Original Research Article

A study of higher circulatory levels of uric acid in cardio vascular disease (CVD) patients

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Abstract

Uric acid is an end product of purine catabolism. It is observed that increased uric acid formation is associated with various inflammatory conditions. Anthropometric parameters as well lipid profile did not show any correlation with CVD. While Blood glucose and related variables were significantly increased in CVD. Increased uric acid levels were observed in CVD group as compared to controls [6.88 (±2.17)/ 4.29 (±1.04)]. No difference in serum uric acid levels were observed in CVD patients according to gender. Post menopausal women showed high uric acid levels than premenopausal [4.89 (±1.10)/ 5.81 (±1.26]. The main enzyme associated with uric acid production is xanthine oxidase. Instead of just formation of uric acid, xanthine oxidase is also involved in various other mechanisms like oxidative stress, endothelial dysfunction etc, which are associated with development of CVD. **Conclusion:** Higher uric acid levels were observed in CVD patients compared to controls. Higher levels of uric acid were found in female CVD patients in post menopausal condition than premenopausal.

Key Words: cardio vascular disease.

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INTRODUCTION

Inflammation is the main key player in Coronary artery disease development and progression[1]. Inflammation is a very wide term and various mechanisms are linked with inflammation. Various inflammatory mediators have been reported to be elevated in Diabetes mellitus, obesity as well Cardio vascular Diseases (CVD)[2-5]. Uric acid is a bioactive molecule which is an end product of purine catabolism. It has a high reducing potential. But its association with CVD is still a question of debate. Uric acid is also believed to involve in oxidative stress, inflammation and ultimately endothelial damage and atherogenesis. Oxidative stress may have a role in atherosclerosis and pathogenesis of coronary artery disease and it has been shown by various studies[6]. Uric acid is a determinant of total antioxidant capacity of plasma (TAOC), and hence expected to protect against progression of atherosclerosis[6,7]. However according to some studies it is one of the factors of the metabolic syndrome and associates to CVD positively[8,9]. In CVD the inflammatory environment is high as inflammatory markers are mainly associated with endothelial dysfunction, atherogenesis which is the central cause for CVD[10,11]. Uric acid (UA) is a potent endogenous antioxidant plays various roles which are not truly identified thoroughly. However, high concentrations of this molecule have been associated with CVD as well kidney dysfunction. The following processes make uric acid a potent factor associated with CVD: oxidative stress, inflammatory processes, and endothelial

injury[12,13].Experimental results suggest that uric acid behaves like other antioxidants, which can shift from the physiological antioxidant action to a pro-oxidizing effect according to their level and to microenvironment conditions[14].

MATERIAL AND METHODS

In the present study included 109 CV D patients and 120 controls. This study was carried out at Dr. D.Y. Patil Medical College, Nerul, Navi Mumbai. Patients presented to outpatient department (OPD) and Indoor patient department (IPD) were recruited in this study. Proper written informed consent was obtained from all the study subjects. The study has been approved by the Institutional Ethics Committee.

Inclusion Criteria: Coronary Artery disease proved by history, clinical examination, blood investigations, Electrocardiogram, Echocardiography and Coronary Angiography. Healthy Controls > 20 yrs of age are included. Age and sex matched healthy individuals without clinical evidence of coronary artery disease and with normal ECG constituted the control group.

Exclusion Criteria: Pregnant women, patients < 20 years of age, with Congenital Heart disease, acute or chronic infection, chronic liver and kidney disease. Fasting venous blood samples were collected from CVD patients and controls. Biochemical tests were performed on autoanalyser using commercially available kits.

Blood Sampling and Methodology: Fasting venous blood samples were collected for biochemical investigations. Routine biochemical parameters like fasting blood sugar, lipid profile etc. were evaluated in clinical laboratory of D.Y Patil hospital and research center, Nerul, Navi Mumbai. Cardiac profile is also evaluated by ECG, ECHO findings as well angiographic results. SPSS software (version 16) was used for Statistical analysis of the data. Demographic and biochemical data were expressed as mean ± S.D. Student 't' test used to test the significance between cases and controls. The '*P*' value < 0.05 considered to be significant while < 0.01 is highly significant.

RESULTS

The following table shows the Demographical Characteristics of study subjects. The present study results showed a male dominance pattern of the disease. Family history has been again showed its involvement in the prevalence of CVD.

Table 1: Demographical Characteristics of study subjects

Variables	Controls (n=120)	CVD (n=109)	*P* value
Age	53.30(± 12.45)	52.47(± 11.23)	NS
BMI	24.50 (±4.08)	24.80 (±3.62)	NS
WC	95.8 (±11.2)	96.88 (± 10.6)	NS
WHR	0.96 (±0.68)	0.99 (±0.56)	NS

[BMI = Body mass index, Wc - Waist Circumference, WHR- Waist Hip Ratio]

Anthropometric parameters did not show any significant difference between CVD patients and normal controls

