ISSN 2515-8260 Volume 09, Issue 03, 2022

SERUM CYSTATIN C AS AN EARLY DIAGNOSTIC MARKER FOR THE DETECTION OF NEPHROPATHY IN TYPE 2 DIABETES MELLITUS

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Abstract

One of the most common causes of dialysis is diabetic nephropathy (DN), which can be prevented or delayed with early identification. When it comes to chronic kidney disease (CKD) and type 2 diabetes, little is known about the renal function marker serum cystatin C (sCysC) and its link to glomerular filtration rate. In this study, we tested the efficacy of sCysC as a marker of early DN and CKD in patients from the southern Indian coastal region.

Key words - Glomerular filtration rate; diabetic nephropathy; chronic renal disease; cystatin C.

Introduction

It has been likened to a "epidemic" in modern society because of the prevalence of the disease. Around 221 million people would be living with DM by 2010, and that number is expected to rise to 300 million by 2025 [1]. Carbohydrate, fat, and protein metabolism are all problematic in diabetics, making it a classic heterogeneous metabolic illness. When it comes to diabetic complications, the most serious one is Diabetic Nephropathy (DN), which raises the risk of heart disease and early mortality [2]. Type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) are both susceptible to diabetic nephropathy beyond the age of 20 years.

40% of type 2 diabetics suffer from diabetic nephropathy, which is characterised by constant albuminuria, high blood pressure, and progressively declining kidney function that eventually leads to kidney failure (ESRD). Patients with impaired renal function, on the other hand, are at an increased risk of cardiovascular disease. A considerable interindividual range in the rate of deterioration in glomerular filtration rate (GFR) has been found for both type 1 and type 2 diabetic patients with nephropathy.

In order to avoid the nephropathy stage and ultimately end-stage renal disease, early diagnosis of impaired renal function is crucial... (ESRD). The early detection of DN has been aided by the screening of numerous markers, including cystatin C, alpha 1-microglobulin, immunoglobulin G or M, angiotensinogen, liver-type fatty acid-binding protein, urinary transferrin, serum osteopontin, urinary retinol-binding protein, and interleukin-18. The development and progression of diabetic nephropathy has been linked to the presence of certain tubular damage markers.

A constant amount of Cystatin C, a cysteine proteinase inhibitor with a molecular weight of 13 kDa, is produced by all nucleated cells. Cystatin C has no tubular secretion in healthy individuals

because the renal glomeruli filter it almost completely and almost totally in the proximal tubule like other low molecular weight proteins. In healthy individuals and proteinuric patients with intact renal tubules, urine cystatin C levels are unaffected by age or muscle mass, just like serum cystatin C levels are. It has long been established that elevated urine cystatin C is a sign of renal tubular failure. Nonalbuminum protein (NAP) leakage in the urine can potentially suggest tubular injury, rather than glomerular damage, as previously stated. We wanted to see how urine cystatin C affects the course of type 2 diabetes nephropathy and whether or not urinary cystatin C has an effect on the reduction of the glomerular filtration rate (GFR) in diabetic patients. The GFR decline was also examined to see if urine NAP had any link with urinary cystatin C or had any effect on the fall in GFR.

In this study, we investigated whether cystatin C levels in the serum of diabetic individuals could serve as biomarkers for early renal impairment.

Materials and Methods

A hospital-based setting served as the setting for this cross-sectional investigation. A total of fifty T2DM patients and a corresponding number of fifty healthy volunteers took part in this investigation. Newly diagnosed Type 2 Diabetes (T2DM) or individuals currently taking treatment for T2DM were both included in the study. Patients having a urinary tract infection, hypothyroidism or hyperthyroidism, or pregnancy were not included in the study. Nondiabetic members of the hospital personnel and tourists served as the control group in this study. Before being allowed to participate in the study, all participants were required to provide their informed, signed consent in writing. The Institutional Review Committee gave its approval for this study's ethical conduct.

