Original Research Article

Interrelationship of serum uric acid levels and cardiovascular disease risk factors in Bangladeshi patients treated with antihypertensive drugs

Abstract

Background. To explore the association between serum uric acid levels and cardiovascular disease (CVD) risk factors in subjects treated with (WD) or without antihypertensive drugs (WOD). ***Methods*.** A total number of 200 subjects were included in his study. Of the total, 40 subjects were healthy control, 59 were hypertensive subjects (taking blood pressure-, and lipid-lowering drugs), and 98 were cardiovascular subjects (without taking blood pressure-, lipid-lowering drugs). Control subjects were with no serious disease. Age ranged from 50 to 70 years. ***Results*.** The hypertensive subjects had higher levels of CVD risk factors, including blood pressure, lipid profile, hypokalemia and elevated serum uric acid levels. Antihypertensive drugs significantly ameliorated the blood pressure, HDL-C levels, LDL-C/HDL-C and TG/HDL-C ratios. Elevated serum uric acid levels were independently correlated with LDL-C. ***Conclusion*.** Elevated serum uric acid and LDL-C levels were positively correlated independently of other measured confounders such as body mass index, high blood pressure, atherogeneic lipids, electrolytes and zinc to hypertension. Finally, our results suggest that corrective measures to control hyperuricemia might be one of the approaches to manage damaging effects of uric acid on cardiovascular diseases during hypertension.

Keywords: Uric acid, LDL-C, Zn, K, Cardiovascular disease, Epidemiology

1. Introduction

The excessive accumulation of uric acid, the metabolic end product of purine, leads to various diseases [1], including gout, in humans. However, hyperuricemia is a risk factor not only for gout, but also for cardiovascular diseases [2, 3]. Hyperuricemia is closely related to obesity, hypertension [4] and dyslipidaemia [5]. Previous studies have demonstrated a strong relationship between serum uric acid levels and coronary heart disease (CHD), with some studies suggesting that uric acid may be an independent risk factor for cardiovascular diseases [4,6-8]. Moreover, a recent meta-analysis showed that hyperuricemia may increase the risk of CHD events, independently of traditional CHD risk factors [9]. However, the nature of the relationship between uric acid and cardiovascular disease remains a subject of debate [10-12]. Recently, a series of controversial and conflicting findings from epidemiological studies have been reported [4-12]. Bangladesh is one of the developing countries, where both the incidence and prevalence of cardiovascular diseases are increasing in an alarming rate [13-15]. Because of an impressive track record for growth and development during the past decades, Bangladesh has been experiencing an increased prevalence of the CVDs. Despite recent advances in treatment for hyperlipidemia and diabetes as well as availability of sophisticated clinical methods, there is an increase in mortality rates for cardiovascular diseases (CVD) every year, demonstrating that cardiovascular risk factors are very high. Therefore, both diagnostic and additional therapeutic

strategies are highly needed to evaluate CVDs, while, on the other hand, prompt and continuous efforts should also be exerted to develop new biomarkers for achieving high diagnostic accuracy in the prediction of risks and treatment of CVDs. In the present investigation on the Bangladeshi population, we have examined whether the serum uric acid could act as an independent risk factor for CVDs. In addition, patients with diabetes have lower serum levels of zinc [16]. There are studies on non-diabetic subjects, which suggest that low serum level of zinc is associated with increased incidence of cardiovascular diseases [17-19]. In this study with CVD patients, we mainly examined the association between serum uric acid level and cardiovascular disease risk factors.

2. Research design and Methods

A total number of 200 subjects were included in his study irrespectively of race, religion and socioeconomic status. Of the total, 40 subjects were healthy control, 59 were cardiovascular subjects (taking blood pressure-, and lipid-lowering drugs), 98 were cardiovascular subjects (without taking blood pressure-, and lipid-lowering drugs). Healthy control subjects were with no serious disease.

