Section: Physiology

Original Research Article

# CORRELATION OF SERUMURIC ACID LEVEL WITH GLYCAEMIC STATUS IN TYPE -2 DIABETES MELLITUS PATIENTS

**Rakesh Kumar[1], Sheela Kumari[2]**

[1]PG Student, Department of Physiology, DMCH, Laheriasarai, India.
[2]Professor, Department of Physiology, Darbhanga Medical College, Laheriasarai, India.

*Received* : 09/06/2023
*Received in revised form* : 05/08/2023
*Accepted* : 23/08/2023

*Keywords:*
*Serumuric acid level, Glycaemic status.*

Corresponding Author:
**Dr. Rakesh Kumar,**
Email: rkjhadmch2k12@gmail.com

DOI: 10.47009/jamp.2024.6.3.188

Source of Support: Nil,
Conflict of Interest: None declared

*Int J Acad Med Pharm*
2024; 6 (3); 917-920

## Abstract

**Background:** Elevated serum uric acid is a consistent feature of the insulin resistance syndromes, which are also characterized by elevated plasma insulin level, blood glucose concentration, serum triglyceride concentration, raised body mass index and waist-hip ratio. **Materials and Methods:** The study comprised of type 1 Diabetes Mellitus cases visiting the inpatient and outpatient at Darbhanga Medical College, Darbhanga Bihar. Age and sex matched healthy volunteers served as controls. Total Number of Subjects was 80, with 40 controls and 40Type 1 Diabetes Mellitus cases. Inclusion Criteria was patients with Type 1 Diabetes Mellitus on treatment in all age groups. Exclusion Criteria was Type 1 Diabetes Mellitus with established micro & macro vascular complications. Patients on drugs which alters serum uric acid levels. **Results:** Out of 40 cases and 40 controls, 20 were male and 20 female cases and 22 male and 18 female controls. Among cases the average age of diabetic person is18.76±6.28 yrs. The numbers of male subjects were higher than female subjects in controls, compared to study group. **Conclusion:** Poor glycemic control is associated with increased serum uric acid levels and increasing duration of type 1 diabetes. was observed between serum uric acid levels in the study group.

## INTRODUCTION

Type 1 diabetes mellitus is characterized by abrupt onset of severe diabetic symptoms and total reliance on exogenous insulin for survival (International Textbook of Diabetes Mellitus). Type 1 Diabetes comprises ~10% of all cases of diabetes mellitus (Belfiore, 2000). Although type 1 diabetes mellitus most commonly develops before the age of 30, an autoimmune beta cell destructive process can develop at any age. There is considerable geographic variation in the incidence of type 1 Diabetes mellitus with the incidence of 1 to 3/100,000 per year (Fauci et al., 2008). Elevated serum uric acid levels and significant renal clearance have been associated with early impaired renal function (Elizabeth Gołembiewska et al., 2005) and poor glycemic control Several studies in type 2 diabetes mellitus have shown the association of high serum uric acid levels as a str predictor of the disease. This study was done to study the significance of serum uric acid in Type 1 Diabetes mellitus, which also helps to know the relationship between glycemic control, duration of diabetes mellitus and uric acid levels. Early raise of these parameters may help in early diagnosis and management of diabetic complications and may help in preventing further progression of the complications in Type 1 Diabetes mellitus. Objectives are to Study the significance of serum uric acid levels in Type 1 Diabetes Mellitus, and to assess the correlation between serum uric acid levels and Glycemic control in Type 1 Diabetes Mellitus. age-adjusted incidence of type 1 diabetes varied from 0.1/100,000 per year (in China and Venezuela) to 36.8/100,000 per year in Sardinia and 36.5/100,000 per year in Finland (Marjatta Karvonen et al., 2000 incidence increased with age and was the highest among children 10–14 years of age (Kumar incidence/prevalence of Type 1 DM in Karnataka per 100,000 persons was 3.8(0.32/year) [males 3.7(0.31/year) and female 4(0.33/year)] (Kumar et al., 2008 ‘vasculopathy’ which may involve the capillary circulation leading to ‘microvascular complications’. It can also accelerate and progress to ‘macrovascular complications’. The potential mechanisms contributing to the initiation and development of the chronic complications include glycation of proteins leading to advanced glycated end (AGE) products, the Polyol Pathway where glucose is reduced to sorbitol and the Haemodynamic Hypothesis. In 1993, researchers announced the DCCT's main findings: intensive glucose control greatly reduces the complications of


