

Study of Renal Function and Serum Electrolyte in Type - 2 DM

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Abstract:

Purpose: - To find out the level of serum Creatinine, serum uric acid, blood urea and serum electrolytes in Type-2 DM patients compare to normal healthy control group.

Method: - A total number of 278 subjects were selected for study at CCM Medical College Hospital Durg. In which 178 subjects are suffering from type-2 DM average range of 30 to 65 years. 100 subjects age, sex matched was selected for control group. Controls were clinically and physically normal and healthy.

Result: - The Mean±SD of serum sodium in diabetic group was 134.72±6.02mmol/L, 133.82±4.98 in male and female respectively and in control group was 139.16±2.83mmol/L. The Mean±SD of serum potassium in diabetic group was 6.28±1.07 mmol/L in male and 5.98±1.02 in female mmol/L and in control group was 4.62±0.46 mmol/L.

The Mean±SD of serum calcium in diabetic group was 10.05±0.79 mg/dl in male and 9.95±0.69 mg/dl in female and in control group was 9.44±0.48 mg/dl.

The present study shows that the activity of blood urea, serum creatinine and uric acid was highly significantly increased found in type-2 DM patients compare to normal healthy group. The activity was 42 ± 19 mg/dl, 2.92 ± 2.43 mg/dl, 12.26 ± 7.81 mg/dl in male and in female it was 39 ± 26 mg/dl, 2.26 ± 2.08 mg/dl and 10.96 ± 6.37 mg/dl and 22 ± 7.48 mg/dl, 0.83 ± 0.31 mg/dl and 5.26 ± 2.84 mg/dl respectively

Conclusion: - This study shows highly significant alterations in Blood Urea, serum creatinine, serum uric acid, Serum Sodium, Serum Potassium and Serum Calcium 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 diabetes mellitus, electrolyte derangement prevails, so routine measurement of serum electrolyte and renal function could not be avoided in type-2 DM patients. Electrolyte imbalance occur even with normal renal function, however the frequency of electrolyte derangement is more with deterioration of the renal function in diabetes mellitus patients. 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.

Keywords: - DM, DN, NIDDM, ESRD, Kidney dysfunction, creatinine, Na, K, Ca, Urea, Uric acid.

Introduction

Diabetes mellitus (DM) is the commonest metabolic abnormality in the world. DM is one of the most challenging health problems in the 21st century. It is affecting millions of peoples, near about 6-7% of the world's population.^[1,2]

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Type-2 diabetes also called as non-insulin dependence diabetes mellitus (NIDDM). NIDDM is the commonest form of diabetes constituting nearly 90% of the diabetic population in any country.^[3]

Diabetes is a chronic endocrine disorder affecting the body's metabolism and resulting in structural changes affecting the organs of the vascular system. Serious complications resulting from diabetes include coronary heart disease, stroke, retinopathy, renal failure, peripheral artery disease, and neuropathy. The two main forms of diabetes are type I diabetes and type 2 diabetes. Type I diabetes is a result of

pancreatic islet β -cell destruction usually due to an autoimmune response which results in insulin deficiency requiring exogenous insulin to prevent serious complications. Type-2 diabetes is characterized by insulin resistance or abnormal insulin secretion. In people with type-2 diabetes, blood sugar must be controlled either through diet, with oral hypoglycemic drugs or in severe cases with exogenous insulin.

If preventive measures are not taken, it is estimated that 438 million people will have diabetes by 2030. India leads the global top ten in terms of the highest number of people with diabetes, with a figure of 50.8 million for 2010. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the “diabetes capital of the world”.^[4] Less glycemic control, smoking, high blood pressure, elevated cholesterol levels, obesity, and lack of regular exercise are considered to be risk factors that accelerate the deleterious effects of diabetes.^[2] Diabetes once regarded as a single disease entity, but is now seen as a heterogeneous group of diseases, characterized by a state of chronic hyperglycemia, resulting from a diversity of etiologies, environmental and genetic, acting jointly. The underlying cause of diabetes is the defective production or action of insulin, a hormone that controls glucose, fat and amino acid metabolism.

