CHAPTER ONE

Introduction

1. Introduction:

Hypertension or high blood pressure is a cardiac chronic medical condition in which the systemic arterial blood pressure is elevated ,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 first figure is the systolic blood pressure, the pressure in the arteries when the heart is contracting. The second, or lower figure, is the diastolic blood pressure, which is the pressure in arteries between heart beats. High blood pressure is above 140/90 mm/Hg. Hypertension is the opposite of hypotension.[1]

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 out obvious medical cause. The remaining 5–10% of cases (Secondary hypertension) is caused by other conditions that affect the kidneys, arteries, heart or endocrine system. Persistent hypertension is one of the risk factors for stroke, myocardial infarction, heart failure and arterial aneurysm, and it is a leading cause of chronic kidney failure. Moderate elevation of arterial blood pressure leads to shortened life expectancy. Dietary and lifestyle changes can improve blood pressure control and decrease the risk of associated health complications, although drug treatment may be necessary in patients for whom lifestyle changes prove to be ineffective or insufficient.[2]

In the year 2000 it is estimated that nearly one billion people or 26% of the adult population had hypertension worldwide , a figure expected to rise to 60% by the year 2020.It is common in both developed [333 million] and undeveloped [639milion] countries however rates vary markedly in different region. It is more common in blacks and native in American and less in white and Mexican American, rates increase with age and is greater in the southeastern united states hypertension is more prevalent in men and those of low socioeconomic status. [3]

1.2 Rationale

Hypertension is one of the non-communicable diseases ,which are common world wide but preventable, especially in the developing countries. Such disease form the biggest challenge to the public health services, as they constitute 47% of the whole burden of disease, a figure expected to rise to 60% by the year 2020.As previous studies reported an association of hypertension with complications and renal impairment , the aim of this study is to assess the plasma urea and creatinine levels in hypertensive patients and correlate them to the duration of hypertension and the outcomes may help in managing hypertension and its complications in Sudanese hypertensive patients.

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1.3 Objectives:

1.3.1 General objective:

To assess the plasma urea and creatinine levels in Sudanese hypertensive patients.

1.3.2 Specific objectives:.

- To compare plasma urea and creatinine levels between hypertensive patients and non hypertensive.
- To correlate between plasma urea and creatinine levels with the 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 is 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 120/80 mmHg, (Millimeters of mercury).[4]

1.4.1.1 Assessment of blood pressure:

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 and determining risk for various medical procedures. [5]

Two methods for measuring a blood pressure exist, the direct and indirect method. The direct method is the criterion 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.[6]The indirect (noninvasive) method is typically used. It involves collapsing the artery with an external cuff, providing an inexpensive and easily reproducible way to measure blood pressure. The indirect method can be performed using a manual cuff and sphygmomanometer or with an automated oscillometric device. The manual method requires auscultation of the blood pressure, whereas the automated system depends on oscillometric devices. [7]

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.[3]

According to the American Heart Association (AHA), approximately 75 million adults in the United States are affected by hypertension, which is defined as a systolic blood pressure (SBP) of 140 mm Hg or more or a diastolic blood pressure (DBP) of 90 mm Hg or more or .Substantial improvements have been made with regard to enhancing awareness and treatment of hypertension. [8]

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. Data from the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, which was released in 2003, reported that 30% of adults were unaware of their hypertension; up to 40% of people with hypertension were not receiving treatment; and, of those treated, up to 67% did not have their BP controlled to less than 140/90 mm Hg. [9]

Hypertension is the most important modifiable risk factor for coronary heart disease (the leading cause of death in North America), 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.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. [10]

1.4.2.1 Signs and symptoms:

In fact, nearly one-third of people who have high blood pressure don't know it. The only way to know if your blood pressure is high is through regular checkups. This is especially important if you have a close relative who has high blood pressure.If blood pressure is extremely high, there may be certain symptoms to look out for, including severe headache, fatigue or confusion ,vision problems ,chest pain, irregular heartbeat ,difficult breathing ,blood in the urine and pounding inyour chest, neck, or ears.Untreated hypertension can lead to serious diseases, including stroke, heart disease, kidney failure and eye problems.[11]

