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Relationship between IL-20 and diabetic nephropathy in AL Anbar governorate

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***Abstract*---**Background: Diabetic syndrome is characterized by increase blood sugar and resistance to insulin. It is linked to macrovascular and microvascular complication such as nephropathy, neuropathy, and retinopathy. The aim of this study to investigate the relationship between Interleukin 20 and diabetic nephropathy. Material and Methods: The study was include 36 of them with type 2 diabetes, 23 of them with diabetic nephropathy, and 25 healthy controls population , all of whom were over the age of 40. ELISA was used to calculate the Interleukin 20 concentration. fasting serum sugar, Glycated Hemoglobin, Urea, Creatinine, Total protein, Albumin, and globulin were all found. Body mass index was also calculated. Result: this study shown that decrease level of Interleukin 20 and chronic kidney disease patient comparing to Healthy controls group , and this also associated with increase in fasting serum sugar , Glycated Hemoglobin , Urea , Creatinine and body mass index in patients group compared to Healthy controls group. Conclusion: serum Interleukin 20 level show significance difference between patients and Healthy controls groups. that's lower in patients groups.

***Keywords*---**interleukin 20, diabetes, chronic kidney diseases anthropometric measurement.

Introduction

Type 2 diabetes (T2DM) is chronic, progressive metabolic disorder caused by a variety of pathogens. The insulin resistance(IR) and a lack of insulin secretion from pancreatic cells are known as the primary causes of T2DM. T2DM

frequently coexists with other metabolic syndrome components such as obesity, increase blood pressure, increase serum level of cholesterol and triglyceride and fatty liver. It is also raises the risk and mortality from cardiovascular event, which rises dramatically with age. However, the pathogenesis of underlying the age related increase in diabetes risk remain unknown (1). T2DM mechanism is well understood. It is widely assumed that there is a feedback between insulin action and insulin secretion under normal conditions. When there is disruption in this feedback, insulin sensitivity and secretion are compromised, resulting in abnormal blood glucose levels. T2DM is distinguished by insulin resistance (IR) and -cell dysfunction. A body growing suggests that an abnormality of lipid profile is linked to IR. In addition to T2DM, IR is a major component of other metabolic disorders (2). In the last 20 years, the prevalence of T2DM has significantly increase . At the time of diagnosis, the majority of T2DM patients are complain from overweight or obesity . T2DM is characterized by increase blood sugar , insulin resistance, and relative insulin secretion impairment. T2DM was once thought to be an adult-onset disease because it only occurred in elderly people. This disease's prevalence in children and adolescents has recently increased. Diabetes and its complications are occurring earlier as younger children become obese and remain obese throughout childhood and adolescence. 28.9 million of the US population with age under 20 are thought to have diabetes and this according to National Diabetes Statistics (3). Type 2 diabetes is the most common type of diabetes , that account for 90-95 percent of all diagnosed cases. The global population with type 2 DM is rapidly increasing. This increase is linked to increase age of population, economic development, increased urbanization, unhealthy diets , and decreased physical activity . Many people go undiagnosed because there are often only few symptoms in the early stages of disease , or symptoms that do occur are not specific to diabetic . However, at this time, the body is already being harmed by high blood glucose levels , so many people experience complications even before being diagnosed with type 2 diabetes. Consistent high blood glucose levels can result in serious complication affecting the heart and blood vessels, the eyes, the kidneys, and the nerves. Angina , myocardial infarction, cerebral vascular accident , peripheral artery disease (PAD), and congestive heart failure (CHF) are all CVDs that come with diabetes (4). T2DM is characterized by systemic low-grade inflammation (5). Diabetes has been shown in previous studies to be a pro inflammatory state (6). The studies show that diabetics have higher levels of C reactive protein (CRP) , toll like receptors 2 (TLR 2), TLR 4 , plasminogen activator inhibitor-1 (PAI-1), and pro inflammatory cytokines interleukin-1 (IL 1), IL 6, and tumor necrosis factors (TNF-). According to gene, high glucose exposure causes an increase in the expression of pro-inflammatory cytokines, chemokines , and other related factors, many of are regulated by the pro-inflammatory transcription factor nuclear factor-B (NF-B) (7). Furthermore, Adiponectin hormone is anti-inflammatory, has been found to be lower in diabetes mellitus patients (8). Its level has also been found to be lower in diabetic patients with microvascular and macrovascular complication . Das et al. established diabetes as a proinflammatory state in our population (9).

Method

This study included 84 people divided into three groups: 25 healthy people (16 males and 9 females as a control group), 23 patients with renal failure (19 males and 4 females), and 36 patients with type 2 diabetes (17 males and 19 females). In the current study, all patients and healthy controls were over the age of 40, and all patients and healthy control samples were over the age of 40 .

