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Evaluating the Association Between Hypertension and Diabetes Mellitus with the Risk of Early Kidney Disease "A Study on the Performance of the Albumin-to-Creatinine " Ratio as a Diagnostic Criterion"

تقييم العلاقة بين ارتفاع ضغط الدم وداء السكري مع خطر الإصابة المبكرة بأمراض الكلى "دراسة عن أداء نسبة الألبومين إلى الكرياتينين كمعيار تشخيصي"

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Abstract

Objectives: This study aims to evaluate the relationship between hypertension and diabetes with an increased risk of early kidney function impairment, as well as to assess the performance of the albumin-to-creatinine ratio (ACR) as a diagnostic criterion in this patient group. **Methods**: The study included 108 participants (males and females) aged between 30 and 80 years. Participants were divided into groups based on their health conditions: hypertensive patients, diabetic patients, those with both conditions, and a control group. Mean and standard deviation (mean ± SD) were calculated, along with the predictive ability of the ACR test. **Results**: The analyses revealed significant differences in several health parameters, with notable increases in blood sugar levels, HbA1C, and systolic and diastolic blood pressure in the diabetes and hypertension groups compared to the control group, with strong statistical significance (P<0.001). Additionally, a significant increase in the albumin-to-creatinine ratio (ACR) was observed, indicating potential deterioration in kidney function. The study also identified important positive and negative correlations between ACR and factors such as age, body mass index (BMI), and kidney function. The ACR test's ability to detect kidney impairment was evaluated, demonstrating good predictive capability with a cutoff value of > 27.59, resulting in an area under the curve (AUC) of 0.916, with a sensitivity of 92.31%, specificity of 80%, and accuracy of 85.71%. **Conclusion**: The ACR test demonstrated excellent performance as a diagnostic tool, highlighting the necessity for its utilization as part of a comprehensive screening strategy.

Keywords: **Hypertension**, **Type2Diabetes**, **Albumin-to-Creatinine Ratio**, **Kidney Complications**, **Brack Al-Shati Hospital**

1.Introduction

Hypertension and diabetes are among the most common chronic diseases worldwide, posing significant health challenges. Hypertension, often referred to as the "silent killer," occurs when blood pressure in the arteries rises abnormally, potentially damaging blood vessels and organs such as the heart and kidneys. Diabetes, on the other hand, affects how the body utilizes glucose, leading to elevated blood sugar levels, and is primarily categorized into two types: Type 1 and Type 2. (**WHO**.,**2023; ADA**.,**2023**)

1.1. Impact of Diabetes and Hypertension on the Kidneys

Diabetic kidney disease (DKD) is a complex condition associated with metabolic disturbances and hemodynamic changes. The classical clinical presentation begins with a slow progression from microalbuminuria to macroalbuminuria, accompanied by glomerular hypertrophy in early stages and a gradual decline in kidney function in later stages. Recent epidemiological studies indicate that patients with DKD experience a variety of symptoms and different rates of progression toward end-stage renal disease (ESRD). Some may show deterioration in kidney function without an increase in albumin levels, but with evident vascular and interstitial fibrosis. Furthermore, patients with DKD have a higher risk of acute kidney injury, yet only a small percentage ultimately progress to ESRD (**Chen et al**., **2020**).

Hypertension negatively affects kidney function, as prolonged high blood pressure can damage blood vessels, increasing the risk of chronic kidney disease (CKD). Many studies have established that hypertension plays a crucial role in the development of CKD, with the presence of small amounts of albumin in the urine serving as an early indicator of the disease. Treatments aimed at reducing albumin levels have been shown to delay disease progression, while careful control of blood pressure contributes to lowering both albumin and protein levels in the urine, which is essential for mitigating complications associated with this condition (**Barry**, **2008**).

2.Materials and methods

The study protocol includes approximately 108 participants of both genders, men and women, aged between 30 and 80 years, recruited from Brack General Hospital based on specific criteria. Patients with heart diseases, kidney failure, type 1 diabetes, tumors, individuals receiving anticoagulant injections, liver diseases, and previous strokes were excluded. The participants were divided into groups, a group suffering solely from high blood pressure, a group suffering solely from type 2 diabetes, a group suffering from diabetes accompanied by high blood pressure, and a control group. Weight, height measurements were taken for each participant in the study, and a questionnaire was conducted for each, including a set of questions and medical history. Blood and urine samples were collected in the morning while considering fasting conditions. The study duration was 4 months from the start date (12/22/2023) to the end date (4/22/2024).

