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RESEARCH ARTICLE

A correlative study of serum uric acid and serum malondialdehyde level in early essential hypertension

Chanchal Shrivastav[1], Suman Sharma[2], Paras Arvindbhai Parekh[1]

[1]Department of Physiology, Ananta Institute of Medical Sciences and Research Center, Rajsamand, Rajasthan, India, [2]Department of Physiology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

Correspondence to: Suman Sharma, E-mail: ishita.ishi@yahoo.in

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ABSTRACT

Background: Hypertension (HT) posing a major public health challenge to the universe in socioeconomic and epidemiological transition. Hyperuricemia in HT is coupled with augmented cardiovascular morbidity and mortality. It also predates the development of HT and suggests that it is not simply a consequence of HT *per se*. Increased urate level along with greater production of oxygen-free radical and augmented oxidative stress may contribute to progression of HT. **Aims and Objectives:** This study aims to assess the correlation between serum uric acid (SUA), serum malondialdehyde (S. MDA) level, and blood pressure in early essential HT. **Materials and Methods:** In this cross-sectional study, after applying inclusion and exclusion criteria, 200 subjects were divided into three groups: 50 subjects as control group, 75 in prehypertensive group, and 75 in hypertensive group. SUA and S. MDA level were estimated in all subjects. Data were analyzed by appropriate statistical methods. **Results:** A significant and positive correlation was observed between SUA and S. MDA level in HT group. Both parameters were correlated positively and significantly with systolic blood pressure (SBP), but not with diastolic blood pressure (DBP) in hypertensive individuals. **Conclusion:** An elevated SUA level is predictive for the evolution of both HT and coronary artery disease. Hyperuricemia plays a role in the formation of free radicals and oxidative stress through increased lipid oxidation. Furthermore, positive correlation with SBP further established its potential role in the etiopathogenesis of essential HT.

KEY WORDS: Essential Hypertension; Hyperuricemia; Serum Malondialdehyde Level; Lipid Peroxidation; Oxidative Stress

INTRODUCTION

Essential hypertension (HT) is being increasingly documented as a part of a complex multifaceted disorder worldwide due to its high incidence and associated risks of renal and cardiovascular disease (CVD), for instance, stroke, myocardial infarction, and heart failure. The effective union between HT and hyperuricemia has been documented for more than a century. Studies from the 1950s and 1960s demonstrated the incidence of hyperuricemia in hypertensive cases to be between 20 and 40%.[1] Later on, it was found that an increasing level of serum urate is an autonomous risk factor of HT.[2]

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Raised serum uric acid (SUA) level is also associated with increased cardiovascular morbidity and mortality rate.[3] Its level is thoroughly controlled by the balance among uric acid production and excretion.[4] Urate is freely filtered in the glomerulus, reabsorbed, secreted, and then again reabsorbed in the proximal tubule. Essential HT may also be linked with hyperuricemia with normal renal functions.[5] Hyperuricemia (>5.5 mg/dl [330 μmol/L]) was detected in almost 90% of teenagers with primary HT, whereas uric acid levels were

significantly lower in controls and youth with any white coat or secondary HT.[6] The finding that uric acid levels were not lifted in secondary HT also cuts down the probability that the hyperuricemia resultants from HT.

There are abundant reports that oxidative stress is amplified in patients with HT. Further, the extreme production of reactive oxygen species (ROS) due to raised urate level, out stripping antioxidant defense mechanisms, has been involved in pathophysiological conditions that influence on the cardiovascular system.[7] Moreover, ROS react with membrane lipids to yield lipid hydroperoxide, a destructive process known as lipid peroxidation. Lipid hydroperoxide decomposes to build various products containing malondialdehyde. In the present study, serum malondialdehyde (S. MDA) was used as a biochemical marker for the assessment of lipid peroxidation.

The significance of both SUA and S. MDA level in the development of essential HT has not been thoroughly investigated, especially in Southern Rajasthan. Hence, this study has been designed to study the correlation between SUA, S. MDA level, and blood pressure among newly diagnosed essential HT.

