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Correlation of Serum Uric Acid and Lipid Profile in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Diabetes complication poses a new challenge in Nepal as the disease is becoming endemic. Identifying risk factor for diabetes can be an essential step in preventing complication related to diabetes. Abnormal Uric acid and lipid profile are the important risk indicators of diabetes mellitus complications, so the study was done to know the association between uric acid and lipid profile in type 2 diabetes.

Methods: A cross-sectional study was done from 118 patients with type 2 diabetes mellitus visiting Nepal Medical College and Teaching Hospital. Three ml of venous blood was analyzed for fasting blood glucose, uric acid, and lipid profile. Correlational analysis was done between fasting blood glucose with triglycerides, high density lipoproteins and uric acid.

Results: A significant positive correlation between fasting blood glucose and triglyceride ($r = .211$, $p = .022$) was found in diabetic. There was significant negative correlation of fasting blood glucose with uric acid ($r = -.196$, $p = .034$) and high-density lipoprotein cholesterol ($r = -.181$, $p = .049$). Uric acid was also found to have significant positive correlation with triglyceride ($r = .235$, $p = .010$) and negative correlation with high density lipoprotein cholesterol ($r = -.420$, $p = .000$).

Conclusions: Negative correlation of serum uric acid with fasting blood glucose and high-density lipoprotein and positive correlation with triglycerides suggests a possible connection of uric acid as a risk factor for diabetes.

Keywords: Diabetes mellitus;f blood glucose; lipid profile; uric acid

INTRODUCTION

Diabetes has already become one of the major endemic non-communicable diseases globally and Nepal is not an exception.[1] It is currently a high-burden disease in Nepal suggesting a possible area for health promotion activities as well as early interventions to help control the disease. A study showed that the prevalence of type 2 DM (T2DM) in Nepal is 8.4%.[2] Hyperuricemia and dyslipidemia are the metabolic abnormalities frequently associated with type 2 diabetic patients. Several studies have been done taking serum UA (Uric Acid) and serum lipid profile individually in T2DM. A case control study done in health institute in Nepal shows positive association between elevated serum UA and serum lipid profile in T2DM.[3] Another study done in India shows there is significant elevation of serum UA in T2DM.[4] But a study done in another neighboring country with similar population characteristics showed that UA level was less in diabetic subjects in comparison to healthy and pre-diabetic.[5] Similar results were found in study done in general population of United States adults.[6] Both parameters are known to have a strong correlation with each other but it has not been properly studied and correlated in case of DM and we need to further explore the relationship of the uric acid level as a marker of dyslipidemia in our diabetic populations. In this context, correlation between serum UA and serum lipid profile in T2DM may be help to know the linkage between UA and lipid profile in T2DM.

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METHODS

A crossectional study was conducted in Department of Biochemistry, Nepal Medical College and Teaching Hospital (NMCTH), Kathmandu for period of one year starting from December 2019. A total of 118 study participants were recruited in the study using convenient sampling method. Physician diagnosed case of T2DM of both gender between age group of 20-70 years were selected for the study. Patients with type 1 DM, gestational diabetes, patients on lipid lowering drugs, patients on treatment for hyperuricemia and who did not give consent were excluded from the study. The selected study participants were measured for FBG (fasting blood glucose), serum UA, serum lipid profile: TC (Total Cholesterol), TG (Triglyceride), HDL-c (High Density Lipoprotein-cholesterol), LDL-c (Low Density Lipoprotein-cholesterol). Five ml of fasting venous blood was drawn from antecubital vein of the selected patients, in a plain vacutainer tube under sterile conditions. Serum was separated by centrifugation and processing was done in Vitros 250 using principle of dry chemistry.

Ethical approval was taken from Nepal Medical College-Institutional Review Committee before the start of study. Written informed consent was taken from each of patients included in this study during collection of data. The data was entered in Microsoft Excel Spreadsheet version 2010 and as a master chart and analyzed using SPSS version 16. Non-categorical data will be presented as mean and standard deviation. Independent t-test was performed to compare the mean of biochemical parameters at 95% confidence interval. Pearson correlation analysis was done in the between all the biochemical parameters against each other and statistical significance of the test will be noted.

RESULTS

Among 118 study participants, 59 were male and 59 were female. Baseline data are shown in Table 1. The average age of study participants was 54.37±11.17 years. Majority {n=40 (33.9%)} of study participants belonged to 61-70 years age category.

Table 1. Baseline characteristics of patients Parameters (n=118).

