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ORIGINAL RESEARCH ARTICLE

Influence of Hyperglycemia on Renal Function Parameters in Patients with Diabetes Mellitus.

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ABSTRACT

Urea & creatinine are the parameters to diagnose functioning of the kidney. Changes in serum creatinine concentration more reliably reflect changes in GFR than do changes in serum urea concentrations. High sugar in the blood can lead to serious health problems, including heart disease and damage to the nerves and kidneys. Study aimed to analyze the effect of hyperglycemic condition on the renal function parameter like serum urea and serum creatinine. In present study a total of 33 hyperglycemic serum samples were analyzed for their urea & Creatinine for percent variation, from their reference range corresponding to blood sugar value. At blood sugar level I (130-190 mg %) the variation among Urea concentration were analyzed. Out of 33 hyperglycemic serum samples, 15 samples were found in this category. While 190-250 mg % hyperglycemic range the level of urea haven't showed significant variation from their reference range. Out of total 13 serum samples, 1 sample showed variation from their normal range which was also around 6.16%. for higher range of sugar concentration (250 – 380 mg %) in blood serum, the urea concentration haven't showed much deviation only one sample found to be deflected from its normal value & the % variation for these sample was observed to be 2.22%. Creatinine level speckled in the range of 91.5– 97.5% from its normal reference range. Thus study was concluded that too much sugar in the blood can lead to diverge the renal function parameter from their normal ranges and causes serious kidneys problems

Key Words: Renal Function, Hyperglycemia and Urea creatinine concentration.

INTRODUCTION

Our body metabolizes most food we eat into glucose which gives you energy. Insulin (a hormone produced by the pancreas) facilitates this process by allowing the glucose to enter all the cells of your body and be used as energy. When we have a shortage of insulin or our body cannot use insulin properly, it results in Diabetes (Ferrannini *et al* 1985). In diabetes, the cells don't receive glucose and most of it is accumulated in the blood. Too much sugar in the blood can lead to serious health problems, including heart disease and damage to the nerves and kidneys. Failing to control diabetes can give rise to many complications (Hofso *et al* 2009).

The above normal blood sugar level can damage your blood vessels and nerves, leading to these complications. Men and women are equally susceptible to diabetes complications; however, men are more affected by several diabetes related health problems as compared to women. Both type 1 (when the body doesn't produce any insulin) and type 2 (when the body either doesn't produce enough insulin or the cells ignore the insulin) diabetes may develop the same complications and can disrupt a variety of bodily systems.

When blood sugar is high, it can put too much stress on kidneys causing serious damage to the blood vessels, leading to kidney disease. In rare, severe cases, this can lead to kidney failure and the need for a kidney transplant. Diabetic kidney disease takes many years to develop. Overall, kidney damage rarely occurs in the first 10 years of diabetes, and usually 15 to 25 years will pass before kidney failure occurs. The kidneys excrete metabolic waste products and regulate the serum concentration of a variety of substances. At some stage during the course of renal disease, the

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following routinely measured substances often become abnormal and the extent of the abnormality generally depends on the severity of the disease. Serum creatinine and urea concentrations change inversely with changes in GFR and are therefore useful in gauging the degree of renal dysfunction (Schutte *et al* 1981).

Urea & creatinine are the parameters to diagnose functioning of the kidney. . Changes in serum creatinine concentration more reliably reflect changes in GFR than do changes in serum urea concentrations. Creatinine is formed spontaneously at a constant rate from creatinine, and blood concentrations depend almost solely upon GFR. Urea formation is influenced by a number of factors such as liver function, protein intake and rate of protein catabolism (Griffin *et al* 2008).

