

Original research article

Assessment of Prognostic markers of Diabetic Nephropathy- Serum Creatinine and Blood Urea Levels in Diabetes mellitus and healthy individuals at tertiary care hospital

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Abstract

Introduction: Diabetes being a chronic progressive disorder severely affecting the end organs like nerves, eyes and kidneys. Hence, diabetic patients are at an increased risk of developing specific complications like nephropathy, retinopathy, neuropathy, and atherosclerosis. Diabetic nephropathy occurs in approximately one third of Type 2 diabetic patients. In diabetic nephropathy, a number of serum markers are deranged. Out of which, plasma creatinine and urea are early indicators of disease progression leading to complications. The morbidity and mortality caused by diabetes mellitus can be reduced by regular screening, early detection, and appropriate treatment of chronic complications. Plasma creatinine and urea are useful clinical tools in assessing renal function.

Objectives: This study is undertaken to measure blood glucose, serum creatinine and blood urea levels in Type 2 diabetic patients and to compare it with non-diabetic subjects. This study aims to signify the role of measuring filtration markers i.e. plasma creatinine and urea levels in assessing renal function.

Material and method: A cross sectional study was done from September 2019 to December 2019. This study included 50 known cases of type II diabetes mellitus attending diabetic Out Patient Department at Sarojini Naidu medical college, Agra of age 40-60 years with duration of 5-10 years and 50 non diabetic healthy controls fulfilling the inclusion criteria.

Biochemical investigations included fasting blood glucose, serum creatinine and blood urea. Statistical analysis was done by using SPSS Software.

Observation and results: The mean values of blood glucose levels (fasting and postprandial) in Group 1 and Group 2 were 140.5 ± 64.98 and 88.58 ± 7.64 and 170.05 ± 65.83 and 123.67 ± 9.25 respectively. Serum creatinine levels in Group 1 and Group 2 were 1.68 ± 0.44 and 0.88 ± 0.11 and blood urea levels in Group 1 and Group 2 were 41.56 ± 6.60 and 29.7 ± 6.09 respectively.

There was a significant increase in blood glucose concentrations, plasma creatinine and urea concentrations in diabetic patients when compared to non diabetic subjects.

Conclusion: The study concluded that in addition to increased blood glucose level in Type 2 diabetes mellitus, plasma creatinine and urea concentration are also significantly increased when compared with non diabetic subjects.

Key words: Diabetes Mellitus, Blood Glucose, Serum Creatinine, Blood Urea

Introduction

Diabetes mellitus is a heterogeneous group of metabolic disorders characterized by hyperglycemia with disturbances of carbohydrate, fat and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin.¹

The worldwide prevalence of Diabetes Mellitus has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 285 million in 2010. Based on current trends, the International Diabetes Federation projects that 438 million individuals will have diabetes by the year 2030. Although the prevalence of both type 1 and type 2 Diabetes Mellitus is increasing worldwide, the prevalence of type 2 Diabetes Mellitus is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population. Diabetic nephropathy is the leading cause of End Stage Renal Disease (ESRD) in the United States and a leading cause of DM-related morbidity and mortality^{1,2}

After many years of diabetes, if blood sugar is poorly controlled, the delicate filtering system of the kidneys starts getting destroyed, initially becoming leaky to larger blood proteins such as albumin which are then lost in urine, a stage known as albuminuria. As the amount of albumin in the urine increases, the kidneys filtering function usually begins to drop, resulting in retention of various wastes in body^{2,3}. The most common lesions involve the glomeruli and are associated clinically with three glomerular syndromes, including non nephritic proteinuria, nephritic syndrome, and chronic renal failure. Diabetes affects the kidney in stages. At the onset of diabetes, the kidneys grow large and the glomerular filtration rate becomes disturbed. The early detection of diabetic nephropathy resulting in timely intervention with particular to glycemic control, can improve long term outcome and retard progression to ESRD. Blood tests for blood urea and creatinine are the simplest way to monitor kidney function⁴ These substances are normal metabolic waste products that are excreted by kidneys. Urea is a by product of protein breakdown. In kidney diseases, these substances (as well as numerous others) are not excreted normally, and so they accumulate in the body thus causing an increase in blood level of urea and creatinine^{3,4}.

