

Uric Acid as a Biomarker for Pre-Diabetic and Type 2 Diabetic Patients

P. Mohanalakshmi^{1*}, N. Muninathan²

¹Associate Professor, Department of Biochemistry, Sri Muthukumaran Medical College and Research Institute, Chikkarayapuram, Chennai, Tamil Nadu, India

²Research Scientist, Department of Research, Meenakshi Medical College Hospital and Research Institute, Meenakshi Academy of Higher Education and Research, Kanchipuram-631552, Tamil Nadu, India

*Corresponding author: P. Mohanalakshmi

| Received: 07.05.2019 | Accepted: 13.05.2019 | Published: 23.05.2019

DOI:10.21276/sijb.2019.2.5.1

Abstract

Background: Several epidemiological studies identify hyperuricemia is an independent risk factor for the development of cardiovascular disease and renal disease, particularly patients with hypertension or congestive heart failure and in women. In the present study to investigate the level of serum uric acid in Type 2 diabetes mellitus and pre-diabetics in south Indian population. **Methods:** Uric acid level was measured by Uricase-PAP methodology in patients with Diabetes (n=50)/Pre diabetes (n=50). Using Chi Square test, uric acid levels in the above two groups were compared based on age, sex and other factors which can affect uric acid level. **Results:** The mean serum uric acid level was lower in type 2 Diabetes Mellitus patients compared with Pre-diabetic patients. P value comparing type2 diabetes mellitus and pre-diabetes was < 0.001. **Conclusion:** The serum uric acid level being higher in pre-diabetes than diabetes mellitus may serve as a potential inexpensive biomarker of deterioration of glucose metabolism.

Keywords: Serum uric acid, Diabetes mellitus, Pre-diabetes.

Copyright @ 2019: This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

INTRODUCTION

Type 2 Diabetes mellitus is a majority of Diabetes present in India for the past few decades. Diabetes Mellitus is the most important risk factor associated with two to four fold increased incidence of coronary artery disease [1].

Individuals with undiagnosed type 2 diabetes are also at significantly higher risk of stroke and peripheral vascular disease than non-diabetes is more in individuals with family history of diabetes, and in members of certain racial or ethnic groups, especially Indians [2].

Diabetes also increases the likelihood of severe carotid atherosclerosis and mortality from stroke is increased almost three folds in patients with diabetes. Both type1 and type 2 diabetes are therefore powerful and independent risk factors for coronary artery disease (CAD), stroke and peripheral arterial disease [3].

Type 2 diabetes mellitus eventually affects more than 150 million adults in the world. India has more than 30 million diabetics and it is known to affect Indians at a much younger age. The prevalence of diabetes is increasing worldwide and it is expected to

affect around 300 million adults all over the world and 57 million in India by the year 2025 [4].

Coronary artery disease is a major cause for mortality which has so many risk factors viz., hypercholesterolemia, hypertension, diabetes mellitus, and cigarette smoking of which Diabetes mellitus is the most important. Hence early detection of Diabetes mellitus even before it is exhibited will help in prevention of CAD [5].

Nearly 120 years have elapsed since uric acid was first described as a potential risk factor in the development of chronic disease. Hyperuricemia as a potential risk factor for Type 2 Diabetes mellitus has ballooned in the last several years with numerous abstracts and research papers, multiple editorials and review articles [6].

The end product of purine ring degradation is uric acid, which is excreted in the urine. Uric acid has a limited solubility, and if it were to accumulate, uric acid crystals would precipitate in tissues of the body with a reduced temperature (such as the big toe). This condition of acute painful inflammation of specific soft tissues and joints is called gout. People who had higher uric acid levels were more likely to get Type 2 Diabetes mellitus [7].

MATERIALS AND METHODS

100 patients were divided into two groups. Group I: Type 2 Diabetes Mellitus Group and Group-II: Pre-diabetes Mellitus patients. Patients' demographic data, including sex, age, and risk factors for diabetes Mellitus were recorded.