Characteristically, diabetes is a long term disease with variable clinical manifestations and progression. Chronic hyperglycemia, from whatever cause, leads to a number of complications like cardiovascular, renal, neurological, ocular and others such as inter current infections.^[5]

DM is associated with a greater risk of mortality from cardiovascular disease which is mainly due to dyslipidemia.^[6] One third or more of the DM patients develop Diabetic Nephropathy (DN) with progressive deterioration of renal function and structure in their life time. DN is the leading cause of end-stage renal disease (ESRD) worldwide. The earliest clinical evidence of DN is the appearance of low but abnormal levels (30-300 mg/day) of albumin in the urine, referred to as Microalbuminuria.^[7] Diabetic nephropathy has become the leading cause of end-stage kidney disease worldwide and is associated with an increased cardiovascular risk.^[8] Electrolytes play an important role in intermediary metabolism and cellular function, including enzyme activities and electrical gradients. Serum concentrations of electrolytes have been shown to change with plasma glucose levels. Disturbances in the levels of some electrolytes are associated with DM.^[9] The kidneys are important organs in the body serving as a natural filter of the blood, and keeping the body chemically balanced. The kidney regulates the concentration of water and soluble substances like sodium salts by filtering the blood, reabsorbing water, glucose and amino acids. It also

excretes wastes such as urea, creatinine, uric acid, electrolytes and extra water, thereby regulating blood volume, blood pressure, levels of electrolytes, metabolites and blood pH, which is a homeostatic function.^[10] If the kidneys fail to remove wastes, these wastes accumulate in the blood and the body, damaging the body and the kidneys themselves leading to renal failure.^[11] Kidney damage usually starts 2 to 5 years after onset of hyperglycemia, if hyperglycemia is not controlled.^[12]

Renal dysfunction leads to accumulation of nitrogenous waste products in the blood above their normal ranges, some of which are toxic. These products include creatinine and urea, whilst urinary albumin excretion rate exceeds 200 mg/minute. Early detection at this stage is vital to preserve kidney function and to delay or prevent end stage renal disease.^[13] Males have greater proportions of skeletal muscles as compared to women resulting in proportionally elevated values of creatinine.

Epidemiology of Diabetes

Diabetes and its complications is a leading cause of death and disability, reducing overall life expectancy and healthy life expectancy. Global estimates place the number of people with diabetes at approximately 200 million and increasing rapidly. Over 2 million Canadians have diabetes and prevalence is increasing annually.^[14] In Canada's largest province, Ontario, the 2005 prevalence estimate of diabetes had already exceeded the rate that was predicted by the World Health Organization (WHO) for 2030.^[15] There is a growing concern that if left unchecked, these trends may slow or even reverse life expectancy gains in the US and other developed countries. In Ontario alone, diabetes has been shown to reduce healthy life expectancy by 2.7 and 2.9 years respectively.^[16] The economic and medical consequences of 4 complications arising from diabetes, including cardiovascular disease and kidney failure, are significant.

Excess body weight or obesity is associated with insulin resistance and is overwhelmingly associated with incidence of type 2 diabetes. Furthermore, it has now been demonstrated through randomized trials that diabetes can be prevented or delayed through reduction in body weight and consequently intervention strategies that target weight reduction or prevention of weight gain are largely recognized as integral to primary prevention of diabetes.^[17]

In addition to obesity several lifestyle, environmental and demographic factors have been associated with diabetes, the main ones being: ethnicity, physical activity, alcohol and tobacco. There is growing evidence that certain ethnic groups are at increased risk for developing type-2 diabetes. Both intervention and observational studies have supported

the reduced incidence of type 2 diabetes associated with increased physical activity. Physical activity can reduce diabetes risk by eliciting physiological changes at the metabolic level related to insulin-stimulating pathways in addition to aiding in the maintenance of a healthy body weight. Several observational studies have now confirmed that shown that moderate alcohol consumption is associated with a reduced risk of developing diabetes whereas smoking appears to increase risk of diabetes.

However analysis of electrolyte is often advised without a true indication in diabetes cases. So we took up a study to analyse serum electrolyte profile in Diabetes Mellitus cases in order to determine whether routine measurement of electrolytes can be safely avoided in diabetes mellitus. As electrolytes are included as one of the kidney function test parameters, an attempt was made to correlate electrolytes with serum creatinine and serum urea levels to see whether in Diabetes Mellitus.

Material and Methods

A total number of 278 subjects were selected for study at CCM Medical College Hospital Durg. In which 178 subjects are suffering from type-2 DM average range of 30 to 65 years. 100 subjects age, sex matched was selected for control group. Controls were clinically and physically normal and healthy.

