



Research Article

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Study of Serum urea and Creatinine in Diabetic and non-diabetic patients in in a tertiary teaching hospital

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Abstract

Introduction: Diabetes is on the rise worldwide and India has more number of diabetics with more than 60 million people diagnosed to suffer from the disease in 2013. Approximately 20% to 30% of all diabetics will develop evidence of nephropathy, although a higher percentage of type 1 patients progress to end stage renal disease. Diabetic nephropathy (DN) is characterised by macro albuminuria and abnormal renal function as represented by a reduction in glomerular filtration and rise in serum urea and creatinine. **Aim & Objectives:** The aim of this study was to study the relationship between blood levels of urea and creatinine with blood glucose levels in diabetic and non-diabetic subjects for their utility in diagnosis of diabetic nephropathy and their comparison with glycemic status. **Material and Methods:** Diabetic and non-diabetic subjects; 100 in each group; attending out- patient department during 15 May to 15 September 2015 were studied. Patients with known kidney disease were excluded. Blood samples were analysed for blood sugar (glucose), serum urea and creatinine to determine presence of kidney disease and hyperglycemia on basis of reference laboratory standards in the institute. **Results:** Out of 100 diabetes samples, 18 had high urea level whereas 15 had increased creatinine level. In control group of 100 sample, there was no one with high urea value and 2 had high creatinine level. There was statistically significant increase in urea level with increased blood sugar level ($p < 0.05$, 95%CI). **Conclusion:** Serum urea and creatinine are useful, simple biomarkers as predictor and prognostic tests of renal failure in diabetic patients, despite some limitations.

Keywords: Blood urea, Creatinine, Diabetes, Nephropathy, Proteinuria.

INTRODUCTION

Diabetes mellitus is characterized by chronic hyperglycemia due to derangement in carbohydrate, fat, and protein metabolism. Diabetes mellitus is associated with absolute or relative deficiencies in insulin secretion, insulin action or both.^[1] Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease.^[2] Diabetic nephropathy affects 30% of all diabetics and it is a leading cause of end stage renal disease. Assessment of a patient's renal function may be used for two different purposes. One is to diagnose impaired renal function, and the other is to detect the presence of a progressive loss of renal function. Diabetic nephropathy is characterised by macro albuminuria more than 300 mg (proteins specifically albumin) in a 24-hour urine collection or macro albuminuria and abnormal renal function as represented by an abnormality in serum creatinine and serum urea. Clinically, diabetic nephropathy is evidenced by proteinuria, decline in glomerular function rate (GFR), hypertension, and has high risk of cardiovascular morbidity and mortality.^[3] In diabetic nephropathy, bio-markers viz. serum urea and creatinine are known to be raised with hyperglycemia in uncontrolled diabetics and usually correlate with severity of kidney damage. Measurement of serum urea and creatinine are easily available tests for this purpose which can assist in detection and prevention diabetic kidney disease at an early stage and can limit the progression to end stage renal disease (ESRD).^[3,4] Creatinine is the breakdown product of creatinine phosphate is released from skeletal muscle at a steady rate. Serum creatinine correlates quite well with the percent of the body that is skeletal muscle. It is filtered by the glomerulus, and a small amount is also secreted into the glomerular filtrate by the proximal tubule (hence at low GFR's, the usual reciprocal relationship breaks down and creatinine tends to underestimate how low the GFR has gotten).^[5,6] Patients with early onset diabetes mellitus have higher GFR levels thus making them a suitable population for study of progressive loss of renal function.^[7]

The aim of our study was to measure serum urea and serum creatinine levels and evaluate their

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correlation in diabetic and non-diabetic subjects in a tertiary hospital and study the variation in serum urea and creatinine levels in relation to blood sugar levels in type 2 diabetic patients in comparison with the levels in non-diabetic control subjects. The variations in serum urea and creatinine levels in type 2 diabetic patients in relation to duration of disease were studied. We studied the usefulness of estimation of the serum creatinine and urea levels in type 2 diabetics as a simple easily available tool for diagnosis and prognosis of diabetic nephropathy.

MATERIALS AND METHODS

100 diabetic subjects as study group and 100 non-diabetic subjects as control group attending out-patient department at the Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pune, during 15 May to 15 September 2015 were studied. Diagnosis of diabetes was done on the basis of WHO criteria. All the subjects between 25-80 years were included in this study. Patients with urinary tract obstruction, congestive cardiac failure, other chronic kidney disease, myopathy or muscular dystrophy were excluded from the study.

