Original Article

Study of Serum and Urinary Cystatin C as A Marker of Nephropathy in Type 1 Diabetic Patients.

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Abstract:

Background: Diabetic nephropathy (DN) is a significant cause of morbidity and mortality in patients with diabetes mellitus (DM). The condition is characterized by persistent albuminuria and may be decline in the glomerular filtration rate (GFR). Serum cystatin C has been proposed as a simple, accurate, and rapid endogenous marker of GFR. **Aim of the study:** To evaluate clinical usefulness of cystatin C levels of serum and urine in predicting DN in patients with type 1 diabetes and to evaluate the association between albuminuria and serum/urine cystatin C. **Subjects and Methods:** The present study included 40 male type 1 diabetic patients 10 of them was normoalbuminuric (group I), 15 patients was microalbuminuric (group II) and 15 patients macroalbuminuric (group III). In addition 10 healthy male individuals served as control group (group IV). Any patients or control with renal disease, hypertension, hepatic disease, thyroid dysfunction and on steroid therapy were excluded. All subjects underwent full history taking and complete clinical examination, and laboratory investigations in the form of urine analysis ,urinary albumin / creatinine ratio (ACR), Serum urea and creatinine, Serum albumin and total protein, Liver enzymes ALT and AST, TSH , Serum and urinary cystatin C, Fasting plasma glucose, glycated hemoglobin (HbA_{1c}), eGFR using MDRD and ultrasound examination of the abdomen and pelvis. **Results:** The cystatin C levels of serum and urine increased with increasing degree of albuminuria, reaching higher levels in macroalbuminuric patients (P <0.001). It was positive correlation between ACR and serum and cystatin C in micro and macroalbuminuric groups and it was negative correlation between serum and urinary cystatin C and eGFR in micro and macroalbuminuric groups **Conclusions:** the serum and urinary cystatin C may serve as a biomarker of diabetic nephropathy in type 1 diabetic patients.

Keywords: Cystatin C, Diabetic Nephropathy, Albuminuria.

Introduction:

The number of people with diabetes is increasing due to population growth, aging, urbanization and the increasing prevalence of obesity and physical inactivity. According to the World Health Organization (WHO), the prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030.(1) Diabetic nephropathy is one of the most important long term complications of diabetes mellitus, recognized as a major cause of the end stage renal disease (ESRD). (2) The onset and course of nephropathy can be favorably influenced by appropriate therapy such as tight glycemic control, effective antihypertensive treatment, lipid lowering strategies, and protein restriction. Such treatment can delay the appearance of microalbuminuria, proteinuria, and (ESRD).(3) General recommendation for subjects with DM is to perform kidney function as screening, in type 1 diabetic subjects five years after diagnosis and type 2 diabetes at the diagnosis.(4) One of these marker is microalbuminuria by using urinary excretion rate of albumin by 24 hr collection of urine equal (30-300mg/24hr) or a spot urine albumin to creatinine (ACR) ratio equal (30-300µg/mg). Microalbuminuria has currently emerged as sensitive indicator of early renal damage. (5) Moreover, impaired renal function may be present even in patients with normal urinary albumin excretion rate.(6) Morphological changes in DN known to start earlier than laboratory abnormality. Also some patient with macroalbuminuria have normal renal structure, while some normoalbuminuric diabetic have

well established nephropathic lesions.[7] Also albumin excretion rate is a predictor of renal disease in hypertension and cardiovascular diseases , so it is not a sensitive marker for DN.[8] Measuring glomerular filtration rate (GFR) is the best functional parameter in renal disease using creatinine clearance. This requires 24h urine collection and blood sample and measure creatinine level in blood and urine and volume of urine. There are several factors that may interfere with the accuracy of the test like incomplete collection of urine.[9] Other methods of assessment of GFR are Cockcroft-Gault formula or modified diet in renal disease formula (MDRD).[10] Gold standard procedures for glomerular filtration rate (GFR) measurement, based on the clearance of Cr^{51}- EDTA or iohexol, are impractical in clinical settings and for larger research studies.[11] Thus, we are still in need of identify more earlier marker early markers of DN needed to be identified. Cystatin C is an alternative and more sensitive marker for estimation of renal function in diabetic subjects for early detection, prevention, and treatment strategies for DN.[12] Cystatin C was first discovered in 1961, is a member of cystatin superfamily (inhibitors of cysteine proteinase). It has a molecular weight of 13,000 KD. Cystatin C is non-glycosylated basic protein, which is produced at a constant rate by all nucleated cells released into blood stream with half-life ~2hr, also present in urine, CSF, saliva, semen and colostrum.[13] The serum concentration does not depend on muscle mass, sex, age and not affected by inflammation, fever.[14]Therefore, the plasma concentration of cystatin C is almost exclusively determined by the GFR making cystatin C an excellent indicator of GFR. It also correlates with the appearance of proteinuria in diabetic subjects.[15] Only a few circumstances have been identified that have impact on the production of cystatin C, such as very large dose of glucocorticoids and thyroid dysfunction. [16]Urinary cystatin C is another marker for nephropathy. In healthy kidney is almost freely filtered by the glomerulus and reabsorbed in proximal tubule and with no tubular secretion and it is virtually absent in final urine like other low molecular weight (LMW) proteins, and only appear with tubular damage. [17] Thus, we explored the possibility of the cystatin C levels of serum and urine as markers of early renal impairment in patients with diabetes. We also evaluated the relationship of albuminuria and serum/urine cystatin C.

