

# ASSOCIATION OF SERUM URIC ACID WITH TYPE II DIABETES MELLITUS

Abdul Jalal Safi, Rashid Mahmood, Mudassir Ahmad Khan, Amin-ul-Haq

*Department of Biochemistry and Department of Physiology,  
Khyber Medical College, Peshawar.*

## ABSTRACT

**Objective:** To find out the association of serum uric acid with type-II diabetes mellitus and to compare the level of serum uric acid between obese and non-obese type-II diabetics.

**Material and Methods:** Fifty obese and fifty non-obese diabetic patients were included in the study one hundred non-diabetic subjects were selected as control group. The results were analysed by t-test for serum uric acid, glucose and lipid profile.

**Results:** The mean level of serum uric acid in obese type-II diabetic patients was 6.07 mg/dl as compared to 5.01 mg/dl in the control group. The difference was significant statistically.

**Conclusion:** Hyperuricemia is significantly associated with type-II diabetes mellitus and can increase the morbidity and mortality from diabetes if not managed in time.

**Key words:** Serum Uric Acid, Type-II Diabetes mellitus and Lipid profile.

## INTRODUCTION

Diabetes mellitus is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin<sup>1</sup>. It may be associated with a number of complications including nephropathy, neuropathy, retinopathy, diabetic foot and macro and micro vascular diseases<sup>2</sup>.

Hyperuricemia is common finding in non-insulin dependent diabetes mellitus<sup>3</sup>. The uric acid, which is the end product of

purine metabolism<sup>4</sup> in human, is found to be raised in many patients with Type-II diabetes mellitus<sup>5</sup>. The actual mechanism of hyperuricemia found in these patients is not known but it has been observed that compensatory hyperinsulinemia in insulin resistant individuals impose an antiuricosuric effect on the kidney<sup>6,7</sup>. The association has also been explained on the basis of genetic predisposition<sup>8,9</sup>. But the relationship of serum uric acid with Type-II diabetes mellitus and obesity has not been demonstrated or explained in the literature; therefore the

present study was designed to look for any association of serum uric acid with Type-II diabetes mellitus.

Cardiovascular disease, particularly coronary artery disease, remains the leading cause of mortality worldwide, despite recent substantial declines. Hypertension and diabetes mellitus, long recognized as risk factors for both stroke and myocardial infarction are important targets for preventive intervention. It has been seen that hyperuricemia is commonly associated with obesity, hypertriglyceridemia, diabetes mellitus and hypertension<sup>3</sup>.

Recently, elevation of serum uric acid has been found to be associated with subsequent morbidity and mortality in the general population among patients with congestive heart failure, diabetics and hypertensive patients<sup>10</sup>. It has been proposed that the serum uric acid levels are linked to the other risk factors, such as hypertension, dyslipidaemia and diabetes<sup>11</sup>. The probable mechanism is that uric acid stabilizes platelet aggregation and enhances thrombotic tendency<sup>12</sup>. Serum uric acid is also associated with body mass index (BMI)<sup>13</sup>.

## MATERIAL AND METHODS

One hundred diagnosed patients suffering from diabetes mellitus having type-II D Mellitus for more than three years were randomly selected from the Outdoor Patients Department, Department of Medicine, Khyber Teaching Hospital, Peshawar. These patients were then divided in to two groups; obese and non-obese. Obesity was taken as body mass index of more than 25 kg/m<sup>2</sup>.

One hundred healthy individuals were selected from among the staff of Khyber Medical College, Peshawar, Khyber College of Dentistry and Khyber Teaching Hospital, Peshawar to constitute the control group. They had no history of any chronic illness

or metabolic disorders. The study was conducted in year 2002. All the subjects were more than 40 years of age.

Similarly diabetic patients suffering from diseases like cardiovascular diseases, kidney disorder and hepatic disorders were also not included in the study.

The male to female ratio was equal in all the groups. The blood samples for all the subjects were analyzed for serum glucose, serum uric acid, serum cholesterol, triacylglycerols, HDL-c, LDL-c and VLDL-c. The samples were selected in simple random manner. The results were statistically analysed by using t-test.

## RESULTS

The average level of serum uric acid in the patients was 6.07 mg/dl as compared to 5.01 mg/dl in the control group. The difference was statistically significant ( $p < 0.05$ )<sup>1</sup>.

