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SERUM URIC ACID - A RISK FACTOR FOR CARDIOVASCULAR DISEASE

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ABSTRACT

Background: Uric acid a metabolite of purine degradation is well known for its antioxidant and prooxidant role. The established biochemical risk factor for cardiovascular disease (CVD) are levels of serum lipid profiles. Elevated serum uric acid levels (SUA) are associated with cardiovascular disease. Oxidative stress has been implicated in number of diseases including cardiovascular disease. Xanthine oxidase an enzyme in biosynthesis of uric acid is a source of free radical generation and thereby contributing to oxidative stress process. The main objective of the present study was to determine the level of uric acid and xanthine oxidase, lipid profile in serum of healthy and cardiovascular disease patients and also to evaluate the association between uric acid, xanthine oxidase and established biochemical cardiovascular risk factor in our study groups. Method: The present study consists of two groups, group-I healthy controls (n= 55, of age >35 years) and group-II CVD patients (n=80,age>35 years). The exclusion criteria of group-I: alcoholic, smokers and pregnant women. The exclusion criteria of group-II: diabetic mellitus, gout, renal, liver and thyroid disease. Serum uric acid and lipid profile are measured using kits in RxL Dimension and it was expressed as mg/dl. Serum xanthine oxidase was measured by Ackermann's method using spectrophotometer and expressed as U/L. Student's t-test was done to compare the results between both groups. The relationship between SUA and SXO was analyzed using correlation studies. Findings: A significant increase ($p<0.001$) in SUA and SXO levels were observed in group-II compared with group-I. A significant association was observed between uric acid, xanthine oxidase and lipid profile in our study population. Limitation: The limitation of our study is that we have not measured the markers of oxidative stress. Conclusion: The result of the present study indicates that uric acid can also be a risk factor for cardiovascular disease.

INTRODUCTION

The association between serum uric acid (SUA) and cardiovascular disease (CVD) has been recognized during the past two decades [1]. Uric acid is the end product of purine metabolism in human, excess accumulation can lead to various disease [2]. Uric acid being both antioxidant and pro-oxidant has a potential risk factor that could contribute to cardiovascular disease pathophysiology. Uric acid is produced from purines by the enzyme xanthine oxidase, this elevation of SUA reflects in the increase of xanthine oxidase pathway. Xanthine oxidase enzyme yields the action of hydroxyl free radicals and H_2O_2 [3]. The action of xanthine oxidase is the major source of reactive oxygen species that disrupt the human cell activities.

Hyperuricemia with increase xanthine oxidase activity leads to oxidative stress. Increase oxidative stress is a major factor responsible for the impaired regulation of vascular tone because it diminishes vasoactive nitric oxide (NO) [4]. Increased levels of uric acid induces increase in generation of mitochondrial free oxygen radical leading endothelial dysfunction and also reduces endothelial NO synthase phosphorylation, thus decreasing NO bioavailability. Xanthine oxidase generated, free oxygen radicals interact with endothelium derived NO to form peroxinitrite ($OON^{-}\cdot$). Peroxynitrite is capable of inducing cell death, thus contributing to various forms of cardiovascular diseases [5].

Uric acid could possibly promote oxygenation of low density lipoprotein cholesterol and lipid peroxidation. This can lead to an increase in platelet adhesiveness, resulting in thrombus formation that can contribute to the development of atherosclerosis, increasing the development of cardiovascular disease [6]. Hence this study was undertaken to estimate SUA levels, xanthine oxidase along with lipid profiles to evaluate the association between them in cardiovascular disease patients compared to healthy individuals.

MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry, Central Hospital Laboratory, Sri Ramachandra Medical College & Research Institute, Sri Ramachandra University from March to November 2014. This study was approved by our Institutional Ethical Committee. The control group (n=100) were individuals who attended the medicine department for master health checkup, Sri Ramachandra University. The case group (n=100) were individuals attending cardiology department. The participants included both the sexes and of >35 years of age. Blood samples were collected after getting their consent.

Serum uric acid and lipid profile were measured using fully automated analyzer (ADVIA 1800 Chemistry) purchased from Diasys Diagnostic System GmbH (Germany) and Accurex (India). Serum xanthine oxidase was measured by spectrophotometrically using Ackermann's method [7] after slight modification. The xanthine oxidase activity is calculated using molar extinction coefficient of uric acid at 290nm.

Student's t-test was used to compare the results between the two groups. The pearson correlation was used to assess the relationship between the measured parameters. The results were expressed as mean ± standard deviation (SD). The p value <0.05 was considered as statistically significant.

