**Sudan University of Sciences and Technology**

**College of Graduate Studies**

# Assessment of Albumin / Creatinine Ratio in Sudanese Hypertensive and Hypertensive Diabetics Patients in Khartoum State

تقيم نسبة الالبيومين للكرياتينين لدى المرضى السودانين المصابين بضغط الدم وضغط الدم والسكرى فى ولاية الخرطوم

A dissertation submitted in partial fulfillment for the requirements of M.Sc. degree in medical laboratory science- Clinical Chemistry

## By:

**Esra Abayazeed Saeed Hassan**

**(B.Sc .in Medical Laboratory Sciences 2014 Sudan University of Sciences and Technology)**

**Supervisor :**

**Dr- Seif Eldeen Ahmed Mohamed**

**Sudan University of Sciences and Technology**

**College of Medical Laboratory Sciences-Clinical Chemistry**

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( يرفع الله الذ ين امنوا منكم والذين اتوا العلم درجات والله بما تعملون خبير)

سوره المجادلة (الايه 11)

# DEDICATION

We dedicate this research

TO

**My teachers**

TO

**My family**

**Who did not spare any effort in scientific scores**

To

**Our colleagues**

To

**All who are suffering from high blood pressure**

To

**All who help me in my research**

# ABSTRACT

**Background:** Hypertension (HTN) is a noteworthy public health concern worldwide due to its significant contribution to the global health burden. It increase risk of serious problems such as heart attacks, strokes, vascular disease and chronic kidney disease.

**Objective**s: This study done to assess albumin/creatinine ratio in Sudanese hypertensive and hypertensive diabetics Patients in Khartoum state.

**Material and method:** The study carried out at Khartoum state in Sharg Alneel hospital, during the period of March to October 2018, including 66 participants and 34 of them are hypertensive (as case) and 32 non hypertensive (as control) measurement of albumin-to creatinine ratio (ACR) in a random urine sample was done for all participants by Roche COBAS and data were analyzed using SPSS in computer program.

**Results** : Albumin/creatinine ratio was high significant elevated in cases ($85.5\pm22.7$ mg/g) when compared to controls ($8.4\pm3.6$ mg/g) with p value 0.00, highly significant increased in albumin/creatinine ratio in hypertensive with diabetes mellitus ($129.4\pm31.61$ mg/g) when compared with hypertensive without diabetes($50.9\pm18.24$ mg/g) with p value 0.00 , insignificant different of albumin/creatinine ratio in male ($94.11\pm49.43$ mg/g) when compared to female ($75.95\pm42.64$ mg/g) with p value 0.263 and significant positive high correlation with age($r= .735$    $p=0.00$) and  significant positive moderate correlation with duration of hypertension($r= .685$   $p=0.00$).

**Conclusion**: This study revealed that albumin/creatinine ratio was increased in hypertensive patients, hypertensive with diabetes mellitus, and the increase was associate with age and duration of hypertension while not associate with gender.

# المستخلص

**خلفية:**جدير بالملاحظة ان الضغط هو مشكلة صحية عامة حول العالم نتيجه لانه يساهم بشكل كبير فى العبء الصحى العالمى . فهو يزيد خطورة الاصابه بالمشاكل الكبيره مثل نوبات القلب' السكتات الدماغيه' وامراض الاوعية الدموية وامراض الكلى المزمنة.

**الهدف :**هذه الدراسه نسبة الالبيومين كرياتينين لدى المرضى السودانين المصابين بضغط الدم وضغط الدم والسكرى فى ولايه الخرطوم.

**المواد والطريقة :**هذه الدراسة تمت بولاية الخرطوم فى مستشفى شرق النيل خلال الفتره من مارس الى 20 اكتوبر . تحتوى 66 شخص, 34 لديهم ضغط و32 ليس لديهم ضغط. حللت نسبة المايكروالبيومين/ كرياتينين على عينة بول عشوائيه بواسطة جهاز الكوباس والبيانات حللت بواسطه برنامج الحزم الاحصائية للعلوم الاجتماعية .

**النتايج :** نسبه الالبيومين/كرياتينين مرتفعه لدى مرضى الضغط( 22.7±85.5 مل جرام لكل جرام)عند مقارنتها مع الاشخاص غير المصابين بالضغط (3.6±8.4 مل جرام لكل جرام) القيمة المعنويه 0.00' والنسبه مرتفعه لدى مرضى الضغط المصابين بالسكرى (31.61±129.4مل جرام لكل جرام) بالمقارنه مع مرضى الضغط غير المصابين بالسكرى (18.24±50.9 مل جرام لكل جرام )القيمة المعنوية 0.00  'وفى الرجال (49.43±94.11 مل جرام لكل جرام) مقارنة بالنساء (42.64±75.95 مل جرام لكل جرام) ولا يوجد فرق ذو دلالة معنوية  (القيمة المعنوية =0.263) ولديه ارتباط قوى بالعمر(معامل الارتباط =735. القيمة المعنوية =0.00) وايضا لديه ارتباط قوى بالمده الاصابه بالضغط (معامل الارتبط =685. القيمة المعنوية =0.00) .

**الاستنتاج :**هذه الدراسه اظهرت ان نسبه الالبيومين/كرياتينين مرتفعه لدى مرضى الضغط 'مرضى الضغط المصابين بالسكرى وزيادة النسبه مرتبطه بالعمر ومدة الاصابه بالضغط ولا ترتبط بالنوع.

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## 1.1 Introduction:

Hypertension is chronic elevation of arterial blood pressure. Most patients that present hypertension eventually cause progressive renal damage. Which further leading to death in 10% of patients due to renal lesion. Hypertension is the growing issue of public health problem of adult population in both developed as well as developing world , which affecting one-person in every four people. Hypertension can lead to injury to glomerular basement membrane causing small sized plasma proteins like albumin to leak into the urine, thus detection of this microalbumin is earliest indicator of renal damage due to hypertension (Sharma et al., 2012).

Hypertension is one of most preventable causes of premature morbidity and morbidity and mortality world wide.

Hypertension if remain undiagnosed it may cause myocardial infraction, stroke (ischemia, and hemorrhagic), nephropathy and retinopathy. Despite widely recognized dangers related to uncontrolled hypertension, the disease remains inadequately treated in most of patients due to asymptomatic behavior even when it progressively damage the multi organ systems(Addo et al., 2007).

Untreated hypertension is associated with a progressive rise in blood pressure, often culminating in a treatment resistant state due to associated vascular and renal damage. albuminuria is associated with glomerular damage and endothelial dysfunction and predictive of development of nephropathy because albumin molecule being small in size is the first protein to enter the urine after glomeruli damage and microalbumin is an independent marker of cardiovascular disease(Matthew and Weir, 2007).

 Study done by Jose Mostaza et al. in span (2005) to calculate albumin/ creatinine ratio in hypertensive patients, the result was as follows the mean of albumin/ creatinine ratio high .

## 1.2 Rationale

Hypertension is one of commoner chronic disease. It is also major risk contributor for coronary heart disease and cardiovascular disease which leading cause of death. It is affect many peoples of different age, sex, and ethnicity. This disease is usually asymptomatic until damaging effect of hypertension such as smoke, renal dysfunction and visual problems are observed. The higher blood pressure increase the risk of complication of the disease (Jorge et al., 2007)

The study aim to highlight parameter of great important as indicator of renal disorder. study done by Sharma et al. in India (2012) correlate between albumin/ creatinine ratio with age, sex and duration of hypertension, the result show high significant of ratio in hypertensive patients compared with controls, statistical significant correlated with age and duration of hypertension.

