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Association Of Serum Uric Acid Level in Diabetic, Prediabetes and Non-Diabetic Individuals: A Comparative Cross Section Study

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Abstract

Aim: To assess the association of serum uric acid level in diabetic, prediabetes and non-diabetic individuals

Study Design: Cross section study

Place and duration: This study was conducted in People's University of Medical Health Science For women Nawabshah Pakistan. From January 2019 to January 2020.

Methodology: Samples of fasting blood sugar, serum uric acid and some other variables of 119 subjects were collected. Total 80 (67.22%) of them were male and 39 (32.78%) were female. Prediabetes was interpreted as fasting blood sugar from 100 to 125 mg/dl. Diabetes was defined as fasting blood sugar equal to or more than 126 mg/dl. Multinomial logistic regression analysis was used for the evaluation of the association between diabetes and serum uric acid.

Results: The lower mean value of serum uric acid for prediabetes patients was 331.8±100.5 µmol/L, the value for the diabetic patients was 295±90.8 µmol/L and it is 372±112.8 µmol/L for nondiabetic individuals ($p<0.001$). Body Mass Index, triglyceride and total cholesterol levels are directly related to the level of serum uric acid, whereas, the level of fasting blood sugar is negatively associated with it. In all the groups, diabetes prevalence reduces with an elevation in concentration of serum uric acid. Hence, there is an inverse relationship between diabetes and serum uric acid according to regression analysis.

Conclusion: There is a negative correlation between serum uric acid and diabetes. Serum uric acid was seen raised in nondiabetic individuals as compared to those who were either diabetic or prediabetic.

Keywords: Diabetes, Prediabetic, Serum Uric Acid, Nondiabetic

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Introduction:

Uric acid is formed as a result of the chemical separation of purine nucleotides present in the diet. It is excreted through urine. A high concentration of uric acid in body is called Hyperuricemia [1]. In hyperuricemia, the equilibrium of its production and expulsion out of the body is disturbed. It can cause several diseases such as gout, metabolic syndrome, cardiovascular diseases and kidney stones. Prevalence of hyperuricemia is seen in individuals who have impaired functionality of the kidneys, hypothyroidism, certain drugs and toxins. Due to the increasing trend of obesity, the graph of hyperuricemia is also increasing in the developing world [2].

Elevated uric acid concentration is also a risk element for hypertension and dyslipidemia. Whereas, the logical reason behind the supposed interrelationship between the raised concentration of serum uric acid and diabetes is not completely understood. Serum uric acid concentration is seen positively related with blood glycemic levels in non-diabetic individuals. This fashion of positive association is not the same in prediabetic and diabetic individuals. In another study, the general population show a reduced risk of gout in diabetic patients [3].

There is variation in the level of serum uric acid in the glycemic state. Some studies show a high level of uric acid in glycemic state while some show its reduction. Impairment of glucose intolerance is seen in presence of hyperuricemia [4]. On the other hand, elevated levels of triglycerides and cholesterol represent insulin resistance and are also associated with a raised level of serum uric acid [5].

To test the association between fasting blood sugar level and serum uric acid concentration, the present study has been carried out in nondiabetic, prediabetic and diabetic individuals.

Methodology:

This comparative cross sectional study was conducted in People's University of Medical Health Science For women Nawabshah Pakistan. From January 2019 to January 2020.

Approval was taken from the ethical review committee of the institute. Subjects were selected after setting strict inclusion criteria. According to the inclusion criteria, the subjects must be above the age of 22 years, and either male or female. The diabetic individuals selected were supposed to be diabetic in accordance with guidelines maintained by American Diabetes Association. Subjects who are lactating mothers, pregnant, have kidney disease, hepatic disorder, cardiovascular disease, have a history of anti-hyperuricemia drugs, or have a positive history of gout were precluded from the present study.

After a gross screening, 119 subjects were selected, and written informed consents were taken. Standard guidelines were set and followed throughout the study. The fasting blood sugar level of all the subjects was taken. Following the collection of samples and determination of the results, subjects were further divided into nondiabetic, prediabetes and diabetic groups.

Data collection was done on the basis of anthropometric characteristics, the health status of the individuals, type of lifestyle and dietary habits. Anthropometric characteristics considered in this study are age, height, weight, BMI and gender. All the measurements were taken keenly and carefully. For minimizing the chances of any kind of errors, measurements were repeated. A questionnaire was cautiously filled for each individual.

Blood samples of all the subjects were recorded after overnight fasting of 10 to 12 hours. The method used for blood collection was venipuncture technique. The blood samples were stored in an ice box. They were carefully transported to the laboratory. After centrifugation and cooling the samples, serum uric acid, glucose level, total cholesterol, HDL, triglycerides, total proteins and serum albumin were measured. Standard protocols were followed in the measurements of all the indices.