Table1: Distribution of Study group subjects

Groups	No of Subjects
Normal Healthy Group	100
Type-2 DM patients	178
Male type-2 DM patients	106
Female type-2 DM patients	72

Table 2: Routine investigations in patients of cardiovascular disease and controls

Biomedical Parameters	Control Subjects (Mean \pm SD)	Type-2 DM patients (Mean \pm SD) Male	Type-2 DM patients (Mean \pm SD) Female	'P' value
Blood Urea (mg/ dl)	22 \pm 7.48	42 \pm 19	39 \pm 26	<0.001
Uric acid (mg/ dl)	5.26 \pm 2.84	12.26 \pm 7.81	10.96 \pm 6.37	<0.001
Serum Creatinine	0.83 \pm 0.31	2.92 \pm 2.43	2.26 \pm 2.08	<0.001
Sodium (mmol/ l)	139.16 \pm 2.83	134.72 \pm 6.02	133.82 \pm 4.98	<0.001
Potassium (mmol/ l)	4.62 \pm 0.46	6.28 \pm 1.07	5.98 \pm 1.02	<0.001
Serum Calcium (mg/dl)	9.44 \pm 0.48	10.05 \pm 0.79	9.95 \pm 0.69	<0.001

* $P < 0.05$ - stastically significant

Sample Collection

5 ml blood sample was collected in plain dry test tube. Serum sample was obtained by centrifugation and sample were immediately separated into another plain dry test tube and stored at -17° C. Serum sample was used to estimate serum creatinine, serum urea by using semi autoanalyser and serum electrolyte by using electrolyte analyzer. Serum creatinine was analyzed using Jaffe's method, blood urea by DAM method, serum sodium / potassium by flame photometry or electrolyte analyzer and uric acid by enzymatic method.

Stastical Analysis:

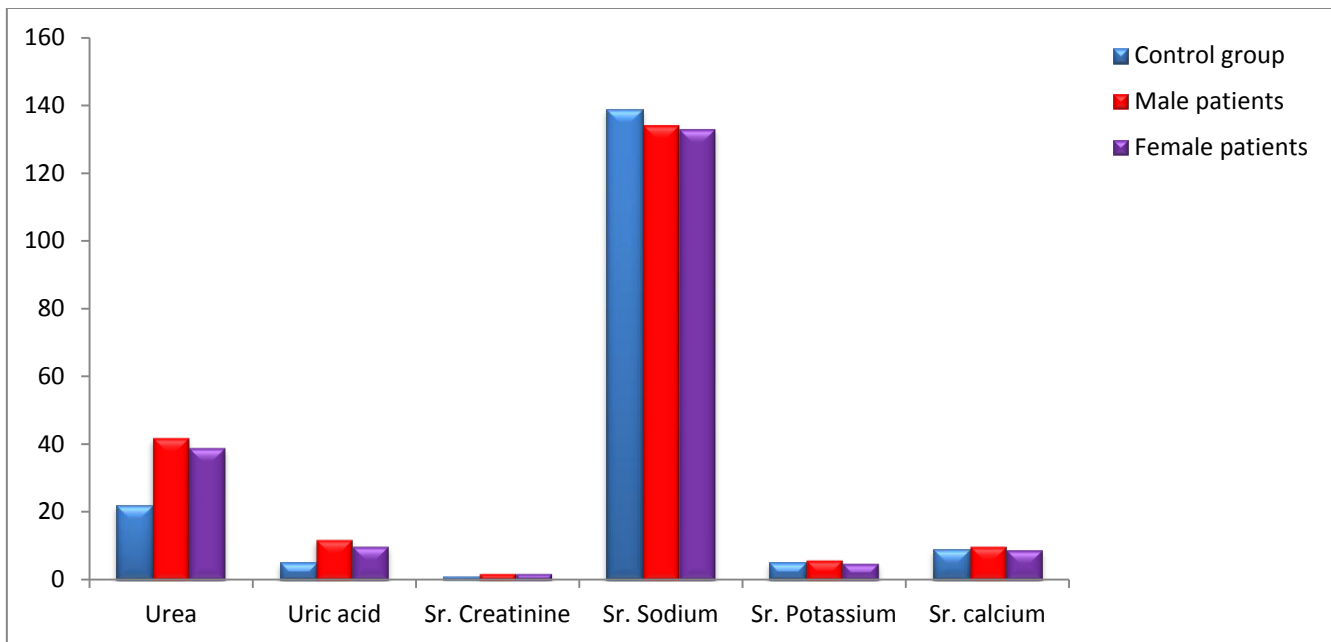
Data were expressed as mean \pm SD. Mean values were assessed for significance by unpaired student -t test. A statistical analysis was performed using the Stastical Package for the Social Science program (SPSS, 23.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.05$ were considered statistically significant.

