shows that Valsartan at doses of 160 mmHg or 320 mg is more effective at lowering blood pressure than losartan 100 mg. For other ARBs at comparable does valsartan achieves comparable antihypertensive efficacy.

**Paolo Verdecchia et al.,[44] (2009)** conducted a study named "Comparative assignment of angiotensin receptor blockers in different clinical settings". The primary outcome was the time to onset of diabetic nephropathy, defined by persistent albuminuria. The primary endpoint was achieved by 14.9% of patients with placebo 9.7% of patients with Irbesartan 150 mg (P=0.08) and 5.2% of patients with Irbesartan 300 mg (p = 0.001). These effects where independent of BP changes. The overall message of the trails examined in this review is that intervention with ARBs at different steps of the cardiovascular diseases Continuum is effective to slow down or black the diseases progression, with consequent measurable benefits. The study result shows that, Telmisartan reduced the cardiovascular event in a broad population of patients with high cardiovascular risk, with a protective effect similar to the ACE- inhibitor comparator Ramipril. Losartan was superior to the beta-blockers atenolol in reducing the risk of stroke in patients with hypertension and LV hypertrophy. In patients with type 2 diabetes and nephropathy, Losartan in addition to conventional therapy reduced proteinuria and the progress to end stage renal disease. In patients with chronic heart failure, losartan proved to be an alternative therapeutic option in patients intolerant to ACE-inhibitors

**Shiho Nakayama et al.,[45] (2008)** studied the effects of Olmesartan and Telmisartan on blood pressure and metabolic parameters in early stage Type-2

Diabeties with hypertension, in this open-label prospective crossover study, they compared the effects of Olmesartan (20 mg/day) and telmisartan (40 mg/day). They analyzed the blood pressure lowering effects of each drugs by 24 hours ambulatory blood pressure monitoring at 0 8 and 16 weeks and metabolic parameters and information makers. Olmesartan lowered means systole and diastole blood pressure more significantly than Telmisatan. While they were no differences between the groups in metabolic parameters.

**Derosa et al.,[46] (2007)** studied the metabolic effects of Telmisartan and Irbesartan in type 2 diabetic patients with metabolic syndrome treated with rosiglitazone. Evaluation were done on mass index, glycosylated hemoglobin, fasting plasma glucose, fasting plasma insulin, homeostasis model assignment index, total cholesterol, low density lipoprotein, and high density lipoprotein-cholesterol, triglycerides, systolic blood pressure, diastolic blood pressure adiponectin and resistin during 12 months of this treatment.in addition to a comparable antihypertensive effect for Telmisartan And Irbesartan after 6 and 12 months, both treatments were associated with significant reduction in TC and LDL plasma level compared with baseline. After six months of treatment, only the Telmisartan group experienced a significant improvement in (HbA(1c)),FPG, Homa-IR, adiponectin and resist in compared with the baseline values, whereas both drug regimens were associated with a significant improvement in these parameters after 12 months, However, the improvements observed in that Telmisartan group were significantly larger than the noted in the Irbesartan group. FPI significantly described only after 12 months of treatment in both groups, but again, the reduction was significantly larger in the Telmisartan- treated subjects. Telmisartan seemed to

Improve glycaemic and lipids control and metabolic parameter of the metabolic syndrome better than Irbesartan.

**Nagel et al.,[47] (2006)** compared Telmisartan 40 mg versus placebo in 20 individuals with insulin resistance (homeostatic model assignment [HOMA] INTEX > 2.3) and abdominal obesity( body mass index [BMI]>25kg/$m^2$ and waist circumference>95cm in males or 80cm in females) in a randomized, crossover trail lasting 12 weeks. Compared to placebo, Telmisartan promoted a significant reduction in the glucose area under curve (AUC) during an oral glucose tolerance test (11%; p=.04). Non-significant changes in the HOMA index (11% reduction; p=.06) and adiponectin (6%; p= increase.09) were also present during Telmisartan treatment.

**R Asmar et al.,[48] (2005)**- conducted a study on effectiveness of an angiotensin receptor blockers in blood pressure control. Variation in blood pressure with individual ARBs are taken into comparison in the study. The study drugs included were Losartan, irbesartan, candesartan, Telmisartan, and Olmesartan. Several newer ARBs have been reported to provide equivalent antihypertensive efficacy to Amlodipine and greater efficacy than Losartan, Valsartan or both. Secondly, increase in dose may improve the antihypertensive efficacy of agents such as Valsartan, although clinical studies are necessary to provide characterization of new, higher- dose monotherapy. Thirdly, fixed dose combinations with hydrochlorothiazide (HCTZ) increase the antihypertensive effect of all ARBs.

**Vitale et Al.,[49](2005)** conducted a study on metabolic effects of Telmisartan and Losartan in hypertensive patients with metabolic syndrome. At baseline and end

of treatment fasting and post pradinal plasma glucose, lipid profile, insulin sensitivity, and the systolic and diastolic pressure were determined. After 3 months' telmisartan reduced 24-hour means SBP and DBP significantly more than Losartan. There was no significant correlations between the decrease in blood pressure and the change in FPG ($p=0.020$) or FPI ($p=0.012$).Both Telmisartan and losartan were well tolerated. On comparison it is founded that the Telmisartan but not losartan, significantly ($p<0.05$) reduce free plasma glucose. The results of this study explains as well as providing Superior blood pressure control, Telmisartan unlike Losartan, displayed insulin sensitizing activity.

**Derosa G et Al.,[50] (2004)** has studied the effects of Telmisartan compared With Eprosartan on blood pressure control, glucose metabolism and lipid profile in hypertension, type 2 diabetic patients. Evaluated the antihypertensive activity, homeostasis and plasma lipid profiles. Compared with baseline, a significant reduction ($p<0.01$) in seated through systolic blood pressure (SBP) was detected after 12-month treatment with either Telmisartan or Eprosartan. The antihypertensive effect of Telmisartan was significantly Superior ($p<0.05$).No change in body mass index or glucose metabolism was observed with either active treatment, or with placebo. Telmisartan, but not Eprosartan, significantly improved plasma total cholesterol ($p<0.01$), Low- density lipoprotein cholesterol ($p<0.01$) and triglycerides ($p<0.05$) compared with Eprosartan. The 12-Month Telmisartan treatment produced a significantly greater reduction in DBP than Eprosartan and significantly improved plasma lipids.

**Michael schupp et Al.,[51] (2004)-**has studied in angiotensin type 1 Receptor blackest includes Peroxisome Proliferator-Activated Receptor-y Activity.

The finding of the study sounds that, ARB Losartan enhanced aP2 expression only at high concentration. Where Eprosartan had no significant effects, Irbesartan and Telmisartan (10 pmol/L) markedly induced transcriptional activity of PPARy. Irbesartan and Telmisartan also induced PPARy activity in an $AT_1R$- Deficient cell model, demonstrating that these ARBs Stimulate PPARy activity independent of their $AT_1R$ blocking actions. The study demonstrates that a specific subset of ARBs induces PPARy activity, there by promoting PPARy-dependent differentiation in adipocytes. The activation of PPARy demonstrates new pleiotropic actions of certain ARBs, providing a potential mechanism for their anti-diabetic effects.

**UjalaVerma et Al.,[52] (2004)** did a study on Antihypertensive efficacy of Carvedilol and Amlodipine in patients of mild to moderate hypertension. Blood pressure was recorded in the sitting and standing position during follow-up visit at 2,4,8 & 12 weeks. Dosage adjustment if needed were made at 4 and 8 weeks of study. Both carvedilol and Amlodipine produced a statistically significant ($p<0.001$) and dose related fall in SBP and DBP. On comparative analysis of the effect of Carvedilol and Amlodipine on BP. Amlodipine produced a greater fall in sitting and standing SBP at all study intervals as compared to Carvedilol, with statistically significant fall at 8 and 12 weeks ($p<0.01$). The finding of the study indicate that Carvedilol has become an alternative treatment for mild to moderate hypertension.

**Daholf B et Al.,[53] (2002)** conducted a study on cardiovascular morbidity and mortality in the losses and LVH ascertained by electrocardiography (ECG).They observed out that blood pressure fell by 30.2/ 16.6 (SD 18.5/10.1)and 29.1/16.8 mm Hg (19.2/10.1) in the Losartan and Atenolol groups, respectively. New-onset diabetes was less frequent with Losartan. Interpretation Losartan prevents more

cardiovascular morbidity and death than atenolol for a similar reduction in blood pressure and is better tolerated. Losartan seems to confer benefits beyond reduction in blood pressure.

**Lerch M et Al.,[54] (1998)** studied the effects of angiotensin II - receptor blockade with losartan on insulin sensitivity, lipid profile, and endothelin in normotensives off spring of hypertensive patients. Insulin sensitivity index (**SI**), determined by the minimal model method of Bergman, fasting plasma insulin and glucose concentrations total and **HDL** cholesterol serum triglycerides, and plasma **ET-1**levels were assessed. Compared with placebo, Losartan administration did not significantly modify SI, fasting plasma insulin and glucose. Plasma **ET-1** levels also did not differ decreased significantly between the placebo and Losartan serum total cholesterol and triglycerides decreased significantly with Losartan treatment. Body weight, BMI, heart rate (**HR**), Blood pressure (**BP**), and 24 hours urinary sodium, potassium, and creatinine values were stable throughout the study. These findings demonstrate that losartan 50 mg daily, does not alter insulin sensitivity and **ET-1** in normotensive offspring of essential hypertension patients. The study shows that the Losartan significantly reduced serum total cholesterol and total triglyceride level...

**Pedro Luis de Pablosvelasco et al.,[55] (1998)** has studied the effects of Losartan and Diltiazem on Blood pressure, Insulin Sensitivity, Lipid Profile and Microalbuminuria in Hypertensive Type 2 Diabetic Patents. At baseline and after 3 months, plasma glucose hemoglobin, uric acid, lipid profile, albumin excretion rate and creatinine clearance, Insulin sensitivity was estimated by an insulin suppression test, and ambulatory blood pressure was monitored for 24 hours Different between the two treatments were not significant. Insulin sensitivity and

lipid profile was not modified any of the treatment and no adverse effects were reported. Both drugs were well tolerated and effectively reduced blood pressure and albuminuria, but did not modify insulin sensitivity or lipid profile

# DRUG PROFILE

# 3. DRUG PROFILES

## 3.1 LOSARTAN POTASSIUM

NAME. : Losartan potassium

BRAND NAME : Cozaar

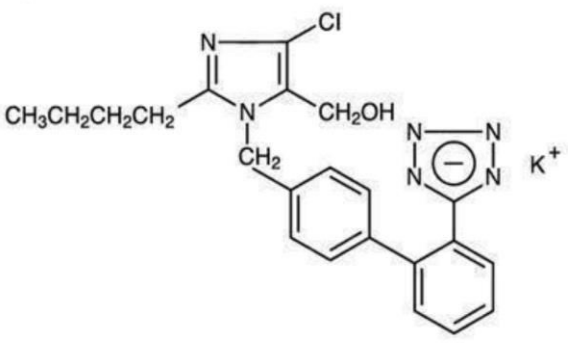
**DESCRIPTION** [56] **:**

Losartan potassium is an anti a potential drug belongs to the class ARB (Angiotensin receptor II antagonist). Losartan potassium is a non peptide molecule Shows high affinity to the angiotensin receptor II. And the drug inhibits the action of the angiotensin receptor II on vascular smooth muscles. As the results of inhibitory Action a reduction in blood pressure is obtained.

**CHEMICAL IUPAC NAME:**

Mono potassium salt of 4-buty1-4chloro-1-[[2'-(1H-tetrazol-5-Y1) [1,r-biphenyl]-4-y1]methy1]-1H-imidazole -5-methanol.

**CHEMICAL FORMULA:** C22H22QKN60



**MOLECULAR WEIGHT** : 461.0 Daltons

**STATE** : White to off white crystalline powder

**MELTING POINT** : 461.01° **C**

**THERAPEUTIC CATEGORY**

Antihypertensive (angiotensin receptor antagonist)

**PHARMACOLOGY:**

Angiotensin II [formed from angiotensin I in a reaction catalyzed by Angiotensin converting enzyme (ACE, kininase II)], is a potent vasoconstrictor, the primary vasoactive hormone of the renin-angiotensin system and an important component in the pathophysiology of hypertension. It also stimulates aldosterone secretion by the adrenal cortex. Losartan and its principle active metabolite block the Vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II the AT1 receptor.