Individuals were declared diabetic, prediabetic and non-diabetic according to American Diabetes Association. Persons having fasting blood glucose ≥126 mg/dL were declared diabetic. If random blood sugar is ≥200 mg/dL or taking hypoglycemic drugs or insulin, then they are also supposed to be categorized as diabetic. Individuals with fasting blood glucose levels 100–125 mg/dL were considered prediabetic. Those who had fasting blood glucose levels less than 100 mg/dL were categorized as non-diabetic.

If the concentration of serum uric acid is more than 7.0 mg/dL or 417 µmol/L in male subjects and more than 6.0 mg/dL or 357 µmol/L in females, then they are considered to be hyperuricemia. The National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) criteria were used to determine the presence or absence of Metabolic Syndrome (MetS) in the subjects. In this study, the components used to determine Metabolic Syndrome are triglycerides (TG≥150 mg/dL), HDL-C (<40 mg/dL for males and <50 mg/dL for females), and fasting blood sugar more than 100 mg/dL.

Software that was used to analyze the statistical data was IBM SPSS version 26. The mean, ranges and standard deviations of the data are presented. Serum electrolytes and other characteristics of the participants in each group were compared by means of One-way ANOVA. The difference in Metabolic Syndrome and hyperuricemia was determined by the application of Chi-square. An independent sample t-test was performed for the determination between baseline characteristics based on gender, and anthropometric measurements. Multinomial logistic regression analysis was applied to study the association between diabetes and serum uric acid level where the presence of diabetes was expressed as 'yes', while the absence of diabetes was categorized as 'no'. The remaining variables were considered continuous variables. Diabetes was taken as a dependent, whereas, serum uric acid as an independent variable. Serum uric acid was utilized as a continuous variable along with other covariates. The correlation between serum uric acid concentration and baseline variables was tested by Pearson's correlation coefficient.

In the regression analysis of the present study, three models were used. The first model was calibrated for gender and age. The model on second number was adjusted for gender, BMI, ages of the subjects, TG, HDL and TC. The third model was calibrated furthermore for remaining variables. First and Second models, total protein and serum albumin were adjusted in the third model.

Result:

A total of 119 participants were considered for the study. Total 80 (67.22%) were male and 39 (32.78%) were female. The average ages of these participants was 38.4±14.8 years. Those who had diabetes were older in age. They were also obese, overweight, hypertriglyceridemic and have high cholesterol levels compared to those who did not have diabetes. Their baseline characteristics have been shown in Table 1. The comparison table depicts that the mean level of serum uric acid in individuals having diabetes (295±90.8 µmol/L) and prediabetic (331.8±100.5 µmol/L) individuals are less than the healthy individuals (372±112.8 µmol/L) with a p-value of <0.001. The prevalence of hyperuricemia across all the participants was 19.1%. The percentage was higher in the prediabetic individuals i.e. 24.3% and low in the diabetic group i.e. 11.9%.

In table 2, a number of subjects, genders, ages, serum uric acid concentration, glucose concentration, hyperuricemia and presence of the metabolic syndrome in each quartile of serum uric acid are presented. According to the result, the ages of the subjects and fasting blood sugar levels are inversely proportional to the serum uric acid.

Serum uric acid of male subjects seems to be higher than the female ones. Likewise, the concentration of serum uric acid is more in young subjects in the non-diabetic category than in older ones in the diabetic and prediabetc section ($p < 0.001$). Uric acid has a negative coalition with the age in non-diabetic ($p < 0.01$) and prediabetic ($p < 0.05$) as per the Pearson correlation coefficient test. Conversely, serum uric acid has a positive association with diabetic individuals ($p < 0.01$). However, this trend is dominantly seen in male participants as compared to female participants.

A significantly negative interrelationship was seen between fasting blood sugar and serum uric acid ($p < 0.01$). Serum uric acid was seemed to be reduced in diabetic and prediabetic individuals as compared to that of non-diabetic participants in both genders. However, male participants had higher serum uric acid in all the quartiles. A multinomial logistic regression analysis was done between diabetes and uric acid concentration by taking serum uric acid as an independent variable and diabetes as a dependent variable. An inverse relation was observed between both variables for all the subjects as mentioned in the table 3.