1.4.2.2 Classification of hypertension:

1.4.2.2.1 Primary hypertension:

Primary (essential) hypertension is the most common form of hypertension, accounting for 90–95% of all cases of hypertension. In almost all societies, blood pressure rises with aging and the risk of becoming hypertensive in later life is considerable.[12]Hypertension results from a complex interaction of genes and environmental factors. Numerous common genetic variants with small effects on blood pressure have been identified as well as some rare genetic variants with large effects on blood pressure but the genetic basis of hypertension is still poorly understood.[13]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, exercise, weight loss and reduced alcohol intake. Stress appears to play a minor role with specific relaxation techniques not supported by the evidence. The possible role of other factors such as caffeine consumption, vitamin D deficiency are less clear cut. Insulin resistance, which is common in obesity is also thought to contribute to hypertension. [14]

1.4.2.2.2 Secondary hypertension:

Secondary hypertension results from an identifiable cause. Renal disease is the most common secondary cause of hypertension. Hypertension can also be caused by endocrine conditions such as Cushing'ssyndrome , hyperthyroidism and hypothyroidism, acromegaly, Conn's syndrome or hyperaldosteronism, hyperparathyroidism and pheochromocytoma. Other causes of secondary hypertension include obesity, sleep apnea, pregnancy, coarctation of the aorta, excessive liquorices consumption and certain prescription medicines and illegal drugs.[15]

1.4.2.3 Pathophysiology:

In most people with established essential (primary) 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 have high cardiac output, an elevated heart rate and normal peripheral resistance. These individuals develop the typical features of established essential hypertension in later life.[16] The increased peripheral resistance in 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. [17]

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. The high pulse pressure in elderly people with hypertension is explained by increased arterial stiffness.[18]

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. [19]

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. Their potential effectiveness is similar to using a single medication. If hypertension is high enough to justify immediate use of medications, lifestyle changes are still recommended in conjunction with medication. [20]

Dietary change such as a low sodium diet is beneficial. A long term (more than 4 weeks) low sodium diet may reduce blood pressure, both in people with hypertension and in people with normal blood pressure. Also 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.[21]

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. [22]

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 combination can be used as well. [23][24]

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.[25]

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. [26] Abnormalities of diastolic function, ranging from asymptomatic heart disease to overt heart failure are common in hypertensive patients. Diastolic dysfunction is an early consequence of hypertension-related heart disease and is exacerbated by left ventricular hypertrophy and ischemia.[27]

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. [28]

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 and 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. [29]

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. [30]

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.[31]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]

1.4.3 Creatinine:

A non protein nitrogenous substance which is a molecule that contains nitrogen atoms but are not proteins. Amino acids, urea, and uric acid are commonly present in the blood plasma. Urea(45%-55%), amino acids 20%, uric acid 20%, (creatine creatinine 5%) and Ammonia. The determination of non protein nitrogenous substances in the blood has traditionally been used to monitor renal function. Nitrogen containing compounds that are not proteins or polypeptides.Urea Nitrogen (Blood) BUN Highest concentration of NPN in blood Major excretory product of protein metabolism These processes release nitrogen, which is converted to ammonia Synthesized in the liver from CO_2 and Ammonia .Uric acid is a final breakdown product of purine metabolism (adenosine/guanine) in liver Most other mammals degrade it further to allantoin.Ammonia Comes from deamination of amino acids Digestive & bacterial enzymes in intestine Also released from muscle during exercise Consumed by parenchymal cells of liver and converted to urea Free ammonia is toxic; however, ammonia is present in the plasma in low concentrations.[34]

