ISSN: 2581 - 3633

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: www.ijmacr.com

Volume – 1, Issue – 1, January – February - 2018, Page No. : 01 - 05

A Case Report on: Role of Serum Uric Acid as a Biomarker for Insulin Resistance

Dr. Surendra Pratap Wasekar

D. Y. Patil Medical College, Pune, Maharashtra, India

Correspondence Author: Dr. Surendra Pratap Wasekar, D. Y. Patil Medical College, Pune, Maharashtra, India

E-Mail Id: surendra.prawasekar@gmail.com

Conflicts of Interest: Nil

Abstract

Objective: The current study has undertaken to explore the role of uric acid as a biomarker for insulin resistance.

Material and Method: The study was conducted on 100 subjects of type 2 diabetic patients in Pune District. Serum uric acid, Fasting plasma glucose, fasting plasma insulin and HOMA- IR were analyzed.

Result: The study showed that there were significantly increased Serum Uric acid, Fasting Plasma Glucose, Fasting Serum Insulin and HOMA-IR values in T2DM subjects as compared to controls ($p < 0.0001$).

Conclusion: There is convincing evidence that there were significant correlation between uric acid and HOMA-IR value. Hyperuricemia is related to risk factors for insulin resistance in type 2 diabetes. The study concluded a significant progressive relationship between increased uric acid level with respect to HOMA-IR levels which is an indices of insulin resistance.

Keywords: Homeostasis model assessment (HOMA-IR), Insulin Resistance, Type 2 Diabetic mellitus (T2DM), Uric acid (UA).

Introduction

Type 2 diabetes is a serious and common chronic disease resulting from a complex inheritance-environment interaction along with other risk factors such as obesity and sedentary lifestyle[1]. Type 2 diabetes and its complications constitute a major worldwide public health problem, affecting almost all populations in both developed and developing countries with high rates of diabetes-related morbidity and mortality[2]. The prevalence of type 2 diabetes has been increasing exponentially, and a high prevalence rate has been observed in developing countries and in populations undergoing “westernization” or modernization[3]. Hyperuricemia, the precursor of gout, is strongly associated with insulin resistance syndrome, an established risk factor for type 2 diabetes[4]. This link may be translated into an independent association between hyperuricemia and the future risk of type 2 diabetes, but little prospective data on the topic are available, particularly in the general population[5]. Indeed, studies of individuals with impaired glucose levels have suggested that hyperuricemia is an independent risk factor for diabetes[6].

Identifying risk factors for the development of type 2 diabetes is essential for its early screening and prevention. Serum uric acid level has been suggested to be associated with risk of type 2 diabetes. Biologically, uric acid plays an important role in worsening of insulin resistance in animal models by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake[7]. However, hyperinsulinemia as a consequence of insulin resistance causes an increase in serum uric acid

concentration by both reducing renal uric acid secretion and accumulating substrates for uric acid production[8]. Therefore, it remains controversial whether serum uric acid is independently associated with the development of type 2 diabetes.

The aim of our study was to examine the independent association between serum uric acid levels and the future risk of insulin resistance in type 2 diabetic mellitus.

Method and Material

This study was conducted during the period from the January 2017 until the end of December 2017 in D. Y. Patil Medical College, Pune, Maharashtra. A total of 100 subjects of type 2 diabeties (60 male and 40 female) having an age group of 45-60 years were participated from urban and rural area of pune. Patients with cardiovascular, thyroid function disorder, and other hormonal disorders that may exaggerate the insulin resistance in type 2 diabetes were excluded from the study. 5 ml of venous blood was obtained after a 12 hour fast from type 2 diabetic patients. Blood samples were transferred into tube, allowed to stand for 15 minutes at room temperature, centrifuged at 3500 rpm for 10 minutes.

Methods

Determination of Serum Uric Acid

Serum uric acid levels were measured with an autoanalyzer by the enzymatic colorimetric Uricase method[9].

Determination of Fasting Glucose

Fasting glucose concentration was measured by the enzymatic colorimetric GOD-POD method[10].

Determination of Fasting Insulin

Fasting serum insulin concentration was assessed by Enzyme Linked Immunosorbent Assay (ELISA) on the strength of double binding test (Sandwich ELISA), using DRG Insulin ELISA Kit (No cat. EIA-2935) of DRG Instruments GmbH (Germany).