Table 1. Demographic characteristics and blood pressures of all the subjects

Variables	Control Subjects (CON)			Patients without drugs (WOD)			Patients with drugs (WD)		
Sex	Male (n=23)	Female (n=17)	All (n=40)	Male (n=29)	Female (n=30)	All (n=59)	Male (n=50)	Female (n=48)	All (n=98)
Age (y)	52.5^{a} ± 0.70	52.1^{a} ±0.90	52.3^{a} ±0.50	57.6^{b} ±1.3	66.9^{c} ±1.3	62.3^{d} ± 1.1	67.8^{c} ± 0.93	62.4^{d} ± 1.10	$65.1^{c,d}$ ± 0.80
BW (Kg)	66.0^{a} ± 1.3	61.4^{a} ±1.8	64.1^{a} ±1.10	64.0^{a} ±1.4	63.0^{a} ±1.1	63.5^{a} ±0.74	64.1^{a} ±1.12	63.1^{a} ±.95	63.6^{a} ±0.74
BMI (kg/m^2)	21.0^{a} ±.14	20.8^{a} ±0.23	20.9^{a} ±.13	27.2^{b} ±0.10	27.5^{b} ±0.18	27.4^{b} ±.10	28.1^{c} ±.25	28.1^{c} ±.14	28.1^{c} ±.12
SBP (mmHg)	122^{a} ±1.97	128^{a} ± 6.5	125^{a} ± 2.75	169^{b} ±2.03	169^{b} ±1.70	169^{b} ±1.30	164^{c} ±1.05	164^{c} ±2.3	164^{c} ± 1.30
DBP (mmHg)	78.5^{a} ±1.5	80.0^{a} ±4.30	79.1^{a} ±1.80	97.3^{b} ±2.5	$92.3^{c,d}$ ±1.50	$94.7^{b,c}$ ±1.50	90.8^{d} ±0.98	88.97^{d} ±1.25	89.8^{d} ±.80

Results are mean ± SEM. Data were analyzed by one-way ANOVA, followed by Fisher's PLSD for post hoc comparison. Values in the same row those share the common superscript are not significantly different at $P<0.05$.

The inclusion criteria for the control and CVD subjects was that the adult subjects must be aged ranging from 50 to 70 years. Subjects with diseases (infection, major surgery, renal failure, liver malfunction, and diabetes), history of using specific steroidal drugs and renal disease and other pre-existing medical conditions or history of illegal drug use and crossing the age limit (40 to 70) were excluded from the study. Blood samples were allowed to clot for thirty minutes and then centrifuged for 10 mins at 3000 rpm and serum samples were collected for the estimation of fasting glucose, serum lipid profile (total cholesterol, HDL-C, LDL-C, TG), serum micronutrients (Na^+, Cl^-, K^+, Zn^{2+}) and uric acid. Uric acid and electrolytes were measured by enzymatic colorimetric methods. Zinc was measured by atomic absorption spectrophotometry.

BMI was calculated as the weight in kilograms per the square of height in meters, and blood pressure was measured while the person was in the sitting position after a 5-min rest. A patient was defined as having hypertension if systolic blood pressure was ≥160 mmHg, if diastolic pressure was ≥95 mmHg, or if the patient was receiving drug for treatment of hypertension.

2.1 Statistical analyses

To investigate the relationship between different parameters, we calculated Pearson correlation coefficients; it is shown as correlation matrix diagonal table. To find out independent (from other confounding factors) correlation, data were subjected to multiple regression analysis. To analyze the differences in the parameters among different subject groups, we performed one-way ANOVA test. We then used Fisher's PLSD test for multiple comparisons. Statistical software used was GraphPad prism 4 and StatView v.4.