Subjects and Methods:

The present study included 40 male type1 diabetic patients from the diabetes and metabolism outpatient clinic of Alexandria Main university hospital. Patients were divided into 3 groups according to ACR. Group I, 10 type 1 diabetic patients with normoalbuminuria (ACR less than 30 mg/g), group II, 15 patients with microalbuminuria (ACR 30-300 mg/g) group III , 15 patients with macroalbuminuria (ACR >300mg/g) and 10 healthy male individuals as group IV.

Detailed medical history and clinical assessment were performed. After taking an informed consent from each subject. Measuring blood pressure and anthropometric data were obtained for each subject. They included weight in kilograms, height in centimeter and calculation of body mass index (BMI) (weight in kilograms/ height in meters squared). [18]

All patients with hypertension, hepatic diseases, renal disease other than DN, thyroid dysfunction and patients on steroids therapy were excluded.

Fasting blood samples were taken for measurement of FBG, HBA1c,[19] BUN, Creatinine,[20] ALT, AST,[21] total protein , serum albumin,[22] and TSH. [23]Early morning urine sample for complete urine analysis and ACR. [24]

The cystatin C levels of serum and urine were measured by the latex agglutination test (Modular P800, Roche, Diagnostics, Mannhein, Germany). [25] The eGFR level was calculated using the Modification of Diet in Renal Disease (MDRD) formula

MDRD = 186 × (serum creatinine [mg/dL])-1.154 × age-0.203. [26]

Statistical Analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. The

distributions of quantitative variables were tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk test and D'Agstino test, also Histogram and QQ plot were used for vision test. If it reveals normal data distribution, parametric tests was applied. If the data were abnormally distributed, non-parametric tests were used. For normally distributed data, comparison the studied groups were analyzed using F-test (ANOVA) and Post Hoc test (Scheffe). Correlations between two quantitative variables were assessed using Pearson coefficient. Kruskal Wallis test was used to compare between different groups and pair wise comparison was assessed using Mann-Whitney test. Significance test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

Results:

All patients and control groups were of male sex and there was statistical significance differences as regard age (P<0.001). As regard the duration of diabetes there was significance difference between diabetic groups (P<0.001) and was longer in macroalbuminuric group 11.40 ± 2.90. All patients and control groups were matched as regard BMI (P=0.807). As regard the patients glycemic control, there was no significant difference between the patients groups for there FPG (P=0.901) also HbA1c% There was no statistically significant difference between the patients groups (P=0.012).

As regard the renal functions, BUN there was statistically significant difference between the patients groups (P=0.002) and also for serum creatinine (P=0.044). For eGFR using MDRD, there was There was statistically significant difference between the patients groups (p<0.001) and was lower in the macroalbuminuric group (79.73 ± 13.39) than in microalbuminuric group (88.0 ± 14.4) and normoalbuminuric group (111.8 ± 12.4) (Table I).

Differences in the cystatin C levels of serum and urine according to albuminuria (TableII, III**):**

There was a statistically significant difference in comparing between patients groups (P<0.001) and the level of serum cystatin C showing stepwise increase with the albuminuria and there was higher in the group of macroalbuminuria (2.79 ± 0.35) than in microalbuminuric group (0.99 ± 0.26) and normoalbuminuric group (0.97 ± 0.17). As regard urinary cystatin C also there was a statistically significant difference between patient groups (P<0.001) and the level of urine cystatin C also showed higher levels in macroalbuminuric group (2.17 ± 0.50) than microalbuminuric group (0.82 ± 0.37) and normoalbuminuric group (0.09 ± 0.08).