Statistical Analysis

The data was statistically analyzed using SPSS version 24 and GraphPad prism version 7. P value of less than 0.05 chosen as the statistical significance level. Descriptive statistics were calculated for each parameter, including mean , standard deviation (SD), and standard error (SE). The Student t-test was used to compare T2DM and (chronic kidney disease) CKD. Using Pearson's correlation (r=1 to 1), the IL-20 characteristics of both T2DM and CKD was investigated. Receiver's operating characteristic(ROC) curve was developed to investigate the distinct ability of IL-20 levels in healthy individuals and patients with T2DM and CKD.

Result

Table 1 show the mean and standard deviation(SD) for healthy controls group (HCs), chronic kidney disease (CKD) and type 2 diabetic (T2DM). and also show the P value , that when it less than 0.05 , it have a significant difference.

Table 1. clinical and anthropometric characteristics of healthy controls, CKD and T2DM groups.

Parameter	Healthy controls		CKD Patients		T2DM Patients		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age years	56.9	5.8	61. 566	3.566	58.22	5.678	0.6780
BMI kg/m^2	25.8	2.205	26.9	4.256	29.33	5.906	0.0122
FSG mg/dL	115.7	10.58	211.5	40.38	202.8	57.24	<0.0001
HbA1c %	5.311	0.6231	6.359	1.283	9.244	2.433	<0.0001
Urea mg/dL	37.92	5.369	158.2	43.43	43.61	10.9	<0.0001
Creatinine mg/dL	0.536	0.1497	3.704	1.279	0.6639	0.171	<0.0001
T. proteins g/dL	8.728	0.6548	7.609	0.7192	8.626	1.121	<0.0001
Albumin g/dL	4.196	0.443	3.125	0.4264	3.967	0.5523	<0.0001
Globulins g/dL	4.532	0.7581	4.484	0.6892	4.659	1.029	0.7236
ALB/GLB	0.9581	0.2244	0.7219	0.1913	0.8957	0.2502	0.0016
Na Ions mmol/L	135.1	10.6	135.3	16.19	139.8	15.01	0.3472
K Ions mmol/L	4	0.6212	4.157	1.077	3.772	1.084	0.3175
Ca Ions mg/dL	9.181	1.562	8.309	1.754	8.917	1.711	0.1893
Uric Acid mg/dL	6.684	1.207	7.491	1.167	6.731	1.172	0.0304
Cr Cl mL/min	177	52.89	26.89	12.72	136.9	60.44	<0.0001
PKC	11.98	2.518	11.39	3.509	12.17	3.296	0.6395
IL-20 ng/mL	1.838	0.6743	0.926	0.2702	1.683	0.6103	<0.0001

Table 2 show the correlation of IL-20 with all other study parameters>

Table (2) : Correlation of IL-20 with all Parameters that have been studied

Correlation of IL-20 with all Studied Parameters		
Parameter	**r (IL-20 ng/mL)**	**p-value**
IL-20 ng/mL	1.000	0.000
Age	-0.206	0.060
FSG	-0.330	0.002
HbA1C	-0.009	0.933
Urea	-0.492	<0.0001
Creatinine	-0.474	<0.0001
Na Ions	-0.020	0.854
T.Protein	0.147	0.177
S.Ca	-0.136	0.217
Albumin	0.397	<0.0001
ALB/GLB	0.310	0.004
globulins	-0.124	0.260
K Ions	-0.170	0.122
BMI	-0.012	0.913
Cr. Cl.	0.371	0.0005
Uric acid	-0.246	0.024