3. Results

The clinical characteristics of the subjects are summarized in Table 1 and Table 2. Participants were relatively older in the cardiovascular disease (CVD) group with (WD) or without drugs (WOD) than those of the control subjects. The age of the female patients were higher in WOD group, while the age of the female subjects were lower in the WD group. The body weight of the subjects was not significantly different among different groups. The body mass indices (BMI) were statistically higher in the CVD patient groups (WOD/WD), the highest values being in the patients with drug (WD) group. The highest systolic blood pressure (SBP) was in the WOD, as compared to that of the WD or control subjects. SBP decreased in the WD group. The highest

Table 2. Parameters of the human subjects

Variables	Control Subjects (Con)			Patients without drugs (WOD)			Patients with drugs (WD)		
Sex	Male (n=23)	Female (n=17)	All (n=40)	Male (n=29)	Female (n=30)	All (n=59)	Male (n=50)	Female (n=48)	All (n=98)
TC	178^{a} ±4.50	173^{a} ±4.50	176^{a} ±3.2	377^{b} ±14.0	378^{b} ±13.4	378^{b} ±9.60	256^{c} ±3.0	251^{c} ±2.90	253^{c} ±2.10
TG	207^{a} ± 3.70	192^{a} ±8.70	200^{a} ±4.40	339^{b} ±23.3	379^{b} ±22.6	359^{b} ±16.3	258^{c} ±14.4	262^{c} ±15.6	260^{c} ±10.5
LDL-C	133^{a} ±3.6	133^{a} ±2.70	133^{a} ±2.30	169^{b} ±1.80	167^{b} ±1.90	168^{b} ±1.30	171^{b} ±1.40	169^{b} ±1.40	170^{b} ±1.0
HDL-C	23.2^{a} ±.80	22.1^{a} ±0.90	22.7^{a} ±0.60	22.1^{a} ±1.10	21.2^{a} ±1.30	21.7^{a} ±0.80	32.0^{b} ±1.10	35.0^{b} ±1.50	33.2^{b} ±1.0
TG/HDLC	9.15^{a} ±0.51	8.88^{a} ±0.34	9.04^{a} ±0.23	16.18^{b} ±1.18	20.21^{c} ±1.88	18.23^{b,c} ±0.80	8.78^{a} ±0.63	8.82^{a} ±0.86	8.80^{a} ±0.50
LDL/HDL	5.96^{a} ±0.26	6.17^{a} ±0.26	6.05^{a} ±0.20	8.28^{b} ±0.48	8.80^{b} ±0.48	8.54^{b} ±0.37	5.65^{a} ±0.19	5.33^{a} ±0.24	5.50^{a} ±0.15
Na	137^{a} ±.20	136^{a} ±0.40	137^{a} ±0.20	138^{a} ±0.80	137^{a} ±0.60	138^{a} ±.40	138^{a} ±0.40	137^{a} ±0.40	138^{a} ±0.40
K	5.56^{a} ±0.14	5.76^{a} ±0.20	5.65^{a} ±0.13	4.32 ±0.14	4.24^{b} ±0.18	4.30^{b} ±0.10	4.49^{b} ±0.14	4.37^{b} ±0.15	4.40^{b} ± 0.10
Cl	104^{a} ±0.40	103^{a} ±0.40	104^{a} ±0.30	103^{a} ±0.4	103^{a} ±0.40	103^{a} ±0.30	103^{a} ±0.30	103 ±0.30	103^{a} ±0.20
Zn	51.0^{a} ±2.1	55.2^{a} ±2.8	52.4^{a} ±1.70	11.8^{b} ±0.20	11.7^{b} ±0.20	11.8^{b} ±.10	10.0^{b} ±0.2	10.4^{b} ±0.30	10.2^{b} ± 0.17
Uric acid	4.40^{a} ±0.30	3.70^{a} ±0.40	4.10^{a} ±0.20	11.7^{b} ±0.14	12.0^{b} ±0.14	12.0^{b} ±0.10	11.4^{b} ±0.08	11.3^{b} ±0.08	11.4^{b} ±0.60

Results are mean ± SEM. Data were analyzed by one-way ANOVA, followed by Fisher's PLSD for post hoc comparison. Values in the same row those share the common superscript are not significantly different at $P<0.05$.

diastolic blood pressure (DBP) was also in the WOD subjects, while it reduced significantly in the WD group.

