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Original Research Article

Correlation between Serum Cystatin C and Creatinine in Apparently Healthy Subjects

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ABSTRACT

Glomerular filtration rate is typically the best indicator for the assessment of kidney function in both healthy and diseased patients. The various methods are used for the estimation of GFR like exogenous substances such as inulin, iohexol, 51 Cr EDTA or 125 I-labeled iothalamate, 24 hours creatinine clearance, 99mTc-DTPA renography. But the inulin clearance is considered as the gold standard for the evaluation of the GFR. These techniques are time-consuming, labor-intensive, expensive, and require administration of substances that make them incompatible with routine monitoring. Serum cystatin C is another marker of renal function that has been proposed as potentially superior to serum creatinine level for estimating renal function, because it is thought to be produced at a constant rate by most nucleated cells. In the present study, the serum cystatin C and serum creatinine levels were estimated in apparently healthy subjects and eGFR-cystatin C and eGFR-creatinine was calculated. It was observed that serum cystatin C shows significant correlation with serum creatinine and negative correlation with eGFR-cystatin C and eGFR-creatinine. Hence, with the help of simple assay and appropriate measures, the kidney disease can be prevented at the early stages.

Keywords: Glomerular filtration rate, cystatin C, creatinine, renal disease.

INTRODUCTION

Glomerular filtration rate (GFR) is conventionally the best indicator for the estimation of renal function in both healthy and diseased patients. GFR is defined as the volume of plasma that can be completely cleared of a particular substance by the kidneys in a unit of time. The inulin clearance is considered as the gold standard for the evaluation of the GFR but due to some technical difficulties and cumbersome procedure its use is mainly limited. [1] As compared to the 24 hours creatinine clearance, 99mTc-DTPA renography is considered to be more simple and accurate, as no blood or urine sampling is required for the calculation of GFR. It is also suggested for clinical use in patients with compromised renal function. [2] The estimation of GFR is decisive for the diagnosis and clinical management of patients with chronic kidney disease (CKD). Serum creatinine is frequently used to estimate GFR. Other than GFR, various factors like age, sex, muscle mass, diet influence the serum creatinine levels. Cystatin C is being considered as a potential renal marker better than serum creatinine. In the recent years, several studies showed that correlation between serum cystatin C and GFR levels. Calculation of GFR using an empirical mathematical formula has been encouraged as a simple, rapid and reliable means of assessing kidney function. [3] The serum cystatin C levels are not influenced by factors such as age, muscle mass, sex. Even though different cystatin C–based formulae are developed, the accuracy and precision of cystatin C methods, irrespective of the formula used is considered better when compared to creatinine-based formulae. [4] In diabetic patients with early

renal changes, estimated GFR-cystatin C (eGFR-cysC) showed better accuracy and precision as compared with eGFR based on creatinine levels. [5] Hence, In the present study the levels of serum creatinine and cystatin C were estimated and the correlation between eGFR-CysC and eGFR-Creatinine was determined in apparently healthy subjects.

MATERIALS AND METHODS

The present study was conducted in the department of Biochemistry, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. 100 apparently healthy subjects in the age range of 17 years and above of either sex were selected. Under all aseptic conditions, 5 ml of venous blood sample was collected from antecubital vein of the subjects after an overnight fasting of 10-12 hours for biochemical analysis. Serum Cystatin C estimation was done by Enzyme Linked Immunosorbent Assay (ELISA) as described by Pergande M. [6] The concentration of serum cystatin C in healthy adult individuals ranges between 0.8-1.2 mg/L depending upon the analytical method used. [7] The serum creatinine estimation was done by Jaffe's Alkaline Picrate method. [8] The reference range of serum Creatinine is 0.5 -1.4 mg/dl. The estimated GFR was calculated using creatinine-based and cystatin C-based equations.