The study was conducted during the period from June to January in the department of Biochemistry, Meenakshi Medical College Hospital and Research Institute, Kanchipuram, Tamil Nadu, India. This study was approved by the institution ethics committee and informed consent from the participants; this study was done.

Source of Chemicals

Phosphotungstic acid and Sodium Carbonate were purchased from Sigma Chemical Company, St. Louis, MO, USA. All other chemicals, reagents and solvents used were analytical grade.

Statistical Analysis

Data were analyzed using the SPSS software package, version 17.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed using range, mean, SD, and median, whereas qualitative data were expressed as frequency and percentage. P value was assumed to be statistically significant at 0.05.

RESULTS

Diabetes mellitus comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM exist and are caused by a complex interaction of genetics, environmental factors, and life-style choices. Depending on the etiology of the DM, factors contributing to hyperglycemia may include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.

Therefore, in the present section, the results obtained during our study of uric acid levels as an early marker of Type 2 Diabetes Mellitus and its correlation of the same in pre-diabetic state are explored in detail.

Prevalence of Glucose in Diabetes Mellitus

The prevalence of Glucose was studied in two groups namely pre-diabetic group of Control (Fasting blood glucose Concentration is 60-110mg/dL) and another test group of Type 2 Diabetes Mellitus (Fasting blood glucose concentration range between 110 to 170 mg/dL). Out of 100 patients 50 had increased Normal prediabetic Patients and 50 belonged to test group of type 2 Diabetes mellitus patients. The percentage prevalence of Normal Glucose level (group 1) and Type 2 Diabetes Mellitus (Test Group II) levels is shown as a pie chart in Figure-1.

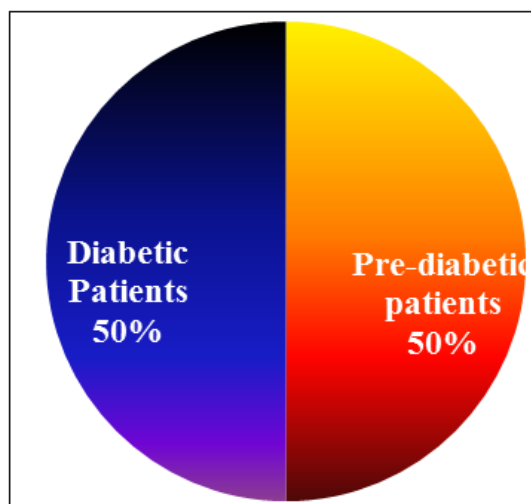


Fig-1: Percentage of Study Groups

The percentage of pre-diabetic mellitus and type 2 Diabetes mellitus group levels are equal to 50%. In our study, Fasting Glucose was estimated in pre-diabetic and type 2 Diabetes mellitus patients of age between 30 to 70 years with history of signs and symptoms, attending in Meenakshi Medical College Hospital and Research Institute, Enathur, Kanchipuram.

Age and Gender wise distribution of mean of serum Uric acid

Table-1 Showed that the age and gender wise distribution of mean of serum uric acid levels. Serum uric acid levels were significantly increased in pre-diabetes mellitus patients compared with type 2 Diabetes mellitus.

Table-1:

Age	Uric acid levels in Type 2 diabetes mellitus		Uric acid levels in Pre-diabetes mellitus	
	Male	Female	Male	Female
30-40	4.18	3.77	5.71	4.63
41-50	2.93	4.66	5.73	4.97
51-60	3.69	4.03	5.86	4.74
61-70	3.33	3.67	5.63	4.52

p<0.001 (highly significant), Pre-diabetes patients compared with type2 DM patients

Role of Serum Uric Acid and Type 2 Diabetes Mellitus

Figure-2 Indicates that the Serum uric acid in the pre-diabetic patients and type 2 diabetes mellitus patients varied from 3.4 to 6.8 and 2.8 to 5.5 mg/dl respectively. The mean and standard deviation of uric

acid among pre-diabetic patients was 5.8 ± 0.83 while in type 2 diabetes mellitus, it was 4.15 ± 0.45 respectively. In Uric acid concentration significantly ($p < 0.001$) decreased in type 2 Diabetes Mellitus when compared pre-diabetic patients.