Correlation studies:

For serum cystatin C (Table IV)

There was positive correlation between serum cystatin C with ACR only in microalbuminuric group (r=0.958, P<0.001) and in macroalbuminuric groups (r=0.818, P<0.001) (figure 1,2).

Also there was a statistically significant negative correlation between serum cystatin C and eGFR in microalbuminuric group (p=0.020, r= -0.593) and macroalbuminuric group (p=0.029, r= -0.562) (figure3,4).

In microalbuminuric group, there was a statistically significant positive correlation between serum cystatin C and ACR, s.Cr, urinary cystatin C (P<0.001, r=0.985, P=0.001, r=0.774, p<0.001, r=0.858 respectively).

In macroalbuminuric group, there was a statistically significant positive correlation between serum cystatin C and ACR, HbA1c, s.Cr and urinary cystatin c (P<0.001, r=0.818, P<0.001, r=0.823, p=0.026, r=0.572, p<0.001, r=0.922 respectively).

In all studied groups there was no statistically significant correlation between serum cystatin C with age, BMI and BUN.

For urinary cystatin C (table V)

In normoalbuminuric group

There was no statistically significant correlation between urinary cystatin C and age, BMI, ACR, HbA1c, eGFR, BUN and s.Cr (P=0.839, 0.300, 0.681, 0.640, 0.603, 0.195, 0.528 respectively).

In microalbuminuric group

There was no statistically significant correlation between urinary cystatin C and age, BMI, HbA1c, BUN (P=0.293, 0.171, 0.878, 0.380 respectively).

There was a statistically significant positive correlation between urinary cystatin C and ACR , s.Cr (P<0.001, r=0.861, p=0.002, r=0.742 respectively) (Figure 3).

There was a statistically significant negative correlation between urinary cystatin C and eGFR (P=0.037, r=0.502).

In macroalbuminuric group

There was no statistically significant correlation between urinary cystatin C and age, BMI, BUN (P=0.610, 0.784, 0.196 respectively).

There was a statistically significant positive correlation between urinary cystatin C and ACR, HbA1c, s.Cr (P<0.001, r=0.831, P<0.001, r=0.849, p=0.008, r=0.653) (figure4).

There was a statistically significant negative correlation between urinary cystatin C and eGFR (p=0.034, r= -0.562).

In the control group:

There was no statistically significant correlation between urinary cystatin C and age, BMI, ACR, HbA1c, eGFR, BUN, s.Cr (P=0.631, 0.888, 0.264, 0.867, 0.680, 0.530, 0.463 respectively).

Table I: Demographic and laboratory data in patients groups.

	Group I (n=10)	Group II (n=15)	Group III (n=15)	Test of sig.
Age(years)	20.0 ±16.70	23.73 ± 5.85	27.80 ± 5.20	$^{F}p<0.001^{*}$
ACR (mg/g)	14(165.0–21.0)	180(40.0–298.0)	10.50(5.0–21.0)	$^{KW}p<0.001^{*}$
FBS (mg/dl)	210.0 ± 182.80	187.67 ± 35.30	182.40 ± 41.92	$^{F}p=0.901$
HBA1c (%)	8.05 ± 0.49	9.27 ± 1.50	9.98 ± 1.72	$^{F}p=0.012^{*}$
e GFR	111.83 ± 12.44	88.02 ± 14.37	79.73 ± 13.39	$^{F}p<0.001^{*}$
BUN (mg/dl)	18.86 + 2.82	27.32 ± 7.46	22.0 ± 5.01	$^{F}p=0.002^{*}$
Serum creatinine (mg/dl)	0.87 ± 0.16	1.14 ± 0.25	1.01 ± 0.28	$^{F}p=0.044^{*}$
Serum cystatin C (mg/dl)	0.97 ± 0.17	0.99 ± 0.26	2.79 ± 0.35	$^{F}p<0.001^{*}$
Urine cystatin C (mg/dl)	0.08 (0.01–0.31)	0.88 (0.33–1.47)	2.29 (1.19–2.73)	$^{KW}p<0.001^{*}$

Group I : Normo albuminemic **Group II:** Microalbuminemic **Group III:** Macroalbuminemic

Table II: Comparison between the studied groups according serum cystatin C (mg/L):