The "reexpressed" Modification of diet in renal disease (MDRD) study equation for standardized serum creatinine: [9]

eGFR (mL/min/1.73 m^2) = 175 x serum creatinine (mg/dL)$^{-1.154}$ x age(years) $^{-0.203}$ x 0.742 (if female) x 1.212 (if black)

CKD-Epidemiology Collaboration (EPI) cystatin C equation adjusted for age, sex, and race: [10]

eGFR = 127.7 x serum cystatin C (mg/L) $^{-1.17}$ x age (years) $^{-0.13}$ x 0.91 (if female) x 1.06 (if black)

RESULTS

Out of 100 healthy subjects, there were 39 females and 61 males. The mean serum cystatin C level was 0.75 mg/L and the mean serum creatinine level was 0.93 mg/dl. There was significant correlation between serum cystatin C and creatinine levels with r = 0.268 and p value= 0.007. The mean eGFR-cysC level was 157.86 ml/min/1.732 m^2 and the mean eGFR-creatinine was 84.29 ml/min/1.732 m^2 and there was significant correlation between eGFR-cysC and eGFR-creatinine with r=0.325, p-value= 0.001.Significant negative correlation between serum cystatin C and eGFR-cysC, eGFR-creatinine and serum creatinine and eGFR-cysC and eGFR-creatinine.

Table 1: Mean and standard deviation of different parameters

	Mean	Std. Deviation	N
Serum cystatin c	0.75 mg/L	0.40 mg/L	100
Serum creatinine	0.93 mg/dl	0.13 mg/dl	100
eGFR of cystatin c	157.86 ml/min/1.732 m^2	112.98 ml/min/1.732 m^2	100
eGFR of creatinine	84.29 ml/min/1.732 m^2	18.15 ml/min/1.732 m^2	100

Table 2: Correlations

		eGFR of creatinine	eGFR of cystatin c	S.cystatin c	S.creatinine
e GFR of creatinine	Pearson Correlation	1	0.325(**)	-0.316(**)	-0.686(**)
	Sig. (2-tailed)		.001	.001	.000
	N	100	100	100	100
e GFR of cystatin c	Pearson Correlation	0.325(**)	1	-0.802(**)	-0.225(*)
	Sig. (2-tailed)	.001		.000	.024
	N	100	100	100	100
S.cystatin c	Pearson Correlation	-0.316(**)	-0.802(**)	1	0.268(**)
	Sig. (2-tailed)	.001	.000		.007
	N	100	100	100	100
S.creatinine	Pearson Correlation	-0.686(**)	-0.225(*)	0.268(**)	1
	Sig. (2-tailed)	.000	.024	.007	
	N	100	100	100	100
** Correlation is significant at the 0.01 level (2-tailed).					
* Correlation is significant at the 0.05 level (2-tailed).					