The difference was more pronounced in the obese group; the serum uric acid was 6.21 mg/dl among the obese patients i.e., an increase of 1.20 mg/dl as compared to an increase of 0.50 mg/dl in the non-obese study group.

The average levels of serum uric acid in female patients were 5.63 mg/dl as compared to 4.31 mg/dl in the female control group with a difference of 1.32 mg/dl ( $p < 0.05$ ). The average levels of serum uric acid in male study group were 6.60 mg/dl as compared to 5.18 mg/dl in the control group, a difference of 0.79 mg/dl ( $p < 0.05$ ) (Table No. 1).

Lipid profile was also measured in both groups (controls and Patients). It was found that lipid profile was abnormal in 48.5% of the patients. But there were 16% patients in whom the lipid profile was normal but serum uric acid levels were more than normal as compared to zero percent in the control

**FASTING BLOOD GLUCOSE, SERUM URIC ACID AND LIPID PROFILE  
OF CONTROL SUBJECTS (n = 100)**

Subjects	Male			Female			Overall		
	Min	Max	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD
Fasting Blood Sugar (mg/dL)	59	110	80.10±10.113	63	112	82.11±11.110	59	112	81.66±10.813
Serum Uric Acid (mg/dL)	3.4	7.8	5.81±1.323	2.7	6.0	4.31±1.490	2.7	7.8	5.01±1.837
Serum Cholesterol (mg/dL)	140	220	180.76±17.699	145	226	184.76±18.131	140	226	182.61±17.613
Triacylglycerols (mg/dL)	96	200	157.66±10.522	100	210	161.33±9.232	96	210	159.01±10.112
HDL-c (mg/dL)	30	72	55.15±6.123	37	96	58.13±7.345	30	96	157.69±7.068
LDL-c (mg/dL)	60	135	100.31±11.136	62	136	103.61±11.360	60	136	102.69±11.179
VLDL-c (mg/dL)	19.2	40	31.53±2.104	20	42	32.26±1.842	19.2	42	31.80±2.002

TABLE - 1

group. 14% of the subjects in the obese group showed elevated serum uric acid with normal lipid profile. This showed that serum uric acid is significantly

associated with Type-II diabetes mellitus, independent of body mass index, hyperlipidaemia and hypertension ( $p < 0.05$ ) (Table No. 2).

**FASTING BLOOD GLUCOSE, SERUM URIC ACID AND LIPID PROFILE  
IN OBESE TYPE-II DIABETIC SUBJECTS (n = 50)**

Subjects	Male			Female			Overall		
	Min	Max	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD
Fasting Blood Sugar (mg/dL)	69	170	132.66±17.652	72	172	134.56±16.131	69	172	133.65±16.781
Serum Uric Acid (mg/dL)	3.6	9.2	5.81±1.323	3.5	8.6	5.91±1.321	3.5	9.2	6.21±1.1.391
Serum Cholesterol (mg/dL)	150	234	180.76±17.699	155	256	198.51±18.121	150	25	194.21±17.912
Triacylglycerols (mg/dL)	100	270	157.66±10.522	108	280	176.11±14.213	100	280	173.17±13.631
HDL-c (mg/dL)	30	63	55.15±6.123	32	67	49.31±7.112	30	67	47.81±7.912
LDL-c (mg/dL)	70	155	100.31±11.136	76	160	119.01±10.623	70	160	116.78±9.987
VLDL-c (mg/dL)	20	54	31.53±2.104	21.6	56	35.22±2.842	20	56	34.62±2.726

TABLE - 2

## DISCUSSION

It was seen that serum uric acid is positively associated with type-II diabetes mellitus. The association was relatively more significant in females, in obese patients and patients with hyperlipidaemia. These results were comparable in most aspects to the similar studies performed by different research workers<sup>14, 15, 16,17,18,19</sup>.

Although a few other researchers observed negative association. Ishihara M et al<sup>19</sup> studied the relationship between the urinary excretion of calcium and uric acid in type-II diabetic patients. They found that in diabetic patients, uric acid clearance/creatinine clearance was higher and the serum level of uric acid was lower than in normal subjects. Their analysis showed that diabetic patient had increased fractional excretion of uric acid. Gonza SL et al<sup>20</sup> observed similar finding in insulin dependent diabetic patients.