RESULT & DISCUSSION

A significant increase in serum uric acid ($p<0.001$) and serum xanthine oxidase ($p<0.001$) was observed in Group-II when compared with Group-I. A similar trend was also obtained in serum lipid profiles (total cholesterol, triglycerides, LDL and HDL) in Group-II when compared to Group-I. Table No:1 represents the uric acid, xanthine oxidase and lipid profiles in serum for both groups I and II.

A significant association was obtained between serum uric acid and xanthine oxidase in the study population as shown in Figure No:1. Similarly, serum uric acid correlated well with total cholesterol, triglycerides and LDL as depicted in Figure No: 2, 3 and 4. A weak but significant correlation was obtained between serum uric acid and HDL ($r = 0.13$, $p<0.05$).

Hyperuricemia has been considered as an independent risk factor for cardiovascular disease and development of metabolic diseases [8]. Some studies show that high concentration of plasma triglycerides are related to hyperuricemia[9]. In the present study, there was a significant increase in serum uric acid, xanthine oxidase level and lipid profiles in CVD individuals when compared to healthy individuals. It was also observed that 60% of CVD patients (group-II) had elevated serum uric acid compared to 20% healthy individuals (group-I). The result of the present study were in concordance with the study by Akpek M, Orscelik O, et al.[10] . However, our results contradicted the study by Hong Euy Lim, Seong Hwan Kin et al.[11]. The increased activity of serum xanthine oxidase observed in this study can be a contributing factor to elevation in serum uric acid group-II.

Some workers proposed that uric acid being a cationic surface agent, attaches itself to larger cholesterol molecules facilitating its contact with intimal surface of vessels, thus accelerating plaque formation,[12] while others reported the deposition of uric acid crystals in the vessel

wall initiating the atherogenic events[13]. Hyperuricemia and dyslipidemia was also observed in group-II and there was a significant association between them in this study. A similar findings was reported by Hammondeh A.J et al. [14], they have noted significant atherogenic dyslipidemia and abnormal ratios in patients with Coronary artery disease and has reported that there is a great diversity in the extent of atherosclerosis and in the expression of clinical disease. This is so called- oxidation hypothesis which states that oxidative modification of LDL-C and other lipoproteins is important and possibly obligatory in the pathogenesis of atherosclerotic lesion. The contribution of atherogenic dyslipidemia to cardiovascular risk is well established based on several epidemiological studies [15].

A direct strong independent association between serum uric acid and cardiovascular risk was noted in PIUMA study as reviewed by Puig and Ruilope (2004)[16]. The studies has indicated that xanthine oxidoreductase - induced oxidative stress is implicated in the pathogenesis of endothelial dysfunction. Uric acid inhibits the bioavailability of nitric oxide which would lead to increase in cardiovascular risk. Though we have observed a correlation between uric acid, xanthine oxidase and lipid profile in CVD patients, the limitation of this study is we have not evaluated the other markers of oxidative stress. The elevated serum uric acid and increased xanthine oxidase activity observed in our study can cause a reduction in nitric oxide level and imbalance in oxidative stress which can play a significant role in pathogenesis of cardiovascular diseases.

Table No:1

Parameters	**Group-I (n =100) [male:64, female:36]**	**Group-II (n=100) [male:60, female:46]**
Uric acid (mg/dl)	4.7 ± 1.34	5.812 ± 1.83***
Xanthine oxidase (U/L)	4.9±2.4	11.15±6.74***
Cholesterol (mg/dl)	156.2±32.14	181.8±43.1***
Triglycerides (mg/dl)	103.1±27.32	172.4±83.1***
LDL (mg/dl)	98.89±35.6	125.4±36.98***
HDL (mg/dl)	41.39±12.4	38.1±11.32**

***p<0.001, **p<0.05

Correlations:

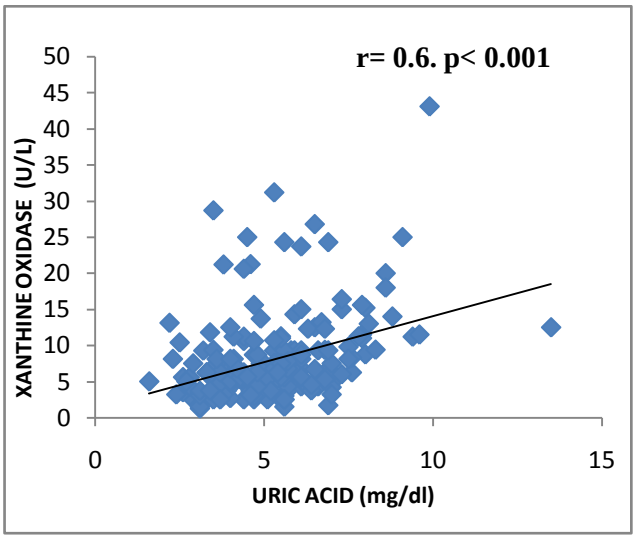

Fig 1: Correlation between SUA and SXO in cardiovascular disease patients.

