



## Evaluation of Serum Cystatin-C and Serum Creatinine Levels in Type-2 DM

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### Abstracts

*Type-2 diabetes has become the most common metabolic disorder in India and is a growing problem with over 40 million diabetic subjects. The "Asian Indian phenotype" is associated with increased insulin resistance, greater abdominal adiposity despite lower body mass index, lower adiponectin and higher high sensitivity C - reactive protein levels and makes Asians more prone to diabetes. Among Indians, the onset of type 2 diabetes occurs at a younger age and hence, they are vulnerable to all the complications of diabetes due to longer duration of the disease. An overnight fasting blood sample was collected from both cases and controls and the samples were centrifuged and separated for the estimations. Estimations of fasting blood glucose, blood urea and serum creatinine were performed using the serum. Estimation of serum cystatin C was done by immunoturbidimetric method. The mean age of cases in this study was  $56.16 \pm 10.47$  with a body mass index of  $25.7 \pm 4.15$ . The mean & S.D. of blood urea, serum creatinine & serum cystatin C were  $36.88 \pm 12.48$ ,  $0.98 \pm 0.32$  &  $1.61 \pm 0.45$  in cases. The study shows significant increase in serum cystatin C levels in diabetic individuals compared to controls. These finding that the measurement of serum cystatin C levels in type-2 DM as a marker of renal impairment.*

**Keywords:** Type-2 DM, cystatin C and marker of renal impairment.

### INTRODUCTION

Type-2 diabetes has become the most common metabolic disorder in India and is a growing problem with over 40 million diabetic subjects. The "Asian Indian phenotype" is associated with increased insulin resistance, greater abdominal adiposity despite lower body mass index, lower adiponectin and higher high sensitivity C - reactive protein levels and makes Asians more prone to diabetes. Among Indians, the onset of type 2 diabetes occurs at a younger age and hence,

they are vulnerable to all the complications of diabetes due to longer duration of the disease.

DM is a metabolic disorder resulting from insufficient insulin secretion, inefficient insulin action or both and covers a wide range of heterogeneous diseases<sup>1</sup>. The prevalence of diabetes is rapidly rising all over the globe at an alarming rate. Although there is an increase in the prevalence of type-1 diabetes, the major driver of the epidemic is the more common form of diabetes, namely type-2 diabetes accounting for more than 90% of all cases<sup>2</sup>.

Diabetic complications result from the toxic effects of chronic hyperglycemia combined with other metabolic derangements. Persons with diabetes are at substantial risk for tissue injury in organs supplied by an endarterial system due to microangiopathy. These microvascular complications include nephropathy, retinopathy and neuropathy<sup>3</sup>. Diabetes is the most common cause of End Stage Renal Disease (ESRD). Approximately 40% of patients with type-1 and 15% of patients with type-2 Diabetes eventually develop ESRD<sup>4</sup>.

In type-2 diabetes, Hyperglycemia starts after forties, usually when the kidneys have already suffered the long term consequences of ageing and other recognized promoters of chronic renal injury like arterial hypertension, obesity, dyslipidemia and smoking<sup>5</sup>. Diabetic nephropathy refers to a characteristic set of structural and functional kidney abnormalities in patients with diabetes. The structural abnormalities include hypertrophy of the kidney, increase in glomerular basement membrane thickness, nodular and diffuse glomerulosclerosis, tubular atrophy and interstitial fibrosis. The functional alterations include an early increase in glomerular filtration rate with intraglomerular hypertension, subsequent proteinuria, systemic hypertension and eventual loss of kidney function<sup>6</sup>.

Although microalbuminuria is the first detectable functional abnormality, Glomerular Filtration Rate (GFR) is the critical renal function<sup>7</sup>. The gold standard for estimation of GFR is clearance of endogenous substances such as inulin, ioxheol, <sup>57</sup>Cr EDTA, <sup>99m</sup>TcDTPA or [<sup>125</sup>I] iothalamate. These techniques are time consuming, labour intensive, expensive and require administration of substances that make them incompatible with routine monitoring<sup>8</sup>. The ideal marker of GFR should be an endogenous molecule which being produced at a constant rate is cleared solely by the kidneys via free glomerular filtration, being neither secreted by tubular cells, nor reabsorbed into peritubular circulation<sup>8</sup>.

Measurement of serum creatinine is simple but the general view is that up to 50% of GFR can be lost before significant elevation of serum creatinine occurs<sup>9</sup>. It also has significant limitations due to inter individual variation in muscle mass and tubular secretion of creatinine. As a result serum creatinine has a poor sensitivity for mild renal dysfunction and in elderly patients, with subsequent under recognition of renal impairment<sup>10</sup>. Cystatin C, a Cysteine protease inhibitor is freely filtered by the renal glomeruli, metabolized by proximal tubule and identified as a promising marker of renal failure. Cystatin C is produced at a constant rate by nucleated cells and released into the blood stream with a half-life of 2 hours. Its concentration is almost totally dependent on GFR, independent from height, gender, age and muscle mass id advantageous<sup>11</sup>.