Determination of Insulin Resistance

The insulin resistance was calculated by a homeostasis model assessment (HOMA-IR) index = Fasting plasma glucose (mg/dl) X fasting plasma Insulin (uU/ml) / 405, as described by Matthews and colleagues 1985[11].

Stastical analysis

Data analysis was performed using Epi info software version 3.5.1. Descriptive statistics, including mean, range, and standard deviations, were calculated for all variables. Proportions were compared using Chi- square tests and chi square for trend at 0.05 level of significance.

Result

Laboratory findings between the study groups (T2DM patients) and control group (Non – diabetic Healthy controls).

Parameters	Study group (no=100) Mean ± S.D.	Control group (no=50) Mean ±S.D.	P value
Serum Uric acid (mg/dl)	6.27± 1.39	4.39 ± 1.24	*p* <0.0001
Fasting Plasma Glucose (mg/dl)	176.34 ± 16.79	86.13 ± 11.36	*p* <0.0001
Fasting Serum Insulin (µIU/ ml)	9.11 ± 1.89	6.23 ± 1.43	*p* <0.0001
HOMA-IR	3.87 ± 0.07	1.32 ±0.04	*p* <0.0001

Table shows comparison of laboratory findings between the study groups (T2DM subjects) and control group (Non – diabetic Healthy subjects). The mean level of Serum Uric acid, Fasting Plasma Glucose, Fasting Serum Insulin and HOMA-IR in T2DM patients were 6.27 ± 1.39 mg/dl, 176.34 ± 16.79 mg/dl, 9.11 ± 1.89 µIU /ml and 3.87 ±

0.07 respectively. On the other hand in controls the mean level were observed as 4.39 ± 1.24 mg/dl, 86.13 ± 11.36 mg/dl, 6.23 ± 1.43 μIU/ml and 1.32 ± 0.04 respectively.

Discussion

It is evident from results that there were significantly increased Serum Uric acid, Fasting Plasma Glucose, Fasting Serum Insulin and HOMA-IR values in T2DM subjects as compared to controls ($p < 0.0001$). Our data suggest that clearance of UA is being reduced with increase in insulin resistance and UA as a marker of diabetes period. A plausible mechanism for the observed results of an association between increasing serum uric acid and diabetes mellitus may be related to the inhibition of uric acid reabsorption in the proximal tubule by high glucose levels in diabetic individuals.

Hyperinsulinemia decreases uric acid clearance by the kidneys; the mechanism is an increased proximal tubular urate transport from the glomerular filtrate to the renal interstitium by stimulation of GLUT 9, one of its major transporters, which leads to hyperuricemia[12].

Our result has shown strong links between uric acid levels and HOMA-IR , a combination of medical conditions that are related to insulin resistance (the body's inability to correctly process insulin) and increase a person's chances of getting heart disease and diabetes[13].

Our results agree with those of Kivity and colleagues[14] who found that high serum uric acid concentrations are associated with diabetes in women, but not in men, and with those from rural areas and colleagues,[15]who found that although hyperuricemia is a strong predictor of metabolic syndrome in both, male and female patients, the risk was higher in women. No explanation is available for this sex difference, but the distinct fat distribution between sexes, the different levels of uric acid in men and women, and the effects of estrogens on renal clearance of urate may explain it.[16,17]

It has been recognized that serum uric acid is positively associated with serum glucose levels in healthy subjects. Recent studies have demonstrated that UA levels are higher in subjects with prediabetic and early Type 2 diabetes then in healthy controls[18]. Furthermore, an elevated serum uric acid level was found to increase chances for developing Type 2 diabetes in individuals with impaired glucose tolerance[19].

Hyperuricemia has been also added to the set of metabolic abnormalities associated with insulin resistance and/or hyperinsulinemia in metabolic syndrome[20]. An elevated uric acid levels, as reported, often precedes the development of obesity , hyperinsulinemia, and diabetes[21]. In addition, uric acid has been implicated in the development of metabolic syndrome and hypertension[22]. Although several studies have implicated the role of uric acid in progression of prediabetic to diabetes, studies related to uric acid levels in diabetes development are controversial and deserve further analysis.

Therefore, in this study we have analyzed and examined potential role of uric acid as a biomarker for impaired glucose metabolism and diabetes progression by analyzing serum levels of uric acid in Type 2 diabetic patients.