	Group I (n=10)	Group II (n=15)	Group III (n=15)	Group IV (n=10)	p
Serum cystatin C (mg/L)					
Min. – Max.	0.65 – 1.17	0.66 -1.43	2.04 – 3.23	0.51 – 0.90	
Mean ± SD.	0.97 ± 0.17	0.99 ± 0.26	2.79 ± 0.35	0.66 ± 0.14	<0.001*
Median	0.98	1.05	2.85	0.66	
p_1	0.093	0.034*	<0.001*		
p_2	<0.001*	<0.001*			
p_3	0.997				

Group I: Normo albuminemic **Group II:** Micro albuminemic **Group III:** Macro albuminemic **Group IV:** Control

p: p value for Kruskal Wallis test for comparing between the different studied groups

p_1 : p value for Mann Whitney test for comparing between group IV and each other groups

p_2 : p value for Mann Whitney test for comparing between group III and each other groups

p_2 : p value for Mann Whitney test for comparing between group II and group I

*: Statistically significant at p ≤ 0.05

Table III: Comparison between the studied groups according to urinary cystatin C:

	Group I (n=10)	Group II (n=15)	Group III (n=15)	Control (n=10)	p
Urine cystatin C (mg/dl)					
Min. – Max.	0.01 – 0.31	0.33 – 1.47	1.19 – 2.73	0.01 – 0.09	
Mean ± SD.	0.09 ± 0.08	0.82 ± 0.37	2.17 ± 0.50	0.05 ± 0.03	<0.001*
Median	0.08	0.88	2.29	0.5	
p_1	0.068	<0.001*	<0.001*		
p_2	<0.001*	<0.001*			
p_3	<0.001*				

Table (IV): Correlation between Serum cystatin C with age, ACR, BMI, HbA1C, eGFR, BUN and serum creatinine

	Group I (n=10)		Group II (n=15)		Group III (n=15)		Group IV (n=10)	
	r	p	r	p	r	p	r	P
Age	0.340	0.336	0.527	0.063	0.238	0.394	0.160	0.658
BMI	0.345	0.328	0.612	0.150	-0.299	0.278	0.240	0.505
ACR	0.125	0.731	0.958*	<0.001	0.818*	<0.001	0.505	0.136
HbA 1C	-0.004	0.992	0.181	0.520	0.823*	<0.001	0.101	0.979
eGFR	0.156	0.666	-0.593*	0.020	0.562*	0.029	-0.639	0.547
BUN	0.378	0.281	0.333	0.225	0.365	0.181	0.241	0.503
Serum Creatinine	-0.125	0.730	0.774*	0.001	0.572*	0.026	0.546	0.103
Urinary cystatin C	-0.550	0.099	0.858*	<0.001	0.922*	<0.001	0.159	0.662

r: Pearson coefficient
***:** Statistically significant at $p \leq 0.05$

Table (V): Correlation between urinary cystatin C with age, ACR, BMI, HbA1C, eGFR, BUN and serum creatinine

	Group I (n=10)		Group II (n=15)		Group III (n=15)		Group IV (n=10)	
	r	p	r	p	r	p	r	P
Age	0.074	0.839	0.291	0.293	0.143	0.610	-0.174	0.631
ACR	-0.149	0.681	0.861*	<0.001	0.831*	<0.001	-0.391	0.264
BMI	-0.365	0.300	0.373	0.171	-0.078	0.784	0.051	0.888
HbA 1C	0.169	0.640	0.043	0.878	0.849*	<0.001	0.061	0.867
eGFR	-0.188	0.603	-0.502*	0.037	-0.549*	0.034	0.150	0.680
BUN	-0.447	0.195	0.539	0.380	0.354	0.196	0.625	0.530
Serum Creatinine	0.227	0.528	0.742*	0.002	0.653*	0.008	-0.263	0.463

