CHAPTER ONE

1. Introduction and Literature Review

1.1 Introduction:

Hypertension chronic medical condition in which the systemic arterial blood pressure is elevated. What that means is that the heart has to work harder than it should to pump the blood around the body. Blood pressure involves two measurements, systolic and diastolic. Normal blood pressure is 120/80 mm/Hg. The range "Systolic" (90-120) and "Diastolic"(60-80) Millimeters of mercury (mmHg). The first figure is the systolic blood pressure, the pressure there is in the arteries when the heart is contracting. The second, or lower figure, is the diastolic blood pressure, which is the pressure in the arteries between heart beats. Hypertension is classified as either primary (essential) hypertension or secondary hypertension; about 90–95% of cases are categorized as "primary hypertension," which means high blood pressure with no obvious medical cause. The remaining 5–10% of cases (Secondary hypertension) is caused by other conditions that affect the kidneys, arteries, endocrine system. \(^{[1]}\) Persistent hypertension is one of the risk factors for stroke, myocardial infarction, heart failure and arterial aneurysm, and is one cause of chronic kidney failure. Over 90-95% percent of adult hypertension is essential hypertension. One of the most common causes of secondary hypertension is primary aldosteronism. \(^{[3]}\)

Sodium is very important cation to maintain osmolality of the body; the mechanisms of controlling osmolality are under the control of hormones that act on the kidney. Abnormality high sodium concentration is (hypernatremia) and abnormality low sodium concentration is (hyponatremia)

Potassium is most intracellular cation influence by the acid base balance, the presence of high concentration of potassium in the blood is called hyperkalemia and low concentration is called hypokalemia.

Three investigators have reported a slight increase in serum sodium concentration in patients with hypertension\(^{[4][5][6]}\), whereas two other studies report no difference.\(^{[7][8]}\)
1.2. Rationale

Hypertension is one of the most common worldwide diseases and is a major risk factor for stroke, myocardial infarction, vascular disease. Hypertension affects approximately 25% of the adult population worldwide, and its prevalence is predicted to increase by 60% by 2025. It is responsible for most deaths worldwide. Primary hypertension, also known as essential or idiopathic hypertension, accounts for as many as 95% of all cases of hypertension. As previous studies reported an association of hypertension with complication and renal impairment, the aim of this study is to assess the plasma electrolytes sodium and potassium levels in hypertensive patients and correlate them with the duration of hypertension and the outcome may be useful to managing hypertension and its complications in Sudanese hypertensive patients.
1.3 Objectives:

1.3.1 General objective:

To assess the levels of plasma Na\(^+\) and K\(^+\) in hypertensive Sudanese patients.

1.3.2 Specific objectives:

1. To compare plasma levels of Na\(^+\) and K\(^+\) between test and control.
2. To correlate between plasma levels of Na\(^+\) and K\(^+\) with duration of disease.
1.4 Literature review

1.4.1 Blood pressure

Is the pressure or force exerted by blood against blood vessels that result in causing pumping of the heart. Blood pressure is measured as systolic and diastolic pressures.”Systolic” refers to blood pressure when the heart beats while pumping blood.”Diastolic” refers to blood pressure when the heart is at rest between beats. You most often will see blood pressure number written with the systolic number above or before diastolic number. The normal blood pressure is Systolic”(90-120) and ”Diastolic”(60-80) Millimeters of mercury (mmHg). [9]

1.4.1.1 Assessment

Is an integral part of clinical practice, Routinely, a patient’s blood pressure is obtained at every physical examination, including outpatient visits, at least daily when patients are hospitalized, and before most medical procedures. Blood pressure measurements are obtained for a wide variety of reasons, including screening for hypertension, assessing a person’s suitability for a sport or certain occupations, estimating cardiovascular risk. Blood pressure measurements are also obtained routinely when following a hypertensive patient to assist with tailoring of medications and treatment of hypertension. [9]

Two methods for measuring a blood pressure exist, the direct and indirect method. The direct method is the gold standard and consists of using an intra-arterial catheter to obtain a measurement. This method, however, is not practical due to its invasiveness and its inability to be applied to large groups of asymptomatic individuals for hypertension screening. [10]