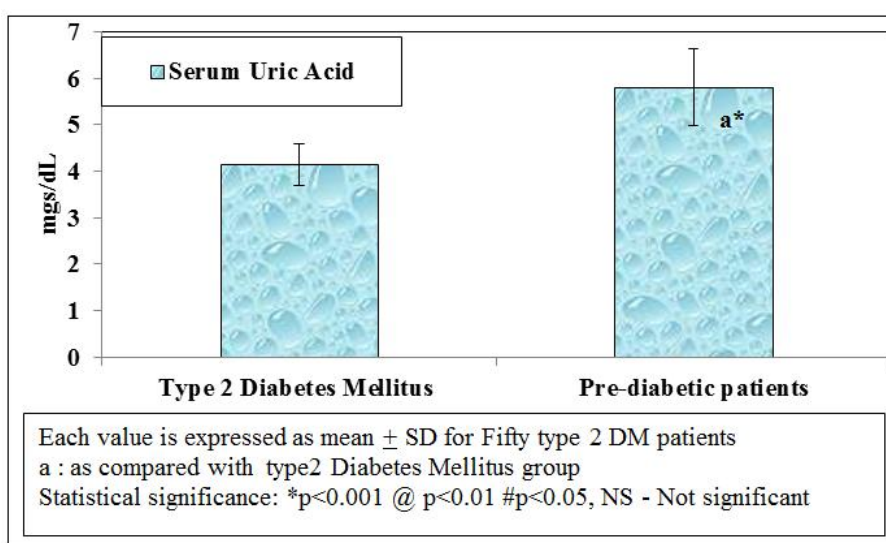


Fig-2: Serum Uric Acid and Type 2 Diabetes Mellitus

Hyperuricemia with Diabetes Mellitus

Table-2 showed that the hyperuricemia is defined as serum uric acid level more than 8 mg/dl in males and more than 6 mg/dl in females. 13 type 2

diabetes mellitus had hyperuricemia while none in controls. In type 2 diabetes mellitus patients with hyperuricemia were significantly present when compared with Pre-diabetes mellitus patients.

Table-2:

Hyperuricemia	Pre- Diabetes Mellitus				Type 2 Diabetes Mellitus			
	Numbers	%	Mean	S.D	Numbers	%	Mean	S.D
Presence	13	26.0	6.20 ^{a*}	0.68	0	-	-	-
Absence	37	74.0	5.53 ^{a*}	0.06	50	100%	4.15	0.45

Each value is expressed as mean \pm SD for Fifty type 2 DM patients
a : as compared with Pre-diabetic patients
Statistical significance: * $p < 0.001$

DISCUSSION

Diabetes mellitus is a group of disorders characterized by chronic hyperglycemia associated with disturbance of carbohydrate, fat and protein metabolism due absolute or relative deficiency of insulin secretion or its action. Type 2 Diabetes mellitus is a one of the risk factor for cardiovascular disease and it also present

average of 25% adults and also increases in prevalence with age and gender type [7].

Hyperuricemia is one of the components of metabolic syndrome. “In the absence of gout the presence of hyperuricemia in patients with type 2 diabetes mellitus is an important marker as well as an added risk factor for atherosclerosis” [8].

In the present study the relation between serum uric acid level and type 2 diabetes mellitus was examined. Uric acid, the end product of purine metabolism is a strong reducing agent and also marker for coronary artery disease in combination with other risk factors among type 2 diabetes mellitus.

Serum uric acid level of diabetic group was significantly lower than prediabetic ($p < 0.001$). These findings were consistent with the previous study, demonstrated that diabetics have lower serum uric acid levels and that prediabetics have higher levels than non-diabetics [8]. The reduced urate level in severe hyperglycemia has been attributed to the uricosuric effect of glycosuria, which might be an explanation of the low uric acid concentration among overt diabetic patients [9]. Furthermore, uric acid concentration might be influenced by the changes in plasma glucose and insulin concentrations [10]. Thus, uric acid fluctuations during prediabetes and diabetes have so far been regarded as a secondary metabolic phenomenon.