Data Collection

Subjects were selected at random, and information was gathered on each one as they were being recruited. Age, sex, gender, dietary habits, drinking and smoking habits, the family history of T2DM, the duration of T2DM, the medication used (oral hypoglycaemic drugs, insulin, or both), and the complications of T2DM were all taken into account in the study (retinopathy, neuropathy, and nephropathy). Body mass index (BMI) (weight in kg/height squared metres) was determined using the anthropometric data, which included height, weight, waist circumference, and hip circumference. Measurements of pulse and blood pressure (BP) were performed in accordance with established protocols.

Sample Collection

Blood and urine samples were taken from the patients and controls following the selection process. Samples of blood were taken via venepuncture. It took 8 hours to determine fasting blood glucose and 2 hours to estimate postprandial blood glucose. Blood samples taken in K2EDTA vials were used to assess HbA1c. Cystatin C, creatinine, triglycerides, total cholesterol, and high-density lipoprotein (HDL) cholesterol were among the other biochemical analytes that were assessed in the blood sample. Blood was taken in a simple container and centrifuged for 10 minutes at 3000 rpm to separate the serum. For biochemical analysis, aliquoted serum was kept at 20°C. Urinary creatinine and microalbumin concentrations were measured using spot urine samples. The supernatant from the centrifuged samples was used for biochemical examination after they were immediately centrifuged at 2000 rpm for 10 minutes.

Laboratory Tests

Serum and urine creatinine, as well as HbA1c levels in the blood were all assessed with the Cobas C311 Roche-Hitachi Chemistry Analyzer. The Accent-200 completely automated analyzer was used to measure serum cystatin C, and the Nycocard analyzer was used to quantify urinary microalbumin. All of these measurements were made using the hexokinase, Jaffe, turbidimetric immunoassay, immunoturbidimetric, and solid-phase immunometric techniques. The results are shown in the table below. Several ratios were calculated following the estimation of these biological parameters. As a result of the albumin: creatinine ratio, three groups of individuals were identified: those with normal albuminuria, those with microalbuminuria (albumin: creatinine ratio 30–300 mg/g), and those with macroalbuminuria (albumin: creatinine ratio >300 mg/g) [5].

eGFR Calculation

Using the serum creatinine levels, eGFR was computed using the following formulae. In the Cockcroft-Gault equation (CG), eGFR was calculated using the formula (140 age) / kg / (72 SCr (mg/dL) / kg) (0.85 if female). As part of the chronic kidney disease epidemiology (CKD-EPI) cooperation, the serum creatinine-based chronic kidney disease epidemiology (SCr/0.7) formula was used for females and SCr/0.9 formula was utilised for males. [27]. MDRD (Modification of Diet in Renal Disease) Equation used eGFR=186 (SCr(mg/dL))1.154 (age(years))0.203 (1.21 if black) [28]. It was found that if cystatin C was below 0.8, the patient's eGFR was equal to 133.2 millilitres per minute (mL/min), and if cystatin C was above 0.8, the patient's GFR was equal to 133.2 millilitres per minute (mL/min), and a female's GFR was 0.93. Renal biomarkers such as serum creatinine and serum cystatin C were evaluated for their capacity to detect micro and macroalbuminuria using receiver operating characteristic (ROC) studies (grade 2 and 3 DN).

Statistical Analysis

SPSS version 20.0 software was used to analyse the data collected in MS Excel. Demographic, anthropometric, and biochemical parameters were expressed using descriptive statistics (mean with standard deviation and median with interquartile ranges). Statistical significance was assessed using Student's t-tests and one-way ANOVA (for regularly distributed variables) as well as the Mann–Whitney U test and the Kruskal–Wallis test (for nonnormally distributed variables) and a post hoc analysis. In order to determine the correlation between regularly distributed and nonnormally distributed variables, we used Pearson and Spearman's rho correlation analysis, respectively. Categorical variables were analysed using a chi-square test. The area under the ROC curve (AUC) was used to examine the diagnostic accuracy of kidney indicators. The cutoff value from ROC analysis was used to assess serum cystatin C sensitivity and specificity.