1.4.2 Hypertension

Hypertension is one of the most common worldwide diseases afflicting humans and is a major risk factor for stroke, myocardial infarction, vascular disease, and chronic kidney disease. Despite extensive research over the past several decades, the etiology of most cases of adult hypertension is still unknown, and control of blood pressure is suboptimal in the general population. Due to the associated morbidity and mortality and cost to society, preventing and treating hypertension is an important public health challenge. Fortunately, recent advances and
trials in hypertension research are leading to an increased understanding of the pathophysiology of hypertension and the promise for novel pharmacologic and interventional treatments for this widespread disease. Furthermore, of those with high blood pressure (BP), 78% were aware they were hypertensive, 68% were being treated with antihypertensive agents, and only 64% of treated individuals had controlled hypertension.\cite{3} In addition, data from NHANES 1999-2006 estimated that 30% of adults 20 years of age and older have prehypertension, defined as an untreated SBP of 120-139 mm Hg or untreated DBP of 80-89 mmHg.\cite{11}

Hypertension is the most important modifiable risk factor for coronary heart disease (the leading cause of death), stroke (the third leading cause), congestive heart failure, end-stage renal disease, and peripheral vascular disease. Therefore, health care professionals must not only identify and treat patients with hypertension but also promote a healthy lifestyle and preventive strategies to decrease the prevalence of hypertension in the general population.

Most individuals diagnosed with hypertension will have increasing blood pressure (BP) as they age. Untreated hypertension is notorious for increasing the risk of mortality and is often described as a silent killer. Mild to moderate hypertension, if left untreated, may be associated with a risk of atherosclerotic disease in 30% of people and organ damage in 50% of people within 8-10 years after onset.\cite{9,10}

1.4.2.1 Signs and symptoms

Although patients with isolated hypertension are usually asymptomatic, so generally speaks it has no symptoms but only there are have complications

1.4.2.2 Classification of hypertension

1.4.2.2.1 Primary hypertension

( Essential hypertension) Primary hypertension is the most common form of hypertension, accounting for 90–95% of all cases of hypertension.\cite{11} In almost all contemporary societies, blood pressure rises with aging and the risk of becoming hypertensive in later life is considerable.\cite{12} Hypertension results from a complex interaction of genes and environmental factors, but the genetic basis of hypertension is still poorly understood. Several environmental factors influence blood pressure. Lifestyle factors that lower blood pressure include reduced
dietary salt intake, increased consumption of fruits and low fat products (Dietary Approaches to Stop Hypertension DASH (Dietary Approaches to Stop Hypertension) diet, exercise, weight loss and reduced alcohol intake. The possible role of other factors such as caffeine consumption, and vitamin D deficiency are less clear cut. Insulin resistance, which is common in obesity and is a component of syndrome X (or the metabolic syndrome), is also thought to contribute to hypertension. Recent studies have also implicated events in early life (for example low birth weight, maternal smoking and lack of breast feeding) as risk factors for adult essential hypertension, although the mechanisms linking these exposures to adult hypertension remain obscure.

1.4.2.2 Secondary hypertension

Secondary hypertension from an identifiable cause such as endocrine conditions such as Cushing’s syndrome, hyperthyroidism, hypothyroidism acromegaly, other causes of secondary hypertension include obesity, pregnancy illegal drugs.

1.4.2.3 Pathophysiology

In most people with established essential hypertension, increased resistance to blood flow (total peripheral resistance) accounting for the high pressure while cardiac output remains normal. There is evidence that some younger people with prehypertension or 'borderline hypertension' have high cardiac output, an elevated heart rate and normal peripheral resistance, termed hyperkinetic borderline hypertension. These individuals develop the typical features of established essential hypertension in later life as their cardiac output falls and peripheral resistance rises with age. Whether this pattern is typical of all people who ultimately develop hypertension is disputed. The increased peripheral resistance in established hypertension is mainly attributable to structural narrowing of small arteries and arterioles, although a reduction in the number or density of capillaries may also contribute. Hypertension is also associated with decreased peripheral venous compliance; which may increase venous return, increase cardiac preload and, ultimately, cause diastolic dysfunction. Whether increased active vasoconstriction plays a role in established essential hypertension is unclear.