**MECHANISM OF ACTION:**

Angiotensin II [formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme (ACE, kininase I)], is a potent vasoconstrictor, the primary vasoactive hormone of the renin-angiostension system and an important component in the pathophysiology of hypertension. It also stimulates aldosterone secretion by the adrenal cortex. Losartan and its principle active metabolite block the Vasoconstrictor and aldosterone-secreting effects of angiotensin I buy selectively blocking the binding of angiotensin II the AT1 receptor found in many tissue,

(e.g., vascular Smith muscle, adrenal gland). There also an AT2 receptor found in many tissues but it is not known to be to be associated with cardiovascular homeostasis. Both Losartan and its principle active metabolic do not exhibit any partial agonist activity at the AT1 receptor and have much greater affinity (about 1000-fold) for the AT1 receptor than for the AT2 receptor. Neither losartan nor it's active metabolite inhibits ACE (kininase I, the enzyme that converts angiotensin l to angiotensin II and degrades bardykinin); nor do they bind to or block other hormone receptors or icon channels know to be important in cardiovascular regulation.

**DOSAGE FORM:**

Form: Tablet

Route: Oral

**PHARMACOKINETIC:**

**ABSORPTION:**

The drugs will observe administration along with the food shows a slight decrease in absorption and it has only minor effects on losartan active metabolite AUC. Systemic bioavailability of losartan is about 33 %

**DISTRIBUTION:**

Volume of distribution is 34 L (losartan) and 12 L (metabolite)

**PROTEIN BINDING**

Losartan and active metabolite are highly binds to plasma protein, primarily albumin. Neither Losartan nor metabolite accumulates in plasma upon repeated daily dosing.

**METABOLISM:**

Losartan undergoes substantial first pass metabolism by CYP-450 2CP and 3A4 enzymes. 14% of an oral dose is converted to an active carboxylic acid metabolite is responsible for most of the angiotensin II receptor antagonist activity.

**ELIMINATION:**

The H2 of Losartan is 2 hr and that of metabolite is 6 to 9 hr. Renal clearance of Losartan is 75 ml/min and that of metabolite is 25ml/min. Biliary excretion contributes to the elimination of losartan and metabolite. About 4% is excreted unchanged in the urine and 6% excreted as active metabolite in urine.

**INDICATION:**

The drug is used alone or in combination with other classes of antihypertensive drugs. It is used in treatment of hypertension, diabetic nephropathy in hypertensive patients with type 2 diabetes mellitus; reduce risk of stroke in patients with hypertension and left ventricular hypertrophy.

**CONTRAINDICATION:**

Losartan potassium tablets are contraindicated in patients who are hypersensitive to any components of this product.

**INTERACTION:**

**Drug - drug:**

Fluconazole: Fluconazole elevates plasma level of losartan which will lead to increase the antihypertensive and adverse effects.

**Indomethacin:** The antihypertensive effects of losartan may be blunted.

**Rifamycins:** Rifamycins like rifampin reduces plasma level of Losartan thus antihypertensive effects of lecithin got reduced.

**Drug and Lifestyle:**

**Alcohol use**: it enhances the hypotensive effects of the drug, Avoid use of alcohol and drug together.

**ADVERSE REACTION:**

The adverse drug reaction Losartan potassium includes, hypertension, orthostatic hypertension, CNS side effects, GI side effects, UTI infection, hypersensitivity reaction

**SPECIAL POPULATION:**

Close monitoring must be practiced in patients with hepatic impairment, renal impairment. During the pregnancy losartan is suggested to be stopped.

**PREGNANCY:**

When used in pregnancy during the second and third trimester drugs that act directly on renin Angiotensin system can use injury and even death to the

developing fetus. When pregnancy is detected discontinued therapy as soon as possible

**Children:**

Safety and efficacy not established in hypertensive patients younger than 6 years of age or in children's

**Renal function:**

Use caution in treating patients who renal function may be depend on the Rennin-Angiotensin Aldosterone System.

**Hepatic function:**

A lower starting does is recommended for patients with hepatic impairment.

**3.2Telmisartan**

**NAME** : Telmisartan

**BRANDNAMES** : Micardis, Taylor, Telday

**DESCRIPTION** [57] :

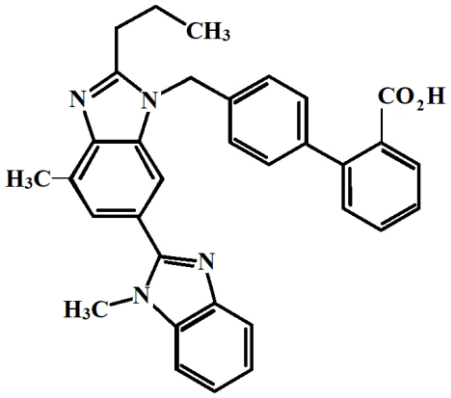
Telmisartan is an antihypertensive drug belongs to the class ARB (angiotensin receptor II antagonist). Telmisartan shows high affinity to the angiotensin receptor II, and the drug inhibit the action of the angiotensin II on Vascular smooth muscles. As the result of inhibitory action a reduction in blood pressure is obtained. As per the suggestions of recent studies, Telmisartan also having beneficial metabolic effects because of PPAR-gamma agonistic action.

**CHEMICAL IUPAC NAME:**

4'-[1(1,4'-Dimethy] -2'-propyl [2,6'-bi-1H-benzimidazonl]-1' - y1) methyl] -[1,1'-biphenyl]-2-carboxylic acid

**CHEMICAL FORMULA: C33H30N402**

CHEMICAL STRUCTURE:




**MOLECULAR WEIGHT** : 514.69 Daltons

**STATE** : white solid

MELTING POINT : **261-263$^0$C**

**THERAPEUTIC CATEGORY: $H_3C$**

Antihypertensive (angiotensin receptor II antagonist)

**PHARMACOLOGY:**

Telmisartan is a non peptide molecule, which orally active. It selectively and inhibits the angiotensin II AT1recetor the subtype. Telmisartan shows much

greater affinity (>3, 000 fold) for the AT1 receptor than for the AT2 receptor. Angiotensin II is the principal factor of rennin angiotensin system. Telmisartan inhibitory action brings out the desirable effects like relaxation of smooth muscle thereby vasodilation, increased renal excretion of salt and water and refused plasma volume. Telmisartan also have beneficial metabolic effects of PPAR -gamma agonistic action. PPAR-gamma is nuclear receptor related to the insulin sensitizing effect, PPAR-gamma agonistic action improve insulin sensitivity and lipid profile in patients with

**METABALIC SYNDROME:**

Telmisartan bind with the angiotensin I ATI receptor in adrenal gland and Vascular smooth muscle, mode of binding is selective and reversible. The systemic vascular resistance is produced by the blockade of the angiotensin II. The angiotensin II is a Vasoconstrictor which produces elevation in blood pressure. Telmisartan is a selective antagonist of angiotensin II receptor because it does not inhibit the angiotensin converting enzyme, other hormone receptors, or ion channels. Studies also suggested that Telmisartan having partial agonist activity towards PPAR gamma. PPAR gamma is an established target for antidiabetic drugs. This sound that telmisartan can improve carbohydrate and lipid metabolism and control insulin resistance

DOSAGE FORM:

FORM: Tablet

ROUTE: Oral

**PHARMACOKINETICS:**

**ABSORPTION:**

The bioavailability of drug depends on dosage. Administration of Telmisartan with food shows a 6% decrease in bioavailability. Peak plasma concentration generally reached at 0.5 -1 hour following oral administration.

**DISTRIBUTION:**

Volume of distribution is 500 L

**PROTEIN BINDING:**

Protein binding is >99.5%, principally albumin and ai-acid glycoprotein

**METABOLISM:**

Metabolized in liver, conjugated into inactive acylgucuronide it has been identified in human plasma and urine.

**ELIMINATION:**

When administered orally duration of action is 24 hours. The drugs is excreted unchanged in the feces via biliary excretion mainly; small amount of drug is eliminated through urine.

**INDICATION:**

The drug is used alone or in combination with other classes of antihypertensive drugs. It is used in treatment of hypertension, diabetic nephropathy in hypertensive patients with type 2 diabetes mellitus, and in congestive heart failure population who can't tolerate ACE inhibitors.

**CONTRAINDICATION:**

Drug is contraindicated in pregnancy and in patient who hypertensive to drugs and its components. Cautious usage is suggested in patients with biliary Obstruction disorders, renal or hepatic insufficiency and in those with an activated rennin- angiotensin system.

**INTRACTION:**

**Drug- Drug**

Digoxin: Telmisartan increase digoxin plasma levels. Digoxin levels must be monitored closely.

Warfarin: Telmisartan decrease the plasma warfarin level, patient must be monitored closely.

**Drug and lifestyle:**

**Alcohol use:** it enhance the hypotensive effects of the drug. Avoid use of alcohol and drug together.

**ADVERSE REACTION:**

Upper respiratory tract infection, sinusitis, pharyngitis, back pain diarrhoea.

**SPECIAL POPULATION:**

Close monitoring must be practiced in patient with hepatic impairment, renal impairment. Drug must not be used in pregnancy and lactation.

**Pregnant patients:**

Use of drug is contraindicated during pregnancy because of potential risk of fetal and neonatal morbidity and death

**Breast feeding patient:**

Assess risk and benefits before continuing drug in breast feeding women. Because it is not known Telmisartan is secreted in human milk.

**Pediatric patients:**

Safety and efficacy in children have not been established

**Geriatric patients:**

No significant difference has been reported compared to younger patient

# AIM AND OBJECTIVE

# 4. AIM AND OBJECTIVES

## SCOPE OF THE STUDY

Hypertension is currently affects, approximately one billion adult globally. It is a major risk factor for cardiovascular diseases (CV) and stroke. The high prevalence of hypertension has contributed to the present pandemic of CV disease, which now account for 30% of all deaths worldwide

As the population ages and the prevalence of contributing factors such as obesity, sedentary lifestyle and smoking rise, this figure is projected in increase by 60 % to 1.56 billion by the year of 2025

The risk of hypertension increases with age and is associated with gender and ethnicity. The morbidity and mortality associated with uncontrolled hypertension result in a substantial economic burden as a result of drug costs, hospitalizations, surgery and other healthcare resources. This cost is compounded by the humanistic burden and effect on quality of life associated with lifestyle modifying adverse events.

Angiotensin receptor blockers (ARBs) have become established as a major class of antihypertensive on the basis of their powerful effects on blood pressure (BP), excellent to liability and Pleiotropic end-organ-protective effects. However, individual ARBs vary in antihypertensive efficacy, which may be important to clinical outcome. It is well established that achieving ambitious BP target improves long-term clinical outcomes in the management of hypertension

The present study was to compare the effect of efficacy of losartan potassium and

Telmisartan, both are belongs to the above mentioned classes of angiotensin receptor blockers (ARBs) of the above Losartan Potassium is the prototype and a Telmisartan is a newly introduced ARB

**AIM:**

- The aim of the present study was to compare the efficacy of Losartan potassium 50mg Vs Telmisartan 40 mg in patients with hypertension.

**OBJECTIVE:**

**PRIMARY**

- To compare the efficacy of Losartan potassium 50mg Vs 40 mg
- To assess the mean change in Systolic Blood Pressure ( SBP) and Diastolic Blood Pressure (DBP) with Losartan Potassium and Telmisartan in a treatment period of three months.

**SECONDARY:**

To assess the mean changes in Fasting blood sugar (FBS) and post Pradinal blood sugar (PPBS).

# 5. PLAN OF WORK

The present dissertation work was planned to conduct a comparative study on efficacy of Losartan versus Telmisartan in hypertensive patient. The study conducted at Krishnagiri Head Quarters & Hospital, Krishnagiri.