Principle of Operation:

Principle HBA1C test

The test uses a sandwich immunodetection method; the detector antibodies in buffer bind to antigens in the sample, forming antigenantibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized-antibodies on test strip. More antigens in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by instrument for ichroma™ tests to show the content of glycated hemoglobin in terms of percent of the total hemoglobin in the blood.

Principle test

The i-STAT System uses direct (undiluted) electrochemical methods. Values obtained by direct methods may differ from those obtained by indirect (diluted) methods.

Measured:

Sodium (Na), Potassium (K), Chloride (Cl) and ionized Calcium (iCa)

The respective analyte is measured by ion-selective electrode potentiometry. In the calculation of results, concentration is related to potential through the Nernst equation.

Glucose (Glu)

Glucose is measured amperometrically. Oxidation of glucose, catalyzed by the enzyme glucose oxidase, produces hydrogen peroxide (H2O2). The liberated H2O2 is oxidized at the electrode to produce a current proportional to the sample glucose concentration.

$$\beta\text{-D-glucose} + H_2O + O_2 \xrightarrow{\text{glucose oxidase}} \text{D-gluconic acid} + H_2O_2$$

$$H_2O_2 \longrightarrow 2H^+ + O_2 + 2e^-$$

BUN/Urea

Urea is hydrolyzed to ammonium ions in a reaction catalyzed by the enzyme urease.

$$\text{Urea} + H_2O + 2H^+ \xrightarrow{\text{urease}} 2NH_4^+ + CO_2$$

The ammonium ions are measured potentiometrically by an ion-selective electrode. In the calculation of results, concentration is related to potential through the Nernst Equation.

Creatinine (Crea)

Creatinine is measured amperometrically. It is hydrolyzed to creatine in a reaction catalyzed by the enzyme creatinine amidohydrolase. Creatine is then hydrolyzed to sarcosine by creatine amidinohydrolase. The oxidation of sarcosine, catalyzed by sarcosine oxidase, produces hydrogen peroxide (H2O2). The liberated hydrogen peroxide is oxidized at the platinum electrode to produce a current which is proportional to the sample creatinine concentration.

Principle albumin test:

Colorimetric assay

At a pH value of 4.1, albumin displays a sufficiently cationic character to be able to bind with bromcresol green (BCG), an anionic dye, to form a blue-green complex.

Albumin + BCG (pH4.1) →albumin-BCG comple

principle of the assay Afinion ACR

principle of the assay Afinion ACR is a fully automated assay for determination of albumin, creatinine and albumin / creatinine ratio in human urine. The Afinion ACR test cartridge contains all reagents necessary for determination of albumin, creatinine and albumin / creatinine ratio in a human urine sample. The sample material is collected using the sampling device integrated in the test cartridge. Albumin is quantified using a solid phase immunochemical assay. In the Afinion ACR Test Cartridge the sample is automatically diluted and aspirated through a membrane coated with anti – albumin antibodies, which concentrates and immobilizes the albumin from the sample. A gold – antibody conjugate then binds to the immobilized

albumin resulting in a red – brown stained membrane. Excess gold – antibody conjugate is removed in a washing step. The Afinion Analyzer measures the colour intensity of the membrane, which is proportional to the amount of albumin in the sample.

Equations Used in This Study to Calculate Estimated Values

In this study, applications from various websites, including MDCalc and Calculator.net, were utilized to calculate estimated values such as the estimated glomerular filtration rate (eGFR) and body surface area (BSA).

The BUN to Creatinine Ratio is calculated using the following formula:

BUN to Creatinine Ratio (mg/dL) = BUN Level / Creatinine Level.

Estimated GFR Calculation

The Estimated Glomerular Filtration Rate (eGFR) can be determined using the 2021 CKD-EPI Creatinine Equation:

$eGFR = 142 \times \min(SCr/\kappa, 1)^{\alpha} \times \max(SCr/\kappa, 1)^{-1.200} \times 0.9938^{Age} \times 1.012$ [if female]

Body Surface Area Calculation

Body Surface Area (BSA) is calculated using the following formula:

$BSA = 0.007184 \times W^{0.425} \times H^{0.725}$.[1]

Corrected Estimated Glomerular Filtration Rate

The corrected eGFR can be calculated using:

Corrected eGFR (mL/min) = eGFR value x BSA / 1.73

3.Statistical Analysis

The following statistical software was utilized for data analysis: SPSS and Excel. Continuous variables were expressed as mean ± standard deviation Comparisons among variables were conducted using one-way analysis of variance (ANOVA). Additionally, the receiver operating characteristic (ROC) curve was employed to assess diagnostic accuracy, and Pearson correlation was applied. All analyses were performed with a significance level set at $p < 0.05$.