Pulse pressure (the difference between systolic and diastolic blood pressure) is frequently increased in older people with hypertension. This can mean that systolic pressure is abnormally
high, but diastolic pressure may be normal or low — a condition termed isolated systolic hypertension. The high pulse pressure in elderly people with hypertension or isolated systolic hypertension is explained by increased arterial stiffness, which typically accompanies aging and may be exacerbated by high blood pressure.\(^{[24]}\)

Many mechanisms have been proposed to account for the rise in peripheral resistance in hypertension. Most evidence implicates either disturbances in renal salt and water handling (particularly abnormalities in the intrarenal renin-angiotensin system) and/or abnormalities of the sympathetic nervous system. These mechanisms are not mutually exclusive and it is likely that both contribute to some extent in most cases of essential hypertension. It has also been suggested that endothelial dysfunction and vascular inflammation may also contribute to increased peripheral resistance and vascular damage in hypertension.\(^{[24]}\)

**1.4.2.4 Managements:**

**1.4.2.4.1 Lifestyle modifications**

The first line of treatment for hypertension is identical to the recommended preventive lifestyle changes and includes dietary changes, physical exercise, and weight loss. These have all been shown to significantly reduce blood pressure in people with hypertension.\(^{[25]}\). If hypertension is high enough to justify immediate use of medications, lifestyle changes are still recommended in conjunction with medication.

Dietary change such as a low sodium diet is beneficial. A long term (more than 4 weeks) low sodium diet in Caucasians is effective in reducing blood pressure, both in people with hypertension and in people with normal blood pressure.\(^{[65]}\) Also, the (Dietary Approaches to Stop Hypertension) diet DASH, a diet rich in nuts, whole grains, fish, poultry, fruits and vegetables lowers blood pressure. A major feature of the plan is limiting intake of sodium, although the diet is also rich in potassium, magnesium, calcium, as well as protein.\(^{[25]}\)

**1.4.2.4.2 Medications**

Several classes of medications, collectively referred to as antihypertensive drugs, are currently available for treating hypertension. Use should take into account the person's cardiovascular risk (including risk of myocardial infarction and stroke) as well as blood pressure readings, in order to gain a more accurate picture of the person's cardiovascular profile; Evidence in those with
mild hypertension (SBP less than 160 mmHg and/or DBP less than 100 mmHg) and no other health problems does not support a reduction in the risk of death or rate of health complications from medication treatment. Medications are not recommended for people with pre hypertension or high normal blood pressure.\textsuperscript{[26]}

1.4.2.4.3 Drug combinations

The majority of people require more than one drug to control their hypertension. In those with a systolic blood pressure greater than 160 mmHg or a diastolic blood pressure greater than 100 mmHg the American Heart Association recommends starting a thiazide and an ACEI, ARB or CCB. An ACEI and CCB combination can be used as well; Unacceptable combinations are non-dihydropyridine calcium blockers (such as verapamil or diltiazem) and beta-blockers, dual renin–angiotensin system blockade (e.g. angiotensin converting enzyme inhibitor + angiotensin receptor blocker), renin–angiotensin system blockers and beta-blockers, beta-blockers and centrally acting agents. Combinations of an \textit{ACE-inhibitor or angiotensin II–receptor antagonist}, a \textit{diuretic} and an \textit{NSAID} (including selective COX-2 inhibitors and non-prescribed drugs such as ibuprofen) should be avoided whenever possible due to a high documented risk of acute renal failure. The combination is known colloquially as a "triple whammy" in the Australian health industry.\textsuperscript{[27]} Tablets containing fixed combinations of two classes of drugs are available and while convenient for the people, may be best reserved for those who have been established on the individual components.\textsuperscript{[28]}

1.4.2.4.4 Resistant hypertension

Resistant hypertension is defined as hypertension that remains above goal blood pressure in spite of concurrent use of three antihypertensive agents belonging to different antihypertensive drug classes.