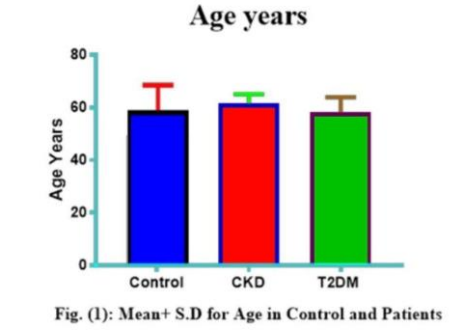

Fig. (1): Mean+ S.D for Age in Control and Patients

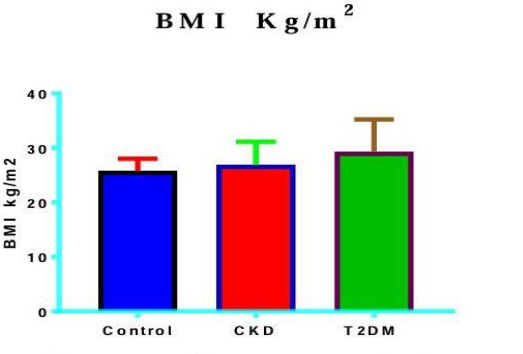

Fig. (2): Mean+ S.D for BMI in Control and Patients

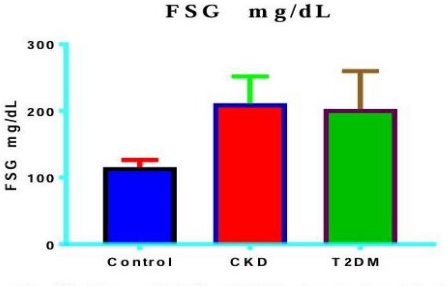

Fig. (3): Mean+ S.D for FSG in Control and Patients

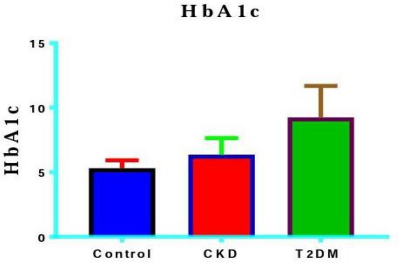

Fig. (4): Mean+ S.D for HbA1c in Control and Patients

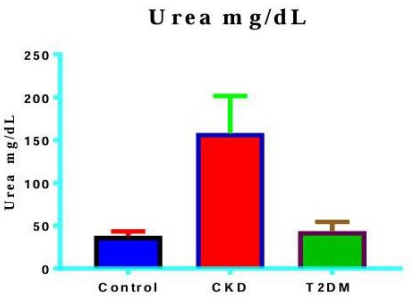

Fig. (5): Mean+ S.D for Urea in Control and Patients

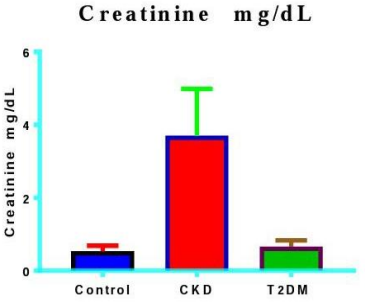

Fig. (6): Mean+ S.D for Creatinine in Control and Patients

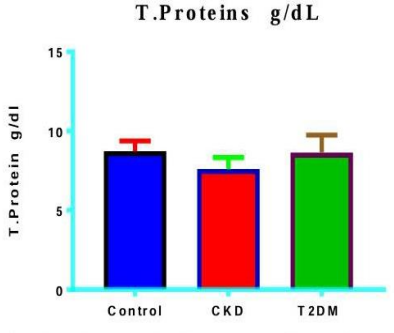

Fig. (7): Mean+ S.D for T.Protein in Control and Patients

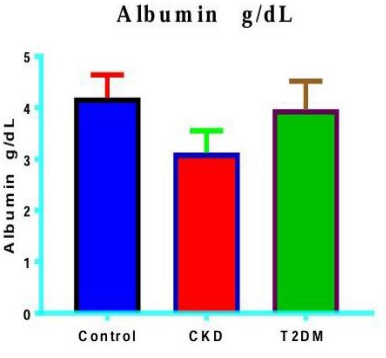

Fig. (8): Mean+ S.D for Albumin in Control and Patients

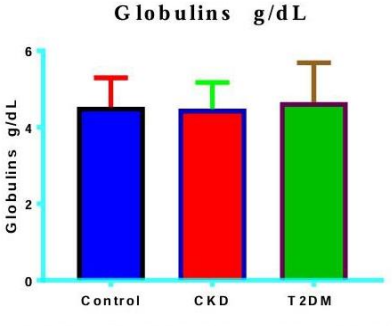

Fig. (9): Mean+ S.D for Glubulins in Control and Patients

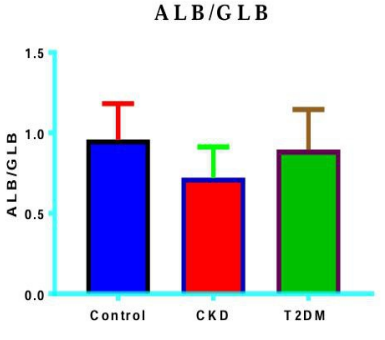

Fig. (10): Mean+ S.D for ALB/GLB in Control and Patients

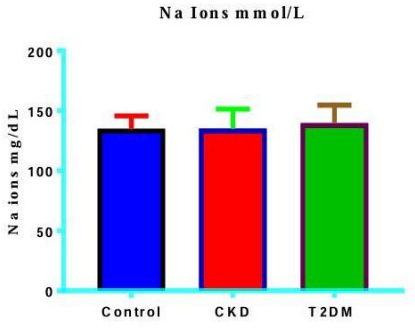

Fig. (11): Mean+ S.D for Na Ions in Control and Patients

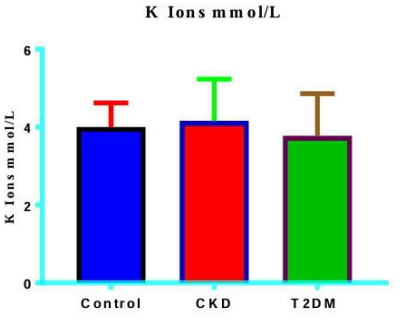

Fig. (12): Mean+ S.D for K Ions in Control and Patients

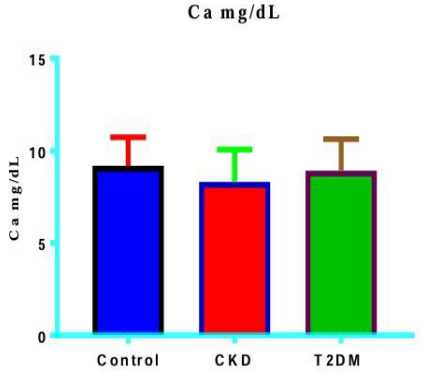

Fig. (13): Mean+ S.D for Ca in Control and Patients