Because hypertension is referred as the silent killer and there was no publish previous study in Sudan. This study was done to assess albumin/creatinine ratio as early indicator of renal dysfunction.

**1.3 Objectives**

**1.3.1General objective:**

To asses albumin/creatinine ratio in Sudanese hypertensive and hypertensive diabetics patients in Khartoum state.

**1.3.2 Specific objectives:**

1-To estimate urine albumin/creatinine ratio in study groups.

2-To calculate and compare ACR in study groups.

3-To compare the mean of albumin/creatinine ratio in case with that of control group.

4-To compare albumin / creatinine ratio in patients of hypertension with diabetes mullets with that with hypertension without diabetes mellitus.

5-To compare albumin / creatinine ratio across the gender.

6-To correlate of between albumin / creatinine ratio and duration of disease.

7-To correlate between albumin / creatinine ratio with age.

**2.1Hypertension {Blood Pressure}:**

Hypertension also known as high blood pressure (HBP), is a long-term medical condition in which blood pressure in the arteries is persistently elevated. High blood pressure usually does not cause symptoms. Long-term high blood pressure however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease, vision loss, chronic kidney disease and dementia (Lackland and Weber, 2015). Blood pressure is quantified as systolic and diastolic pressure in millimeters of mercury(mm Hg). The systolic pressure represent the peak pressure due to ventricular contraction during systole, where as diastolic pressure represents the pressure during ventricular relaxation in diastole.

Blood pressure is expressed by two measurements, the systolic and diastolic pressures, which are the maximum and minimum pressures respectively. For most of adults, normal blood pressure at rest is within the range of 100-130 millimeters mercury (mmHg) systolic and 60-80 mmHg diastolic. For most adults, high blood pressure is present if the resting blood pressure is persistently at or above 130/80 or 140/90mmHg (Poulter et al.,2015). Different numbers apply to children. Ambulatory blood pressure monitoring over a 24 hour period appears more accurate than office-based blood pressure measurement (Poulter et al.,2015).

**2.1.1 Classification of Hypertension:**

High blood pressure is classified as either primary (essential) high blood pressure or secondary high blood pressure (Poulter et al., 2015).  Primary hypertension was previously termed (essential hypertension) because long standing view that high blood pressing was same time (essential) to perfuse diseased and sclerotic arteries – it is now recognized that the diseased and sclerotic arteries were most often the consequence of the hypertension and thus the term (essential hypertension) is redundant and the primary hypertension is preferred.  About 90-95% of cases are Primary, defined as high blood pressure due to non specific lifestyle and genetic factors (Poulter et al., 2015). The remaining 5-10% of cases are categorized as secondary high blood pressure, define as high blood pressure due to an identifiable causes, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of the birth control pills(Poulter et al., 2015).

## 2.1.2 Causes of Hypertension:

The exact cause for hypertension is difficult to predict because hypertension is difficult to predict because hypertension results from complex interaction of genes and environment factors (Addo et al., 2007).

Primary ( essential) hypertension:

Hypertension result s from a complex interaction of genes and environmental factors. Numerous common genetic variants with small effects on blood pressure have been identified (Ehret et al.,2011) as well as some rare genetic variants with large effects on blood pressure. Also genome-wide association studies (GWAS) have identified 35 genetic loci related to blood pressure,12 of these genetic loci influencing blood pressure were newly found (Katoet al., 2015).

Secondary hypertension :

It is result of identifiable causes, which may be caused by kidney damage or impaired function (The accounts for most secondary forms of hypertension ).Tumor or over activity of adrenal gland ,thyroid dysfunction, coarctation of aorta,, pregnancy related condition, sleep Apnea syndrome, medication, recreational drugs, drinks and food(Williams et al., 2007).

## 2.1.3 Risk Factors:

Several risk factors have been identified:

Genetic variation:

Having a personal family history of hypertension increases the likelihood that an individual develops it (Loscalzo, Joseph, Anotony S.; Braunwald, Eugene; et al,2008). High blood pressure tends to run in families (Balam-Ortiz *et al*.,2012).

Race :

Essential hypertension is four times more common in black than white people, accelerates more rapidly and is often more severe with higher mortality in black patients (Loscalzo et al.,2008).

Age:

Hypertension can also be age-related and if this is the case, it is likely to be multifactorial. Once possible mechanism involves a reduction in vascular compliance due to the stiffening of the arteries. This cab build up due to isolated systolic hypertension

with a widened pulse pressure. A decrease in glomerular filtration rate is related to aging and this result in decreasing efficiency of sodium excretion. The developing of certain diseases such as renal microvascular disease and capillary rarefaction may relate to this decrease in efficiency of sodium excretion. There is experimental evidence that suggests that renal microvascular disease is an important mechanism for inducing salt sensitive hypertension (Kosugi et al., 2009)

Obesity:

Obesity can increase the risk of hypertension to five fold as compared with normal weight, and up to two-thirds of hypertension cases can be attributed to excess weight (Haslam and James,2005). More than 85% of cases occur in those with a Boy Mass Index (BMI) greater than 25 (Haslam and James,2005). A definitive link between obesity and hypertension has been found using animal and clinical studies; from these it has been realized that many mechanisms are potential causes of obesity-inducing hypertension. These mechanisms include the activation of the sympathetic nervous system as well as the activation of the rennin- angiotensin- aldosterone system (Rahmouni et al.,2005) .

Salt:

Which is an environmental factor that has received the greatest attention. Approximately one third of essential hypertensive population is responsive to sodium intake. When sodium intake exceeds the capacity of the body to excrete it through the kidney, vascular volume expands secondary to movement of fluid into the intra-vascular compartment. This causes the arterial pressure to rise as the cardiac output increases. As arterial pressure increases in response to high sodium chloride intake, urinary sodium excretion increases and the excretion of the salt is maintained at expense of increased vascular pressures (Loscalzo et al.,2008).

 Too little potassium in diet:

 potassium helps balance the amount of sodium in cells, if don't get enough potassium in diet or retain enough potassium may accumulate too much sodium in blood. Also some authorities claim that potassium might both prevent and treat hypertension(Eva May Nunnelley Hamilton et al.,1991).

Alcohol:

Excessive alcohol consumption will increase blood pressure over time. Alcohol also contains a high density of calories and may contribute to obesity. A2018 review found that any alcohol increased blood pressure in males while over one or two drinks increased the risk in females (Roerecke et al.,2018)

Ranin:

Renin elevation is another risk factor. Ranin is an enzyme secreted by the juxtaglomerular apparatus of the kidney and linked with aldesterone in a negative feedback loop. In consequence some hypertensive patients have been defined as having low renin and other as having essential hypertension. low rennin hypertension is more common in African Americans than white Americans and may explain why African Americans tend to respond better to diuretic therapy than drugs that interfere with the renin- angiotensin system. High rennin levels predispose to hypertension by causing sodium retention through yhe following mechanism : Increased rennin increased→ angiotensin II → Increased vasoconstriction, thirst/ ADH and aldesterone →Increased sodium reabsorption in the kidneys→ Increased blood pressure.

