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Serum Uric Acid as a Potential Concomitant with Carotid Atherosclerosis

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ABSTRACT

Background: Common carotid intima-media thickness (CC-IMT) measured by ultrasonography as a non-invasive method is nowadays known as a marker for early atherosclerosis.
Objectives: Survey the relationship between serum uric acid and carotid intima-media thickness considering hypertension.
Materials and Methods: This study was designed as a comparative cross-sectional study in northern Iran in 2013–2014. The samples for uric acid level were taken from 90 patients. Data were collected through questionnaires and a non-invasive ultrasound technique was used to measure IMT. The analysis of data was done by one-way ANOVA and Tukey post hoc tests and logistic regression model using SPSS software version 21. The significance level was set as 0.05.
Results: Patients in the 3 groups were the same age and gender. The measured carotid intima-media thickness was significantly different among the groups (p=0.004). Using multivariate logistic regression and entering all variables, The intima-media thickness of the carotid in the group with hypertensive and hyperuricemia was significantly higher than that of the other research groups (p<0.05).
Conclusion: An association was found between serum uric acid level and increased thickness of carotid intima-media and hyperuricemia can be considered as a risk factor for atherosclerosis.

Keywords: Uric Acid; Carotid Intima-Media Thickness; Hypertension

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Introduction

Common Carotid Intima-Media Thickness (CC-IMT), measured non-invasively by ultrasound, is today known as a marker for atherosclerosis (1) and its increment is generally known as a primary sign of initiation of atherosclerosis (2). Some studies have introduced serum uric acid level as an independent risk factor for cardiovascular diseases (3,4). Nietoa *et al*. investigated the association between serum

uric acid level and carotid atherosclerosis. Their result showed that future incidence of atherosclerosis is significantly associated with higher concentration of serum uric acid (5).

Normal blood level of uric acid is highly important for proper body functioning. Uric acid blood level is considered abnormal above 7mg/dl in men and 6mg/dl in women (ranges from 3-7 mg/dl) (6). Measurement of uric acid level is used as an important method in prevention of certain health problems (7).

Few studies have investigated the contemporaneous effect of blood pressure and uric acid level on CC-IMT. For instance, Tavil *et al.* investigated the association between serum uric acid level and CC-IMT in patients with hypertension and showed that irrespective of hypertension, serum uric acid level is associated with atherogenesis, and the patients with high serum uric acid levels are at greater risk of coronary heart and cerebrovascular diseases compared to people with normal levels of serum uric acid (8).

Although most studies acknowledge the association of serum uric acid level with coronary and cerebrovascular diseases (3,9,10), few have investigated the association of serum uric acid level with carotid atherosclerosis and cerebrovascular IMT (3,9). The present study was conducted in an Iranian population with the aim to investigate the association of serum uric acid level with CC-IMT considering hypertension.

Materials and Methods

The present comparative cross-sectional study was conducted in Poursina Hospital an academic hospital in the North of Iran in 2013-2014.The samples were selected from patients aged between 40 years and 70 years having data of blood pressure and serum level of uric acid.

The case group included the patients with hypertension and hyperuricemia (+HTN+HU) and two control groups included the patients with hypertension and no hyperuricemia (+HTN-HU), and with normal blood pressure and no hyperuricemia (-HTN-HU).

Measurement of IMT was performed by non-invasive ultrasound method using Madison-v10 device and 5-12 MHz linear transducer. The ultrasound device used in measurement had a sensitivity of 0.1mm. All measurements were performed by one radiologist. Patients were first place in a supine position and their heads were tilted by 45 degrees away from the side being examined. By moving the transducer, transverse and longitudinal planes were scanned in B-mode, so as to identify the areas of greatest thickness in both carotids. Attempt was made to obtain a high quality still image of the longitudinal section. Zoom was used for greater accuracy in all patients, and measurement was performed electronically by the same device. IMT was measured at three points and the highest thickness was recorded for each.

