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Evaluation Of Serum Uric Acid And Lipid Profile In Type 2 Diabetes Mellitus.

Gunasundari C[1], Gayathri MS[2]*, and C Satish Kumar[3].

[1]Assistant Professor, Department Of Biochemistry, Government Kilpauk Medical College Chennai, Tamil Nadu, India
[2]Assistant Professor, Department Of Biochemistry, Government Stanley Medical College, Chennai, Tamil Nadu, India
[3]Assistant Professor, Department Of Biochemistry, Government Villupuram Medical College, Villupuram, Tamil Nadu. India

ABSTRACT

Hyperuricemia and dyslipidemia are the metabolic abnormalities frequently associated with type 2 diabetic patients. In the present study, the levels of serum uric acid and serum lipid profile were evaluated and correlated for the risk of cardiovascular disease in type 2 diabetes mellitus. Sixty-five type 2 diabetes mellitus patients and sixty-five healthy controls were included in this study. 5ml of fasting venous blood was drawn and Serum was separated and analysed for Glucose, Urea, Creatinine, Total cholesterol, TGL, LDL, HDL and Uric acid using semi autoanalyzer. The results were statistically analysed by using t-test and Pearson correlation.(SPSS version 20.0) The mean value of uric acid for control is 4.74 and that of case is 5.68 and the P value is 0.001 which is statistically significant. The serum levels of total cholesterol, TGL, LDL and uric acid were raised in diabetic patients and was statically significant. But the level of serum HDL was significantly decreased in type 2 diabetes . The study shows a significant positive correlation (p < 0.05) between serum uric acid and Total Cholesterol, TGL and LDL and a significant negative correlation (p < 0.05) between serum uric acid and HDL. The present study proves that hyperuricemia is positively associated with dyslipidemia in type 2 DM. As there is a parallel rise in uric acid along with total cholesterol, TGL, LDL levels in type-2 diabetes patients, the estimation of serum uric acid and serum lipid profile is highly beneficial in type-2 diabetes mellitus patients to assess the dyslipidemia induced cardiovascular complications.
Keywords: Type 2 Diabetes mellitus, serum uric acid, serum lipid profile, cardiovascular disease