Creatinine is formed from creatine. Muscle contains 98% of total body creatinine. Creatinine leaves muscle and enters blood from where it is removed by kidneys. If the kidneys are failing, serum creatinine levels increase.⁵ The use of serum creatinine as a marker of glomerular filtration originated from the work of Rehberg in 1926⁶ Plasma creatinine is a more sensitive index of kidney function compared to plasma urea level because its level change a little except in renal disease and creatinine fulfils most of the requirements for a perfect filtration marker. A quick and simple way to check renal function in diabetics is to draw blood sample for serum creatinine and urea tests. These tests should be performed when patients are diagnosed as diabetics and at time of follow up. Early detection of renal damage may help to delay the process^{5,7}.

The morbidity and mortality caused by diabetes mellitus can be reduced by regular screening, early detection, and appropriate treatment of chronic complications. This study aims to signify the role of measuring plasma creatinine and urea levels in diabetes mellitus. This can help in identifying the earlier and asymptomatic stage of diabetic nephropathy so that suitable preventive measures can be taken.

Therefore, this study was undertaken to measure plasma glucose, creatinine and urea concentrations in type 2 diabetic patients and to compare it with non diabetic subjects, as creatinine and urea concentrations are useful clinical tools in assessing renal function.

Materials and methods

A cross sectional study was undertaken in the Department of Physiology in collaboration with Department of Biochemistry and Department of Medicine, Sarojini Naidu Medical

College and hospital, Agra, India for 4 month duration from September 2019 to December 2019 in 100 subjects who fulfilled the study protocol.

Sample size

This study was done from September 2019 to December 2019 and 100 subjects of both sexes who fulfilled the inclusion criteria were taken for study. Of them, patients of 40-60 years of age with a history of diabetes since 5-10 years attending the diabetic OPD were selected. Diabetes in this study was defined based on laboratory findings of a fasting and post prandial plasma glucose levels. The healthy individuals of same age and sex matched attending the outpatient department and staff members were taken as control and their fasting blood sugar was performed before start of study to confirm they are non diabetics.

Inclusion and exclusion criteria:

Subjects included in the study were divided into 2 Groups:

Group-I: 50 Type 2 diabetes mellitus patients of both sexes, of age group 40-60 years.

Group-II: 50 Non-diabetic healthy subjects, of both sexes, of age group 40- 60 years as a control group.

Patients with diseases such as muscle dystrophy ,dehydration, glomerulonephritis pyelonephritis, eclampsia and preeclampsia, rhabdomyolysis that have higher than normal plasma creatinine and urea levels were excluded from the study, also the patients on certain drugs that may affect the test were excluded from the study. These drugs include aminoglycosides, cimetidine, heavy metal chemotherapy drugs (e.g. cisplatin) and nephrotoxic drugs (e.g. cefoxitin). A written and informed consent was obtained from each participant and procedure explained in their mother tongue. Ethical permission was taken from institutional ethical committee.

Table 1: Blood sugar levels (fasting and post prandial) study groups⁸:

Parameters (mg/dl)	Non diabetics	Diabetics
Fasting Plasma Glucose	70-110 mg/dl	≥126 mg/dl
2-h Plasma Glucose	110-140 mg/dl	≥200 mg/dl

Blood sample collection and analysis

Blood samples of all these subjects were collected to study the parameters such as blood urea and serum creatinine with relation to blood sugar level. Under aseptic conditions 2ml of the patient's intravenous blood was collected for measuring serum creatinine, fasting blood glucose and serum urea. For biochemical investigations serum was separated by centrifugation at 4000 rpm for 10 minutes and analysed on same day.