**The plan of work includes:**

i. Submission of the protocol for getting the approval from ethical committee

ii. To get the consent letter from patient.

iii. Select hypertensive patient for study

iv. To design a data collection form

v. Select monitoring parameters.

vi. Patients divided into two GROUPS A& B

vii. Each groups containing 30 patients

viii. Prescribing drugs for GROUP A: losartan potassium 50 mg

ix. Prescribing drugs for GROUP B:telmisartan 40 mg

x. Checking of SBP and DBP FBS and PPBS on specified visit

Carrying out statistical analysis and recorded

# METHODOLOGY

# 5. METHODOLOGY

**Study site** Krishnagiri Head Quarters& Hospital, Krishnagiri

**Study design** Prospective observational study

**Duration of study** 3 months

**Dosage** Losartan potassium 50 mg

- A total of 60 patients were enrolled in the treatment
- A prospective and observational study was carried out to compare efficacy of losartan potassium vs. telmisartan 40 mg in patients with hypertension.
- The selected patients were divided into two groups. GROUP A, GROUP B.
- Group A(30 patients) were to be treated with losartan potassium 50 mg
- Group B (30 patients) were to be treated with telmisartan 40 mg

**STUDY CRITERIA INCLUSION CRITERIA**

- Patients aged between 30 - 59 years
- Patients who is having sustained Diastolic blood pressure > 90 mm Hg accompanied by elevated systolic blood pressure >140 mm Hg
- Patients who agreed with prescribed consent form

**EXCLUSION CRITERIA**

Patients with secondary hypertension.

- Patient who having other medicines with known effects on blood pressure.

- Patient who refuse to participate in study or withdrawing prescribed consent
- Pregnant and lactating women.

**PARAMETERS**

**Primary parameters**

- Systolic Blood Pressure
- Diastolic Blood Pressure
- FBS.
- PPBS.

**Secondary parameters**

- Height.
- Weight.
- BMI.

**STATISTICAL ANALYSIS:**

- The information collected regarding all the selected cases were recorded in a master chart. Data analysis was done with the help of computer (Microsoft Excel 2007)
- Using this software range, frequencies, percentage, means, standard deviations, and 'p' values were calculated. The student T-test was used to test the significant difference of quantitative variables, Chi square test was under to test the significant difference of qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

# OBSERVATION AND RESULTS

# OBSERVATION AND RESULTS

The work entitled comparative study of efficacy of losartan potassium 50 mg Vs Telmisartan 40 mg in patients with hypertension was carried out in department of general medicine at Krishnagiri Head Quarters & Hospital, Krishnagiri. A total number of 60 patients were enrolled in this study. These patients were diverted into two groups (A & B). Group A (30 patients) were treated with losartan potassium 50 mg and group B (30 patients) Telmisartan 40 mg

All primary and secondary parameters were recorded in that initial visit, systolic and diastolic blood pressure recorded at each follow-up of 15 days interval and the FBS and PPBS and weight were recorded at the end of the study. All the recorded parameters were compared to assess the efficacy

**Group A**: Losartan potassium 50 mg **Group B**: telmisartan 40 mg

## A. CHARACTERISTICS OF CASE STUDY

**Table 2: Age distribution**

| Age Group ( in years ) | GROUP A | | GROUP B | |
|---|---|---|---|---|
| | No. | % | No. | % |
| 30-39 years | 3 | 10 | 2 | 6.67 |
| 40-49 years | 11 | 36.66 | 12 | 40 |
| 50-60 years | 16 | 53.34 | 16 | 53.33 |
| TOTAL | 30 | 100 | 30 | 100 |
| Range | 38-59 | | 30-60 | |
| Mean | 50.17 | | 50.47 | |
| SD | 6.62 | | 6.25 | |

Out of 60 patients, 30 patients were of group A, out of these 3 patients (10%) between the age group of 32- 39 years, 11 patients (36. 66 %) between the age group of 40-49 years, 16 patients (53.34%) between the age group of 50 -60 years.

Out of 60 patients 30 patients were of group B out of these two patients (6.67 %) between the group of 32- 39 years 12 patients (40%) is between the age group of 40 -49 years 16 patients (53.33%)between the age group of 50-50 years.

**Age distribution**

**REQUENCY**

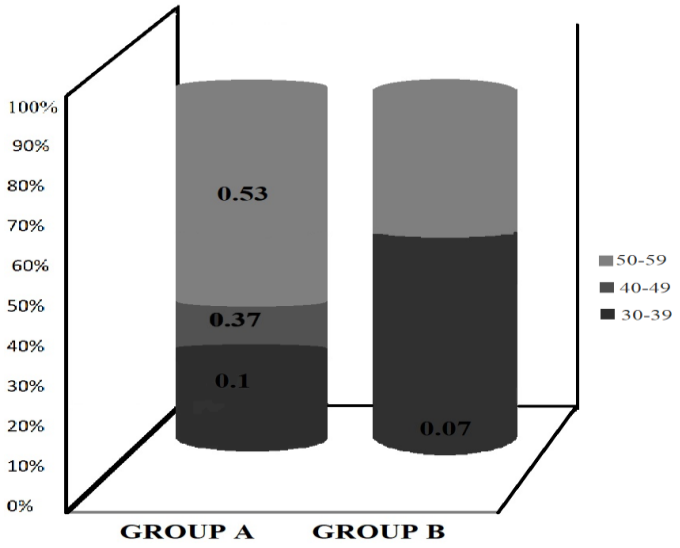



**Fig No.1**

The mean age of group A was 50.17 + 6.62 years and group B was 50.47 + 6.25.

**Table 3: Sex distribution**

| Age group ( in years) | GROUP A | | GROUP B | |
|---|---|---|---|---|
| | No. | % | No | % |
| Male | 18 | 60 | 20 | 66.67 |
| Female | 12 | 40 | 10 | 33.34 |
| Total | 30 | 100 | 30 | 100 |

A total of 60 patient were screened and randomized into two treatment group. Out of which 30 patients were of GROUP A, 18 patients (60%) were males, 12 patients (40%) were females. In case of GROUP B, 20, patients (66.67%) were males, 10 patients (33.34%) females.

**Sex distraction**

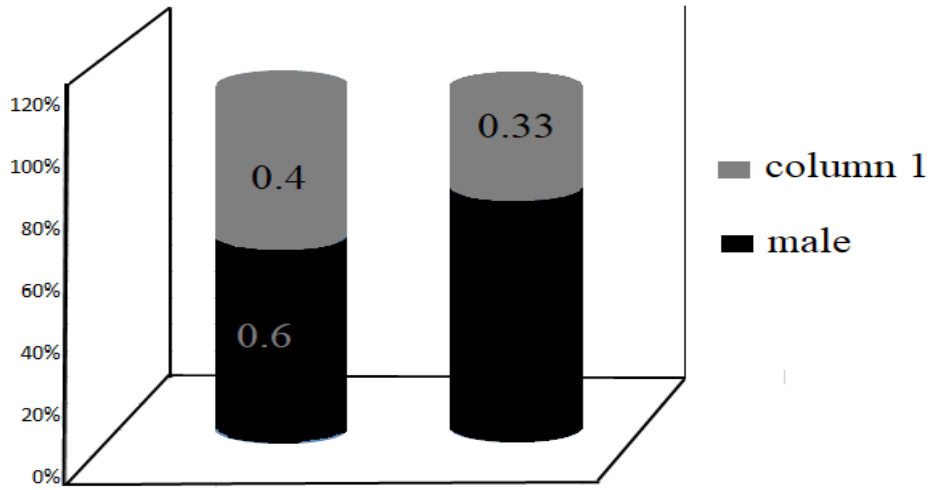


TABLE 4: PHYSIOLOGICAL PARAMETERS

| AGE GROUP (IN YEARS) | GROUP A | | GROUP B | | 'P' VALUE |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Weight (In Kg) | **74.1** | **5.97** | **70.57** | **5.84** | |
| Height (In Cm) | **163.77** | **6.3** | **161.77** | **6.95** | **0.1767** |
| BMI | **27.64** | **1.73** | **26.99** | **1.92** | |

The average weight of patient were 74.1+5.97 in GROUP A and 70.57+ 5.84 in GROUP B. The average height of patients was 163.77 + 6.32 in GROUP A and 161.77+ 6.95 in GROUP B. The average BMI of patients were 27.64 + 1.73 in GROUP A and 26.99 + 1.92 in GROUP B.

**Physiological parameters**

**Fig, no 3**

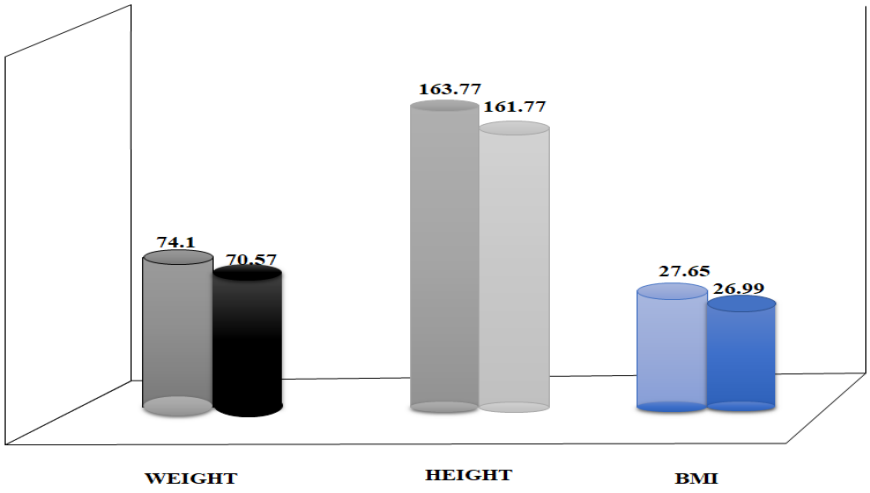


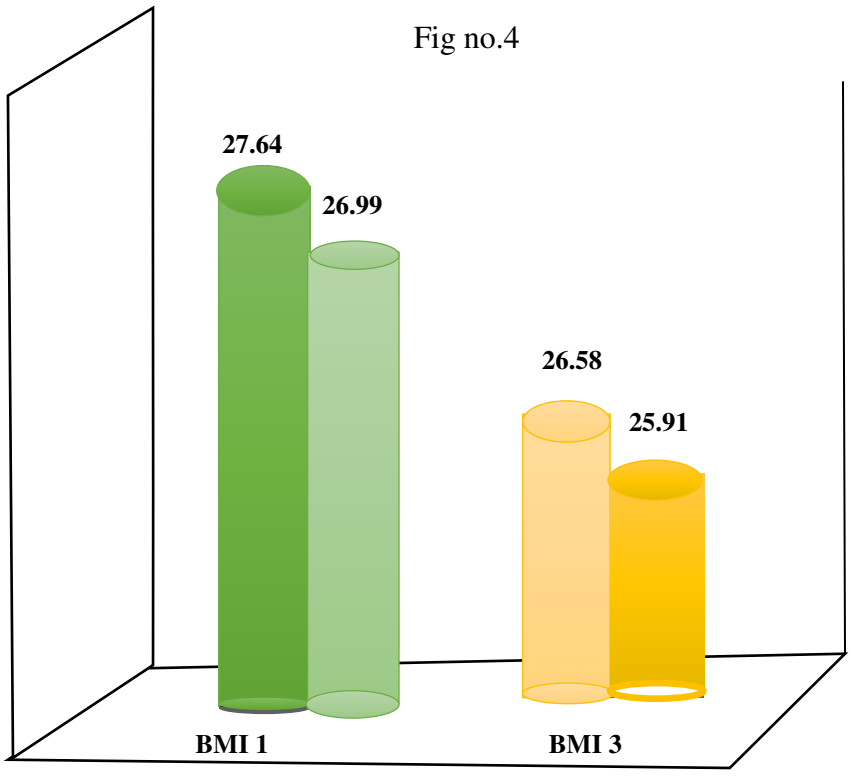
**Table 5: Change in BMI**

| BMI | GROUP A | | | GROUP B | | |
|---|---|---|---|---|---|---|
| | First Visit | Final Visit | Difference | First Visit | Final Visit | Difference |
| MEAN | 27.64 | 26.58 | 1.05 | 26.99 | 25.91 | 1.08 |
| SD | ±1.73 | ±1.75 | ±0.39 | ±1.9 | ±1.71 | ±0.71 |

The average BMI of patients after 3 month were 26.58 + 1.75 in GROUP A with difference of 1.05 + 0.39 from initial vale 2.64 and 25.91+ 1.71 in GROUP B with difference of 1.08 ±0.71 from initial 26.99

Change in BMI

Fig no.4



**B.EFFICACY OF THE TWO REGIMENS**

Tale 6: Change in Systolic Blood Pressure (SBP) – in mm Hg

| SBP vales at | SBP Values | | | | **'p'** values |
|---|---|---|---|---|---|
| | GROP A | | GROP B | | |
| | Mean | SD | Mean | SD | |
| First visit | 152.93 | 6.53 | 148.80 | 7.28 | 0.02 |
| Second visit | 147.06 | 6.30 | 140.94 | 7.12 | P<0.001 |
| Third visit | 142.87 | 6.50 | 134.06 | 7.11 | P<0.001 |
| Forth visit | 137.48 | 6.77 | 127.80 | 6.99 | P<0.001 |
| Fifth visit | 131.14 | 6.6 | 122.00 | 6.90 | P<0.001 |
| Sixth visit | 125.00 | 6.96 | 115.53 | 6.40 | P<0.001 |
| Decrease (first visit – sixth visit) | 27.94 | 3.09 | 33.27 | 3.42 | P<0.001 |

The systolic blood pressure showed significant reduction in the both group. The reduction was greater in GROUP B who was treated with Telmisartan 40 mg, than in GROUP A who were treated with Losartan potassium 50 mg.