*Corresponding author

INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder characterized by the presence of chronic hyperglycemia associated with impairment in the metabolism of carbohydrates, lipids and proteins. It was first reported in Egyptian manuscript about 3000 years ago[1]. In 1936, the distinction between type 1 and type 2 DM was clearly made [2]. Type2 DM was first described as a component of metabolic syndrome in 1988 [3]. The origin and etiology of DM may vary greatly but always it include defects in either insulin secretion or insulin response or both at some point in the course of disease. Mostly patients with diabetes mellitus have either type 1 diabetes (which is immune-mediated or idiopathic) or Type 2 DM (formerly known as non-insulin dependent DM). Type 2 DM is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency [4].The worldwide prevalence of diabetes has continued to increase dramatically. Globally, as of 2011, an estimated 366 million people had DM, with type 2 making up about 90% of the cases [5,6]. The number of patients with type 2 DM is increasing in every country with 80% of people with DM living in low- and middle-income countries. Among the top ten countries with the largest number of diabetic patients, five are in Asia.[1].China tops the list with 90.0 million followed by India which has 61.3 million people affected by diabetes. The numbers are expected to rise to 129.7 million and 101.2million, respectively by 2030. These estimates are likely to be underestimations as the prevalence data are mostly available for urban areas and reports from rural areas are very few. India is a large rural nation and the recent available studies indicate rising prevalence of the diabetes in the rural areas also [7-9].The prevalence of diabetes is reaching a pandemic proportion which is mostly due to rapid lifestyle transitions and by a narrowing in the urban-rural divide in living conditions. Although there are disparities in the sample selection and screening criteria, the prevalence estimates are increasing both in the urban and rural regions of India. A recent study in Kerala, concluded that the rural population has a higher prevalence of diabetes than the urban population [10].In India, prevalence of Diabetes mellitus ranges from 0.4 to 3.9% in rural areas and from 9.3 to 16.6% in urban areas. Diabetes causes dysfunction of various organs like heart, kidneys, eyes, nerves and blood vessels. Age adjusted mortality rates among diabetics is 1.5 to 2.5 times greater than general population. Most of this excessive mortality is mainly attributed to cardiovascular disease [11].The hyperglycemia observed in diabetes mellitus if not controlled may lead to various life threatening complications such as micro and macro vascular diseases [12].Uric acid is the end product of purine catabolism. Excessive serum uric acid accumulation can cause various diseases. For more than 50 years, increased serum levels of uric acid have been implicated in cardiovascular disease. Different mechanisms have been suggested through which uric acid may be involved in the atherosclerotic process and its clinical complications. Uric acid may act as a prooxidant, particularly at increased concentrations, and may be a marker of oxidative stress [13, 14].Uric acid promotes vascular smooth muscle proliferation and also upregulates the expression of platelet-derived growth factor and monocyte derived chemotactic protein1 [15- 17]. This would enhance the atherogenesis and its progression. As a result of insulin resistance, there is a decrease in excretion of uric acid due to reduced effect of insulin, [18, 19]. The prevalence of dyslipidemia in type 2 diabetes is double with respect to the general population .Dyslipidemia is an important risk factor for cardiovascular disease (CVD) and plays a major role in the progress of atherosclerosis. [20]. These are more complex abnormalities that are caused by interrelationship among obesity, insulin resistance and hyperinsulinism [21].According to Freedman et al (1999), when the overweight subjects were compared with their respective thinner counterparts, they presented 2.4 to 7.1 times higher probability to have an elevated total cholesterol, LDL cholesterol, triglycerides[22]and blood pressure as well as 12.6 times higher probability to have hyperinsulinemia. It is worth to emphasize that the fatty tissue is exclusively related to risk factors, such as the altered insulin and lipid profile, which can contribute to the development of the insulin resistance syndrome, which comprises several risk factors for the emergence of cardiovascular complications [23]. In patients with type 2 diabetes, which is equivalent to CHD [4], it is most commonly characterized by elevated TG and reduced HDL-C [25]. These abnormalities can be present alone or in combination with other metabolic disorders. The prevalence of dyslipidaemia varies depending on the population studies, geographic location, socio economic development and the definition used [26,27].In patients with type 2 diabetes mellitus, the risk of cardiovascular disease and cardiovascular mortality is significantly increased relative to healthy individuals[28, 29].Dyslipidemia is a major causative factor for the increased cardiovascular risk associated with type 2 diabetes ,which includes abnormalities in all lipoproteins [30–32].Type 2 DM is associated with various plasma lipid and lipoprotein (LP) abnormalities that are recognized as predictors for coronary heart disease [33]. Hypertriglyceridemia and reduced HDL cholesterol is the most common dyslipidemia in patients with noninsulin-dependent diabetes mellitus, but essentially any pattern of dyslipidemia may be present [34]. Dyslipidemia is a major risk factor for coronary

heart disease (CHD). Cardiovascular disease is a cause of morbidity and mortality in patients with type 2 diabetes mellitus due to associated abnormalities in lipids such as serum triglycerides (TC) 69%, serum cholesterol 56. 6%, low-density lipoprotein cholesterol (LDL) 77% and high density lipoprotein cholesterol (HDL) 71% [35,36]. Early detection and treatment of hyperlipidemia in Patients with type-2 diabetes can prevent the progression of cardiovascular disease associated with atherogenic abnormalities and minimize the risk for atherogenic Coronary artery disease. Hyperuricemia and hyperlipidemia are the metabolic abnormalities frequently associated with type 2 diabetic patients. In present study the levels of biochemical parameters like serum uric acid and serum lipid profile were evaluated and correlated for the risk of cardiovascular disease in type 2 diabetes mellitus

MATERIALS AND METHODS

This study was conducted during the period of July 2016-December 2016 as a cross sectional study in the department of Diabetology, department of Biochemistry in Government kilpauk Medical College,Chennai.65 patients with type 2 diabetes mellitus on oral hypoglycemic drugs less than five years duration in the age group of 40 years-60 years. cases are selected from OPD of department of diabetology, Government Kilpauk Medical College, Chennai.65 healthy non diabetic individuals in the age group of 40 years-60 years, age and sex matched.