MATERIALS AND METHODS

This cross-sectional case–control study was conducted among 200 subjects in the Department of Physiology, Geetanjali Medical College and Hospital (GMCH), Udaipur. All the subjects were chosen randomly from medicine outpatient department, family members or attendants of established hypertensive patients, individual's comings to hospital for health checkup, and healthy volunteers such as clinical and non-clinical staff of a tertiary care hospital. This study was ethically approved by the institutional ethical committee of GMCH, Udaipur (Ref. No. GU/UCE/EC/2013/299 dated15/05/2013).

Inclusion Criteria

All the sex-matched subjects, aged between 20 and 50 years old were broadly divided into three groups:

- 50 participants with normal blood pressure (systolic blood pressure [SBP] = 90–119 mmHg and diastolic blood pressure [DBP] = 60–79 mmHg) were taken as control group
- 75 cases of prehypertension (preHT) (SBP = 120–139 mmHg and DBP = 80–89 mmHg) were taken as preHT group
- 75 cases of newly diagnosed cases of essential HT (SBP = 140–159 mmHg and DBP = 90–99 mmHg) were taken as HT group.

Exclusion Criteria

The subjects suffering with gout, diabetes mellitus, gestational HT, and/or secondary HT caused by renal disorders, metabolic disorders, fluid volume disturbances, endocrinal disorders, etc., were excluded from the study groups. Smokers, alcohol consumers, and patients on medication for HT were also excluded from the study. After diagnosis, a written informed voluntary consent was taken from all the participants after explaining their participation in the study in their local language. All the data from three groups were collected in the detailed pro forma along with required physical examination. For biochemical analysis, blood sample (5 ml) was drawn after an overnight fasting (12 h) by venous puncture and serum was separated by centrifugation at 3000 rpm for 10 min. SUA level and S. MDA were estimated using commercially available reagents or kits.[8,9]

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 16. Significance testing of difference for mean of three groups was done by analysis of variance test (ANOVA). $P < 0.05$ was used to establish statistical significance. The correlation between different parameters was assessed by Pearson coefficient of correlation test.

RESULTS

Figures 1 and 2 showing that the difference in mean of SUA level and S. MDA level between control, preHT, and HT group was highly significant ($P < 0.0001$). Table 1 shows that SUA level was significantly and positively correlated with SBP

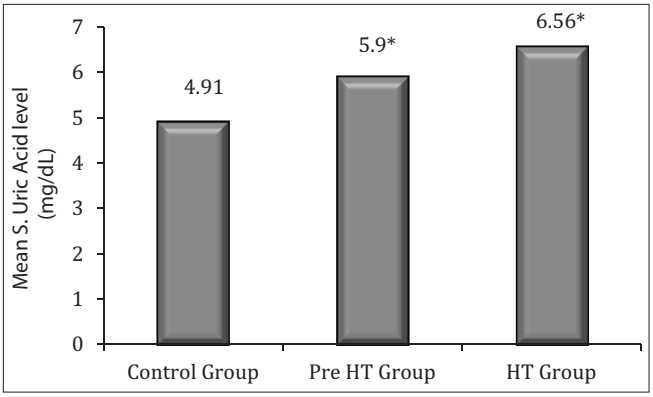

Figure 1: Comparison of mean serum uric acid level among different groups (*significant with $P < 0.001$)

Table 1: Correlation of serum uric acid levels with various parameters

Parameters	Control group		Hypertension group	
	r value	*P* value	*r* value	*P* value
SBP	−0.234	NS	+0.478	<0.001
DBP	−0.230	NS	+0.202	NS
S. MDA	+0.236	NS	+0.574	<0.001

