Assessment of Albumin: Creatinine Ratio and Estimated Glomerular Filtration Rate among Hypertensive Patients at Al-Jazeera State

A dissertation submitted in partial fulfilment for the requirement of Master degree in Medical Laboratory Science (Clinical Chemistry)

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February, 2021
(لَتُبْلَوُنَّ فِي أَمْوَالِكُمْ وَأَنْفُسِكُمْ وَلَتَسْمَعُنَّ مِنَ الَّذِينَ أُوتُوا الْكِتَابَ مِنْ قَبْلِكُمْ وَمِنَ الَّذِينَ أَشْرَكُوا أَذًى كَثِيرًا ۚ وَإِنْ تَصْبِرُوا وَتَتَّقُوا فَإِنَّ ذََٰلِكَ مِنْ عَزْمِ الأُمُورِ)

[سورة آل عمران 186]
DEDICATION

To my father,

Who taught me the meaning of life

To my mother,

Praying for me to successful

To my brother and sister,

For their support and kindness

To my friends and colleagues,

The persons, whom we love, respect and appreciate

To everyone from whom I learned.
ACKNOWLEDGEMENTS

Thanks first and last to ALLAH who enabled me to conduct this study by the grace of him and give me strength and patience. I am extremely grateful to my supervisor: Dr. Abdelgadir Ali El-Mugadam for him kind help and guidance, during all stages of the study and for reading the draft manuscript.

Words can never help to express my feelings towards every one stand beside me to carry work. So I would like to thanks all those who offered me assistance and help me to complete this work.

Finally, I am thanks my college to allow me to conduct this study and provide any assistance required. Special thanks go to the member of clinical chemistry for their continued support.
ABSTRACT

hypertension has much serious effect on human body and cause different diseases such as coronary heart disease, cerebrovascular disease and chronic kidney disease. This study conducted to determine the albumin creatinine ratio and eGFR in Sudanese hypertensive patient at Al-Gezera state.

The study hypothesized that there is no difference in albumin: creatinine ratio and eGFR levels between hypertensive patients and normotensive group. This hypothesis was tested by cross sectional comparative study during the period from September 2019 to November 2020. The study was included 60 hypertensive patients and 40 normotensive individuals. A structured questionnaire was designed to obtain demographic and clinical data. Urine samples were collected from all participants in clean urine container, then investigated for levels of urine albumin and urine creatinine by using full-automated cobas system international analyzer in Al-Gezeria Hospital for Renal Diseases and Surgery to calculate albumin: creatinine ratio. Venous blood samples were collected from all participants in heparin-containing container and investigated for plasma creatinine level using automated biosystem biochemical system international analyzer in AL-Daraga center to calculate eGFR.

The results showed that, significant (p <0.05) increased difference in albumin: creatinine ratio and significance (p <0.05) decreased difference in eGFR in hypertensive patients when compared to normotensive group was found, the level of was increased in uncontrolled hypertensive patients and in hypertensive patients had DM and also found the level of eGFR was decreased in >61year age and in>8 years’ duration of hypertension.

Therefore, albumin: creatinine ratio and eGFR had associated with hypertension
مستخلص الأطروحة

ارتفاع ضغط الدم له عدة أثار خطيرة على جسم الإنسان و بسبب أمراض مختلفة منها مرض الشريان التاجي، مرض وعائي دماغي و مرض الكلي المزمن.

أجريت هذه الدراسة في ولاية الجزيرة لمعرفة مدى تأثير ارتفاع الضغط على مستوى نسبة الألبومين إلى الكرياتينين و معدل الترشيح الكلوي.

افتُرضت هذه الدراسة أنه لا يوجد فرق في مستوى نسبة الألبومين إلى الكرياتينين و معدل الترشيح الكلوي بين مرضى ارتفاع ضغط الدم والأشخاص الذين لا يعانون من ارتفاع ضغط الدم. تم اختبار هذه الفرضية بإجراء دراسة مقارنة مقطوعة في الفترة من سبتمبر 2019 حتى نوفمبر 2020. الدراسة مكونة من 60 مريض ارتفاع ضغط الدم و 40 شخص لا يعانون من ارتفاع ضغط الدم. تم إعداد استبيان لكل المشاركين شمل المميزات الشخصية والسريرية. أُخذت عينات بول من جميع المشاركين في حاويات بول نظيفة. تم قياس مستويات الألبومين والكرياتينين في البول باستخدام جهاز تحليل عالمي "اتوماتيكي" في المستشفى الجزيرة لامراض و جراحة الكلى لحساب نسبة الألبومين إلى الكرياتينين و جمعت عينات دم وريدي من جميع المشاركين في حاويات خالية تحتوي على الهيبرين. تم قياس مستوى الكرياتينين باستخدام جهاز "اتوماتيكي" في مركز الدرجة لحساب معدل الترشيح الكلوي.

أظهرت النتائج أن توجد فروق معنوية في مستوى نسبة الألبومين إلى الكرياتينين و معدل الترشيح الكلوي عند مرضى ارتفاع ضغط الدم مقارنة بالأصحاء و أن مستوى نسبة الألبومين إلى الكرياتينين يزيد بشكل واضح عند مرضى الضغط غير منتظمين في العلاج و عند الذين لديهم مرض السكري مع الضغط و أن مستوى معدل الترشيح الكلوي يقل عند مرضى الضغط فوق سن الواحد و ستون عام و الذين لديهم ضغط أكثر من ثمانية أعوام.

خلصت الدراسة الا أن نسبة الألبومين إلى الكرياتينين و معدل الترشيح الكلوي لها علاقة زيادة الضغط.
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<td>ACR</td>
<td>Albumin creatinine ratio</td>
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<tr>
<td>AKI</td>
<td>Acute kidney injury</td>
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<td>Ang II</td>
<td>Angiotensin II</td>
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<td>ARV</td>
<td>Average real variability</td>
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<td>BP</td>
<td>Blood pressure</td>
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<td>CVD</td>
<td>Cardiovascular disease</td>
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<td>CKD</td>
<td>Chronic kidney disease</td>
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<td>DBP</td>
<td>Diastolic blood pressure</td>
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<tr>
<td>eGFR</td>
<td>Estimated Glomerular filtration rate</td>
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<td>ERF</td>
<td>End-stage renal failure</td>
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<td>ESRD</td>
<td>End stage renal disease</td>
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<td>GFR</td>
<td>Glomerular filtration rate</td>
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<td>HTN</td>
<td>Hypertension</td>
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<tr>
<td>KDIGO</td>
<td>Kidney Disease Improving Global Outcomes</td>
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<td>MAU</td>
<td>Microalbuminuria</td>
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<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
</tr>
<tr>
<td>SBP</td>
<td>Systolic blood pressure</td>
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<td>UACR</td>
<td>Urine albumin to creatinine ratio</td>
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<td>UAE</td>
<td>Urine albumin excretion</td>
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1. INTRODUCTION