Serum total cholesterol (TC) and triacylglycerol (TG) levels were significantly higher in the patients without drugs (WOD), as compared to those of the control subjects. However, the subjects (WD) who took drugs had significantly lower levels of TC or TG, when compared to those of the WOD subjects. The levels of HDL-C levels increased in the subjects who took drugs (WD). The levels of LDL-C were not reduced significantly; the TG/HDL-C and LDLC/HDL-C ratios were, however, significantly reduced in the subjects with drugs (WD) (Table 1, 2). When compared to those of the control subjects, the levels of Na or Cl were not altered either in the subjects with drugs (WD) or without (WOD) drugs. The levels of K were significantly decreased in the patients of both the WOD and drug-taking (WD) groups. The levels of Zn were declined in both of the WD and WOD subjects. Finally, the levels of serum uric acid were higher both in the subjects of WD and WOD groups (193% in the patients of WOD group and 178% in the patients of WD group). The (small) differences in age, body weight and/or blood pressure between male vs. female were not reflected in the biochemical parameters.

Correlation is a technique for investigating the relationship between two quantitative, continuous variables, for example, age and blood pressure. Pearson's correlation coefficient (r) is a measure of the strength of the association between the two variables. We had 14 interval-level variables (including TG/HDL-C and LDL-C/HDL-C ratios 16 variables) and we analyzed the relationships among all of them (i.e., between all possible pairs of variables). The results are shown in Table 3 as a *correlation matrix*. It listed the variable names down the first column and across the first row. To locate the correlation for any pair of variables, one needs to find the value in the table for the row and column intersection for those two variables. For instance, to find the correlation (r) between variables serum total cholesterol (TC) and systolic blood pressure (SBP), one needs to look for where row TC and column SBP meet (in this case, its r = 0.494). Serum uric acid levels were positively associated with age, BW, BMI, SBP, DBP,TC, TG, LDL-C, HDL-C and negatively associated with K and Zn. Subjects with the highest uric acid levels exhibited a higher prevalence of hypertension (as indicated by the increased SBP/DBP), central obesity (as indicated by the increased BMI, TC,TG and LDL-C).

As expected, other cardiovascular risk factors including age, BW, SBD, DBP, TC,TG, LDL-C, HDL-C, K or Zn were also correlated at different extents (see the correlation matrix Table 3). The Pearson's correlation, which is performed by bivariate regression analysis, does not assure about the two-variables whether they are actually dependent on each other and/or independent from each other. In multiple regression analysis, we thus included all the independent variables into the model and analyzed which ones are statistically significant. It is possible for several independent variables to be individually correlated with a dependent variable, but not all of them will be statistically significant in the same multiple linear regression model. In Person's correlation analysis, almost all parameters were correlated (Table 3); however, in multiple correlation analysis (Table 4), the serum uric acid was correlated with LDL-C significantly. In other words, all 14 parameters (except Na and Cl) were correlated with serum uric acid (Table 3), but not all 14 parameters add on collectively to predict better the dependent variable i.e. serum uric acid. On the statistical model, serum LDL-C only had "add independent information" about serum uric acid. In other ways, "the relationship between serum uric acid and LDL-C" was

independent from the 'confounding effects' of other cardiovascular risk factors (age to Zn) (Table 4).

Table 3. Correlation coefficient matrix analysis among different variables measured.

