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STUDY OF RENAL BIO-PROFILE IN TYPE 2 DIABETIC SUBJECTS WHO VISIT OUT PATIENT CLINIC AT OUR TERITIARY HOSPITAL, AT CM MEDICAL COLLEGE, DURG, INDIA

Biochemistry

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ABSTRACT

Background: Diabetes is a common metabolic syndrome, widely prevalent in most of the developing and developed nations. Diabetes Mellitus simply means high blood glucose level, is a silent killer and it kills 10 years before our time as per the study conducted by Oxford University.
Diabetic subjects develop one or the other complications (microvascular or macrovascular) during their life span. One of most common complication in uncontrolled diabetes is progression of renal impairment to nephropathy. The simple, cheap and cost-effective markers which are used to evaluate renal function are measurement of serum creatinine and serum urea.
The objectives of our study include: To determine and compare the levels of, fasting blood sugar, urea, creatinine and uric acid in type 2 Diabetic subjects and Healthy subjects and to study the association of between fasting blood glucose, post prandial blood glucose, serum urea and creatinine.
Materials and Methods: After informed consent, fasting and postprandial blood sample was collected both in fluoride tube and red stoppered tube for the estimation of fasting blood glucose, post prandial blood glucose, serum urea and creatinine levels using Fully Automated Biochemistry Analyzer.
Results: The results of this study indicate that, the fasting blood glucose, post prandial blood glucose, serum urea and creatinine levels are elevated in type 2 diabetic subjects as compared to controls and there is increased prevalence of elevated creatinine and urea levels in type 2 diabetic subjects. Estimation of serum urea and creatinine levels are highly useful cost-effective, cheap and affordable renal biomarkers, which can be used for detecting the renal impairment in type 2 diabetic subjects. Hence, these biomarkers can be used on routine basis for follow-up checkups in type 2 diabetic subjects.

KEYWORDS

type 2 diabetes, urea, creatinine, fasting blood glucose, post prandial blood glucose and renal biomarkers

INTRODUCTION

Diabetes is a common metabolic syndrome, widely prevalent in most of the developing and developed nations. Diabetes Mellitus simply means high blood glucose level, is a silent killer and it kills 10 years before our time as per the study conducted by Oxford University. As per International Diabetes Federation, there are about 382 million people worldwide living with diabetes, and India ranks among top three countries. Diabetes is a condition in which the body either does not produce sufficient insulin or does not respond properly to insulin [1].

Diabetes is broadly classified as Type 1 diabetes and type 2 diabetes. Type 1 diabetes is due to absolute lack of insulin and in type 2 diabetes there is decreased action of insulin due to insulin resistance and relative deficiency of insulin. In both the conditions, the blood glucose levels are increased (hyperglycemia) [2]. Specially in type 2 diabetes is more common in genetically pre-disposed individuals which runs in families, the combination of less physical activity and excess caloric intake can lead to obesity which in turn, leads to a state of decreased insulin sensitivity (insulin resistance) [3]. Further, decrease in β-cell mass and abnormalities of β-cell function can both be demonstrated in patients with type 2 diabetes and individuals at increased risk for diabetes [4]. Most type 2 diabetics are often obese [5]. Uncontrolled Diabetes leads to development of macrovascular and microvascular complications: the macrovascular complications include cerebrovascular accidents, coronary artery disease, peripheral vascular disease and the microvascular complications include nephropathy, retinopathy and neuropathy [6].

Diabetic nephropathy is the leading microvascular complication affecting the diabetic subjects, leading to end stage renal disease. It affects approximately 30% of all diabetic population who have uncontrolled diabetes. Assessment of a renal function tests in these patients on regular basis is very important for two reasons. 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 characterized by macroalbuminuria i.e excretion of more than 300 mg of protein (especially albumin) per 24 hours of urine and abnormal renal function tests characterized by elevation of blood urea and serum creatinine. Clinically, diabetic nephropathy is characterized by decline in glomerular function rate (GFR), proteinuria, hypertension, and high risk of cardiovascular morbidity and mortality. Measurement of serum urea and creatinine are easily available tests used for detection, assessment and further prevention of diabetic kidney disease at an early stage and can limit the progression to end stage renal disease (ESRD) [7, 8].

Creatinine is anhydride of creatine and is a breakdown product of creatinine phosphate. It is released from skeletal muscle at a steady rate. Serum creatinine levels positively correlate with skeletal muscle mass and a small amount creatinine is also secreted into the glomerular filtrate by the proximal tubule [9,10]. Patients with early onset diabetes mellitus have higher GFR levels thus making them a suitable population for study of progressive loss of renal function [11]. Chronic kidney disease (CKD) is one of the main causes of morbidity and mortality in both developing and developed countries secondary to uncontrolled diabetes [12]. Hence, there is a need to find out whether diabetics patients who attend medicine outpatient clinic are developing kidney dysfunction, so that they can be offered regular follow ups and timely advice. Hence, we have taken up this study to assess renal function tests in diabetic patients.

