EFFECTS OF HYPERGLYCEMIA ON RENAL FUNCTION IN TYPE-2 DIABETES MELLITUS PATIENTS

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Abstracts: **Background:** Diabetes mellitus is one of the most common metabolic abnormality in the world. Type-2 diabetes (NIDDM) is the commonest form of diabetes constituting 90% of the diabetic population in any country. Diabetic nephropathy has become leading cause of end-stage kidney disease worldwide. There is progressive change in the structure and function of the kidney. Death rates and rate of renal function decline increases as the disease progresses. **Objectives:** To evaluate the effect of hyperglycemia on renal function in type-2 DM patients and to compare it with those of non-diabetic healthy subjects. **Methods:** 50 type-2 DM patients of both sexes having DM for more than 1 year between 40-60 years attending medicine OPD & 50 nondiabetics of both sexes of same age without hypertension, any renal diseases like stones, gestational DM, endocrine disorders, alcohol abuse were recruited. The renal function tests, Fasting Blood Sugar, S.creatinine, Blood urea were performed and compared by using suitable statistical methods (unpaired student t-test, p value and pearson correlation coefficient). **Result:** Diabetics have high FBS, S.creatinine and Blood urea as compare to nondiabetics. **Conclusion:** Increase in Blood sugar had direct relationship with Serum creatinine and Blood urea in type-2 DM patients.

Key Words: Type-2 DM, Hyperglycemia, Renal Function Tests.

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Introduction:

Diabetes mellitus is one of the most common metabolic abnormalities in the world[1]. There are 347 million people in the world who have diabetes[2]. Type 2 diabetes comprises 90% of people with diabetes around the world[2]. According to the Diabetes Atlas 2003 published by the International Diabetes Federation, the number of people with diabetes worldwide was 194 million and expected to rise to 333 million by 2025[3]. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "diabetes capital of the world"[4]. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030[5].

In 2004, an estimated 3.4 million people died from consequences of high blood sugar. More than 80 per cent diabetes deaths occur in low and middle income countries. WHO projects that diabetes will be the 7th leading cause of death in 2030[2].

Diabetes mellitus is a syndrome of impaired carbohydrate, fat and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin[6]. Chronic hyperglycemia, from whatever cause, leads to a number of complications – cardiovascular, renal, neurological, ocular and others such as intercurrent infections[5].

Diabetic nephropathy has become the leading cause of end-stage kidney disease worldwide and is associated with an increased cardiovascular risk[7]. About 20–30% of patients with type-1 or type-2 diabetes develop evidence of nephropathy, but in type-2 diabetes, a considerably smaller fraction of these progresses to ESRD[8]. Diabetic Nephropathy is due to a progressive change in the structure and function of the kidney owing to multiple diabetes associated factors. Death rates and rate of renal function decline increases as the disease progresses.

Easy, simple and quick method to access the renal function in diabetic patients is measurement of serum creatinine and blood urea level in their blood sample[9].

Material and Methods:

50 type-2 DM patients of both sexes having DM for more than 1 year between 40-60 years and 50 nondiabetics of both sexes of same age group without hypertension, any renal diseases (like renal stones, glomerulonephritis), gestational DM, endocrine disorders (like cushing's syndrome),

alcohol abuse attending medicine OPD were recruited. Samples were selected randomly. This study was approved by the institutional ethics committee (IEC) and an informed oral consent was obtained from the study participants. Detailed history regarding age, sex, age of onset and duration of diabetes, presenting complaints, past history of any other disease, any medications for treatment of diabetes, dosages and regularity of treatment, family history of diabetes, drug history of any nephrotoxic drug like aminoglycosides, personal history like smoking and alcohol consumption were taken. Clinical examination was done to look for any microvascular or macrovascular complications and findings were noted.

For Fasting Blood Sugar (FBS) fasting venous blood sample is collected in fluoride bulb and for this patients were advised to don't take any caloric intake for at least 8 hours before taking blood sample. For serum creatinine and blood urea 5 ml venous blood sample is collected in EDTA bulb. For serum separation blood was spun for 10 minutes at 1500 rpm in centrifuge machine. Serum creatinine, Blood urea and Blood glucose were estimated by Semi auto analyzer machine.

FBS was estimated by GOD – POD (Glucose Oxidase Peroxidase) method[10]. Estimation of Serum creatinine was done by the Modified Jaffe's method[10]. Blood urea was estimated by Modified Berthelot method[10].