	Age	BW	BMI	SBP	DBP	TC	TG	LDLC	HDLC	TG/HDL	LDL/HDL	Na	K	Cl	Zn	UA
Age	1.000															
BW	0.124	1.000														
BMI	0.560	-0.074	1.000													
SBP	0.422	-0.036	0.854	1.000												
DBP	0.191	-0.020	0.517	0.534	1.000											
TC	0.216	0.034	0.571	0.494	0.425	1.000										
TG	0.148	0.114	0.386	0.235	0.215	0.418	1.000									
LDLC	0.454	0.010	0.761	0.573	0.413	0.465	0.195	1.000								
HDLC	0.325	0.027	0.300	0.231	-0.043	-0.177	-0.273	0.234	1.000							
TG/HDL	0.003	0.039	0.218	0.128	0.174	0.428	0.797	0.073	-0.644	1.000						
LDL/HDL	-0.092	-0.038	0.116	0.035	0.200	0.390	0.313	0.160	-0.818	0.760	1.000					
Na	0.106	0.093	0.110	0.073	0.056	0.074	0.066	0.132	0.123	-0.043	-0.105	1.000				
K	-0.256	0.018	-0.482	-0.562	-0.226	-0.393	-0.120	-0.334	-0.203	-0.026	-0.004	-0.017	1.000			
Cl	-0.025	-0.054	-0.067	-0.089	-0.192	-0.129	0.020	0.019	0.110	-0.022	-0.076	-0.002	0.022	1.000		
Zn	-0.520	0.061	-0.943	-0.938	-0.513	-0.593	-0.377	-0.768	-0.195	-0.251	-0.181	-0.136	0.542	0.098	1.000	
UA	0.541	0.006	0.928	0.835	0.516	0.586	0.315	0.793	0.231	0.182	0.132	0.137	-0.511	-0.057	-0.943	1.000

Results were obtained from bivariate analyses. No correlation, r = 0 to ± 0.25; Poor correlation, r = ± 0.25 to ± 0.50; Moderate/good correlation, r = ±0.50 to ±0.75; Very good to excellent correlation r = ± 0.75 to ± 1.0 . *Ref: Dawson B, Trapp RG. Basic and Clinical Biostatistics. 4th Ed. New York: Lange Medical Books/McGraw-Hill; 2004.*

4. Discussion

The results of the present investigation on Bangladeshi population clearly point to the following facts: (i.) the subjects with or without drugs were hypertensive; (ii.) the hypertensive subjects had higher body mass index (BMI), when compared to those of the control subjects; (iii.) the cardiovascular disease risk factors, including higher serum total cholesterol, LDL-C, TG, higher LDL-C/HD-LC or TG/HDL-C ratio, lower-serum HDL-C were accompanied with increased systolic and diastolic blood pressure *i.e*. hypertension. Most importantly, the CVD-risk factors were accompanied with the increases in the serum uric acid levels; (iv.) correlation coefficient matrix, as carried out by bivariate regression analyses, revealed significant positive relationships between uric acid versus age, BMI, SBP, DBP and dyslipidemia-related risk factors, namely, TC, TG, LDL-C, HDL-C, TG/HDL-C and LDL-C/HDL-C ratios, and significant negative relationship with K and Zn; (v.) the anti-lipidemic/hypertensive drugs ameliorated TC, TG, HDL-C, TG/HDL-C and LDLC/HDLA ratios, blood pressures of the hypertensive subjects; however, they did not have effects on the levels of electrolytes (Na, K, Cl), trace element Zn and serum uric acid. These results might suggest a critical role of uric acid in the regulation of dyslipidemia, in other words, hyperuricemia and dyslipidemia may share a common pathophysiology of cardiovascular diseases in hypertension. Our study corroborated well with the reports of Peng et al., (2015) [20], where they also noted the positive relation between dyslipidemia and serum uric acid. Nakagawa et al (2006) [21], Moriarity et al., (2000), [12] also reported that the relation between serum uric acid and TG is linear. Our results are also consistent with increased uric acid level and hypertriglyceridemia [22]. There is a debate on

whether uric acid may exert an atherogenic effect independently of other known cardiovascular risk factors. It is possible for several independent variables to be individually correlated with a dependent variable (as seen after bivariate regression analyses), but all of them might not be statistically significant in the same multiple linear regression model. This led us to analyze the correlation of serum uric acid with all other measured parameters by multiple regression analysis, which can statistically infer about whether a given relationship is independent from the confounding effects of other cardiovascular risk factors. Interestingly, among all parameters, serum uric acid was found to significantly correlate independently from other confounding CVD risk factors (age, BW, BMI, SBP and DBP,TC, TG, HDL, Na/Cl/K/Zn) with serum LDL-C levels and the correlation was positive (Table 4). With our experimental data limit, we are not sure as why serum uric acid was independently correlated with LDL-C only. Correlation provides information on association rather than a cause- and-effect relationship between variables. Thus there is a possibility of a considerable effect of other uninvestigated confounding factors on the correlation between serum uric acid and LDL-C. Although it is very difficult to assume about these unknown factors, however, blood levels of antioxidants, oxidized LDL-C, kidney filtration rate and action of other pharmacologically active substances are believed to contribute to the independent relationship between uric acid versus LDL-C. LDL-C may modify the endothelial functions of the blood vessels of the cardiovascular systems [23].