Diabetes:

Hypertension can also be caused by insulin resistance and/ or hyperinsulinemia, which are components of syndrome X, or the metabolic syndrome. Insulin is a polypeptide hormone secreted by cells in the islets of langerhans, which are contained throughout the pancreas. Its main purpose is to regulate the levels of glucose in the body antagonistically with glucagon through negative feedback loops. Insulin also exhibits vasodilatory properties. In normotensive individuals, insulin may stimulate sympathetic activity without elevating mean arterial pressure. Recent studies claim that obesity is a risk factor for hypertension because of activation of renin- angiotensin system (RAS) in adipose tissue (Segura and Ruilope,2007) , and also linked renin- angiotensin system with insulin resistance, and claims that any one can cause the other (Saitoh,2009) .

Smoking:

Smoking does not directly cause high blood pressure. However it is a known risk factor for other serious cardiovascular disease.

Vitamin deficiency:

It has been suggested that vitamin D deficiency is associated with cardiovascular risk factors (Lee et al.,2008). It has been observed that individuals with a vitamin D deficiency have higher systolic and diastolic blood pressures than average. Vitamin D inhibits rennin secretion and its activity, it therefore acts as a" negative endocrine regulator of the renin- andiotensin system". Hence, a deficiency in vitamin D lead to an increase in renin secretion. This is one possible mechanism of explaining the observed link between hypertension and vitamin D levels in the blood plasma(Forman et al.,2007).

Lack of exercise :

Regular physical exercise reduces blood pressure. The UK National Health Service advises 150 minutes (2 hours and 30 minutes) of moderate intensity aerobic activity per week to help prevent hypertension.

Sex :

The life time risk is the same for males and females, but men are more prone to hypertension at younger age, the prevalence tends to be higher in older women.

Using tobacco:

Not only does smoking or chewing tobacco immediately raise blood pressure temporarily, but the chemicals in tobaccos can damage the lining of artery walls, this can cause arteries narrow and increase risk of heart disease, secondhand smoke can also increase heart disease risk.

Stress:

levels of stress increase blood pressure, if try to relax by eating more, using tobacco or drink alcohol may only increase problems with high blood pressure.

Certain chronic condition :

Also may increase risk of high blood pressure such as kindey disease, diabetes and sleep apnea. Sometimes pregnancy contributes to blood pressure as although blood pressure is most common in adult may be at risk too .For some children blood pressure caused by problems with the kidneys or heart. But for growing number of kids, life style habits, such as unhealthy diets obesity and lack of exercise, contribute to blood pressure.

**2.1.4 Signs and Symptoms:**

Hypertension is rarely accompanied by symptoms, and its identification is usually through screening, or when seeking healthcare for an unrelated problem. Some with high blood pressure report headaches (particularly at the back of the head and in the morning), as well as lightheadedness, vertigo, tinnitus (buzzing or hissing in the ears), altered vision or fainting episodes (Fisher and Williams,2005). These symptoms, however might be related to associated anxiety rather than high blood pressure itself (Marshall et al.,2012).

On physical examination, hypertension may be associated with the presence of changes in the optic fundus seen by ophthalmoscopy. The severity of the changes typical of hypertensive retinopathy is graded from I – IV; grades I and II may be difficult to differentiate (Wong et al.,2007). The severity of the retinopathy correlates roughly with the duration or the severity of the hypertension (Fisher and Williams,2005).

**2.1.5 Complications Of Hypertension:**

The excessive pressure on artery walls caused by high blood pressure can damage Blood vessels as well as organs the higher blood pressure and long it goes uncontrolled  the greater the damage. Uncontrolled high blood pressure can lead to complications including:

 Heart attack or stroke:

Blood pressure can cause hardening and thickening of arteries (Atherosclerosis) which can lead to heart attack, stroke or other complications(Balam-Ortiz *et al*., 2012).

Aneurysm:

 Increase blood pressure can cause blood vessels to weaken and bulge forming an aneurysm, if aneurysm raptures, it can be life the retaining.

Hear failures:

Too pump blood against blood pressure in vessels heart has to work harder, this cause the walls of hearts pumping chamber to thicken (left ventricular hypertrophy). Eventually the thickened muscle may have a hard time pumping enough blood to meet the body needs, which can lead to heart failure.

Trouble with memory or understanding :

Uncontrolled high blood pressure may also affect ability to think, remember and learn. Trouble with memory or understanding concepts is more common in people with high blood pressure.

Complications affecting the heart :

Hypertensive heart disease is result of structural and functional adaptations (Steinmetz and Nickenig, 2009) , leading to left ventricular hypertrophy (Hennersdorf and Strauer,2006) , diastolic dysfunction(Hennersdorf and Strauer,2007) , CHF, abnormality of blood flow due to atherosclerotic coronary artery disease (Steinmetz and Nickenig, 2009), microvascular disease (Agabiti-Rosei E,2008) and cardiac arrhythmias (Hennersdorf and Strauer,2006). Individuals with left ventricular hypertrophy are at increased risk for stroke , CHF and sudden death (Wachtell et al.,2008). Aggressive control of hypertension can regress or reverse left ventricular hypertrophy and reduce the risk of cardiovascular disease (Petrovic´ and Stojimirovic´,2008). Left ventricular hypertrophy are seen in 25% of hypertensive patients and can easily be diagnosed by using echocardiography (Herpin,1999). Underling mechanisms of hypertensive left ventricular are 2 types: mechanical, mainly leading to myocyte hypertrophy; neuro-hormonal. Mainly resulting in a fibroblastic proliferation (Herpin,1999).

Abnormalities of diastolic function, ranging from asymptomatic heart disease (Parekh and Maisel,2009) to overt heart failure (Verma and Solomon,2009), are common in hypertensive patients. Patients with diastolic heart failure have a preserved ejection fraction, which is a measure of systolic function (Okoshi et al.,2007). Diastolic dysfunction is an early consequence of hypertension-related heart disease and is exacerbated by left ventricular hypertrophy (Hennersdorf and Strauer,2007) and ischemia.

Complications affecting the brain:

Hypertension is an important risk factor for brain infarction and hemorrhage (White,2009). Approximately 85% of strokes are due to infarction and the remainder are due to hemorrhage, either intracerebral hemorrhage or subarachnoid hemorrhage (Loscalzo et al.,2008). 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 ischemia and hemorrhage strokes (Loscalzo et al.,2008).

Hypertension is also associated with impaired cognition in an aging population (Iadecola et al.,2009). Hypertension-related cognitive impairment and dementia may be a consequence of a single infarct due to occlusion of a "strategic" larger vessel (Solans-Laque´et al.,2008) or multiple lacunar infarcts due to occlusive small vessel disease resulting in subcortical white matter ischemia (Erkinjuntti and Gauthier,2009). Several clinical trials suggest that antihypertensive therapy has a beneficial effect on cognitive function, although this remains an active area of investigation (Zekry,2009). Cerebral blood flow remains unchanged over a wide range of arterial pressures (mean arterial pressure of 50-150 mmHg) through a process termed autoregulation of blood flow(Hall et al.,2006). Signs and symptoms of hypertensive encephalopathy may include severe headache, nausea and vomiting (often of a projectile nature), focal neurologic signs, and alterations in mental status. Untreated, hypertensive encephalopathy may progress to stupor, coma, seizures and death within hours (Müller-Wiefel,1988). It is important to distinguish hypertensive encephalopathy from other neurologic syndromes that may be associated with hypertension example: cerebral ischemia, hemorrhage or thrombotic stroke, seizure disorder, mass lesions, pseudotumor cerebri, delirium tremens, meningitis, acute intermittent porphyria, traumatic or chemical injury to the brain and uremic encephalopathy (Loscalzo et al.,2008).