The current definition of hypertension (HTN) is systolic blood pressure (SBP) values of 130 mmHg or more and diastolic blood pressure (DBP) more than 80 mmHg. Most cases of hypertension are idiopathic (essential hypertension) and it may due to other disease (secondary). More than one billion adults worldwide have hypertension with up to 45% of adult populace being affected with disease and the prevalence rises with age accounting for up to 60% of population above 60 years of age. (Iqbal and Jamal, 2019)

Hypertension is one of the most influential risk factor for mortality worldwide. epidemiological studies have reported that hypertension is strongly associated with the risk of coronary heart disease, cerebrovascular disease and chronic kidney disease. However, there remains a lack of understanding of the determinants of hypertension (Yadav et al., 2016).

Chronic kidney disease (CKD) is persistent kidney damage accompanied by reduction in the glomerular filtration rate (GFR)and the presence of albuminuria. In 2009, more than 57000 people in U.S were classified as having end stage renal disease (ESRD). The rise in incidence of CKD is attributed to an aging populace and increases in HTN, diabetes and obesity. It is associated with electrolyte imbalance, mineral and bone disorder, anemia, dyslipidemia and hypertension. Hypertension occur in 85%to 95% of patients with CKD (stage 3_5). Uncontrolled hypertension is risk factor for developing CKD and rapid progression of CKD (Buffet and Ricchetti, 2012).

Microalbuminuria is an indicator and predictor of early kidney disease, marker of vascular dysfunction and predictor for morbidity and mortality of cardiovascular disease (CVD). The prevalence increase with disease duration. Some studies found that microalbuminuria related to the risk of hypertension whereas others indicated higher blood pressure predicted further risks of microalbuminuria (Zhang et al., 2018).

In study done by Mani (2016) in rural Africans to study albuminuria in hypertensive patients, found that the prevalence of albuminuria is about 40% in untreated
hypertensive population and about 25% among hypertensive patients treated with β-blockers. The prevalence increase with age, duration and severity of hypertension.

1.1 Rationale:
High blood pressure is silent killer and it affects renal function. albuminuria develops from progressive, subclinical and functional changes within kidney and represents a marker of early renal disease. Estimation of GFR reflect renal status. So early detection of albuminuria and GFR in hypertensive patients can help to avoid or minimize complication associated with renal impairment.
1.2 Objective:

1.2.1 General objective:

Assessment of albumin: creatinine ratio and estimated GFR among hypertensive patients at Al-Jazeera state.

1.2.2 Specific objective:

1. To measure urine albumin and creatinine in hypertensive and normotensive individuals, and to calculate and compare the albumin: creatinine ratio in each subject.

2. To measure plasma creatinine in hypertensive and normotensive individuals and to calculate and compare estimated glomerular filtration rate (eGFR).

3. To correlate between ACR, eGFR, age of hypertensive patients, duration of hypertension, presence of diabetes mellitus with hypertension and controlled of hypertension.
1. LITERATURE REVIEW

2.1 Hypertension:

The National Institute for Health and Care Excellence (NICE) defines high blood pressure (BP) (or hypertension) as a clinic blood pressure of 140/90 mmHg or higher confirmed by a subsequent ambulatory blood pressure monitoring day time average of 135/85 mmHg or higher. Hypertension has been identified by WHO as one of the most significant risk factors for morbidity and mortality worldwide and is responsible for the deaths of approximately nine million people annually. Hypertension does not just develop in old adult, over 2.1 million people under 45 years old has high blood pressure in England in 2015. This is important because treating hypertension results in significant reduction in risk of subsequent cardiovascular disease (Kitt et al., 2019).

Hypertension is a disease that affects one billion individual worldwide. It increases the risk for develop of cerebral, cardiac and renal events. The majority of patients have essential hypertension. Despite the widely recognized dangers related to uncontrolled hypertension, the disease remains inadequately treated in most patients, due to its asymptomatic nature even when it progressively damages multiple organ systems (Hitha et al., 2008).

Hypertension is classifying in to primary or secondary hypertension. Primary (essential or idiopathic) hypertension is systemic of unknown cause that results from dysregulation of normal homeostatic control mechanisms of blood pressure in the absence of detectable known secondary causes and it affect over 95% of all cases of hypertension. Secondary hypertension is systemic hypertension due to: reno-vascular disorder (renal vascular stenosis and intra-renal vasculitis), renal parenchymal disorder (acute glomerulonephritis, chronic nephritis, hydro-nephrosis and diabetic nephropathy), endocrine disorder (Acromegaly, Cushing syndrome, aldosteronism, phaeochromocytoma, hypo and hyper-thyroidism and adrenal hyperplasia), acute stress, neurological disorder, pregnancy-induced hypertension, increase cardiac output and iatrogenic hypertension (Khatib and El-Guindy, 2005).
2.1.1 Pathophysiology of hypertension:
Elevated blood pressure may be due to elevated cardiac output, elevated peripheral vascular resistance, or combination of both. Each of these mechanism is regulated by hemodynamic, neural, humoral and renal processes, all of which vary in their contribution from one individual to another. As persons grow older, the predominant cause of hypertension tends to be elevated peripheral vascular resistance with increased stiffness of vessels which manifests as isolated systolic hypertension. Familial clustering implies a genetic predisposition whose interaction with environmental factors, such as salt intake calories and degree of physical exercise, ultimately determines how severe the rise of blood pressure will be (Jordan et al., 2018).

2.1.2 Signs and symptoms of high blood pressure:
One of most dangerous aspect of hypertension is that you may not know that you have it, one third of people who has high blood pressure don’t know it. The symptoms of high blood pressure include: severe headache, fatigue, vision problems, chest pain, difficulty breathing, irregular heartbeat and blood in urine. Untreated hypertension can lead to serious disease: stroke, heart disease, kidney disease and eye problems (Web, 2018).

A study done on Germany to study the prevalence of symptom generally attributed to hypertension, dizziness and headache were significantly more prevalence in untreated hypertensive as compared with normotensives whereas tiredness was less in hypertensive. In untreated and treated the overall prevalence of symptoms increased with blood pressure levels (Middeke et al., 2008).