In ischemia and/or hypoxia-reperfusion condition, which is typically seen during atherosclerosis, the production of uric acid is accelerated. Xanthine oxidase (XO) is actively present in the vascular endothelial cells. Production of uric acid by the xanthine oxidase may harvest free radicals. Moreover, the uric acid and xanthine oxidase have been found in greater concentration in atherosclerotic vessels than in healthy vascular tissues. This might be one of the underlying

Table 4. Multiple correlation between uric acid (dependent variable) and 13 independent variables (X)

(X)	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	6.441	25.887	6.441	0.249	0.810
Age	0.027	0.034	0.066	0.776	0.460
Body	-0.036	0.035	-0.064	-1.028	0.334
BMI	0.358	0.254	0.321	1.411	0.196
Systolic	-0.010	0.036	-0.059	-0.291	0.778
Diastolic	0.000	0.049	0.001	0.007	0.994
TC	0.001	0.003	0.044	0.517	0.619
TG	-0.008	0.005	-0.335	-1.549	0.160
LDLC	0.044	0.014	0.334	3.128	0.014
HDLC	-0.004	0.086	-0.009	-0.044	0.966
TG/HDLC	0.218	0.111	0.481	1.960	0.086
LDL/HDLC	-0.297	0.323	-0.256	-0.917	0.386
Na	0.005	0.102	0.005	0.049	0.962
K	-0.353	0.285	-0.098	-1.241	0.250
Cl	-0.067	0.092	-0.048	-0.727	0.488
Zinc	-0.077	0.054	-0.390	-1.424	0.192

Data were subjected to multiple coreltion analysis.

mechanisms for which LDL-C was positively (independent from other confounding factors) correlated with the uric acid levels in the present investigation. Ruggiero et al. (2007) reported that levels of serum uric acid are low in the presence of carotenoid antioxidants in the serum [24]. Holvoet et al., (2001, 2004) reported that oxidized LDL-C is associated with coronary heart disease and it (oxidized LDL-C) can act as a useful diagnostic marker for identifying patients with coronary artery disease [25, 26] and is highly linked with the pathophysiology of the cardiovascular diseases [27]. Endothelial dysfunction also impairs endothelial-dependent vascular relaxation, which is produced by nitric oxide (NO). The free radicals generated during uric acid production also stimulate the production of reactive nitrogen species (RNS), such as peroxynitrite ($ONOO^{\bullet}$), which in turn can mediate further vascular endothelial cell dysfunction in the setting of atherogenesis [28]. The net consequence is that high serum uric acid confers damage to endothelial integrity by over-production of reactive free radical species, which, in turn, are important contributors to vascular disease.