An informed written consent was obtained from the subjects and approval for the study was obtained from the Institute ethics committee.

5 ml of venous blood sample was collected for estimation of blood sugar, serum urea and serum creatinine. Blood sugar was estimated by GOD – POD method.^[8,9] Estimation of creatinine was done by the

modified Jaffe’s method^[9,10] and urea was estimated by Urease-Berthelot’s method^[10,11] by using Cobas Integra (Roche) fully automated analyser. The normal ranges for these biomarkers were 70 – 110 mg/dl and 110 - 140 mg/dl for fasting and postprandial blood sugar respectively; 15-40mg/dl for serum urea; and 0.6 - 1.2 mg/dl and 0.5 - 1.1 mg/dl for serum creatinine for males /females respectively. The mean age of the control group was matched to the mean age of diabetic patients.

The values of standard deviation for serum urea, serum creatinine and blood sugar levels were calculated using EPI INFO 7 software. The coefficient of correlation ‘r’ value was calculated using the line of best fit in Primer of Biostatistics software.

RESULTS AND OBSERVATIONS

The total number of patients were 200 (100 diabetics & 100 controls). Out of 100 control subjects 29 were females and 71 were males whereas amongst diabetics 32 were females and 68 were males.

Out of the 100 control subjects, all of them had normal urea level 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 100 diabetic subjects 18 of them had raised serum urea levels and 15 had raised serum creatinine levels (Table 1).

Table 1: Comparison of serum urea and serum creatinine levels in diabetics and non-diabetic controls

Investigations	Diabetics n=100	Controls n=100
Raised serum Urea (mg/dL)	18	0
Raised serum Creatinine (mg/dL)	15	2

Patients with diabetes more than six years’ duration were found to have higher serum urea and serum creatinine levels compared to diabetics of lesser duration. On comparison between the duration of diabetes mellitus and the serum urea levels a significant increase was seen in the individuals having diabetes since 11-15 years however no such significant changes were seen in the serum creatinine levels.

The mean (± S.D) blood sugar fasting and post prandial in control was found to be 88.05±8.96 and 124.67±8.94 respectively, whereas in diabetics it was found to be 133.88±68.993 and 168.01±74.87 respectively. Thus, the mean fasting and post prandial blood sugar levels are higher in the diabetic subjects in comparison to the non-diabetic control subjects. (Table 2)

Table 2: Mean serum urea, creatinine, & blood sugar levels in diabetic patients compared to healthy controls

Investigations	Controls n=100 Mean Value ±SD	Diabetics n=100 Mean Value ±SD
Age of the individuals	48.71±15.74	54.11±16.40
Blood Sugar (Fasting)	88.05±8.96	133.88±68.993
Blood Sugar (Post) prandial)	124.67±8.94	168.01±74.87
Serum Urea	18.31±4.55	29.22±20.32
Serum Creatinine	0.89±0.21	1.13±0.77

The mean (± S.D.) urea level in control group was found to be 18.31±4.55 whereas in diabetics it was found to be 29.22±20.32. The mean (±S.D.) creatinine levels in controls was found to be 0.89±0.21 and in diabetics it was found to be 1.13±0.77. Thus, the mean serum urea and creatinine levels are also visibly higher in the diabetics in comparison to the non-diabetic control group. (Figure 1)

A strong positive correlation between the serum urea levels and blood sugar levels both fasting and post prandial was seen with an “r value” of 0.76 and 0.83 respectively. The line of best fit in the graphs below is

an upward curve thus representing a positive correlation between the two variables. (Figures 2,3)

On the other hand, it was observed that there was a weak positive correlation between serum creatinine levels and blood sugar both fasting and post prandial, with a “r value” of 0.28 and 0.40 respectively. The line of best fit in the graphs below is a weak upward curve thus representing weak positive correlation between the two variables. (Figure 4, 5)

