Pre -diagnosis of Renal Failure in patients with Diabetes Mellitus

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Abstract

Background: Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Diabetes is the leading cause of kidney disease. About 1 out of 4 adults with diabetes has kidney disease.

Methods: Five ml venous blood sample were withdrawn from every subject by aseptic venipuncture from an anticubital vein in a fasting state. The blood was left to clot in plain polypropylene tube at 25oC for 30 min, centrifuged and the separated serum was divided into 2 tubes. This assay is based on the quantitative sandwich enzyme immunoassay technique (ELISA technique).

Results: The present study demonstrated that serum fasting and postprandial blood glucose levels were statistically significantly higher in diabetes with renal insufficiency compared to diabetic or control groups. serum cystatin C showed much more significance than creatininein detection reduced GFR in diabetic patients.

Conclusions: Cystatin C may be useful for early detection of renal insufficiency in a variety of renal disease for which early treatment is critical. So cystatin C might be superior indicator of GFR compared to creatinine in diabetic patient.

Keywords: Renal Failure; Diabetes Mellitus; cystatin C; glomerular filtration rate.

Introduction: Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both [1]. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels [2].

Diabetes mellitus is one of the most common chronic diseases in human populations across the globe, with a current prevalence of 6.7%, representing about 285 million adults in 2016. Moreover, the prevalence of diabetes continues to rise in both the Western world and in the developing countries as changing lifestyles lead to reduced physical activity, and increased obesity. Thus, predictions for the next 20 years show that diabetes will become epidemic, reaching a prevalence of 8.7% (about 439 million adults throughout the world) by 2030[3].

In the past years, the number of people with diabetes is increasing due to population growth, aging, urbanization and the increasing prevalence of obesity and physical in activity, according to the World Health Organization (WHO) [4]. Diabetes is the leading cause of kidney disease. About 1 out of 4 adults with diabetes has kidney disease [5].

Epidemiological studies report that there has been a 40% increase in the prevalence of chronic kidney disease (CKD) in recent years with a- corresponding doubling of the incidence of end stage renal disease [6]. Topreventthis increase, screening for chronic kidney disease and early intervention are necessary [7]. Glomerular Filtration Rate; is the best global index of renal function [8]. To evaluate glomerular filtration rate (GFR) in patients with kidney renal failure serum creatinine (Scr) is frequently used but the low precision and sensitivity of serum creatinine (Scr) and the influence of muscle mass, age and gender on its relationship with glomerular filtration rate,leading to search for new marker [9].

Cystatin C was used as an alternative and more sensitive endogenous marker for the estimation of glomerular filtration rate (eGFR) than serum creatinine [10].

We aim To evaluate the role of serum cystatin C as early marker for detection of renal disease in diabetic patients.

Serum Samples of patients: Five ml venous blood sample were withdrawn from every subject by aseptic venipuncture from an anticubital vein in a fasting state. The blood was left to clot in plain polypropylene tube at 25oC for 30 min, centrifuged and the separated serum was divided into 2 tubes: The first tube was used for the assay of serum glucose level, kidney function tests including serum creatinine and urea using automatic auto analyzer. The second tube was stored at -70oC for the assay of cystatin C. The retrospective analysis covered the period between November 2012 and October 2017 within the laboratories of Mansoura University hospital.

Subjects: The present studycomprised80 subjects;25patientswith acute diabetic complication(renal insufficiency) (15 male and 10 female)and25patients without diabetic complication(13 male and 12 female) .In addition, 30 healthy individual (19 male and 11 female) with age ranging from 25 to 65 years were served as a control group. The patients were selected from Internal and External Medicine Center, Mansoura University. They were classified into the following groups: Group A (patients with diabetes suffering from renal insufficiency). This group included 25 patients. Group B (Patients with diabetes mellitus), this group included 25 patients.

Statistical analysis of the data: 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. Significance of the obtained results was judged at the 5% level. F-test (ANOVA)For normally quantitative variables, to compare between more than two studied groups, and Post Hoc test (LSD) for pair wise comparisons . Kotz S, Balakrishnan N, Read CB, Vidakovic B. Encyclopedia of statistical sciences. 2nd ed. Hoboken, N.J.: Wiley-Interscience; 2006. Kirkpatrick LA, Feeney BC. A simple guide to IBM SPSS statistics for version 20.0. Student ed. Belmont, Calif.: Wadsworth, Cengage Learning; 2013.

