ORIGINAL ARTICLE

A COMPARATIVE ASSESSMENT OF SERUM CREATININE AND CYSTATIN C AS A SIGNIFICANCE OF NEPHROPATHY IN DIABETIC PATIENTS

Balqees Sadoon Jasim[1], Salim Hussein Hassan[1] and Maytham Salim AL-Nasrawii[1]

[1]*Community Health Department, Technical Institute of Karbala, AL-Furat Al-Awsat Technical University, Iraq*

Corresponding author: Balqees Sadoon Jasim
Email: *balqees2018m@gmail.com*

ABSTRACT

The critical micro-vascular complications of diabetes ultimately result in renal dysfunction known as diabetic nephropathy (DN). Measurement of glomerular filtration rate (GFR) is considered to be an important parameter in renal function assessment, evaluating GFR by Creatinine level. Recently, Cystatin C is used as a substitute indicator in several studies to assess diabetic nephropathy. This work was conceived to determine whether serum cystatinC would replace serum creatinine (Scr) in patients with type2 diabetes for early evaluation of nephropathy. A Case-Control Study was enrolled on 30 Patients with diabetic and 30 apparently healthy as control, aged between 25 - 83 years. Levels of serum cystatine C and serum Creatinine were calculated for both groups. Serum Creatinine, as well as serum cystatin C levels, was significant relationship with diabetic pt. in compared to non-diabetic individuals. ROC analysis noted the cystatinC was more predict indicator in diagnosed Diabetic Nephropathy (DNP) from Serum Creatinine level. In Type 2 diabetics, CystatinC is a good marker for uncontrolled diabetic nephropathy relative to serum creatinine.

Keywords: Diabetic Nephropathy, Cystatin C.Serum Creatinine, Type 2 DM

INTRODUCTION

Diabetic Nephropathy (DN) is a common microvascular diabetes disorder and a potential cause of end-stage renal disease. With the rapidly increasing incidence of diabetes worldwide and as survival time of diabetic patients is prolonged, the prevalence ratio of diabetes-caused chronic kidney diseases is also increasing each year [1]. The pathway involved includes improvements in peripheral nerves and metabolic disturbances in the blood vessels [2]. Diabetic nephropathy characterized by excessive proteins excretion, especially urinary albumin, decreased glomerular filtration rate (GFR) and increased blood involvement resulting in renal failure at the endpoint. [3]. Moreover, 25-40 % of people those had type1 or type2 DM reported diabetic nephropathy [4]. Early diagnosis of diabetic nephropathy is critical, and fast treatment reduces renal disease progression [5].

The presence of albumin in urine "Proteinuria" identified in more than 50 % of Type 2 diabetes patients, its seen shortly after diagnosis in other cases. The occurrence of microalbuminuria was found at the time of diagnosis of type 2 diabetes it has been linked to the hyperglycemia itself, which after sufficient glycemic regulation will revert to normal albuminuria. However, Micro-albuminuria can also reflect incipient nephropathy, especially if persistent [6]. The appearance of micro-albuminuria in the urine of diabetic persons heralds the onset of renal failure. Micro-albuminuria suggests serious damage to the glomerular blood vessels and may also suggest a lack of renal autoregulation in diabetes [6, 7].

Cystatin C (Cys C) is a secreted protein found in cerebrospinal fluid, saliva, urine, and semen [8]. Serum Cys C is considered as a renal secreted enzyme and can represent glomerulus filtration function [9]. After degradation of renal tubular reabsorption, nearly no effect is detected under physiological conditions Cys C stability factor. Cys C is constantly produced via glomerular filtration excretion in the renal tubules that is reabsorbed completely degraded [8]. Many diabetic patients with renal failure requiring renal dialysis GFR " Glomerular Filtration Rate". in renal clearance might be estimated and status the renal function to further evaluated in diabetic patients [10].

Routinely estimated of GFR (eGFR) was still based solely on serum creatinine and although reported with cystatin C to improves the accuracy of GFR estimation compared to equations based on single biomarkers [11, 12]. Besides, the combination of cystatin C-based equations with creatinine appears to reinforce the correlation between decreasing eGFR and cardiovascular diseases [13]. It has been investigating the relationship of cystatin C with renal function with persons for more than 25 years. To evaluate renal function, cystatin C has been identified as having a better diagnostic ability than creatinine, especially to identify the small reductions of glomerular filtration rate. Cys.C has appeared recently as a strong indicator of cardiovascular disorders and worse outcomes in patients without the renal disease [14].

The purpose of this study was to proof that Cys C serum is an optimal endogenous indicator of glomerular function and can be used in diabetic patients as a precise and reliable assessment indicator for evaluating glomerular filtration function compared to Creatinine.