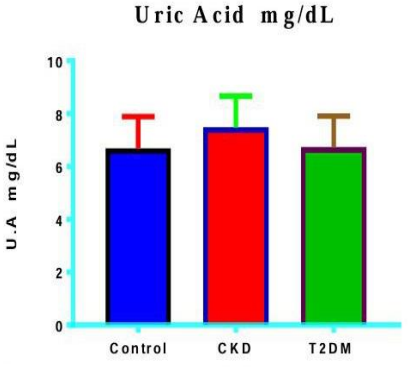

Fig. (14): Mean+ S.D for Uric Acid in Control and Patients

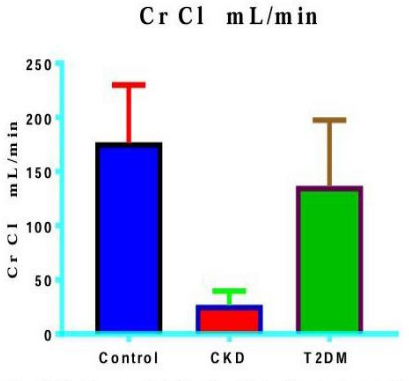

Fig. (15): Mean+ S.D for Cr Cl in Control and Patients

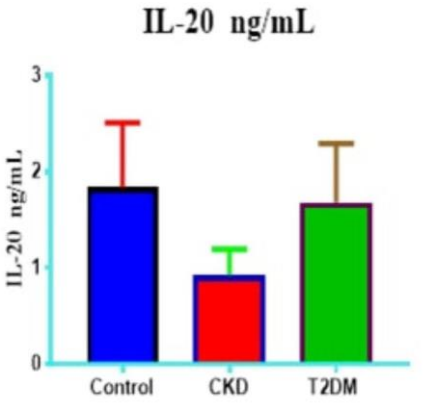

Fig.(16): Mean+ S.D for IL-20 in Control and Patients

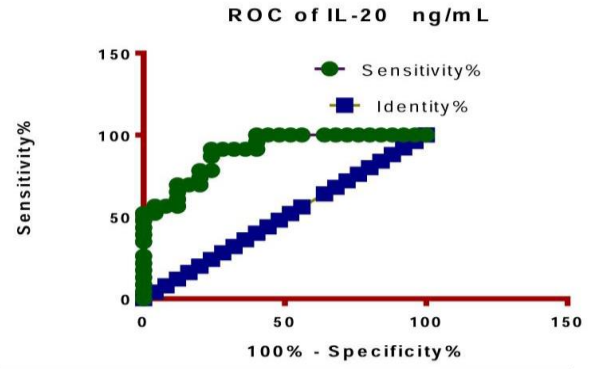

Fig.17.ROC curve displaying AUC of IL-20

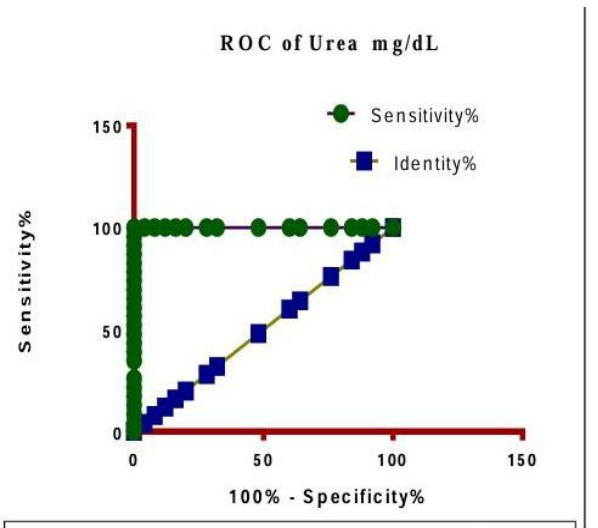

Fig.18.ROC curve displaying AUC of Urea

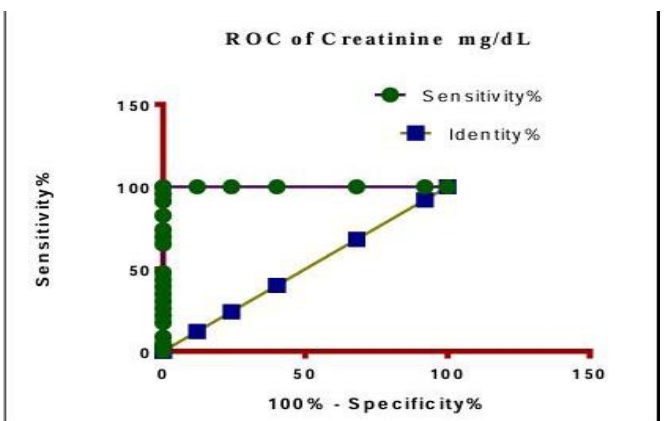

Fig.19.ROC curve displaying AUC of Creatinine

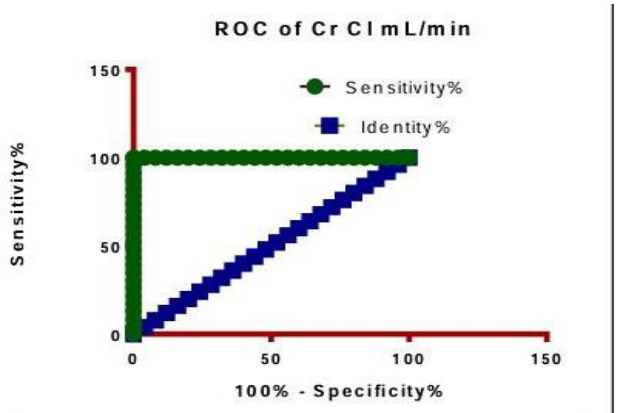

Fig.20.ROC curve displaying AUC of Cr Cl

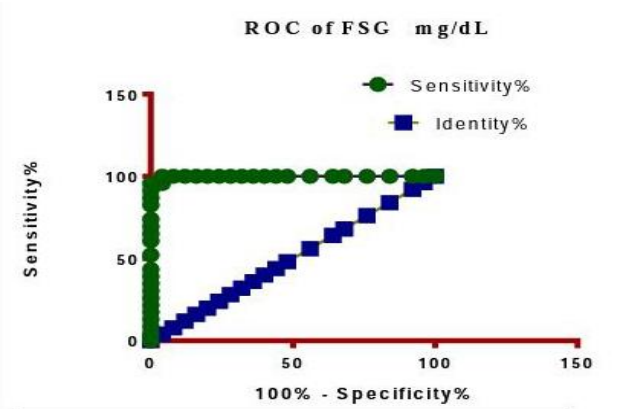

Fig.21.ROC curve displaying AUC of FSG

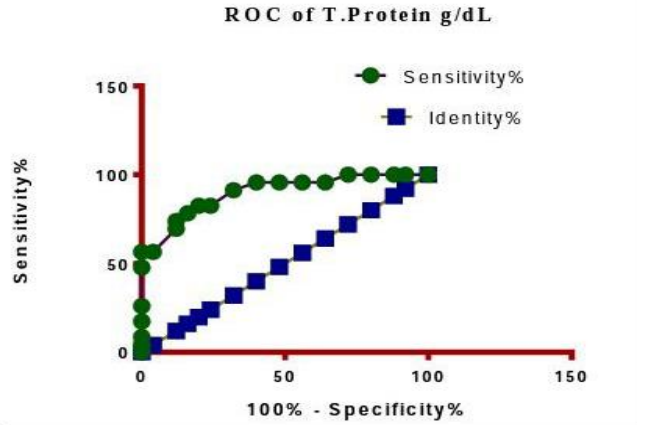

Fig.22.ROC curve displaying AUC of T.Protein

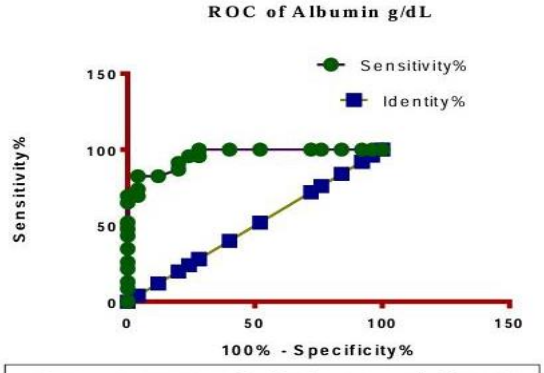

Fig.23.ROC curve displaying AUC of Albumin

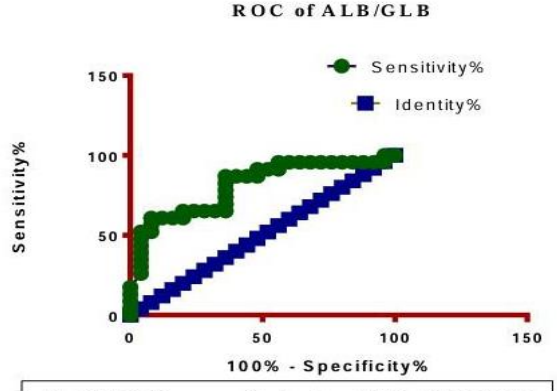

Fig.24.ROC curve displaying AUC of ALB/GLB

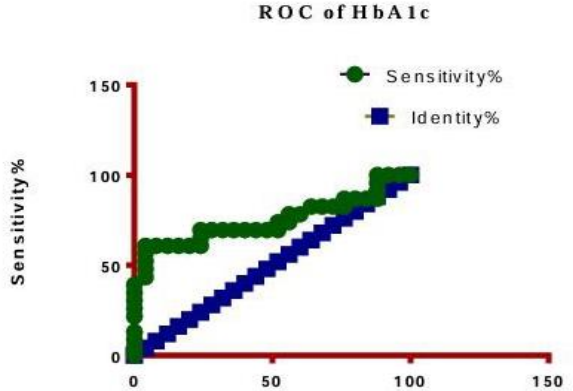

Fig.25.ROC curve displaying AUC of HbA1C

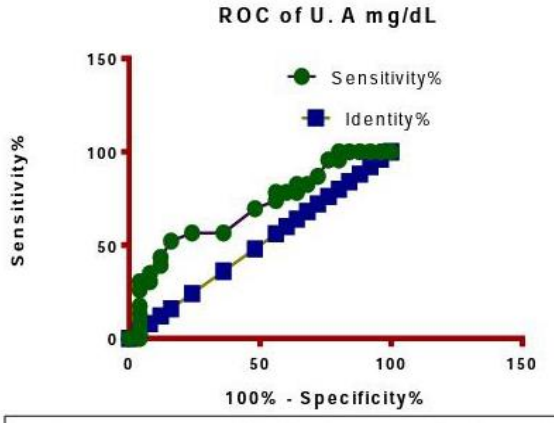

Fig.26.ROC curve displaying AUC of Uric Acid

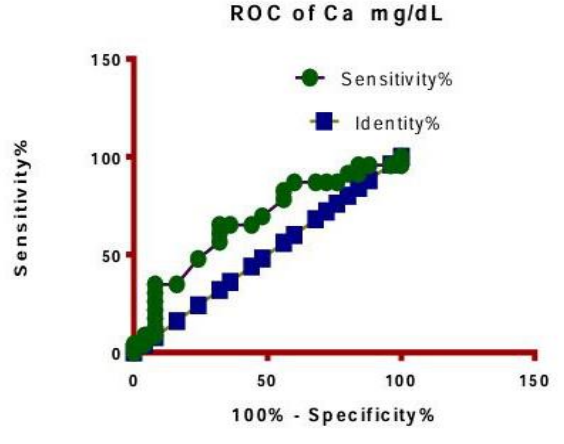

Fig.27.ROC curve displaying AUC of Calcium ion

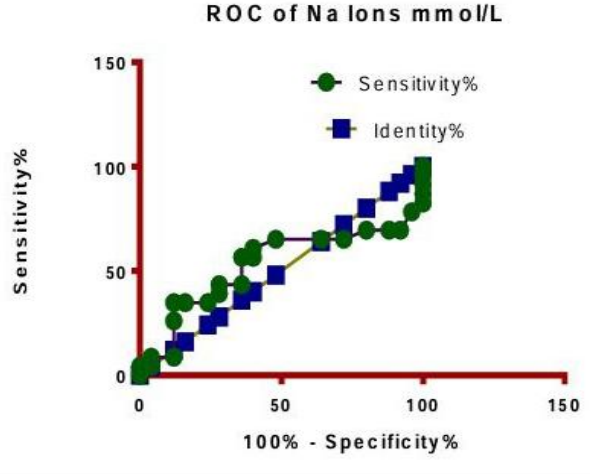

