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A STUDY TO COMPARE SERUM LEVEL OF CYSTATIN C IN DIABETIC NEPHROPATHY AND HEALTHY SUBJECTS AT TERTIARY CARE HOSPITAL, BIKANER

Medical Biochemistry

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ABSTRACT

Diabetic nephropathy is defined as a clinical syndrome characterised by persistent albuminuria, decreases in GFR, raised arterial blood pressure and enhanced cardiovascular morbidity and mortality. Diabetic nephropathy is one of the most common micro vascular complications of diabetes. The aim of the study is to estimate the cystatin c level in Diabetic nephropathy and healthy control groups. It was an observational cross sectional study, carried out in Department of Biochemistry, S. P. Medical College and Department of Nephrology & associated groups of PBM Hospital, Bikaner and Rajasthan. 90 participants with diabetic nephropathy and 90 as healthy controls were enrolled. In this study, an analysis of blood Urea, serum Creatinine and serum Cystatin C was done in both the groups. We found that the mean blood urea, serum Creatinine, serum Cystatin C level were higher in participants with DN as compare to healthy control 135.31mg/dlvs33.77mg/dl, 3.45mg/dlvs0.96mg/dl, and 4.59µg/mlvs0.63µg/ml respectively and all the parameters were statistically significant ($p<0.001$). The correlation between Cystatin C and Creatinine was found to be 0.924. We conclude that, the serum cystain c can be used instead of serum creatinine in basic renal function test due to its ability to increase in the early stages of DN

KEYWORDS

Cystatin C, Diabetic Nephropathy, Diabetic Kidney Disease, Renal marker, Urea, Creatinine.

INTRODUCTION

Diabetic nephropathy is defined as a clinical syndrome characterised by persistent albuminuria, a relentless decline in GFR, raised arterial blood pressure and enhanced cardiovascular morbidity and mortality[1]. Diabetic nephropathy is one of the most common micro vascular complications of diabetes and gives rise to morbidity and mortality in diabetic patients[2].

According to IDA, globally the total number of people with diabetes is estimated to increase from 415 million (8.8%) in 2015 to 642 million (10.4%) in 2040. In US (2013-2016)[3], 40% patients with diabetes develop diabetic nephropathy[4].

Diabetic nephropathy progresses through a number of clinical stages, including nephrotic proteinuria, hyperfiltration, micro- and macroalbuminuria, and progressive chronic kidney disease that ultimately results in end-stage renal disease (ESRD). The final common route of DN is renal fibrosis. Numerous factors contribute to this fibrosis, such as aberrant glucose metabolism linked to oxidative stress, alterations in renal hemodynamics, inflammatory processes, and an excessive renin-angiotensin-aldosterone system (RAAS).

Stages Of Diabetic Nephropathy:-

A sequence of stages in the occurrence of renal changes in diabetes[5,6] is as following:-

- Stage1 is pre- nephropathy. The GFR is increased i.e. >=120 ml/min/1.73m^2.
- Stage2. Other name is silent nephropathy.
- Stage3. Also known as incipient nephropathy. In this, microalbuminuria (30-299mg/g of creatinine) with drop down in GFR (30-60 ml/min/1.73m^2) is present.
- Stage4 is Overt nephropathy. Macroalbuminuria (>=300mg/g of creatinine) or persistent proteinuria (>=0.5gm/24 hr) and GFR 15-30ml/min1.73/m^{2}are classical finding of this stage.
- Stage 5 is defined when ESRD reached with GFR <15 mL/min/1.73 m^2.

Cystatin C is a member of the human cystatin superfamily. It is found in all body tissues, fluids and a potent inhibitor of lysosomal proteinases and extracellular inhibitor of cystatin proteases. It is a low molecular mass protein that is freely filtered at the glomerular and then reabsorbed and fully catabolized, but not secreted by proximal renal tubules. In the past few years, Cystatin C has been proposed as a more reliable marker of renal function than serum creatinine[7]. It is also considered as an independent risk factor for all cause and cardiovascular mortality among elderly persons with chronic kidney disease or without renal impairment[8].

After evaluating the divergent research studies related to this disease and parameter, my study may highlight the risk of further kidney damage. Our findings will have an implication and improvement on monitoring of kidney function parameter and inflammatory markers.

METHODS

Study Design:- It is an observational cross sectional study.
Study Place:- This study was carried out in Department of Biochemistry, Sardar Patel Medical College and Department of Nephrology & associated groups of PBM Hospital, Bikaner and Rajasthan.
Study Population:- Subjects with diabetic nephropathy and healthy controls.
Sampling Technique:- Purposive Sampling Technique
Sample Size:- 90 Diabetic nephropathy cases and 90 healthy controls were included in this study.

Inclusive Criteria

- Clinically diagnosed with Type 2 Diabetes mellitus based on Fasting blood glucose level ≥126 mg/dl after 8 hour fasting or 2 hr PP glucose ≥200 mg/dl as per the criteria by ADA 2021[9].
- All had ≥ 30 mg/ml albumin in urine.
- Age between 45-70 years.

Exclusive Criteria

- Patients with previous history of liver disease, pulmonary disease, malignancy, pregnancy, coagulation abnormalities.
- Alcohol addiction and smoking habit.
- Type 1 diabetes
- Pregnant women.