Ethical Considerations:

Permission to carry out the project was sought from authorities in charge of the concerned department, including the Consultant and the Ward Incharge. Ethical approval was obtained from the Joint Research Ethics Committee of the College.

Results and Discussion:

There were 106 males and 72 females patients selected for study group and 100 normal health for control group. Levels of serum creatinine, serum urea, serum electrolytes and serum uric acid are given in following table.



The present study showed decrease in serum sodium in type-2 diabetics when compared to controls. The Mean±SD of serum sodium in diabetic group was 134.72 ± 6.02 mmol/L, 133.82 ± 4.98 in male and female respectively and in control group was 139.16 ± 2.83 mmol/L. In a study done by Shenqi Wang et al.,^[9] the serum sodium was significantly lower in diabetics with Mean±SD 141.0 ± 2.4 mmol/L. Similar findings were consistent with the study done by San-E Ishikawa et al.,^[18] Under physiological conditions, most of the sodium is reabsorbed in the proximal tubule of the kidney. Hyperglycemia-induced osmotic diuresis, which can increase excretion, is thought to be a primary mechanism underlying the decreased serum concentrations of sodium. It has been observed that cellular membrane electrolyte transporter $\text{Na}^+ - \text{K}^+ - \text{ATPase}$ dysfunction in diabetic subjects, can be secondary to hyperglycemia which leads to electrolyte disturbances within cells.^[9]

The present study showed increase in serum potassium in type-2 diabetics when compared to controls. The Mean±SD of serum potassium in diabetic group was 6.28 ± 1.07 mmol/L in male and 5.98 ± 1.02 in female mmol/L and in control group was 4.62 ± 0.46 mmol/L. In a study done by Shenqi Wang et al.,^[9] the serum potassium was significantly higher in diabetics with Mean±SD 4.26 ± 0.37 mmol/L. Similar findings were consistent with the study done by San-E Ishikawa,^[18] and Abdul Rahman Al-Ajlan,^[19] Hyperosmolality would promote cellular dehydration, thus providing an increase in potassium efflux from the cells.^[18]

The present study showed increase in serum calcium in type-2 diabetics when compared to controls. The Mean±SD of serum calcium in diabetic group was 10.05 ± 0.79 mg/dl in male and 9.95 ± 0.69 mg/dl in female and in control group was 9.44 ± 0.48 mg/dl. These findings are in tune with findings of Shenqi Wang et al.,^[9] which shows that serum

calcium was significantly higher in diabetics. Similar findings were consistent with the study done by J Levy et al.,^[20] Ca^{2+} is mainly reabsorbed in the proximal tubule. Its reabsorption is coupled to Na^+ absorption, and it appears to compete with Mg^{2+} for transport in the loop of Henle.

The present study shows that the activity of blood urea, serum creatinine and uric acid was highly significantly increased found in type-2 DM patients compare to normal healthy group. The activity was 42 ± 19 mg/dl, 2.92 ± 2.43 mg/dl, 12.26 ± 7.81 mg/dl in male and in female it was 39 ± 26 mg/dl, 2.26 ± 2.08 mg/dl and 10.96 ± 6.37 mg/dl and 22 ± 7.48 mg/dl, 0.83 ± 0.31 mg/dl and 5.26 ± 2.84 mg/dl respectively. Similar findings observed by N. A. A. Amartey^[21] and showed that the renal function of diabetics has been investigated through this study. Some of the diabetics were having kidney dysfunction due to their elevated blood creatinine and uric acid levels. The study has also shown that the BMI of some of the diabetics fell in the range of overweight and obese; thus, confirming a correlation between BMI and diabetes mellitus. In the diabetic females, there was a strong positive correlation between FBS and BMI. DM is the major cause of renal morbidity and mortality, and diabetic nephropathy is one of chronic kidney failure. Blood urea and creatinine is widely accepted to assess the renal functions. Good control of blood glucose level is absolute requirement to prevent progressive renal impairment. In order to monitor the control of blood glucose level along with blood sugar blood urea can also be important parameter as we found that there is strong correlation of blood sugar and urea level.