Fig.28.ROC curve displaying AUC of Sodium ion

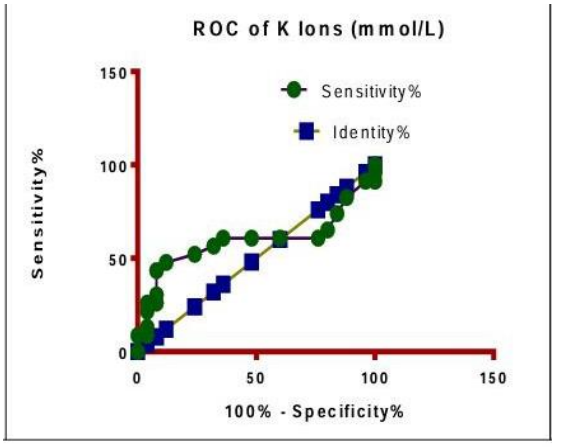

Fig.29.ROC curve displaying AUC of Potassium ion

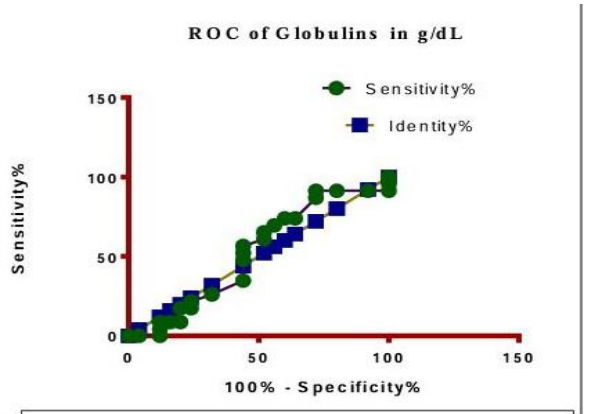

Fig.30.ROC curve displaying AUC of Globulin

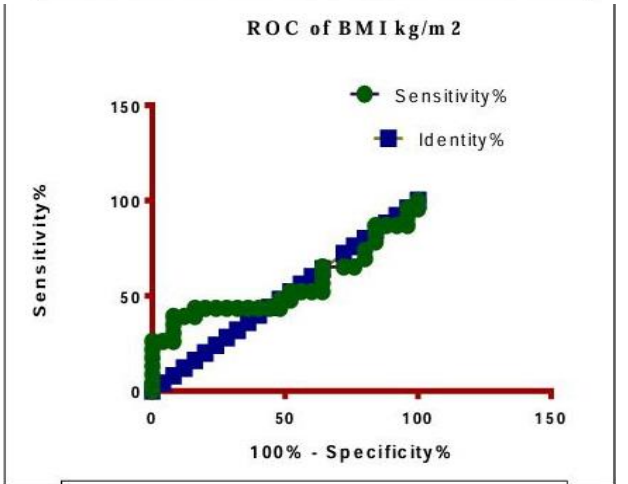

Fig.31.ROC curve displaying AUC of BMI

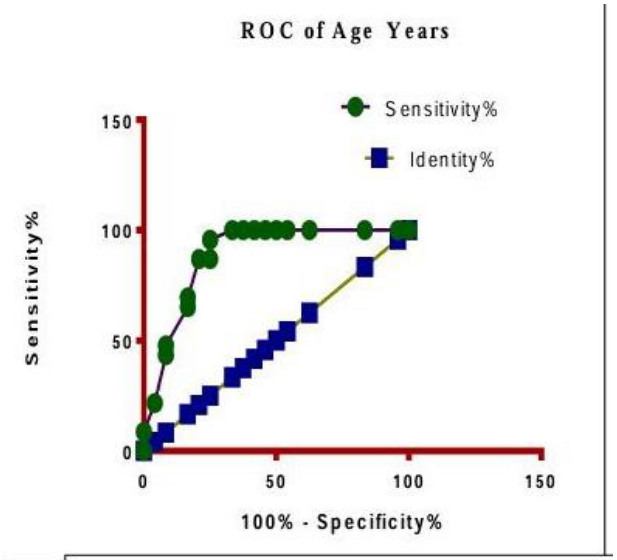

Fig.32.ROC curve displaying AUC of Age

Table 3. The area under the ROC curve for all biomarkers studied

Table 3. The area under the ROC curve for all biomarkers studied

Parameter	AUC	Std. Error	95% confidence interval	P-value
Age years	0.8841	0.05151	0.7831 to 0.985	<0.0001
BMI kg/m^2	0.5513	0.08845	0.378 to 0.7247	0.5427
FSG mg/dL	0.9983	0.002928	0.9925 to 1.004	<0.0001
HbA1c %	0.7496	0.07547	0.6016 to 0.8975	0.0031
Urea mg/dL	1	0	1 to 1	<0.0001
Creatinine mg/dL	1	0	1 to 1	<0.0001
T. proteins g/dL	0.9009	0.04338	0.8158 to 0.9859	<0.0001
Albumin g/dL	0.9574	0.0245	0.9094 to 1.005	<0.0001
Globulins g/dL	0.5217	0.08547	0.3542 to 0.6893	0.7964
ALB/GLB	0.807	0.06405	0.6814 to 0.9325	0.0003
Na Ions mmol/L	0.5287	0.08899	0.3543 to 0.7031	0.7335
K Ions mmol/L	0.593	0.08968	0.4173 to 0.7688	0.2695
Ca Ions mg/dL	0.6704	0.07901	0.5156 to 0.8253	0.0431
Uric Acid mg/dL	0.6948	0.07663	0.5446 to 0.845	0.0208