Creatine is a nitrogenous organic acid that occurs naturally in vertebrates and helps to supply energy to all cells in the body, primarily muscle. This is achieved by increasing the formation of Adenosine triphosphate (ATP).It is naturally produced in the human body from amino acids L-arginine,. glycine, and L-methionine primarily in the kidney and liver. It is transported in the blood for use by muscles. Approximately 95% of the human body's total creatine is located in skeletal muscle and to a lesser extent n the brain to be used as an energy compound during times of increased energy demands by the phosphocreatine system which rapidly resynthesizes ATP from ADP with the use of phosphocreatine (PCr) through a reversible reaction with the enzyme creatine kinase (CK) and producing creatinine.[35]

Creatinine is a break-down product of creatine phosphate in muscle, and is usually produced at a fairly constant rate by the body (depending on muscle mass).In chemical terms, creatinine is a spontaneously formed cyclic derivative of creatine. It is chiefly filtered out of the blood by the kidneys (glomerular filtration and proximal tubular secretion). There is little-to-no tubular reabsorption of creatinine. If the filtering of the kidney is deficient, creatinine blood levels rise. Therefore, measuring serum creatinine is commonly used as an indicator of renal function. However, in cases of severe renal dysfunction a complete estimation of renal function can be

also made when creatinine levels in blood and urine used to calculate the creatinine clearance (CrCl), which reflects the glomerular filtration rate (GFR).[36]

In a study done by Peter; Brown, Ronald and Hunter 2003, July said that an Increase blood urea and serum creatinine measured in 10,940 persons for 10 years in a community-based, randomized, controlled trial of treatment for hypertension. Participants were randomized to one of two treatment groups, stepped care and referred care. The primary end point of the study was all-cause mortality, with morbid events involving the heart, brain, and kidney as secondary end points. Loss of renal function, ascertained by a change in serum creatinine, was among these secondary events. For persons with a serum creatinine concentration greater than or equal to 1.7 mg/dl, 8-year mortality was more than three times that of all other participants.The incidence of decline in renal function was greater in men, blacks, and older adults, as well as in those with higher entry diastolic blood pressure. So an elevated serum creatinine concentration is a very potent independent risk factor for mortality. [37]

1.4.3.1 Diagnostic significance of creatinine:-

Measuring serum creatinine is a simple test and it is the most commonly used indicator of renal function. A rise in blood creatinine level is observed only with marked damage to functioning nephrons. Therefore, this test is not suitable for detecting early-stage kidney disease. A better estimation of kidney function is given by the creatinine clearance (CrCl) test.A normal result is 0.7 to 1.3 mg/dL for men and 0.6 to 1.1 mg/dL for women.Females usually have a lower creatinine than males, because they usually have less muscle mass.[38]

Higher-than-normal levels may be due to acute tubular necrosis, Dehydration, Diabetic nephropathy, Pyelonephritis and Reduced kidney blood flow (shock, congestive heart failure),Rhabdomyolysis and urinary tract obstruction.

Lower-than-normal levels may be due to muscular dystrophy (late stage) and Myasthenia gravis,diuretics, such as coffee and tea, cause more frequent urination, thus potently decreasing creatinine levels and also pregnancy.[39]

1.4.4 Urea:

Urea or carbamide is an organic compound with the chemical formula CO $(NH_2)_2$. The molecule has two —NH_2 groups joined by a carbonyl (C=O) group. It is solid, colorless, and odorless (although the ammonia that it gives off in the presence of water, including water vapor in the air, has a strong odor). It is highly soluble in water and non-toxic. Dissolved in water, it is neither acidic nor alkaline. The body uses it in many processes, the most notable one being nitrogen excretion. Urea is widely used in fertilizers as a convenient source of nitrogen. Urea is also an important raw material for the chemical industry.[40]