Urea excretion also depends upon hydration status and the extent of water re-absorption as well as upon GFR. Blood urea levels are quite sensitive indicators of renal disease, becoming elevated when renal function drops to around 25-50% of normal. Creatinine is breakdown product of creatinine phosphate is released from skeletal muscle at a steady rate. (Only a small amount comes from meat in the diet.) 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). If the urine volume goes up, the serum creatinine does go down slightly. Creatinine is generally considered a somewhat more sensitive and specific test of renal function than BUN. Serum Creatinine may serve as a surrogate marker of muscle mass, and a possible relationship between low serum Creatinine and type 2 diabetes has recently been demonstrated. (Hjelmesh *et al* 2010).

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 over time. The first is a cross-sectional assessment at a particular moment. Minimizing diagnostic errors is important, so accuracy of the GFR is critical, specifically in the neighborhood of the threshold for chronic renal failure (CRF; 60 ml/min per 1.73 m^2). The second is a longitudinal assessment to detect systematic decreases in renal function (a negative trend) and requires repeated measurements over time. The most important result is whether a downward trend (slope) is present, regardless of the initial GFR value. Therefore, accuracy of the slope rather than the individual GFR measurements is the primary concern (Hsu C-Y *et al* 2002).

In patients with CRF, trends of renal function over time are determined using one of several approximations of GFR based on serum creatinine. These approximations, however, perform adequately only in advanced disease (GFR <60 ml/min per 1.73 m^2) (Mogensen CE, 1997). In patients who have normal or elevated renal function but are suspected of losing renal function over time, creatinine-based measures are unreliable for detecting trends (K. DOQI 2002).

Onset of type 2 diabetes was at an early age, many have elevated GFR, and their risk for developing ESRD is high. These characteristics make this a suitable population for studying early renal function decline that is generalizable to many type 2 diabetes populations and to the type 1 diabetes population. This study sought to determine how accurately serial determinations of serum cystatin C detect trends (particularly systematic decreases) in renal function over time that have been documented by measurements of iothalamate clearance in patients with normal or elevated GFR. For comparison, we also report how accurately the trends obtained with three commonly used creatinine-based approximations of GFR reflect the trend in iothalamate clearance (Nelson RG et al, 1996).

Blood urea nitrogen is assessed with creatinine test. Serum creatinine proves useful in diagnosing renal failure and diseases. A directly proportional relationship exists between creatinine levels and renal function. Both the blood urea nitrogen (BUN) and creatinine levels are helpful in achieving the BUN to creatinine ratio. This test is a diagnostic tool in recognizing the causative factor for abnormal levels, such as de-hydration, as its consequences in higher **BUN** to creatinine ratio. This is credited to the fact that BUN levels are more than creatinine levels, during dehydration. Both BUN and creatinine levels are increased in the case of kidney malfunctioning or urinary flow damage. As kidneys fail, BUN levels

will rise, as well as the level of creatinine in blood. If levels of creatinine rise, your kidneys may be malfunctioning. Creatinine levels usually rise later than BUN, so it tends to indicate a more chronic condition. So the study aimed to analyze the effect of hyperglycemic condition on the renal function parameter like serum urea and serum creatinine.

MATERIALS AND METHODS

A total of 33 blood samples were collected from hyperglycemic patients from the district hospital of Mandsaur district MP India. Five milliliters (5ml) venous blood was collected at 09.00 hr every morning after overnight fast. The blood was dispensed into plane dry glass test tubes. Serums were isolated by centrifuging in a laboratory centrifuge at 2000g for three minutes immediately after blood clotting and retraction at room temperature. The serums were refrigerated at 4 0 C.

Sample Analysis

Serum creatinine & urea were analyzed by Auto Analyzer at the B. R. Nahata College of Pharmacy, Mandsaur MP India. Serum Creatinine was estimated by Jaffe's method. Creatinine in alkaline medium reacts with picric acid to produce orange red complex. (Bartels,H.*et al*, 1972 ;Bowers,L.D.*et al*. 1980).