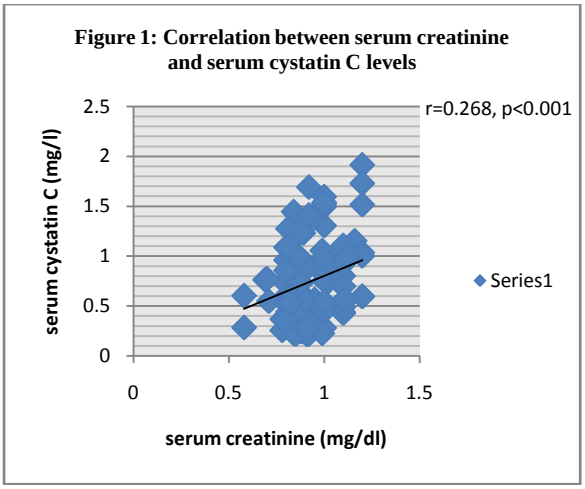

Figure 1: Correlation between serum creatinine and serum cystatin C levels

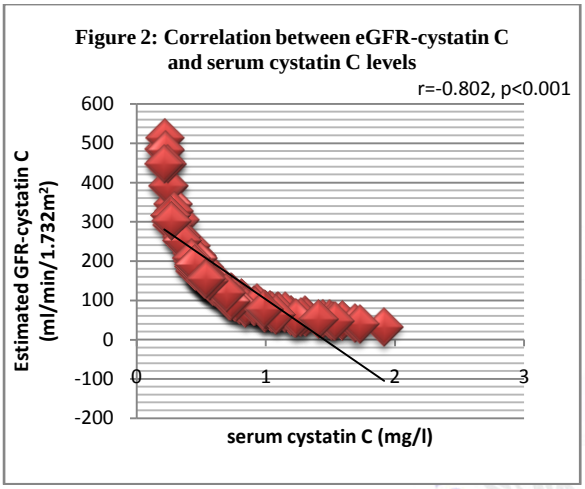

Figure 2: Correlation between eGFR-cystatin C and serum cystatin C levels

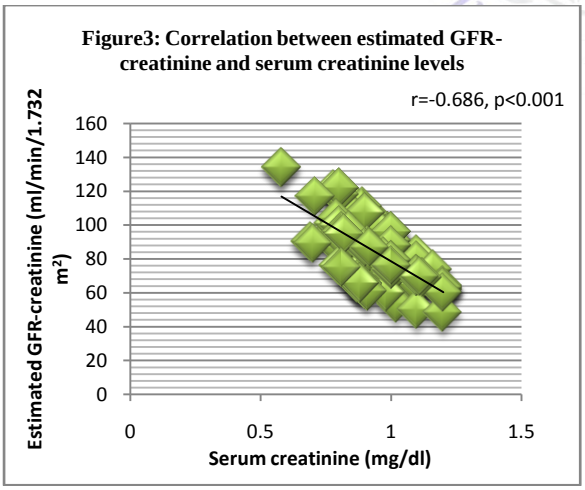

Figure3: Correlation between estimated GFR-creatinine and serum creatinine levels

DISCUSSION

In the present study significant correlation was observed between serum creatinine and serum cystatin C levels. And the significant negative correlation was also observed between serum cystatin C and eGFR-cysC, eGFR-creatinine and serum creatinine and eGFR-cysC, eGFR-creatinine. There was also significant positive correlation between eGFR-cys C and eGFR-creatinine. It was also observed that in subjects with very low serum cystatin C level, the GFR level is on the higher side. But this is not the case with the serum creatinine and eGFR-creatinine. Dhupper et al also observed a strong correlation between serum cystatin C and eGFR-cys C than serum creatinine and eGFR-creatinine. [11] In another study conducted by Tsai JP et al reported a strong positive correlation between serum cystatin C and serum creatinine level. [12] Similar results were observed by Dsa J et al in their study conducted in chronic kidney disease patients. They also observed a positive correlation between serum cystatin C and serum creatinine levels, while both serum creatinine and serum cystatin C had negative correlation with eGFR. [13] In a study conducted by Vinge et al among 42 healthy adults, it was suggested that eGFR - cys C concentrations was a better marker then eGFR-creatinine concentrations for estimating kidney function. [14] Domingueti et al, in the study conducted on type I diabetic patients also demonstrated that GFR < 60 ml/min/1.73m^2 estimated by cystatin C and creatinine based equations showed association with macroalbuminuria, thus suggestive of renal injury. [15] Serum cystatin C is more sensitive than serum creatinine in diagnosis of early kidney disease. It is already known that if there is more than 50% reduction in GFR, then there is rise in serum creatinine levels above the normal upper reference range. Cystatin C is being considered as a potential replacement for serum creatinine as a filtration marker. Most studies show that serum levels of cystatin C are more closely correlated with GFR than serum creatinine; however, the few studies that have compared serum cystatin C to estimates based on serum creatinine, age, sex and race. For diabetes patients, Pucci et al observed a higher predictive value in the early detection of reduced renal function (determined by the iohexol plasma clearance method) when the

GFR was estimated by cystatin C compared with GFR estimation by the creatinine-based MDRD and Cockroft-Gault formulae. [16] It was described that poor precision and accuracy of creatinine-based eGFR equations was seen with the range of 60–89 mL/min/1.73 m^2 (determined by the isotopic 51-creatinine EDTA method). Nonetheless, the evidence accumulates for better accuracy and precision of eGFR-CysC compared with eGFR -creatinine levels in subjects with diabetes, especially in early changes of kidney function. [5]

CONCLUSION

Thus, in the present study it was found that serum cystatin C shows significant correlation with serum creatinine and negative correlation with eGFR-cysC and eGFR-creatinine in apparently healthy subjects. There are certain limitations of this study. Firstly, the sample size was small. Secondly, the actual GFR was not estimated. Lastly, the GFR was not estimated using other equations like CKD-EPI creatinine based equation, CKD-EPI creatinine and cystatin C based equation. Though, the serum cystatin C assay is quite expensive when compared with serum creatinine. But, the renal disease can be prevented at the early stages before the appearance of signs and symptoms by this simple assay and appropriate action.

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Competing Interests

The data used in the study was a part of the MD (Biochemistry Thesis) of Dr. Pallavi Mahajan at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. The author declares no conflict of interest.

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