1.4.4.1 Physiology of urea:

Urea is synthesized in the body of many organisms as part of the urea cycle, either from the oxidation of amino acids or from ammonia. Urea production occurs in the liver and is regulated by N-acetyl glutamate. Urea is found dissolved in blood and is excreted by the kidney as a component of urine. In addition, a small amount of urea is excreted (along with sodium chloride and water) in sweat. amino acids from ingested food that are not used for the synthesis of proteins and other biological substances are oxidized by the body, yielding urea and carbon dioxide, as an alternative source of energy. The oxidation pathway starts with the removal of the amino group by a transaminase; the amino group is then fed into the urea cycle. [41] Ammonia (NH_3) is another common byproduct of the metabolism of nitrogenous compounds. Ammonia is smaller, more volatile and more mobile than urea. If allowed to accumulate, ammonia would raise the pH in cells to toxic levels. Therefore many organisms convert ammonia to urea, even though this synthesis has a net energy cost. Being practically neutral and highly soluble in water, urea is a safe vehicle for the body to transport and excrete excess nitrogen. The handling of urea by the kidneys is a vital part of human metabolism. Besides its role as carrier of waste nitrogen, urea also plays a role in the countercurrent exchange system of the nephrons, that allows for re-absorption of water and critical ions from the excreted urine.[36] Urea is reabsorbed in the inner medullary collecting ducts of the nephrons, thus raising the osmolarity in the medullary interstitium surrounding the thin ascending limb of the loop of Henle, which in turn causes water to be reabsorbed. By action of the urea transporter 2, some of this reabsorbed urea will eventually flow back into the thin ascending limb of the tubule, through the collecting ducts, and into the excreted urine. This mechanism, which is controlled by the antidiuretic hormone, allows the body to create hyper osmotic urine, that has a higher concentration of dissolved substances

than the blood plasma. This mechanism is important to prevent the loss of water, to maintain blood pressure, and to maintain a suitable concentration of sodium ions in the blood plasma.[42]

1.4.4.2 Diagnostic significance of urea:

azotemia (*azot*, "nitrogen" + -emia, "blood condition") is a medical condition characterized by abnormally high levels of nitrogen-containing compounds (such as urea, creatinine, various body waste compounds, and other nitrogen-rich compounds) in the blood. It is largely related to insufficient filtering of blood by the kidneys.It can lead to uremia if not controlled.Azotemia has three classifications, depending on its causative origin, but all three types share a few common features. All forms of azotemia are characterized by a decrease in the glomerular filtration rate (GFR) of the kidneys and increases in blood urea nitrogen (BUN) and serum creatinine concentrations. [43]

1.4.4.2.1 Prerenal azotemia:

Prerenal azotemia is caused by a decrease in blood flow (hypoperfusion) to the kidneys. However, there is no inherent kidney disease. It can occur following hemorrhage, shock, volume depletion, congestive heart failure, adrenal insufficiency, and narrowing of the renal artery among other things.[43]

Renal Plasma Flow (RPF) is decreased due to hypoperfusion which results in a proportional decrease in GFR. In turn, the decreased flow and pressure to the kidney will be sensed by baroreceptors in the Juxtaglomerular cells.This leads to sympathetic nerve activation, resulting in renal afferent arteriolar vasoconstriction and renin secretion . Renin is secreted from granules in the JG cells, and once in the blood stream, it acts as a protease to convert angiotensinogen to angiotensin I, which is converted by angiotensin converting enzyme, to angiotensin II, which, in turn, stimulates aldosterone release. Increased aldosterone levels results in salt and water absorption in the distal collecting tubule. [44]

1.4.4.2.2 Primary renal azotemia:

Renal azotemia (acute renal failure) typically leads to uremia. It is an intrinsic disease of the kidney, generally the result of renal parenchymal damage. Causes include renal failure,

glomerulonephritis, acute tubular necrosis, or any other kind of renal disease. However, in addition to not being normally filtered, what urea does get filtered is not reabsorbed by the proximal tubule as it normally would be. This results in higher levels of urea in the blood and lower levels of urea in the urine as compared to creatinine. Creatinine filtration decreases, leading to a higher amount of creatinine in the blood. Third spacing of fluids such as peritonitis, osmotic diuresis, or low aldosterone states such as Addisons Disease.[44]