The actual mechanism of hyperuricemia found in many diabetic patients is not known but different theories have been presented. Quinones et al., (1995)<sup>14</sup> observed that hyperuricemia is a frequent finding in insulin resistant states. He found that insulin induces change in fractional uric acid and sodium excretion co-related with one another and physiological hyperinsulinemia acutely reduces urinary uric acid and sodium excretion in coupled patients. Moriwaki et al., (1995)<sup>7</sup> studied the effects of glucose infusion on the renal clearances of uric acid, Xanthine and oxyipurinol and found that the effect was not related to osmotic diuresis but induced by glycosuria and/ or hyperglycemia.

Muscelli and coworkers (1996)<sup>16</sup> observed the effect of insulin or urinary excretion in normal subjects and found that hyperinsulinemia caused a significant decrease in the urinary excretion of uric acid. Quinones et al., (1995)<sup>14</sup> also found a similar reason. They observed that in insulin

resistant individuals compensatory hyperinsulinemia imposes a chronic antinatriuretic and antiuricosuric pressure on the kidney.

The association of serum uric acid with diabetes mellitus has also been explained on the basis of genetic predisposition<sup>17,21</sup>. Hyperuricemia may result in acute gouty arthritis, nephrolithiasis and nephropathy<sup>22, 23</sup>. Hyperuricemia with diabetes mellitus may specially give rise to complications like overt nephropathy<sup>2</sup> and stroke<sup>7</sup>.

## CONCLUSION

Hyperuricemia is a common finding in Type-II diabetes mellitus adding to the morbidity and mortality of these patients. In this study it was found that serum uric acid is significantly associated with type-II diabetes mellitus in general and obese patients in particular independent of body mass index, hyperlipidemia and hypertension.

## REFERENCES

- 1- Marks, V. and Teale, J.D., Hypoglycemia in Adults. Baillier's Clinical Endocrinology and Metabolism. 1993; (3): 705-729.
- 2- Kumar, P. J. and Clark, M. L., Diabetes mellitus and other disorders of Metabolism. Clinical Medicine. A Textbook for Medical Students and Doctors. W.B Saunders, London, 5<sup>th</sup> Ed., 2002; 1092-1100.
- 3- Kelley, N. W. and Palella, T. D., Gout and Other Disorders of Purine Metabolism. Harrison's Principles of Internal Medicine. McGraw Hill Book Company, New York, 15<sup>th</sup> Ed., Vol.2., 2001; 1994-97.
- 4- Murray, R. K., Granner, D. K., Mayes, P. A. and Rodwell, V. W., Metabolism of Purine and Pyrimidine Nucleotides. Harper's Biochemistry. Appleton and Lange, Stamford, 25th Ed., 2000; 395.
- 5- Lehto, S., Niskanen, L., Ronnema, T. and Laakson, M., Serum Uric Acid is a strong predictor of stroke in Patient with Non-insulin Dependent Diabetes Mellitus. Stroke, 1998; 29(3): 635-639.
- 6- Clausen, J. O., Borch, J. K., Ibsen, H. and Pedersen, O., Analysis of the relationship