Multiple CVD risk factors increase with a decline in glomerular filtration rate and one of such factors is serum uric acid. When uric acid level becomes high, it decreases the glomerular filtration rate. Furthermore, older age, hypertension, diabetes and elevated TG are independently associated with chronic kidney diseases [29]. The prevalence of reduced glomerular filtration rate is high in hypertensive patients [30]. Moreover, high levels of uric acid correlate with decline of glomerular filtration rate [31], and this is why the serum uric acid can act as a marker of kidney disease [32]. Ryu et al. (2013) [33] found that uric acid may cause loss of cell-to-cell contact in the renal tubular cells of rats. Therefore, the increase in serum uric acid might suggest either increased production and/or decreased excretion of uric acid through tubular systems of the kidneys. Besides anti-lipiemic drugs, diuretics and angiotensin II blockers were most prevalent drugs as medication for the drug taking cardiovascular patients in our investigation. Patients taking angiotensin receptor bolckers/diuretics had lower levels (~ 6%) of uric acid when compared to those of the patients who did not start taking drugs, however, the difference did not rich significance (WOD: 11.3±0.06 vs WD: 12.0±0.10). Diuretics work with kidneys to excrete sodium from urinary system via urine. In turn, the sodium takes water from blood, and the water is also excreted. Diuretics are thus commonly used to treat hypertension because they lower blood pressure by helping our body eliminate sodium and water through our urine. However, some diuretics can also cause to eliminate more potassium in the urine. This can lead to low potassium levels in the blood (hypokalemia). Hypokalemia is present in patients with cardiovascular disease [34]. In our case, the levels of either Na or Cl were not altered significantly in the subjects of either the WD or WOD groups. Hypokalemia were not observed in the patients of WD group, as compared those of the WOD group. Still, the levels of K were, as compared to those of the controls, were higher in hypertensive patients. We speculate that it may relate to the impairments of kidney tubular functions in the hypertensive patients. Angiotensin II type 1 receptor blockers (ARB) are a frequently used class of antihypertensive drugs. Nishida et al. (2013)[35] reported that the ARB losartan decreases the serum uric acid level. But in this investigation the angiotensin II blockers did not significantly affect the serum uric acid level in the patients with drug group (WD). Serum uric acid was accompanied with CVD risk factors. No evidence exists that reducing hyperuricemia is harmful. So reducing the uric acid in the serum, as one of the independent markers of cardiovascular diseases, may help people to be free from cardiac problems as well as gout complications.

Other markers those were measured in this experiment was trace element zinc. The levels of zinc exhibited significantly negative correlation with age, BW, BMI, SBP/DBP, TC, TG, and LDL-C. Several studies indicate that zinc is vital to vascular endothelial cell integrity [36, 37]. Zinc is inversely correlated with the atherosclerotic lesion formation [38]. Therefore, zinc can slow down the progression of atherosclerosis [39, 40]. The hypertensive subjects had zinc value 10.2±0.17 µg/dL compared to 52.4±1.7 µg/dL in the control subjects. There was a big difference between the values of the control versus hypertensive subjects of WD and WOD groups. Subjects with serum zinc concentration greater than the baseline (>10.2±0.17µg/dL) of the controls had a higher risk for cardiovascular risk factors. In our study the deficiency of zinc levels caused uric acid to increase (Table 2 and 3). A relevant study was done in South Africa by a group of researchers. They stated that dietary zinc deficiency caused uric acid to increase by disturbing the glomerular filtration rate (Rasheed et al, 2012)[41]. Again, the serum zinc level exhibited negative correlation with the serum uric acid. The relationship of zinc and uric acid however was not independent from other confounding relationships (Table 4). The cause-effect relationship between serum uric acid and zinc is not clearly understood.

5. Conclusion

The debate is still ongoing on 'whether serum uric acid can act as an independent marker for cardiovascular disease or it simply results from the synergistic effects of other known cardiovascular risk factors'. The major finding of this study is that hypercholesterolemic subjects had increased prevalence rate of elevated serum uric acid levels and that increased LDL-C is the strongest predictor of hyperuricemia in our investigation. The results are consistent with numerous published reports. However, the underlying pathophysiological mechanisms linking elevated LDL-C and hyperuricemia are currently unknown. The control of dyslipidemia by the antihypertensive drugs did not correct or alter the uric acid levels in our investigation. Thus, it is urgent to develop appropriate treatment guidelines for hyperuricemia. Finally, understanding the mechanisms of the relevance of elevated serum uric acid levels in cardiovascular disease (CVD) and the biological basis of the link of LDL-C with elevated uric acid might help clinicians to identify and treat CVD patients, as well as help patients prevent these potentially devastating complications. Further research is essential to understand the relationship between serum uric acid and other cardiovascular risk factors.

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