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Cystatin C and Urinary Enzymes as Early Diagnostic Markers for Diabetic Nephropathy

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Introduction

Diabetes mellitus refers to a group of metabolic disorders characterised by hyperglycemia. Diabetes mellitus is one of the world's most common noncommunicable diseases and a leading cause of death. India has the highest prevalence of diabetes mellitus in the world, with over 50 million people affected, and this figure is expected to rise to 87 million by 2030. As the number of diabetic patients rises, so will the number of diabetic complications. It has been discovered that Asians have a higher prevalence of diabetes complications than Europeans. Diabetic nephropathy, also known as diabetic kidney disease, is one of the most common complications of diabetes.

Diabetic Nephropathy, also known as diabetic kidney disease, is one of the most common long-term microvascular complications of Type 1 and Type 2 Diabetes Mellitus. In developing countries, it is one of the leading causes of End Stage Renal Disease (ESRD). The appearance of microalbuminuria is part of the routine classical evaluation of diabetic nephropathy.

Urinary microalbumin is not widely available, is difficult to standardise, is relatively expensive, and appears in urine only after significant glomerular damage has occurred. Urinary albumin levels are also increased in urinary tract infection, after exercise, fever, posture, hyperglycemia, marked hypertension, congestive cardiac failure, and it may also be affected by the patient's state of hydration and the method of sample collection. It is well known that the presence of microalbumin in a diabetic patient indicates the presence of glomerular involvement in early renal damage. Recent research suggests that tubular involvement may occur before glomerular involvement, as several tubular proteins and enzymes can be detected before the appearance of microalbuminuria and a rise in serum creatinine. As a result, it would be better prognostically if we could detect Diabetic Nephropathy at an earlier stage, prior to the appearance of microalbuminuria.

Cystatin C is an endogenous cysteine proteinase inhibitor with a low molecular weight. The kidney is the primary site of Cystatin C catabolism, as glomerular

filtration removes more than 90% of Cystatin C from circulation. Because it is produced at a constant rate and completely removed from circulation by glomerular filtration and proximal tubule reabsorption, cystatin C has been proposed as a useful early marker for glomerular damage. Cystatin C level detection tests are not widely available (the immunoassay is expensive), and not all assays have been universally calibrated.

Tubular damage is indicated by urinary enzymes such as alkaline phosphatase, gamma glutamyl transferase, and lactate dehydrogenase. In the proximal tubule lumen, ALP and GGT are found in the luminal brush border of the epithelial cell membrane. Lactate dehydrogenases are found in cell cytoplasm and become more active before the onset of microalbuminuria. Tubular damage markers can serve as an early diagnostic marker for diabetic nephropathy because it occurs before glomerular damage. Urinary enzymes ALP, GGT, and LDH can serve as early markers for diabetic nephropathy, and tests to detect their levels are widely available and cost effective, reducing the burden on patients with lower socioeconomic status.

Methodology

The study was carried out at the Indes Medical College Indore among patients who attended the Medicine OPD, Department of Medicine, and the Department of Surgery. The study was carried out with the approval of the institutional scientific and ethical committee, and informed, written consent was obtained from all study participants. A total of 200 people took part in the study. The participants were assigned to one of three groups:

1. 60 diabetic patients identified using WHO/ADA criteria

2. 60 subjects were patients with early diabetic nephropathy, as defined by the presence of microalbuminuria, and

3. 60 age and gender matched healthy controls.

Data Collection:- Following an overnight fast and taking the standard safety procedures, a sample of five millilitres of venous blood was collected in a simple vial. A second urine sample in the form of a spot was taken in a clean container early in the morning. After allowing the samples to coagulate for a period of 30 minutes at room temperature, the serum was extracted by centrifuging the samples for 10 minutes at a speed of 1500 revolutions per minute. The serum that was collected in this manner was used for testing the following parameters:

fasting blood sugar, post-prandial blood sugar, serum urea, and serum creatinine. In accordance with the procedures outlined by the manufacturer, the samples were placed in appropriately labelled and aliquoted tubes before being chilled to a temperature of -200 degrees Celsius and kept in a refrigerator. The acquired urine samples will be put to use in the analysis of urinary creatinine, microalbumin gamma glutamyl transpeptidase, lactate dehydrogenase, and alkaline phosphatase levels.