Blood pressure was measured using mercury sphygmomanometer of 5mmHg precision attached to the right arm of the person after a 5-minute rest in sitting position. Systolic and diastolic blood pressures were measured according to Korotkoff phases 1-5. Increases in blood pressure were determined according to the Joint National Committee jnc8 criterion, which defines hypertension in 60-year-old or older people as diastolic pressure above 90mmHg and systolic pressure above 150mmHg, and in people younger than 60 years, as systolic pressure

above 140mmHg and/or diastolic pressure above 90mmHg on three occasions with a one-week interval, or receiving antihypertensive medication. Patients with secondary hypertension were excluded.

Other factors such as fasting blood sugar, total cholesterol, HDL, LDL, and triglyceride were also measured. Venous blood samples were also taken for routine biochemical tests. Uric acid level was measured by Coulometric method. Serum uric acid level in excess of 6mg/dl in women and 7mg/dl in men was identified as hyperuricemia.

Mean±standard deviation (CI 95%) was used to describe data. Qualitative data and the ratio differences between the groups were assessed using Chi-square test. The normal distribution of quantitative data was examined using Kolmogorov-Smirnov test, and the means of normally distributed data were compared with one-way ANOVA test in the three groups. Tukey post hoc test was used to determine the exact significance between the groups. Significance level was set as 0.05.

Logistic regression analysis by was used to determine the association of serum uric acid level with CC-IMT by controlling the effect of other variables. Considering cut-off point of 1 mmfor IMT the subjects were divided into two groups with IMT≥1 mm and <1 mm.

Results

The present study recruited 90 subjects in three groups of 30. Demographic details of three groups are shown in Table 1.

Table 1. Demographic details of three groups of study

Variable	Normal blood pressure and no hyperuricemia Frequency	Hypertension and no hyperuricemia Frequency	Hypertension plus hyperuricemia Frequency	*p-value*
	N (%)	N (%)	N (%)	
Gender				
Male	15 (50)	18 (60)	18 (60)	**0.621**
female	15 (50)	12 (40)	12 (40)	
Age				
40-50	10 (33.3)	6 (20)	7 (23.3)	
51-60	12 (40)	12 (40)	12 (40)	**0.710**
61-70	8 (26.7)	12 (40)	11 (36.7)	

Mean age of patients was 53.12±10.13 years in -HTN-HU group, 56.11±11.9 years in +HTN-HU, and 55.9±11.7 years in +HTN+HU group. As shown in table 1 three groups were the same in terms of age and gender. However, significant differences were found among the three groups in mean of fasting blood sugar and cholesterol values, but no significant difference was observed in terms of mean LDL and HDL (Table 2). The results obtained showed significant differences among the three groups in CC-IMT and serum uric acid level (Table 2).

Table 2. Mean values of study variables in three groups of study

Variable	Normal blood pressure and no hyperuricemia	Hypertension and no hyperuricemia	Hypertension plus hyperuricemia	*p-value*
	Mean (SD)	Mean (SD)	Mean (SD)	
CC-IMT	0.73 (0.07)	0.83 (0.15)	0.91 (0.32)	0.004
Serum uric acid level	5.36 (0.28)	5.32 (0.28)	11.17 (1.1)	0.001
Fasting blood sugar	92.93 (6.73)	97.5 (10.18)	100.23 (9.5)	0.008
Cholesterol	166.6 (9.2)	184.16 (11.05)	187.63 (20.9)	0.001
LDL	178.2 (12.3)	181.6 (13.3)	183.9 (7.06)	0.1
HDL	42.3 (2.38)	42.93 (3.62)	42.6 (2.23)	0.672

Tukey post hoc test showed a significant difference in means of CC-IMT between -HTN-HU and +HTN+HU groups (p=0.003), but no such a difference was observed between -HTN-HU and +HTN-HU groups (p=0.146), or between +HTN+HU and +HTN-HU groups (p=0.282). Tukey post hoc test results showed a significant difference in mean fasting blood sugar between +HTN+HU and the other two groups (p<0.0001), but no such a difference was observed between -HTN-HU and +HTN-HU groups (p=0.123).

