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ROLE OF CYSTATIN C IN DIABETIC NEPHROPATHY

[1] Bhagwan Singh Meena, [2] B.K. Agarwal, [3] Mahesh Kumar, [4] MS Chandel
[1,2,3] Department of Biochemistry, Index Medical College, Indore. India
[4] Academic Registrar, Index Medical College, Indore, India
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Corresponding author: Mahesh Kumar

Abstract:
Background: Diabetic Nephropathy is consider as one of the major micro-vascular problems of diabetes mellitus and has become the most general single factor of end stage of kidney disease. It is defined traditionally by kidney morphological and modification like: glomerular hyper filtration, glomerular and kidney hypertrophy, increased urinary albumin excretion (> 300 mg/24 hours), increased GBM (Glomerular Basement Membrane) thickness and mesangial expansion and also accumulation of extracellular proteins comprising laminin, collagens and fibronectin worldwide. Cystatin C is a low molecular weight protein and freely filtrates by kidney. Cystatin c doesn't affected via age, sex, weight and diet.
Objective of the study: The role of cystatin c level in early detection of DN.
Materials and methods: The investigation was conducted on 100 DN subjects of both sex and aged 20 or more and 100 age and sex matched healthy control subjects. Cystatin C of each subject was measured in untimed serum specimens.
Results: the present investigation shows that the cystatin c in serum was elevated significantly in DN individuals as compared to controls.
Conclusion: This study concluded that the cystatin C could be better serum marker for early recognition of DN.
Keywords: Diabetic nephropathy (DN), Cystatin C**,** Kidney disease

Introduction

Diabetic Nephropathy (DN): DN is treated as one of the chief micro-vascular complications of diabetes mellitus and has become the most commonly single factor of end-stage of kidney disease. It is delineated commonly by renal morphological and function activity alterations like; glomerular and kidney hypertrophy, glomerular hyper-filtration, elevated glomerular basement membrane (GBM) thickness, elevated urinary albumin excretion (> 300 mg/ 24 hours), and mesangial expansion and also aggregation of extracellular proteins comprising laminin, collagens and fibronectin).1,2,3 In 2015 the pervasiveness of diabetes was 8.8%, ages from 20 to 70 years affecting a people of about 440 million populations by the year 2035.[4] The main clinical features of diabetes is chronic tissue damage. For short-term elevation in hyperglycemia doesn't show in severe clinical problems. The duration and severity of hyperglycemia is the major causative factor in initiating organ damage.

About 2/3 of the patients with diabetic nephropathy develop ESRD or renal failure requiring either dialysis or renal transplantation. In the US the DN is the most general element of ESRD or chronic kidney failure and reports that for > 1/3 of subjects entered in long-term dialysis curicculums.[5] Patients with nephropathy frequently develop other complications, in particularly cardiovascular disease including hypertention and stroke, resulting in increased risk of early mortality.[6,7] In subjectswho have type 1 diabetes, forty years after onset of the disease, the mortality rate is 90% for those patients with nephropathy but only 30% for those patients without renal disease.[7] Hence, kidney problems of DM are crucial, glomerulosclerosis and vascular disease are the most essential factors of renal failure in the diabetic subjects.

Cystatin C: Cystatin C (also cystatin 3; formerly *gamma* trace, post-*gamma* globulin, neuroendocrine basic polypeptide) is a monomeric 13.3 kDa globular, nonglycosylated protein. It has a high isoelectric point (pI=9.3) and in all bodily fluids, is positively charged. The third amino acid residue, proline, is hydroxylated to hydroxyproline in approximately every second cystatin C molecules. No other posttranslational modifications occur, physiologically.[7]

Chromosome 20 is the place where gene cst3 lodges, is actually the code for human cystatin C.[9] transcript possess a N-terminal hydrophobic signal, by sequence of 26 amino acids. Which is divided before secretion of the 120 amino acid polypeptide.[10] Its level is highest of all known LMW (approximately 13.3 kiolodalton) cystatins. In all human ECF its value approximately can be 1-10 mg/L.[11,12] The concentration of cystatin C in urine is remarkably lower, approximately 0.1 mg/L.[13,11]

