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CYSTATIN C IN DIABETIC PATIENTS

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ABSTRACT

Early identification of renal function impairment is crucial in diabetic patients. Clinically, serum cystatinc may be the most sensitive indicator of the glomerular filtration rate. The aim of this study wasto propose the use of cystatinc test to evaluate kidney function in type 2 diabetic patients. The study was done on 60 patients with type 2 diabetic and 20 healthy subjects, serum level of glucose ,total protein ,urea ,creatinine and cystatinc were measured and studied. The estimating glomerular filtration rate (eGFR) was estimated by using Hoek formula.The statistical results of biochemical tests showed high significant differences (P< 0.005) in mean serum levels of glucose, urea, creatinine, cystatinc and insignificant changes (P > 0.05) in mean serum levels of total protein for diabetic patients as compared with control mean. However, high significant negative correlation was appeared between eGFR values and serum levels of creatinine for both groups.Cystatin C-based GFR estimates showed high correlation to serum creatinine levels. Thus, we recommend cystatin C for GFR estimation in diabetic patients.

Keywords: Cystatin C. Creatinine. Type 2 Diabetes Mellitus. Glomerular filtration rate.

1. INTRODUCTION

The glomerular filtration rate (GFR) is essential for theclinical assessment of renal function. An optimal GFR biomarker should be constantly produced at the same level, independent of age, body or muscle mass, and exclusively eliminated by glomerular filtration without tubular secretion orreabsorption[9]. The urinary clearance of exogenous substances,such as ^{51}Cr-EDTA and inulin, are accepted as gold standards for GFR assessment. However, because of costs and inconvenience, plasma creatinine, creatinine clearance and creatinine-based estimation formulas are most commonlyused to measure renal function[1].

Creatinine is of limited value in early renal insufficiency since plasma levels only rise if the GFR decreases below 60mL/min/1.73 m². As it is generated by muscle metabolism,plasma levels are dependent on muscle mass, age, and gender. In addition, creatinine undergoes tubular secretion whichvaries with renal function[2].

Cystatin C, an endogenous 13 kDa protein of the cystatinsuperfamily of cysteine proteinase inhibitors, is expressed ata constant rate in all nucleated cells. It is freely filtered in theglomeruli without significant tubular secretion. Thus, plasmalevels should be unaffected by muscle mass, age, race, or gender [10].

1.1 Patients and Methods

Sixty patients,(32 females ,28 males) their ages ranging from (40-65) year, with type 2 diabetic and 20 control subject (9 females, 11 males) aged (40-60) year recruited from Al-yarmouk hospital. Diagnoses are made based on clinical symptoms and biochemical tests. Patients with liver disease, renal failure, heart failure and patients on high dose steroid treatment(effect on cystatin c level) were excluded from the study.

Blood samples are aspirated to measure serum levelsof glucose,creatinine,urea,total Proteinsby Photometric Colorimetric Test and serum levels of cystatinc (Cys C) that assayed by the quantitative sandwich enzyme immunoassay technique (ELISA).

The estimating glomerular filtration rate (eGFR) was estimated by using Hoek formula[3]:eGFR (ml /min/ 1.73 m^2) = [80.35/S.Cystatin C (mg/L)] – 4.32

All blood samples were obtained after receiving patients' informed consent and followeda standardized protocolthat approved by the institutional ethics committee of each study site. Results are shown as mean ± SD with 95% confidence interval (CI), and *P* values of 0 < 0.05 were regarded to be statistical significant. All statistical analyses were performed using SPSS version 16.

1.1.1 RESULT

The Results of biochemical tests tended to show high significant differences (P< 0.005) in mean serum levels of glucose, urea, creatinine, cystatin c for diabetic patients compared with control mean. Whereas insignificant changes (P > 0.05) were appeared in mean serum levels of total protein for diabetic patients as compared with control mean (Table 1; Figure 1 and 2).

Moreover, there were high significant negative correlation between eGFR values and serum levels of creatinine for control group (r= -

0.7464, *P <0.001*), and for diabetic group (r= -0.826, *P <0.001*), (Figure 3 and 4 respectively).

1.1.2 DISCUSSION

The GFR is accepted as the best overall index of renalfunction. The current guidelines emphasize the need toassess kidney function using predictive serum creatinine-based equations rather than just serum creatinine[4]. For clinicians, a GFR below 60ml/min/1.73 m^{2}is very important because such valuesindicate the presence of renal insufficiency and represent an increasedrisk of cardiovascular events and mortality in these patients[5]. However, the use of serum creatinine and serum creatinine-based equations has some limitations, and the development of new markers for more accurateevaluation of renal function was essential. In recent years,serum cystatin C was proposed as a new endogenousmarker of GFR, and various serum cystatin C-basedequations were developed[6]. In the study of Larsson et al., two different serum cystatinc formulas were developed and compared with iohexol clearance as the reference GFR method. In a study of 100 adult patients with different renaldiseases was concluded by the authors that cystatinc formulas presented reliable GFR data based on a single measurement of serum cystatinc concentrations[7].