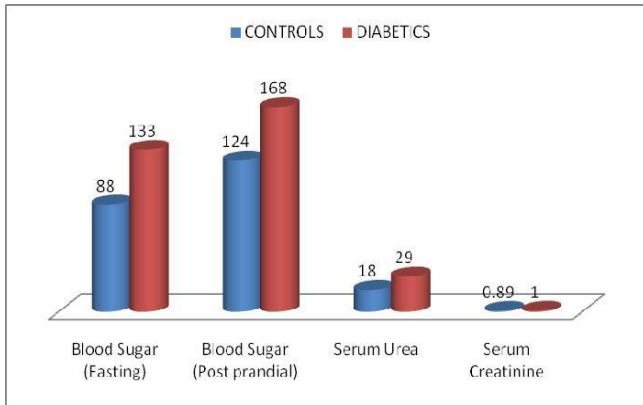


Figure 1: Mean of serum urea, creatinine and blood sugar in diabetics and controls

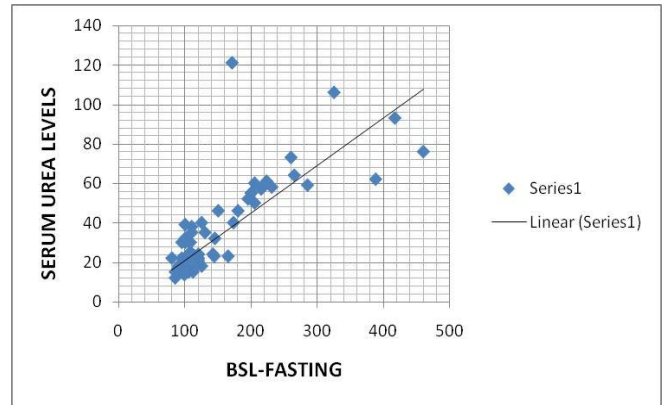


Figure 2: Scatter plot showing relationship between fasting blood sugar and serum urea levels in diabetics. “r” value=0.76 (strong correlation)

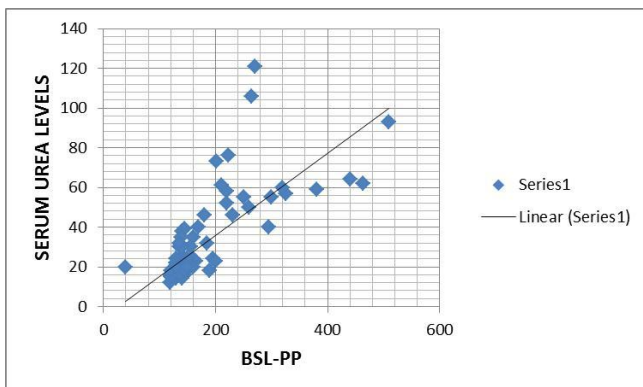


Figure 3: Scatter plot showing relationship between post prandial blood sugar and serum urea levels in diabetics. “r” value=0.83 (strong correlation)

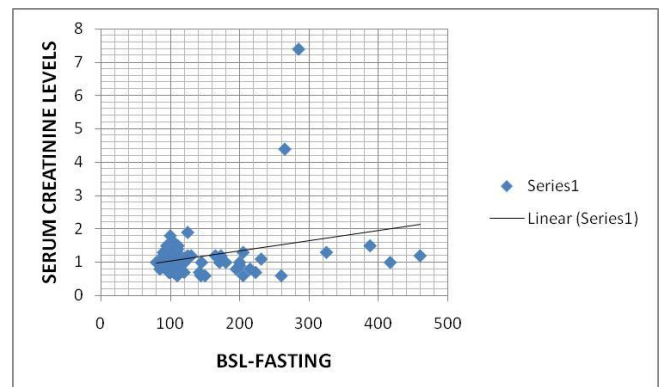


Figure 4: xScatter plot showing relationship between fasting blood sugar and serum creatinine levels in diabetics. “r” value=0.28 (weak correlation)

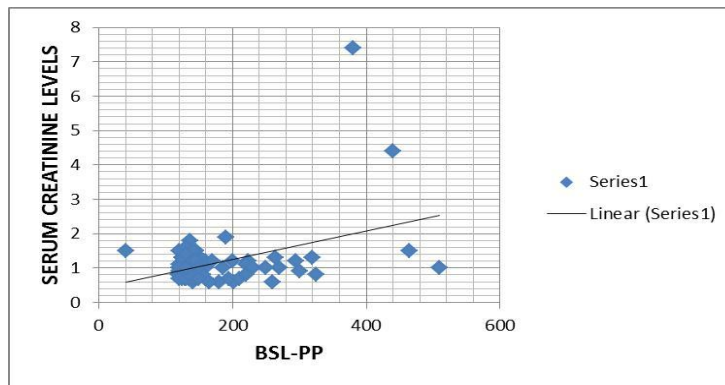


Figure 5: Scatter plot showing the correlation between blood sugar levels post prandial and serum creatinine levels in diabetics. “r” value=0.40 (weak correlation)