Results

The total number of participants in the research group was 210. 70 of the 210 participants had a diagnosis of diabetes mellitus according to WHO/ADA criteria, 70 of the 210 subjects had an early diagnosis of diabetic nephropathy as determined by the presence of microalbuminuria, and 70 of the 210 subjects were healthy controls who were matched for age and gender.

In this study out of 310 respondents, 24.22 percent were between the ages of 35 and 45 years old, 26.88 percent were between the ages of 46 and 55 years old, 24 percent were between the ages of 55 and 65 years old, and 24 percent were over 65 years old.

The gender breakdown of those that participated in the study, There were a total of 210 individuals, and females made up 49% of the sample while males made up 51%.

In the current investigation, it was discovered that the urine levels of alkaline phosphatase in participants who had diabetes mellitus and diabetic nephropathy were substantially greater than in the group that served as a control (p value 0.01).

It was discovered that the urine levels of Gamma glutamyl transpeptidase in patients with diabetes mellitus and diabetic nephropathy were considerably greater than in the group that served as a control (p value less than 0.01).

In the current investigation, it was discovered that the urine levels of Lactate Dehydrogenase in participants who had diabetes mellitus and diabetic nephropathy were considerably greater than in the group that served as a control (p value 0.01).

The urine albumin creatinine ratio and urinary enzyme levels were not observed to have a significant association with one another.

There was not observed to be any significant association between serum cystatin C and urine enzymes.

Conclusions

This research was carried out with the purpose of determining whether or not there is a possibility for urine enzymes to serve as early markers of diabetic nephropathy. The ratio of urine albumin to creatinine and the levels of cystatin C in the serum were used to arrive at a diagnosis. All of the individuals in the study had their levels of the urine enzymes ALP, GGT, and LDH tested.

In comparison to the results of earlier studies, the levels of enzymes found in the urine of diabetic nephropathy patients were significantly elevated.

ubjects. Additionally, it was discovered that the levels of urine enzymes were higher in diabetes individuals who did not have nephropathy compared to non-diabetic participants; however, the difference was not statistically significant. Additionally, correlation analyses of urinary enzyme levels with albumin to creatinine ratio (urine) and cystatin C levels (serum) were carried out. The findings did not demonstrate any significant association (either positive or negative) between the enzyme levels and the previously identified indicators of diabetic nephropathy (ACR and cystatin C).

Both an elevated ratio of albumin to creatinine in the urine and elevated levels of cystatin-C in the serum are known to be indicators of glomerular damage. The findings of our research indicate that diabetic nephropathy predominantly has an effect on the glomerular function of the kidneys since elevated urine enzyme levels indicate that tubular dysfunction of the nephrons is present when the kidneys are affected.

Our findings lend credence to the hypothesis that glomerular destruction is the fundamental pathology in diabetic nephropathy, disproving the hypothesis that tubular dysfunction is present in the disease's early stages. Additionally, the study had a few shortcomings.

We were limited in our ability to follow up with the patients to check for shifts in the study's parameters in relation to the passage of time because of time constraints. Using the urine indicators, we were unable to determine whether or not there was a connection between the severity of diabetes and its longevity. Given the high and rising prevalence of diabetes mellitus in the current global context, it would have been helpful to produce a more trustworthy conclusion if

the sample size had been increased. It is possible that in the future prospective cohort studies will be carried out where similar parameters can be estimated. This would assist us in gaining a better understanding of the pathology of diabetic nephropathy, which is the most common and most dreadful of the complications that are associated with diabetes.

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