Bland and Altman analysis showed that the simple formula {GFR = -4.32 + 80.35 x 1/serum cystatinC(mg/L)}, gave more accurate and more precise GFR estimates than obtained with the Cockcroft and Gault formula. The day-to-day variation (biological and analytical) for cystatinc was small in diabetic patients[3].

The serum concentrations of creatinine and cystatinc are namely inversely related to their clearances. Therefore, the reciprocals of creatinine and cystatinc can be usedfor the calculation of the GFR[8].

In our study, we compared serum cystatinc

-based equation to serum creatinine levels in patients with type 2 diabetic. The results of our study indicate that cystatinc formula is a reliable marker of GFR inthese patients.

1.1.3 CONCLUSION
The serum cystatinc -based equation which requires just one variable (serum cystatinc concentration) could beused for evaluation of renal function in patients withtype 2 diabetic.

Table 1: Clinical and biochemical characteristics of the studied groups

|	Control	Diabetic Group
-Number	20	60
-Female	9	32
-Male	11	28
-Age range (year)	(40-60)	(40 - 65)
Mean ± SD //		
-Age (year)	50± 7	55 ±10
-Glucose (mg/dl)	96.4 ±5	143.6 ±10 **
-Urea (mg/dl)	31.2 ±7.8	38.5 ±8.45**
-Total protein (g/dl)	7.06 ±0.55	7.2 ±1.06
-Creatinine (mg/dl)	0.98 ±0.15	1.24 ±0.23 **
-Cystatin C (mg/L)	0.75 ±0.2	0.97 ±0.22 **
-eGFR (ml/min/1.732m^2)	98.7 ±19.5	85.3 ±20.07 **

(**) high significant differences ($P< 0.005$)
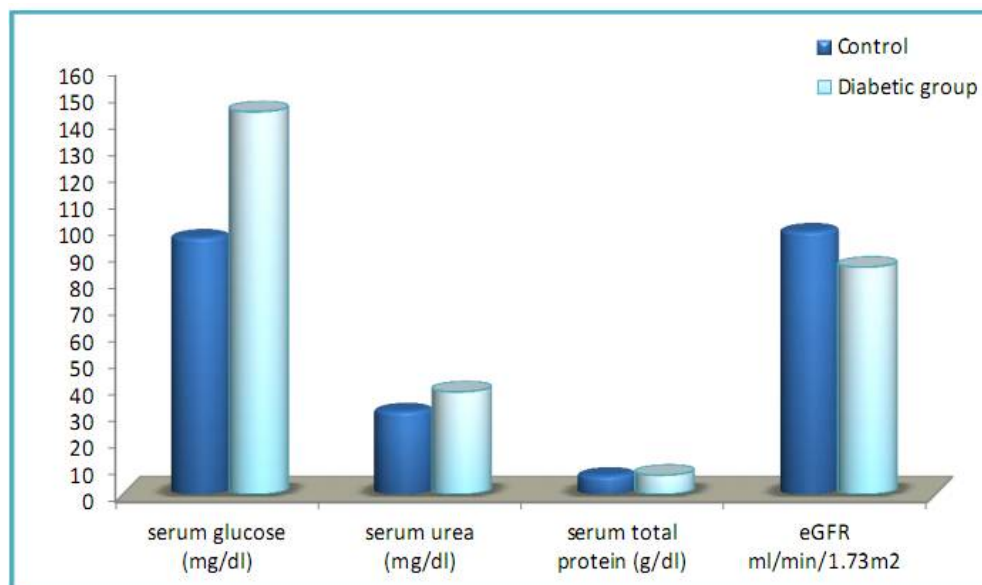
Fig. 1: The mean serum levels of glucose (mg/dl), urea (mg/dl), total protein (g/dl) and eGFR (ml/min/1.73 m^2) for control and diabetic patients.
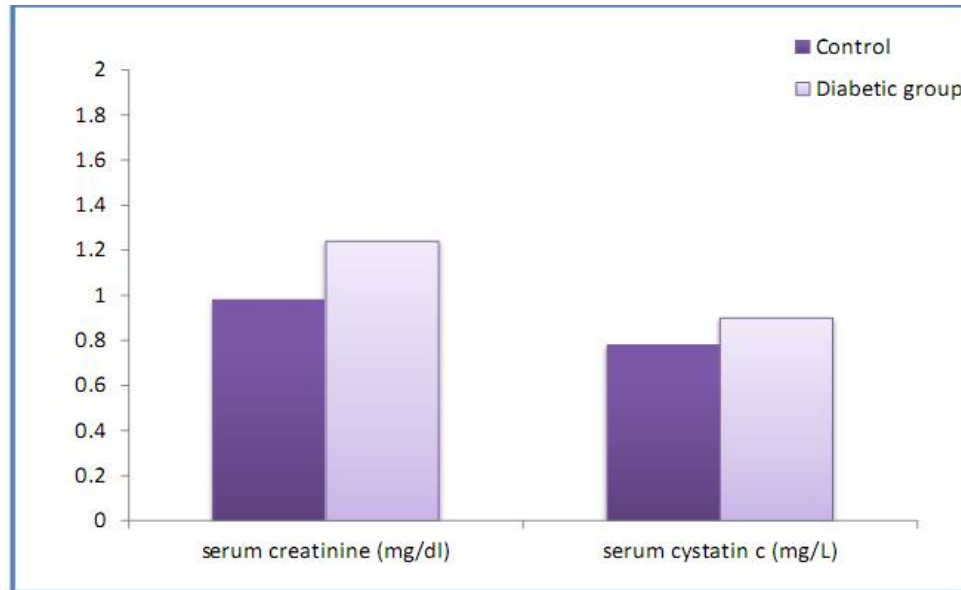
Fig. 2: The mean serum levels of creatinine (mg/dl) and cystatin c (mg/L) for control and diabetic patients.