2.1.3 Management and Treatment of hypertension:
Lifestyle adjustments are the standard first-line treatment of hypertension: regular physical exercise (at least 5 days of the week), stress reduction, reducing salt intake, managing body weight, moderating alcohol consumption and use of medications include: diuretic (thiazides, chlorthalidone and indapamide), beta and alpha-blockers, calcium channel blockers, central agonists, vasodilators, angiotensin converting
enzyme inhibitors and angiotensin receptor blockers. The choice of medication depends on the individual and any underlying medical conditions they may experience (Felman, 2019).

2.2 The kidney:

2.2.1 Renal anatomy:

The kidneys are paired, bean-shaped organs located retroperitoneally on either side of the spinal column. Macroscopically, a fibrous capsule of connective tissue encloses each kidney. It is composed of two regions: an outer region (cortex) and an inner region (medulla). Each kidney contains approximately 1 million nephrons (functional units of the kidney). Each nephron comprises five basic parts: the glomerulus, the proximal convoluted tubule, the long loop of Henle, the distal convoluted tubule and the collecting duct (Bishop, 2010).

2.2.2 Renal physiology:

2.2.2.1 Mechanism of urinary protein excretion:

Under normal circumstances, urine is almost free of protein (proteinuria<4mg/m²/h or protein-creatinine ratio of <180 mg/g (20 mg/mmol)). There is physiological condition of proteinuria: orthostatic proteinuria, febrile proteinuria and exercise proteinuria. Water and small solutes (5kDa) can pass the glomerular filter freely. For larger molecules, permeability is inversely related to molecular size. The LMW proteins (10 and 20 kDa) such as β-2 microglobulin, cystatin C and many other macromolecules pass the glomerular filter in considerable amounts then reabsorbed in the proximal tubule and digested at low pH in lysosomes and do not enter the circulation.

The intact glomerular membrane is almost impermeable to albumin due its larger size and negative charge causing reflection of this anionic molecule. Filtered albumin is not only reabsorbed in clathrin-coated pits on the surface of proximal tubular cells following binding to cubulin but also via fluid-phase endocytosis, absorbed albumin can leave the cell intact after binding to the neonatal Fc receptor (FcRn) rather than being degraded in lysosomes. Substantial amounts of albumin will be detected in the
urine of individuals with defective tubular protein reabsorption but normal glomeruli, and does not necessarily imply a glomerular origin of albuminuria (Bökenkamp, 2020).

2.2.2.2 kidney roles in hypertension regulation:

The kidney plays a central role in the long-term control of arterial pressure by regulating sodium balance and extracellular fluid volume. The renin angiotensin system is important in the regulation of arterial pressure through its chronic effects on the pressure natriuresis relationship. Under physiological condition, angiotensin II is important in causing the long-term relationship between arterial pressure and sodium excretion. An inability to suppress Ang II formation in response to increases in sodium intake can lead to salt-sensitive hypertension. Ang II decrease pressure natriuresis by enhancing tubular reabsorption (directly enhancing tubular sodium transport or indirectly through aldosterone stimulation) or reducing glomerular filtration (Ang II interacts with various local autocrine and paracrine factors such as: eicosanoids, adenosin and superoxide to influence glomerular filtration rate) (Granger and schnackenberg, 2000).

2.2.3 Renal function:

The mean biological functions of kidneys are: (1) Excretion (excretion of the waste products of protein metabolism, drugs and toxins), (2) Homeostatic regulation (water, electrolyte, and acid-base homeostasis) and (3) Endocrine function (it synthesize renin, erythropoietin, 1,25-dihydroxy vitamin D3, and the prostaglandins) (Burtis, 2008).

2.2.4 Renal disorder:

Kidney disease is an increasing global problem, with a significant economic impact, especially in the developed world. Failure of renal function may occur rapidly, producing acute kidney injury (AKI) and this is potentially reversible. Chronic kidney disease (CKD) develops insidiously over many years, and is irreversible, leading to end-stage renal failure (ERF). Glomerulonephritis is a group of renal diseases characterized by pathological changes in glomeruli, usually with an immunological basis and it presented as: an acute nephritic syndrome with hematuria, hypertension
and edema, as acute or chronic kidney disease, or as proteinuria leading to nephrotic syndrome (proteinuria, hypo-proteinaemia and edema). Many disorders affect renal tubular function, but most are rare. Their metabolic and clinical consequences range from being trivial (as in isolated renal glycosuria) to being serious (as in cystinuria) (Marshal et al., 2012).

Kidney Disease Improving Global Outcomes (KDIGO) stages of chronic kidney disease (CKD):

Stage 1 GFR greater than 90 ml/min/1.73 m²
Stage 2 GFR-between 60 to 89 ml/min/1.73 m²
Stage 3 GFR 45 to 59 ml/min/1.73 m²
Stage 3b GFR 30 to 44 ml/min/1.73 m²
Stage 4 GFR of 15 to 29 ml/min/1.73 m²
Stage 5-GFR less than 15 ml/min/1.73 m² (end-stage renal disease) (Gounden, 2020).

2.2.5 Renal function tests:

There are several clinical laboratory tests that are useful in investigating and evaluating kidney function. Clinically, the most practical tests to assess renal function is to get an estimate of the glomerular filtration rate (GFR) and to check for proteinuria (albuminuria) (Gounden, 2020).

2.2.5.1 Glomerular Filtration Rate:

The best overall indicator of the glomerular function is the glomerular filtration rate (is the rate in milliliters per minute at which substances in plasma are filtered through the glomerulus or the clearance of a substance from the blood). The normal GFR for an adult male is 90 to 120 mL per minute. Endogenous and exogenous markers of GFR are used. The creatinine (by-product of creatine phosphate in muscle) is most commonly used endogenous marker, produced at a constant rate by the body, cleared from the blood by the kidney and it amount produced per day depends on muscle bulk.
Serum creatinine utilized in GFR estimating equations and Creatinine clearance (Gounden, 2020).

The eGFR is a test that is used to assess how well your kidneys are working. The test estimates the volume of blood filtered by kidneys over a given period of time. The eGFR test involves a blood test which measures a chemical called creatinine. Creatinine is a breakdown product of muscle. Creatinine is normally cleared from the blood by the kidneys. If your kidneys are not working properly, the level of creatinine in the blood goes up. The eGFR is then calculated from your age, sex and blood creatinine level. The eGFR does not diagnose any specific kidney disease but is a test to assess how well your kidneys are working (Tidy and Jackson, 2017).

So the use of serum cystatin C and its equation as marker of GFR is better than serum creatinine and equations based on serum creatinine (Salgado et al., 2013).

