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Evaluation of Serum Levels of Cystatin C in patients of Type 2 Diabetes Mellituswith progression of nephropathyand healthy controls in north western regions of Punjab.

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Abstract

Diabetic nephropathy is classically defined by the presence of proteinuria, in the absence of other renal disease. It is a common problem that is most likely to occur in patients who have poor glycemic control, hypertension, glomerular hyper filtration, or a genetic predisposition. The lifetime risk of nephropathy is estimated to be equivalent in type 1 and type 2 diabetes. **Material and Method:** Our study was conducted on 50 Diabetic Patients type 2 with albuminuria and 50 healthy subjects in Department of Biochemistry and Department of Medicine Government Medical College Amritsar. Serum Cystatin C levels, Blood Urea, Serum Creatinine were estimated on both subjects and controls. Results were collected and analyzed statically. **Results and conclusions:** The p value of Serum Cystatin C both in Subjects and controls was <0.005 which is statically significance. This shows that the Cystatin C levels has a statical significance in progression of disease.

Keywords: Cystatin, Lysosomal, Blood Urea, Serum

Introduction

Diabetic nephropathy is a complication with high morbidity and mortality as well as a major cause of end-stage renal disease. Although glomerular dysfunction is thought to be a major factor for the development and progression of diabetic nephropathy, tubulointerstitial damage may also play an important role in the pathogenesis of diabetic nephropathy.[1,2] Recently, several studies have shown that some tubular damage markers have clinical implications as biomarkers for the nephropathy.[3,4]Cystatin C is a 13-kDa cysteine proteinase inhibitor and is produced by all nucleated cells at a constant rate.[5] In healthy subjects, cystatin C is almost freely filtered by the renal glomeruli and almost entirely reabsorbed in the proximal tubule like other low molecular weight proteins; there is no tubular secretion of cystatin C.[6] It has been shown that Cystatin C is able to modulate lysosomal protein turnover after cellular internalization via endocytosis, thereby indicating the role of Cystatin C in modulating target tissue homeostasis after cellular

reuptake *in vivo*. Moreover, Cystatin C also contributes to endothelial cell (EC) tubule formation and shows angiogenic characteristics *in vitro* Cystatin C is mainly removed from the blood stream by renal glomerular filtration, and is almost completely reabsorbed in the distal tubule without tubular secretion.[7] Unlike serum creatinine, Cystatin C is not susceptible to external factors such as age, diet, or body mass. Cystatin C has been shown to be superior to serum creatinine as a marker in assessment of renal function and improves estimates of glomerular filtration rate (GFR) compared to creatinine-based methods alone.[8,9] In addition, studies have suggested that Cystatin C could be an independent factor in the prediction of all-cause mortality, CVD and incident congestive heart failure in subjects with coronary heart disease (CHD).[10,11] Our study was conducted to assess the Serum levels of Cystatin C in Different groups of Diabetes Mellitus type 2 so that progression of disease can be studied in details. Permission from Institution Ethical Committee was taken before the study.