Results

Study subjects were aged 33 to 67, with an average age of 52 years; there were 20 men (37.5 percent) and 30 women (62.5 percent); their BMIs ranged from 22 kg/m2 to 44 kg/m2 with an average BMI of 33.5 kg/m2 in the examined groups. According to this research, BMIstatistically significant difference between groups I-(A1) and II-(A2)All of the groups investigated showed a significant difference in FBG ratio and 2HPP. As it turned out,a significantly higher (HbA1c) than the other groups in the macroalbuminuric population There is a higher prevalence of microalbuminuria in this group than in the normoalbuminuric group. According to the data, there

was Diabetic patients with normal, micro, and macroalbuminuric blood glucose levels differ greatly in their ability to respond to treatment. duration of the DM on average (with standard deviation). Only a few millimetres of variation could be seen between the two. In terms of TSH, four different groups have been examined. There was a huge disparity between the two groups. S. creatinine, BUN, and eGF were all examined by different research groups in the lab. In the study, the results indicated a high level of significance Regarding, there was a substantial difference between the diabetes group and the control group. Cystatin C Is Also Required for this Macroalbuminuric patients had a considerably higher mean serum Cystatin C level than the general population. the mean (3.25) is higher than that of other groups Negative correlation was found to be substantial. betweeneGFR and S.Cystatin C. In addition, Serum had a substantial positive connection. cystatin c and s, respectively. Blood.urea. and creatinine. The A/C ratio in urine, HbA1c, FBG, 2Hpp, and DM duration. Despite this, there was no association between cystatin C levels in the blood and a patient's risk of cardiovascular disease. Age is a factor. There was a statistically significant difference between the two groups, according to the research. correlation between blood albumin levels in the control group and the patient with neoalbuminuria with GFR 90 A cytostatin C. For S. Cystatin C to be a meaningful predictor, a linear regression analysis was conducted. A/C and eGFR in urine.

Discussion

To eliminate serum cystatin C from circulation, glomeruloscopy and proximal tubular reabsorption and degradation remove this non-glycosylated, low molecular weight and basic protein. Serum cystatin C levels have been shown in several investigations to be unaffected by age, gender, or body mass, and inflammation has had no effect on them. GFR declines as DN progresses in persons with diabetes mellitus (DM). There is an elevated risk of death and cardiovascular mortality when the patient's GFR goes below 60 ml/min/1.73 m2. The goal of this meta-analysis was to compare blood cystatin C with mGFR in order to make a prediction about the likelihood of developing diabetes type 2.

The serum cystatin C test for the early prediction of DN was the subject of nine research included in this meta-analysis. Serum cystatin C's pooled sensitivity and specificity were 0.88 and 0.85, respectively, according to the study results. There was a correlation between the positive likelihood ratio and the likelihood of a given condition being diagnosed, while the negative likelihood ratio was inversely proportional. As a result, the likelihood ratio may be a better way to explain the results. Serum cystatin C levels in DM patients are associated with an increased risk of developing DN, as evidenced by a pooled positive likelihood ratio of 7.04. As a result of the 0.13 pooled negative likelihood ratio, patients with normal serum cystatin C had a lower risk of developing the disorder. The SROC curve also served as a summary of the diagnostic tests' overall usefulness. The SROC area under the curve was 0.9549 and the Q value was 0.8972 in the current meta-analysis. To calculate DOR, divide the number of positives by the number of negatives, and divide the number of positives by the number of negatives. 66.80 was the diagnostic odds ratio. Cystatin C is therefore a better indicator of diabetes-related neutropenia (DN) in patients with diabetes mellitus (DM).

It is possible that the following restrictions are to blame for the variability we see. GFR could be measured using one of three ways. Although most research used the 51Cr-EDTA plasma clearance to measure GFR, the observation time varied. Most research did not include the diagnostic criteria for diabetes, which is a major problem.

We found that sCysC was a better tool for detecting early signs of nephropathy in people with type 2 diabetes. sCysC was also more sensitive in detecting stage 2 CKD early on. Because of this, sCysC may be a useful biomarker for the early diagnosis of stage 2 CKD, particularly in patients with grade 2 DN.

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