Relation Between Serum Uric Acid and Non Insulin Dependent Diabetes Mellitus(NIDDM)

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Abstract: Background & Objectives: NIDDM is an independent risk factor for cardiovascular disease. NIDDM increases the risk for all manifestations of atherosclerotic vascular disease, coronary heart disease, cerebro-vascular disease and peripheral vascular disease. Coronary heart disease mortality and morbidity rates are two to four times higher in diabetic patients than in non-diabetic subjects. NIDDM is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency. The aim of the study was to assess the relation between serum uric acid and NIDDM. Methods: The study group included 30 NIDDM cases and 30 control of both sex. Fasting blood samples were collected from both cases and controls in Dhiraj General Hospital, Pipariya, vadodara. Fasting blood sugar, and serum levels of uric acid, creatinine, lipid profile assayed by standard IFCC protocol. Results: There was a significant increase in fasting blood sugar, serum creatinine, uric acid, and lipid profile with exception to high density lipoprotein in NIDDM cases as compared to control. However the correlation bet ween uric acid and other parameter was not very relevant. Conclusion: The study showed significant increase in serum uric acid with the increase in blood sugar value in NIDDM. Elevated uric acid levels are associated with increased risk of cardiovascular mortality in NIDDM. [Nayak M et al NJIRM 2013; 4(5) : 72-75]

Key Words: Cardiovascular disease, Hyperuricemia, NIDDM.

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Introduction: Non-insulin dependent diabetes mellitus has emerged as major health problem in India .In the year 2000, there were 30 million people with diabetes in India. NIDDM is a disorder affecting insulin production or action, which may lead to serious complications, including eye disease (Diabetic retinopathy), Kidney disease, neuropathy, and cardiovascular disease. However, despite its serious health implications, NIDDM may not present any obvious symptoms, and people may have the illness for several years prior to diagnosis.[1]

A Several population-based studies[2] have shown that subjects with NIDDM have a twofold to fourfold greater risk of all manifestations of atherosclerotic vascular disease, stroke, compared with non diabetic subjects. The increased risk of cardiovascular disease is only partly explained by the adverse effects of NIDDM on classic risk factors or risk factors clustering with hyperinsulinemia (elevated levels of total triglycerides, decreased HDLcholesterol, hypertension, and glucose intolerance).[3]

Serum uric acid, an end product of purine metabolism, has been shown to be associated with an increased risk of hypertension, cardiovascular disease and chronic kidney disease in previous epidemiological studies. Also, an elevated level of uric acid is a risk factor for peripheral arterial disease, insulin resistance, and components of the metabolic syndrome. Elevated serum uric acid is highly predictive of mortality in patients with heart failure or coronary artery disease and of cardiovascular events in patients with diabetes.[4] However, the potential mechanism by which elevated serum uric acid can have direct or indirect effect on cardiovascular system is not very clear because of its association with established risk factors like diabetes mellitus, hypertension, obesity and others. Elevated uric acid is one of the metabolic abnormalities associated with hyperinsulinemia as seen in NIDDM and impaired glucose tolerance.[5] Hyperuricemia could be an "innocent bystander," a nonspecific marker of adverse pattern of risk factors. However, we do not exclude the possibility that hyperuricemia could play a role in the pathogenesis of atherosclerosis. Overwhelming evidence suggests that hyperuricemia is linked to reduced HDL cholesterol, hypertriglyceridemia, hyperinsulinemia and reduced insulin sensitivity, components of the metabolic syndrome.[6] This comparative studies show relation between serum uric acid and NIDDM.

Material and Methods: The present prospective study was conducted in Department of, clinical Chemistry, Dhiraj General Hospital, S.B.K.S.medical institute & Research centre Piparia, Vadodara, Gujarat. The study included 30 non insulin dependent diabetes mellitus (NIDDM) as case and 30 non diabetic people as control. Approval was taken from research ethics committee of S.B.K.S medical college, Piparia, Vadodara, before starting the study.

Inclusion criteria:

I) Age >18 year
II) Both Male and Female
III) Known cases of NIDDM
IV) Indoor Patients of Dhiraj General Hospital.
V) 30 Non Diabetes Subject as control

Exclusion Criteria:

I) Patient with cardiovascular disease such as myocardial infarction(MI), and other vascular disease
II) Comorbid major psychiatric diagnosis
III) Comorbid chronic illness requiring daily medical management.
IV) Patients with sickness like liver disease and history of renal disorder.

After consent was given venous blood sample were collected after 12 hours overnight fasting. Each test tube containing a blood sample was immersed in crushed ice before analysis. The samples were centrifuged for 10 min at a speed of 4000 r.p.m. (R-8 CLABORATORY CENTRIFUGE), to separate the serum Into a 12 × 75 mm test tubes. Serum Uric Acid, creatinine, Total cholesterol, Triglyceride, HDL and blood sugar were measured by using available kits in TRANSASIA (ERBA MANNHEIM) CHEM-5 PLUSV2 which has open system with photometric accuracy. Standard IFCC protocols were used for all analysis .LDL concentration was calculated using Freidwald Formula Anthropometric measure like Body Mass index (BMI), Waist and hip circumference in cm, Waist Hip ratio (WHR) and Waist Height ratio (WHtR) were taken into both case and controls.

Statistical analysis:

Stastical analysis were performed using commercially available software (SAS version 9.1 ;) The responses were noted and the data obtained were analysed using Descriptive statistics (frequency distribution, percentages ,mean, standard deviation, standard error of mean, mean differences, and 95%confidence interval) .Also t – test and Analysis of Variance (ANOVA) were used and significance judged at P<0.05.pearson correlation was used to assess the relation between uric acid with different parameters.

