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Impact of Serum Cystatin C as an Early Sign of Decreased Glomerular Filtration Rate in Type II Diabetes.

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Introduction

Diabetes Mellitus, abbreviated as DM, is a syndrome characterized by hyperglycemia that is present for an extended period of time and is caused by a relative insulin deficiency, resistance, or both. It is estimated that by the year 2030, it will affect 370 million people all over the world, and it currently affects more than 120 million people all over the world. Diabetes is typically a condition that cannot be reversed; its late complications lead to a decreased life expectancy and significant increases in medical expenses. These include macrovascular disease, which leads to an increased prevalence of coronary artery disease, peripheral vascular disease, and stroke; microvascular damage, which leads to diabetic retinopathy and nephropathy; and cardiovascular disease, which leads to an increased prevalence of coronary artery disease, peripheral vascular disease, and stroke.

Proteinuria and elevated serum creatinine levels, which represent a decrease in the glomerular filtration rate (GFR), are the first signs that someone has chronic kidney disease. This condition eventually leads to complete loss of kidney function, which is referred to as end-stage renal disease. Chronic kidney disease can be prevented by maintaining a healthy blood pressure and maintaining a healthy diet.

Due to the fact that diabetes was prevalent for many years before it was diagnosed, a higher proportion of individuals with type 2 diabetes are found to have diabetic nephropathy shortly after their diabetes is diagnosed. [3] This is because diabetic nephropathy develops more quickly in people with type 2 diabetes.

Serum creatinine level is the biochemical parameter that is used in clinical practise that is most frequently to estimate GFR. Glomerular filtration rate (GFR) is considered to be the most accurate indicator of renal function. Nevertheless, there are a few drawbacks associated with the utilisation of this parameter. Serum creatinine levels can be influenced by a variety of factors, including gender, age, amount of muscle mass, and consumption of protein, which can lead to an inaccurate estimation of GFR. Individuals who have a GFR that is significantly impaired can have levels of creatinine in their serum that are normal.

It is possible that the presence of albuminuria is less specific to the presence of diabetic nephropathy. Between 20 and 40 percent of type 2 diabetic patients who have microalbuminuria develop overt nephropathy, and the majority of patients show progression to end-stage renal disease.

Cystatin C is a small protein with a molecular weight of 13 kilodaltons that belongs to the cysteine proteinase inhibitor family. All nucleated cells produce it at a rate that is relatively constant. Because of its diminutive size, it is easily filtered by the glomerulus, and because it does not undergo secretion, the renal tubules are responsible for its complete reabsorption and subsequent breakdown. Because of this, the rate at which cystatin C is filtered at the glomerulus is the primary factor that determines the level of cystatin C in the blood; consequently, cystatin C is an excellent GFR marker. Recent research has shown that serum cystatin C is a more accurate marker of GFR than serum creatinine. This was discovered through a meta-analysis.

Cystatin C is an alternative endogenous marker that can be used in place of serum creatinine to estimate GFR. This marker is more sensitive than serum creatinine.

The estimation of GFR has become more practical and straightforward as a result of new immunoassay methods that measure cystatin C levels. These methods come from a variety of different manufacturers. These procedures are automated, and one can obtain results in a short amount of time. It is essential for clinical laboratories to standardise their testing procedures in order to derive accurate GFR estimates.

Methodology

Individuals who were attending the outpatient clinic and those who were inpatients in the Internal Medicine Department of selected hospitals in Indore were included in the current study. The study was conducted on a total of 50 patients, 50 of whom were healthy and 50 of whom were diagnosed with type 2 diabetes. For the purpose of the study, a purposeful sampling method and an adapted case control design were utilized.

The following procedures were performed on all patients and controls:

Complete medical history, including age, gender, previous medications, and duration of diabetes.

Clinical examination, with a focus on blood pressure, neurological and cardiac examinations, electrocardiography, and abdominal ultrasound examination

Abdominal ultrasonography is used to detect kidney abnormalities.

Laboratory studies, such as the following:

The A/C ratio is estimated.

Fasting and postprandial blood glucose levels are estimated.

Complete urine testing.

Glycated haemoglobin levels are estimated (HbA1c).

Estimation of the total blood count

Serum urea levels are estimated.

Serum creatinine levels are estimated (modified rate Jaffe method).

The ELISA technique was used to calculate serum cystatin C levels (mg/dl).