r: Pearson coefficient
***:** Statistically significant at $p \leq 0.05$

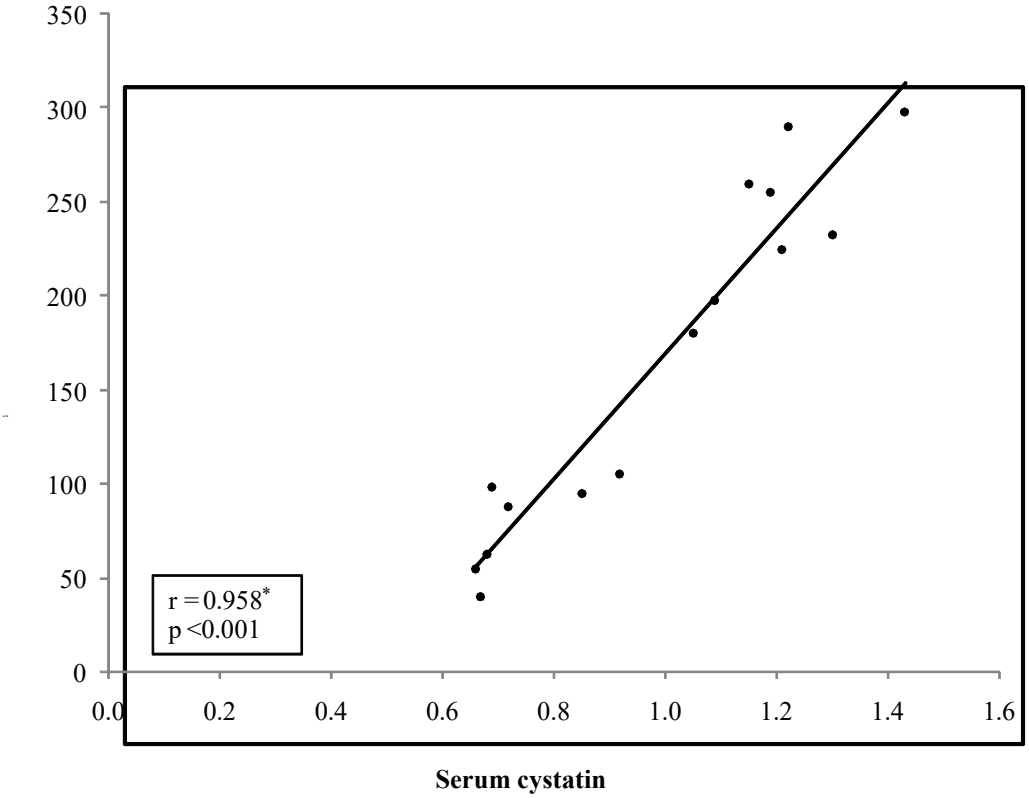

Figure 1: Correlation between Serum cystatin with ACR in group II

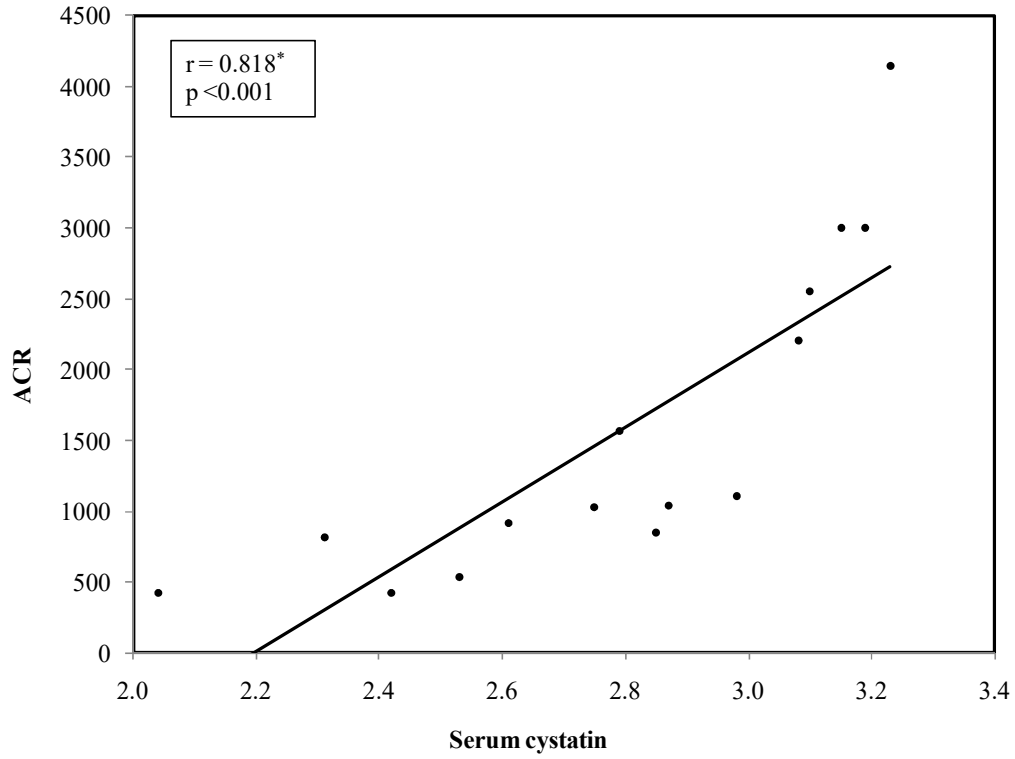

Figure 2: Correlation between urine cystatin with ACR in Group III

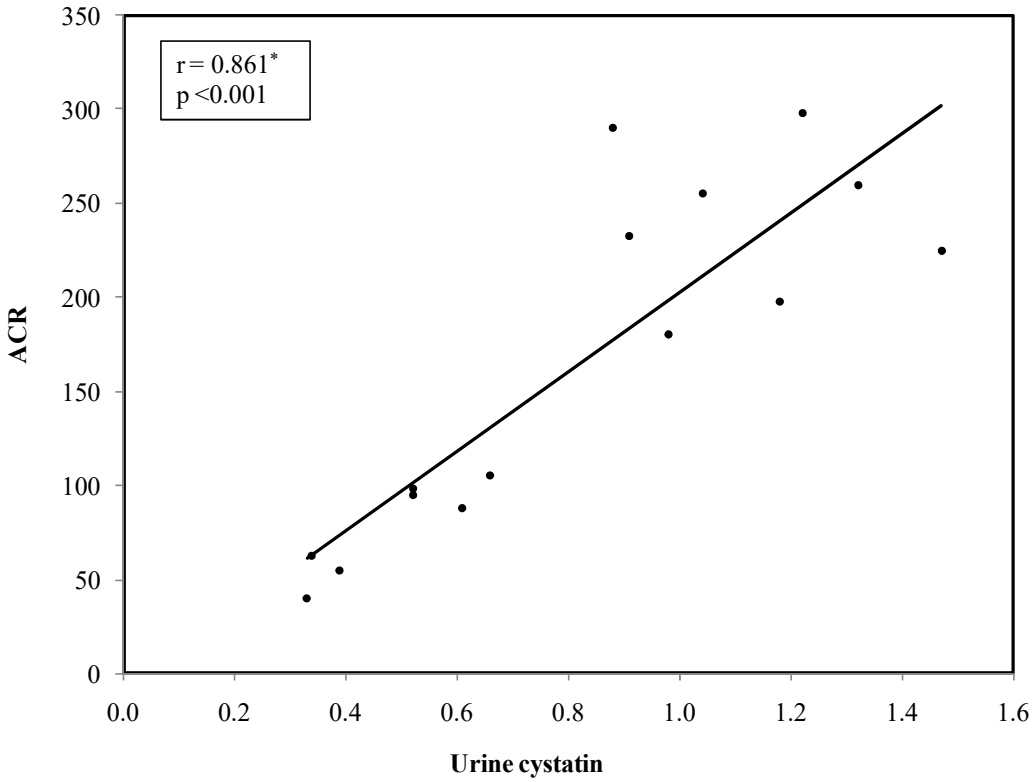

Figure (3): Correlation between urine cystatin with ACR in group II

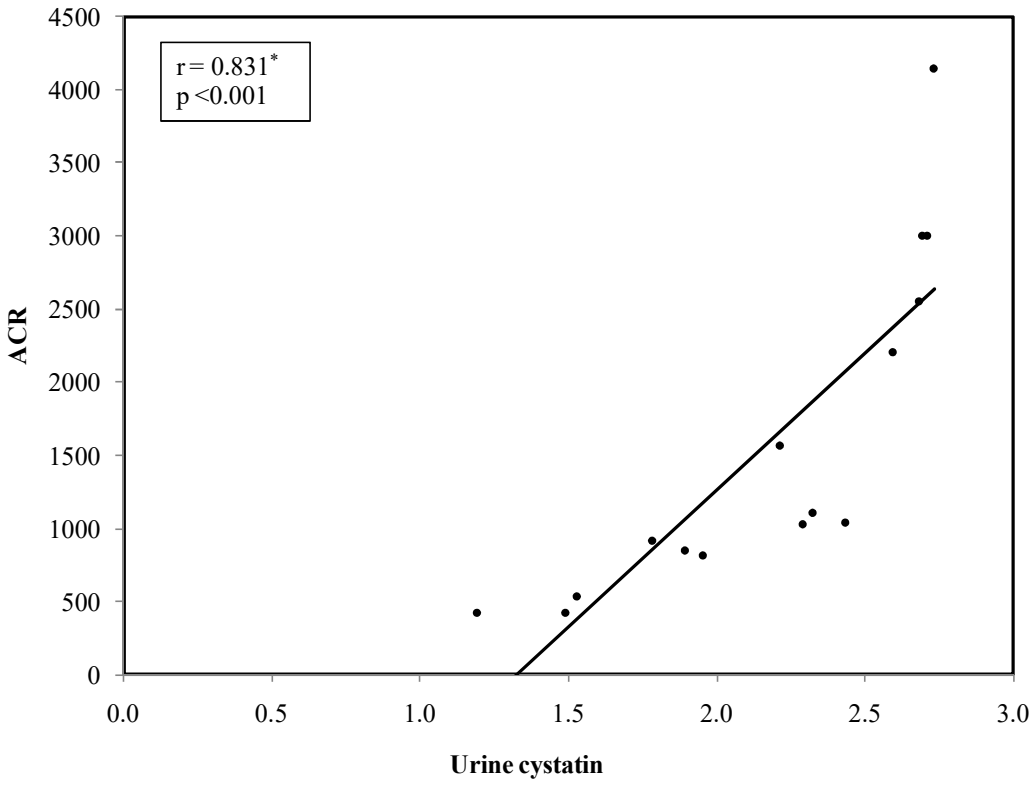

Figure 4 : Correlation between uArine cystatin with ACR in group group III

Discussion:

Data presented in our study dealt with 40 type 1 diabetic patients as cases and 10 healthy individual as controls. There was statistical significant difference between the patients groups and the control groups regarding to age (P < 0.001). The groups of micro and macroalbuminuria were older than the others groups their mean age were (23.7 ± 5.9 and of 27.8 ± 5.2 years respectively). Also the diabetes duration was longer in micro and macroalbuminuric groups (mean 8.53 ± 3.54 years and 11.40 ± 2.90 respectively) than in normoalbuminuric groups (mean 3.69± 1.90 years). This data was confirmed by the fact that DKD takes years to develop in type 1 diabetic patients. It is rare to see DN earlier than 3 years after the diagnosis of diabetes; it is usually seen after 5 to 15 years in patients with type 1 diabetes. (27)

In our study, there was no significant correlation between serum, urinary cystatin C and the age in the control group and the patients groups. This data matched with Filler et al (28) who found that measuring of cystatin C not affected by the age. Also Uchida K et al(29) found that measuring of urinary cystatin C was not affected by the age. In contrast, Christensson et al (30) reported that there was significant positive correlation noticed between serum cystatin C and age.

