EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 6
91-94
Year: 2017

EVALUATION OF CYSTATIN C FOR EARLY DETECTION OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH HYPERTENSION AND TYPE 2 DIABETES MELLITUS-KHARTOUM STATE

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Article Received on 07/04/2017 **Article Revised on 28/04/2017** **Article Accepted on 19/05/2017**

ABSTRACT

Background: Cystatin C is a marker used for early detection of chronic kidney disease in high risk patients (hypertension and type 2 diabetes mellitus). Chronic kidney disease is a common serious complication of hypertension and diabetes mellitus and associated with increased risk of mortality, progression to kidney failure. Elevation of cystatin C in serum could occur in diabetic and/or hypertensive patients even before the appearance of clinical chronic kidney disease markers and it is useful marker for detecting early nephropathy. Many previous studies and literature discussed the clinical efficiency and relevance of cystatin c as an endogenous renal marker for detecting early renal impairment. Serum cystatin C could be the most sensitive indicator of glomerular filtration rate. Therefore, in our study we examined the correlation between serum cystatin c, hypertension and diabetes mellitus. **Method:** Cross-sectional study in which 75 participants were included, categorized into three groups, 25 patients with type 2 diabetes mellitus, 25 hypertensive patients, and 25 apparently healthy subjects as control group. Cystatin C was measured by sandwich immune-detection method among control, diabetic and hypertensive groups without clinically recognized CKD. Renal function tests (serum creatinine and blood urea) were measured used Jaffe reaction and Berthelot reaction respectively. **Results:** Elevated serum cystatin C levels were found to be associated with diabetes and hypertension (P. value = 0.001. 0.0028 respectively), insignificant with the duration of hypertension and diabetes (P. value = 0.988, 0.169 respectively), and insignificant correlation with serum creatinine levels (P. value =0.914) when P value cut off is at 0.05. **Conclusion:** The findings of our study showed that cystatin C levels could be used as a maker for early CKD detection in patients with type2 diabetes mellitus and in hypertensive patients. The underlying biological processes remain to be determined.

KEYWORDS: Cystatin C, Diabetes mellitus, hypertension, chronic kidney disease.

INTRODUCTION

Diabetes mellitus is metabolic disease characterized by high level of glucose.[1]

The level of serum cystatin c has been proposed as simple accurate and rapid endogenous marker of glomerular filtration rate in research and clinical practice.

Cystatin C, a cysteine protease inhibitor, is freely filtered by the renal glomeruli, metabolized by the proximal tubule and identified as a promising marker of renal failure.[2] Cystatin C may have a role in identifying persons with CKD who have the highest risk for complications than SCr.[3]

Cystatin C is measuring of kidney function that appears more sensitive than creatinine to factors other than glomerular filtration rate.[4]

Chronic kidney disease is a common and serious complication of diabetes associated with increased risk of mortality, progression to kidney failure.[5]

The levels of cystatin C in serum may be elevated in diabetic patients even before the appearance of traditional chronic kidney disease markers and it can be used as marker for detecting nephropathy. The study done by Surendar J *et al*, ound that cystatin C levels were highest in type 2 diabetic patients.[6]

Serum cystatin C may be the most sensitive indicator of glomerular filtration rate.[7,8]

MATERIALS

Components of ichromacystatin c: Cartridge box, ID chip, instruction foruse, Box containing detection buffer tubes.

Instrument of ichroma tests:ichroma reader, chroma D, ichroma printer.

METHODS

A case control study was conducted among 75 consisted of diabetic patients (n=25), hypertensive patients (n=25) and healthy control group (n=25).

The control group comprised of twenty five healthy adults with normal blood sugar, blood pressure and renal function test.

Cystatin C was measured by sandwich immune-detection method. The detector recombinant protein in buffer bind to antibody in sample forming recombinant protein antibody complexes and migrates onto nitrocellulose matrix to be captured by the other immobilized antigen on test strip.

The more antibodies in sample forms the more recombinant protein antibody complex and leads to stronger intensity of fluorescence signal on detector recombinant protein, which is processed by instrument for i-chroma tests to show cystatin C concentration in sample.

Serum creatinine and blood urea were analyzed used Jaffe reaction and Berthelot reaction in full-automated chemistry analyzer (C 311 Cobas).

Statistical analysis was done using SPSS and Microsoft Excel.

Table 1: Mean±SD of measured parameters.

Parameters	Cystatin C	Glucose	Urea	creatinine
Control	0.889±0.145	96.68±14.28	21.3±8.38	0.824±0.252
Hypertensive	1.526±0.345	90.05±12.66	19.04±5.14	0.93±0.22
DM	1.687±0.623	215.3±91.17	24.4±8.37	0.868±0.270

RESULT

In our study the age of patients and healthy control ranged from 32 years to 80 years. The age of diabetic patients ranged from 36-75 years, for hypertensive it ranged from 40-72 years. The range of healthy control was from 32-80 years. The females in the healthy control were 11, and males were 14. In the diabetic group, females were 20 and males were 5. In the hypertensive group, females were 15 and males were 10 (figure 1).

The mean of Cystatin C levels among normal was 0.8896± 0.14587 mg/l, among diabetic patients was 1.6872+/- 0.62330 mg/l and among hypertensive was 1.5264+/- 0.34543 mg/l (Table 1).

Our study showed serum cystatin C level was significantly increased in diabetics and hypertensive patients when compared to control group (P. value = 0.001, 0.028 respectively) (Table 2)(Table 7). Insignificant difference was observed with the duration of hypertension and duration of type 2 diabetes mellitus (P. value = 0.988, 0.169) (Table 3) and (Table 4). There is no correlation between serum creatinine levels and cystatin C levels among diabetic patients (Table 5).