Results: The average age of the study group was 58.7±8.7 yrs in cases and 45.6±16.9 yrs in control. Study group consist of no patients were below 30 years or less, 16 patients (53,3%) were in between 31 to 60 years of age and 14 patients (46.7%) were above 60 years of age. The maximum numbers of patients were in the age group of 31 to 60 years. While in non diabetic subject the maximum number of patient 17(56%) were in age group 31 to 60 years. (Table-1)

Table. 1: Age distribution of study groups

AGE	NUMBER (N=60)		Percentage of total
	Cases (NIDDM)	Controls (NON DIABETIC)	
<30 year	0	23% (n=7)	11.66%
31 to 60 year	53.3% (N=16)	56% (n=17)	55% -
>60 year	46.7% (N=14)	21% (n=6)	33.33% -

In the present study, gender distribution shows out of 60 patients 36 were male & 24 were female. Out of 36 male patients 19 (67.3%) had type 2 diabetes. out of 24female patients 11(33.7%) had type 2 diabetes. So this suggests that male patients had higher incidence of diabetes as compared to female counterparts. (Table-2)

Parameters like Waist, Waist/Hip ratio, Waist/Height, body mass index were also measure. They were significantly elevated in cases · as compared to control and there is statistically significance found between those two groups in this study. (Table-3)

The important biochemical parameters were measured. In diabetic subject the serum uric acid

level was significantly high as compared to control groups .the serum creatinine level is slightly elevated in cases. The all the lipid profile were significantly higher in case group as compare to control group. (Table-4)

Table.2: Gender distribution of study groups

Sex	Number (N=60)		% (N=60)	P Value
	Diabetic	Non Diabetic		
Male	67.3% (N=19)	56.7% (N=17)	60%	>0.05
Female	33.7% (N=11)	43.3%(N =13)	40%	

Table:3 Mean of anthropometrics parameters of study groups

Parameters	Cases N = 30	control N = 30	P VALUE
Age (years)	58.7±8.7	45.6±16.9	<0.0004
Waist cm	86.21±2.95	82.76±3.38	<0.001
Waist/Hip ratio	0.99±0.01	0.88±0.03	<0.001
Waist /Height	0.57±0.04	0.52±0.04	<0.001
Body Mass Index	27.94± 1.8	24.55±2.1	<0.001

Table:4 Mean of biochemical parameters of study groups

Biochemical parameters	Case N = 30	Control N = 30	P Value
Uric acid(mg/dl)	7.3±1.2	4.7±1.0	<0.001
FBS(Mg/dl)	190±20.23	88±8.8	<0.001
Creatinine (Mg/dl)	1.1±0.3	0.42±0.24	<0.001
T.chol(MG/dl)	210.12±18.43	134.31±16.78	<0.001
TGL(mg /dl)	205±36.44	130.12±22.45	<0.001
HDL(Mg/dl)	30.11±5.66	47.21±3.6	<0.001
LDL(Mg/dl)	183.2±18.69	113.56±15.49	<0.001

Discussion: NIDDM is a heterogeneous syndrome Characterized by insulin resistance and /or defective insulin secretion.[7] Metabolic syndrome is characterized by abdominal obesity with visceral adiposity, impaired glucose tolerance due to insulin resistance with hyperinsulinemia, hypertriglyceridemia, increased low density lipoprotein cholesterol, decreased high-density lipoprotein cholesterol, and hyperuricemia. Hyperuricemia resulting from euglycemic hyperinsulinemia may precede the onset of type 2 diabetes, hypertension, coronary artery disease, and gout in individuals with metabolic syndrome [8]
In humans, uric acid is the most abundant aqueous antioxidant, accounting for up to 60% of serum free radical scavenging capacity and is an important intracellular free radical scavenger during metabolic stress. Uric acid, although one of the major antioxidants in circulation can induce oxidative stress in a variety of cells including vascular smooth muscle cells and thus, mediate progression of cardiovascular disease . pathogenic mechanism appears to involve decreased nitric oxide (NO) bioavailability in vascular smooth muscle and endothelial cells and direct scavenging of NO by uric acid . Decrease in endothelial NO production by uric acid, has been also associated with endothelial dysfunction and insulin resistance. In addition, uric acid has been implicated in the development of hypertension and elevated levels of uric acid have been reported particularly in newly diagnosed hypertension.[9]

Derek G. Cook'[10] found that there is positive correlation between higher serum uric acid level (7.0±0.4) and blood glucose concentration (FBS 182±10mg/dl). J.A.robes at el[11] shows significantly positively correlation between serum uric acid concentration and NIDDM. The highest quartile of uric acid was also associated with incident type 2 diabetes in the Rotterdam study (4,536 adults followed for 10 years) [12] A cross-sectional study of 1877 Turkish men and women showed that those in the highest uric acid for a diagnosis of diabetes.[13]

Hyperuricemia has been associated with insulin resistance; however, there are few studies where the association of hyperuricemia-insulin resistance and beta cell function is evaluated. A modest

positive association between concentrations of uric acid and incidence in type 2 diabetes mellitus was observed in a cohort of a Chinese population[14] Cohort studies support the fact that uric acid is a risk factor for developing DM2; in a meta analysis by Kodama et al.[15]the authors concluded that the variability of the results and control of confounding variables should be considered in the final analysis of competitive models for interpreting the results regarding the role of uric acid as a risk factor for developing DM2. Omar Khalid Alboqai et al[16] reported that the positive correlation between serum uric acid level and obesity has been recognized for a long time. Serum uric acid level was found to be positively associated with body weight, BMI, body fatness.

Conclusion: The study reveals positive correlation between serum uric acid and blood sugar in NIDDM. Uric acid can play an important role in the function of the beta cell in patients with DM2. Hence, estimation of Serum uric acid while monitoring case of NIDDM will help to decrease incidence of cardiac and renal complications.

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