2.2.5.2 Microalbuminuria:

The microalbuminuria (MAU) refers to presence of relatively of protein in urine 30-300mg/day which below the detection threshold of standard urine dipstick test. Now defined as urine albumin excretion (UAE) between 20 and 200 μg/min or 30-300mg in overnight or 24-h urine collection. The importance of microalbuminuria as an independent predictor of progressive renal disease and cardiovascular mortality was thereafter realized in number of prospective and epidemiological studies particularly in patients with diabetes and hypertension (Singh and Satchell, 2011).

**Causes of microalbuminuria:**

Increased amounts of protein in the urine may be due to: defects in permselectivity of the glomerular filtration barrier to plasma proteins (glomerulonephritis or nephrotic syndrome), incomplete tubular reabsorption of proteins (interstitial nephritis), increased plasma concentration of proteins (multiple myeloma-Bence Jones protein, myoglobinuria) and urinary tract inflammation or tumor (Gounden, 2020).
most probable cause for MAU in hypertensive are changes in hemodynamics that cause an elevation in intra-glomerular pressure and a generalized angiopathy due to endothelial dysfunction that cause renal and systemic trans-vascular albumin leakage (Crippa, 2002).

**Measurement of microalbuminuria**

Quantitative albumin-specific immunoassays, usually using nephelometry or immunoturbidimetry, are widely used. A 24-hour urine collection is preferred, but a random urine sample that uses a ratio of albumin to creatinine can be also be used. An albumin/creatinine ratio of 20–30 mg/g is indicative of microalbuminuria. Although many urine dipstick methods are not sensitive enough to detect these low levels of albumin, newer dipstick methods are now available for specific detection of albumin and the albumin/creatinine ratio (Bishop, 2010).

**previous studies:**

- In study done by Glassman, *et al* (2018) to study the Change in Blood Pressure and Urine Albumin-Creatinine Ratio in a randomize clinical trial comparing Aflibercept, Bevacizumab and Ranibizumab for Diabetic Macular Edema, they found that 38% of participants (95 had normal blood pressure, 220 had borderline, 206 had mild and 139 had moderate blood pressure elevation) had no albuminuria, 30% had micro-albuminuria and 32% had macro-albuminuria.

- The prevalence of MAU in patients with left ventricular hypertrophy was 36.8% (Talle *et al.*, 2015).

- A study by (Mule *et al.*, 2016) among patients with primary hypertension has shown that MAU was detected in 26% of patients. Average real variability (ARV) (short term Bp variability) of 24-hr term systolic BP was significantly higher in patient with MAU (9.8(8.5-11.1) mmHg) compared with those without it (9.1(8-10.2(mmHg).

- A study published by (Catena *et al.*, 2017) in Non-Diabetic Treatment-naive Patients with Hypertension, they demonstrated that an increase of the urine albumin to creatinine ratio (UACR) was associated with significant and progressively high blood
pressure, high-density lipoprotein cholesterol, plasma aldosterone levels and glomerular filtration.

-A study done by (Oliveras et al., 2014) to evaluate the association between different levels of urinary albumin excretion and blood pressure control in treated hypertensive patients. They found that lack of blood pressure control is more prevalence among patients with MAU than in patients with normo-albuminuria but found no difference between patients with optimal or high –normal UAE.

-A study of (Alharf et al., 2016) compared two definitions of MAU in a cohort hypertensive patients attending two specialist clinics in Scotland: conventional ACR >2.5-25 in males or >3.5-25 mg/mmol in females and low-grade ACR 1.2-2.5 in males or 1.7-3.5 mg/mmol in females. The prevalence of MAU(C) was 11% in overall whereas MAU(L) 11.1% in overall.

-In study done by (Parving et al., 1974), they found that MAU prevalence in hypertensive patients stands at 40% in untreated population and increases with age and hypertension severity.

-In study done among rural Africans with hypertension they found that obesity, blood pressure levels and duration since diagnosis were not associated with albuminuria among rural Africans with hypertension (Rasmussen JB et al., 2016).

-In study done by (Mani, 2016) in rural Africans to study albuminuria in hypertensive patients, found that the prevalence of albuminuria is about 40% in untreated hypertensive population and about 25% among hypertensive patients treated with β-blockers. The prevalence increase with age, duration and severity of hypertension.

-In study done by (Marudhaiveeran, Radhakrishnan and Alphonse, 2014) to study prevalence of microalbuminuria among patients with essential hypertension, they found that 64% of study population had hypertension and they were statistically Signiant association between hypertension and presence of microalbuminuria.

-Study done by (Pedersn and Kornerup, 1976) on hypertensive patients who found that there was no significant difference in GFR in hypertensive patients and control
population, GFR decrease with increasing blood pressure in both groups and it decrease in control subjects but not in hypertensive patients with increasing age.

The prevalence of HTN with ACR was observed in subject with and without obesity end abdominal obesity, in all groups HTN increased as ACR increased (P value <0.001) (Yoon et al., 2014).

-In study done by (Hitha et al.,2008) to investigate the Microalbuminurinia in Patients with Essential Hypertension and its Relationship to Target Organ Damage: An Indian Experience they found that, the prevalence of microalbuminuria among hypertensive patients increased steadily with age. It prevalence in more than 10 years of hypertension than in less duration. It prevalence in irregular treatment than regular treatment.

-A study done by James et al (2015) found that low eGFR and high ACRs are associated with higher risks of acute kidney injure among individuals with or without diabetes and with or without hypertension when compared with common reference of eGFR of 80 ml/min/1.73m².

-A study found that positive correlations were detected between cystatin C and eGFR (r= -0.503, p< 0.001). eGFR correlated with age (r= -0.339, p= 0.001) (Okura, 2010).
2. MATERIALS AND METHODS

3.1 Study area and duration:

The study was conducted in Al-Daraga center in Wad Madani city, Al-Gazira state from September 2019- November 2020.

3.2 Study design:

It was a cross sectional comparative study.

3.3 Study population:

Study was confined on Sudanese hypertensive patients which included 30 Sudanese hypertensive patients, 30 Sudanese hypertensive and diabetic patients attending the health center regulatory for follow up and from different regions of Al-Gazira and 40 normotensive volunteers.

3.3.1 Inclusion Criteria:

Include essential hypertensive patients (male and females of age 30 to 90 years), beside non-hypertensive individuals as controls, whom voluntarily accepted to participate in this study were included.

3.3.2 Exclusion criteria:

Individuals with: Secondary hypertension, renal diseases, thyroid diseases and cardiovascular diseases were excluded.