Serum urea was estimated by Berthelot method. Urease breaks down the urea into ammonia & CO_2 in alkaline medium .Ammonia liberated from the breakdown of urea reacts with hypochlorite & salicylate to form dicarboxyindophenol. This reaction is catalyzed by the presence of Nitroprusside.The intensity of the colour produced by the reaction is directly proportional to the concentration of urea present in the sample (Fawcett, J.K, Scott, J.E 1960).

RESULT AND DISCUSSION

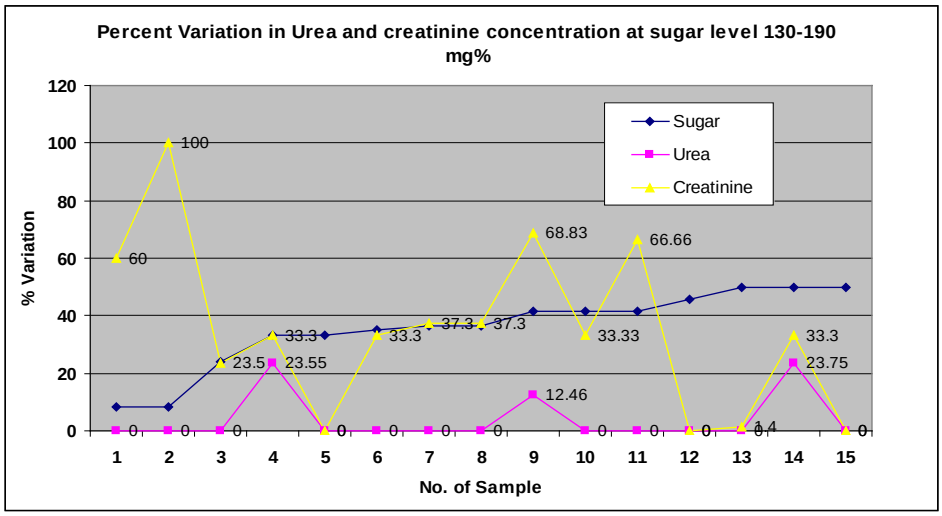
In present study a total of 33 hyperglycemic serum samples were analyzed for their urea & Creatinine for percent variation, from their reference range corresponding to blood sugar value. In these samples the blood sugar level selected from ranges 130-380 mg %. All hyperglycemic serum samples were then categorized into 3 major categories indicated as level I, II and III (**Table 1**).

Table 1:Urea and Creatinine concentration and blood sugar level.

Sample no	Sugar 80-120 mg%	Percent variation	Urea 10-50 mEq.	Percent variation	Creatinine 0.6-1.5 mg/dl	Percent variation
Urea & Creatinine concentration & Blood Sugar level I 130-190 mg%						
1	130	8.3	35.613	0.0	2.4	60
2	130	8.3	12.587	0.0	3	100
3	149	24.16	25.6	0.0	0.459	23.5
4	160	33.33	7.645	23.55	2	33.3
5	160	33.33	11.60	0.0	0.661	0.0
6	162	35	16.548	0.0	0.4	33.3
7	164	36.6	47.619	0.0	2.06	37.3
8	164	36.6	47.619	0.0	2.06	37.3
9	170	41.6	56.23	12.46	0.187	68.83
10	170	41.6	16.548	0.0	0.4	33.33
11	170	41.6	36.202	0.0	0.2	66.66
12	175	45.83	44.76	0.0	1.4	0.0
13	180	50	27.594	0.0	1.521	1.4
14	180	50	7.625	23.75	2	33.3
15	180	50	23.913	0.0	1	0.0
Urea & Creatinine concentration & Blood Sugar level I 190-250 mg%						
1	200	66.66	10.90	0.0	0.5483	8.61
2	200	66.66	16.548	0.0	0.4	33.3
3	205	70.83	26.928	0.0	0.411	31.5
4	220	83.33	40	0.0	0.21	65
5	220	83.33	12.220	0.0	1.333	0.0
6	229	90.83	53.084	6.168	1.046	0.0
7	230	91.66	42.87	0.0	0.8	0.0
8	230	91.66	36.881	0.0	0.3	50
9	230	91.66	42.42	0.0	2	33.3
10	240	100	20.446	0.0	0.8	0.0
11	245	104.16	24.282	0.0	0.4	33.3
12	250	108.33	35.171	0.0	0.9	0.0
13	250	108.33	16.388	0.0	0.666	0.0
Urea & Creatinine concentration & Blood Sugar level I 250-380 mg%						
1	275	129.16	14.44	0.0	1.298	0.0
2	280	133.33	21.214	0.0	.015	97.5
3	280	133.33	24.669	0.0	.8	0.0
4	300	150	51.11	2.22	.0507	91.55
5	380	216.66	24.669	0.0	.8	0.0