Blood sugar levels were estimated by glucose oxidase and peroxidase method (GOD- POD) end point assay method⁹. Blood urea was estimated by Urease-Berthelot's method¹⁰ while serum Creatinine was estimated by Alkaline Jaffe's Picrate method¹¹. The normal range for blood sugar levels, fasting is 70-110 mg/dl, post prandial is 110- 140 mg/dl. Similarly, the normal range for blood urea is 6-20 mg/dl (< 60 years) and 0.9-1.3 mg/dl and 0.6- 1.1 for serum creatinine in males and females respectively.¹²

Statistical analysis

The data collected was analyzed using Microsoft excel 2007. The data was analysed and compared by using unpaired student 't' test. The values were expressed as mean \pm SD. A p value of <0.05 was considered to be statistically significant. A p value of < 0.001 was considered to be statistically highly significant.

Results and observations:

Table 2: Comparison of blood urea and serum creatinine levels in diabetics and non – diabetics.

Parameters	Group I n=50	Group II n= 50
Raised serum urea(mg/dl)	14	0
Raised serum creatinine (mg/dl)	19	2

Group 1- Diabetics, Group 2- Non diabetic subjects

Out of the 50 non diabetic subjects, all of them had normal urea levels and only 2 had abnormal serum creatinine levels. The raised creatinine in normal subjects is likely due to increased muscle mass and high protein meal intake. Out of the 50 diabetic subjects, 14 of them had raised serum urea levels and 19 had raised serum creatinine levels. (Table 2)

Table 3: Plasma glucose, Serum Creatinine and blood urea concentrations in Type 2 diabetes mellitus and non - diabetics.

Parameters(mg/dl)	Group I n = 50 Mean \pm SD	Group II n = 50 Mean \pm SD	'P' value
Blood Glucose (fasting)	140.5 \pm 64.98	88.58 \pm 7.64	< 0.0001 (HS)
Blood Glucose (Post prandial)	170.05 \pm 65.83	123.67 \pm 9.25	< 0.0001 (HS)
Serum creatinine	1.68 \pm 0.44	0.88 \pm 0.11	< 0.0001 (HS)
Blood urea	41.56 \pm 6.60	29.7 \pm 6.09	< 0.0001 (HS)

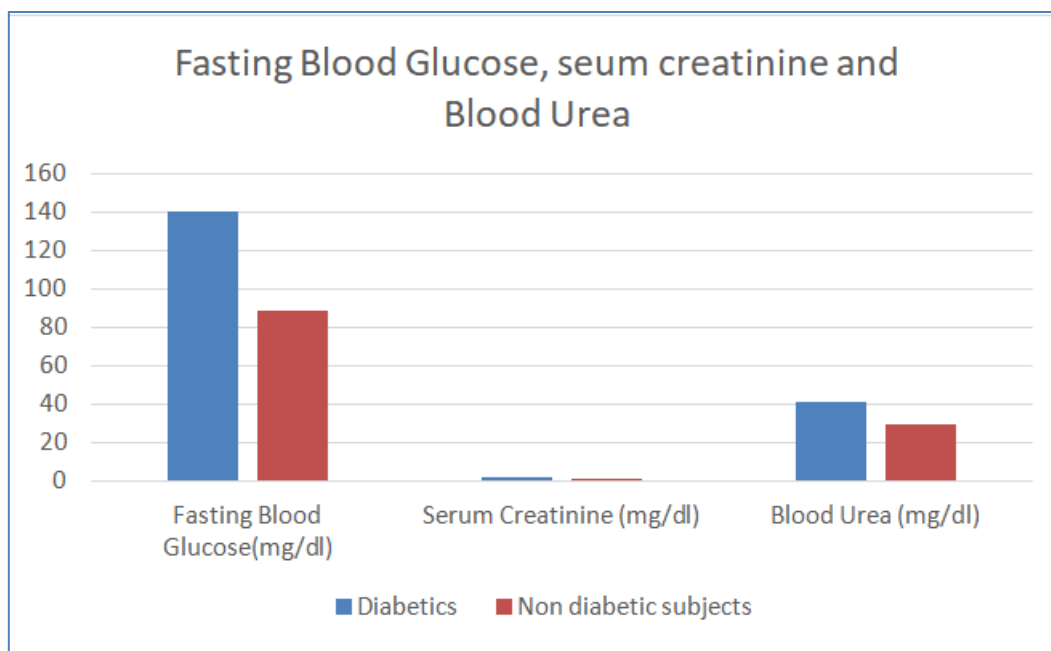
Group 1- Diabetics, Group 2- Non diabetic subjects, HS- Highly Significant SD- Standard Deviation