3.4 Methodology:

3.4.1 Data collection:

Data was collected using structured questionnaire, data from urine analysis for ACR and data from blood sample for creatinine estimation to calculate GFR was recorded in the same form.

3.4.2 Ethical consideration:
The study protocol was institutional ethic approve by Sudan University of Sciences and Technology Faculty of Graduate studies before initiation of study. Informed consent was obtained from each participant before collection sample.

3.4.3 Quality controls and managements:

The cases were selected carefully. Urine and blood were collected with care and adequate safety precaution to ensure test results are reliable. Quality assurance and standard operating system was followed for all biochemical tests to achieve validity and reliability of test results. weight was estimated carefully after shoes and bag taken off by scale balance and readings less than has been rounded.

3.4.4 Sample collection and processing:

Sterile urine containers were used for spot urine sample (second voided) collection and the quantitative albumin and creatinine level determined for albumin: creatinine ratio calculation, Heparinized blood containers were used for blood sample collection to estimation of plasma creatinine for GFR calculation.

3.4.5 Methods of estimation:

3.4.5.1 Estimation of urinary Albumin:

Estimated by used of cobas c311 systems for the quantitative immunological determination of human albumin in urine.

Principle:

Human albumin forms a precipitate with a specific antiserum which is determined turbidimetrically at 340nm.

Reagents/materials:

Roche COBAS c311Albumin (turbidimetric)- 100tests
Cassette ALBT2

R1- TRIS buffer: 50mmol/L, PH 8.0 PEG: 4.2% and EDTA:2.0 mmol/L preservative
R2- polyclonal anti-human albumin antibodies (sheep): dependent on titer, TRIS buffer 100mmol/L and PH 7.2 preservative.


**Calculation:**

The COBAS c311 system automatically calculates the albumin concentration of each urine sample.

**Reference values:**

Random urine: less than 20 mg albumin/ g creatinine. (see appendix (1))

3.4.5.2 Estimation of urinary creatinine:

Estimated by used of cobas c311 systems for kinetic colorimetric Jaffe method determination of human creatinine in urine.

**Principle:**

\[ \text{creatinine} + \text{picric acid Alkaline PH} \rightarrow \text{yellow orang complex with picrate} \]

**Reagents/materials:**

R1_ potassium hydroxide:900mmol/l, phosphate:135mmol/l, PH≥13.5, preservative (stabilizer).

R3_ picric acid:38mmol/l, PH 6.5, non-reactive buffer.

**Calculation:**

The COBAS c311 system automatically calculates the creatinine concentration of each urine sample.

**Reference values:**

Males:3450-22900μmol/l (39-259mg/dl)

Females: 2470-19200μmol/l (28-217mg/dl)

3.4.5.3 Calculation of albumin: creatinine ratio:

Urinary albumin: creatinine reported as ratio:
Urine albumin(mg/L)/Urine Creatinine(g/L) = mg albumin / g Creatinine. (see appendix (2))

3.4.5.4 Estimation of plasma creatinine:

Principle:
Creatinine in the sample reacts with picrate in alkaline medium forming a colored complex (Jaffe method). The complex formation rate is measured in short period to avoid interference.

Composition of reagent:

A. Reagent 5×50 ml. sodium hydroxide 0.4 mol/l, detergent.

B. Reagent 5×50 ml. picric acid 25 mmol/l

Auxiliary reagent: bio-chemistry calibrator (bio-system cod. 18011)

Reagent preparation:
Working reagent: mix equal volumes of reagent A and reagent B (stable for one month).

Procedure and calculation:
The A15 analyzer automatically do the procedure and calculate the analyte concentration of each sample. (see appendix)

Reference values of blood creatinine:
Male: 0.9-1.3mg/dl(80-115μmol/l)
Female: 0.6-1.1mg/dl(53-97μmol/l)

3.4.5.5 Calculation of eGFR:

\[
\text{eGFR (ml/min)} = \frac{(140 - \text{Age (years)}) \times \text{weight (kg)}}{72 \times \text{Serum creatinine (mg/dl)}} \times (0.85 \text{ if female})(\text{Bishop, et al. 2010})
\]

Reference values of eGFR:
Male: 97-137 ml/min/1.73m²
Female: 88-128 ml/min/1.73m²

3.5 Statistically analysis:

The mean, standard deviation (SD), and the correlations between albumin creatinine ratio, eGFR, age, duration of hypertension, DM with hypertension and controlled of hypertension. For all statistical comparisons a P-value of < 0.05 was considered statistical significant. All statistical procedures were performed using SPSS software, version 20.
# 4. RESULTS

## Table (4.1): Demographic data of two groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HT N= 60</th>
<th>Healthy Control N= 40</th>
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</thead>
<tbody>
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<td></td>
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<td>Percent</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>Female</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
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<td>100</td>
</tr>
<tr>
<td><strong>Age Groups</strong></td>
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<td></td>
</tr>
<tr>
<td>30 - 60 Years</td>
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<td>51.7</td>
</tr>
<tr>
<td>≥61 Years</td>
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<td>48.3</td>
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<tr>
<td>Total</td>
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<td>100</td>
</tr>
<tr>
<td><strong>Classification of GFR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>51</td>
<td>85</td>
</tr>
<tr>
<td>Stage 2</td>
<td>7</td>
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<td>Stage 4</td>
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<td>3.3</td>
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<td>Total</td>
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<td>100</td>
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<td><strong>ACR</strong></td>
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<td></td>
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<tr>
<td>Micro-albuminuria</td>
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<td>45</td>
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<tr>
<td>Normal</td>
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<td>46.7</td>
</tr>
<tr>
<td>Macro-albuminuria</td>
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<td><strong>Duration of Disease</strong></td>
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<td>50</td>
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<td>100</td>
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<td><strong>DM with HTN</strong></td>
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</tr>
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<td>50</td>
</tr>
<tr>
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</tr>
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<td>Total</td>
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</tr>
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Table (4.2): Means ± SD of study parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HTN= 60 Means ± SD</th>
<th>Normotensive = 40 Means ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR</td>
<td>9.40 ± 23.62</td>
<td>3.18 ± 2.57</td>
</tr>
<tr>
<td>eGFR</td>
<td>101.22 ± 21.12</td>
<td>111.03 ± 18.56</td>
</tr>
<tr>
<td>Age</td>
<td>60 ±1 1.74</td>
<td>57±12.43</td>
</tr>
</tbody>
</table>