In our study all patients and healthy controls were of male sex. Regarding to measuring cystatin C, there was conflicting evidence regarding whether cystatin C levels vary by gender or not. Some authors like Croda-Todd et al (31) and Finney H et al (32) found that there was statistically significant differences as regarding measuring cystatin C in adults males and females and was higher in male gender than female. In contrast, Erlandsen JE et al (33) and Uhlmann EJ et al (34) reported that there was no significant difference as regarding measuring cystatin C in both gender.

Regarding BMI, in our study, there was no statistically significant difference between the patients groups and the control group (P=0.807) and there was no statistical significance correlation between serum and urinary cystatin C with BMI. The same result was reported by Galteau et al (35) who have reported a moderate but biologically insignificant correlation between BMI and cystatin C. In contrast, Al Wakeel JS et al (36) and Muntner P et al (37) have reported a significant correlation between serum cystatin C and BMI.

Regarding HbA1c, in our study, there was a statistically significance difference between the patients groups regarding HbA1c (P=0.012) and the mean levels were higher in macroalbuminuric group (mean=9.98± 1.72). There was positive significance correlation between ACR and HbA1c in the macroalbuminuric groups (P=0.002).

In our study there was statistically significance positive correlation between serum and urinary cystatin C with HbA1c only in macroalbuminuric group (P <0.001). The same result was reported by Jeon YK, et al. (17) as cystatin C as a marker of DN is also related to increase level of HbA1c and poor glycemic control. In contrast, Tian et al(38) observed there was non-significant correlation between cystatin C and glucose level indicating that serum cystatin C levels are independent of blood glucose level.

In our study, there was no significance correlation between BUN and serum and urinary cystatin C but there was statistical significance positive correlation between serum Creatinine and serum and urinary cystatin C in the groups of micro and macroalbuminuric groups. The same result was reported by Tian et al(38) there was significant positive correlation between serum cystatin C and each of serum creatinine suggesting that serum cystatin C increased similar to serum creatinine for measuring renal function in diabetic patients.

In our study, there was a significant negative correlation between eGFR with serum cystatin C only in the microalbuminuric (P=0.020) and macroalbuminuric groups (P=0.029) not with normoalbuminuric group (P=0.666). As cystatin C is produced at a constant rate by nucleated cells and released into the blood stream with a half-life of ~2 h and is freely filtered and almost completely taken up and degraded, but not secreted, by proximal tubular cells, so with the occurrence of pathological changes in diabetic

kidney the filtration capacity is decreased with subsequent retention of cystatin C and increased serum level.