- between fasting Uric Acid and the Insulin sensitivity index in a Population-based sample of 380 Young healthy Caucasians. *Eur J Endocrinol.*, 1998; 138(1):63-69.
- 7- Moriwaki, Y., Yamamoto, T., Takahashi, S., Suda, M. and Higashino, K., Effect of Glucose infusion on the Renal Transport of Purine bases and Oxypurinol. *Nephron*, 1995; 69 (4): 424-427.
  - 8- Wang, G., Li, Q., Niu, T., Chen, C. and Xo, X., Association of GYS1 and Beta (3)-AR gene with postprandial Hyperglycemia and Serum Uric Acid in Type 2 Diabetes mellitus. *Chin Med J Engl.*, 2002; 115 (9): 1308-1311.
  - 9- Shearman, D. J. C., Disease of the Alimentary Tract and Pancreas. *Davidson's Principles and Practice of Medicine*. Churchill Livingstone, Edinburgh, U. K., 19<sup>th</sup> Ed., 2002; 644-646.
  - 10- Alderman, M., Uric Acid in Hypertension and Cardiovascular Disease. *Can J Cordiol.*, 1999; 15:20-25.
  - 11- Milionis, H. J. and Elisaf, M. S., Management of Hypertension and Dyslipidaemia in Patients Presenting with Hyperuricemia. *Curr Med Res Opin.*, 2000; 16 (3):164-170.
  - 12- Lehninger, A. L., Nelson, D. L. and Cox, M. M., Biosynthesis of Amino Acid Nucleotides and related molecules. *Principles of Biochemistry*. CBS Publishers and Distributors, New Delhi, 2nd Ed., 1993; 727-730.
  - 13- Ying, Li., Stamler, J., Xiao, Z., Folsom, C., Tao, S. and Zhang, H., Serum Uric Acid and its Correlates in Chinese Adult Populations, Urban and Rural, of Beijing. *The PRC, USA Collaborative Study in Cardiovascular and Cardiopulmonary Epidemiology. International J Epidemiol.*, 1997; 26:288-296.
  - 14- Quinone, G. A., Natali, A., Baldi, S., Frascerra, S., Sanna, G., Ciociara, D. and Ferrannini, E., Effect of Insulin on Uric Acid excretion in Humans. *Am J Physiol.*, 1995; 268(1): 1-5.
  - 15- Iwaski, N., Ogata, M., Tomonaga, O., Kuroki, H., Kasahara, T., Yano, N. and Iwamoto, Y., Liver and Kidney function in Japanese patients with Maturity-onset Diabetes of the Young. *Diabetes Care*, 1998; 21 (12): 2144-2148.
  - 16- Muscelli, E., Natali, A., Bianchi, S., Bigazzi, R., Galvan, A.Q., Sironi, A.M., Frascerra, S., Ciociaro, D. and Ferrannini, E., Effect of Insulin on Renal Sodium and Uric Acid handling in Essential Hypertension. *Am J Hypertens.*, 1996; 9 (8): 746-752.
  - 17- Edwards, C.R.W., Baird, J.D., Frier, B.M., Shepherd, J. and Toft, A.D., Endocrine and Metabolic Diseases, including Diabetes Mellitus. *Davidson's Principles and Practice of Medicine*. Churchill Livingstone, Edinburgh, U. K., 19<sup>th</sup> Ed., 2002; 644-648.
  - 18- Guan, M. P., Xue, Y. M., Shen, J., Zhou, L., Gao, F., Liu, S.Q. and Li C. Z., Serum Uric Acid in Type 2 Diabetic patients complicated by stroke. *Di Yi Jun Yi Da Xue Xue Bao.*, 2002; 22(1): 70-71.
  - 19- Ishihara, M., Shinoda, T. and Yamada, T., Co-occurrence of Hypercalciuria and Hypouricemia in Type 2 Diabetic patients. *Diabet Med.*, 1989; 5(5): 406-411.
  - 20- Gonzalez, S. L., Gaeica, E. J., Martinez, B. A. and Fernandez, P. J., Quiles, J. L. and Hernandez, J., Renal metabolism of Uric Acid in Type-I Insulin-nondependent diabetic patients: Relation to Metabolic compensation. *Horm Metab Res.*, 1997; 29 (10): 250-253.
  - 21- Bo, S., Cavallo, P.P., Gentile, L., Repetti, E. and Pagano, G., Hypouricemia and Hyperuricemia in Type-II Diabetes: Two Different Phenotypes. *Eur. J Clin Invest.*, 2001; 31(4):318-321.
  - 22- Mikkelsen, W., Moge, H. J. and Valkenburg, H., The distribution of Serum Uric Acid values in a Population unselected as to Gout or Hyperuricemia, Tecumseh, Michigan; 1950-1960. *Am J Med.*, 1965; 39: 242-251.
  - 23- Kelley, W. N. and Wortman, R. L., Gout and Hyperuricemia. *Textbook of Rheumatology*. W. B. Saunder and Company, Philadelphia, 5th Ed., 1997; 1323-1328.

**Address for Correspondence:**

Dr. Abdul Jalal Safi  
 Department of Biochemistry  
 Khyber Medical College, Peshawar.