Dementia :

Narrowed or blocked arteries can limit blood flow to the brain, leading to certain type of dementia (vascular dementia). A stroke that interrupts blood flow to the brain also can cause vascular dementia .

Complications affecting the eye:

Hypertensive retinopathy is a condition characterized by a spectrum of retinal vascular signs in people with elevated blood pressure (Walsh,1982). It was first described by liebreich in 1859. The retinal circulation undergoes a series of pathophysiological changes in response to elevated blood pressure (Tso and Jampol,1982). In the initial, vasoconstrictive stage, there is vasospasm and 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 lead 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, changes in the arteriolar and venular junctions and alterations in the arteriolar light reflex(example: widening and accentuation of the central light reflex or copper wiring) (Wong and Mitchell,2004). This is followed by an exudative stage, in which there is disruption of blood-retina barrier, necrosis of smooth muscles and endothelial cells, exudation of blood and lipid and retinal ischemia. These changes are manifested in retina as microaneurysms, hemorrhage, hard exudates and cotton-wool spots. Swelling of the optic disk may occur at this time and usually indicatesseverely elevated blood pressure (example malignant hypertension). In contrast, other retinal vascular complications of hypertension such as macroaneurysms and branch-vein occlusions, are not uncommon in patients with chronically elevated blood pressure. These stages of hypertensive retinopathy however, may not be sequential (Tso and Jampol,1982). For example, signs of retinopathy that reflect the exudative stage, such as retinal hemorrhage or microaneurysms, may be seen in eyes that do not have features of sclerotic stage(Tso and Jampol,1982), the exudative signs are nonspecific, since they are seen in diabetes and other conditions.

Complications affecting the kidneys:

Renal system is group of organs it work together to produce, store and release urine. The organs in work together to form renal system: kidneys, bladder, ureters and urethra. Kidneys are vital part of renal system. The one function of kidneys such as regulate blood pressure. The also work to regulate the PH balance in body as well as electrodes such as sodium and potassium. also kidneys transport into ureters before the urine exist the body the kidney make important hormones such as Renin it involve in control blood pressure .Hypertension is leading cause of kidney disease and kidney failure (end stage of renal and kidney disease), Hypertension can also cause damage blood vessels and filters in the kidney making removal of waste from the body difficult(National Kidney and Urologic Diseases information clearinghouse3, MD 20892-3580)

Hypertension is a risk factor for renal injury and end stage renal disease (ESRD) (Krzesinski and Cohen,2007) . Renal risk appears to be more closely to systolic than to

diastolic blood pressure (Marin et al.,2005) , and black men are at greater risk than white men for developing ESRD at every level of blood pressure (Lindhorst et al.,2007). The atherosclerotic, hypertension-related vascular lesions in the kidney primarily affect the preglomerular arterioles (Marin et al.,2005) , resulting in ischemic changes in the glomeruli and postglomerular structures (Loscalzo et a.l,2008). Glomerular injury may also be a consequence of direct damage to the glomerular capillaries due to glomerular hyperperfusion. Glomerular pathology progresses to glomerulosclerosis(Kwoh et al., 2006) and eventually the renal tubules may also become ischemic and gradually atrophic. The renal lesion associated with malignant hypertension consists of fibrinoid necrosis of afferent arterioles (Ono and Ono,1997), sometimes extending into the glomerulus and may result in focal necrosis of the glomerular tuft.

Complications associated diabetes and hypertension :

Diabetes has several complications of which one is hypertension or high blood pressure. Data indicate that at least 60-80% of individuals whom develop diabetes will eventually develop high blood pressure. The high blood pressure is gradual at early stages and may take at least 10-15 years to fully develop. Beside diabetes, other factors that may also increase high blood pressure include: obesity, insulin resistance and high cholesterol levels. In general, fewer than 25% of diabetics have good control of their blood pressure. The present of high blood pressure in diabetes is associated with a 4 fold increase in death chiefly from heart disease and strokes. The chief reason why people with diabetes develop high blood pressure is hardening of the arteries. Diabetes tends to speed up the process of atherosclerosis. The other fact about diabetes is that it affects both large and small vessels in the body. Over time, blood vessels become clogged with fatty deposits, become non-compliant and lose of their elasticity. The process of atherosclerosis is a lot faster in diabetic individuals whom do not have good control of their blood sugars. The high blood pressure eventually lead to heart failure, strokes, blindness, kidney failure, loss of libido and poor circulation of blood in the eye. When the blood supply to the feet is compromised, the chances of infections and amputations also increases. All diabetics should know that even mild elevations in blood pressure can be detrimental to health. Studies have shown that diabetics with even a slight elevation in blood pressure have 2-3 times the risk of heart disease compared to individuals without diabetes .

### 2.1.6 Diagnosis of Hypertension :

Typical tests performed

**Table (2-1)Test performed for diagnosis of hypertension**

| System | Test |
|---|---|
| Kidney | Microscopic analysis, protein in the urine, BUN and/ or creatinine |
| Endocrine | Serum sodium, potassium, calcium, TSH |
| Metabolic | Fasting blood glucose, HDL, LDL, and total cholesterol, triglycerides |
| Other | Hematocrit, electrocardiogram and chest radiograph |

**Sources: Harrison´s Principles of Internal Medicine (Loscalzo et al.,2008)  and others.**

Hypertension is diagnosed on the basis of a persistently resting high blood pressure. The American Heart Association recommends at least two separate health care visits. For an accurate diagnosis of hypertension to be made, it is essential for proper blood pressure measurement technique to be used (Viera, 2017). Improper measurement of blood pressure is common and can change the blood pressure reading by up to 10 mmHg, which can lead to misdiagnosis and misclassification of hypertension. Correct blood pressure measurement technique involves several steps.  Proper blood pressure measurement requires the person whose blood pressure is being measured to sit quietly for at least five minutes which is then followed by application of a properly fitted blood pressure cuff to a bare upper arm. The person should be seated with their back supported, feet flat on the floor and with their legs uncrossed (Viera, 2017). The person whose blood pressure measured should avoid talking or moving during this process. The arm being measured should be supported on a flat surface at the level of the heart. The blood pressure cuff should be deflated slowly (2-3 mmHg per second) while listening for the Korotkoff sounds (Vischer and Burkard, 2017). The bladder should be emptied before can a persons blood pressure is measured since this increase blood pressure by up to 15/10 mmHg. Multiple blood pressure readings (at least two) spaced 1-2 minutes apart should be

obtained to ensure accuracy. Ambulatory blood pressure monitoring over 12 to 24 hours is the most accurate method to confirm the diagnosis (Siu,2015). An exception to this is those with very high blood pressure readings especially when there is poor organ function. Initial assessment of the hypertensive people should include a complete history and physical examination. Once diagnosis of hypertension has been made, healthcare providers should attempt to identify the underlying cause based on risk factors and other symptoms if present.