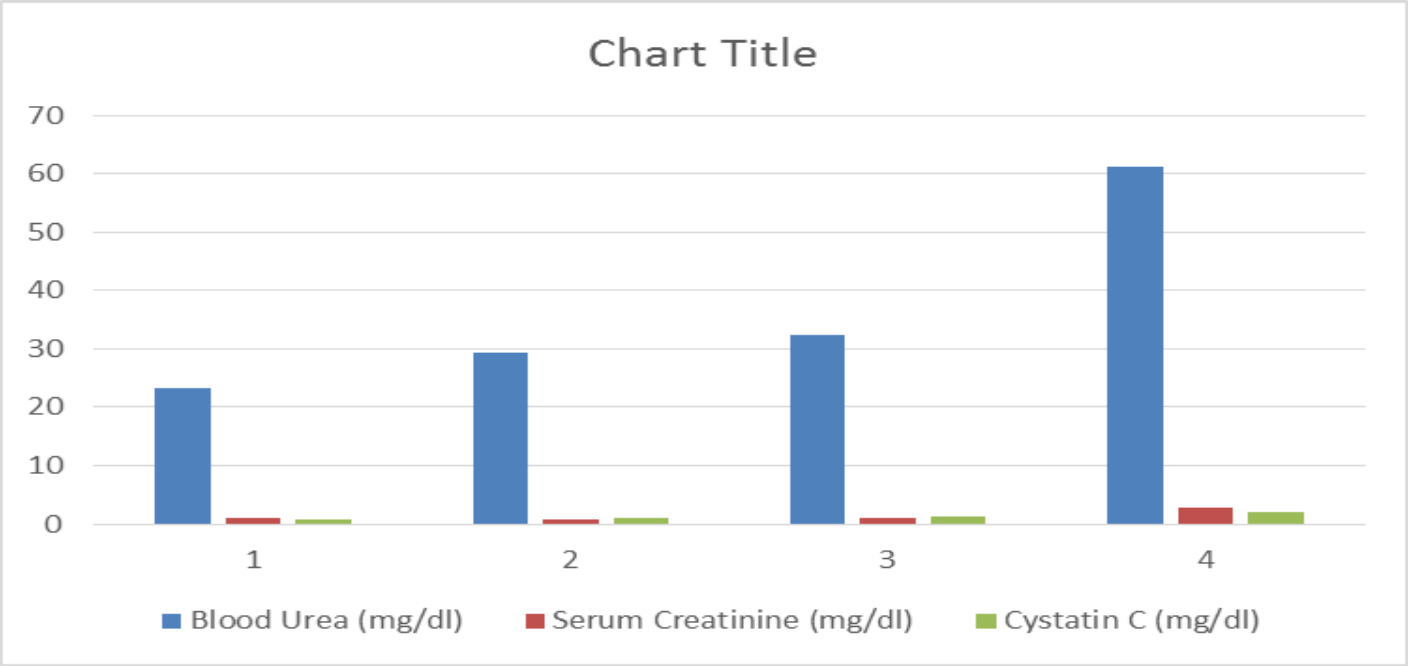
Material and Method

Our study was designed to be a comprehensive case control observational study and was conducted in Department of Biochemistry with collaboration of Department of Medicine Government Medical College Amritsar on 50 known cases of Type 2 Diabetes Mellitus with progression of nephropathy and age and sex matched normal individuals as controls. Cases were then divided in 3 groups depending upon presence of Micro albumin in Urine. 5 ml of venous blood was collected from both patients and controls and serum Levels of Cystatin C was estimated on ELISA. Blood urea and Serum Creatinine were also analyzed on Semiautoanalyzers. Results were collected and analyzed statically to find p value and significance.

Results

Table showing Blood Urea, Serum Creatinine, Serum Cystatin C in Controls and patients of Type 2 Diabetes Mellitus in different groups

Parameter	Control	Normoalbuminuria	Microalbuminuria	Macroalbuminuria	P value
Blood Urea (mg/dl)	23.35±5.91	29.41±8.9	32.45±9.22	61.21±26.56	<0.003
Serum Creatinine (mg/dl)	0.98±0.19	0.88±0.22	0.99±0.337	2.91±0.66	<0.002
Cystatin C (mg/dl)	0.88±0.33	0.91±0.34	1.24±0.43	1.98±0.55	<0.005



Discussion

Our study showed a stastical significance association of Serum levels of Cystatin C in patients of Diabetes Mellitus type 2 with different states of Micro albuminuria. The Mean value of Serum Cystatin C in Normoalbuminuria ,Microalbuminuria and Macroalbuminuria were 0.91+0.34,1.24+0.43,1.98+0.55 with p value 0.005.Some of the most important findings about Cystatin C are in the area of renal disease. Vijay *et al.*demonstrated that there was an increased urine Cystatin C level in T2DM with early diabetic nephropathy as compared to patients without nephropathy, and the increase of Cystatin C level was positively correlated with microalbuminuria.[12] Zhang *et al.* reported that serum Cystatin C was more sensitive than serum creatinine for estimation of GFR in T2DM.[13]Cystatin C is a good marker of incipient renal disease and represents an ideal endogenous index reflecting the GFR.[14] Serum Cystatin C could be a more precise indicator than serum creatinine because it is less affected by other factors, thereby reflecting renal function much more precisely inearly renal function lesions of T2DM.A recent study that included 523 T2DM patients revealed that, compared to the T2DM with non-subclinical atherosclerosis group, there was an increased serum Cystatin C level in the subclinical atherosclerosis group, and the concentration of Cystatin C was correlated with brachial-ankle pulse wave velocity, suggesting a potential role of Cystatin C in predicting arterial stiffness.[16] Other studies have also found an association of serum Cystatin C with vascular complications, carotid arterial wall elasticity and subclinicalatherosclerosis in T2DM.[16,17] A study by Vaduganathan*et al*. revealed that the renal biomarker of Cystatin C was independently associated with subsequent cardiovascular (CV) risk.[18]

Conclusion

Our study concluded that Serum levels of Cystatin C is associated with the progression of Nephropathy in Type 2 Diabetes Mellitus. There is a strong association with state of albuminuria with the serum levels of Cystatin C in Diabetes Mellitus Patients. So measuring the levels of Serum Cystatin C can decrease the progression of

Nephropathy in Type 2 Diabetes Mellitus patients but more studies are required on larger populations.

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