4.1 Comparison between normotensive individuals and hypertensive patients for the levels of albumin: creatinine ratio and eGFR:
The levels of albumin: creatinine ratio statistically were significant (P<0.05) increased difference between hypertensive and normotensive individual (1.46 ± 0.59 mg/g and 1.37 ± 0.34 mg/g respectively) and the levels of eGFR statistically were significantly (P<0.05) decreased different between hypertensive and normotensive (101.22 ± 21.1 ml/min/1.73m² and 111.03±18.7 ml/min/1.73m² respectively). (see table 4.3)

4.2.1 Study of albumin: creatinine ratio and eGFR levels with variables:

4.2.1 Age of hypertensive patients:
The levels of eGFR statistically were significantly (P< 0.05) by age of hypertensive patients which decreased in >61 years’ age (93.3 ± 19.9 ml/min/1.73m²) than in 30-60 years’ age (108.6 ± 19.8 ml/min/1.73m²), whereas levels of albumin: creatinine ratio statistically were insignificantly (P> 0.05) by age of hypertensive patients which increased in >61 years’ age (1.45 ± 0.53 mg/g) than in 30-60 year’ age (1.40 ± 0.48 mg/g). (see table 4.4.a)

4.2.2 Duration of hypertension:
The levels of albumin: creatinine ratio and eGFR statistically were insignificantly (P> 0.05) by duration of hypertension but the level of albumin: creatinine ratio increased in >8 years’ duration (1.57 ± 0.70 mg/g) than in 1-7 years’ duration (1.34 ± 0.42 mg/g), whereas level of eGFR decreased in >8 years’ duration (96.9 ± 24.6 ml/min/1.73m²) than in 1-7years’ duration (105.5 ± 16.1ml/min/1.73m²). (see table 4.4.b)
4.2.3 Presence of DM with hypertension:
The levels of albumin: creatinine ratio statistically were significantly (P< 0.05) by presence of DM with hypertension which increased in patients with hypertension and DM (1.66 ± 0.69 mg/g) than in patients with hypertension only (1.25 ± 0.37 mg/g), whereas levels of eGFR statistically were insignificantly (P> 0.05) by presence of DM with hypertension, decreased in patients with hypertension and DM (96.7 ± 22.2 ml/min/1.73m²) than in patients with hypertension only (105.7 ± 19.4 ml/min/1.73m²). (see table 4.4.c)

4.2.4 Controlled of hypertension:
The levels of albumin: creatinine ratio statistically were significantly (P< 0.05) by controlled of hypertension which increased in uncontrolled patients (1.85 ± 0.88 mg/g) than in controlled patients (1.41 ± 0.53 mg/g), whereas levels of eGFR statistically were insignificantly (P> 0.05) by controlled of hypertension, decreased in uncontrolled patients (84.2±33.9 ml/min/1.73m²) than in controlled patients (103.1±18.8 ml/min/1.73m²). (see table 4.4.d)

4.3 Correlation between albumin creatinine ratio, eGFR and social characters:
The albumin: creatinine ratio level had negative, significant (P<0.05) and (weak correlation with DM with HTN) and (moderate correlation with GFR), whereas it had positive, (significant (P<0.05) and weak correlation with duration) and (insignificant (P>0.05) and moderate with age). On the other hand, eGFR level had positive, weak and insignificant (P>0.05) correlation with DM with HTN whereas it had negative, weak and (insignificant (P>0.05) correlation with duration), (significant (P<0.05) with age) and (moderate and significant (P<0.05) with ACR). (see table 4.5)
Table (4.3): Comparison between normotensive individuals, hypertensive for the levels albumin: creatinine ratio and eGFR

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Hypertensive</th>
<th>Normotensive</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin: creatinine ratio</td>
<td>1.46±0.59</td>
<td>1.37±0.34</td>
<td>0.02*</td>
</tr>
<tr>
<td>eGFR</td>
<td>101.22±21.1</td>
<td>111.03±18.7</td>
<td>0.046*</td>
</tr>
</tbody>
</table>

*: Significant at 5 %

Table (4.4.a): Levels of albumin: creatinine ratio and eGFR for hypertensive patients associated with age

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Age</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 - 60 year</td>
<td>&gt; 61 year</td>
</tr>
<tr>
<td>Albumin: creatinine ratio</td>
<td>1.40±0.48</td>
<td>1.45±0.53</td>
</tr>
<tr>
<td>eGFR</td>
<td>108.6±19.8</td>
<td>93.3±19.9</td>
</tr>
</tbody>
</table>

*: Significant at 5 %, ns: No significant difference

Table (4.4.b): Levels of albumin: creatinine ratio and eGFR for hypertensive patients associated with duration of hypertension

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Duration of hypertension</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-7 years</td>
<td>&gt;8 years</td>
</tr>
<tr>
<td>Albumin: creatinine ratio</td>
<td>1.34±0.42</td>
<td>1.57±0.70</td>
</tr>
<tr>
<td>eGFR</td>
<td>105.5±16.1</td>
<td>96.9±24.6</td>
</tr>
</tbody>
</table>

ns: No significant difference
Table (4.4.c): Levels of albumin: creatinine ratio and eGFR for hypertensive patients associated with DM with hypertension

<table>
<thead>
<tr>
<th>Parameters</th>
<th>DM with hypertension</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DM+HT</td>
<td>HT</td>
</tr>
<tr>
<td>Albumin: creatinine ratio</td>
<td>1.66±0.69</td>
<td>1.25±0.37</td>
</tr>
<tr>
<td>eGFR</td>
<td>96.7±22.2</td>
<td>105.7±19.4</td>
</tr>
</tbody>
</table>

*: Significant at 5 %, ns: No significant difference

Table (4.4.d): Levels of albumin creatinine ratio and GFR for hypertensive patients associated with controlled of hypertension

<table>
<thead>
<tr>
<th>Parameters</th>
<th>controlled of hypertension</th>
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<tbody>
<tr>
<td></td>
<td>Controlled</td>
<td>Not controlled</td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
<tr>
<td>Albumin: creatinine ratio</td>
<td>1.41±0.53</td>
<td>1.85±0.88</td>
</tr>
<tr>
<td>eGFR</td>
<td>103.1±18.8</td>
<td>84.2±33.9</td>
</tr>
</tbody>
</table>

*: Significant at 5 %, ns: No significant difference

Table (4.5): Correlation between albumin: creatinine ratio, GFR and variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>r &amp; P</th>
<th>ACR</th>
<th>eGFR</th>
<th>Age</th>
<th>Duration</th>
<th>DM with HTN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR</td>
<td>R</td>
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<td>-0.5879</td>
<td>0.06409</td>
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<td>-0.3151</td>
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<tr>
<td></td>
<td>P</td>
<td>-</td>
<td>P&lt;0.0001</td>
<td>P=0.6266</td>
<td>P=0.0344</td>
<td>P=0.0142</td>
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<tr>
<td>eGFR</td>
<td>R</td>
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<tr>
<td></td>
<td>P</td>
<td>P&lt;0.0001</td>
<td>-</td>
<td>P=0.000</td>
<td>P=0.0630</td>
<td>P=0.0981</td>
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</table>