Adults:-

Classification in adults (persons with systolic and diastolic in different categories are assigned to the higher category)

**Table (2-2) Categories of hypertension in adults**

| Category | Systolic mmHg | Diastolic mmHg |
|---|---|---|
| Hypotension | <90 | <60 |
| Normal | 90-119 | 60-79 |
| Prehypertension (high normal elevated) | 120-129 | 60-79 |
| Stage 1 hypertension | 130-139 | 80-89 |
| Stage 2 hypertension | >140 | >90 |
| Hypertensive crises | ≥180 | ≥120 |
| Isolated systolic hypertension | ≥160 | <90 to 110 |

**2.1.7 Management of Hypertension:**

According to one review published in 2003, reduction of blood pressure by 5 mmHg can decrease the risk of the stroke by 34%, of ischemic heart disease by 21%, and reduce the likelihood of dementia, heart failure and mortality from cardiovascular disease(Law et al.,2003).

Lifestyle modifications:

The first line of treatment for hypertension is lifestyle changes, including dietary changes, physical exercise, and weight loss. Though these have all been recommended in scientific advisories , a Cochrane systematic review found no evidence for effects of weight loss diets on death, long-term complications or adverse events in persons with hypertension (Semlitsch et al.,2016). The review did find a decrease in blood pressure. Their potential effectiveness is similar to and at times exceeds a single medication, If hypertension is high enough to justify immediate use of medications, lifestyle changes are still recommended in conjunction with medication.

Dietary changes shown to reduce blood pressure include diets with low sodium(Aburto et al.,2013), the DASH diet, vegetarian diets and green tea consumption. Increasing dietary potassium has a potential benefit for lowering the risk of hypertension. The 2015 Dietary Guidelines Advisory Committee (DGAC) stated that potassium is one of the shortfall nutrients which is under-consumed in the united states(Scientific Report of the 2015 Dietary Guidelines Advisory Committee).

Physical exercise regimens :

Which are shown to reduce blood pressure include isometric resistance exercise, aerobic exercise, resistance exercise and device-guided breathing.

Stress reduction techniques :

Such as biofeedback or transcendental meditation may be considered as an add-on to other treatments to reduce hypertension, but do not have evidence for preventing cardiovascular disease on their own(Nagele et al.,2014).

-Medications :

Several classes of medications, collectively referred to as antihypertensive medications, are available for treating hypertension. First-line medications for hypertension include: thiazide-diuretic, calcium channel blockers, angiotensin converting enzyme inhibitors and angiotensin receptor  blockers (James et al.,2013). These medications may by used alone or in combination (ACE inhibitors and ARBs are not recommended for use in combination); the latter option may serve to minimize counter-regulatory mechanisms that act to revert blood pressure values to pretreatment levels. Previously beta blockers such as atenolol were thought to have similar beneficial effects when used as first-line

therapy for hypertension. However, a Cochrane review that included 13 trials found that the effects of beta-blockers are inferior to that of other antihypertensive medications(Wiysonge et al., 2017). Most people require more than one medication to control their hypertension.

## 2.2 Microalbuminuria:

Microalbuminuria is a term to describe a moderate increase in the level of urine albumin. It occurs when the kidney leaks small amounts of albumin into the urine, in other words, when an abnormally high permeability for albumin in the glomerulus of the kidney occurs.

Microalbumin is early indicator of kidney damage. It occurs due to loss of systemic endothelial glycocaly x-aprotein- rich surface layer on the endothelium(Klausen et al., 2007).

One function of kidney is conserve plasma proteins so not execrated in to urine. There are two mechanism that prevent protein from passing into using the glomeruli provide barrier that keeps larger plasma protons the blood vessels and small protein reabsorbed by the tubule(S. C. Satchell and J. E. Tooke, 2008).

The albumins are a family of globular proteins, the most common of which are the serum albumins. Albumins are commonly found in blood plasma and differ from other blood proteins in that they are not glycosylated.

Synthesis:

Albumin is synthesized in the liver as preproalbumin which has an N-terminal peptide that is removed before the nascent protein is released from the rough endoplasmic reticulum. The product, proalbumin, is in turn cleaved in the Golgi vesicles to produce the secreted albumin.

Properties:

Albumin is a globular, water-soluble serum protein. It is negatively charged, the glomerular basement membrane is also negatively charged in the body; some studies suggest that this prevents the filtration of albumin in urine. According to this theory, that charge play a major role in the selective exclusion of albumin from the glomerular filtrate. A defect in this property results in nephrotic syndrome leading to albumin loss in

the urine. Nephroitic syndrome patients are sometimes given albumin to replace the lost albumin.

Function:

Serum albumin is the main protein of human blood plasma(Farrugia and Albert,2010). It binds water, cations, fatty acids, hormones, bilirubin, thyroxine (T4) and pharmaceuticals (including barbiturates): its main function to is to regulate the oncotic pressure of blood. Alpha-fetoprotein (alph-fetoglobulin) is a fetal plasma protein that blinds various cations, fatty acids and bilirubin. Vitamin D-binding protein binds to vitamin D and its metabolites, as well as to fatty acids. The isoelectric point of albumin is 4.9 .

Structure :

The 3D structure of human serum albumin has been determined by X-ray crystallography to a resolution of 2.5 aͦngstroͦms (250 pm) (Sugio et al., 1999). Albumin is a 65-70 KDa protein. Albumin comprises three homologous domains that assemble to form a heart shaped protein (He et al.,1992). Each domain is a product of two subdomains that possess common structural motifs (He et al.,1992). The principal regions of ligand binding to human serum albumin are located in hydrophobic cavities in subdomains IIA and IIIA, which exhibit similar chemistry. Structurally the serum albumins are similar, each domain containing five or six internal disulfide bonds.

Medical uses:

For the patients with low blood volume, there is no evidence that albumin reduce mortality when compared with cheaper alternatives such as normal saline, or that albumin reduces mortality in patients with burns and low albumin levels. Therefore, the Cochrane Collaboration recommends that it not be used, except in clinical trials(Roberts et al., 2011). In acoustic droplet vaporization (ADV) albumin is sometimes used as a cancer treatment by means of occlusion therapy (Lo Andrea et al.,2007). Human serum albumin may be used to potentially reverse drug/ chemical toxicity by binding to free drug/ agent (Ascenzi et al., 2018).

Albumin is normally filtered by the glomerulus and reabsorbed in proximal tubule of kidney, therefore only minute quantities of albumin are normally present in the urine. Daily albumin excretion is in range of 5 – 10 mg and urine Albumin/Cretainine ratio is in the range of 0-29 mg albumin / g creatinine.

Microalbuminuria can be determined by measuring the concentration of albumin in either grandma (spot) sample or a timed collection(usually 24 hours) of urine. Random sample of urine is the preferred method (Mundel and Shankland,2004). Other method short time collection of urine example 4 hours.

## 2.3 Creatinine:

Creatinine formed from creatine , the loss of a water molecule from creatine results in the formation of creatinine ,which come from amino acids motioning and arginine then transport to the brain and muscle then converted to phosphocreatine. It produce at constant rate in the body, it is transferred to the kidney by blood plasma,  and is excreted through the kidney  in the urine. Creatinine is not reabsorbed into body from kidney hence any failure on part of kidney to excrete. Creatinine is one of nitrogenous end products of metabolism, it is small molecule (113 daltons) that distribute throughout total body water.

