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Association of uric acid and dyslipidemia in newly detected type 2 Diabetes Mellitus

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Abstract
Background: *Cardiovascular disease has been suggested to be associated with higher levels of serum uric acid. Dylipidemia in Diabetes mellitus has been linked with cardiovascular complications in these patients. We undertook this study to evaluate the association of uric acid and dyslipidemia in newly detected type 2 Diabetes Mellitus.*
Materials and Methods: *The study group comprised of 100 newly detected type 2 diabetic patients in the age group of 30-60 years visiting medicine Out Patient Department. As a control group 100 age and sex matched healthy participants were taken. The blood samples were used for measuring various parameters. Serum uric acid was estimated by uricase method. LCAT activity was assessed by measuring the difference between esterified and free Cholesterol. Determination of free and esterified cholesterol was done by using digitonin precipitation method. HDL cholesterol level and total cholesterol was measured by Cholesterol oxidase Peroxidase method. Triacylglycerol estimation was done by Glycerol 3-Phosphate Oxidase – Peroxidase method. VLDL and LDL cholesterol was calculated by formula. Fasting blood glucose was measured by Glucose Oxidase Peroxidase method.*
Results: *Study found that serum uric acid, LDL, VLDL, Total Cholesterol, Triacylglycerol were significantly increased in type 2 DM when compared to control group. Activity of LCAT and levels of HDL were significantly decreased in newly detected type 2 DM when compared to control group.*
Conclusion: *Hyperuricemia is found to be associated with dyslipedimia along with decreased LCAT activity in Diabetes mellitus patients. Thus uric acid can be used as a potential biomarker of deterioration of glucose metabolism and dyslipedemia.*

Introduction

Uric acid is a ubiquitous end product of purine metabolism in humans that is mainly excreted in urine[1]. Uric acid acts as a potent peroxynitrite scavenger and antioxidant[2]. However, high levels of serum uric acid, termed hyperuricemia, are associated with gout, kidney stones, metabolic syndrome, hypertension, renal disease, and

cardiovascular disease[3]. Life style related diseases, such as metabolic syndrome, or type 2 Diabetes mellitus often have a common pathological foundation. DM will be a leading cause of morbidity and mortality in the foreseeable future[1]. 50% of diabetic's deaths occur due to cardiovascular disease[4]. Low HDL is a strong risk factor for the development of cardiovascular disease. The cardioprotective role of HDL is related to its role in RCT[5]. HDL plays a central role in RCT by promoting the efflux of cholesterol from peripheral tissues and also by acting as the major site for the esterification of cholesterol by LCAT[6]. Human LCAT is a 416 amino acid glycoprotein circulating in plasma associated with lipids and apolipoproteins in the HDL fraction[7]. LCAT is the enzyme that generates almost all of the cholesterol esters in plasma. It plays a key role in reverse cholesterol transport and is activated by apo A-I in HDL[8]. It promotes reverse cholesterol transport by maintaining a free cholesterol gradient between HDL and peripheral tissues[9]. Hence the present study was undertaken to evaluate the association of uric acid and dyslipidemia in newly detected type 2 Diabetes Mellitus.

Materials and Methods

The study group comprised of 100 newly detected type 2 diabetic patients in the age group of 30-60 years visiting medicine Out Patient Department. The diagnosis of Diabetes Mellitus was done by senior physicians and confirmed by estimating Fasting Blood Glucose (>126mg/dl) and 2hour Oral Glucose Tolerance Test (>200mg/dl) values on two occasions as per American Diabetic Association's revised criteria. As a control group 100 age and sex matched healthy participants were taken. The study was conducted at department of Biochemistry.

After obtaining informed written consent, 10ml of 12 hours fasting venous blood sample was collected from diabetic patients and the control group under all aseptic conditions. The blood samples were used for measuring various parameters. Serum uric acid was estimated by uricase method[10]. LCAT activity was assessed by measuring the difference between esterified and free Cholesterol[11]. Determination of free and esterified cholesterol was done by using digitonin precipitation method[11]. HDL cholesterol level[12] and total cholesterol was measured by Cholesterol oxidase Peroxidase method[12]. Triacylglycerol estimation was done by Glycerol 3-Phosphate Oxidase – Peroxidase method[12]. VLDL and LDL cholesterol was calculated by formula[12]. Fasting blood glucose was measured by Glucose Oxidase Peroxidase method[13].