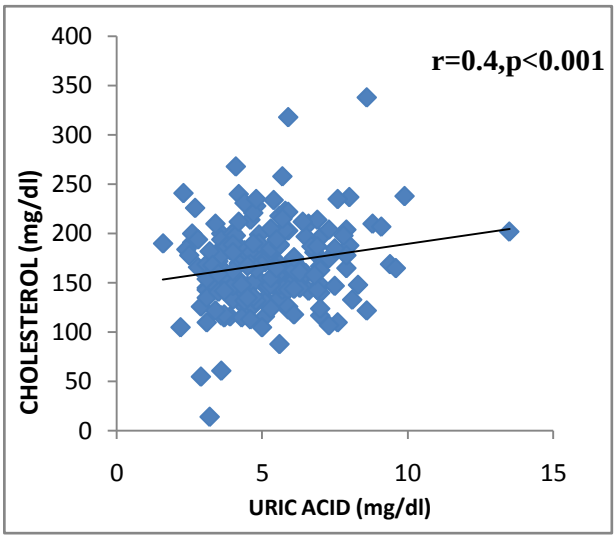

Fig 2: Correlation between SUA and Cholesterol in cardiovascular disease patients

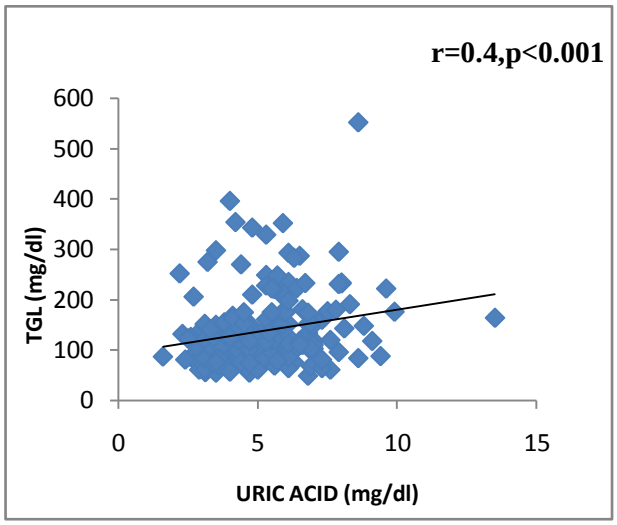

Fig 3: Correlation between SUA and Triglycerides in cardiovascular disease.

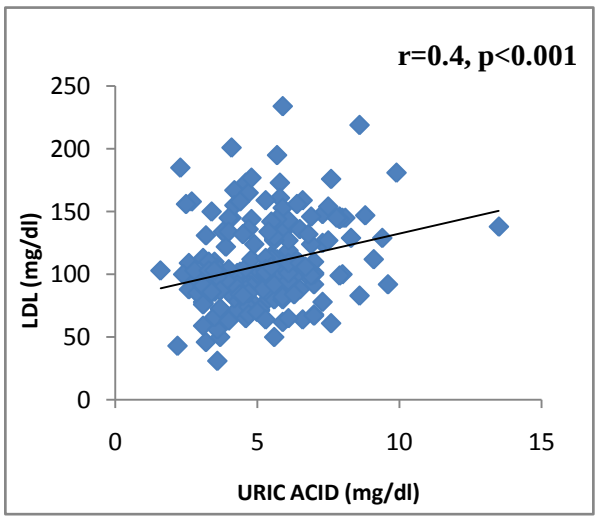

Fig 4: Correlation between SUA and LDL in cardiovascular disease patients.

CONCLUSION

A significant increase in serum uric acid and xanthine oxidase levels was observed in patients with cardiovascular diseases compared to the healthy individuals. The changes indicates its involvement in the pathogenesis of cardiovascular disease and that serum uric acid can be a risk factor for cardiovascular diseases.

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