Parameters (n=118)	Mean ± SD
Age (Years)	54.37±11.17
FBG (mg/dl)	160.02±58.87
UA (mg/dl)	5.84±1.32
TC (mg/dl)	177.13±44.4
TG (mg/dl)	213.07±105.24
HDL-c (mg/dl)	34.76±9.84
LDL-c (mg/dl)	97.42±40.32
VLDL-c (mg/dl)	42.63±21.05
Non-HDL-c (mg/dl)	140.01±43.53
TC/HDL-c	5.28±1.72
LDL-c/HDL-c	2.92±1.39
HbA1c (n=73) * (%)	8.08±2.21
Urea (mg/dl)	25.92 ± 12.05
Creatinine (mg/dl)	0.77 ± .35

*FBG=fasting blood glucose, UA= uric acid, TC= total cholesterol, TG= triglyceride, HDL-c= high density lipoprotein cholesterol, LDL-c= low density lipoprotein cholesterol, VLDL-c= very low-density lipoprotein cholesterol. * Only 73 subjects were tested for glycated hemoglobin (HbA1c).*

Table 2. Correlation analysis of FBG, UA, lipid profile and HbA1c.

	UA	HbA1c	TC	TG	HDL-c	LDL-c	VLDL-c	NON-HDL-c	TC/ HDL-c
FBG	-.196* .034	.833** .000	.014 .877	.211* .022	-.181* .049	-.037 .690	.211* .022	.062 .506	.157 .089
UA	1	-.420** .000	.006 .946	.235* .010	-.232* .011	-.045 .630	.235* .010	.056 .548	.149 .107
HbA1c	-	1	.205 .082	.081 .494	-.147 .215	.268* .022	.081 .498	.267* .022	.302** .009

**Correlation is significant at 0.05 level (2-tailed) **correlation is significant at 0.01 level (2-tailed); FBG=fasting blood glucose, UA = uric acid, TC= total cholesterol, TG= triglyceride, HDL-c= high density lipoprotein cholesterol, LDL-c= low density lipoprotein cholesterol, VLDL-c= very low-density lipoprotein cholesterol, HbA1c = Glycated hemoglobin.*

Table 2 shows correlation analysis of FBG, UA, lipid profile and HbA1c. There was significant negative correlation of fasting blood glucose with uric acid (r = -.196, p =.034) and high-density lipoprotein cholesterol (r = -.181, p = .049) and significant positive correlation between fasting blood glucose and triglyceride (r =.211, p = .022). Uric acid was also found to have significant positive correlation with triglyceride (r = .235, p = .010) and negative correlation with high density lipoprotein cholesterol (r = -.420, p = .000).

Table 3. Mean values of age, FBG, UA and lipid profile categorized by gender.

SEX	Female	Male	Mean difference	p-value
Age (years)	54.31±11.4	54.44±10.9	.136	.948
FBG (mg/dl)	159.9±61.6	160.1±56.5	.237	.983
UA (mg/dl)	5.5±1.2	6.1±1.3	.5492	.024
TC (mg/dl)	182.3±42.5	171.9±46.1	-10.356	.207
TG (mg/dl)	181.6±.09	244.4±124.2	62.746	.001
HDL-c (mg/dl)	38.27±9.9	31.25±8.4	-7.017	.000
LDL-c (mg/dl)	105.50±40.13	89.32±39.20	-16.1797	.029
VLDL-c (mg/dl)	36.34±14.01	48.91±24.85	12.57	.001
NON-HDL-c(mg/dl)	142.22±40.40	137.80±46.7	-4.4186	.548
TC/HDL-c	4.92±1.4	5.6±1.9	.7107	.025
LDL-c/HDL-c	2.8±1.1	2.9±1.6	.1156	.654
HbA1C (%)	8.3±2.3(35)	7.8±2.1(38)	-.4463	.393

FBG=fasting blood glucose, UA=uric acid, TC=total cholesterol, TG= triglyceride, HDL-c= high density lipoprotein cholesterol, LDL-c= low density lipoprotein cholesterol, VLDL-c= very low-density lipoprotein cholesterol, HbA1c = glycated hemoglobin

Table 3 shows mean values of age, FBG, UA, HbA1c and lipid profile categorized by sex. The mean values of FBG, UA, TG, VLDL-c, TC/HDL-c and LDL-c/HDL-c were higher in male compared to female. Mean difference between male and female were significant for UA, TG, HDL-c, LDL-c, VLDL-c and TC/HDL-c.

The mean value of TG and TC/HDL-c was above the normal range and mean value of UA, TC, HDL-c, LDL-c, non-HDL-c, were within the normal range. Out of total study participant 28.8% had borderline high TC. According to NCEP ATP III classification, (reference here please, if possible) 73.7% (n= 87) study participant had low HDL-c (≤40mg/dl) and 1.7% (n=2) study participant had high HDL-c. For atherogenic index, 29.7% study participant had high TC/HDL-c. Out of 118 study participants, only 73 were tested for HbA1c. The mean value of HbA1c was 8.08±2.21. Urea and creatinine were also studied and was found to be within the normal range.

Table 4. Mean values of UA, TG and HDL-c according to FBG category.

FBG (mg/dl)	UA (mg/dl)	TG (mg/dl)	HDL-c
≤125 n= 33 (28%)	6.08±1.2	190.45±92.2	36.91±9.9
126-200 n= 63 (53.4%)	5.9±1.3	212.90±108.3	35.27±9.9
>200 n = 22 (18.6%)	5.2±1.3	213±105.2	34.76±9.8

FBG=fasting blood glucose UA=uric acid, TG=triglyceride, HDL-c=high density lipoprotein cholesterol.