*: Significant correlation at 5%, ns: No significant difference
5. DISCUSSION

5.1 Discussion:

Hypertension is one of the most influential risk factor for mortality worldwide. Epidemiological studies have reported that hypertension is strongly associated with the risk of coronary heart disease, cerebrovascular disease and chronic kidney disease. However, there remains a lack of understanding of the determinants of hypertension. (Yadav et al. 2016)

This study conducted to study the effect of hypertension on the albumin creatinine ratio and estimated GFR on Sudanese hypertensive patients compared to control group. The results obtained from present study indicated that, there were significantly different of albumin creatinine ratio and GFR of hypertensive patients when compared with controls. This results were agreed with study done by (Zhang YP et al., 2013) on elderly subjects, which they found that there were significant low GFR in hypo and hypertensive groups compared with normotensive group and proteinuria more prevalent when systolic blood pressure was more than 140mmg or less than 90mmgh.

In current study, the level of albumin: creatinine ratio was significant (p<0.05) increase in uncontrolled of treatment hypertensive patients than in controlled. The study also found insignificantly (p> 0.05) increase in ACR between hypertensive patients age >61 years than in 30-60 years and duration >8 years than in 1-7 yeas duration. this agreed with (Jong et al., 2012). This results were agreed with study done by (Hitha B et al., 2008), which they found that, the prevalence of microalbuminuria among hypertensive patients increased steadily with age and it prevalence in more than 10 years of hypertension than in less duration. It prevalence in irregular treatment than regular treatment.

This study also showed that there was significant (p<0.05) increase in ACR between hypertensive patients have DM than in patients not have DM.
On the other hand, the level of eGFR was significantly \((p < 0.05)\) reduced in cases when compared to control. Similar result was also reported on cohort study done by (Mancusi, C et al., 2018) on hypertensive patients which found that 10% of patients presented with GFR decline and they were older, more likely to be diabetic, with low GFR and have high systolic and diastolic blood pressure.

The level of eGFR was significantly \((p < 0.05)\) decreased in >61 year age than in 30-60 year and also in >8 years’ duration than 1-7 years’ duration. But the level of eGFR is insignificant decreased in cases who have DM than in who not have and in uncontrolled patient than controlled patients.

The present study shows that, ACR has negative, significant and weak correlation with DM with HTN, whereas it had positive, (significant and weak correlation with duration) and (insignificant and moderate with age). On the other hand, GFR level had positive, weak and insignificant correlation with DM with HTN whereas it had negative, weak and (insignificant correlation with duration) and (significant with age).
CONCLUSION AND RECOMMENDATIONS

5.2 Conclusion:

This study demonstrates significantly increased difference in albumin creatinine ratio and GFR in hypertensive patients when compared with normotensive group. Thus, albumin creatinine ratio and GFR level activity associated with age, duration of hypertension, presences of DM with hypertension and controlled of hypertension.

5.3 Recommendations:

1- Further study should be carried out and other renal function tests must be included.
2- The health ministry must play an obvious role in health education for the community to know the hazard and complication of hypertension.
3- Screening tests for microalbuminuria should be applied for all patients with essential hypertension.
4- Estimation of microalbuminuria for uncontrolled patients and patients have DM with hypertension.
5- Estimation of GFR for hypertensive patients age > 61 year and hypertension duration > 8 years.
6- Further research include matching between case and control.
7- Further study should divide diabetic patients to type 1 and type 2.
8- Further study should calculate body mass index for GFR calculation.
9- Further study should compare between hypertension and type of drugs used.
REFERENCES


### Appendix (1)

<table>
<thead>
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<th>REF</th>
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<th>Analyzer(s) on which cobas c pack(s) can be used</th>
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<tbody>
<tr>
<td>04469658 190</td>
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<td>07 6743 3</td>
<td>cobas c 311, cobas c 501/502</td>
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<td>03121305 122</td>
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<td>Code 489</td>
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<td>Precinorm PUC (4 x 3 mL)</td>
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<td>Diluent NaCl 9 % (50 mL)</td>
<td>07 6869 3</td>
<td></td>
</tr>
</tbody>
</table>

### English

**System information**

For cobas c 311/501 analyzers:

ALBU2: ACN 253 (Albumin in urine)

ALBS2: ACN 128 (Albumin in serum)

ALBC2: ACN 412 (Albumin in CSF)

For cobas c 502 analyzer:

ALBU2: ACN 8253 (Albumin in urine)

ALBS2: ACN 8128 (Albumin in serum)

ALBC2: ACN 8412 (Albumin in CSF)

**Intended use**

In vitro test for the quantitative determination of albumin in human urine, serum, plasma and CSF (albumin CSF/serum ratio) on Roche/Hitachi cobas c systems.

**Summary**

Albumin is a non-glycosylated protein with a molecular weight of 66000 daltons. It is synthesized in liver parenchymal cells at a rate of 14 g/day. Quantitatively, albumin is normally the most important protein component (> 50 %) in plasma, CSF and urine. A small, but abnormal albumin excretion in urine is known as microalbuminuria. Causes of microalbuminuria can be glomerular (e.g. due to diabetic microangiopathy, hypertension, minor glomerular lesion), tubular (inhibition of reabsorption) or postrenal. Albumin is also a marker protein for various forms of proteinuria.

In selective glomerular proteinuria, 100-3000 mg albumin/g creatinine are excreted in the urine. Non-selective glomerular proteinuria is characterized by elevated excretion of high-molecular weight proteins (IgG more than 10 % of the albumin value). Glomerular proteinuria is recognized by a discrepancy between albumin and total protein (albumin accounting for less than 30 %, with concurrent elevation of total protein). Simultaneous elevation of albumin and microproteins is found in glomerulotubular proteinuria occurring due to overloading of tubular reabsorption in glomerulopathy (e.g. nephritic syndrome), combined glomerular tubulointerstitial nephropathy or in renal failure following diabetic nephropathy or other causes (overflow proteinuria). Albumin has two main functions in plasma: maintaining the oncotic pressure (80 % due to albumin in plasma) and transport. It is the most important transport protein for substances having low water solubility (such as free fatty acids, bilirubin, metal ions, hormones and pharmaceuticals).