Table 2: Biochemical Characteristics of study subjects

Variables	Controls (n=120)	CVD (n=109)	*P* value
FBS (mg%)	98.32 (±19.18)	138.22 (±46.27)	0.001
HbA1c (mg%)	5.68 (±1.29)	7.40 (±1.90)	0.001
Insulin (µu/L)	9.89 (±6.34)	11.99 (±9.0)	0.005
TG (mg%)	121.34 (±46.7)	140.23 (±70.38)	NS
TC (mg%)	178.45 (±38.05)	182..28 (±52.56)	NS
LDL (mg%)	107.19 (±34.92)	111.94 (±43.05)	NS
HDL (mg%)	44.694 (±12.44)	39.56 (±14.44)	0.001
Sr. Uric Acid	4.29 (±1.04)	6.88 (±1.17)	0.001

[TG = Triglycerides, TC = Total Cholesterol, LDL = Low density Lipoprotein, HDL = High density Lipoprotein, Sr. UA= Serum Uric Acid]

The present study observed a significant increase in blood sugar and related variables like serum insulin and Glycosylated hemoglobin fractions in CVD patients than control group. While from lipid parameters only HDL levels shown to be lower in CVD than controls. But other lipid variables did not show any significant increase in CVD group than control.

Table 3: Serum Uric acid in Men and women with CVD

Variables	CVD (109)		*P* value
	Male (67)	Female (42)	
Sr. Uric Acid	5.74(±1.90)	5.60 (±1.84)	NS

As per the results there is no much difference in male and female subjects in CVD group. Various studies showed a gender difference in serum uric acid levels but the present study could not find any difference between male and female.

Table 4: Serum Uric acid Women with CVD: Pre and Post Menopausal period

Variables	Female with CVD (42)		*P* value
	Pre menopuasal CAD (18)	Post menopausal CAD (24)	
Sr. Uric Acid	4.89(±1.10)	5.81 (±1.26)	0.005

The above table indicates that in post menopausal women concentration of uric acid is high. The hormonal status in women is not evaluated in this study.

DISCUSSION

The present study found higher levels of uric acid in CVD patients compared to controls. From a longer time a debate is going on about the role of uric acid in CVD. According various studies uric acid levels are increased in CVD patients[11,12]. Further it has also been observed that in atherosclerotic plaques, uric acid levels are found to be elevated six-fold, reflecting accelerated purine oxidation within these plaques[13]. Actually oxidative stress is one of the major factors for atherogenesis as well endothelial dysfunction[8]. The effects associated with atherogenesis, endothelial dysfunction and oxidative stress are not only mediated by uric acid, but xanthine oxidase might have been involved in it. Uric acid is an end product formed by the action of an overactive enzyme known as xanthine oxidase. High Uric acid production indicates the hyper activity of xanthine oxidase. The basal expression of xanthine oxidase is low in humans but it increases in the conditions like hypoxia, elevated levels of inflammatory markers as well as steroid treatment have been shown to unregulated transcription[14]. Xanthine oxidase is one of the important players in generation of reactive oxygen species which ultimately leads to endothelial damage[15]. Uric acid is considered as a marker of inflammation and also involved in detrimental effects caused on endothelium (16). Higher levels of uric acid possibly produce the adverse effects on the vasculature have been linked to increased chemokine and cytokine expression, induction of the renin-angiotensin system, and to increased vascular C-reactive protein (CRP) expression[16-18]. It also infiltrates vascular smooth muscle cells, stimulates chemokine and cytokine expression and ultimately leads endothelial damage. Xanthine oxidase also stimulates pro inflammatory effect on endothelial cells, causing reduced nitric oxide bioavailability[14,15]. Hence hyper active xanthine oxidase produces excess of uric acid with other detrimental effects on endothelium. Instead of evaluating endothelial dysfunction it's easy and cost effective to estimate serum uric acid which is one of the routine biochemical investigations. Furthermore, it has been observed that in it is associated with inflammatory cytokines. Uric acid also shows a positive correlation with inflammatory cytokine interleukin (IL)-6 and tumor necrosis factor-α in vitro[17]. Further, it has been observed that hyperuricemia-induced endothelium injury and vascular dysfunction is via increased expression of inflammatory cytokines. Increased xanthine oxidase enzyme activity may be associated with a corresponding increased production of uric acid, free oxygen radicals, potentially activating the atherosclerotic process. This is further supported by studies showing that xanthine oxidase inhibition is associated with improved endothelial function, cardiovascular risk, and plaque progression in preclinical and clinical studies[19,20]. Uric acid is a routine and inexpensive biomarker, routinely investigated and can be retrieved easily by the clinician from the previous reports of the patients. Circulatory levels of uric acid helps to tract the inflammatory status of the CVD patients in an inexpensive way. For these reasons, uric acid might represent a useful additive tool as much as a CVD risk marker. Thus, in view of available evidence, progressive uric acid elevation with levels higher than 6 mg/dL could be considered an "alarm" for increased CVD risk. Further it has been also observed a higher uric acid level in post menopausal women connects it with various factors like hormonal status, high xanthine oxidase activity, inflammatory environment which results in endothelial dysfunction and risk of CVD[21]. But elevated levels of uric acid indicate the risk of CVD which is suggested in various studies. More studies in post menopausal women with a large sample size, all associated parameters need to be performed for better understanding of the path physiology, clinical consequences of hyperuricaemia and risk of cardiovascular disease.

Limitations: This study has its own limitations like small sample size.

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