Data Collection

Ethical approval certificate has been taken from institutional ethical committee. An informed consent was obtained from all participants those are diagnosed with diabetic nephropathy and healthy controls. From each participant following data was collected: Age, gender, other profile and Biochemical parameters, including complete physical examination of each participant were done very carefully.

Sample Collection and Processing:-

Blood sample was collected by venupuncture using aseptic technique and subjected to the following assays:-

- Serum Cystatin C :- Estimated by ELISA.
- Serum urea and Serum Creatinine:- Estimated by enzymatic method using fully auto analyzer.

Statisitcal Analysis

Data is entered in MS Office Excel work sheet in the form of master chart and analysis is performed with IBM SPSS. These data are classified and analyzed as per aims and objectives. Quantitative data is expressed in the form of Mean±SD. To compare categorical variables, the χ^2 test or t test are performed. Inference is drawn with the use of appropriate test of significance. Correlation of parameters is done using Pearson's correlation test. Result is considered as statistically significant if $p<0.05$.

Observation Tables And Graphs

Table 1: Comparison Of Mean Urea, Creatinine And Cystatin C Between Diabetic Nephropathy Group And Healthy Control Group

Subjects / Parameters	Controls (n=90) Mean±SD	Case (n=90) Mean±SD	P value
Urea (mg/dl)	33.77±12.61	135.31±35.16	<0.001*
Creatinine (mg/dl)	0.96±0.30	3.45±1.82	<0.001*
CYSTATIN C (µg/ml)	0.63±0.328	4.59±1.93	<0.001*

*Highly significant

Table 2: Correlation of CREATININE with CYSTATIN C in Diabetic Nephropathy

PARAMETER	CREATININE	p-value
CYSTATINC	0.924	0.001

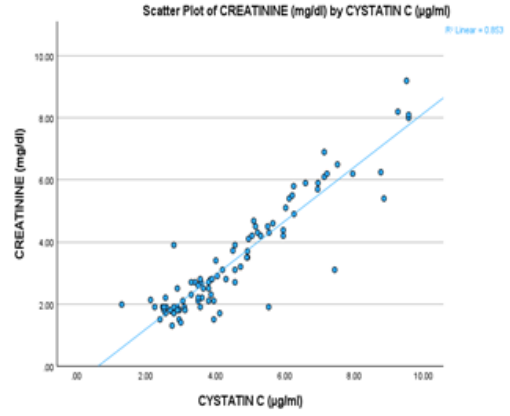

Figure 2:- Correlation of CREATININE with CYSTATIN-C in Diabetic Nephropathy Subjects.

RESULTS

Mean Urea level between Case and Control group was 135.31±35.16 mg/dl and 33.77±12.61mg/dl as observed in table 1. Its concentration is significantly higher in case group (p<0.001). These findings are in close agreement with the previous studies Akpinar[10] et al and Sun[11] et al which have suggested that impairment of urea level is because of reduction in kidney function in diabetic patients due to hyperglycemia induced damage led to become diabetic nephropathy.

In the same table, mean creatinine level was shown to be higher in DN group (3.45±1.82 mg/dl) in contrast to healthy group (0.96±0.30 mg/dl) which is statistically significant (p<0.001) as per the t-test. In light of our results, there is a positive asasociation between serum creatinine and DN which explains that there is insufficient filtration or incapability of kidney's to filter blood, and this has a similarity with other research articles of Takir[12] et al and Dejenie[13] et al et al.

Cystatin C level was also significantly elevated in case group as compare to control group that was 4.59±1.93 µg/ml vs 0.63±0.32 µg/ml with p value <0.001 as per the table 1. Our findings support the positive association between cystatin c and DN with p value <0.001 and was also concluded by Rina[14] et al and Elsayed[15] et al,. Thus, glomerular dysfunction in early stages of DN triggers serum cystatin c to rise. Slight change in its concentration can be crucial.

As per the table2 and figure 2, creatinine is positively correlated with cystatin c and r value for this is 0.924 (p<0.001).

DISCUSSION

Diabetic nephropathy is an under-recognised disesae as a worldwide burden of disease, the prevalence of DN is rising steadily in low to middle income countries with uneven growth. It has extended epidemic proportions worldwide. In early kidney dysfunction, renal cells become hypertrophied and leads to hyperfiltration but in this stage serum level of creatinine is not markedly elevates so diabetic nephropathy remains unidentified.

Analysis of mean urea level, creatinine and cystatin c were found considerably higher in DN subjects than healthy subjects (p<0.001). Thus, there is insufficient filtration or incapability of kidney's to filter blood in diseased state. It was indicated that glomerular dysfunction in early stages of DN triggers serum cystatin c to rise and even slight change in its concentration can be crucial.

As per my study, cystain c can be used instead of serum creatinine due to its ability to remain stable even in the change in muscle mass, presence of metabolites such as bilirubin, ketones and various drugs like antidiabetic medications and the most importantly it increases in the early stages of Diabetic nephropathy. To avoid untimely complication of diabetes and diabetic nephropathy one should actively try to add cystatin c as renal function marker for early renal dysfunction.

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