The mean systolic blood pressure reduction in GROUP B was (33.27 ±3.42) & GROUP A was (27.94 ± 3.09) at the end of 3 month, which shows that the regimen have better impact on systolic blood pressure then GROUP A with statistically significant 'p' value less than 0.001

**Change in systolic blood pressure (SBP)**

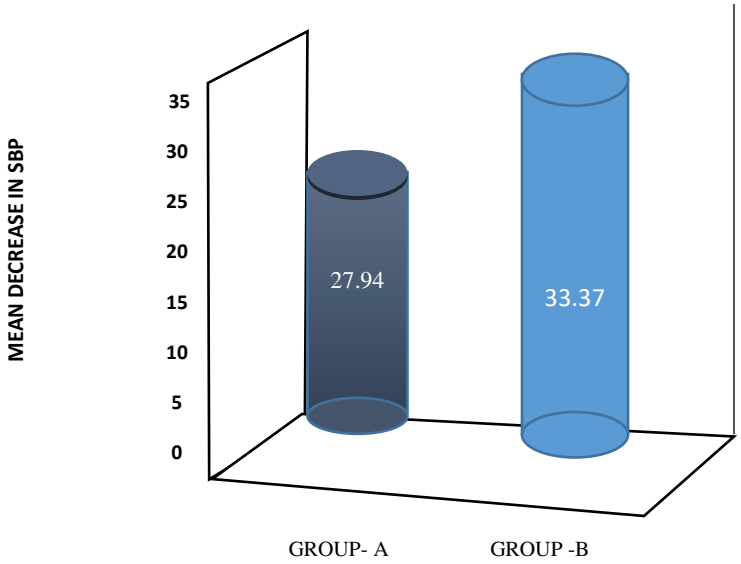
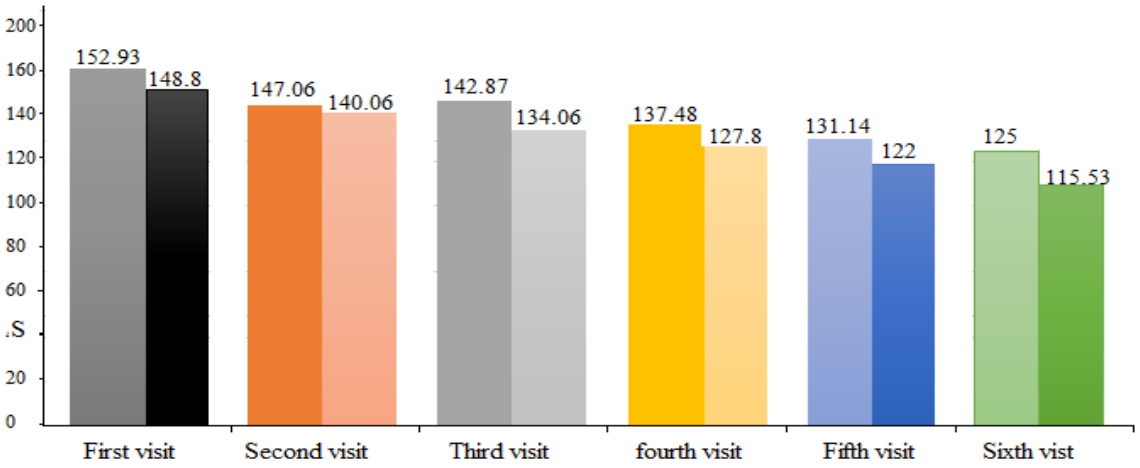



**Fig No .5 Change in Systolic Blood Pressure in Week Intervals.**




The SBP values of GROUP A and GROUP B were initially 152.93 + 6.53 & 148.8 +7.8 respectively and that was changed to 147.06+6.30 & 140.94+7.12 on second visit, then it changed to the levels of 142.87+6.50 & 134.06 + 7.11, 137.48 +6.77 & 127.8+6.99, 131.14+6.60 & 122+6.96, & 115.53+6.40 in further third, fourth fifth , sixth visits

**Table 7**

| DBP vales at | DBP Values | | | | 'p' Values |
|---|---|---|---|---|---|
| | GROUP A | | GROUP B | | |
| | Mean | SD | Mean | SD | |
| First visit | 93.73 | 3.39 | 93.27 | | 0.0561 |
| Second visit | 90.74 | 2.94 | 88.80 | 2.99 | 0.01 |
| Third visit | 87.33 | 2.53 | 85.14 | 3.18 | 0.004 |
| Forth visit | 85.60 | 2.75 | 85.14 | 3.18 | P<0.001 |
| Fifth visit | 84.20 | 2.59 | 81.20 | 3.22 | P<0.001 |
| Sixth visit | 82.20 | 2.53 | 78.80 | 3.13 | P<0.001 |
| Decrease (first visit – sixth visit) | 11.54 | 2.27 | 14.47 | 2.33 | P<0.001 |

The diastolic blood pressure showed significant reduction in the both group. The reduction was greater in GROUP B who was treated with Telmisartan 40 mg, than GROUP A who are treated with Losartan Potassium 50 mg.

Diastolic blood pressure decreased significantly in GROUP B (14.47±2.33) than in GROUP A (11.54±2.27) at the end 3 months, which showed that the regimen B had a significantly better impact on systolic blood pressure ($p<0.05$) than group A

Change in diastolic pressure

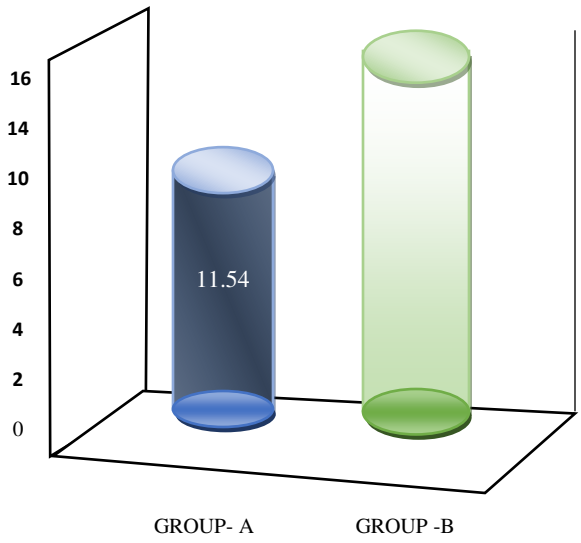



Fig No.7

**Change in Diastolic Blood Pressure in 2 week interval.**

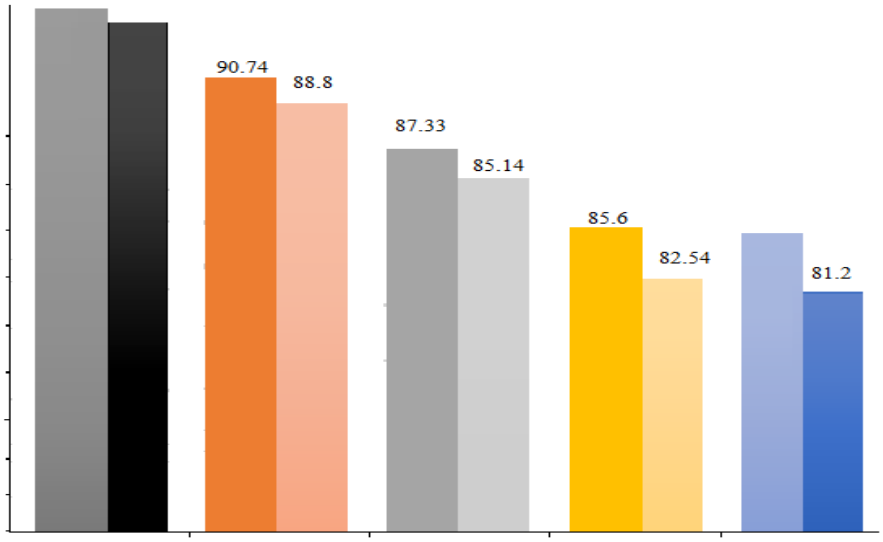



Fig No.8

Initial DBP values of GROUP A and GROUP B were 93.73 ± 3.39 & 93.27 ± 2.75 respectively and that was changed to 90.74 + 2.94 & 88.80 +2.99 on second visit , then it changed to the levels of 87.33 + 2.53 & 85.14 + 3.18,85.60 + 2.75 & 82.54 + 3.32 , 84.20 + 2.59 & 81.27 + 3.32, 82.20+2.53 & 78.80 + 3.13 in further third, fourth, fifth and sixth visits respectively

**Tale 8: Fasting Blood Sugar (FBS) Values**

| FBS values at | FBS values | | | | 'p' Values |
|---|---|---|---|---|---|
| | GROP A | | GROP B | | |
| | Mean | SD | Mean | SD | |
| **First visit** | **145.47** | **16.40** | **136** | **13.06** | **0.0163** |
| **Sixth visit** | **138.06** | **15.83** | **123.16** | **13.32** | **0.0002** |
| **Decrease (first visit – sixth visit)** | **7.40** | **1.35** | **12.83** | **4.86** | **0.0001** |

The fasting blood sugar vales reduced significantly in both group, the reduction of fasting blood sugar was greater in GROUP B 12.83 ± 4.86 than GROUP A 7.40 ± 1.35. The GROUP B shows better significant reduction in fasting blood sugar than GROUP a at the end of 3 month study with a value of <0.05

Change in FASTING BLOOD SUGAR (FBS)

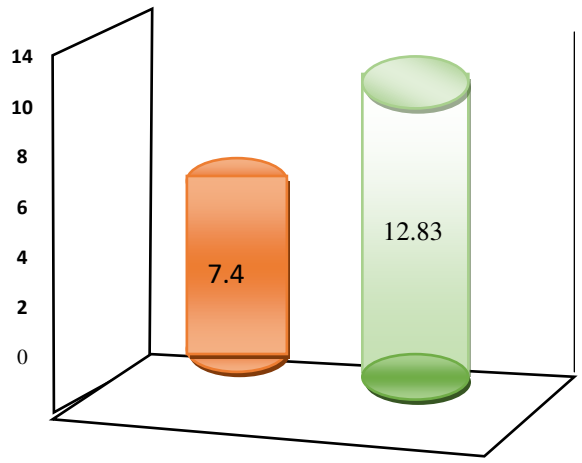



**Fig.No. 9**

**Tale 9: Change in Post Prandial Blood Sugar (PPBS)**

| DBP vales at | DBP Values | | | | 'p' Values |
|---|---|---|---|---|---|
| | GROP A | | GROP B | | |
| | Mean | SD | Mean | SD | |
| **First visit** | **247** | **21.81** | **247.87** | **17.0** | **0.8643** |
| **Fourth visit** | **229.81** | **19.92** | **217.47** | **15.81** | **0.0098** |
| **Sixth visit** | **85.60** | **2.75** | **82.54** | **3.3** | **P<0.001** |
| **Decrease (first visit – sixth visit)** | **17.14** | **3.69** | **30.40** | **8.9** | **0.0001** |

The PPBS vales reduced significantly in both groups, the reduction of fasting blood sugar was greater in GROUP B 30.40 ±8.92 than in GROUP A 17.14 ± 3.69.