Creatinine results in rise the creatinine levels in body. Variation from normal creatinine level could indicate kidney dysfunction and muscle problems. Creatinine must be determined in plasma or serum not whole blood because erythrocytes contain considerable amounts of non creatinine chromogens. Normal level of urine creatinine may vary with age, muscle mass and gender. Normal range of urine creatinine is 70-140 mg/dl(Landry and Bazari, 2011)

## 2.4 Albumin /Creatinine Ratio:

It is a ratio between urine micro albumin(mg/L) and urine creatinine (mg/L) the ratio express in mg/g. albumin/ creatinine ratio test is designed as early indicator for kidney damage. The kidney contain tiny blood vessels cluster that filter wastes from blood, the hypertension can damage this delicate filtering system. Microalbumin can detect this damage at earliest stages, prompt treatment can help prevent kidney failure. Reference range of albumin/ creatinine ratio in random urine sample less than 35 ug/ mg (for both males and females)(Mundel and Shankland,2004).

Factors that affect albumin/creatinine ratio: various exercise, present of fever, urinary infection, congestive heart failure,   acute severe elevation of blood pressure or blood sugar or menstruation.(Mundel and Shankland, 2004)

**2.5 Back ground studies of albumin / creatinine ratio:**

The study was conducted by Sabharwal in India (2011) to assess the prevalence microalbuminuria in hypertensive patient as well as to correlate of albumin/creatinine ratio with duration of hypertension the results showed that the prevalence of microalbuminuria in males females was found to be 34% and 30.7% respectively(Pagana and Pagana, 2011).

Much attention has been paid with regard to study done by Jorge Polonia et al, in portugal (2011)to determine the prevalence of microalbuminuria in sample of non-diabetic hypertensive patients, microalbuminuria was significally more frequent in patients with uncontrolled(29) than in controlled(20) hypertension(p<0.01).(Pagana and Pagana, 2011).

Poudel et al, in (2012) has calculated themicroalbumin/creatinine ratio in essential hypertension patients. The result of the mean of microalbumin/creatinine ratio was found be to 40ug/mg (Sharma et al., 2012).

Other study done by Sharma et al. in India (2012) correlate between albumin/ creatinine ratio with age, sex and duration of hypertension and urinary were as follows: the values of mean. Urinary micro albumin was higher in hypertensive group as compared to control group and the increase was statistically significant (p≤ 0.0000005).

In a further evaluation, female hypertensive patients had higher urinary microalbumin values as compared to male, the different was statistically insignification (p≤ 0.47). The mean of urinary microalbumin when compared with the duration of hypertension and it was statically significant that the patients of having hypertension for more than 5 years of duration had higher mean urinary micro albumin level and it was statistically significant (P valve ≤ 0.001) .

 Hypertensive patient with age 40 years and less had been mean urinary microalbrmin level of 22.8 + 7.07 ug/mg of creatinine as compared to those of age above 40, having mean urinary microalbumin level 51.8 + 6.1ug/mg of creatinine and difference was statistically significally (p≤0.01).(Bakker, 2005)

 Another study done by Muhammad Yakoob Ahmadani, Asher Fawwad, Abdul Basit, Zafar Iqbal Hydri in Pakistan(2012) to calculate albumin/creatinine ratio in hypertensive patients, result was as follows albumin/creatinine ratio in hypertensive patients, result

was follows the mean of albumin/creatinine ratio was found 83ug/mg.(Sharma et al., 2012).

Study done by  Basu et al. in Kolkata in (2006) to calculate albumin/creatinine ratio in hypertensive patients, result was as follows the mean of albumin/creatinine ratio  was found 54.4ug/mg.(Redon and Pascual, 2006)

Study done by Jose Mostaza et al. in span (2005) to calculate albumin/ creatinine ratio in hypertensive patients, the result was as follows the mean of albumin/ creatinine ratio was found 67ug/mg.(Roberto et al., 2005).

**3.1 Materials :**

**3.1.1 Study design:**

This study design was cross sectional case control.

**3.1.2 Study area:**

This study was conducted in Khartoum state Khartoum North Province and ShargAnile hospital.

**3.1.3 Study population:**

This study was conducted on 66 persons, 34 of them with hypertension as case group (15 hypertensive with diabetes, 18 male and 16 female, age 30-70 years) and 32 are non-hypertensive as control group .

**3.1.4 Study period:**

The study start in March 2018 and ended in June 2018.

**3.1.5 Selection criteria:**

Cases were selected according to :

**Inclusion criteria:**

Hypertensive patients and apparently healthy individuals of both sexes were enrolled in this study.

**Exclusion criteria:**

Individuals suffering from  primary and secondary renal diseases were excluded.

**3.1.6 Ethical consideration:**

Permission of this study were obtained from the scientific committee of Clinical Chemistry department , college of medical laboratory science in Sudan University of Science and Technology and local authorities in the area of the study. A written informed consent was obtained from each participates and demographic data was collected by Questionnaire (appendix II).

Questionnaire was including full information about patients name, age, gender and duration of disease.

**3.1.7 Collection of Sampling:**

3ml of venous blood sample was collected from each participant, the blood sample was drawn in heparin containers, then centrifuged at 4000rpm for three minutes to get plasma.

The plasma prepared was collected into 1.5ml eppendroff tubes and kept frozen at (-20c) until analysis.

## 3.2 Methodology:

### 3.2.1 Estimation of albumin / creatinine ratio:

**Principle:**

Human albumin forms precipitate with specific antiserum is determined turbidimeterically at 340.

## 3.3 QUALITY CONTROL METHOD:

The precision and accuracy of all methods used in this study were checked each time by commercial prepared control sera.

## 3.4 Statistical analysis:

The data obtained from all participants were recorded and analyzed by used Statistic Package for Social Science (SPSS) version on programmed computer.

T.test was used to find out the difference between mean of compared group.

Person correlation was used to find out the relationship between others variables in the study.

# 4 Results

This study was conducted on 34 patients with hype tension as a test group and 32 apparently healthy subjects age and sex matched to the test group as a control group .

In this study (18) of patients (53%) are male, (16) of patients (4t%) are female,(15) of patients (44.1%) with  diabetes mellitus , (19) of patients (55.9%) with without diabetes mellitus.

The results were compared according to the objectives of the study as illustrated below:

Table (4-1) Shows highly significant increase between the ratio of albumin/creatinine in the hypertensive group (case) (85.5±22.7 mg/g) when compared with that of the control group (8.4±3.6) with p value 0.00.

Table (4-2) Shows insignificant difference of albumin/cratinine ratio between male (94.11±49.43 mg/g) when compared with that of the female (75.95±42.64 mg/g) with P value o.263.

Table (4-3)     Shows highly significant increase of albumin /creatinine ratio in hypertensive patients with diabetes mellitus (DM)  (129.4±31.61 mg/g) when compared with that of the   hypertensive patients without  diabetes mellitus (50.9±18.24 mg/g) with p value 0.00 .

Figure (4- 2): shows significant positive moderate correlation between the albumin /creatinine ratio and duration of   hypertension.

(r=.685 p. value 0.00)

Figure (4-3): shows significant positive high correlation between the albumin /cratinine ratio and age in the hypertensive patients.

(r= .735   p. value 0 .00)

Table (4 - 1) Comparison of albumin / creatinine ratio levels in study groups.

| Variable | Case N=34 | Control N=32 | p.value |
|---|---|---|---|
| Albumin/Creatinine  Ratio | 85.5±22.7 | 8.4±3.6 | 0.00 |

The table show the mean ± standard deviation and probability (p.value).

T.test  was used for comparison.

p.value<0. 05 consider significant.

Table( 4 - 2): Comparison of albumin / creatinine ratio levels across gender.

| Variable | Male N = 18 | Female N = 16 | P.VALUE |
|---|---|---|---|
| Albumin/creatinine ratio | 94.11±49.43 | 75.95±42.64 | 0.263 |

The table show the mean ± standard deviation and probability (p.value).