1.4.4.2.3 Postrenal azotemia:

Blockage of urine flow in an area below the kidneys results in postrenal azotemia. It can be caused by congenital abnormalities, blockage of the ureters by kidney stones, pregnancy, compression of the ureters by cancer, prostatic hyperplasia, or blockage of the urethra by kidney or bladder stones. Like in prerenal azotemia, there is no inherent renal disease. The increased resistance to urine flow can cause back up into the kidneys, leading to hydronephrosis. The increased nephron tubular pressure causes increased reabsorption of urea, elevating it abnormally relative to creatinine. [44]

Low plasma urea level always is indication of low protein diet or malnutrition haemodilution,liver diseases, pregnancy, excessive amounts of liquid ingestion may cause overhydration .Women and children may have lower urea levels than men because of how their bodies break .[45]

CHAPTER TWO

2. Materials and Methods

2.1 Materials:

2.1.1 Study design:

This is a quantitative, descriptive, analytical, cross - sectional and hospital-based study.

2.1.2 Study area and period:

This study was conducted in Khartoum state, capital and central of Sudan country at Omdurman town. Patients enrolled in this study were came to Aldosuogi specialized hospital during the period from March 2014 to July 2014.

2.1.3 Study Population:

The Study included Sudanese hypertensive males and females above 40 years old.

2.1.4 Sample size:

Population of this study was categorized into a study group of 60 hypertensive patients who attended to Aldosuogi specialized hospital and a control group of 40 healthy subjects (non hypertensive).

2.1.5 Inclusion criteria:

Sudanese patients with hypertension were included as a test group and healthy subjects as control.

2.1.6 Exclusion criteria:

Patients with renal disease, muscular diseases,other cardiovascular diseases and diabetes were excluded.

2.1.7 Ethical consideration:

Firstly the permission of this study was obtained from medical directors of Aldosuogi specialized hospital, then all participants were told about the research aims and benefits during interview and all of them were agreed to participate in addition to all samples were taken from participants after their agreement.

2.1.8 Data collection and clinical examination:

Clinical data for every patient was collected by questionnaire using refer card for patient while clinical examinations done by clinicians in above mentioned hospital.

2.1.9 Sample collection:

Blood sample "3ml" were from subjects of study group after fulfillments of questionnaire as well as control group, using disposable syringe and sprit for sterilization the area of collection. Collected blood was drawn in heparin containers and gently mixed with anticoagulant. The sample in heparin containers was separated by centrifuged it at 3000 rpm for 5 min. Hemolyzed and lipaemic samples were rejected and excluded from the study. Obtained plasma was tested for urea and creatinine using bio-system (BTS 302).

2.2 Methods

2.2.1 Measurement of Creatinine:

Jaffe, colorimetric-kinetic alkaline picrate method.

2.2.1.1 Principle:

The assay is based on the reaction of Creatinine with alkaline picrate forming a red complex. The time interval chosen for measurements ,avoids interferences from the other plasma constituents. The intensity of the color formed is proportional to the Creatinine concentration in the sample. [46, 47, 48]

2.2.1.2 Reagent content:

Reagent (A) sodium hydroxide 0.4mol/l.Reagent (B) picric acid 25mmol/l. Creatinine standard was creatinine aqueous primary standard 2mg/dl. Equal volume from regent (A) and (B) mixed to obtain working reagent stable for 10 days at 15-25°C. [46.47,48]

2.2.1.3 Procedure:

The three ml blood sample in heparin container was separated by centrifuged it at 3000 rpm for 5 min and the test was done as follow:

1-Assay conditions:

Wavelength…….500nm

Cuvette……1 cm. light path

Temperature……37°C /15-25°C

2-Adjust the instrument to zero with distilled water

3-Pepette into acuvette:

	Blank	Standard	Sample
WR(ml)	1.0	1.0	1.0
Standard (2mg/dl)(µl)	ـــــ	100	ـــــ
sample(µl)	ـــــ	ـــــ	100

4- Mixed and start stopwatch.