The GROUP B shows better significant reduction in PPBS than GROUP A at the end of 3 month study with vales < 0.05

Change in Post Prandial Blood Sugar PPBS

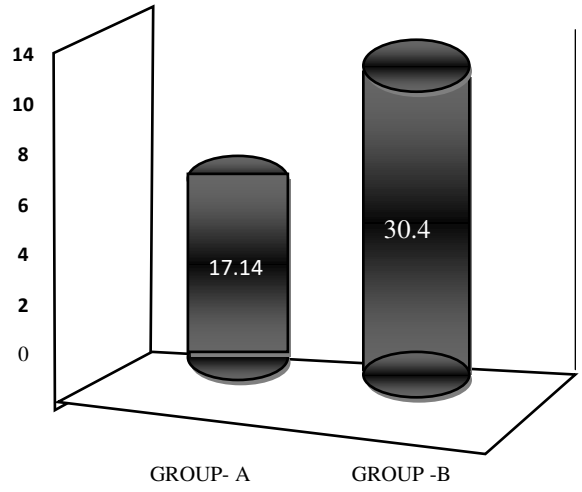



Fig No.10

**Table 10: change in Fasting Blood Sugar – FBS (patients Treated with Metformin HCL 500 mg**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 137.3 | 19.79 | 119.166 | 130.9 | 9.33 | 114.145 | 0.315 |
| Sixth visit | 130.9 | 19.77 | 113.160 | 120 | 10.78 | 102-137 | 0.105 |
| Decrease (first visit – sixth visit) | 6.4 | 0.97 | 5-8 | 10.92 | 1.89 | 8-14 | P<0.001 |

A total number of 11 & 13 patients who were under anti diabetic treatment with Metformin HCL 500 mg belong to hypertensive patient GROUP A (Losartan potassium 50 mg ) and were in hypertensive category GROUP B respectively

The observed change in Fasting Blood Sugar value was from 137.3 ± 19.79 to 130.9 19.77 with a mean decrease of 6.4 ± 0.97 in GROUP A, and that was from 130.9 ± 9.33 to 120 ± 10.78 in GROUP B with a mean decrease of 10.92 ± 1.89 GROUP B have better reduction in FBS than GROUP A. Change in Fasting Blood Sugar FBS (Metformin HCL 500 mg )

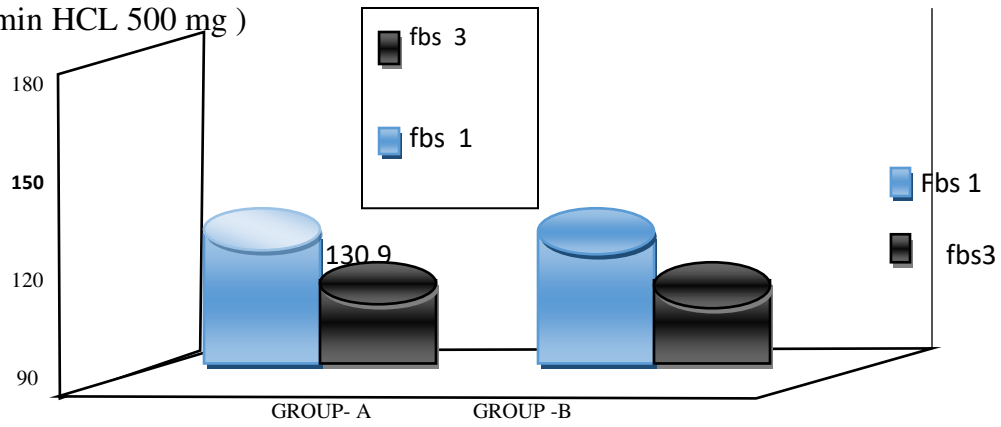



Fig No.11

**Table 11: Change in Post Prandial Blood Sugar -PPS (Patient Treated with Metformin HCL 500 mg)**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 229.8 | 19.86 | 200-256 | 245.77 | 16.74 | 215-274 | 0.048 |
| Sixth visit | 214.3 | 17.26 | 190-240 | 217.6 | 15.01 | 198-236 | 0.628 |
| Decrease (first visit – sixth visit) | 15.5 | 4.03 | 10-21 | 28.15 | 6.58 | 17-38 | P<0.001 |

A total number of 11& 13 patient who were under anti diabetic treatment with metformin HCL 500 mg belong to hypertension patient category GROUP A ( Losartan Potassium 50 mg ) and GROUP B ( Telmisartan 40 mg ) respectively.

The observed change in Post prandial Blood Sugar value was from 229.8 ± 19.86 to 214.3 ± 17.26 with a mean decrease of 15.5 4.03 GROUP A, and that was from 245.77 ± 16.74 to 21.6 ± 15.01 in GROUP B with a mean decrease of 28.15 6.58 GROUP B have better reduction in PPBS than GROUP A

**Fig. 12 Change in Post Prandial Blood Sugar –PPBS (Metformin HCL 500 mg)**

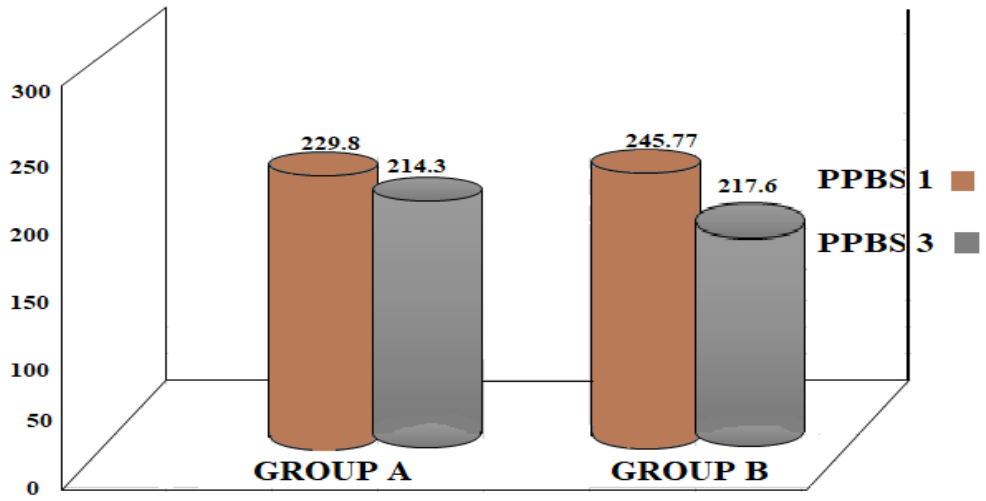


**Table 12: Change in Fasting blood Sugar -FBS (Patient Treated with Glimepiride 1 mg + Metformin HCL 500 mg)**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 229.8 | 19.86 | 200-256 | 245.77 | 16.74 | 215-274 | 0.048 |
| Sixth visit | 214.3 | 17.26 | 190-240 | 217.6 | 15.01 | 198-236 | 0.628 |
| Decrease (first visit – sixth visit) | 15.5 | 4.03 | 10-21 | 28.15 | 6.58 | 17-38 | P<0.001 |

A total number of 7 & 9 patient who were under anti diabetic treatment with metformin HCL 500 mg + Glimepiride 1 mg, belong to hypertension patient category GROUP A ( Losartan Potassium 50 mg ) and GROUP B ( Telmisartan 40 mg ) respectively.

The observed change in Post Prandial Blood Sugar value was from 150.28 ± 12.84 to 142 ± 12.61 with a mean decrease of 8.28 ± 1.11 in GROUP A, and that was from 143 ± 16.84 to 127.11 ± 18.65 in GROUP B with a mean decrease of 15.88 ± GROUP B have better reduction in FPBS than GROUP A

**Change in Fasting blood Sugar -FBS (Patient Treated with Glimepiride 1 mg + Metformin HCL 500 mg)**

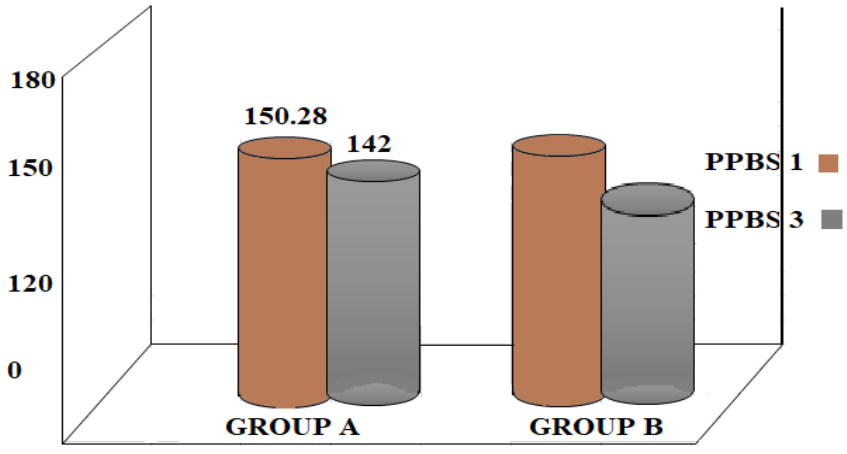



**Fig. No 13**

**Tale 13: Change in Post Prandial Blood Sugar – PPBS (patient treated with Glimepiride 1 mg + metformin HCL 500mg**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 262 | 13.35 | 130-67 | 253.56 | 15.63 | 220-270 | 0.2581 |
| Sixth visit | 245 | 11.46 | 122-158 | 216.4 | 13.65 | 200-246 | P<0.001 |
| Decrease (first visit – sixth visit) | 17.28 | 3.59 | 7-10 | 37.11 | 9.94 | 20-49 | P<0.001 |

A total number of 7 & 11 patient who were under anti diabetic treatment with metformin HCL 500 mg + Glimepiride 1 mg, belong to hypertension patient category GROUP A ( Losartan Potassium 50 mg ) and GROUP B ( Telmisartan 40 mg ) respectively.

The observed change in Post prandial Blood Sugar value was from 262 ± 13.35 to 245 ± 11.46 with a mean decrease of 17.28 ± 3.59 in GROUP A, and that was from 253.56 ± 15.63 to 216.4 ± 13.65 in GROUP B with a mean decrease of 37.11 ± 9.94 GROUP B have better reduction in PPBS than GROUP A

**Change in Post Prandial Blood Sugar – PPBS (Glimepiride 1 mg + metformin HCL 500mg**

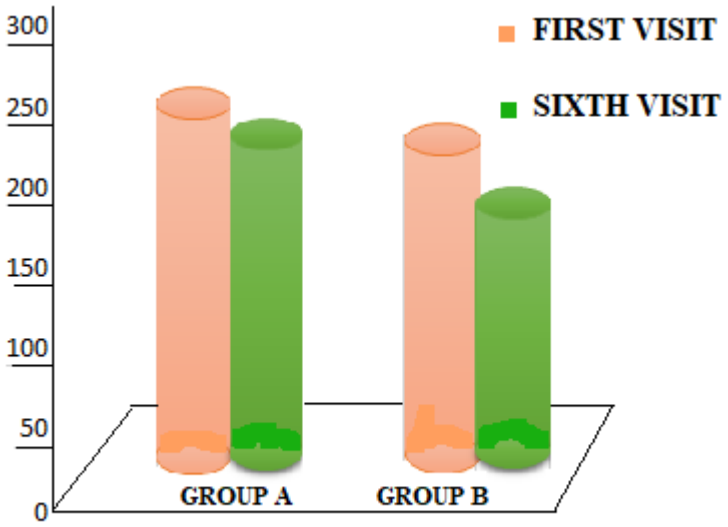



**Fig No.14**

**Tables 14: Change in Fasting Blood Sugar - FBS (Patients Treated with Glimepiride 1 mg)**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 155.43 | 16.19 | 129-180 | 132.4 | 6.06 | 124-140 | 0.013 |
| Sixth visit | 147.57 | 15.05 | 124-170 | 119.8 | 6.02 | 114-128 | 0.003* |
| Decrease (first visit – sixth visit) | 7.85 | 1.77 | 5-10 | 12.6 | 2.61 | 9-16 | 0.0036* |

A total number of 7 & 5 patient who were under anti-diabetic treatment with Glimepiride 1 mg, belong to hypertension patient category GROUP A (Losartan Potassium 50 mg ) and GROUP B ( Telmisartan 40 mg ) respectively.

The observed change in Post prandial Blood Sugar value was from 155.43 ± 16.19 to 147.57 ± with a mean decrease of 7.85 ± 1.77 in GROUP A, and that was from 132.4 ± 6.06 to 119.8 ± 6.02 in GROUP B with a mean decrease of 12.6 ± 2.61 GROUP B have better reduction in FBS than GROUP A.