4.The Results

4.1Comparison of Patient Groups with Control Group.

The data extracted from the four groups (Control, Hypertension, Diabetes, and Both) reveal significant differences in several health parameters. Fasting blood sugar FBS (P<0.001) and hemoglobin A1C HbA1C (P<0.001) levels were significantly elevated in the Diabetes and Both groups compared to the Control group. Systolic blood pressure SBP (P<0.001) levels exhibited significant differences, with a marked increase observed in the Hypertension group. Additionally, diastolic blood pressure DBP (P=0.034) displayed significant associations between the Control and Hypertension groups. The albumin-to-

[1] MDCalc eGFR Calculation.
Calculator.net BSA Calculator.[1]

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creatinine ratio ACR (P<0.001) also demonstrated a significant increase in the Diabetes and Both groups. In contrast, other parameters, such as age, body mass index (BMI), and the BUN: Creatinine Ratio did not exhibit significant differences, with P values exceeding 0.05. Furthermore, through the utilization of multiple comparisons (LSD), significant differences were confirmed between.

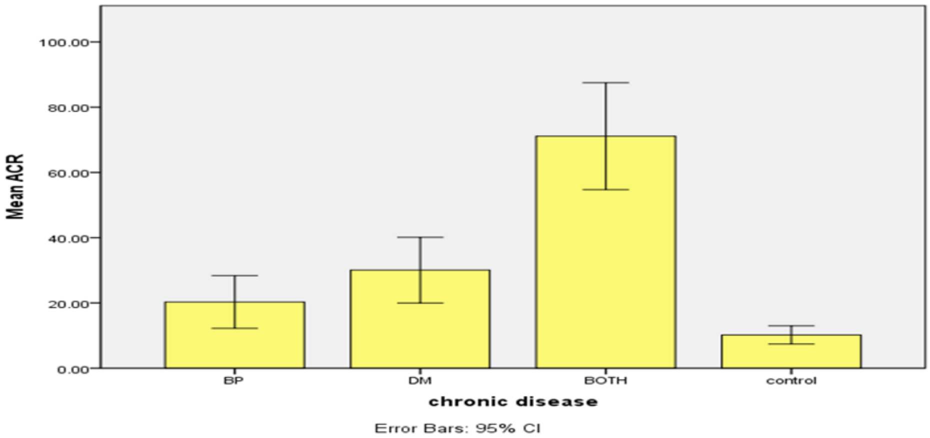


Figure1: Mean Albumin-to-Creatinine Ratio (ACR) in Patients with Chronic Diseases Compared to Control Group.

Table1: Comparing of Health Parameters Among Groups with LSD Method P1: Control VS BP, P2: Control VS DM, P3: Control VS Both, P4: BP VS DM, P5: BP VS Both, P6: DM VS Both

Parameters	Mean±SD				P value	Significant pairwise comparisons
	Control(24)	Hypertension(27)	Diabetes(27)	Both(30)		
Age(years)	51.58±10.89	53.59±10.61	54.26±9.67	55.23±10.85	0.642	
BMI(kg/m^2)	29.22±8.30	30.19±4.64	29.30±4.07	31.53±5.06	0.376	
FBS(mg/dl)	93.23±13.38	99.72v10.07	146.81±66.07	152.04v60.98	<0.001 *	P2, P3, P4, P5: <0.001
HbA1C(%)	5.26±0.59	5.42±0.63	7.56±2.08	8.14±2.43	<0.001 *	P2, P3, P4, P5: <0.001
SBP (mmHg)	124.55±16.56	132.74±15.69	119.81±10.96	128.57±20.11	<0.001 *	P1:>0.001,P3:0.003,P4:0.003, P6:0.034
DBP (mmHg)	74.58±8.33	80.37 ±10.18	73.15±7.98	78.00±11.72	0.034*	P1:0.037,P4:0.008