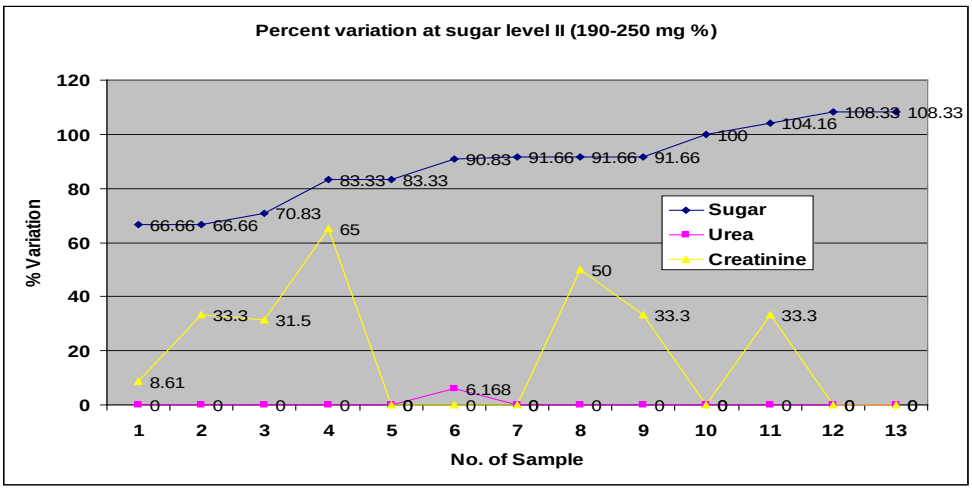
At blood sugar level I (130-190 mg %) the variation among Urea concentration were analyzed. Out of 33 hyperglycemic serum samples, 15 samples were found in this category. Out of these 12 samples were in the normal range indicated no variation from its reference range and 3 samples showed deviation from their reference range.

The percent variation value varied from 12.46 – 23.75 for Urea. When study data were analyzed for creatinine concentration it was found that, out of total 15 only 3 samples were found in their reference range whereas 12 serum samples showed variation from their reference value. The percent variation for Creatinine was found between 1.4 – 100%. The analysis showed that at hyperglycemic level Creatinine showed maximum variation from their reference range as compared to Urea The concentration of urea haven't showed significant fluctuation from their normal range (**Fig 1**).



(Fig 1)- Percent Variation at sugar level I (130-190 mg %).