Exclusion Criteria

Patients on hypolipidemic drugs, steroids and oral contraceptives were excluded. Known cases of hypothyroidism, hyperthyroidism, hyperuricemia, Cushing's syndrome, kidney diseases, hepatic diseases, alcoholics, smokers, tobacco chewers and patients with Type 1 Diabetes Mellitus and Hypertension were also excluded from the study.

Limitations

The duration of diabetes before the formal diagnosis was unknown. Because of limited resources the direct methods available for measuring LCAT activity could not be used. The LCAT activity was indirectly measured as the difference between esterified cholesterol and free cholesterol.

Statistical Analysis

The results are expressed as mean±SD. The results are further subjected to students 't' test, differences between means are considered significant at $p< 0.05$.

Results

Study found that serum uric acid, LDL, VLDL, Total Cholesterol, Triacylglycerol were significantly increased in type 2 DM when compared to control group. Activity of LCAT and levels of HDL were significantly decreased in newly detected type 2 DM when compared to control group (Table:1).

Table no 1: Biochemical parameters in newly detected Type 2 DM and Control participants.

Sl.No	Parameters	Newly detected type 2 DM (n=100)	Controls (n=100)	p value
1	Serum uric acid	7.595 ± 0.08559, n=100	4.620 ± 0.05822, n=100	<0.05
2	LCAT activity (IU/ L)	59.00 ± 0.9863, n=100	91.74 ± 0.6497, n=100	<0.001
3	HDL(mg/dl)	33.29 ± 0.4691, n=100	48.76 ± 1.684, n=100	<0.01
4	LDL(mg/dl)	130.3 ± 3.371, n=100	95.98±3.916, n=100	<0.01
5	VLDL(mg/dl)	43.51 ± 2.106, n=100	29.74 ± 1.970, n=100	<0.01
6	Total Cholesterol(mg/dl)	208.0 ± 3.379, n=100	175.1 ± 3.988, n=100	<0.05
7	Triglycerides(mg/dl)	220.7 ± 10.35, n=100	155.6 ± 10.72, n=100	<0.05
8	FBS (mg/dl)	156.05±41.14	74.34±15.09	<0.001

n = number of participants, p< 0.05 – significant, p>0.05 - non significant.

Discussion

The prevalence of diabetes and the cardiovascular complications associated with diabetes are increasing globally. Diabetic patients who are hyperuricemic appear to be at increased risk for developing diabetic complications, especially cardiovascular disease[14].

Present study found that the levels of uric acid were significantly (<0.001) increased in newly detected type 2 diabetes patients compared to the control group (Table 1). This is in line with data published in previous studies in which hyperuricemia has been associated with the higher risk of developing impaired glucose tolerance and type 2 Diabetes[15,16,17]. Many reasons have been suggested to explain the relationship between hyperuricemia and diabetes, reduced renal clearance or increased proximal tubular reabsorption of uric acid due to the insulin resistance[18].

Present study found that in newly detected type 2 diabetes patients the activity of LCAT was significantly reduced (p<0.001) on comparison with the control group (Table: 1). Durucan and coworkers found significantly lowered LCAT activity in diabetics[19]. A. Ghanei concluded that LCAT activity is considerably lower in diabetics compared with non-diabetics[20]. Hyperglycemia and oxidative stress in newly detected type 2 DM may lead to nonenzymatic glycation of LCAT. This may reduce the activity of LCAT in newly detected type 2 DM.

This study found that there was a significant increase in the levels of Triglyceride, Total Cholesterol and LDL levels in patients suffering from Diabetes Mellitus compared to the control group. Also there are significantly decreased levels of HDL in Diabetic patients compared to the control group. This study found significantly higher levels of uric acid in newly detected type 2 DM patients when compared to the control participants. Diabetes mellitus associated with hyperinsulinemia leads to increased tubular reabsorption of sodium and also decreases the ability of the kidney to excrete uric acid. Studies have shown that uric acid is a predictor of hyperinsulinemia[21] this may be attributed to the its ability to inhibit endothelial function by impairing nitric oxide production[22].

Conclusion

Uric acid levels were significantly increased in Type 2 Diabetes mellitus patients compared to the control participants. Hyperuricemia is found to be associated with dyslipedimia along with decreased LCAT activity in Diabetis mellitus patients. Thus uric acid can be used as a potential biomarker of deterioration of glucose metabolism and dyslipedemia.

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