5- Read the absorbance (A1) after 30 seconds and after 90 seconds (A2) of the sample edition.

6- Calculate: Delta (A) = ΔA= A2-A1.[46,47,48]

2.2.1.4 Calculation:

Creatinine mg/dl=$\frac{\Delta Abs\ of\ T}{\Delta Abs\ of\ std} \times con\ of\ std$

Conversion factor: mg/dl× 88.4 = µmol/L.

2.2.1.5 Reference range:

Serum or **plasma**:

- Male = 0.7-1.2mg/dl or 62-106 µmol/l. [46,47,48]
- Female = 0.5-0.9mg/dl or 44-80 µmol/l. [46,47,48]

2.2.2 Measurement of Urea:

Enzymatic, colorimetric, endpoint-Berthelot method.

2.2.2.1 Principle:

Urea catalyses the conversion of urea to ammonia. In modified Berthelot reaction the ammonium ions react with a mixture of salicylate, hypochlorite. And nitroprusside to yield a blue –green dye (indophenols). The intensity of this dye is proportional to the concentration of urea in the sample. [48, 49]

2.2.2.2 Sample:

Three ml of venous blood was collected by using sterile disposable syringes. Poured into heparin containers, then centrifuged at 3000 rpm for 5 minutes and obtained plasma was not need to be diluted before assaying.

2.2.2.3 Reagent content:

Reagent A, sodium salicylate 62mmol/l, sodium nitroprusside 3.4mmol/l and phosphate buffer 20mmol/l,PH 6.9,urease>500U/ml. Reagent B sodium hydroxide 150mmol/l, sodium hypochlorite 7mmol/l. Urea standard 50mg/dl. The reagent and standard were ready for used. [48, 49]

2.2.2.4 Procedure:

The sample in heparin container was separated by centrifuged it at 3000 rpm for 5 min and the test was completed as follow:

	Blank	Standard	Sample
Sample (ml)	_	_	0.01
Standard (50mg/dl) (ml)	_	0.01	_
Reagent1 (ml)	1.0	1.0	1.0

Mixed and incubated for 10 minutes at 20-25°C. Or 5 minutes at 37°C

Reagent2 (ml)	1.0	1.0	1.0

Mixed and incubated for 10 min at 16-25°C or 5 min at 37°C, the absorbance of the sample and standard were measured against blank at wavelength 600nm[48,49].

2.2.2.5 Calculation:

Urea (mg/dL) = $\frac{Abs\ of\ T}{Abs\ of\ std} \times con\ of\ std$

To convert mg/dl to mmol/l, divide 6.01. [48,49]

2.2.2.6 Reference value:

- Plasma= 10-50mg/dl or 1.66-8.30mmol/l. [48,49]

2.3 Data analysis:

Data was analyzed by independent t-test and bivariate correlation by the programmed computer (SPSS).

CHAPTER THREE

RESULTS

3.Results:

- This study was conducted on 60 patients with hypertension as test (cases) group and 40 as control group (healthy volunteers).The two groups were age and gender matched,male account for 70% (n=42) from the cases and 67.5% (n=27) from control group, while female account 30% (n=18) from the cases and 32.5% (n=13) from control group with age means equal to 58.8± 8.2 in cases and 40.6± 8.6 in control..
- Table (3-1) illustrate that the mean of plasma urea and creatinine in mg/dl was significantly higher in the study group than the control group. (40± 13.4 vs 28 ±5.2, p.value 0.000) for urea and (1.14± 0.28 vs 0.99 ±0.26, p.value 0.01) for creatinine.
- Figure (3-1) shows a significant positive weak correlation between plasma urea and the duration of hypertension. (r=0.34,p.v=0.004)
- Figure (3-2) shows a significant positive moderate correlation between plasma creatinine and the duration of hypertension. (r=0.58, p.v=0.000).