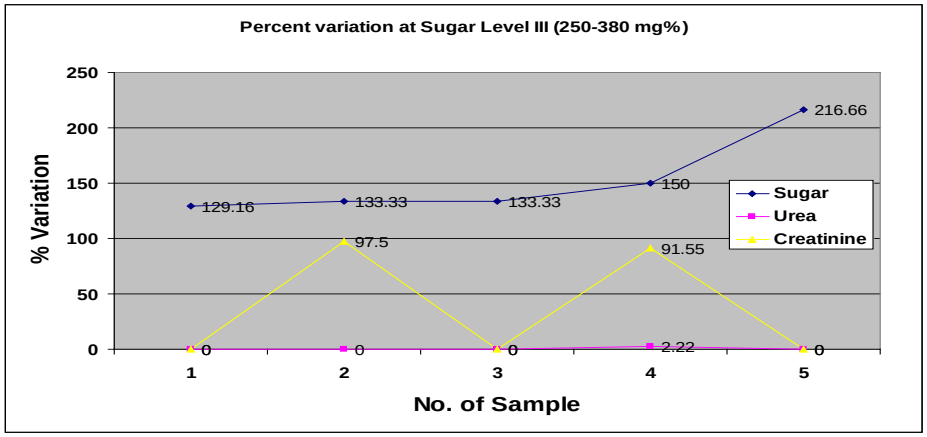
When data analyzed for 190-250 mg % hyperglycemic range the level of urea haven't showed significant variation from their reference range. Out of total 13 serum samples, 1 sample showed variation from their normal range which was also around 6.16% whereas for Creatinine, Out of 13 samples 6 sample showed no variation from their normal range whereas rest showed variation from their normal value the percentage variation for these sample varied from 8.61 to 65 %from their reference range. In this category also percentage variation of creatinine showed more variation as compared to Urea (**Fig 2**).



(Fig 2) – Percent Variation at Sugar level II (190-250 mg%)

Out of 33 serum samples 5 samples were identified for highest hyperglycemic range. The study data indicated that when urea & Creatinine variation observed for higher range of sugar concentration (250 – 380 mg %) in blood serum, the urea concentration haven't showed much deviation only one sample found to be deflected from its normal value & the % variation for these sample was observed to be 2.22%. Creatinine

level speckled in the range of 91.5– 97.5% from showed that for very high range of blood sugar its normal reference range. Study creatinine concentration variation found very high as compare to other two categories (**Fig 3**).



(Fig 3) – Percent Variation at Sugar level II (250-380 mg %)

Similarly In 2010 Hjelmesh *et al* found the population of 1, 017 consecutive morbidly obese subjects with an eGFR > 60 ml/min our initial hypothesis of an inverse association between serum creatinine and Type 2 diabetes mellitus. After these breakpoints increasing creatinine levels did not decrease the odds further. Adjustments for known modifiable and non-modifiable risk factors left the piecewise effect for both women and men largely unchanged.

Emre Sinan *et al* 2006 found that, a total of 112 patients were evaluated, 56 of whom had gestational diabetes. All of the patients had single estimations of serum uric acid, creatinine, albumin and liver enzymes carried out on booking between the 24th and 28th gestational weeks. Creatinine levels were significantly higher in the diabetic group than in the control group [0.6±0.15 vs. 0.43±0.1 mg/dL (53.04±13.26 µmol/L vs. 38.01±8.84 µmol/L), $p<0.001$]. Uric acid levels were also higher in the diabetic patients, but this elevation was not statistically significant [4.42±1.09 vs. 4.1±0.84 mg/dL (260.78±64.31 µmol/L vs. 241.49±49.56 µmol/L), $p>0.05$]. There were no differences in mean albumin concentrations or liver function tests. Their study concluded that, patients with gestational diabetes had significantly higher levels of creatinine than normal pregnant women (Emre Sinan *et al* 2006).

Bruce A *et al* 2005, draw the conclusion that the longitudinal behavior of cystatin C provides convincing evidence that sequential measurements of cystatin C are an accurate and precise alternative to gold standard methods for measuring the urinary clearance of exogenous markers to quantify trends in renal function and detect declining renal function. This finding has major implications for clinical research because it demonstrates the existence of a practical, inexpensive, and accurate alternative for investigating trends in renal function in epidemiologic studies. Although creatinine-based estimates may provide sufficient accuracy for diagnosing the presence of CRF, unlike cystatin C, they do not have sufficient precision for detecting longitudinal trends in GFR in the normal and hyperfiltration ranges. Validation of cystatin C in this range of renal function permits epidemiologic research into the timing and determinants of the initiation of early renal function decline and the early intervention to prevent chronic kidney disease in patients with type 1 or type 2 diabetes, for whom hyperfiltration is a common feature of the early stages of kidney complications.