Inclusion Criteria

* Patients with type 2 diabetes mellitus in the age group of 40-60 years.
* Both genders (male & female) are included
* Those who are on treatment with oral hypoglycemic drugs are included.

Exclusion Criteria

* Type 1 diabetes mellitus
* Pregnant women GDM
* Patients on treatment with statins, insulin, uricosuric drugs
* Patients with hypertension
* Individuals with history of alcoholism
* Patients with malignancy (leukemia, lymphoma, myeloma)
* Patients with arthritis, cardiac and renal disease

Sample Collection

5ml of fasting venous blood was drawn from antecubital vein of patients in a plain vacutainer tube under sterile conditions after fulfilling the selection criteria. Serum was separated by centrifugation at 3000 rpm for 15minutes and the separated serum was stored at -20^0c for further analysis.

Serum Glucose was estimated by Glucose oxidase- peroxidase method. (GOD/POD) (END POINT METHOD) , serum Urea was estimated by UV – GLDH, serum Creatinine was estimated by Jaffe's Method, serum Total cholesterol was measured by Cholesterol Oxidase Peroxidase Method (CHOD-POD), End point assay, TGL was measured by Glycerol phosphate, oxidase peroxidase method, End point assay and LDL was calculated by using Friedwalds formula, LDL Cholesterol = Total Cholesterol – HDL Cholesterol – Triglyceride/5,HDL was measured by Precipitation End Point Method and Uric acid was estimated by URICASE/ POD, End point assay

Statistical Analysis

This study done to evaluate serum Uric acid and Lipid profile in Type 2 Diabetes Mellitus patients was done in total of 130 subjects, of which 65 with known diabetes mellitus were taken as cases and 65 individuals without diabetes mellitus were taken as controls. Statistical analysis was performed using SPSS software, Version 20.0 .If the P value is 0.000 to 0.010 then denoted by **,it imply significant at 1 level (Highly Significant),If the P value is 0.011 to 0.050 then denoted by *,it imply significant at 5 level (Significant),If the P value is 0.051 to 1.000 then no star,it imply Not Significant at 5 level (Not Significant) and P value of <0.05 is considered significant .Pearson's correlation was used

RESULTS

Table 1: Age Between Cases And Controls

Age in years	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
	Control	65	48.55	5.403	.670	0.215
	Cases	65	49.74	5.441	.675	0.215

Age based distribution into cases and controls have showed no statistically significant difference.

Table 2: Comparison Of Fasting Blood Sugar Between Cases And Controls

	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
	Control	65	91.31	12.993	1.612	
Glucose	Cases	65	174.00	39.502	4.900	0.001**

The mean glucose value of cases is 174.00 and that of controls is 91.31 and the P value is 0.001 which is statiscally highly significant.

Table 3: Comparison Of Urea Between Cases And Controls

	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
Urea	Control	65	20.23	3.673	.456	0.001**
	Cases	65	24.54	5.951	.738	

The mean value of urea for control is 20.23 and for case is 24.54 and the P value is 0.001 which is statistically significant.

Table 4: Comparison Of Creatinine Between Cases And Controls

	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
Creatinine	Control	65	0.940	.1599	.0198	0.019*
	Cases	65	1.011	.1786	.0222	

The mean value of creatinine for control is 0.940 and that of case is 1.011 and the P value is 0.019 which is statistically significant.

Table 5: Comparison Of Total Cholesterol Between Cases And Controls

	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
Total Cholesterol	Control	65	142.20	24.627	3.055	0.001**
	Cases	65	218.00	42.059	5.217	

Comparison between cases and control groups for total cholesterol shows highly significant difference in mean and the P value is 0.001 .