Table (3-1): comparison between plasma urea and creatinine in (mg/dl) in hypertensive patients and non-hypertensive.

Variable	Test group (HTN) (n=60)	Control group(non-HTN) (n=40)	P. value
Urea (mg/dl)	40± 13.4	28 ±5.2	0.000
Creatinine (mg/dl)	1.14± 0.28	0.99 ±0.26	0.010

- The table shows the mean± Std. deviation and probability (P).
- Independent t- test was used for comparison.
- P- Value ≤ 0.05 was considered significant.

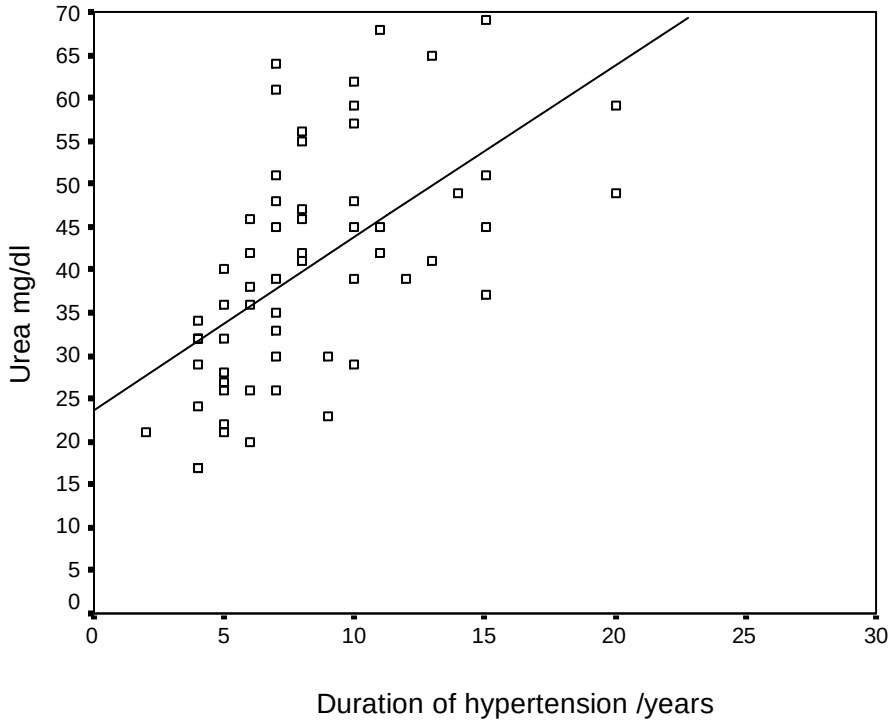

Fig (3-1): A scatter plot shows the correlation between plasma urea level (mg/dl) and duration of hypertension (years), (r=0.34, P=0.004).