Cr Cl mL/min	1	0	1 to 1	<0.0001
IL-20 ng/mL	0.8991	0.04237	0.8161 to 0.9822	<0.0001

Discussion

The age show non-significant difference as all groups have been taken above forty years . Type 2 diabetic is characterized by systemic low-grade inflammation (5). Serum IL-20 in this study have significant difference according to p value and according to the mean it is level was lower in patients with type 2 diabetes and kidney failure than in healthy controls group . and this also was shown in many

research (10).and the opposite were high level of IL-20 have been shown in other researches (11). T2DM, also known as metabolic syndrome, is characterized by dyslipidemia, impaired glucose tolerance, and increase in blood pressure (12). It has been discovered that 70% of obese adults have at least one of the syndromes major criteria (13). Low production capacity of IL-10(i.e., a pro-inflammatory cytokine response) was found to be associated with high plasma sugar, high HbA1c, type 2 diabetes, and dyslipidemia in one study (14). This study also found that patients with T2DM who developed diabetic nephropathy had a higher BMI than the healthy control population with significant difference , as well as higher fasting blood glucose (FSG) and Glycated Hemoglobin(HBA1c) levels than the healthy controls. These finding may explained by the fact that pro-inflammatory cytokines have long been linked to the development of the metabolic change and type 2 diabetes. Human experiments have shown that pro-inflammatory cytokines cause an increase in blood glucose and insulin resistance (15,16). Pro-inflammatory cytokines, by increasing lipolysis, also contribute to dyslipidemia (17). Diabetic mellitus impairs cellular functions such as phagocytosis, chemotaxis , and pathogen killing by macrophages, monocytes, and neutrophils. When diabetic monocytes, macrophages, and neutrophils were compared to control cells, most studies found a decrease in normal cellular function as well as changes in enzyme activity and cytokine secretion (18). Long-term diabetic complications and immune compromise occur in hyperglycemic conditions(19), causing many problems in DM such as atherosclerosis, nephropathy, and neuropathy (20). This study also found that patients with Type 2 DM have higher levels of serum urea and creatinine, as well as higher levels of FSG and HBA1c when compared to a healthy control group. According to studies on circulating monocytes from hyperglycemic patients, there is a high level of CD11c expression and a lower level of CD206 expression compared to normal glycemic control monocytes. Elevated CD11c levels are associated with increased insulin resistance, obesity, triglyceridemia, and low serum IL-10 levels. In high glucose conditions, they may exhibit M1 inflammatory polarization (21). Interleukins is a cytokine, which is a type of small protein (22), and this study found a decrease in total protein and albumin in diabetic and CKD patients, which could explain why IL-20 levels were lower in these patient groups and also low protein diabetic patient indicate renal injury, this may due to change in basement membrane of renal glomeruli that will lead to leakage of albumin and some other proteins (23) . The globulin show no significant difference and this result may be due to compensatory increase in globulin due to decrease albumin in renal injury (24). The uric acid have been shown significant difference ,with higher level among patient with chronic kidney disease, this also was the result of some research (25). The endothelial dysfunction was associated with reduced eGFR that leads to the retention of substances like uric acid (26). The sodium (Na^{+2}) , potassium (K^{+2}) and calcium (Ca^{+2}) show non-significant difference .

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