Conclusion

Identifying risk factors for the development of type 2 diabetes is essential for its early screening and prevention. Serum uric acid level has been suggested to be associated with risk of type 2 diabetes. Our study suggests that serum uric acid level is positively associated with the development of insulin resistance in type 2 diabetes regardless of various study characteristics. Further research should attempt to determine whether it is effective to utilize serum uric acid level as a predictor of type 2 diabetes for its primary prevention.

Reference

[1]. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci. 2014 Sep 6;11(11):1185-200.

[2]. Tripathi BK, Srivastava AK. Diabetes mellitus: complications and therapeutics. Med Sci Monit. 2006;12(7):RA130-147

[3]. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus-present and future perspectives. Nat Rev Endocrinol. 2011;8(4):228-236.

[4]. Wang T, Bi Y, Xu M, Huang Y, Xu Y, et al. Serum uric acid associates with the incidence of type 2 diabetes in a prospective cohort of middle-aged and elderly Chinese. Endocrine 2011; 40: 109–116.

[5]. Bhole V, Choi JW, Kim SW, de Vera M, Choi H. Serum uric acid levels and the risk of type 2 diabetes: a prospective study. Am J Med 2010; 123: 957–961.

[6]. Yamada T, Fukatsu M, Suzuki S, Wada T, Joh T. Elevated serum uric acid predicts impaired fasting glucose and type 2 diabetes only among Japanese women undergoing health checkups. Diabetes Metab 2011; 37: 252–258.

[7]. Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C, Mu W, Krotova K, Block ER, Prabhakar S, Johnson RJ. Hyperuricemia induces endothelial dysfunction. Kidney Int 2005; 67: 1739– 1742.

[8]. Satoru Kodama et al. Association Between Serum Uric Acid and Development of Type 2 Diabetes. Diabetes Care. 2009 Sep. 32(9): 1737–1742.

[9]. Yunsheng Zhao et al. Uricase based methods for determination of uric acid in serum. Microchimica Acta January 2009:Jan 164(1-2):1–6.

[10]. Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Ann.Clin.Biochem 1969; 6:24-7.

[11]. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC: Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28:412–419, 1985.

[12]. Liuqing Xu, Yingfeng Shi, Shougang Zhuang, and Na Liu. Recent advances on uric acid transporters. Oncotarget. 2017 Nov 21; 8(59): 100852–100862.

[13]. Cesar I. Elizalde-Barrera et al. Serum uric acid levels are associated with homeostasis model assessment in obese nondiabetic patients: HOMA and uric acid. Ther Adv Endocrinol Metab. 2017 Oct; 8(10): 141–146.

[14]. Kivity S, Kopel E, Steinlauf S, et al. The association between serum uric acid and diabetes mellitus is stronger in women. J Womens Health 2013; 22: 782–789.

[15]. Nagahama K, Inoue T, Kohagura K, et al. Hyperuricemia predicts future metabolic syndrome: a 4-year follow-up study of a large screened cohort in Okinawa, Japan. Hypertens Res 2014; 37: 232–238.

[16]. Yamada T, Fukatsu M, Suzuki S, et al. Elevated serum uric acid predicts impaired fasting glucose and type 2 diabetes only among Japanese women undergoing health checkups. Diabetes Metab 2011; 37: 252–258.

[17]. Liu Y, Jin C, Xing A, et al. Serum uric acid levels and the risk of impaired fasting glucose: a prospective study in adults of north China. PLoS One 2013; 8: e84712.

[18]. Kodama S, Saito K, Yachi Y, Asumi M, Sugawara A, Totsuka K, et al. The association between serum uric acid and development of type 2 diabetes mellitus. A Meta-Analysis. Diabetes Care. 2009;32(9):1737–1742.

[19]. Nakanishi N, Okamoto M, Yoshida H, Matsuo Y, Suzuki K, Tatara K. Serum uric acid and risk for

development of hypertension and impaired fasting glucose or Type II diabetes in Japanese male office workers. Eur. J. Epidemiol. 2003;18(6):523–530.

[20]. Chen LY, Zhu WH, Chen ZW, Dai HL, Ren JJ, Chen JH, et al. Relationship between hyperuricemia and metabolic syndrome. J. Zhejiang. Univ. Sci. B. 2007;8(8):593–598.

[21]. Dehghan A, van Hoek M, Sijbrands EJ, Hofman A, Witteman JC. High serum uric acid as a novel risk factor for type 2 diabetes. Diabetes Care. 2008;31(2):361–362.

[22].Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk N. Engl. J. Med. 2008;359(17):1811–1821.