Statistical analysis: The results were expressed as mean ± standard deviation. Statistical analysis was done by unpaired student t-test to compare between the groups and Pearson correlation coefficient to correlate between the parameters using Graphpadprism version-5 software. $p<0.05$ was considered as statistically significant.

Result:

Following observations were made from the study of renal function tests in 50 type-2 DM patients and 50 non diabetics.

Table-1 shows maximum number of type-2 diabetic patients in the age group of 50-54 years (17 patients, 34 %) and least patients in the group of 40-44 years (8 patients, 16 %). The sex distribution among the patient group showed female preponderance. The youngest patient was 40 years and the oldest patient was 60 years old. The Mean±SD of age was 50.46±5.23 years.

Table: 1 Distribution of Type-2 DM patients according to age and sex

Age(Years)	Sex		No. of cases	% of cases
	Male	Female		
40-44	3	5	8	16
45-49	8	7	15	30
50-54	8	9	17	34
55-60	4	6	10	20
Total	**23**	**27**	**50**	**100**
Mean±SD	**50.46±5.23**			

Table: 2 Duration of DM in Type-2 DM patients

Duration(Years)	No. of cases	% of cases
1-5	19	38
6-10	16	32
>10	15	30
Total	**50**	**100**
Mean±SD	**7.52±4.07**	

Table-2 shows maximum number of type-2 diabetes mellitus patients had duration of diabetes mellitus between 1 to 5 years (19 patients, 38 %). The Mean±SD of Duration of type-2 DM was 7.52±4.07 years.

The observed values of various renal function parameters are provided in Table-3. There was significant increase in the levels of FBS, S.creatinine and Blood urea ($p<0.0001$) in type-2 diabetic patients when compared to healthy controls.

Table: 3 Comparison of renal function tests in type-2 DM patients and non diabetic subjects

Parameters	Type-2 DM cases (n=50)	Non diabetic controls (n=50)	P value
	Mean±SD	Mean±SD	
FBS (mg/dl)	237.74±64.33	89.1±7.19	<0.0001* * *
S.creatinine (mg/dl)	1.60±0.78	0.85±0.16	<0.0001* * *
Blood urea (mg/dl)	28.58±13.42	15.06±3.42	<0.0001* * *
*P<0.05-significant			

Table: 4 Correlation coefficient of FBS with renal function parameters in type-2 DM patients

	S.creatinine	Blood urea
FBS	0.4755	0.4693
P value	0.0005***	0.0006***
*P<0.05-significant		

Table-4 shows that Blood sugar had positive correlation with Serum creatinine (r= 0.4755) and Blood urea (r= 0.4693) in type-2 DM patients.

Discussion:

The researchers in this study compared and analysed FBS, S.creatinine, Blood urea in type-2 DM patients and non diabetic controls.

The present study showed that the Maximum numbers of type-2 diabetic patients were in the age group of 50-54 years having mean age 50.46±5.23 years. Study done by Butheinah A Al-Sharafi et al[11] also founded that people with age between 45-54 years were affected more by diabetes and mean age for male and female were 50.3±12.5 years and 50.7±10.7 years respectively.

In the present study, the numbers of type-2 diabetics were more in females than males. Male: Female ratio was 0.8:1. These findings are in tune with findings of Butheinah A Al-Sharafi et al[11] which shows that the number of type-2 diabetics were more in females than males. Male: Female ratio was 0.7:1.

In present study maximum number of type-2 diabetic patients had duration of DM between 1-5 years. The Mean±SD of duration of DM was 7.52±4.07 years. These findings are in tune with findings of Butheinah A Al-Sharafi et al[11] which shows maximum number of type-2 diabetics with duration < 5 years.

In present study diabetics were found to have higher FBS level than controls with Mean±SD 237.74±64.33 mg/dl and 89.1±7.19 mg/dl in diabetics and in controls respectively. Similar findings were consistent with the study done by Manjunatha goud B K et al[12] which shows that the diabetics had more FBS level with Mean±SD 169.29±138.32 mg/dl and in control group it was 83.30±13.15 mg/dl. Study done by S W Masram et al[13] also had same results which favours the results of the present study. It was found in their study that diabetics had higher FBS level than controls with Mean±SD 223.82±37.59 mg/dl and in control group it was 88.29±10.78 mg/dl. Similar findings were consistent with the study done by Aftab Begum et al[14] which shows that the Mean±SD of FBS level in diabetics was 162.32±57.09 mg/dl and in control group was 86.98±9.66 mg/dl. Result of present study also tuned with the study done by Olarewaju M Oluba et al[15] in which diabetics had more FBS when compared to controls with Mean±SD in male diabetics was 178.5±67.2 mg/dl and in male controls it was 83.4±10.7 mg/dl. The Mean±SD of FBS level in female diabetics was 179.3±54.9 mg/dl and in female controls it was 85.5±12.3 mg/dl. Similar findings were consistent with the study done by Tejal J Wagle[9] and L Siva et al[16].