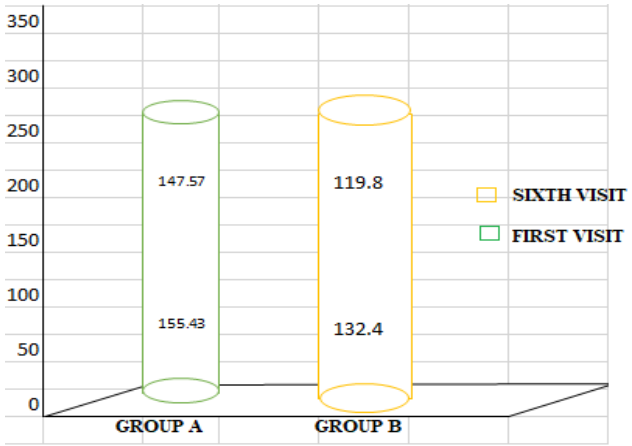



**Fig. no. 15**

**Tables 15: Change in Post prandial Blood Sugar (Patients Treated with Glimepiride 1 mg)**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 256.14 | 23.31 | 219-279 | 236.8 | 15.6 | 210-250 | 0.139 |
| Sixth visit | 237 | 22.42 | 202-264 | 209.8 | 17.21 | 190-236 | 0.046 |
| Decrease (first visit – sixth visit) | 19.14 | 3.71 | 15-24 | 27 | 9.94 | 14-39 | 0.081 |

A total number of 7 & 5 patient who were under anti-diabetic treatment with Glimepiride 1mg, belong to hypertension patient category GROUP A (Losartan Potassium 50 mg ) and GROUP B ( Telmisartan 40 mg ) respectively.

The observed change in Post prandial Blood Sugar value was from 256.14 ± 23.31 to 237 ± 22.42 with a mean decrease of 19.14 ± 3.71 in GROUP A, and that was from 236.8 ± 15.62 to 209.8 ±17.21 in GROUP B with a mean decrease of 27±9.94 GROUP B have better reduction in PPBS than GROUP A.

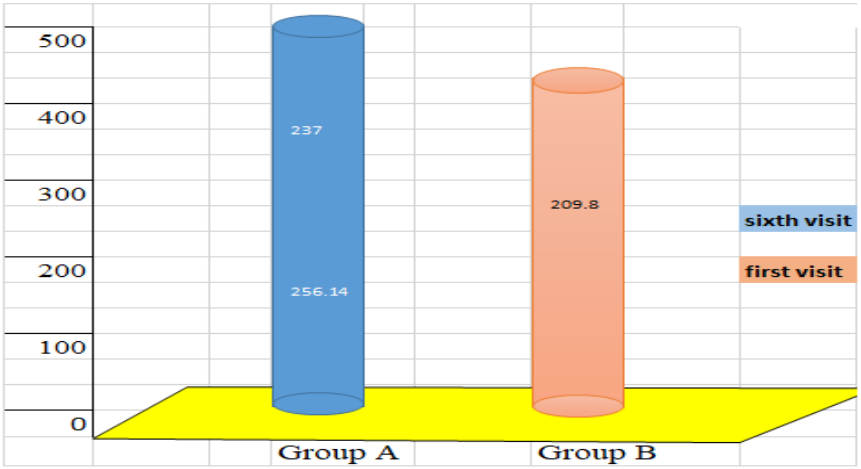


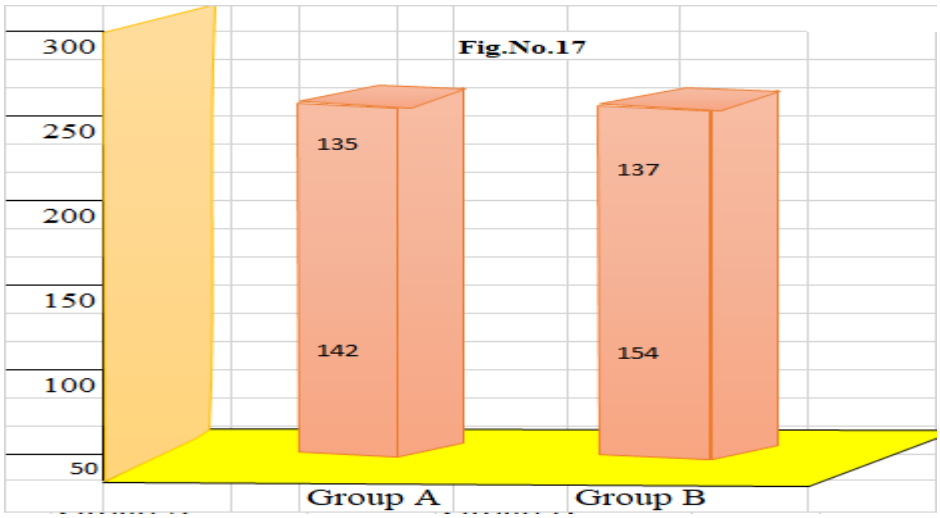

**Fig. no. 16**

**Table 16: Change in Fasting Blood Sugar (Patient Treated with Voglibose 0.2 mg)**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 142 | 2.12 | 141-144 | 154 | | 154 | |
| Sixth visit | 135 | 2.82 | 133-137 | 137 | - | 137 | |
| Decrease (first visit – sixth visit) | 7.5 | 0.71 | 7-8 | 17 | | 17 | |

A total number of 2 & 1 patient who were under anti-diabetic treatment with Voglibose 0.2 mg, belong to hypertension patient category GROUP A (Losartan Potassium 50 mg ) and GROUP B ( Telmisartan 40 mg ) respectively.

The observed change in Post Prandial Blood Sugar value was from 142.5±2 to 135±2.82 with a mean decrease of 7.5±0.71 in GROUP A, and that was from 154 to 137 in GROUP B with a mean decrease of 17. GROUP B have better reduction in FBS than GROUP A. Change in Fasting Blood Sugar-FBS (Voglibose 0.2 mg)



**Tale 17: Change in Post Prandial Blood Sugar (Patients Treated with voglibose 0.2 mg)**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 139 | 3.46 | 137-143 | 137.5 | 17.68 | 125-150 | 0.886 |
| Sixth visit | 131.7 | 3.79 | 129-136 | 127.5 | 16.26 | 116-139 | 0.675 |
| Decrease (first visit – sixth visit) | 7.33 | 0.58 | 7-8 | 10 | 1.41 | 9-11 | 0.053 |

A total number of 2 & 1 patient who were under anti-diabetic treatment with Voglibose 0.2 mg, belong to hypertension patient category GROUP A (Losartan Potassium 50 mg ) and GROUP B ( Telmisartan 40 mg ) respectively.

The observed change in Post Prandial Blood Sugar value was from 259 ± 1.41 to 241.5 ± 2.12 with a mean decrease of 17.5 ± 3.53 in GROUP A, and that was from 270 to 246 in GROUP B with a mean decrease of 24. GROUP B have better reduction in PPBS than GROUP A

**Change in Post Prandial Blood Sugar – PPBS (Voglibose 0.2 mg)**

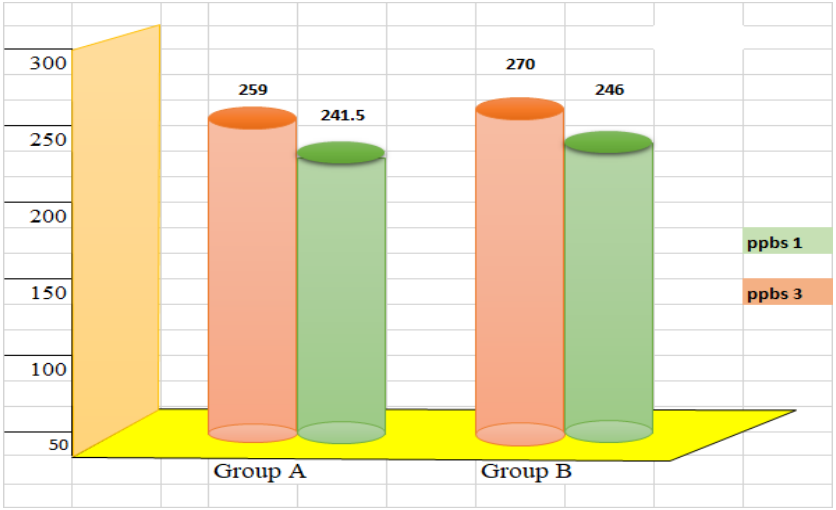


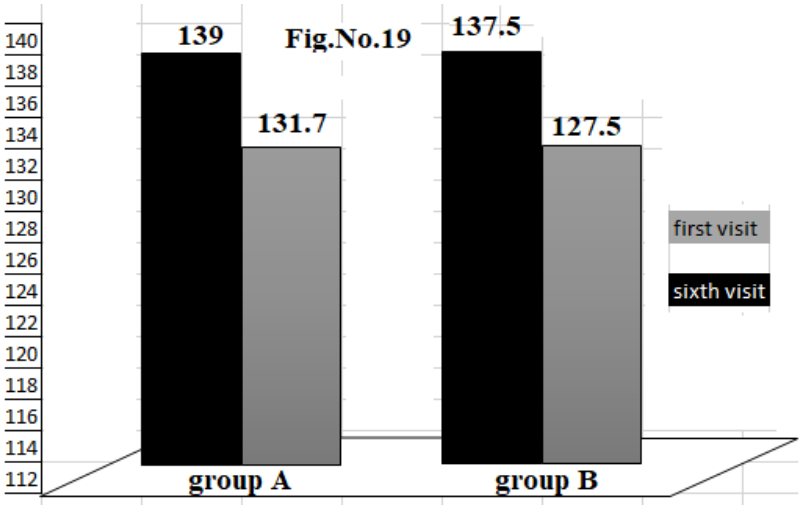
**Table 18: Change in Fasting blood Sugar (Patients Treated with Metformin HCL 500 + Voglibose 0.2 mg)**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 139 | 3.46 | 137-143 | 137.5 | 17.68 | 125-150 | 0.886 |
| Sixth visit | 131.7 | 3.79 | 129-136 | 127.5 | 16.26 | 116-139 | 0.675 |
| Decrease (first visit – sixth visit) | 7.33 | 0.58 | 7-8 | 10 | 1.41 | 9-11 | 0.053 |

A total number of 3 & 2 patient who were under anti-diabetic treatment with Metformin HCL 500 mg + Voglibose 0.2 mg, belong to hypertension patient category GROUP A ( Losartan Potassium 50 mg ) and GROUP B ( Telmisartan 40 mg ) respectively.

The observed change in Post Prandial Blood Sugar value was from 139 ± 3.46 to 131.7 ± 3.79 with a mean decrease of 7.33 ± 0.58 in GROUP A, and that was from 137.5 ± 17.68 to 127.5 ± 16.06 in GROUP B with a mean decrease of 10 ± 1.41 GROUP B have better reduction in FBS than GROUP A

**Change in Fasting Blood Sugar – FBS (Metformin HCL 500 mg + Voglibose 0.2 mg)**



**Tale 19: Change In Post Prandial Blood Sugar (patients treated with metformin HCL 500mg + Voglibose 0.2 mg) 500mg + Voglibose 0.2 mg)**

| FBS values at | FBS values | | | | | | 'p' Values |
|---|---|---|---|---|---|---|---|
| | GROP A | | | GROP B | | | |
| | Mean | SD | Range | Mean | SD | Range | |
| First visit | 238.3 | 10.41 | 230-250 | 252.5 | 24.75 | 235-270 | 0.419 |
| Sixth visit | 221 | 7.54 | 214-229 | 226 | 24.04 | 209-243 | 0.742 |
| Decrease (first visit – sixth visit) | 17.33 | 3.21 | 15-21 | 26.5 | 0.71 | 26-27 | 0.032* |

A total number of 3 & 2 patient who were under anti-diabetic treatment with Metformin HCL 500 mg + Voglibose 0.2 mg, belong to hypertension patient category GROUP A ( Losartan Potassium 50 mg ) and GROUP B ( Telmisartan 40 mg ) respectively.