Cystatins are reversibly binding, non-covalent, competitive inhibitors of cysteine proteinases/peptidases of the papain family (C1), and some - like cystatin C - also inhibit legumain family proteases (C13).[14,15] The cystatin C is primarly inhibit cysteine proteinases of host and microbial origin occurs in extracellular fluid.[14,10] In humans, cystatin C is a most important cysteine protease

inhibitor in cerebrospinal fluid (~8 mg/L), milk (~3 mg/L) and seminal plasma (~50 mg/L).[11,12] In plasma, kininogen and *alpha*-2-macroglobulin are more abundant cysteine protease inhibitors.[12]

Cystatin C is active as a monomer. It may, however, undergo dimerization through domain swapping, and the formed dimer is inactive.[16,17] During intracellular trafficking, prior to secretion from the endoplasmic reticulum in a monomeric form, the precursor of cystatin C is transiently dimerized and becomes inactive.[18]

According to current data, diagnostic role of cystatin C may be categorized in three classes:

1. The cystatin C is a biomarker of kidney function.

2. It may show a role in prediction of cardiovascular disease.

3. In neurological disorders.

The present investigation was undertaken to find out whether serum cystatin C is increased in DN & compared with a group of healthy subjects.

Materials and methods:

The investigation was conducted on 100 DN subjects of both sex and aged 20 or more and 100 age and sex matched healthy control subjects. An untimed blood sample was collected from each subject without adding any preservatives. Immediately after collection, turbidimetric immunoassay quantitatively analyzed the serum samples for cystatin C.

The mean (± SD) cystatin C of test group (DN subjects) was compared with that of control group by Student's unpaired t test. A p value of less than 0.05 was considered as significant.

Results:

Table: 1 Shows statistical analyzes projected that the Cystatin C of diabetic nephropathy patients found to be significantly elevated.This was observed that the average (mean ± standard deviation) Cystatin C concentration was found in the control group was 0.68 ± 0.16 and in the test group, it was 2.57 ± 1.75. The Cystatin C level was found significantly higher comparison to that in the control group, with a p value of < 0.001.

Table 1: Cystatin C in control group (healthy subjects) and test group (DN). All the values are mean ± SD.

	Control group	Test group	P value
Cystatin C	0.68 ± 0.16	2.57 ± 1.75	<0.001*

* Highly significant

** Non-significant

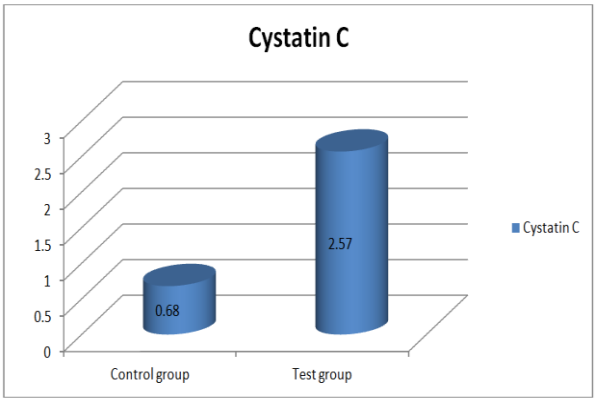

Figure 1: Cystatin C in control group (healthy subjects) and test group (DN).

Discussion and Conclusion

In the present study, the mean cystatin C concentration was found to be significantly higher in the DN as compare to control group.

Guo et al., (2017)[19] suggested that the elevated Cys C level in initial stage of DN and also reported that urine albumin, glomerular filtration dysfunction and Hcy level also increase.

Gupta et al., (2017)[20] suggested that the for nephropathy and decreased renal function in diabetic subjects, the serum Cystatin C level can be used as an early marker, than microalbuminuria and serum creatinine are generally used marker.

Takir M et al., (2016)[21] concluded cystatin-C concentration in serum was reported as a useful early detection marker in patients who have diabetic nephropathy.

Kachhawa et al., (2016)[22] concluded that the serum cystatin C determination is a useful and early detection marker for the evaluation of renal disease in the course of diabetes patients.

Our results are in conformity with these four previous reports. As the subjects included in the present study were otherwise healthy, the increased cystatin C could only be due to DN. Increase in serum cystatin C could be an early indicator of DN. This shows that DN individuals should be screened for cystatin C could be a quick and convenient alternative technique.

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