T.test  was used for comparison.

p.value<0. 05 consider significant.

Table( 4 - 3): Comparison of albumin / creatinine ratio levels between hypertensive diabetic patients and hypertensive non diabetics.

| Variable | hypertensive patients with (DM) n= 15 | hypertensive patients without (DM) n= 19 | p.value |
|---|---|---|---|
| Albumin/creatinine ratio | 129.4±31.61 | 50.9±18.24 | 0.00 |

The table show the mean ± standard deviation and probability (p.value).

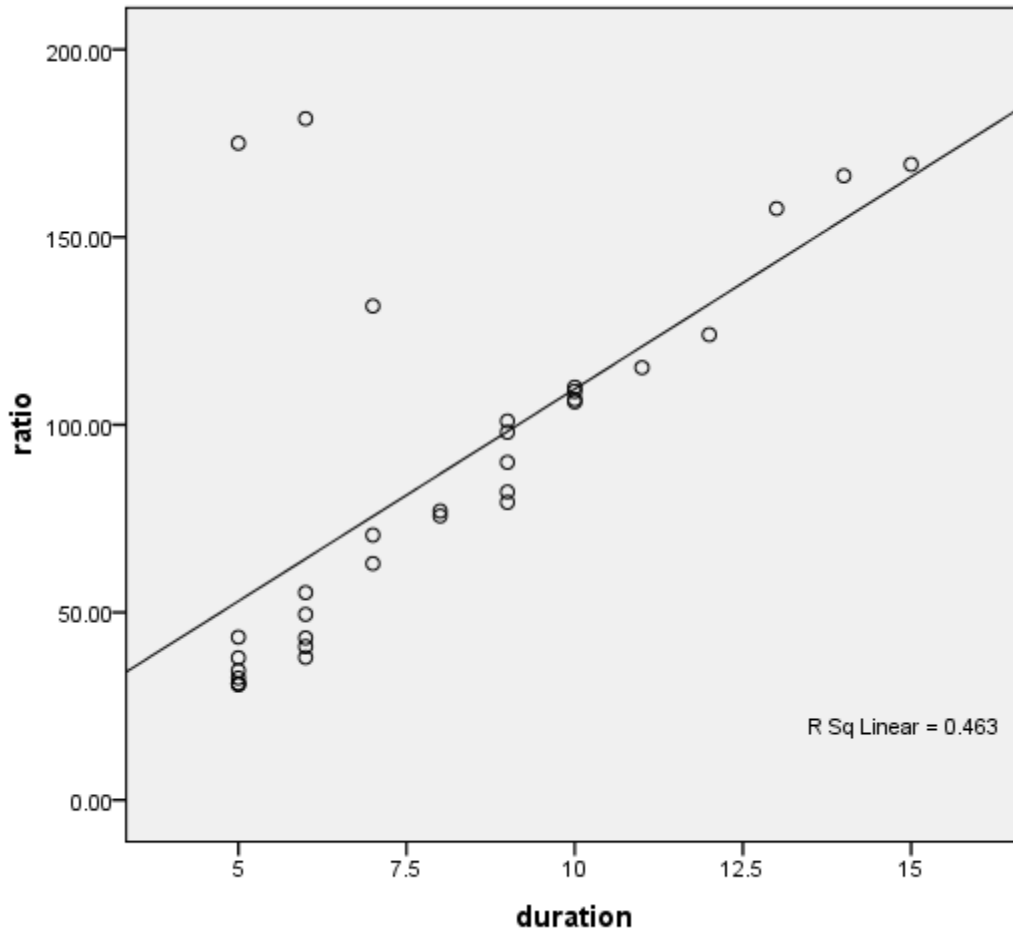T.test was used for comparison.

p.value<0. 05 consider significant.

Figure (4 - 2)  Correlation between  albumin /creatinine ratio and duration of hypertension  (r=.685   p. value 0.00)
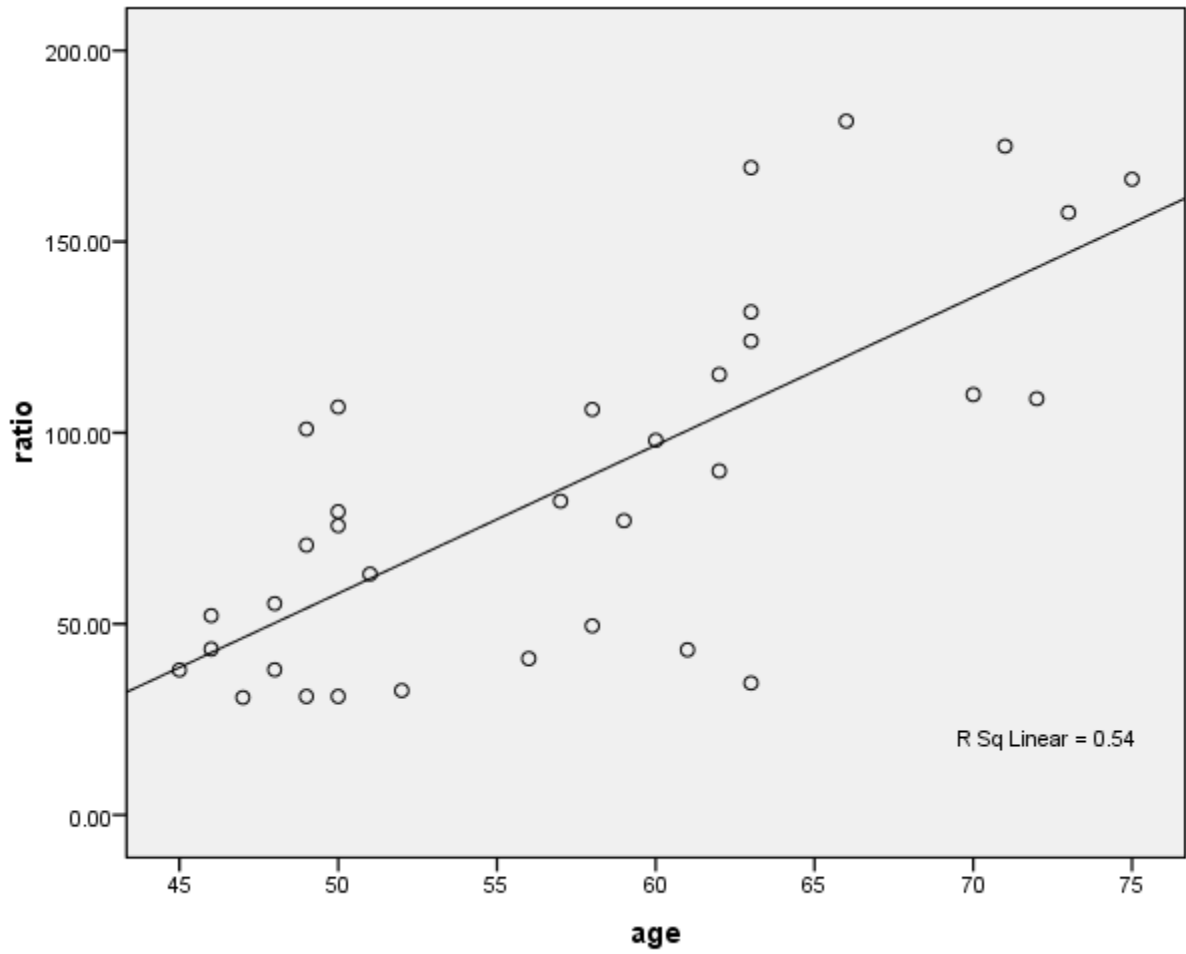
Figure (4 - 3) Correlation between albumin /cratinine ratio and age.(r=.735  p. value 0.00)

**5.1 DISCUSSION:-**

Hypertension (HTN) is a public health worldwide due its significant contribution to increase risk of serious problems such as heart attacks, strokes, vascular disease and chronic kidney disease.