$$y = -0.0042x + 1.3007$$
$$R^2 = 0.5571$$
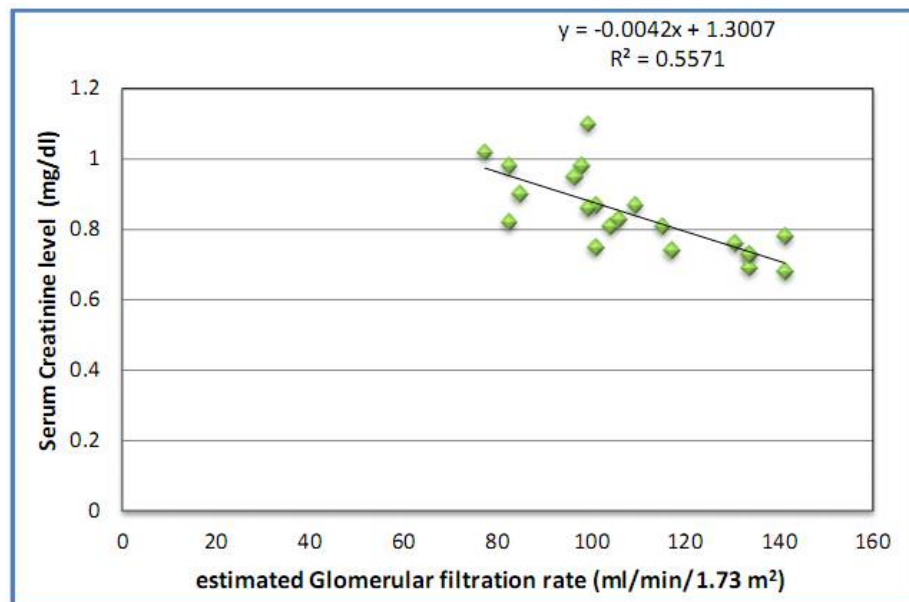
Fig. 3: The correlation coefficient (r) between estimated glomerular filtration rate values (ml/min/1.73 m^2) and serum creatinine levels (mg/dl) for control group.
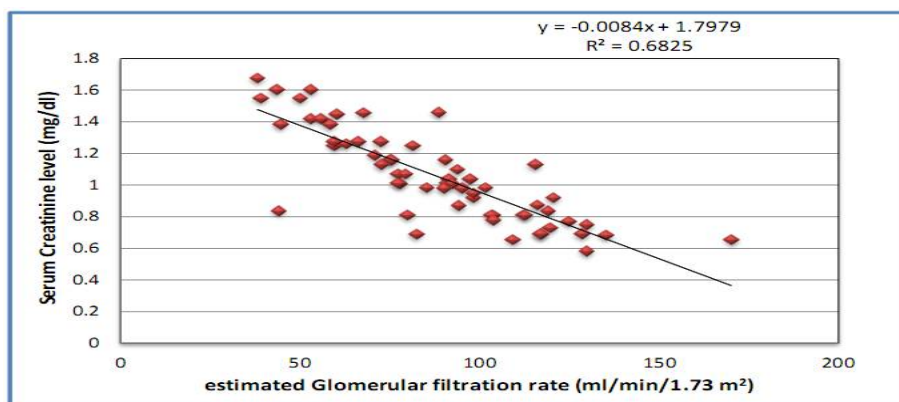
Fig. 4: The correlation coefficient (r) between estimated glomerular filtration rate values (ml/min/1.73 m^2) and serum creatinine levels (mg/dl) for Diabetic patients.

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