Parameters		Mean±SD				P value	Significant pairwise comparisons
		Control(24)	Hypertension(27)	Diabetes(27)	Both(30)		
BUN:Creatinine Ratio(mg/dl)		14.61 ±6.45	14.16±4.91	15.15±5.79	16.21±6.54	0.600	
Ccr (mL/min)		102.79±32.27	98.17±32.92	101.43±27.64	104.31±32.27	0.912	
GFR (ml/min)		102.72±19.49	96.22±22.36	101.26±20.98	104.63±21.60	0.574	
ACR(mg/g)		10.21±6.62	20.29±3.93	30.06±25.48	71.12±43.90	>0.001 *	P2:0.015, P3, P5, P6: <0.001
Albumin(g/dl)		4.02±0.33	4.21±0.44	4.20±0.23	4.02±0.33	0.099	P1:0.026,P2:0.032
Electrolyte (mmol/l)	Na	144.83±9.88	144.00±8.05	143.11±11.07	140.82±6.37	0.375	
	K	4.55±0.79	4.44±0.97	4.79±0.96	4.60±0.76	0.520	

4.2. Pearson Correlation of Various Health Parameters with Albumin-to-Creatinine Ratio (ACR) Across Different Patient Groups.

The table illustrates the correlation between the albumin-to-creatinine ratio (ACR) and various health parameters across four groups: Control, Hypertension, Diabetes, and Both. A significant positive correlation was found between age and ACR in the Diabetes group (R = 0.521, P = 0.005), indicating that older age is associated with higher ACR. Additionally, a significant negative correlation was observed for BMI in the Diabetes group (R = -0.461, P = 0.016), suggesting that higher BMI is linked to lower ACR. In terms of kidney function, a significant negative correlation with ACR was also present in both Ccr (R = -0.388, P = 0.046) and GFR (R = -0.432, P = 0.025) for the Diabetes group. No significant correlations were found for fasting blood sugar, hemoglobin A1C, blood pressure measurements, albumin, or electrolytes across the groups.

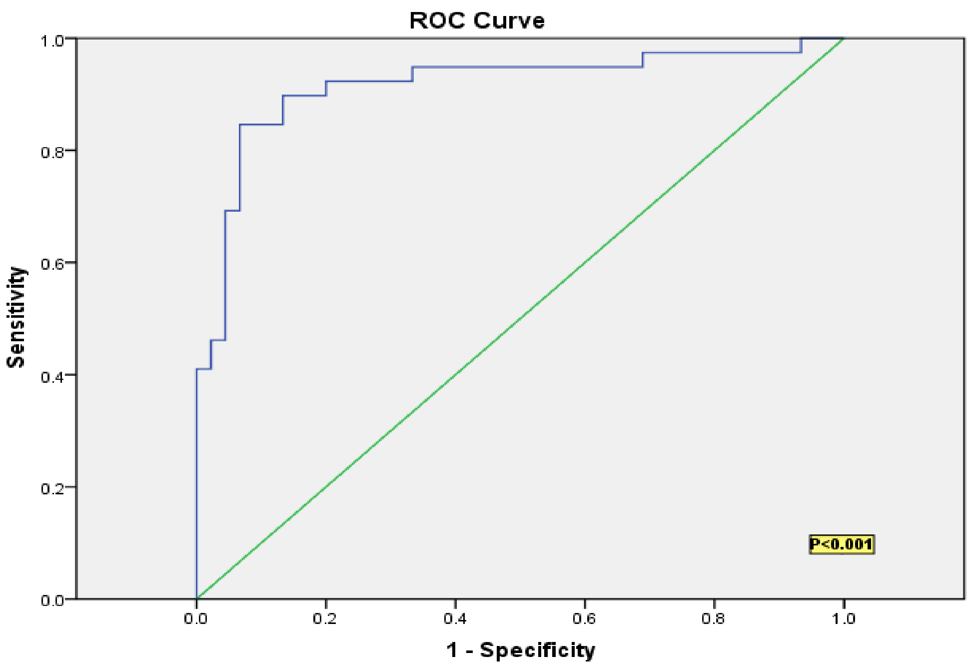
Table2: Pearson Correlation of Various Health Parameters with Albumin-to-Creatinine Ratio (ACR) Across Different Patient Groups.