OBJECTIVES OF THE STUDY:

The objectives of this study include

1) To determine and compare, the serum levels of glucose (fasting and post prandial), urea, creatinine and uric acid in type 2 Diabetic subjects and Healthy subjects.
2) To study the association of between fasting blood glucose, post prandial blood glucose, serum urea and creatinine.
3) To study the usefulness of estimation of serum creatinine and urea levels in type 2 diabetic subjects as a simple easily available cost effective tool for diagnosis and prognosis of diabetic nephropathy.

MATERIALS AND METHODS

Source of data: A case-control Study of Renal Bio-Profile in Type 2 Diabetic Subjects, was conducted at Chandulal Chandrakar Memorial Medical College, Kachandur, Durg from February 2018 to July 2018 in age and sex matched type 2 diabetic subjects and controls. Written informed consent was taken from the study subjects. Type 2 Diabetic subjects and controls participated voluntarily in the study. Detailed medical history and relevant clinical examinations were carried out in both cases and controls. Inclusion Criteria: 60 WHO proven and confirmed cases of type 2 diabetic subjects and 60 controls, in the age group of 25-75 years and sex matched were included in the study.

Exclusion criteria: Admitted patients in the hospital for any cause,

subjects suffering from urinary tract infections, urinary tract obstruction, antibiotic usage (cephalosporin's), chronic kidney disease, hypothyroidism (thyroid myopathy), myopathies, muscular dystrophy, diagnosed cases of hypertensive and diabetic nephropathy and congestive cardiac failure were excluded from the study. Sample collection: Under aseptic precautions about 6 mL of fasting venous blood and 2 mL post prandial blood sample, was drawn from antecubital vein of study subjects using a sterile disposable syringe. Plain vacutainer containing 4 mL of blood was subjected for centrifugation and the serum was separated. The biochemical parameters were analyzed by Automated Clinical Biochemistry Analyzer (Mispa Nano). Parameters measured in the present study include, fasting blood glucose, past prandial blood glucose, urea, creatinine and uric acid. Serum glucose levels were estimated by Glucose-Oxidase Peroxidase method, urea is estimated by DAM method and creatinine by Enzymatic method. The reference ranges for urea and creatinine were 10-50 mg/dL and 0.6-1.1 mg/dL (males) and 0.5-0.8 mg/dL (females) respectively.

STATISTICALANALYSIS

Mean and standard deviations were used to describe the data. Students't' test was used for comparison between controls and study subjects. Relationship between variables was assessed by Karl Pearson's coefficient of correlation. P-value of 0.05 or less was considered as statistically significant.

RESULTS

A total of 62 type 2 diabetic subjects and 62 controls, aged 25-75 years were involved in the study. The mean age of controls and type 2 diabetic subjects were 38.7 10.25 and 48.45 10.8 years respectively. Out of 62 controls, 61.6% were males and 23 (38.3%) were females. Out of 62 types 2 diabetic subjects, 38 (63.3%) were males and 22 (36.6%) were females (Table 1)

Table 1: Shows age wise and gender wise distribution of controls and type 2 diabetic subjects

	Controls	Type 2 Diabetic Subjects
Total Number (120)	**60**	**60**
Total Males (75)	**37**	**38**
Total Females (45)	**23**	**22**
Age (Mean SD)	**38.7 10.2**	**48.4 10.8**

Table 2: Shows Comparison of Serum Values of Blood Glucose (Fasting and Postprandial), Urea and Creatinine in Controls and Type 2 Diabetic Subjects expressed in Mean and SD

Parameters	Controls	Type 2 Diabetic Subjects	p value
Fasting blood glucose (mg/dL)	**86 13.3**	**236 92**	**<0.001**
Post prandial blood glucose (mg/dL)	**112 16.4**	**276 96.6**	**<0.001**
Serum Urea (mg/dL)	**17.9 4.86**	**42.9 30.4**	**<0.001**
Serum Creatinine(mg/dL)	**0.68 0.18**	**1.51 1.31**	**<0.001**

Shows that the mean and SD values of fasting blood glucose, post prandial blood glucose, urea and creatinine are increased in type 2 diabetic subjects compared controls. The increase in these levels are highly statistically significant.

Table 3: Shows Comparison of Serum Values of Blood Glucose (Fasting and Postprandial), Urea and Creatinine between males and females among Type 2 Diabetic Subjects

Parameters	Males	Females	p value
Age (in years)	**47.4 10.1**	**50.1 11.7**	
Fasting blood glucose (mg/dL)	**252.8 102**	**209 62.8**	**0.08**
Post prandial blood glucose (mg/dL)	**283 103**	**253 80**	**0.24**
Serum Urea (mg/dL)	**34.1 33.6**	**42.9 30.4**	**0.80**
Serum Creatinine (mg/dL)	**1.6 1.5**	**1.2 0.6**	**0.18**

Shows that there is no significant difference mean and SD values of fasting blood glucose, post prandial blood glucose, urea and creatinine levels between males and females among type 2 diabetic subjects.