Table 6: Comparison Of TGL Between Cases And Controls

	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
TGL	Control	65	103.00	27.295	3.385	0.001**
	Cases	65	176.78	63.605	7.889	

The mean value of TGL for control is 103.0 and that of case is 176.7 and the P value is 0.001 which is statistically highly significant.

Table 7: Comparison Of HDL Between Cases And Controls

	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
HDL	Control	65	49.92	4.25	0.527	
	Cases	65	24.20	5.51	0.68	0.001**

Statistically significant difference was observed between the mean value of HDL for control and cases and the P value is 0.001 which is statistically highly significant.

Table 8: Comparison Of LDL Between Cases And Controls

	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
LDL	Control	65	71.677	23.6155	2.9291	0.001**
	Cases	65	155.089	40.6039	5.0363	

The mean value of LDL for control is 71.67 and that of case is 155.08 and the P value is 0.001 which is statistically highly significant.

Table 9: Comparison Of Uric Acid Between Cases And Controls

	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
Uric Acid	Control	65	4.740	0.5249	0 .0651	0.001**
	Cases	65	5.689	1.6384	.2032	

Comparison of uric acid levels between cases and control groups showed statistically significant difference in the mean and the P value is 0.001 which is statistically highly significant.

Table 10: Pearson Correlation Between Serum Uric Acid And Lipid Profile In Type 2 Diabetes Mellitus

	R –VALUE	P -VALUE	SIGNIFICANCE
Uric acid vs.Total cholesterol	0.498	0.0001**	SIGNIFICANT
Uric acid vs.TGL	0.254	0.04*	SIGNIFICANT
Uric acid vs.LDL	0.448	0.0001**	SIGNIFICANT
Uric acid vs.HDL	−0.292	0.018*	SIGNIFICANT

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

This table shows correlation between serum uric acid and lipid profile in type 2 Diabetes mellitus. Total cholesterol, TGL and LDL were positively correlated with serum uric acid level and the correlation was statistically significant. High density lipoprotein cholesterol(HDL) was negatively correlated with serum uric acid and the correlation was statistically significant.

DISCUSSION

In this cross sectional study ,65 patients with type 2 diabetes mellitus were taken as cases and 65 healthy individuals were taken as controls. This study evaluated the levels of serum Uric acid and Lipid profile in type 2 diabetes and compared them with healthy controls. The serum uric acid level was correlated with lipid profile in type 2 DM. The serum uric acid level was found to be increased in diabetic patients than the healthy individuals and was statistically significant . The serum levels of total cholesterol, TGL, LDL were also raised in diabetic patients when compared with healthy controls and was statiscally significant. But the level of serum HDL was significantly decreased in type 2 diabetes than the healthy control group. The study shows a normal renal profile in the patient and the control group, which signifies that the hyperuricemia under study is not due to decreased excretion of uric acid. The study proves a statistically significant positive correlation (p < 0.05) between serum uric acid and Total Cholesterol, TGL and LDL and a significant negative correlation (p < 0.05) between serum uric acid and HDL. Therefore, it is inferred that hyperuricemia is associated with dyslipidemia in type 2 Diabetes Mellitus and these patients are at a high risk for developing CVD. The increase in uric acid levels observed in the present study indicates a definite rise in uric acid levels in diabetic patients with a close relationship to cholesterol levels. The observed increase in uric acid levels in type-2 diabetic patients indicates a positive relationship of uric acid levels with cholesterol levels in type-2 DM subjects suggesting, the rise in uric acid parallels the increase in cholesterol levels [37].Many life threatening complications of type-2 diabetes mellitus specifically micro angiopathy have been attributed to diabetes induced dyslipidemia. As there is a parallel rise in uric acid along with cholesterol levels in type-2diabetic subjects, an estimation of uric acid levels in serum may be an additional significant criteria to assess dyslipidemia as well as to control the dyslipidemia induced complications in type-2 diabetes mellitus The morbidity and mortality due to cardiovascular complications is higher in type 2 diabetes. Studies on the risk factors which increase the prognostic efficiency for cardiovascular risk in diabetic subjects are very few. In this study, there is increase in Total Cholesterol, LDL-Cholesterol, Triacylglycerol and decrease in HDL-Cholesterol in diabetic cases compared to non diabetics indicating atherosclerotic changes indiabetics. Serum uric acid levels were found to increase profoundly in diabetic subjects compared to non diabetics [38]. These results agree with that obtained in a study done by Safi et al [39], who found the average level of serum uric acid in the diabetic patients was 6.07 mg/dl as compared to 5.01 mg/dl in the control group. It was observed that serum uric acid is positively associated with type 2 diabetes mellitus and the association was relatively more significant in patients with hyperlipidemia. Also these results were comparable to similar studies performed by different research workers .[40-43] In the present study all lipid fractions with exception to HDL are significantly elevated in patients with type 2 diabetes, supporting the fact that high morbidity and mortality in diabetes may be due to derangement in lipid profile. Uric acid can promote LDL oxidation, a key step in progression of atherosclerosis by stimulating granulocyte adherence to the endothelium. High range of glycaemia can promote non enzymatic glycosylation of LDL which in turn can be phagocytosed into the arterial wall independent of receptor mechanism [44,45]. Phagocytosed uric acid can transverse through dysfunctional endothelium, this in turn leads to plaque formation. [46,47] Diabetics with elevated uric acid levels are at increased risk for developing cardiovascular disease [48]. Hyperglycemia is a well-known risk factor for hyperuricemia [51] and also hyperuricemia is a risk factor for the development of diabetes. Such counter influence leads to a vicious cycle, which may drive the development of co-morbidities such as Cardiovascular disease (CVD) in general and Coronary artery disease (CAD) in specific.