Some previous studies on the role of cystatin C in detecting early renal failure in diabetic patients were contradictory. Some authors showed that cystatin C was more effective than creatinine in detecting initial reduction of GFR in T2DM as well as in T1DM. Mussap et al[39], Xia et al[40], and Harmoinen et al[41] showed that serum cystatin C was more sensitive than serum creatinine for estimation of GFR in T2DM patients and Tan et al[42] showed the same in T1DM patients. In contrast to these result, Oddoze et al [43] found that serum creatinine was better than serum cystatin C for the estimation of GFR in microalbuminuric and proteinuric diabetic patients. Oddoze et al selected a heterogeneous group of type 1 and type 2 diabetic patients.

In our study, there was no correlation between urinary cystatin C and eGFR in normoalbuminuric (P=0.603) group but there was negative significance correlation between urinary cystatin C and eGFR in microalbuminuric (P=0.037) and macroalbuminuric (P=0.034) groups.

Sang Soo et al[44] reported that urinary cystatin C was not associated with a decline in eGFR in normoalbuminuric patients. It is necessary to assess tubular damage independent of albuminuria in patients with early development and progression of DN because tubular damage may play a significant role in the normoalbuminuric renal insufficiency. Stefan et al [45] reported that increased urinary cystatin C reflects structural and functional renal tubular impairment independent of GFR.

The mean value of the cystatin C was significantly higher in the macroalbuminuric group compared to normoalbuminuric group, and it also significantly higher in the macroalbuminuric(P<0.001) group compared to microalbuminuric (P<0.001) group, In agreement with these results, Mojiminiyi et al [46] found that cystatin C was significantly higher in patients with DN than in normoalbuminuric diabetic patients, which can be explained in that there is already impaired renal function in DN patients. In addition, Yang et al[47] reported that serum cystatin C concentration increased significantly in patients from normo- to macro- and micro- to macroalbuminuria.

In our study, there was strong positive correlation between serum cystatin C and ACR only in the microalbuminuric group (P<0.001) and macroalbuminuric group (P<0.001) and there was no correlation in the normoalbuminuric group (P=0.731).

The strong correlation between serum cystatin C in the micro and macroalbuminuric groups may be due to decrease eGFR in these groups in comparing to normoalbuminuric group.

In contrast to our study Jeon YK et al[17] found that in normoalbuminuric patients, the cystatin C levels of serum and urine were significantly increased in patients with GFR ≤ 60 mL/min/1.73 m2 than those with GFR > 60 mL/min/1.73 m2. It was thought that this increment was probably due to the tubular phase before glomerular manifestation. He suggested that the cystatin C levels of serum and urine are related to subclinical tubular impairment and can be an earlier measurable markers of renal involvement before onset of albuminuria.

The level of urinary cystatin C was higher in groups of microalbuminuric (P <0.001) macroalbuminuric group (P<0.001) in comparing to normaalbuminuric group and control group. There was strong positive correlation between the urinary cystatin C and ACR in microalbuminuric group (P <0.001) and macroalbuminuric group (P<0.001) and there was no correlation in the normoalbuminuric group (P=0.681).

From these result, urinary cystatin c can use parallel to microalbuminuria to diagnosis of DN and for follow up the progression of the disease. The same result was reported by Kim SS et al [48] who reported that several tubular markers as urinary cystatin C increase more in diabetic patients thanin healthy controls, and this correlated with the severity of albuminuria. Also Sang SK et al[44] reported that urinary cystatin C mainly increased in the macroalbuminuria group

and was not significantly different between the microalbuminuria and normoalbuminuria groups.

In our study, there was no correlation between serum and urinary cystatin C in control group but there was a statistically positive correlation between serum and urinary cystatin C in the micro and macroalbuminuric groups. As in the micro and macralbuminuric group the eGFR were relative lower than the others group so the serum cystatin C increased and also urinary cystatin C secondary to decrease the reabsorption capacity of renal tubules. The same result reported by Jeon YK, et al. [17] In contrast to our result, Sang SK et al [44] reported that urinary cystatin C was a predictor of renal impairment independent of serum cystatin C. Although serum cystatin C itself, an indicator for the eGFR, is very important for predicting renal dysfunction.

Conclusion:

The present study supports the importance of cystatin C measuring in serum and urine as a marker of diabetic nephropathy and its correlation with albuminuria in type 1 diabetic patients.

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