The “r value” for serum creatinine levels in males is 0.78, since it is close to +1 thus it represents a positive correlation. Males have higher serum creatinine levels likely due to higher muscle mass and protein intake.

The “r values” for the remaining parameters of BSL and serum urea, on comparison with gender were found to be non-significant (NS) and show a negative correlation. (Table 3)

Table 3: Sex wise correlation of blood sugar, serum urea and creatinine levels in diabetics

Parameters	Diabetics	“r value”		Significance	
		M	F	M	F
Blood Sugar (Fasting)	133.88±68.993	-0.2	-0.23	NS	NS
Blood Sugar (Post Prandial)	68.01±74.87	-0.25	-0.3	NS	NS
Serum Urea	29.22±20.32	-0.25	-0.23	NS	NS
Serum Creatinine	1.13±0.77	0.78	0.24	S	NS

DISCUSSION

The trend between blood sugar and serum urea levels in diabetics has shown a strong relation as evidenced by "r value". The "r value" for the fasting blood sugar and serum urea levels was 0.76 and that of post prandial blood sugar and serum urea was 0.83 thus establishing a strong relationship between them. However, the association between hyperglycemia and the serum creatinine levels showed a weaker link. Our study shows that poorly controlled blood sugar levels would cause increase in the serum urea levels and thus increase the chances of the patient suffering from diabetic nephropathy. This corroborates with the findings of other studies which reported that hyperglycemia is one of the major causes of progressive renal damage.^[6,8] An increase in urea level is seen when there is damage to the kidney. Increase in blood urea level in the presence of high blood sugar level in diabetic patient indicates damage to the kidney. Studies conducted by Anjaneyulu et al had found that increase urea and serum creatinine in diabetic rats indicates progressive renal damage.^[6]

In our study, duration and severity of diabetes strongly correlated with serum urea levels, but not so with serum creatinine levels. This finding is in accordance with the fact that serum creatinine and urea are established markers of Glomerular Filtration Rate (GFR). Serum creatinine is a more sensitive index of kidney function compared to serum urea level. This is because creatinine fulfills most of the requirements for a perfect filtration marker.^[12,13]

In our study high serum creatinine level was seen more in males than females, which could be because of storage of creatinine as a waste product in muscle mass and the presence of high muscle mass in males as reported earlier.^[12,14] There was no relationship between sex and the blood sugar levels likewise significant relation between sex and urea level was also not observed. Similar observations have been reported by the study conducted by Shrestha et al.^[8,15] The results of our study were in accordance with various studies which showed that raised plasma creatinine and urea levels in diabetic patients may indicate a pre-renal problem.^[12,16]

Serum levels of urea and creatinine can be used as useful prognostic markers and predictors of renal damage in diabetic patients.^[12] Effective control of blood sugar levels can stop progression to diabetic nephropathy and thus remarkably reduce the morbidity and mortality associated with this metabolic disease. The tendency of occurrence of renal function tests value at the higher reference limits in cases of type 2 diabetes mellitus reflects the initiation of nephropathy changes. Estimation of Renal function tests is simple, reliable, economic and sensitive that can now be considered as an adjunct in the management and long duration treatment of Type 2 diabetes mellitus disorder.^[17,18]

CONCLUSION

Good control of blood glucose level helps to prevent progressive renal impairment and diabetic nephropathy is one of major cause of chronic renal failure. In order to prevent the progression of diabetes mellitus to diabetic nephropathy, vigilant monitoring of serum urea and creatinine are simple biomarkers available in patients with proteinuria if microalbuminuria screening test cannot be performed. We would like to conclude that blood urea and serum creatinine levels are simple tests helpful in diabetics who are poorly controlled to assess the renal function.

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Authors' Contribution:

SB -concept, design of the study, final approval of manuscript

AB-compilation, manuscript writing

AA-data collection and compilation, literature search

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