Correlation with ACR	Control		Hypertension		Diabetes		Both	
	R	P	R	P	R	P	R	P
Age(years)	0.239	0.261	-0.065	0.747	0.521	0.005*	-0.087	0.649
BMI(kg/m^2)	-0.097	0.653	0.249	0.210	-0.461	0.016*	-0.241	0.199
FBS(mg/dl)	0.364	0.080	-0.040	0.844	0.031	0.879	0.096	0.612
HbA1C(%)	-0.003	0.990	-0.132	0.511	0.100	0.621	0.064	0.736
SBP (mmHg)	-0.219	0.304	-0.327	0.096	0.279	0.158	0.115	0.544
DBP (mmHg)	-0.318	0.130	-0.205	0.305	-0.103	0.608	0.024	0.901
BUN:Creatinine Ratio(mg/dl)	-0.026	0.903	0.030	0.883	-0.006	0.978	-0.104	0.585
Ccr (mL/min)	0.038	0.860	-0.189	0.345	-0.388	0.046*	-0.176	0.351
GFR (ml/min)	-0.243	0.252	-0.244	0.219	-0.432	0.025*	-0.130	0.493
Albumin(g/dl)	-0.025	0.908	0.055	0.785	-0.045	0.824	-0.002	0.994
Na(mmol/l)	0.005	0.981	0.133	0.507	0.249	0.210	0.194	0.305
K(mmol/l)	-0.124	0.509	-0.150	0.455	0.219	0.272	-0.021	0.913

4.3. Evaluation of the predictive Ablity of the Albumin-to-Creatinine Ratio Test in Kidney Dysfunction Compared to (GFR+Microalbuminurea) Leves.

The results of the Albumin-to-Creatinine Ratio (ACR) test demonstrate exceptional performance in distinguishing between positive and negative cases, with a p-value of less than 0.001, indicating strong statistical significance. Additionally, the area under the ROC curve reached 0.916, reflecting the high efficacy of the test. Furthermore, the established threshold of greater than 27.59 serves as an appropriate cutoff point. The sensitivity of the test was recorded at 92.31%, meaning it accurately identifies 92.31% of individuals with kidney dysfunction. Meanwhile, the specificity was 80%, and the overall accuracy was 85.71%, indicating the test's effectiveness in correctly identifying negative cases.

TEST	AUC	Cutoff	Specificity	Sensitivity	Accuracy
ACR- test	0.916	>27.59	80%	92.31%	85.71%



The Figure2: displays Analysis of the Area Under the Curve for ACR test.

5.Discussion

AlShurbaji et al. (2023) highlighted the severity of diabetes, describing it as a silent epidemic rapidly spreading worldwide, posing an increasing threat to public health. The results of this study, based on four groups (the control group, the hypertension group, the diabetes group, and the diabetes with hypertension group), revealed significant differences in various health parameters, illustrating the detrimental effects of diabetes on blood sugar levels and the associated risks of hypertension. This underscores the necessity of monitoring blood pressure in these populations. Notably, an increase in the albumin-to-creatinine ratio (ACR) was recorded in both the diabetes and mixed groups, indicating a potential deterioration in kidney function. A significant positive relationship between age and ACR was observed in the diabetes group, suggesting that advancing age may be correlated with elevated ACR levels, reflecting the impact of aging on kidney health. Additionally, a notable negative correlation was found between body mass index (BMI) and ACR, emphasizing the importance of weight management as part of healthcare for diabetic patients. Furthermore, the results indicated negative associations with ACR for both glomerular filtration rate (GFR) and creatinine clearance, suggesting that kidney function deterioration may be linked to increased ACR levels. These findings highlight the importance of monitoring various health parameters, particularly among patients with diabetes and hypertension, and underscore the complex relationships between age, weight, and kidney function, necessitating special attention from healthcare providers to improve patient outcomes. Moreover, a study by **Ghaderian et al**. (**2014**) indicated that diabetes and hypertension are the primary factors contributing to chronic kidney disease (CKD). In recent years, the main causative factors have shifted from glomerulonephritis to these conditions, attributed to lifestyle modifications and rising obesity rates in developed countries. In contrast, the causes of end-stage renal disease (ESRD) remain largely unknown for many patients in developing nations due to delays in healthcare delivery, where challenges in identifying causes in advanced stages hinder kidney biopsy procedures, leading to inconclusive anatomical results. Therefore, it is essential to educate at-risk individuals, such as those with hypertension and diabetes, about the importance of early detection and effective treatment to preserve kidney function, contributing to improved overall health outcomes. Additionally, a study by **Azeem et al**. (**2022**) identified diabetes mellitus (DM) as one of the most significant public health issues globally, as evidenced by global statistics regarding its prevalence. Diabetes leads to numerous health complications, including cardiovascular diseases, blindness, and kidney failure, imposing economic and social burdens on individuals and nations. Genetic factors and unhealthy lifestyle choices contribute to the disease's spread, increasing the need for effective strategies for awareness and control of diabetes within the community. Another study indicated that hereditary hypertension is associated with an increased likelihood of developing chronic kidney disease (CKD) and decreased kidney function, where each 10 mmHg increase in systolic blood pressure raises the odds of CKD by 37%, while each 5 mmHg increase in diastolic blood pressure increases these odds by 19%. Furthermore, a strong relationship was observed between hypertension and increased kidney filtration, suggesting that self-regulation of blood pressure may not provide complete renal protection against moderate increases in blood pressure, according to a study by (**Staplin et al**. **2022**). The findings of this study align with other research regarding the effectiveness of the albumin-to-creatinine ratio (ACR) in detecting early kidney impairment. The

