INTRODUCTION:

Hypertension is a public health problem that affects >25% of the adult population worldwide.\(^1,2\) Prevalence increases with age, with a 90% residual lifetime risk in normotensive individuals aged 55 to 65 years.\(^3\) Hypertension has been identified as the leading risk factor for mortality and ranks as the third-leading cause of disability-adjusted life-years.\(^1,4\) Despite the availability of numerous antihypertensive agents, the diagnosis, management, and control of hypertension are far from ideal, with control rates of 6% to 30% in different communities worldwide.\(^1\) Nonadherence to antihypertensive treatment has been associated with lower rates of blood pressure (BP) control and higher rates of cardiovascular events.\(^5-7\) The greater the number of daily doses prescribed, the poorer the compliance.\(^8\) In a review of studies in which compliance was monitored electronically, compliance was significantly higher with medications administered once or twice daily compared with those administered 3 or 4 times daily.\(^9\)

Current guidelines and results from recent clinical trials have refocused attention on the treatment of hypertension. Emphasis has been placed on identifying patients at high risk and treating to lower levels of blood pressure, particularly in patients with diabetes or target organ damage. Most patients will require combination therapy to achieve adequate blood pressure control. Therefore, a number of antihypertensive agents may be appropriate for first-line or add-on therapy.\(^10\)

Long-acting calcium antagonists are useful in treating essential hypertension because they are generally well tolerated and have been found to decrease blood pressure in various types of patients, such as elderly people with hypertension, those with diabetes, and those with stable angina pectoris.\(^11-13\)

Amlodipine is a long-acting dihydropyridine calcium channel blocker that reversibly blocks the cellular calcium L-type channel.\(^14\) Its slow association and dissociation at the calcium binding site ensure a gradual onset and extended duration of pharmacodynamic activity.\(^14\) The high oral bioavailability (60%-65%), long half-life (35-50 hours), and low renal clearance (7 mL/min per mg) ensure a sustained antihypertensive effect for >24 hours after a single oral amlodipine dose.\(^14-17\) Amlodipine has a 23% hepatic extraction
ratio with no significant presystemic or first-pass metabolism. Amlodipine is highly bound (>95%) to plasma protein, is readily taken up by hepatic tissue, and is slowly redistributed into the systemic circulation.$^{18}$

The renin-angiotensin-aldosterone system has a key function in the pathogenesis of hypertension, making blockade of this system an ideal target for antihypertensive therapy. All known clinical effects of angiotensin II, including vasoconstriction, aldosterone release, and augmented catecholamine release, are mediated by the AT$_1$ angiotensin II type 1 receptor.$^{19}$

Losartan potassium is an angiotensin II type 1 receptor antagonist. After oral dosing, plasma concentrations peak at 1 hour, and the half-life of elimination is only 2 hours. Despite this, single daily doses of losartan appear to lower blood pressure throughout the day, perhaps owing to the formation of a more slowly excreted, active metabolite. Currently, losartan is indicated for hypertension, although it may be useful in congestive heart failure as well.$^{20}$

**Risk Factor:-**

**A) Non- Modifiable Risk Factors:**

- **Family History:**
  Studies show that the tendency to develop high blood pressure runs in families. People who have parents, siblings, or close relatives (aunts, uncles and grandparents) with hypertension are at greater risk of developing the disease. The chances of getting hypertension are about twice as high if either parent or a sibling has hypertension.

- **Increasing Age:**
  As people get older they are at greater risk to develop hypertension due to:
  - Increased weight
  - Reduced elasticity of arteries.

- **Diabetes:**
  The prevalence of high blood pressure among adults with diabetes is about twice that of all adults. Blood pressure levels should be maintained at less than 130/80 mm Hg in persons with diabetes.
Gender:
Hypertension more commonly occurs in males until about age 50. From the ages of 50 to 60 the occurrence of hypertension is about equal in males and females. After age 60, hypertension more commonly occurs in females.[23]

B) Modifiable Risk Factors:

Overweight and Obesity:
There is a positive correlation between elevated body mass index (BMI) and blood pressure. However, not all obese people have high blood pressure and not all persons with hypertension are obese. Individuals who are overweight are more prone to develop severe complications of high blood pressure than those who are not overweight. Obesity (BMI > 30 kg/m2) is an increasingly prevalent risk factor for the development of hypertension and cardiovascular disease.