ISSN (O): 2687-5365; ISSN (P): 2753-6556

type 1 diabetes (complications Trial, 1993). Long term studies like UKPDS has proved that maintaining euglycemia significa microvascular complications in type1 Diabetics (UKProspective Diabetes Study, 1998). The severity of the metabolic abnormality can progress, regress, or stay the same. Thus, the degree of hyperglycemia reflects the severity of the underlying metabolic process and its management. Over recent years there has been renewed debate about the association between raised serum uric acid concentration and diabetic complications. Several large studies have identified the value, in populations, of serum uric acid concentration in predicting the risk of cardiovascular events, such as MI. This has directed several research studies towards the potential mechanisms by which uric acid might have direct / indirect effects on the diabetic complications. Xanthine oxidase activity is increased in the setting of ischemia or oxidative stress. The consequences are an increase in uric acid production and raised SUA concentrations, and increased hydrogen peroxide synthesis, which stimulates further liberation of free radicals (Waring et al., 2000; William et al., 2005). Uric acid can stimulate vascular adherence of neutrophils and their subsequent degranulation, so that peroxide and superoxide free radicals are liberated in close proximity to the endothelium and impair vascular endothelial function through leukocyte activation (William et al., 2005. Hyperglycemia induces both an oxidative stress (glucose autoxidation and advanced glycosylation endproducts (AGE) – ROS oxidation products and a reductive stress through pseudohypoxia with the accumulation of NADH and NAD(P)H in the vascular intima. This redox stress consumes the natural occurring local antioxidants. Once these local intimal antioxidants are depleted uric acid can undergo the paradoxical antioxidant – prooxidant switch or the urate redox shuttle (Melvin et al., 2004). E. Gołembiewska showed that in type 1 diabetes there is significant renal uric acid clearance, pronounced with poor glycemic control which leads to hypouricemia despite an approximately two fold uric acid synthesis (Gołembiewska et al., 2005). Serum uric acid levels, related with CRP levels in chronic kidney disease patients was shown by Caravaca, 2005. With M. Suliman, serum uric acid levels showed a high association with all-cause mortality. Moreover, uric acid level was associated with calcium/phosphate metabolism, dyslipidemia, and inflammation (Suliman et al., 2006; Carlos et al., 2007). CRP and UA are associated with an increase of arterial stiffness in male and female subjects, was shown by Nobukazu Ishizaka et al., 2005. Mild hyperuricemia was shown to significantly increase renal tubular injury and inflammation in a model of CP-induced ARF in the rat. Serum uric acid concentration in the high-normal range is associated with impaired renal function in patients with type 1 diabetes was shown by Elizabeth T. Rosolowsky (Elizabeth et al., 2008). Further, it is proposed that fructose- and purine-rich foods that have in common, the raising of uric acid may have a role in the epidemic of metabolic syndrome and renal disease that is occurring throughout the world (Pietro Cirillo et al., 2006). Hyperuricaemia is also associated with possible confounding factors including elevated serum triglyceride and cholesterol concentrations, fasting and post-prandial plasma insulin concentrations, waist-hip ratio and body mass index (Green et al., 1992; Gołembiewska et al., 2005; Seppo Lehto et al., 1998; Waring et al., 2000). About one quarter of hypertensive patients have co-existent hyperuricaemia (Kumar et al., 2008) and, interestingly, asymptomatic hyperuricaemia predicts future development of hypertension, irrespective of renal function was explained by Richard J Johnson et al., 2003. Uric acid also has a predictive role in high-risk patient groups. For instance, diabetes mellitus is a very powerful risk factor for cardiovascular disease, and a prospective study of 1017 Type 2 DM patients showed that serum uric acid concentration >295 µmol/l conferred a hazard ratio of 1.91 of fatal or non-fatal stroke during 7-year follow-up study (Seppo Lehto et al., 1998). Although there is overwhelming evidence that elevated serum uric acid concentrations are strongly associated with increased cardiovascular risk and poor outcome, prospective population studies are often confounded by co-existent risk factors. It remains unclear whether uric acid is an independent predictor of poor cardiovascular outcome (Waring et al., 2000). Paolo Verdecchia study demonstrates a strong independent association between SUA and CV risk in initially untreated and asymptomatic adult subjects with essential hypertension (Paolo Verdecchia et al., 2000). Elevated serum uric acid is a consistent feature of the insulin resistance syndromes, which are also characterized by elevated plasma insulin level, blood glucose concentration, serum triglyceride concentration, raised body mass index and waist-hip ratio (Bonora et al., 1996; Agamah et al., 1991). Uric acid concentrations were significantly higher in subjects with impaired glucose metabolism according to Vaidotas Urbanavicius et al., 2008.