Table 4: Shows comparison of urea and creatinine in controls and type 2 Diabetic subjects in both males and females

Parameters	Controls n = 60	Type 2 Diabetic Subjects n = 60
Increased Urea (mg/dL)	0	13 (21.6%)
Increased Creatinine (mg/dL)	3 (0.05%)	23 (38.3%)

Shows that there is increase in serum urea and creatinine levels in type 2 diabetic subjects as compared to controls. Out of 60 type 2 diabetic subjects 13 had increased urea levels with a prevalence of 21.6% and 23 out of 60 had elevated creatinine levels with a prevalence of 38.3%.

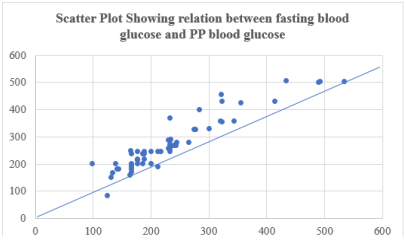

Figure 1: Scatter plot showing the relationship between fasting blood glucose and post prandial blood glucose (r = 0.93)

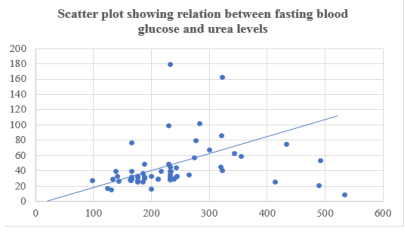

Figure 2: Scatter plot showing the relationship between fasting blood glucose and urea levels in type 2 diabetic subjects (r = 0.22)

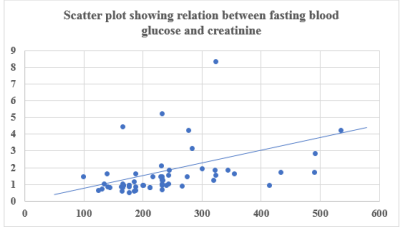

Figure 3: Scatter plot showing the relationship between fasting blood glucose and creatinine levels in type 2 diabetic subjects (r = 0.39)

DISCUSSION

In the present study, we found that the serum levels of urea and creatinine are elevated compared to control subjects participated in the study. We found positive association between fasting blood glucose, post prandial blood glucose, urea and creatinine levels. The prevalence of elevated serum urea levels was 13% among type 2 diabetic subjects and for serum creatinine was 38.3%. The prevalence of elevated creatinine among type 2 diabetic subjects was more significant compared to the elevated urea levels.

This study shows that poorly controlled blood sugar levels positively associated with increase in the serum urea levels and thus there is increase in the chances of the patient suffering from diabetic nephropathy. This finding is in accordance with other studies conducted in the past, which reported that hyperglycemia is one of the leading cause of progressive renal damage. In this study, the duration and severity of diabetes are strongly correlated with serum urea levels, but not so with serum creatinine levels. Urea is the end product of protein catabolism, produced as a result of oxidative deamination of amino acids in which ammonia generated is transported to the liver for the formation of urea through the urea cycle. Azotemia is a condition characterized by abnormal elevation of blood nitrogen and may indicate renal disease or a disorder that causes a secondary increase of blood urea [13]. Uremia is a condition in which there is an elevated blood urea level due to kidney malfunction [14].

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 [15, 16]. Creatinine is produced after the pyrophosphate cleavage of phosphocreatine to produce energy for muscle activity [17]. Serum creatinine level is one of the important biomarker for assessing renal function. Age, gender, protein intake, and muscle mass influence serum creatinine levels [18]. In this study, we did not find statistically significant difference in fasting blood glucose, post prandial blood glucose and serum urea levels between type 2 diabetic males and females. Where as serum creatinine levels were slightly elevated in males compared to females, this increase was not statistically significant. In our finding sex was not the determining factor for the diabetes. There was no relationship between sex and the blood sugar levels likewise significant relation between sex and urea level was also not observed. This result is supported by various researchers who showed that sex wise variation occurs only in serum creatinine level but not in blood sugar level and urea level. High serum creatinine level was seen 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 [19].

The prevalence rate of increased urea and creatinine levels in type 2 diabetic subjects was 21.6% and 38.3% and in controls it was 0% and 0.05% respectively. In controls, out of 60 subjects only 3 males had increased creatinine levels, in the same controls the serum urea level was normal. This finding, may be due to increased muscle mass and increased dietary protein intake on the day of the sample collection.

CONCLUSION

In this present study, we investigated renal biomarkers, serum urea and creatinine in type 2 diabetic subjects. We found elevated creatinine and urea levels in type 2 diabetic subjects with increased duration of diabetes and had positive correlation with fasting serum glucose and post prandial glucose levels. Good glycemic control helps to prevent progressive renal impairment and diabetic nephropathy in type 2 diabetic subjects. Vigilant monitoring of serum urea and creatinine in type 2 diabetic subjects could serve as cost-effective and simple biomarkers to screen for renal impairment, in type 2 diabetic subjects with proteinuria. 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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