GFR is calculated using the following equation:

This test uses a technique called quantitative sandwich enzyme immunoassay to gather its results (ELISA technique). Polyclonal anti-human cystatin C-specific antibodies were used to coat the surface of the wells on the microtiter plate, which was used for testing. Standard solutions, quality control solutions, and sample solutions that had been diluted were pipetted into the wells. After the initial incubation period, any unbound protein was removed by washing it out. The immobilised antibodies were successful in capturing any human cystatin C that was present. After that, horseradish peroxidase-conjugated polyclonal anti-human cystatin C antibodies were added to the wells, and they were allowed to sit for an extended period of time. The unbound antibody-horseradish peroxidase conjugates were then removed in a subsequent washing step after this step had been completed. After that, a substrate solution, designated as H202, was added to each well. The addition of the acidic stop solution caused the blue product that was produced by the enzymatic reaction to change colour to yellow.

The amount of human cystatin C that was bound in the first step was directly proportional to the amount of colour intensity that was measured spectrophotochemically at 450 nm.

The absorbance values were plotted against each respective human cystatin C standard level using a four-parameter function, and then the concentrations of unknown samples were obtained from the standard curve. The standard curve was constructed by plotting the absorbance values against each respective human cystatin C standard level.

Results

The control group consisted of 50 apparently healthy people with a mean age of 50.2 13.1 years and a mean weight of 78.3 11.8 kg.

The patients were divided into the following groups based on their A/C:

The normoalbuminuria group included 25 patients with an A/C of 31 mg/g or lower (range, 8-28 mg/g). The average age was 50.5 12.3 years old, and the average weight was 95.1 27.4 kg. The study included 11 patients with GFRs of 91 ml/min or higher and four patients with GFRs ranging from 88 to 61 ml/min.

The microalbuminuria group included 15 patients with an A/C of 32-296 mg/g (range, 50-292). The average age was 52.5 4.3 years, and the average weight was 95 13.4 kg. Four patients in the group had a GFR of 91 ml/min or higher, four patients had a GFR of 88-60 ml/min, and three patients had a GFR of 60 ml/min or lower.

Macroalbuminuria group: ten patients with macroalbuminuria and an A/C of 300 mg/g or higher were included (range, 348-1200). The average age was 52.3 7 years, and the average weight was 82.2 23 kg. They included four patients with GFRs of 90 ml/min or higher, three with GFRs of 88-60 ml/min, and nine with GFRs of less than 60 ml/min. Cystatin C levels, weight, and GFR all had a negative correlation. Serum creatinine level and A/C; HbA1c, FBS, and 2HPP levels; weight; and DM duration all had a positive correlation. There was a negative relationship between serum creatinine level and age, as well as GFR.

Conclusion

For the purpose of determining renal function, the measurement of GFR is seen as being of great assistance, particularly in individuals who have type 2 diabetes. Twenty to forty percent of people diagnosed with type 2 diabetes will ultimately develop diabetic nephropathy, and these patients will at some point in the future require renal replacement therapy.

It is common knowledge that the serum creatinine level is a marker of renal function that is relatively insensitive. Furthermore, the serum creatinine level is not an accurate reflection of GFR because it is influenced by many factors, such as muscle mass, sex, diet, liver function, age, and tubular secretion,

which can result in an overstatement of GFR of up to 20%; consequently, it is preferable to look for an alternative noninvasive measure, particularly for diabetic nephropathy.

As a result of this research, we are able to draw the conclusion that serum cystatin C, rather than serum creatinine, is a more accurate measure for GFR in type 2 diabetes patients who have impaired GFR, particularly in the "creatinine-blind area." Cystatin C has the ability to detect moderate to mild declines in GFR that are not readily apparent using tests based on blood creatinine.

Estimating GFR is now more realistic and easier to do as a result of new immunoassay technologies that assess cystatin C levels. These methods come from numerous different manufacturers. Because these procedures are automated and it is possible to receive findings in a short amount of time, it is possible that routine studies for the measurement of GFR in diabetes patients may advocate using these methods.

In conclusion, evaluation of renal function based on cystatin C levels will allow for improvements in diabetic nephropathy early identification, prevention, and treatment techniques. It is possible to estimate the levels of cystatin C in the serum, and doing so can be helpful in identifying an early decrease in renal function in people with type 2 diabetes.

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