Metabolic Syndrome:
Individuals with metabolic syndrome are at an increased risk for coronary heart diseases and diabetes. Metabolic syndrome is defined as the presence of three or more of the following conditions:
- Elevated waist circumference (men equal to or greater than 40 inches; women equal to or greater than 35 inches)
- Elevated triglycerides (equal to or greater than 150 mg/dL)
- Reduced HDL cholesterol (men less than 40 mg/dL; women less than 50 mg/dL)
- Elevated blood pressure (equal to or greater than 130/85 mmHg)
- Elevated fasting glucose (equal to or greater than 100 mg/dL)

Sodium Intake:
Studies have shown that diets containing excessive sodium can produce hypertension in genetically predisposed animals and probably people. Low sodium diets have been known to lower blood pressure in some hypertensive patients.

Smoking:
Smoking is the most important preventable cause of premature death in the United States. Smoking increases blood pressure and leads to coronary heart disease. A blood pressure should never be taken on a client who has smoked in the last 30 minutes, as the reading will be elevated.[23]

Angiotensin Receptor Blockers:-
ARBs antagonise the action of angiotensin II in a highly selective manner at the angiotensin II AT1-receptor. Angiotensin II receptors are subclassified into AT1 and AT2 receptors. The AT1-receptor mediates all the classical effects of angiotensin II e.g. vasoconstriction, aldosterone release, sympathetic activation and other potentially harmful effects on the cardiovascular system. The functional role of the AT2-receptor is unclear. Many ARBs or active metabolites bind to the AT1-receptor in a manner which is competitive but slowly surmountable, so that duration of action is prolonged. Reduction in blood pressure secondary to vasodilation following angiotensin receptor blockade is greatest when the renin-angiotensin system is activated (e.g. following diuretic therapy or renal artery stenosis) but ARBs also lower blood pressure when there is normal or low activity of the renin-angiotensin system. ARBs do not produce cough as it is major adverse effect with ACE inhibitors.\(^ {22}\)

**Calcium Channel Blocker:**

Calcium antagonists have attracted a great deal of interest as antihypertensive agents because they reduce peripheral vascular resistance uniformly. They have reliable clinical effects in patients regardless of race, age, gender, or comorbid conditions. They reduce blood pressure through inhibition of calcium influx into the cell through the L-type calcium channel. In hypertensive patients, there is an abnormal influx of calcium into the cytosol, where it binds with calmodulin. There are several other properties of calcium antagonists that facilitate blood pressure reduction.\(^ {24}\) First, there is considerable evidence that calcium antagonists interfere with a2 (and possibly a1) adrenergic receptor-mediated vasoconstriction. They also dampen the vascular responses to angiotensin II and reduce the synthesis of aldosterone. Interestingly, patients with low renin and angiotensin II activity exhibit the greatest vasodilatory responses to calcium antagonists, which suggest a more important role for calcium-mediated vasoconstriction in these patients. Alternatively, amlodipine and others may partially inhibit local angiotensin-converting enzyme (ACE) activity that results in increased activity of the vasodilatory kinins and nitric oxide.\(^ {25}\) An equally important property of calcium antagonists is that they facilitate natriuresis by several mechanisms. They cause increases in atrial natriuretic peptide, and
the dihydropyridines, in particular, cause preferential dilation of the afferent arteriole, resulting in reduced tubular sodium re-absorption and improved renal blood flow.\textsuperscript{26}

**Drug Profile:**

1 **Losartan:**

**Mechanism of action & pharmacological actions**

Losartan is a selective, competitive Angiotensin II type 1 (AT1) receptor antagonist, reducing the end organ responses to angiotensin II. Losartan administration results in a decrease in total peripheral resistance (afterload) and cardiac venous return (preload). All of the physiological effects of angiotensin II, including stimulation of release of aldosterone, are antagonized in the presence of losartan. Reduction in blood pressure occurs independently of the status of the renin-angiotensin system. As a result of losartan dosing, plasma renin activity increases due to removal of the angiotensin II feedback.\textsuperscript{22}

**Dosage:** 50 mg once a day. In liver disease or volume depletion 25 mg once a day.\textsuperscript{22}

2 **Amlodipine:**

**Mechanism of Action:**

Amlodipine selectively inhibits the transmembrane influx of calcium ions into the vascular smooth and cardiac muscle. A decrease in intracellular calcium inhibits the contractility of the myocardial smooth muscle cells. This results in the dilation of coronary and systemic arteries with a greater pharmacological effect on the vascular smooth muscle than the cardiac muscle. The ultimate effect of amlodipine is a reduction in peripheral vascular resistance and reduction in blood pressure. Amlodipine does not significantly affect sinus node function, cardiac conduction, or have negative inotropic effects at clinical doses. The gradual pharmacological effect of amlodipine does not produce tachycardia caused by other peripheral vasodilators. Serum calcium levels are unaffected by amlodipine.\textsuperscript{22}

**Dosage:** 5 mg once a day. Initially 2.5 mg once a day, Max. 10 mg once a day.\textsuperscript{22}