Therefore, the results of this study strongly suggest and recommend that SUA can be an independent predictor of the development of type 2 diabetes [11]. This study has some limitations. The participant's average age was 58.72 years at baseline so the role of uric acid in predicting incident of type 2 diabetes among younger adults needs further study. Because of the less number of new type 2 diabetes cases, this study had limited power for excluding complete effectiveness of uric acid prediction among IGT and normoglycemia groups [12].

Uric acid > 5 mg/dl should be considered as a "Red flag" in those patients at risk for cardiovascular disease. In this study 78.57% of diabetic patients have serum uric acid level > 4 mg/dl, while only 30% of the control have serum uric acid > 4 mg/dl. In these patients the clinician should strive to utilize global risk reduction programme to reduce the complications of atherogenic process [13].

CONCLUSION

In the present study, we conclude that the Uric acid level above 4 mg/dl in diabetic population. In the present study, we conclude that the Uric acid level is a one of the prognostic and diagnostic marker for type 2 diabetes mellitus and pre-diabetic patients.

REFERENCE

1. Tuomilehto, J. (2006). Modeling of primary prevention of the development of type 2 diabetes. *Przeglad Lekarski*, 63(4), 3-6.
2. Stratton, I. M., Adler, A. I., Neil, H. A. W., Matthews, D. R., Manley, S. E., Cull, C. A., ... & Holman, R. R. (2000). Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Bmj*, 321(7258), 405-412.
3. Cox, J. H., Cortright, R. N., Dohm, G. L., & Houmard, J. A. (1999). Effect of aging on response to exercise training in humans: skeletal muscle GLUT-4 and insulin sensitivity. *Journal of Applied Physiology*, 86(6), 2019-2025.
4. Mellitus, D. (2005). Diagnosis and classification of diabetes mellitus. *Diabetes Care*, 28, S37.
5. Alderman, M. H., Cohen, H., Madhavan, S., & Kivlighn, S. (1999). Serum uric acid and cardiovascular events in successfully treated hypertensive patients. *Hypertension*, 34(1), 144-150.
6. Ramachandran, A. (1990). Decreased insulin sensitivity in off springs whose both parents have NIDDM. *Diabetes Medicine*, 7(1), 331-334.
7. DeFronzo, R. A., Hendler, R., & Simonson, D. (1982). Insulin resistance is a prominent feature of insulin-dependent diabetes. *Diabetes*, 31(9), 795-801.
8. Godsland, I. F., & Stevenson, J. C. (1995). Insulin resistance: syndrome or tendency?. *The Lancet*, 346(8967), 100-103.
9. Yudkin, J. S. (1995). Coronary heart disease in diabetes mellitus: three new risk factors and a unifying hypothesis. *Journal of internal medicine*, 238(1), 21-30.
10. Johnson, R. J., Kang, D. H., Feig, D., Kivlighn, S., Kanellis, J., Watanabe, S., ... & Mazzali, M. (2003). Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease?. *Hypertension*, 41(6), 1183-1190.
11. Tkác, I., Bomba, J., & Cvanigová, A. (1990). Uric acid--a risk factor or atherosclerosis marker in type 2 diabetes?. *Vnitri lekarstvi*, 36(8), 763-768.
12. Woo, J., Swaminathan, R., Cockram, C., Lau, E., & Chan, A. (1994). Association between serum uric acid and some cardiovascular risk factors in a Chinese population. *Postgraduate medical journal*, 70(825), 486-491.
13. Bedir, A., Topbas, M., Tanyeri, F., Alvur, M., & Arik, N. (2003). Leptin might be a regulator of serum uric acid concentrations in humans. *Japanese heart journal*, 44(4), 527-536.