The observed change in Post prandial Blood Sugar value was from 238.3 ± 10.41 to 221 ± 7.54 with a mean decrease of 17.33 ± 3.21 in GROUP A, and that was from 252.5 ± 24.75 to 226 ± 24.04 in GROUP B with a mean decrease of 26.05 ± 0.71 GROUP B have better reduction in PPBS than GROUP A change in post prandial blood sugar PPBS (Metformin HCL 500mg + Voglibose 0.2 mg)

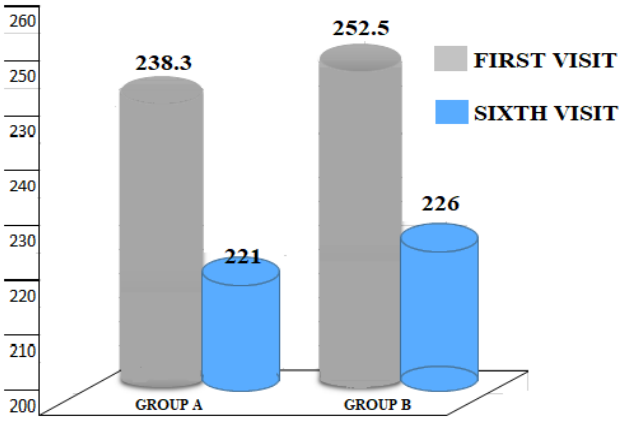



**Fig.No.20**

# DISCUSSION

# DISCUSSION

Angiotensin II receptor antagonist provide a more specific blockade to the Renin- Aldosterone System and have better tolerability when compared with ACE inhibitors. In addition, the evidence Available thus far for this new classes of antagonists has established that their efficacy is equal to that of ACE inhibitors in hypertension. Therefore, it is conceivable that Angiotensin II Receptor blockers will take a growing place in the management of hypertensive patients. However, the place of Angiotensin II receptor antagonist in the management of hypertension will of course, depend on the result of morbidity and mortality trials.

In this study comparison of efficacy of Losartan and Telmisartan in hypertensive patients was carried out. Patients with hypertension were enrolled for the study as per inclusion and exclusion criteria. They are divided into GROUP A (30 patients who were treated with Losartan Potassium 50 mg) & GROUP B (30 patients who were treated with Telmisartan 40 mg). The Parameters that used to the efficacy comparison were -SBP, DBP, and FBS & PPBS. SBP & DBP Were recorded from baseline to 3 months in an interval of 15 days. And the FBS and PPBS were recorded in the baseline and at the end of study. Then the comparison was done with help of computational statistical method.

In this prospective study we observed that both Losartan Potassium and Telmisartan reduces the blood pressure. Telmisartan was significantly superior to the Losartan in reduction of Systolic Blood Pressure and Diastolic Blood Pressure with a p-value($<0.05$) and Telmisartan the same shows superior reduction blood sugar level than less than Potassium with significant p value $<0.05$.

**AGE:**

A number of 60 patients were enrolled for the study and their age distribution was as below -30 patients were of group A, out of these 3 patients (10%) between the age group of 32-39 years, 11 patients (36.66%) between the age group of 40 -49 years, 16 patients (53.34%) between the age group of 50 to 60 years.

Out of 60 patients, 30 patients were of group A, out of these two patients (6.67%) between the age group of 30-39 years, 12 patients (40%) between the age group of 40 - 49 years, 16 patient (53.33%) between the age group of 50 - 60 years.

The age GROUP A was 50.17 ± 6.62 years and group B was 50.34 ± 6.25 years. A total number of 32 patients comes under the age category 50 - 60 years ie, 53.33% of total study population this will cement the age correlation of hypertension. "As the age increases the risk of hypertension also increases"

**SEX:**

A total of 60 patients were screened and randomized into two treatment group. Out of which 30 patients were GROUP A, 18 patients (60%) were male, 12 patients (40%) were female. In case of GROUP B, 20 patients (66.67%) were male, 10 patients (33.34%) were female.

In our study population number of males with hypertension where higher than the females, this may be due to the lifestyle difference between the males and females, especially using of tobacco and alcohol

**PSYCHOLOGICAL PARAMETER**

The average weights of patients were 74.1± 5.97 in GROUP A and 70.57± 5.84 in GROUP B. The average BMI of patients were 27.64 ± 1.73 in GROUP A and 26.99 ± 1.92 in GROUP B. There was no statistically significant difference in the mean weight and BMI of 2 group ($p > 0.05$)

**SYSTOLIC BLOOD PRESSURE**

That mean systolic blood pressure of GROUP A and GROUP B where (152.93±6.53mmHg & 148.8+7.28mmHg respectively, at the baseline (first visit). The GROUP A who were treated with Losartan Potassium 50mg showed a mean reduction of (27.94+3.09 mmHg) but that was lower than that produced by the Telmisartan in GROUP B (33.27+3.42 mmHg).

Both of the study drugs produced reduction in the systolic blood pressure during the Study time and of that, the Telmisartan 40mg is found to be superior in SBP reduction which is Satisfactory significant when compared to Losartan Potassium 50mg with a p value $<0.05$

**DIASTOLIC BLOOD PRESSURE**

The mean diastolic blood pressure of GROUP A and GROUP B were (93.73+3.37 mmHg & 93.27+2.75 mmHg) respectively, at the best line (first visit). The Group A who were treated with Losartan Potassium 50mg showed a mean reduction of (11.54+2.27 mmHg) but that was Lower than that produced by the Telmisartan 40mg in GROUP B (14.47+2.33 mmHg).

Both of the study drugs produced reduction in the Systolic Blood Pressure

During the study time and of that the Telmisartan 40 mg is found to be superior in SBP production which is static still significant when compare to Losartan Potassium 50 mg with a p Value <0.05.

**EFFECT OF STUDY DRUGS IN BLOOD SUGAR LEVEL OF STUDY**

**POPULATION**

**FASTING BLOOD SUGAR (FBS)**

The fasting blood sugar values reduced in both groups the reduction of fasting blood sugar was greater in GROUP B (Telmisartan 40mg) 12.803 + 4.86 then GROUP A(Losartan Potassium 50 mg)7.40 + 1.35

The GROUP B shows better reduction in fasting blood sugar than GROUP A at the end of 3 months study with a statistically significant p value of < 0.05

The Fasting Blood Sugar changes among the study population who were under different anti diabetic therapy was observed as follows

**Metformin HCL 500 mg:**

Values were decreased from baseline value 137.3± 19.79 to 130.9±19.77 with a decrease of 6.4 ±0.97 in GROUP A and in GROUP B it was from baseline value 130.9 ±9.33 to 120 ±10.78 with a decrease of 10.92 ±1.89. It was found to be higher reduction in GROUP B then in GROUP A

**METFORMIN HCL 500 MG +GLIMEPIRIDE 1MG**

Value were decreased from base line value 150.28 ±12.84 to 142 ±12.61with a decrease of 8.28±1.11 in GROUP A and in GROUP B it was from baseline

value 143 ±16.85 to 127.11 ±18.65 with a decrease of 15.88±7.47. It was found to be higher reduction in GROUP B then in GROUP A.

**Glimepiride 1 mg:**

Values were decreased from baseline value 155.43 ±16.19 to 147.57±15.05 with a decrease of 7.85 ±1.77 in GROUP A and in GROUP B it was from baseline value 132.4 ± 6.06 to 119.8± 6.02 with a decrease of 12.6 ±2.61. It was found to be higher reduction in GROUP B then in GROUP A.

**Voglibose 0.2 mg:**

Values were decreased from baseline value 142.5 ± 2.12 to 135± 2.82 with a decrease of ± 0.71 in GROUP A and in GROUP B. It was from baseline value 154 to 137 with a decrease of it was Found to be higher reduction in GROUP B then in GROUP A.

**Metformin HCL 500mg+Voglibose 0.2 mg:**

Values were decreased from base line value 139±3.97 with a decrease of 7.33 ± 0.58. In GROUP A and in GROUP B it was from base line value 137.5±17.68 to 127.5± 16.26 with a decrease of 10±1.41. It was found to be higher reduction in GROUP B than in GROUP A.

**POST PRANDIAL BLOOD SUGAR (PPBS)**

The PPBS values reduced in both groups, the reduction of post prandial blood sugar was greater in GROUP B (Telmisartan 40mg)30.40+8.92 than in GROUP A (Losartan Potassium 50mg)17.14±3.69

The GROUP B shows better significant reduction in PPBS then. GROUP A at the end of 3 month Study with a p values <0.05

From the above finding it can assess that the partial PPAR-Gamma activity of Telmisartan Sound for the superior reduction in blood sugar values.

The post prandial blood sugar changes among the study population who were under different antidiabetic therapy were observed as follows.

**Metformin HCL 500 mg:**

Values were decreased from base line value 229.8+19.86 to 214.3+17.26 with a decrease Of 15.5 + 4.03 in GROUP A and GROUP B it was from baseline value 245.77+16.74 to 217.6+15.01 with decrease of 28.15+6.58. It was found to be higher resolution in GROUP B then in GROUP A

**Metformin HCL 500 mg + Glimepiride1 mg:**

Values were decreased from baseline value 150.29 +12.84 to 142 + 12.61 with a decrease of 8.28 + 1.11 in GROUP A and in GROUP B it was from baseline value 253.56+15.63 to 216.4 +13.65 with a decrease of 37.11+ 9.94 it was found to be higher than reduction in GROUP B then in GROUP A

**Glimepiride 1 mg:**

Values were deserved from base line value 256.14+23.31 to 237+22.42 with a decrease of 19.14+3.71 in GROUP A and GROUP B it was from baseline value 236.8+15.62 to 209. 8±17.21with a decrease of 27±9.94.It was found to be higher reduction in GROUP B than in GROUP A

**Voglibose 0.2 mg**:

Values were decreased from base line value 259±1.41 to 241.5 ± 2.12 with a decrease of ±3.53 in GROUP A and in GROUP B It were from baseline value 270 to 246 with a decrease of 24. It was found to be higher reduction in GROUP B then in GROUP A

**Metformin HCL 500 mg +Voglibose 0.2 mg:**

Values were decreased from baseline value 238.3 ±10.41 to 221± 7.54 with a decrease of 17.33±3.21 in GROUP A and in GROUP B it was from baseline value 252.5±24.75 to 226±20.04 with a decrease of 26.5±0.71 It was found to be higher reduction in GROUP B then in GROUP A

# CONCLUSION

# 8. CONCLUSION

In this present prospective observation study, treatment of hypertension with two study drug Losartan potassium 50 mg and Telmisartan 40 mg were carried out in a population of 60 patients. They were instructed to follow a healthy diet with proper exercise.

After 3 months study it is observed that both of the study drugs have good impact on Blood pressure lowering. But the Telmisartan 40mg showed superior reduction in blood pressure when compare to losartan potassium 50 mg

The second objective of the study i.e.; effect of study drugs Losartan Potassium 50 mg and Telmisartan 40 mg in blood sugar levels of population on diabetic therapy. The FBS and PPBS where parameters observed for the study, there was reductions in FBS and PPBS values in both GROUP A GROUP B. And it is observed that the reduction is higher in group B when compare with GROUP A. It can be suggested that the partial PPAR gamma agonist activity of Telmisartan accounts for the higher reduction in blood sugar levels.

# BIBLIOGRAPHY

# BIBLIOGRAPHY

**1.** Wolf -Mair k et al, hypertension prevalence and blood pressure level in 6 European countries, Canada and the United States, JAMA 2003;289(18);page number 2363-2 369

**2.** Gupta R, trends in hypertension epidemiology in India HUM hypertension 2004: 18; PG no 73-80.

**3.** Madhuri Devabhaktuni, fixed combination of amlodipine and atorvastatin in cardiovascular risk management patient perspective vascular health and risk management 2009; page number 3377 - 387

**4.** Stella- Maria G et al., Effect of antihypertensive Treatment with Angiotensin II receptor Blockers on lipid Profile: An Open Multi Drug Comparison Trail, Hellenic J Cardial,2006;47:pg no: 21-28

**5.** Franz H. messerli et al; Efficacy and safety of Coad ministered amlodipine and atorvastatin in patient with Hypertension and dyslidemia: result of the avlon trial. The journal of clinical Hypertension, 2006;vol(8) ;pg no:8

**6.** George Nickening, should angiotensin II receptor blockers and statins be combined. Circulation, Journal of the American heart Association, 2004: 110:pg no; 1013 - 1020..

**7.** Marry J Mycok, Lippincott's illustrated reviews. Pharmacology 2nd edition, Judith E Thomson; 1998; pg no: 179-191.

**8.** R S Sathoker, Pharmacology and pharmacotherapeutics. 19th edition. Popular prakashan; 2005; pg no ; 404-407

**9.** Padmaja udaykumar, medical pharmacology,3rd edition; CBS publishers: 2011;pgno: 169-177

**10.** Rogar Walker, Clinical pharmacy and therapeutics,3rd edition; Churchill living stone; 1994; pg no: 265-275.

**11.** Anderson JL ST segment elevation acute myocardial infarction and complication of myocardial infraction. Saunders Elsevier,2011;chap 73.