Mimran et al, 1994 and Hoy et al, 2001 reported on a close correlation between baseline albuminuria and decline GFR. This suggested that microalbuminuria may be a marker of early intra-renal vascular dysfunction.

This study done to detect renal impairment in patients with hypertension in Khartoum state Sudan.

The result of this study showed highly significant elevation in albumin/creatinine ratio in hypertensive patients compare with control (mean ± SD), this agree with the result of (Pontremoli et al, 1997) who find a prevalence of microalbuminuria (average ≥ 30mg) was observed in 8% of hypertensive patients,(Basu et al, 2001) who found that the mean of urinary microalbumin was higher in hypertensive patients of Kalkata region. However, a higher ratio was reported by (Yakoob et al, 2003) who has calculated albumin /creatinine ratio in Pakistan hypertensive patients.

To study the effect of duration of hypertension in albumin/ceatinine ratio it is found that there was significant positive moderate correlate (p. value 0.00), this agree with the result of (Sharma et al, 2012) who has found there was statistical significant (p. value ≤0.001).

The study also showed that albumin/creatinine ratio was positively highly correlated with age of patients (r=.735 p=0.00),this result agree with result of(Mimran et al, 1999) who reported that age-related value was observed and associated with a higher level of albuminuria, (Fesler et al, 2003) observed that the existence of hypertension was associate with a marked acceleration of the age-related decline in GFR and (Sharma et al, 2012) who found the mean of ratio was statistically significant (p≤0.01) with age.

Hypertensive patients with diabetic showed highly significant difference compare with non diabetic (p. value 0.00), this indicate that renal impairment was more obvious in this groups, this agree with (Berrut et al, 1997) , (Keane et al, 2003) and(Pinto-Sietsma et al, 2000) whom report that albuminuria is a well-known predictor of poor renal outcomes in patients with diabetes and in hypertension. Also (Ribstein et al, 2001) in cross-sectional

study have the relationship age versus GFR is steeper in patients with impaired glucose tolerance or diabetes discovered during an oral glucose tolerance test.

Women excrete less creatinine than men and microalbuminuria are different in men and women when using ACRs (Connell and Hollis, 1994). The result in this study showed that there was insignificant statistical difference of albumin/creatinine ratio between male compare with that of female (p. value o.263).

**5.2 CONCLUSION :-**

From this study it was concluded that :

Albumin/creatinine ratio is highly elevated in hypertensive patients, hypertensive patients with diabetes mellitus and the study is associate with age and duration of the disease and not associate with gender.

**5.3 Recommendation :-**

-Screening for microalbuminuria is recommended for patients with hypertension to assess early impairment of renal function.

-Testing for albuminuria at the time of initial diabetes diagnosis and yearly there after.

-Patients with microalbuminuria need further evaluation and management of chronic kidney disease (CKD)and prevention of cardiovascular disease (CVD).

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## Appendix " I "
## Informed Consent

هذه دعوة منى:الباحثة/ اسراء ابايزيد سعيد حسن طالبة ماجستير ـ مختبرات طبية ـ كيمياء سريرية ـ بجامعة السودان للعلوم والتكنولوجيا لمشاركتكم فى برنامج بحث هدفه قياس نسبه الالبيومين/كرياتينين فى عينه البول لدى السودانين المصابين بضغط الدم وضغط الدم والسكرى فى ولايه الخرطوم كمؤشر لتاثيرمرض ضغط الدم على وظائف الكلى.

اذا رغبتم فى انجاح هذا البرنامج فانى وفريق البحث سنقوم:-

باخذ عينه من البول لقياس معدل المايكروالبيومين/كرياتينين

بملء استماره بمعلومات تخصكم لها علاقه بموضوع البحث

اى معلومه تخصكم فى الاستمارة سوف تكون سرية

مشاركتكم فى البرنامج تسعدنا وتساعد فى انجاح هدف البحث

لكم كامل الحرية فى اختيار عدم المشاركة ٫ او الانسحاب من برنامج البحث اى وقت تشاءون

يمكنكم الحصول على اجابهلاى سؤال عن برنامج البحث ( الخرطوم اركويت 0995421788)

التاريخ  ..............................

توقيع المتبرع ............................

توقيع الباحث  ...............................

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**Sudan University of Science and Technology**

**Collage of Graduate Studies**

**Questionnaire**

1.Date:……………………..

2.Gender:    male(    )                    female(    )

3.Age:…………………

4.Duration of hypertension………….. ….. years

5.Other disease

Diabetes:  yes(  )            no(  )

6.Investigation

Albumin/creatinine ratio………………………..mg/g

## Appendix " III "

**Specimen:**

For qualitative albumin determination in urine use random urine sample.Use only fresh urine and no preservation. Centrifuge the specimen containing precipitates prior to analysis. Do not freeze urinespecimens stability in urine: one month at 4 c.

**Reagents and materials:**

Roche COBAS.

- 100 tests.

*R1:TRIS buffer 50 mmol/L, PH8.0 PEG: 40.2%, EDTA:2-0 mmol/L; preservative.

*R2 polyclonal anti-human albumin antibodies (sheep) dependent on titer TRIS buffer 100 mmol/L, plt 7.2 preservative

*R3 reagent for Ag excess check, albumin in diluted serum (human), Nacl 150 mmol/L phosphate preservative precaution and waning: Exercise the Normal precaution required for handling all laboratory reagents.


**Equipment instrumentation:**

COBAS Integra:

**\*Calibration**

**Calibrator:**

$$S_1 = H_2 o S_2 - 6 \, CFAS \, puc$$

**Calibration mode:**RCM

**\*Calibration frequency:-**

The instrument should be calibrated:

1/ Atinitial installation.

2/ if necessary after instrument service or repair.

3/ if dictated by Quality Control results.

4/ if dictated to do by Rochesupport personnel.

5/ with each new lot of reagent cassette.

**Calibrator preparation, storage and procedure:**

Refer to COBAS Integra user manual located in chemistry department.

**Quality Control:**

Control sera with known values was used for calibration of instrument

**Procedure Notes:**

-AMR ( AnalyticalMagerment Range):12-200mg/L.

-If value is greater than 200 mg / L, it automatically to rerun using a 1:10 dilution. Results are automatically multiplied by factor of 10. Expended range is 12-2000mg/L.

-Report relies of less than 12 mg/L .

-Report relies of greater than 2000 mg/L .

**Calculation:**

The COBAs Integra system automatically calculatesthe albumin concentration calculates the albumin concentration of each sample for more details, please refer to user manual.

Random urine reported as ratios:

Urine albumin( mg/L) urine creatinine (g /L)= mg albumin /gcreatinine .

**Interpretation:**

*Random urine <20 mg Albumin /g Creatinine.

*limitation:

Criterion: Recovery within +/ - 10% of initial value