CONCLUSION

The present study concluded that, at hyperglycemic level Creatinine showed maximum variation from their reference range as compared to Urea The concentration of urea haven't showed significant fluctuation from their normal range when tested percent variation at sugar level I. whereas at sugar concentration increased up to 250 mg% also percentage variation of creatinine showed more variation as compared to Urea. For very high range (Up to 380 mg %) of blood sugar creatinine concentration variation found very high as compare to other two categories Thus study was concluded that too much sugar in the blood can lead to diverge the renal function parameter from their normal ranges and causes serious kidneys problems

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REFERENCES

1. Hofso D, Jenssen T, Bollerslev J, Roislien J, Hager H, Hjelmesaeth J: Anthropometric characteristics and type 2 diabetes in extremely obese Caucasian subjects: a cross-sectional study**.** *Diabetes Research and Clinical Practice* 2009, 86:e9-11.
2. Ferrannini E, Smith JD, Cobelli C, Toffolo G, Pilo A, DeFronzo RA: Effect of insulin on the distribution and disposition of glucose in man**.** *Journal of Clinical Investigation* 1985, 76:357-364.
3. Schutte JE, Longhurst JC, Gaffney FA, Bastian BC, Blomqvist CG: Total plasma creatinine: an accurate measure of total striated muscle mass**.** *Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology* 1981, 51:762-766.
4. Bartels, H *et al* ., (1972), Clin Chem. Acta, 37:193
5. Bowers, L. D. *et al* (1980), Clin. Chem., 26:551.
6. Fawcett, J.K.,Scott, J.E.,J.Clin.Path; 1960;13:156-159.
7. Harita N, Hayashi T, Sato KK, Nakamura Y, Yoneda T, and Endo G, *et al.*: Lower serum creatinine is a new risk factor of type 2 diabetes: the Kansai healthcare study**.** *Diabetes Care* 2009, 32:424-426.
8. Griffin KA, Kramer H, Bidani AK: Adverse renal consequences of obesity**.** *American Journal of Physiology - Renal Physiology* 2008, 294:F685-F696.
9. Hjelmesh, Jo Rslien, Njord Nordstrand, Dag Hofs, Helle Hager and Anders Hartmann, 'Low serum creatinine is associated with type 2 diabetes in morbidly obese women and men: a cross-sectional study' *BMC Endocrine Disorders* 2010, 10:6
10. Emre Sinan Gungor, Nuri Danisman and Leyla Mollamahmutoglu, 'Relationship between serum uric acid, creatinine, albumin and gestonal diabetes mellitus' Clinical laboratory medicine, vol. 44 issue 8, Pages 974-977, 2006.
11. Bruce A. Perkins, Robert G. Nelson, Betsy E.P. Ostrander, Kristina L. Blouch, Andrzej S. Krolewski, Bryan D. Myers and James H. Warram* Detection of Renal Function Decline in Patients with Diabetes and Normal or Elevated GFR by Serial Measurements of Serum Cystatin C Concentration J Am Soc Nephrol 16: 1404-1412, 2005.
12. Hsu C-Y, Chertow GM, Curhan GC: Methodological issues in studying the epidemiology of mild to moderate chronic renal insufficiency. *Kidney Int* 61 : 1567 – 1576, 2002.
13. K. DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. *Am J Kidney Dis* 39: S1 –S266, 2002.
14. Mogensen CE: How to protect the kidney in diabetic patients: With special reference to IDDM. *Diabetes* 46: S104 –S111, 1997.
15. Nelson RG, Bennett PH, Beck GJ, Tan M, Knowler WC, Mitch WE, Hirschman GH, Myers BD: Development and progression of renal disease in Pima Indians with non-insulin-dependent diabetes mellitus. Diabetic Renal Disease Study Group. *N Engl J Med* 335: 1636 –1642, 1996.