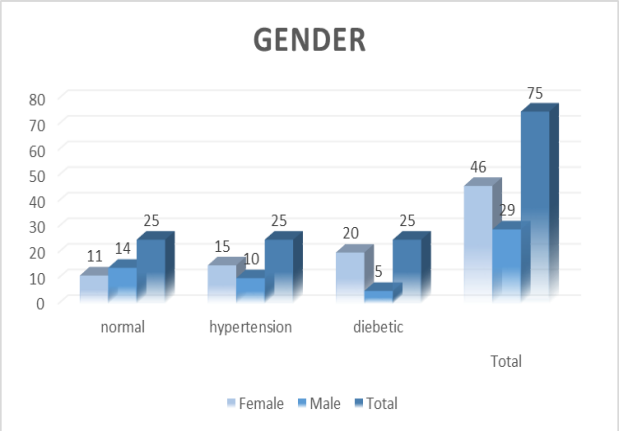

Figure 1: The numbers of individuals in the study, males and females.

Table 2: The association between cystatin c levels and blood glucose level in diabetic patients, there is a significant correlation between both variables.

Parameter	DM
Cystatin C	1.687±0.623
Glucose	215.3±91.17
P. Value	0.001
R	0.612

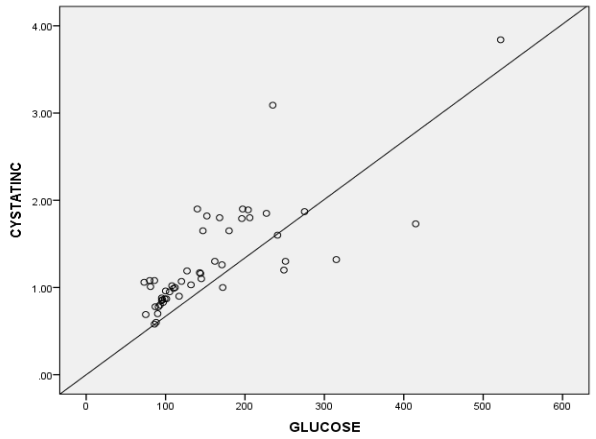

Figure 2: Relationship between glucose and cystatin C level among diabetic patients (P. Value 0.001, R 0.612).

Table 3: There is no significant association between cystatin C and duration of hypertension.

Parameter	Hypertension
Cystatin C	1.526±0.345
Duration	11.92±7.26
P. Value	0.988
R	0.003

Table 4: There is no association between cystatin C levels and duration of diabetes mellitus.

Parameter	DM
Cystatin C	1.687±0.623
Duration	10.24±8.14
P. Value	0.169
R	0.284

Table 5: There is no correlation between Creatinine and cystatin C levels among diabetic patients.

Parameter	DM
Cystatin C	1.687±0.623
SCr	0.868±0.270
P. Value	0.914
R	0.023

Table 6: There is no correlation between creatinine and cystatin c levels among hypertensive patients.

Parameter	HT
Cystatin C	1.526±0.345
SCr	0.93±0.22
P. Value	0.874
R	0.033

Table 7: showed serum cystatin C was significantly increased in hypertensive patients compared to control group.

Parameter	HT
Cystatin C	1.526±0.345
P. Value	0.028
R	0.44

DISCUSSION

The main objective of the study was to assess the rate and possible clinical applications of cystatin C as biomarker for fluctuations in glomerular filtration rate (GFR) in patients with type 2 diabetes mellitus and/or hypertension. This was important because findings could help clinicians in early detection of chronic kidney disease (CKD), as well as avoiding misclassification of CKD patients in Sudan.

Diabetes and hypertension are two of the most important factors accounting for cardiovascular disease development, which in itself is a major precursor for CKD.

In our study, we found that serum creatinine did not show any significant correlation when compared with cystatin c in diabetes mellitus and hypertensive patients. In Y. KOC, E and coworkers' study, it showed there were no significantly difference between serum creatinine, cystatin C in hypertensive patients ($p > 0.05$).[9]

It is an established fact that creatinine exceeds normal levels only when 50% of glomerular filtration rate (GFR) has already been lost.[10,11] So more sensitive biomarkers are needed. Serum cystatin C could be the most sensitive indicator of glomerular filtration rate.

The present work investigated the relationship between serum cystatin C and serum levels of glucose, creatinine and duration of hypertension among patients and compared with control group.

Serum Cystatin C concentrations are less influenced by muscle mass and diet than creatinine.[12]

Our results showed a strong correlation between glucose levels and cystatin C in Sudanese diabetes mellitus and hypertensive patients throughout a wide range of kidney function levels. The study done by Surendar J *et al*, ound that cystatin C levels were highest in type 2 diabetic patients.[13]

CONCLUSION

Cystatin C was significantly increased in high risk population and correlation with glucose levels in diabetes mellitus and hypertensive patients.

This study of persons with diabetes suggests that the use of cystatin C to estimate kidney dysfunction before appearance of clinical symptoms and markers. Neither creatinine nor cystatin C is a perfect marker of glomerular filtration.[14] Serum cystatin C levels in diabetes mellitus and hypertensive patients were significantly associated with kidney function across a wide range of cystatin c, even in subjects with presumably normal kidney function this can provide a

vital link in diagnosis of worsening renal function at an early stage.

ACKNOWLEDGMENT

Iam so thankful to allah and I would like to express my special thank to my teachers (Dr Tarig, Dr Ayman, Safa). Who gave me the golden opportunity to do this wonderful paper,which also helped me in doing a lot of research. Secondly I would also like to thank my parents, brothers and my friend (Zeinab) who helped me a lot in finalizing this paper within the limited time frame.
Iam really thankful to them.

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