Depressed albumin levels are caused by hyperhydration, hepatocellular synthesis insufficiency, secretion disorders in the intravascular space, abnormal distribution between the intravascular and extravascular space, catabolism and loss of albumin, acute phase reactions and congenital analbuminemia.

Blood brain barrier disorders can be reliably quantified with the aid of the albumin CSF/serum ratio. Elevated albumin ratios are indicative of a blood brain barrier disorder.

By simultaneously determining IgG in CSF and serum while taking into account the individual albumin ratios, it is possible to differentiate between IgG originating from the blood and CNS-synthesized immunoglobulin. IgG predominates in multiple sclerosis, chronic Hiv encephalitis, neurosphyllitis and herpes simplex encephalitis.

A variety of methods, such as radial immunodiffusion, nephelometry and turbidimetry, are available for the determination of albumin.

**Test principle**

Immunoassay.

Anti-albumin antibodies react with the antigen in the sample to form antigen/antibody complexes which, following agglutination, are measured turbidimetrically.

**Reagents - working solutions**

- **R1** TRIS buffer: 50 mmol/L, pH 8.0; PEG: ≥ 4.2 %; EDTA: 2.0 mmol/L; preservative
- **R2** Polyclonal anti-human albumin antibodies (sheep): dependent on titer; TRIS buffer: 100 mmol/L; pH 7.2; preservative
- **R3** Reagent for antigen excess check. 
  *Albumin in diluted serum (human); NaCl: 150 mmol/L; phosphate buffer: 50 mmol/L; pH 7.0; preservative*

R1 is in position A, R2 is in position B and R3 is in position C.

**Precautions and warnings**

For in vitro diagnostic use.

Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods used are approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A. However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.

**Reagent handling**

Ready for use.

**Storage and stability**

ALBT2

Shelf life at 2-8 °C: See expiration date on cobas c pack label.

On-board in use and refrigerated on the analyzer: Diluent NaCl 9 %

12 weeks
Appendix (2)

CREJ2
Creatinine Jaffé Gen.2
Order information

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<td>07 6928 2</td>
<td>Roche/Hitachi cobas c 311, cobas c 501/502</td>
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<td>System-ID 07 6869 3</td>
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</table>

English
System information
For cobas c 311/501 analyzers:
CREJ2U: ACN 690 (Rate blanked, compensated, serum and plasma)
CRJ2U: ACN 691 (Rate blanked, urine)
SREJ2U: ACN 773 (STAT, compensated, serum and plasma, reaction time: 4)
SCREJ2U: ACN 774 (STAT, urine, reaction time: 4)
For cobas c 502 analyzer:
CREJ2U: ACN 8690 (Rate blanked, compensated, serum and plasma)
CRJ2U: ACN 8691 (Rate blanked, urine)
SREJ2U: ACN 8773 (STAT, compensated, serum and plasma, reaction time: 4)
SCREJ2U: ACN 8774 (STAT, urine, reaction time: 4)

Intended use
In vitro test for the quantitative determination of creatinine in human serum, plasma and urine on Roche/Hitachi cobas c systems.

Summary
Chronic kidney disease is a worldwide problem that carries a substantial risk for cardiovascular morbidity and death. Current guidelines define chronic kidney disease as kidney damage or glomerular filtration rate (GFR) less than 60 mL/min per 1.73 m² for three months or more, regardless of cause. The assay of creatinine in serum or plasma is the most commonly used test to assess renal function. Creatinine is a breakdown product of creatine, which is produced at a fairly constant rate by the body (depending on muscle mass). It is freely filtered by the glomeruli and, under normal conditions, is not re-absorbed by the tubules to any appreciable extent. A small amount is also actively secreted. Since a rise in blood creatinine is observed only with marked damage of the nephrons, it is not suited to detect early stage kidney disease. A considerably more sensitive test and better estimation of glomerular filtration rate (GFR) is given by the creatinine clearance test based on creatinine’s concentration in urine and serum or plasma, and urine flow rate. For this test a precisely timed urine collection (usually 24 hours) and a blood sample are needed. However, since this test is prone to error due to the inconvenient collection of timed urine, mathematical attempts to estimate GFR based only on the creatinine concentration in serum or plasma have been made. Among the various approaches suggested, two have found wide recognition: that of Cockcroft and Gault and that based on the results of the Jaffé test. While the latter equation was derived from data obtained with the conventional Jaffé method, a newer version of the second is usable for IOMS-traceable creatinine methods. Both are applicable for adults. In children, the Bedside Schwartz formula should be used.

In addition to the diagnosis and treatment of renal disease, the monitoring of renal dialysis, creatinine measurements are used for the calculation of the fractional excretion of other urine analytes (e.g., albumin, α-amylase). Numerous methods were described for determining creatinine. Automated assays established in the routine laboratory include the Jaffé alkaline picrate method in various modifications, as well as enzymatic tests.

Test principle
This kinetic colorimetric assay is based on the Jaffé method. In alkaline solution, creatinine forms a yellow-orange complex with picrate. The rate of dye formation is proportional to the creatinine concentration in the specimen. The assay uses “rate-blanking” to minimize interference by bilirubin. To correct for non-specific reaction caused by serum/plasma pseudo-creatine chromogens, including proteins and ketones, the results for serum or plasma are corrected by -28 μmol/L (-0.3 mg/dL).

Alkaline pH
Creatinine + picric acid → yellow-orange complex

Reagents - working solutions
R1  Potassium hydroxide: 900 mmol/L; phosphate: 135 mmol/L; pH ≥ 13.5; preservative; stabilizer
R3  Picric acid: 38 mmol/L; pH 6.5; non reactive buffer

(STAT R2)
R1 is in position B and R3 (STAT R2) is in position C.

Precautions and warnings
For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user or request.
For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:
Appendix (3)

بسم الله الرحمن الرحيم

Sudan University of Sciences and Technology

College of Graduate Studies

Questionnaire Paper for Master Degree Research

Questionnaire No ( )

Assessment of Albumin: Creatinine Ratio and GFR among Hypertensive Patients at Al-Jazeera state

Name:

Age:

Family history of hypertension:

Last blood pressure measured:

Duration of hypertension:

Controlled of hypertension:  Yes ( )  NO ( )

Presence of DM:  Yes ( )  NO ( )

Medications used:

Other diseases:

Telephone:

Lab results:

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<thead>
<tr>
<th>Urine ALB</th>
<th>Urine Creatinine</th>
<th>ACR</th>
<th>Plasma creatinine</th>
<th>Body weight</th>
<th>GFR</th>
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