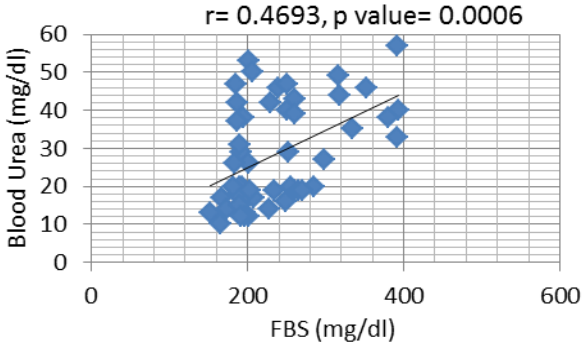

Figure-1: Correlation between FBS and Blood urea in type-2 DM patients

In present study it was found that diabetics had higher level of blood urea than controls with Mean±SD 28.58±13.42 mg/dl and in controls it was 15.06±3.42 mg/dl. Blood sugar had direct positive correlation with blood urea in type-2 DM patients (Figure-1). Study conducted by Manjunatha goud B K et al[12] had same findings which shows that the Mean±SD of blood urea in diabetics was 69.69±69.71 mg/dl and in controls it was 33.62±27.17 mg/dl. Similar findings also tuned with the study done by Olarewaju M Oluba et al[15] which favours the results of present study. In that study Mean±SD of blood urea in male diabetics was 28.1±13.9 mg/dl and in male controls it was 20.0±7.00 mg/dl. The Mean±SD of blood urea in female diabetic group was 28.7±15.6 mg/dl and in female control group it was 19.0±5.20 mg/dl. Similar findings were consistent with the study done by L Siva et al[16] and Jiji Inassi[17].

If the kidneys are failing to function normally, the blood urea levels increase abnormally. Increased catabolism of proteins coupled with the diminished ability to excrete the nitrogenous waste might have accounted for the raised urea in diabetic patients. Enhanced activities of urea cycle enzymes in diabetic condition might have also lead to increased production of urea nitrogen[16].

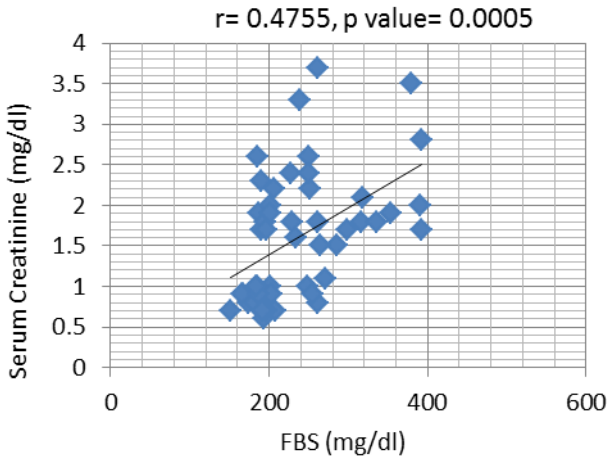

Figure-2: Correlation between FBS and Serum creatinine in type-2 DM patients

The present study showed increase in serum creatinine in type-2 diabetics when compared to controls. The Mean±SD of serum creatinine in diabetic group was 1.60±0.78 mg/dl and in control group was 0.85±0.16 mg/dl. Blood sugar had direct positive correlation with serum creatinine in type-2 DM patients (Figure-2). These findings are in tune with findings of Manjunatha goud B K et al[12] which shows that the Mean±SD of serum creatinine in diabetic group was 2.23±3.03 mg/dl and in control group it was 1.11±1.18 mg/dl. Similar findings were consistent with the study done by Olarewaju M Oluba et al[15] which shows that the Mean±SD of serum creatinine in male diabetic group was 1.2±1.20 mg/dl and in male control group was 0.8±0.20 mg/dl. The Mean±SD of serum creatinine in female diabetic group was 1.1±0.50 mg/dl and in female control group was 0.8±0.20 mg/dl. Similar findings were consistent with the study done by Tejal J Wagle[9], L Siva et al[16] and Jiji Inassi[17].