## MATERIALS AND METHODS

The study comprised of type 1 Diabetes Mellitus cases visiting the inpatient and outpatient at Darbhanga Medical College, Darbhanga Bihar. Age and sex matched healthy volunteers served as controls. Total Number of Subjects was 80, with 40 controls and 40Type 1 Diabetes Mellitus cases. Inclusion Criteria was patients with Type 1 Diabetes Mellitus on treatment in all age groups. Exclusion Criteria was Type 1 Diabetes Mellitus with established micro & macro vascular complications. Patients on drugs which alters serum uric acid levels. All conditions which increase/decrease


ISSN (O): 2687-5365; ISSN (P): 2753-6556

serum uric acid levels. Blood - samples were collected after an informed written consent. Study design was Comparative study with random sampling. Data for the study was collected from all those who fulfilled the inclusion and exclusion criteria after taking a detailed case history and age and sex, detailed medical history including conventional risks factors, clinical examinations and relevan were included as part of the methodology.[5] ml plain venous blood sample after overnight fasting and 2 hour postprandial were obtained by venepuncture. For HbA1C estimation 2 ml of EDTA blood sample was collected. This was followed by centrifugation and processed immediately. Determinations of Serum uric acid was estimated by uricase method 2010), Glycosylated haemoglobin by immunoturbidimetric method, Fasting and post prandial blood sugars by glucose oxidase / peroxidase method. The statistical software using SPSS 17, Systat 8.0, MS word and MS Excel were used for the analysis of data.

## RESULTS

Out of 40 cases and 40 controls, 20 were male and 20 female cases and 22 male and 18 female controls. Among cases the average age of diabetic person is18.76±6.28 yrs. The numbers of male subjects were higher than female subjects in controls, compared to study group. Though statistically non-significant, the controls and cases were age and sex matched as far as possible. Statistically, the mean age of duration of diabetes is 6.67±4.0 and HbA1c is 9.7%. The mean serum uric acid (SUA) is 2.36 mg/dl in study group compared to controls. There was statistically significant correlation at 4% level between duration of diabetes and serum uric acid indicating SUA increases with the duration of diabetes mellitus. SUA also increased with increase in HbA1cindicating increase in SUA levels with poor control of diabetes.

**Figure 1: Distribution of cases and controls of SUA and HbA1c**

When t – test is applied we get significant 2 tailed correlations between SUA and HbA1c with their respective controls at 4% level. This indicates increased uric acid levels in diabetics compared to controls. It is further significantly increased in uncontrolled diabetics compared to controlled diabetics.

When diabetic patients are grouped depending on the duration of diabetes, there exists significant mean difference in SUA at 5-10 yr, >10yr of diabetic duration compared to controls at 4% level.

At different levels of HbA1c glycemic control and serum uric acid levels are studied at different levels of HbA1c <7%, 8

Distribution of cases and controls of SUA and HbA1c test is applied we get significant 2 tailed correlations between SUA and HbA1c with their respective controls at 4% level. This indicates increased uric acid levels in diabetics compared to controls. It is further significantly increased in diabetics compared to controlled diabetics. depending on diabetic duration: When only diabetic duration is considered irrespective of age and sex the results Paired Samples Test of SUA depending on duration of diabetes patients are grouped depending on the duration of diabetes, there exists significant mean difference in SUA at 10 yr, >10yr of diabetic duration compared to controls at 5% HbA1c: To know the significance of and serum uric acid levels are studied at different levels of HbA1c <7%, 8-9% and >11%. Descriptive Statistics of SUA at different levels of HbA1c

The serum uric acid levels increased significantly with increase in HbA1c levels. At HbA1c >9, the levels are statistically significant compared to controls.

**Figure 2: Distribution of SUA in cases & controls depending on glycemic control (HbA1c)**

## DISCUSSION

Comprehensive results obtained from various studies conducted upon patients with diabetes mellitus point towards a close relationship between serum levels of acute reactants like uric acid and diabetes mellitus. Several studies have implicated hyperurecemia in the pathogenic process leading to endothelial dysfunction, which contribute to various local and systemic complications in long Hyperuricemia has been shown to be linked to a number of conditions and disorders like gout, hypertens mellitus. Several mechanisms have been proposed on how uric acid is elevated, reabsorption from kidney. Elevated levels of uric acid have been shown to be an independent marker in many conditions like hypertension (Carmine Zoccali 2006), DM, stroke, cardiovascular disease and renal disease. It remains unclear whether an increased UA level is the cause or a consequence of some of these conditions. In this background, an assessment of serum uric acid in relation to type 1 diabetes mellitus patients has been made. The present study was carried out on 40 type 1 diabetes mellitus cases and serum uric acid as measured spectrophotometrically. There was significant elevation in the serum uric acid levels in type 1 diabetics, compared to healthy controls. Higher levels were observed in patients with poor control of diabetes even though the values were not in pathological levels. Serum uric acid levels were directly related to serum glucose levels and with HbA1c. Increased serum uric acid levels were directly proportional to the duration of diabetes. In our study 29 cases of type 1 diabetes had HbA1c >11% indicating poor control and there was significant mean difference at 4% level of serum uric acid compared to controls indicating increasing serum uric acid levels with poor control of diabetes. Similar finding was found with Nobukazu Ishizaka


ISSN (O): 2687-5365; ISSN (P): 2753-6556

et al., 2005 and by Golembiewska serum uric acid concentration in the high associated with poor glycemic control and increasing duration of diabetes in Type 1 diabetes mellitus.