ACR test demonstrated excellent performance in distinguishing between positive and negative cases, with a P-value (<0.001) indicating strong statistical significance. Additionally, the area under the ROC curve, which reached 0.916, reflects the high effectiveness of the test, while the specified threshold (>27.59) serves as an appropriate cutoff point. The sensitivity recorded was 92.31%, indicating that the test can accurately identify 92.31% of affected individuals, with specificity reaching 80%. Moreover, the test's accuracy stands at 85.71%, demonstrating its reliability in identifying negative cases, suggesting that the ACR test is a trustworthy and effective tool for diagnosing kidney impairment. In a study conducted by **Amelia et al**. (**2021**), it was found that blood sugar levels and HbA1c were strongly associated with increased ACR levels, which serve as an indicator of diabetic nephropathy. ACR can be utilized as a screening tool for diabetic nephropathy and other complications of type 2 diabetes, such as cardiovascular complications and retinopathy. In a comparative study between ACR and MMP-7 for detecting impaired kidney function in diabetic patients, the ROC analysis conducted by **Sarangi et al**. (**2025**) revealed that the AUC value for ACR in urine was 0.782, with a sensitivity of 81.3% and a specificity of 64.4%. Diabetic nephropathy is considered a chronic complication of diabetes, where the presence of albumin in urine is an early indicator of its progression. Additionally, a study by **Bhaisare et al**. (**2020**) showed that 80.95% of patients exhibited proteinuria, with 59.04% showing positive results for urinary protein in a 24-hour test. The study also demonstrated the effectiveness of the albumin-to-creatinine ratio (ACR) as a diagnostic tool, with a sensitivity of 100% and a specificity of 46.51%. A strong relationship was established between ACR and levels of creatinine, urea, HbA1c, and anemia, reinforcing its role in assessing the impact of diabetes on kidney function and monitoring its complications.

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الاستبانة

الاسم:

رقم العينة ( ) **السكن** **الجنس** **العمر( )**

الوزن:( ) **الطول( )**

نوع المرض المزمن الذي تعاني منه	سكري	ضغط الدم	سكري وضغط الدم	سليم ظاهرياً
مدة الإصابة بالمرض السكري	اقل من سنة	5 – 1سنوات	10 – 5سنوات	اكثر من 10سنوات
مدة الإصابة بضغط الدم	اقل من سنة	5 – 1سنوات	10 – 5سنوات	اكثر من 10سنوات
ما هو العلاج المستخدم حاليا ؟ واسم العلاج	ادوية مخفضة للسكر	ادوية مخفضة لضغط	لايوجد	
ما مدي التزامك بالعلاج؟	ملتزم جدا	ملتزم إلي حد ما	غير ملتزم	
هل يوجد في تاريخ عائلتك من أصيب بمرض السكري؟	نعم	لا		
هل يوجد في تاريخ عائلتك من أصيب بضغط الدم؟	نعم	لا		
النظام الغذائي	عشوائي	منتظم		
هل تمارس الرياضة أو المشي يومياً	نعم	أحياناً	لا	
هل تعاني من امراض مزمنة	نعم	لا		
نوع المرض المزمن..				

تم تعبئة الاستبيان بمقابلة شخصية مع المريض..

TEST	RESULT
FBS	
HbA1C	
Albumin Levels Test	
HTN	
Kidney function test	
Microalbuminuria	
Electrolyte	
BMI	

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Equipment used in the study:

Centrifuge

Model: Tuttligen Hettich D.78532

Manufacturer: Andreas Hettich GmbH & Co

Country of Manufacture: Germany

Roche Cobas Integra 400 plus Chemistry Analyzer

Model: Roche Cobas Integra 400 Plus

Manufacturer: Roche (Germany)

I CHROMA

Measurement of HbA1C

i-CHROMA™ II

Model: iCHROMA

Manufacturer: Boditech (Korea)

i-STAT 1 Analyzer

Manufacturer: Abbott (U S A)

Model Number: G-300

Afinion 2 Analyzer

Measurement of Lipid profile

ACR-test