Creatinine is a more sensitive index of kidney function compared to blood urea level. Creatinine fulfills most of the requirements for a perfect filtration marker. When the kidney fails to function properly serum creatinine level increases due to increase protein catabolism and decrease excretion of nitrogenous waste products[16].

Conclusion:

This study shows highly significant alterations in Blood glucose, Blood urea, Serum creatinine levels

in patients with type-2 DM suggesting renal damage. Screening tests for the complications of diabetes mellitus are strongly recommended at the time of diagnosis not only for early detection of DM but also to prevent the progression to end stage renal disease.

In view of the fact that the present study comprised of a small group of patients, further studies with more number of patients may be required to evaluate our observations.

Good control of blood glucose level is absolute requirement to prevent progressive renal impairment.

References:

1. A Ramachandran, C Snehalatha. Type 2 Diabetes Mellitus-The Epidemic of the 21st Century: The Indian Scenario. INT.J.DIAB.DEV.COUNTRIES 1999; 19: 158-164.
2. WHO: Diabetes Fact Sheet No.312. Reviewed October 2013.
3. Executive Summary. Diabetes Atlas. Second Edition. 2003: 11.
4. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of Type 2 Diabetes: Indian Scenario. Indian J Med Res 2007; 125: 217-30.
5. K Park. Chapter-6; Diabetes Mellitus. In: Park's Textbook of Preventive and Social Medicine. 22nd edition. Jabalpur: M/s Banarsidas Bhanot publishers. 2013: 362-367.
6. Arthur C Guyton, John E Hall. Chapter-78; Insulin, Glucagon, and Diabetes Mellitus. In: Guyton and Hall Textbook of Medical Physiology. 12th edition. New Delhi: Elsevier. 2011: 939-954.
7. Enyioma N Obineche and Abdu Adem. Update in Diabetic Nephropathy. Int J Diabetes & Metabolism 2005; 13: 1-9.
8. American Diabetes Association. Nephropathy in Diabetes Mellitus. Diabetes Care 2004; 27 Suppl 1: S79-S83.
9. Tejal J Wagle. Genderwise Comparison of Serum Creatinine and Blood Sugar Levels in Type-2 Diabetic Patients. Bombay Hospital Journal 2010; 52(1): 64-68.
10. Carl a. Burtis, Edward R. Ashwood, David E. Bruns. Chapter-25, 26. In: Teitz Textbook of Clinical Chemistry and Molecular Diagnostics. Fifth Edition, 2012.
11. Butheinah A Al-Sharafi, Abdallah A Gunaid. Prevalence of Obesity in Patients with Type-2 Diabetes Mellitus in Yemen. Int J Endocrinol Metab 2014; 12(2): e13633: 1-5. DOI: 10.5812/ijem.13633.
12. Deepa K, Manjunatha goud B K, Oinam Sarsina Devi, Devaki R N, Bhavna Nayal, Asha Prabhu, et al. Serum Urea, Creatinine in Relation to Fasting Plasma Glucose Levels in Type-2 Diabetic Patients. International Journal of Pharmacy and Biological Sciences 2011; 1(3): 279-283.
13. S.W. Masram, M.V. Bimanpalli, Suresh Ghangle. Study of Lipid Profile and Glycated Hemoglobin in Diabetes Mellitus. Indian Medical Gazette 2012: 257-265.
14. Aftab Begum, Siraj Ahmed Shirbadgi, S. Chandrasekharappa. Serum Lipid Assessment: A Cardiovascular Risk Factor in Asymptomatic Type-2 Diabetics. International Journal of Advances in Pharmacy, Biology, and Chemistry 2014; 3(1): 184-188.
15. Blessing O Idonije, Oloruntoba Festus, Olarewaju M Oluba. Plasma Glucose, Creatinine and Urea Levels in Type-2 Diabetic Patients Attending A Nigerian Teaching Hospital. Research Journal of Medical Sciences 2011; 5(1): 1-3.
16. L Siva, SV Mythili, JamunaRani, P Sai Kumar. Biochemical and Haematological Aberrations in Type-I and Type-II Diabetic Patients in South India-A Comparative Study. International Journal of Research in Pharmaceutical and Biomedical Sciences 2012; 3(2): 967-977.
17. Jiji Inassi, Vijayalakshmy R. Role of Duration of Diabetes in the Development of Nephropathy in Type-2 Diabetic Patients. National Journal of Medical Research 2013; 3(1): 5-8.

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