These findings suggest that the measurement of serum cystatin C levels in type-2 DM as a marker of renal impairment.

## MATERIAL AND METHOD

The study will comprise cases of Type 2 Diabetes Mellitus visiting the inpatient and outpatient of G. R. Medical College Gwalior (M.P.) A part of the analysis of blood has been carried out at Laboratory Medicine, Department of Biochemistry, Medanta-The Medicity Hospital, Gurgaon.

**Study Design:** The study shall be carried out in 300 subjects out of which 100 subjects treated as controls groups and 200 subjects shall be of Type 2 Diabetes Mellitus. Suffering from nephropathy. Age and sex matched healthy volunteers will serve as controls.

**Inclusion criteria:** Cases of Type 2 Diabetes Mellitus suffering from nephropathy, hypertension, obesity etc.

**Exclusion criteria:** Patients on Glucocorticoids, nephrotoxic drugs, endocrine disorders, rheumatoid disease, malignancy, fever, dehydration.

Before starting analysis the written consent from all subjects were taken. The study (synopsis) was approved by institutional ethical committee and was carried out by keeping all norms in mind.

The clinical manifestations of disease, personal history of patients were recorded in study proforma.

### Collection of Blood Sample

An overnight fasting blood sample was collected from both cases and controls and the samples were centrifuged and separated for the estimations. Estimations of fasting blood glucose, blood urea and serum creatinine were performed using the serum. Estimation of serum cystatin C was done by immunoturbidimetric method.

### Statistical Analysis

Data were analyzed by SPSS student t-test and one way ANOVA. A P-value <0.05 was considered statistically significant.

## RESULTS AND DISCUSSION

In the present study, a total of 200 cases and 100 controls were studied. Table 1 shows the Basic characteristics of study population and Table 2 shows the Comparison of Blood Urea, Sr. Creatinine and Sr. Cystatin C between cases and controls.

**Table No. 1** Basic characteristics of study population:

Parameters	Cases (n=200)	Controls (n=100)
Age (Years)	56.16±10.47	50.2±10.3
BMI kg/m <sup>2</sup>	25.7±4.15	22.04±1.4

**Table No. 2** Comparison of Blood Urea, Sr. Creatinine and Sr. Cystatin C between cases and controls:

Parameters	Cases (n=200)	Controls (n=100)	P- Value
Urea mg/dl	36.88±12.48	29.89±8.73	<0.0001
Creatinine mg/dl	0.98±0.32	0.81±0.14	<0.0001
Cystatin C mg/dl	1.61±0.45	0.64±0.18	<0.0001

(Statistically significant P value <0.05)

The mean age of cases in this study was 56.16±10.47 with a body mass index of 25.7±4.15 (Table 1). This is comparable to studies by Punyakrit Deb et al.<sup>12</sup> and Nazmu Saquib et al.<sup>13</sup>. The mean & S.D. of blood urea, serum creatinine & serum cystatin C were 36.88±12.48, 0.98±0.32

& 1.61±0.45 in cases. The study shows significant increase in serum cystatin C, serum creatinine and blood urea levels in diabetic individuals compared to controls. These findings are similar to a study conducted by Borges et al.<sup>14</sup>. There was a positive correlation between serum cystatin C and serum creatinine (r= 0.17) among cases in this study. This is in conformity with a study done by Buysseheart M et al. Who found a linear relationship between serum cystatin C and serum creatinine (r=0.92).<sup>15</sup> Gold standard methods of assessing GFR are replaced by an estimated GFR derived from, endogenous substances. Serum creatinine is the most widely used substance to estimate GFR. Creatinine concentration is influenced by sex, age diet and muscle mass. It only increases once GFR reduction of about 50% is present. This leads to falsely high or low values, limiting its usefulness as an ideal marker of GFR.<sup>16</sup> Cystatin C is a low molecular weight protein produced at a constant rate by all nucleated cells. It is freely filtered by glomerulus, completely reabsorbed and catabolized in the proximal tubule. Serum cystatin C is reported to be modulated by several non-renal factors like steroids, thyroid status, smoking, C-reactive protein and malignancy. Despite these limitations evidence continues to suggest superiority of serum cystatin C when compared with serum creatinine in patients with early and moderately decreased renal function.<sup>7,8</sup> The present study showed that the serum cystatin C can be used as a marker for determining GFR in type-2 DM compared to serum creatinine.

## CONCLUSION

These findings suggest that the serum cystatin C was a good marker of impaired renal function and its more sensitive marker in most study groups when compared with creatinine. Cystatin C had a good correlation with creatinine. Further studies can be done with higher sample size using other parameters like urine microalbumin and gold standard methods for better evaluation of cystatin C as a marker of renal impairment.

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