Table 1: Baseline characteristics of all the subjects

Variables	**All**	**Diabetes**	**Prediabetes**	**Non-Diabetes**	**p-value**
Number	119	42	37	40	-
Female	39	16	13	10	-
Male	80	27	24	29	-
Age in years	39.5±16.5	48.5±13.4	38.7±18.1	30.6±12.6	0.000
Glucose (mg/dL)	148.8±78.1	220.7±83.4	112.2±8.3	90.1±8.2	0.000
BMI	25.1±3.6	26.1±4.1	23.9±3.5	24.5±4.6	0.048
Serum Uric Acid (µmol/L)	324.8±105.4	289±99.1	339±102.7	371.1±110.5	0.000
Hyperuricemia	16 (19.1%)	5 (11.9%)	9 (24.3%)	8 (20%)	0.000
Triglyceride (mg/dL)	192.2±125.4	245.8±152.7	161.2±96.4	190.4±125.3	0.000
Total Cholesterol (mg/dL)	207.2±32.5	257.4±109.6	186.4±53.5	175.3±54.0	0.000
HDL (mg/dL)	35.8±16.4	36.9±18.2	36.1±12.5	33.1±11.5	0.265
Albumin (g/dL)	48.0±12.9	46.9±16.1	48.9±13.7	47.8±8.9	0.684
Total protein (g/dL)	79.2±25.9	80.9±30.0	75.0±22.1	79.9±26.4	0.301

Table 2: Ages, fasting blood sugar level and metabolic syndrome of the subjects according to serum uric acid quartiles

Variables	**Q1 (≤249 µmol/L)**	**Q2 (250–321 µmol/L)**	**Q3 (322–387 µmol/L)**	**Q4 (>387 µmol/L)**	**p-values**
Number	29	31	30	29	-
Female	16	11	8	4	-
Male	15	20	22	23	-
Serum Uric Acid (µmol/L)	205.8±36.9	291.7±20.8	256.4±17.8	478.2±80.6	0.000
Glucose level (mg/dL)	175.3±85.3	140.5±75.3	140.1±80.3	129.2±65.2	0.005
Metabolic syndrome (%age)	38.2	31.5	22.2	24.1	0.000

Table 3: Multinomial logistic regression analysis for evaluating serum uric acid level and diabetes

	Model 1	**Model 2**	**Model 3**
B	-0.005	-0.005	-0.006
Standard Error	0.002	0.002	0.002
Wald	8.315	5.215	6.655
df	1	1	1
Odd Ratio	0.995	0.995	0.994
p-value	0.003	0.022	0.011

Discussion:

The presented study was carried out for the assessment of the association between blood sugar and uric acid level in non-diabetic, prediabetic and diabetic patients. Not many studies have been conducted in this regard with close results. In the present study, hyperuricemia was seen in 19.1% of participants. The percentage was higher in healthy participants as compared to prediabetic and diabetic individuals. Older participants in diabetes and prediabetes group had a lower level of serum uric acid, whereas, younger individuals in the nondiabetic group had a higher concentration of serum uric acid ($p < 0.001$). According to the Pearson correlation coefficient test, the ages of the participants were inversely related to the level of serum uric acid in the prediabetic and non-diabetic groups, however, it was positively correlated with diabetic participants. Male individuals had a prevalence of diabetes as compared to female participants. The hypothesis that an increase in serum uric acid in young individuals leads them to be prediabetic and it is less in developed diabetes disease, was supported by observing an increased level of serum uric acid in young participants [6].

Male participants had a higher concentration of serum uric acid compared to female participants. This finding of the present study is consistent with a previous study which proves that men have a higher tendency of having higher serum uric acid than female patients [7]. According to the present study, it was observed that serum uric acid level was lower in diabetic individuals. It was positively associated with prediabetic and nondiabetic individuals. This result of the present study is consistent with another study carried out by Rao et al. according to which a comparison of serum uric acid in prediabetic patients and patients having diabetes mellitus type 2 was done. The results of the study depicted a high level of uric acid in prediabetic individuals and significantly lower in type 2 diabetic patients [8].

Serum uric acid was inversely related to diabetes in a multinomial logistic regression analysis. This relationship was observed in all the models of the regression analysis. On the other hand, a positive association has been reported by many studies. Xiong et al. reported that an increase in uric acid promotes diabetes mellitus and its chronic complications [9]. Most of the studies that had been conducted previously were carried out for the individuals who had existing co-morbidities such as hypertension, diabetes, old age, high risk of kidney diseases and cardiovascular diseases [10].

Conclusion:

The concentration of serum uric acid is higher in nondiabetic and prediabetic individuals and lower in diabetic patients in the present study. The results of this study support the hypothesis that an increased level of serum uric acid can potentially cause diabetes, however, its level is significantly lower in the advanced stage of diabetes.

Conflict of interest:

None

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