Conclusion

This study shows highly significant alterations in Blood Urea, serum creatinine, serum uric acid, Serum Sodium,

Serum Potassium and Serum Calcium 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 diabetes mellitus, electrolyte derangement prevails, so routine measurement of serum electrolyte and renal function could not be avoided in type-2 DM patients. Electrolyte imbalance occur even with normal renal function, however the frequency of electrolyte derangement is more with deterioration of the renal function in diabetes mellitus patients. 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.

References

- [1] Adegate E, Schattner P, Dunn E. An Update on the Etiology and Epidemiology of Diabetes Mellitus. *Ann N Y Acad Sci.* 2006; 1084: 1-29
- [2] American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2006; 29 (1): S43-48.
- [3] 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.
- [4] Mohan V, Sandeep S, Deepa R, et.al. Epidemiology of Type 2 Diabetes: Indian Scenario. *Indian J Med Res.* 2007; 125: 217-230.
- [5] K Park. Park's Textbook of Preventive and Social Medicine, 22nd edition, Chapter-6: Diabetes Mellitus, 2013; P. 362-367.
- [6] Samatha P, Venkateswarlu M, Siva Prabodh V. Lipid Profile Levels in Type 2 Diabetes Mellitus from Tribal Population Of Adilabad In Andhra Pradesh. *JCDR* 2012; 6(4):590-92.
- [7] Parving HH. Microalbuminuria in essential hypertension and diabetes mellitus. *Journal Hypertension Supplement* 1996; 14: 89-94.
- [8] Enyioma N Obineche and Abdu Adem. Update in Diabetic Nephropathy. *Int J Diabetes & Metabolism.* 2005; 13:1-9.
- [9] Shenqi Wang, Xuhong Hou, Yu Liu, et.al. Serum Electrolyte Levels in Relation to Macrovascular Complications in Chinese Patients with Diabetes Mellitus. *Cardiovascular Diabetology.* 2013; 12(146): 1-10.
- [10] McClellan, W. The kidneys and how they work. National Kidney and Urologic Disease Information Clearing House, 2009; 09, 3195 - 3200.
- [11] Glodny, B., Unterholzner, V. and Taferner, B. Normal kidney size and its influencing factors. *British Medical Council: Urology,* 2009; 9, 19 - 22.
- [12] Fioretto, P., Bruseghin, M., Berto, I., et al. Renal protection in diabetes: Role of glycemic control. *Journal of American Society Nephrology,* 2006;17(4), S86-9.
- [13] Deepa, K., Manjunatha goud, B.K., Oinam Sarsina, D., 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.
- [14] Ramachandran A et al. Rising prevalence of NIDDM in an urban population in India. *Diabetologia* 1997; 40: 232-7.
- [15] Manuel D, Schultz S. Diabetes in Ontario: An ICES Practice Atlas. Hux, J. E., Booth, G. L., Slaughter, P. M., and Laupacis. Toronto, Institute for Clinical and Evaluative Sciences. 2003; 94; 4-77-4.
- [16] Calonge N et al. Screening for type 2 diabetes mellitus in adults: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine* 2008; 148: 846-U63.
- [17] Kovacevic MS, Mach L, Roberts G. Bootstrap variance estimation for predicted individual and population-average risks. *Proceedings of the Survey Research Methods Section. American Statistical Association* 2008.
- [18] San-E Ishikawa, Minori Higashiyama, Tomoatsu Nakamura, et.al. Inverse Distribution of Serum Sodium and Potassium in Uncontrolled In patients with Diabetes Mellitus. *Endocrine Journal.* 1999; 46(1): 75-80.
- [19] Abdul Rahman Al-Ajlan. Incidence of Hyperkalemia in Patients of Type-1 and Type-2 Diabetes Mellitus in Saudi Arabia. *Middle East Journal of Family Medicine.* 2007; 5 (3): 27-29.
- [20] J Levy, Z Stern, A Gutman, Y Naparstek, et.al Plasma Calcium and Phosphate Levels in an Adult Noninsulin-Dependent Diabetic Population. *Calcified Tissue International.* 1986; 39(5): 316-318.
- [21] N. A. A. Amartey et. al. Plasma Levels of Uric Acid, Urea and Creatinine in Diabetics Who Visit the Clinical Analysis Laboratory (CAn-Lab) at Kwame Nkrumah University of Science and Technology, Kumasi, Ghana. *Journal of Clinical and Diagnostic Research.* 2015 Feb, Vol-9(2): BC05-BC09