METHODS

In the duration from February 2019 to July 2019, case-control study was conducted at Imam Hussein Medical City in Holy Karbala. In totally 60 subjects were participating in this study divided into two groups:
- Diabetic subjects (n = 30)
- Apparently healthy control (n = 30)

All diabetics patients were recruited from the out-patient clinic of Imam Hussein Medical City and diagnosed by specialists. Blood samples (3-5ml) have been collected to determine biochemical testing included random blood sugar, serum Creatinine, Serum cystatin C, by automated chemistry analyzer (Mendary Com.) and Glycated hemoglobin HbA1c % according to the procedure that provided with kits (i. Chroma II) device. The average amount of GFR was measured by applying the formula "Modification of diet in renal disease" **MDRD-eGFR** [15]:

$$\text{MDRD-eGFR}= 186\times (\text{serum creatinine [mg/dL]})\text{-}1.154 \times \textbf{age-0.203} \times \textbf{(0.742 if female)}$$

The cystatin C-based estimated GFR (CysC-eGFR) equation [16]:

$$\text{CysC-eGFR}=78/ (\text{serum cystatin C in mg/L})+4$$

Statistical analysis.

Data were present in mean ± SD. The results were performed by using SPSS (Statistical Software for Social Sciences) version 25. To assess the significant difference between variables, t-test and Chi-square are employed. Also, receiver operating characteristic" ROC" analysis was conducted to determine the accurate marker for renal function when we compare the serum creatinine and cystatin C levels for indicating DN. P-value < 0.05 was considered statistically significant.

RESULTS

Studied groups divided into two category group I (Diabetic patients) and group II (healthy control). A total of (60) subjects were (30) male and (30) female, on the other hand, was found statically significant between both groups according to the mean age, RBS and HbA1c, as detailed in Table (1). Comparison of serum ceatinine level among groups revealed that the significant difference between both groups (P=0.0001). Moreover the Mean ± SD of Serum Cystatin C level for the Group I was 1.13±0.36 mg/l and for the Group II was 0.705±0.104mg/l. There were highly significant differences when compared between studied groups (p=0.001). For study groups, Group I, and Group II, the Mean ± SD of GFR by creatinine dependent formula were119.74 ± 21.97, 74.37 ± 26.01 respectively, there was highly statistically significant differences (p=0. 0001). While the Mean ± SD of GFR by cystatin C based formula for Group I, and Group II were 115.46 ± 28.21, 90.18 ± 28.56 respectively, with highly statistically significant differences(p=0. 001).

As shown in Table (2), for Serum Creatinine (ROC = 0.153) the region under the curve was high, and serum Cystatin C (ROC area = 0.092), also explain the test result variables of serum creatinine and cystatin C which reveals that has at least one tie between the positive and negative actual state group, statistics may be biased.

ROC figure observing line reference between sensitivity/specificity "rate true positive result/rate of false-positive results", in this figure noted that the Cys C is more predict marker in diagnosed DNP from Serum Creatinine level.

Table 1: Clinical characteristics and comparative analysis in sample groups

Parameters (M±Sd)		Group I DM patients	Group II Healthy control	P-value
Gender	Male	17	13	0.3
	Female	13	17	
Age		61.13±9.59	52.03±11.68	0.002
RBS		252.90±103.48	121.23±8.91	0.0001
HbA1c		8.22±1.65	5.591± 0.502	0.0001
Serum Creatinine (mg/dl)		0.907± 0.24	0.66± 0.084	0.0001
Serum Cystatin C (mg/l)		1.13± 0.36	0.705± 0.104	0.0001
GFR by Creatinine		119.74 ± 21.97	74.37 ± 26.01	0.0001
GFR by Cystatin C		115.46 ± 28.21	90.18 ± 28.56	0.001

Table 2: The area under the ROC curve for prediction of Serum Creatinine and Cystatin levels in diabetic patients