## CONCLUSION

Poor glycemic control is associated with increased serum uric acid levels and increasing duration of type 1 diabetes. was observed between serum uric acid levels in the study group. Hence this study highlights the facts that all type 1 diabetes should be screened periodically for serum uric acid levels and blood sugars to detect and to prevent future complications. Since type 1 diabetes mellitus is an inflammatory process, elevated levels of acute phase reactants like serum uric acid probably act as diagnostic marker for the development of pan systemic compl diagnostic and early marker for the development of diabetic complications. Follow up studies are needed to confirm that this level of serum uric levels is a risk factor for diabetic complications in type 1 diabetes and to determine whe reduction would prevent the complications.

## REFERENCES


1. Agamah ES, Srinivasan SR, Webber LS, Berenson GS. Serum uric acid and its relation to cardiovascular disease risk factors in children and young adults from a biracial community: the Bogalusa Heart Study. 118:241–9.
2. Belfiore F, Mogensen CE. 2000. New concepts in Diabetes and its treatment. Karger publications, 4.
3. Bonora E, Targher G, Zenere MB, Saggiani F, Cacciatori V,
4. Tosi F, Travia D, Zenti MG, Branzi P, Santi L, Muggeo M. 1996. Relationship of uric acid concentration to cardiovascular risk factors in young men. Role of obesityand central fat distribution. The Atherosclerosis Risk Factors Study Disord, 20:975–80.
5. Caravaca F, Martín MV, Barroso S Luna E, Sánchez-Casado E reactive protein levels in patients with chronic kid disease. Nefrologia, 25(6):645
6. Carlos A. Roncal, Wei Mu, Byron Croker, Sirirat Reungjui, Xiaosen Ouyang, Isabelle Tabah elevated serum uric acid on cisplatin failure. Am J Physiol Renal Physiol, Carmine Zoccali, Raffaele Maio, Francesca Mallamaci, Giorgio Sesti, and Francesco Perticone and Endothelial Dysfunction in Essential Hypertension Am Soc Nephrol., 17: 1466–90
7. Diabetes Control and complications Trial (DCCT) Group: The effect of intensive treatment of diabetes on the development and progression of long insulin-dependent diabetes mellitus. 329:977-986, 1993.
8. Elizabeth T. Rosolowsky, Linda H. Ficociello, Nicoholos J Maselli, Monika A. Niewczas, Amanda L. Binns, Bijan Roshan, et al. 2008. High Associated with Impaired Nonproteinuric Patients with Type 1 Diabetes Soc Nephrol., 3: 706-713.
9. Fauci, Braunwald, Kasper, Hauser, Longo and Jameson et al. 2008. Principles of Internal Medicine, Harrison's 17th edition. Mc Graw-Hill.
10. Gołembiewska E, Ciechanowski K, Safranow K, Kedzierska K, Kabat-Koperska J. 2005. Renal handling of uric acid in patients with type 1 diabetes in relation to glycemic control. Arch Med Res., 36(1);32-35.
11. Green A, Gale EA, Patterson CC. 1992. Incidence of childhood-onset insulin-dependent diabetes mellitus: the EURODIAB ACE Study. Lancet., 339:905–909.
12. International Textbook of Diabetes Mellitus by K.G.M.M. Alberti, 2nd Edition.
13. Kumar P, Krishna P, Reddy SC, Gurappa M, Aravind SR, Munichoodappa C. 2008. Incidence of type 1 diabetes mellitus and associated complications among children and young adults: results from Karnataka Diabetes Registry 1995-2008. J Indian Med Assoc., 106 (11):708-11.
14. Lawrence A. Kaplan and Amadeo J. Pesce, 2022. Clinical Chemistry, 5th Edition. 2010.
15. Marjatta Karvonen, Maarit Viik-Kajander, Elena Moltchanova, Ingrid Libman, Ronald Laporte, Jaakko Tuomilehto, 2023.
16. Incidence of Childhood Type 1 Diabetes Worldwide: Diabetes Care, 23:1516–1526. Melvin R. Hayden and Suresh C Tyagi, 2024.




ISSN (O): 2687-5365; ISSN (P): 2753-6556