1. The mean values of fasting blood glucose levels in Group I and Group II were 140.5 \pm 64.98, 88.58 \pm 7.64 respectively; the increase was statistically highly significant ($p < 0.0001$). (Table 3)

2. The mean values of blood glucose levels (post prandial) in group I and group II were 170.05 \pm 65.83 and 123 .67 \pm 9.25 respectively. The increase was statistically highly significant ($p < 0.0001$). (Table 3)

3. The mean values of serum creatinine levels in Group I and Group II were 1.68 \pm 0.44, 0.88 \pm 0.11 respectively. The increase was statistically highly significant ($p < 0.0001$). (Table 3)

4. The mean values of blood urea levels in Group I and Group II were 41.56 \pm 6.60, 29.7 \pm 6.09 respectively. The increase was statistically highly significant ($p < 0.0001$). (Table 3)



Graph 1: Showing mean blood glucose, serum creatinine and blood urea in study groups

Discussion

In the present study, blood glucose, serum creatinine and blood urea levels were measured in total 100 subjects of both sexes in the age group 40-60 years.

There was an increase in blood glucose, serum creatinine and blood urea levels values in diabetic group.

When diabetics were compared with non-diabetic subjects, it was found that the diabetic group had increased blood glucose, serum creatinine and urea levels. This difference was found to be statistically significant. (Table 1), indicating the derangement of kidney function. This hints towards the burden of kidney disease in type 2 diabetes mellitus. High blood sugar levels damage million of nephrons resulting in inability of kidneys to maintain fluid and electrolyte homeostasis. Creatinine is filtered by glomerulus and thus ,serum creatinine level is considered as an indirect measure of glomerular filtration. Diminishing of glomerular filtration rate results in rise of plasma concentrations of serum creatinine and urea. The rate of increase and the final concentration of serum creatinine depend on many factors including severity and time course of resolution of renal injury, rate of generation of creatinine, volume of distribution of creatinine and extra renal elimination^{13,14}.

Alder et al (2003) demonstrated that raised plasma creatinine and urea levels in diabetic patients may indicate a pre renal problem such as volume depletion. Wagle (2010) in their submission suggested that high creatinine levels in diabetic patients may be due to impaired function of nephrons and high urea leaves in diabetic patients could be attributed to a fall in the filtering capacity of the kidney thus leading to accumulation of waste products within the system.⁵

Kasper Rosing et al studied progression of nephropathy in type 2 diabetes mellitus in 2004, according to this study, diabetes mellitus type 2 is single most common cause of end stage renal disease but decrease in kidney function varies among individuals.¹⁵

Bauza, Mosquera A (2003) suggested that hyperglycemia is one of the major causes of progressive renal damage. An increase in urea level and creatinine level is seen when there is damage to the kidney or kidney is not functioning properly. Research conducted by

Anjaneyulu et al 2004 had found that increase urea and serum creatinine in diabetic rats indicates progressive renal damage.¹⁶

According to Mitch and Walser (1986) if a graph of reciprocal of plasma creatinine is plotted over time; a straight line will be obtained. Thus if a patient is losing kidney function at a constant rate, one could be able to extrapolate the graph out of time and get a rough idea of when kidney will fail completely and when initiation of dialysis may be required and to determine efficacy of treatment to halt progression of renal failure. Plasma creatinine is also helpful in recognizing when there is an acute drop in kidney function in addition to chronic loss. Thus plasma creatinine is used for monitoring disease progression.¹⁷

Conclusion

Diabetes Mellitus is the major cause of renal morbidity and mortality and diabetic nephropathy is one of the causes of chronic kidney failure. Blood urea and creatinine are widely accepted to assess the renal functions as they are established markers of glomerular filtration rate. These tests should be performed when patients are diagnosed as diabetics and at time of follow up, annually. Early detection of renal damage may help to delay the process. Good control of blood glucose level is absolute requirement to prevent progressive renal impairment. This study will be very helpful to clinicians to begin necessary medical therapy where needed at the earliest.

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