In our study, diabetic patients had higher total cholesterol, triglycerides, LDL cholesterol and lower HDL cholesterol than nondiabetic patients, which is consistent with published reports[50].We also observed higher serum uric acid levels among diabetics than nondiabetics with significant positive correlation between serum uric acid levels and hyperlipidemia.

CONCLUSION

In the present study, the levels of serum uric acid and serum lipid profile were evaluated in type 2 Diabetes mellitus patients and healthy individuals. The serum levels of Uric acid, Total cholesterol, TGL, LDL were raised and the High density lipoprotein cholesterol was decreased in type 2 diabetic cases when compared to healthy control group indicating atherosclerotic changes in type 2 diabetes mellitus patients. Also there is a significant positive correlation between the levels of serum uric acid with total cholesterol, TGL, LDL and a significant negative correlation between serum uric acid with HDL in type 2 DM.The present study proves that hyperuricemia is positively associated with dyslipidemia in type 2 DM. As there is a parallel rise in uric acid along with total cholesterol, TGL, LDL levels in type-2 diabetes patients, the estimation of serum uric acid along with serum lipid profile is highly beneficial in type-2 diabetes mellitus patients to assess the dyslipidemia induced cardiovascular complications. Hyperuricemia and dyslipidemia are significant risk factors which can lead to possible cardiovascular disease and increase the morbidity and mortality in type 2DM.So treatment of hyperuricemia and dyslipidemia may prevent or decrease the development of cardiovascular disease in type2 DM. Further research is needed to determine the assessment and treatment of hyperuricemia and dyslipidemia for reducing the risk of cardiovascular disease in type 2 DM

Limitations Of The Study

- The sample size is relatively small, which was not enough to correlate serum uric acid with other parameters like fasting blood glucose, urea and creatinine
- Selection of individuals with prediabetic state like impaired fating glucose, impaired glucose tolerance also would have provided more information regarding the association of serum uric acid with progression of type 2 diabetes mellitus
- A large scale study taking into account of body mass index, impaired fasting glucose (IFG),impaired glucose tolerance(IGT), metabolic syndrome is however needed to avail a better understanding of this association between serum uric acid and dyslipidemia .

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