Table 4 shows that the mean values of UA and HDL-c were decreased with increasing FBG range and mean value of TG was increased with increasing FBG range. In our study, it was also found that mean values of age, FBG and HDL-c were high for male with normal serum UA. Similarly, mean values of FBG, TC, TG, HDL-c, LDL-c, VLDL-c, non-HDL-c and TC/HDL-c were high for female with normal serum UA.

DISCUSSION

Relationship of serum uric acid level with serum lipid and fasting blood glucose has variable results in different populations. In our study, a significant negative correlation was found between serum UA and FBG (Table 2). Some studies done in different populations matches with the finding of our study .[5,7,8] A study have postulated that with increasing blood glucose in diabetic patient, there is more likelihood of more uricosuria effect of glucose that leads to increased excretion of UA.[5] UA is transported by glucose transporter 9 from lumen to proximal tubules and its reabsorption may be affected by several inorganic and organic ions and glucose which results in decline reabsorption and increase excretion of UA.[7] It is likely that the most of study participants in our study were in later stages of diabetes as we enrolled only the known cases of diabetes. This might explain the negative association of serum UA with FBG in our study. However, our study does not have data to show the duration of diabetes. Contrary to our result, there are some studies which have proved a positive association between UA and development of T2DM.[3,9,10]

There are also some studies which do not show any association of serum UA with FBG.[11,12] The present study revealed negative correlation between serum UA and HbA1c. Levels of serum urea and creatinine of the study participants were found to be in the normal range in our study. From this, we can assume that the negative association between serum UA and FBG is not due to the impairment in the kidney function but it may be a possible link with hyperglycemia.

Our study showed a significant difference in TG, HDL-c and LDL-c with in gender category. The dyslipidemia is more in male than female in our study which is in agreement with the previous hospital based study done in other metropolitan city of Nepal.[13] Several studies have concluded that diabetic dyslipidemia is more in female than male.[14,15] The difference may have resulted due to age distribution, treatment status for diabetes and dyslipidemia, glycemic status, and nature of study population.[13] Though mean value of serum UA was higher in male in comparison to female, more number of female had high UA in our study. A study done among Chinese men and women aged 30-89 years reported that UA level was associated with insulin resistance and plasma glucose levels more strongly in women than in men.[9]

In the present study, a significant positive correlation of FBG with TG and negative correlation with HDL-c were also found. However, correlation with other lipid parameters was not significant. The cause for increased TG level in hyperglycemia has been explained by the effect of insulin resistance. As insulin activate the LPL (Lipoprotein Lipase) activity in adipose tissue (decrease in muscle), insulin resistance causes decrease in LPL activity leading to hypertriglyceridemia.[16] Along with it, hyperglycemia also increases transfer of HDL ester to VLDL-c which decreases HDL1-c.[16] Insulin affects the liver apoprotein production and regulates the enzymatic activity of LPL and cholesterol ester transport protein, which causes dyslipidemia.[17] The activity of hepatic lipase, the enzyme controlling HDL-c catabolism, is enhanced in insulin resistant states, which seems to be responsible for the observed increase in HDL-c catabolism.[18] The TG rich HDL-c has short half-life as they are more prone to catabolism via different lipase primarily hepatic lipase. Hypertriglyceridemia is a major contributing factor to the accelerated HDL-c catabolism seen in T2DM. It has been recently observed that both raised VLDL1-c production and decreased VLDL1-c catabolism are independent factors associated with increased HDL-c catabolism in insulin-resistant states.[19]

In the present study, positive correlation was found between UA and lipid profile, significant for increased TG and decreased HDL-c. There is not specific reason explained behind it, some researchers suggested that due to over production of fatty acid from increased TG, there will be increased formation of adenosine triphosphate which is the precursor for UA synthesis.[20] A study done to see the effect of visceral fat accumulation on UA metabolism in male obese subjects suggested potential mechanism for the same. The study explained it on the basis that TG synthesis accelerates the de novo synthesis of ribose-5-phosphate to phosphoribosyl pyrophosphate through the common metabolic pathway nucleotinamide adenine dinucleotide phosphate and as a result, UA production increases.[21]

Lack of determination of Urinary UA level to see whether there is increase in UA excretion in urine or not can limit some of the finding of the study. Moreover, the sample size is relatively small, further studies with larger sample size and diverse participants are required to validate our findings, however the study still provides some glimpse of how biochemical parameters of diabetes correlated and give some guide to some possible associations and decision making.

CONCLUSIONS

In our study, serum UA level was found to be negatively associated with blood glucose. However, hyperuricemia was positively associated with hypertriglyceridemia in DM. Our study suggested that UA might be a possible indicator for dyslipidemia in the DM. UA is correlated with fasting blood glucose and lipid profile which can be early marker for T2DM. More multicentric studies done at different centers can give more robust information and guide to use of UA as a marker for T2DM.

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CONFLICT OF INTEREST

The authors declare no conflict of interest

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