Results:

Table (1): Shows that cystatin C has a higher sensitivity, specificity and accuracy than creatinine in studied diabetic subjects. **Fig** (1):The ROC (Receiver Operator Characteristic)Curve plots to assess the diagnostic efficiency of serumCystatin C & serum Creatinine estimated GFR. **Table (2):** Shows that cystatinC has a more significant positive correlation(r=0.719, P <0.001 for cystatin C and r =0.63, P <0.001

for creatinine) in diabetic group and indiabetic with renal insufficiency (r=0. 872, P <0.001 for cystatin C and r =0.75, P <0.001 for creatinine). **Figure (2):** Correlations between eGFR and reciprocal of serum cystatin C, reciprocal of serum creatinine in diabetic group.

Table (1) : Sensitivity, specificity, and accuracy of cystatin C and serum creatinine in studied subjects.

	Serum cystatin C (mg/dl)	**Serum creatinine (mg/dl)**
Sensitivity	94.4 %	88.3 %
Specificity	85.6%	80.4 %
Accuracy	91.5 %	85.7 %

Figure (13): Non parametric ROC plots of cystain C and creatinine

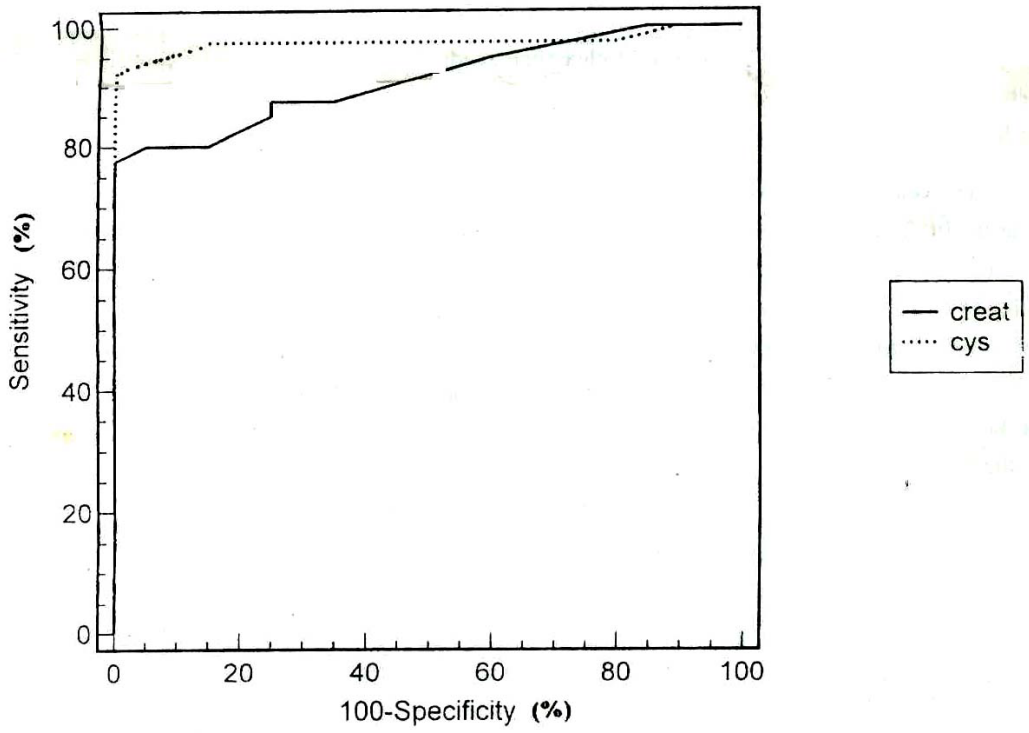
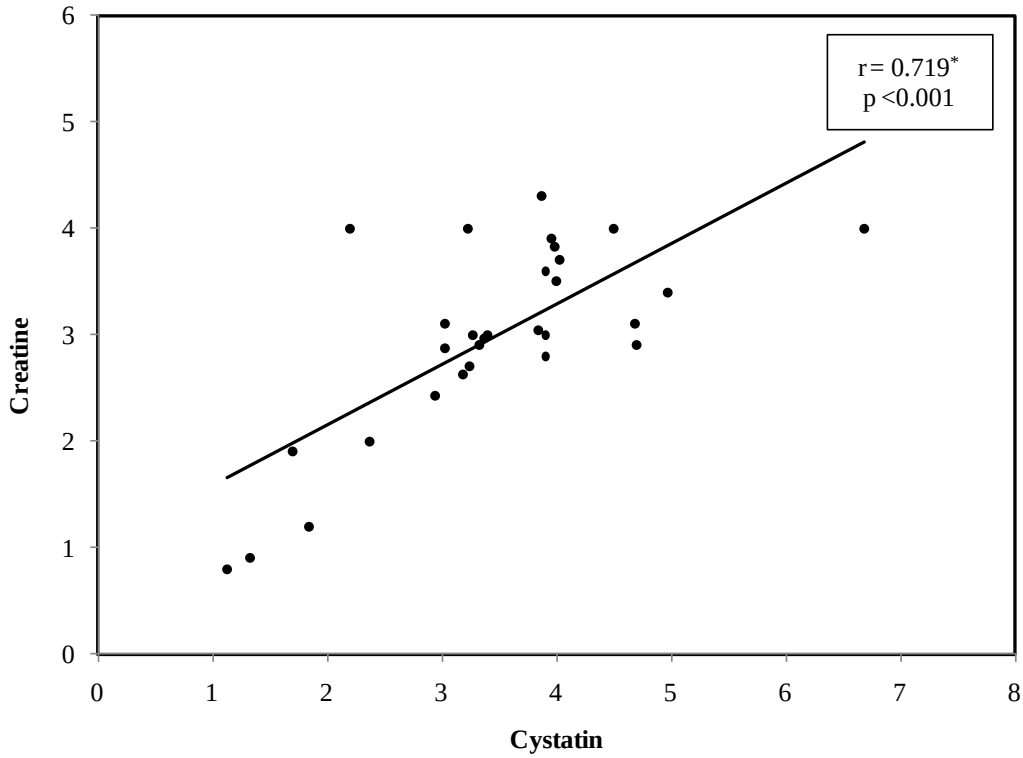