Test Result Variables	Area.	S.E	(p-value)	Asymptotic Confidence Interval 95%	
				Lower Bound	Upper Bound
S Cr	0.153	0.056	0.000	0.044	0.263
CYS.C	0.092	0.042	0.000	0.010	0.174
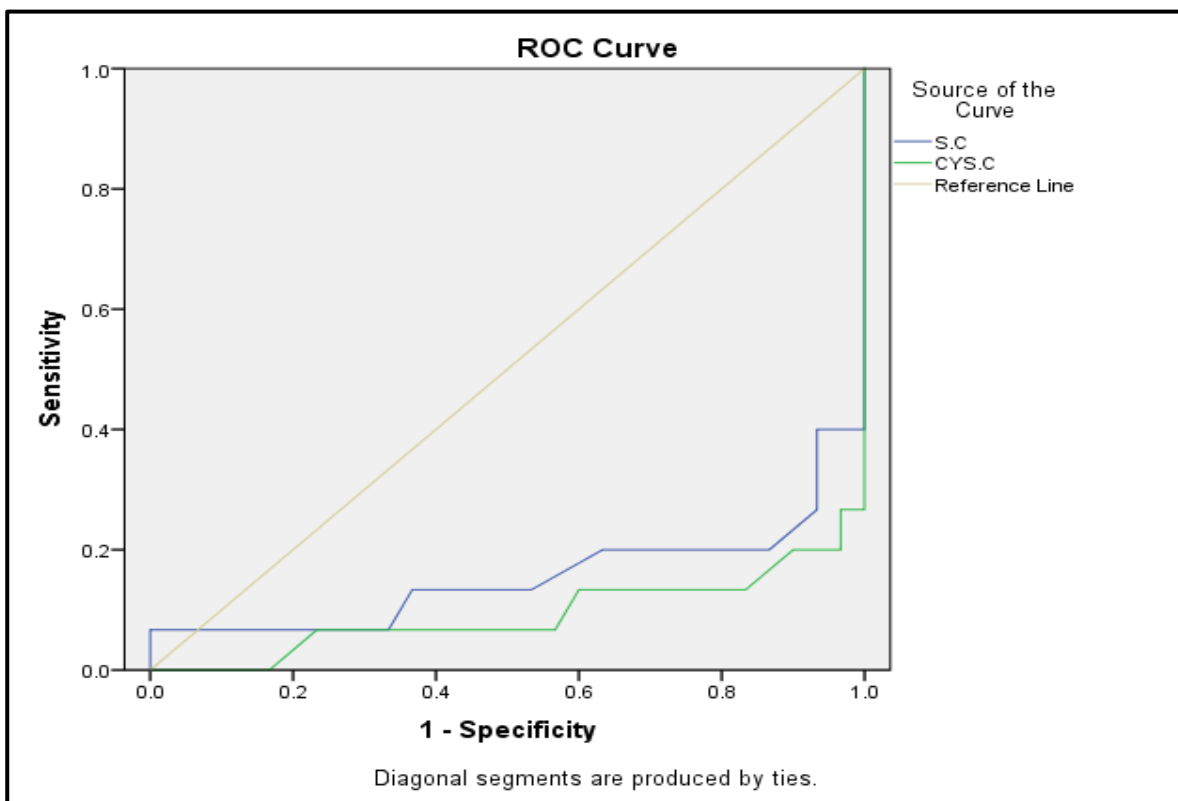
Figure 1: ROC analysis of serum creatinine and cystatin C (CysC) to determine the specificity and sensitivity in the diagnosis of DPN

DISCUSSION

DN has a complex pathogenesis and it's a severe microvascular complication of diabetes diseases and it's conceding the main cause of the diabetes-related mortality and mutilation. Epidemiological surveys have shown that the mortality rate of DM patients with DN is 30-fold higher than in those without kidney disease complications; therefore, early diagnosis and treatment of DN is important for improving the quality of life of DM patients [17]. Recently, different criteria were studied in serum and urine which played an important significant role in early warning indicators of acute renal complications and dysfunction like " cystatin C, kidney injury molecule-1" [18]. Cystatin C has been identified as a better diagnostic ability than serum creatinine for assessing the functionality of the kidney, especially to identify the slight reductions in glomerular filtration levels [19].

Gold standard GFR measurement techniques shall be replaced by an approximate GFR extracted from endogenous substances. Serum creatinine is the product most used to measure GFR. The concentration of creatinine is affected by gender, age, nutrition, and muscle mass[20,21].

It only rises until there is a GFR decline of nearly 50 %. This results in mistakenly high or low values which restrict its usefulness as an ideal GFR marker [22]. Several non-renal causes such as steroids, thyroid status, smoking, C-reactive protein and tumor have reportedly modulated serum cystatin C. Despite these limitations, research shows that serum cystatin C is advantageous in patients with early to moderately reduced renal function relative to serum creatinine. [23].

Our study has revealed that the serum cystatin C levels were more predict marker in diagnosed early renal impairment in Diabetes Mellitus compared with the level of serum creatinine. This is in matched with other researches. Gupta et al concluded that serum Cystatin C may be considered as an early marker use of to measure renal function [24]. Shetty et al, 60 type 2 diabetic patients were examined and divided evenly into 3 classes " Group A comprised of 20 subjects " non-diabetic", Group B consisted of 20 diabetic patients with usual serum creatinine (< 1.2 mg/dl), and Group C consisting of 20 diabetic subjects with significantly elevated serum creatinine (1.2-1.8 mg/dl)". This indicates that the serum levels of cystatin C were a fast and stronger predictor of incipient DN in type 2 diabetes with serum creatinine[25]. Also, another study made by Huda, showed the Cys C is a better marker of impaired renal function and its more sensitive marker compared to Serum Creatinine [26].

Serum Cys C is the most appropriate marker for calculating GFR, instead of serum creatinine, and for predicting kidney malfunction progression [27]. So the study indicates that serum cystatin C can be used instead of serum creatinine to measure GFR in type 2 diabetes mellitus. These results are similar to Kumar research [28].

CONCLUSION

In conclusion, the findings of this search suggest that the assessment of cystatin C in serum in patients with type 2 diabetes is an effective, practical, noninvasive approach for assessing kidney dysfunctions. Further studies with greater sample size and a prospective model would be required to validate the possible use of cystatin C as a useful biomarker for early diagnosis of diabeticnephropathy.

Conflict of interest
The authors declare no potential conflict of interest.

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