**12.** Badr KF., Vascular injury to the kidney. In eds Harrison's principals of internal Medicine, 17th Ed. New York, NY; McGrew Hill: 2008: chap 280.

**13.** Good maan & Gilman's, The Pharmacological Basis of therapeutics,10th edition; The Mc Grew Hill: 2001:pg.no ; 845 - 866.

**14.** KD Tripathi, Essential of Medical pharmacology,4th edition, Jay pee brothers: 1999: pg no : 539-550.

**15.** National high blood pressure education program working Group Report on primary Prevention of Hypertension. Arch inter Med,1993 : 153: pg no : 186 - 208

**16.** N Murugesh, A Concise Text Book of Pharmacology, 6theditio, Sathya publishers ; pg no : 133-139

**17.** Joseph Dippiro, Pharmacotherapy Hand book, 7th edition, Mc Grew Hill : 2009; pg. no: 111-114

**18.** Arm V Chobanin et al., The Seventh report of Joint National committee on Prevention, Detection, Evaluation, and treatment of high Blood Pressure. The JNC 7 Repot, 2003; pg. no: 2560-257.

**19.** Trials of Hypertension Prevention Collaborative Research Group, Effects of Weight loss and sodium reduction intervention blood pressure and hypertension incidence in overweight people with high normal blood pressure. The Trails of hypertension prevention phase II. Arch intern med,1997;157(6): pg. no:657-667

**20.** Blair SN et al., Cardiorespiratory fitness and Risk of Nonfatal Cardiovascular Disease in Men and Women. AM J Hypertension, 2007; 20(6):pg.no:608-615.

**21.** Maxwell et.al. BP change on obese hypertension subjects during rapid weight loss. Comparison of restricted v unchanged salt intake. Arch intern Med,1984; 144(8):pg.no:1581-1584

**22.** Kagan A et al., Dietary and other risk factors for stroke in Hawaiian Japanese men. Stroke Journal of the American heart association, 1985;16: pg.no :390-396

**23.** Niels AG et al., Effects of Sodium Restriction on blood pressure, Renin, Aldosterone, Catecholamine, Cholesterols, and Triglyceride A Meta-analysis. JAMA,1998; 279 (17): pg.no :1383-1391

**24.** Sacks FM et al., effect on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (dish) diet. N Engl J med 2001; 344(1): pg. no: 3-10

**25.** Nelson l et al., effect of change levels of physical activity on blood pressure and hemodynamics in essential hypertension. Lancet 1986; 2 (8505); pg. no: 473-476

**26.** Kohno et al., Renal depressor mechanisms of physical training in patient with essential hypertension.am j hypertension, 1997;10(8):pg.no:859-868

**27.** Jonas MA et al., statement on smoking and cardio vascular disease for health care professionals. Circulation stroke,jornal of the American heart Association, 199;86:pg. no: 1664-1669

**28.** La Croix AZ., Smoking and Mortality among older men and women in three communities. N Engl J Med, 1991:324(23):pg.no; 1619-1625.

**29.** Davey GK et al., Hypertension and blood pressure among meat eaters, fish eaters, Vegetarians and Vegans in EPIC-Oxford. Public Health Nutr,2002;5(5): pg.no:645-654

**30.** Lawrence J et al., Approaches to prevent and treat hypertension. A Scientific Statement from the American Heart Association. Hypertension Journal Of The American Heart Association, 2006; 47:pg.no: 296 308

**31.** Psaltopoulou T et al., Olive oil the Mediterranean diet and arterial blood pressure: the Greek European prospective investigation into cancer and nutrition (EPIC) study [1-3] AM J Clin Nutr, 2004; 80:pg.no: 296-308.

**32.** Epstein BJ et al., Can the renin-angiotensin system protect against stroke? A focus on angiotensin II receptor blockers. Pharmacotherapy, 2005; 25(4):pg.no: 531- 539

**33.** Weber M et al., Achieving blood pressure goals: should angiotensin II receptor blockers become first-line treatment in hypertension?.J Hypertension Suppl, 2009; 27(5): pg no: 9-14.

**34.** George nickening et al., Clinical Evidence for the Cardiovascular benefits of Angiotensin Receptor lockers.JRAAS,2006;7:pg.no:1-6

**35.** National clinical guidelines for the management in primary and secondary care

**36.** National diabetic information clearing house. US Department of health and human services 2006 page number 111

**37.** National diabetic fact sheet. Department of Health and Human services centers for disease control and prevention 2007;pg.no:1-14

**38.** L H Bosenberg et al., The mechanism of action of Oral antidiaetic drug. JEMDSA, 2008; 13(3):pg.no.80-88.

**39.** Dr. P R Anand Vijay Kumar et al., To Compare the Pleiotropic Effect of Telmisartan and in Olmesartan in hypertensive patients with Metabolic Syndrome Based on ATP III Criteria. Iosar journal of Pharmacy 2013; 3(1):PG.no; 59-67.

**40.** Yuiji Shimizu et al., metabolic effect of combined telmisartan and nifedipine CR therapy in patients with essential hypertension. Int J Gen Medicine, 2012; 5: pg.no:753- 758

**41.** Nazia Yasmeen et al., Efficacy and tolerability of Different Anti-hypertensive drugs in Patients with Mild to Moderate Hypertension in a Tertiary Care hospital. Scholars reach

Library, Archives of Applied Science Research, 2011; 3(1):pg.no:436-443

**42.** Se Kjeldsen et al; The Effects of losartan vs. candesartan in reducing cardiovascular events in the primary treatment of hypertension. J Hum Hypertens,2010;24(4)pg.no:263-273

**43.** RM Nixon et al; Valsartan vs. Other angiotensin II receptor blockers in the treatment of hypertension int j clinpract,2009;63(5):pg no:766-775

**44.** Paolo Verdecchia et al., Comparative assessment of angiotensin receptor blockers in different clinical setting. Vasc Health Risk Manag 2009;5:pg.no: 939-948

**45.** Shiho Nakayama et al., comparison of Effect of Olmesartan and Telmisartan on blood pressure and metabolic parameters in Japanese Early-stage type-2 Diabetics with Hypertension. Hypertension Research, (2008); 31: pg no: 7-13.

**46.** Derosa G et al., Metabolic effects of telmisartan and irbesartan in type 2 diabetic patients with metabolic syndrome treated with rosiglitazone. J clin pharm Ther, 2007; pg.no:261-268.

**47.** Nagel et al., the effect of telmisartan on glucose and lipid metabolism in nondiaetic, insulin-resistant subject metabolism. Clinical and Experimental, 2006; pg no: 1149-1154.

**48.** Asmar R et al., Targeting effective blood pressure control with angiotensin receptor locker. Int j pract,2006;60(3):pg.no:315-320

**49.** Cristiana Vitale et al., Metabolic effect of telmisartan and losartan in hypertension patients with metabolic syndrome. Cardio vascular Diabetology, 2005; 4(6); pg.no:1-8.

**50.** Derosa G et al., effects of telmisartan compared with eprosartan on blood pressure control, glucose metabolism and lipid profile in hypertensive,typr2 diabetic patients: a randomized ,dole-hand, placebo-controlled 12 month study Hypertens,2004;27:pg.no:457-464.

**51.** Schpp M et al., Angiotensin type 1 receptor lockers induce peroxisome proliferator-activated receptor-g activity. Circlation 2004; 109: pg no: 2054-2057.

**52.** Ujala Verma et al., Antihypertensive Efficacy of carvedilol and Amlodipine in patients of mild to moderate hypertension-A Comparative Study. J K science, 2004; 6(4); pg.no:193-196.

**53.** Dahlof B et al., Cardiovascular morbidity in the Losartan Intervention for Endpoint reduction in Hypertension study (LIFE): a randomized trial against atenol.Lancet:2002;359:pg no:995-1003

**54.** Letch met et al., effects of angiotensin receptor II blockade with losartan on insulin sensitivity, lipid profile, and endothelia in normotensive off spring of hypertensive patient. J Cardiovasc Pharmacol, 1998; 31(4):pg.no:576-580.

**55.** Pedro Luis de Palos Velasco et al., Effects of Losartan and Diltiazem on blood Pressure,Inslin Sensitivity, Lipid Profile and Microalminria, in Hypertensive Type 2 Diabetic Patients.1998;16(5):pg.no:361-370

**56.** Indian Pharmacopoeia. 2007; vol (1):pg.no:1319-1321.

**57.** The Merck index, An Encyclopedia of CHEMICALS, DRUGS AND BILOGICALS,13th edition Merck research laboratories,2001;pg.np:1628-1629

# ANNEXURE

# PROFORMA

**COMPARTIVE STUDY ON EFFICACY LOSARTAN VERUS TELMISARTAN IN HYPERTENSION PATIENTS**

DEMOGRAPHICDATA:

1. NAME: 2.AGE: 3.SEX: M/F 4.OPNO:

5. WEIGHT: 6. HEIGHT: 7.BMI:

7. ADDRES:

8. PAIENT HISTORY:

9. DIAGNOSIS:

10. DRUG USED: LOSARTAN POTASSIUM 50 MG ☐

TELMISARTAN 40 MG ☐ IR

11. OTHER CO-MORBIDITIES:

12. OTHER DRUGS USED:

BASE LINE (First Visit) DATE:

PARAMETERS

PRIMARY

**SYSTOLIC BLOOD PRESSURE: mm Hg DIASTOLIC BLOOD**

**PRESSURE: mm Hg SECONDARY**

FBS:

PPBS:

PARAMETERS

SYSTOLIC BLOOD PRESSURE: mm HG

DIASTOLIC BLOOD PRESSURE: mm HG

THIRD VISIT **DATE:**

PARAMETERS

SYSTOLIC BLOOD PRESSURE: mm HG

DIASTOLIC BLOOD PRESSURE: mm HG

FOURTH VISIT **DATE:**

PARAMETERS

SYSTOLIC BLOOD PRESSURE: mm HG

DIASTOLIC BLOOD PRESSURE: mm HG

FIFTH VISIT **DATE:**

PARAMETERS

SYSTOLIC BLOOD PRESSURE: mm HG

DIASTOLIC BLOOD PRESSURE: mm HG

SIX VISIT DATE:

PARAMETERS

PRIMARY

SECONDARY

SYSTOLIC BLOOD PRESSURE: mm HG FBG:

DIASTOLIC BLOOD PRESSURE: mm HG PBS:

Body weight: Kg

Pharmacist signature Physician signature

# ABBREVIATION

| ABBREVIATIONS | DESCRIPTION |
|---|---|
| **ACE** | **Angiotensin Converting Enzyme** |
| **ARBs** | **Angiotensin Receptor Blockers** |
| **AUC** | **Area Under Curve** |
| **BP** | **Blood Pressure** |
| **BMI** | **Body Mass Index** |
| **$C^{2+}$** | **Calcium ion** |
| **CCBs** | **Calcium Channel Blockers** |
| **CHD** | **Coronary Heart Diseases** |
| **CHF** | **Congestive Heart Failure** |
| **CNS** | **Central Nervous System** |
| **CI** | **Cardiac Index** |
| **CVS** | **Cardio Vascular System** |
| **CVD** | **Cardio Vascular Disease** |
| **CYP450** | **Cytochrome P 450** |
| **DASH** | **Dietary Approaches to Stop Hypertension** |
| **DBP** | **Diastolic Blood Pressure** |
| **DM** | **Diabetes Mellitus** |
| **ECG** | **Electrocardiogram** |
| **UTI** | **Urinary Tract Infection** |
| **VLDL** | **Very Low Density Lipoprotein** |
| **LVH** | **Left Ventricular Hypertrophy** |
| **WHOS** | **World Health Organisation** |

| | |
|---|---|
| **HMGCoA** | **Hydroxy – 3- Methyl Glytaryl Coenzyme - A** |
| **mm Hg** | **Millimeters of Mercury** |
| **NaCl** | **Sodium Chloride** |
| **NCEP-ATP III** | **National Cholesterol Education Program Adult Treatment Panel** |
| **NSAID** | **Non Steroidal Anti-Inflammatory Drug** |
| **OD** | **Once-daily** |
| **OGTT** | **Oral Glucose Tolerance Test** |
| **PPAR** | **Peroxisome Proliferator Activated Receptor** |
| **SBP** | **Systolic Blood Pressure** |
| **SD** | **Standard Deviation** |
| **SI** | **Insulin Sensitivity Index** |
| **TC** | **Total Cholesterol** |
| **TG** | **Triglycerides** |