Table (10): Correlations betweeneGFRcystatin C andeGFRcreatinine in diabetic and diabetic group with renal insufficiency.

Groups	**Serum creatinine (mg/dl)**	**Serum cystatin C (mg/l)**
Diabetic group R	0.629	0.719
P	< 0.001*	<0.001*
Diabetes mellitus with renal insufficiency	**Serum creatinine (mg/dl)**	**Serum cystatin C (mg/l)**
R	0.754	0.872
P	<0.001	<0.001

Figure (14): Correlations between eGFR and reciprocal of serum cystatin C, reciprocal of serum creatinine in diabetic group.



Discussion Diabetes is the leading cause of kidney disease. About 1 out of 4 adults with diabetes has kidney disease [5]. GFR is considered the most accurate measurement of kidney disease and is reduced before the onset of clinical symptoms; it is measured or predicted using different methods [11]. There is no simple and practical way to measure GFR directly. To estimate the GFR, an endogenous substance in the blood that is cleared by the kidney is used; this substance is currently serum creatinine [12]. The Cockcroft-Gault and Modification of Diet in Renal Disease Study equations are serum creatinine-based equations that are used to estimate GFR [13]. GFR determinations using creatinine-based equations are not precise; hence, other substances, such as cystatin C, are being explored to estimate GFR [14].

The primary limitation of using creatinine level is that the level is determined not only by GFR but also by muscle mass and dietary intake. Lower serum creatinine levels may less reliably detect impaired GFR in patients with certain characteristics like older age, female sex, chronic illness with muscle wasting, amputation, or a vegetarian diet higher serum creatinine levels are associated with, muscular body habitus, and high protein diet [15]. Although estimating equations attempt to adjust for these factors, the result is not precise [16]. Several new biochemical markers have the potential to be markers of chronic kidney disease progression. These new markers might reflect the early diminished GFR compared with traditional markers; these include the following: N-acetyl-β-glucosaminidase, neutrophil gelatinase, fatty acid binding protein, and cystatin C [17].

Cystatin C is produced at a constant rate by all nucleated cells. Because of its small size, it is freely filtered by the glomerulus and is not secreted but is fully reabsorbed and broken down by the renal tubules [18]. In the present study the correlation of eGFR cystatin C was stronger than the correlation with eGFR creatinine and creatinine clerance in diabetes mellitus and renal insufficiency with diabetes. These results confirm those reported by Rao [19] and also observed in our study, the correlations between eGFR and creatinine or cystatin C were higher in patients with decreased than in those with normal GFR. These results agreed with Shelkh [20] who found that the regressions with GFR were superimposable in the subgroup with reduced GFR, whereas in patients with normal renal function the relationship between cystatin C and GFR was stronger than between GFR and the other variables. This

different behavior is due not only to the wider range of GFR values of patients with reduced renal function but also to the role played by different pathophysiological factors. Also this result agreed with Herget [21] who reported that serum cystatin C levels started to increase when GFR was 88 ml/min/1.73 2m, while serum creatinine level began to increase when GFR was 75ml/min 1.73 2m. These data indicate that serum cystatin C may detect mild reduction in GFR than serum creatinine

In summary, Cystatin C may be useful for early detection of renal insufficiency in a variety of renal disease for which early treatment is critical**.** So cystatin C might be superior indicator of GFR compared to creatinine in diabetic patient.

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Abbreviations

(DM) Diabetes mellitus, **(CKD)** chronic kidney disease, **(GFR)** glomerular filtration rate, **(Scr)** serum creatinine, **(eGFR)** estimation of glomerular filtration rate.

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