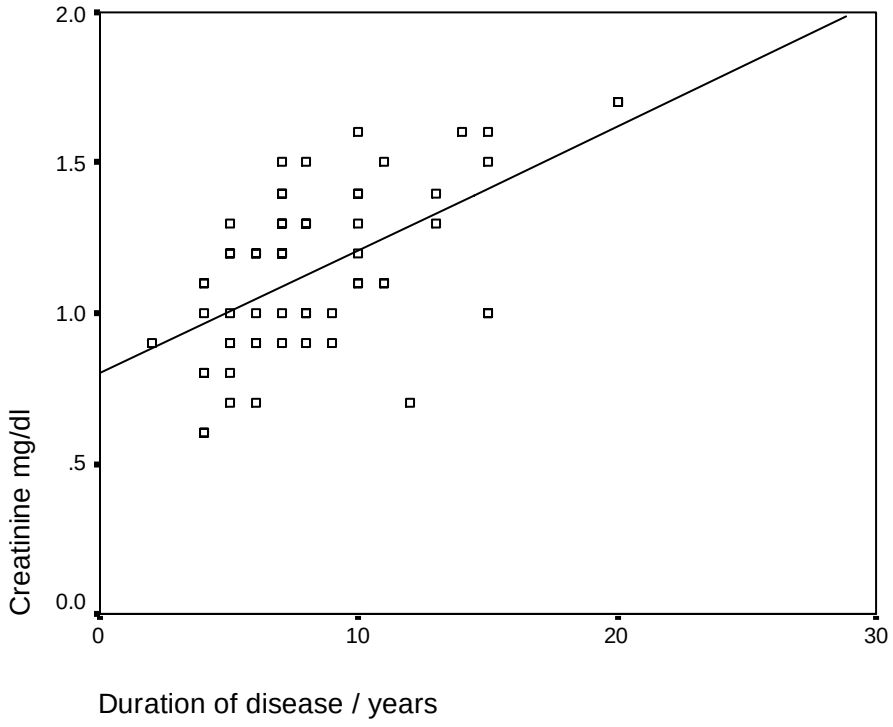

Fig (3-2): A scatter plot shows the correlation between plasma creatinine level (mg/dl) and duration of hypertension (years), (r=0.58, P=0.000).

CHAPTER FOUR

4.Discussion:

Hypertension is a cardiac,chronic medical condition in which the systemic arterial blood pressure is elevated, it can affects vital organs including kidneys,causing impairment in function and serious complications,so plasma urea and creatinine should regularly checked for their levels.[6]

In this study there was a significant increase in the mean of plasma urea level (mg/dl) in the test group when compared with the control group (40± 13.4 vs 28 ±5.2, p.value 0.000), this result agreed with the result observed by (Bulpitt and Breckenridge 2000) whom reported that there was a significant increase in plasma urea level. [50]

A significant increase in the mean of plasma creatinine level (mg/dl) in the test group when compared with the control group (1.14± 0.28 vs 0.99 ±0.26, p.value 0.01) ,this result agreed with the result observed by (Bulpitt and Breckenridge 2000) whom reported that there was a significant increase in plasma creatinine level. [50]

The present data demonstrated that there is a significant weak positive correlation between plasma urea level (mg/dl) and duration of hypertension (r=0.34, P= 0.004) , this result agree with the result observed by (Peter; Brown, Ronald and Hunter 2003),whom reported that there was a relation between the duration of hypertension and plasma urea level.[37]

A significant moderate positive correlation between plasma creatinine level (mg/dl) and duration of hypertension (r= 0.58, P= 0.000) expressed by the result and agree with the result observed by (Peter; Brown, Ronald and Hunter 2003) ,whom reported that there was a relation between the duration of hypertension and plasma creatinine level.[37]

4.1 Conclusion:

From the results of this study it is concluded that, in Sudanese patients with hypertension:

- Plasma levels of urea are significantly raised in hypertensive patients.
- Plasma levels of creatinine are significantly raised in hypertensive patients.
- There is a significant weak positive correlation between urea and duration of hypertension disease.
- There is a significant moderate positive correlation between creatinine and duration of hypertension disease.

4.2 Recommendations:

From the results of this study, it is recommended that:

- Renal function tests should be checked regularly in hypertensive patients, especially in those with prolong period of the disease.
- Health education, diet control and exercise are important factors to achieve good control of hypertension.
- Further studies with large sample size and using other biochemical tools to get more about Hypertension and to avoid complications.

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Questionnaire

Assessment of Plasma Urea and Creatinine in Sudanese Hypertension Patients

- ***Name :*** ***……..***
- ***Number:……***
- ***Sex: ……..***
- ***Age: ……***
- ***Duration of disease :……***
- ***Urea …….mg/dl***
- ***Creatinine …….mg/dl***

Date …….. ***sig ……***