1.4.2.5 Complications of Hypertension

Complications of hypertension are clinical outcomes that result from persistent elevation of blood pressure. Hypertension is a risk factor for all clinical manifestations of atherosclerosis since it is a risk factor for atherosclerosis itself. It is an independent predisposing factor for heart
failure, coronary artery disease, stroke, renal disease and peripheral arterial disease. It is the most important risk factor for cardiovascular morbidity and mortality in industrialized countries[29].

1.4.2.5.1 Complications affecting the heart

Hypertensive heart disease is the result of structural and functional adaptations leading to left ventricular hypertrophy, diastolic dysfunction, CHF, abnormalities of blood flow due to atherosclerotic coronary artery disease and microvascular disease, and cardiac arrhythmias. Individuals with left ventricular hypertrophy are at increased risk for stroke, CHF, and sudden death. Aggressive control of hypertension can regress or reverse left ventricular hypertrophy and reduce the risk of cardiovascular disease. Left ventricular hypertrophy is seen in 25% of the hypertensive patients and can easily be diagnosed by using echocardiography. Underlying mechanisms of hypertensive left ventricular hypertrophy are of 2 types: mechanical, mainly leading to myocyte hypertrophy; neuro-hormonal, mainly resulting in a fibroblastic proliferation.

Abnormalities of diastolic function, ranging from asymptomatic heart disease to overt heart failure are common in hypertensive patients. Patients with diastolic heart failure have a preserved ejection fraction, which is a measure of systolic function. Diastolic dysfunction is an early consequence of hypertension-related heart disease and is exacerbated by left ventricular hypertrophy and ischemia.

1.4.2.5.2 Complications affecting the brain

Hypertension is an important risk factor for brain infarction and hemorrhage. Approximately 85% of strokes are due to infarction and the remainder are due to hemorrhage, either intracerebral hemorrhage or subarachnoid hemorrhage. The incidence of stroke rises progressively with increasing blood pressure levels, particularly systolic blood pressure in individuals >65 years. Treatment of hypertension convincingly decreases the incidence of both ischemic and hemorrhagic strokes[30].

Hypertension is also associated with impaired cognition in an aging population, Hypertension-related cognitive impairment and dementia may be a consequence of a single infarct due to occlusion of a "strategic" larger vessel or multiple lacunar infarcts due to occlusive small vessel disease resulting in subcortical white matter ischemia. Several clinical trials suggest that
antihypertensive therapy has a beneficial effect on cognitive function, although this remains an active area of investigation.

1.4.2.5.3 Complications affecting the eye:

Hypertensive retinopathy is a condition characterized by a spectrum of retinal vascular signs in people with elevated blood pressure. The retinal circulation undergoes a series of pathophysiological changes in response to elevated blood pressure. In the initial, vasoconstrictive stage, there is vasospasm and an increase in retinal arteriolar tone owing to local autoregulatory mechanisms. This stage is seen clinically as a generalized narrowing of the retinal arterioles. Persistently elevated blood pressure leads to intimal thickening, hyperplasia of the media wall, and hyaline degeneration in the subsequent, sclerotic, stage. This stage corresponds to more severe generalized and focal areas of arteriolar narrowing, widening and accentuation of the central light reflex.\[^{[31]}\]

1.4.2.5.4 Complication affecting the kidneys

Hypertension is a risk factor for renal injury and ESRD. Renal risk appears to be more closely related to systolic than to diastolic blood pressure, and black men are at greater risk than white men for developing ESRD at every level of blood pressure.

The atherosclerotic, hypertension-related vascular lesions in the kidney primarily affect the preglomerular arterioles, resulting in ischemic changes in the glomeruli and postglomerular structures. Glomerular injury may also be a consequence of direct damage to the glomerular capillaries due to glomerular hyperperfusion. Glomerular pathology progresses to glomerulosclerosis, and eventually the renal tubules may also become ischemic and gradually atrophic. The renal lesion associated with malignant hypertension consists of fibrinoid necrosis of the afferent arterioles, sometimes extending into the glomerulus, and may result in necrosis.\[^{[32]}\]

Clinically, macroalbuminuria (a random urine albumin/creatinine ratio > 300 mg/g) or microalbuminuria (a random urine albumin/creatinine ratio 30–300 mg/g) is early markers of renal injury. These are also risk factors for renal disease progression and for cardiovascular disease.\[^{[33]}[34]\]