Tukey post hoc test also showed a significant difference in mean values of blood cholesterol between -HTN-HU and the other two groups (p<0.0001), but no such difference was observed between +HTN-HU and +HTN+HU groups (p=0.631).

The results of CC-IMT based on cut-off point=1mm for three groups are presented in table 3, showing a significant difference in the frequency of patients with IMT≥1mm and IMT<1mm among the three groups (p=0.004).

Table 3. Comparison of the frequency of subjects with IMT ≥1mm and IMT <1mm among the three groups of study

Group/CC-IMT	Normal blood pressure and no hyperuricemia	Hypertension and no hyperuricemia	Hypertension plus hyperuricemia	*p-value*
	N (%)	N (%)	N (%)	
≥1mm	0 (0)	3 (10)	9 (30)	p=0.002
<1mm	30 (100)	27 (90)	21 (70)	

The results of multivariate logistic regression analysis showed an association between serum uric acid level and increased thickness of carotid intima-media (Table 4).

Table 4. The final logistic regressionmodel of the association between serum uric acid level and CC-IMT* by controlling the confounding factors

Variable	B	S.E	Wald	Sig	Exp (B)
Age	-0.99	1.43	0.474	0.4	0.37
Gender	-0.771	2.92	0.07	0.79	0.46
Hypertension	7.04	3.57	0.000	0.99	1.91
Uric acid level	12.69	5.71	4.92	0.026	3.26
Fasting blood sugar	1.037	0.487	4.528	0.050	2.821
Cholesterol	1.292	0.598	4.67	0.06	0.27
Triglyceride	-0.879	0.447	3.874	0.059	0.415
HDL	-2.751	1.346	4.175	0.061	0.064
LDL	-4.87	0.253	3.693	0.055	1.627
Constant	335.394	3.57	0.009	0.9	4.5
* Common Carotid Intima- Media Thickness					

It was found that by controlling gender, blood pressure, serum sugar level, serum cholesterol, HDL, LDL and triglyceride, abnormal uric acid level exacerbated the odds of IMT>1mm by 3.2 times.

Discussion

Normal uric acid level is essential for optimal functioning of the body (8). High level of serum uric acid in some people leads to diseases such as hypertension, heart and chronic renal disease (11).

In the present study, serum uric acid level was independently associated with increased CC-IMT. The present study results agree with those of other studies. Previous studies have shown that patients with high serum uric acid levels are more exposed to the risk of

cardiovascular diseases than patients with normal levels of uric acid (8). On the other hand, several studies have presented evidence showing association of high serum uric acid levels (as a risk factor) with mortality due to cardiovascular diseases (12-14). Tavila *et al.* studied the association of uric acid with CC-IMT in patients with hypertension in 2007. Their results suggested that hypertension and hyperuricemia were significantly associated with CC-IMT, and their linear regression analysis showed that high serum uric acid level was independent from IMT, but associated with it (8).

In the present study, no significant difference was found in terms of gender among the three groups of patients, and thus the role of gender as a confounding factor was eliminated from statistical analysis. In agreement with the present study results, Nietoa *et al.* study showed that carotid atherosclerosis was not associated with gender or serum uric acid level (5). This was also confirmed in Tavila *et al.* study (2007) (8).

No statistically significant difference was found in values of LDL, HDL, and triglyceride among the three groups of patients (15,16).

However, a significant difference was observed in fasting blood sugar among the three groups, whose effect as a confounding factor was eliminated from logistic regression analysis. Considering the significant association found in the present study between serum uric acid level and increased CC-IMT; measuring uric acid levels in patients with one of the components of metabolic syndrome is recommended as a measure for preventing the synergistic effect of this risk factor and reducing the prevalence of atherosclerosis.

Conclusion

The present concluded that hyperuricemia can be considered as risk factors for atherosclerosis.

Conflict of Interest

Authors have no conflict of interest.

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