S. MDA: Serum malondialdehyde, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

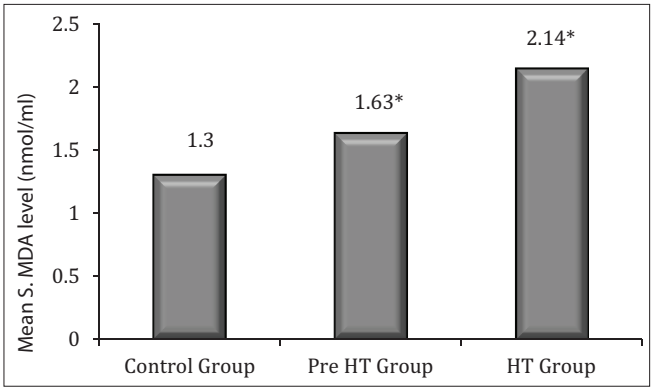

Figure 2: Comparison of mean serum malondialdehyde level among different groups (*significant with $P < 0.001$)

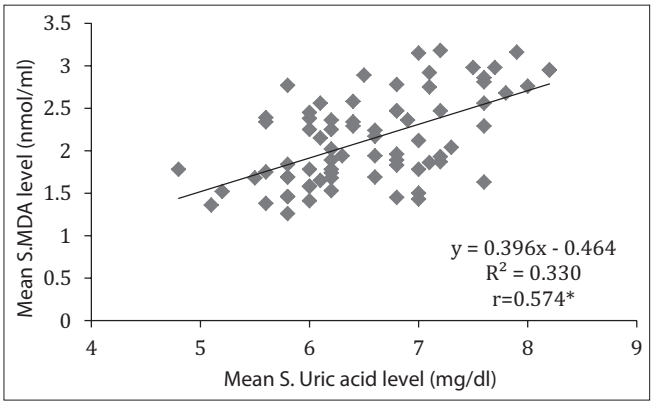

Figure 3: Correlation between serum uric acid levels and serum malondialdehyde levels (*significant with $P < 0.001$)

($r = +0.478$, $P < 0.001$) and S. MDA ($r = +0.574$, $P < 0.001$), whereas no significant correlation was found with DBP ($P > 0.05$). Figures 3-5 showed that S. MDA was significantly and positively correlated with SBP ($r = +0.486$, $P < 0.001$) and SUA ($r = +0.574$, $P < 0.001$), whereas no significant correlation was found between S. MDA and DBP ($P > 0.05$).

DISCUSSION

In this study, we found that the mean of SUA level and S. MDA level in hypertensive group was significantly higher as compared to prehypertensive and controls ($P < 0.001$). The increased trend in mean SUA level was observed from control to prehypertensive and prehypertensive to hypertensive cases [Figures 1 and 2]. Results also showed that SUA and S. MDA were significantly and positively correlated with each other and SBP ($P < 0.001$), whereas no significant correlation was observed with DBP ($P > 0.05$) for the same.

Masuo *et al*. assessed the linear relationship of SUA and SBP and showed an average raise of 23 mmHg per 1 mg/dl increase in SUA within non-obese young men.[10] Another study on 125 children (age group 6–18 years) with essential HT proved the association of SUA with SBP ($r = 0.80$) and DBP ($r = 0.66$).[6] In support to our study, Acharya and Mishra found that S. MDA level was significantly and positively correlated

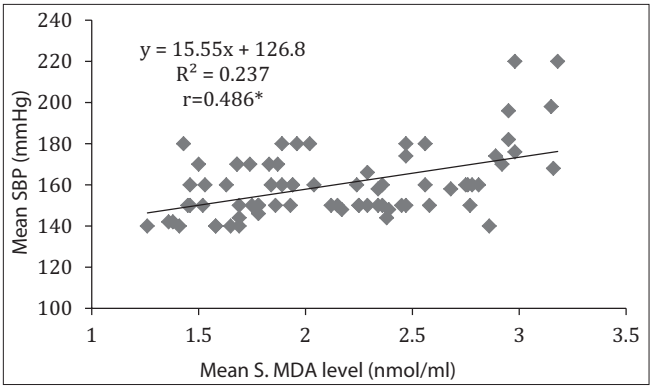

Figure 4: Correlation between serum malondialdehyde levels and systolic blood pressure (*significant with $P < 0.001$)

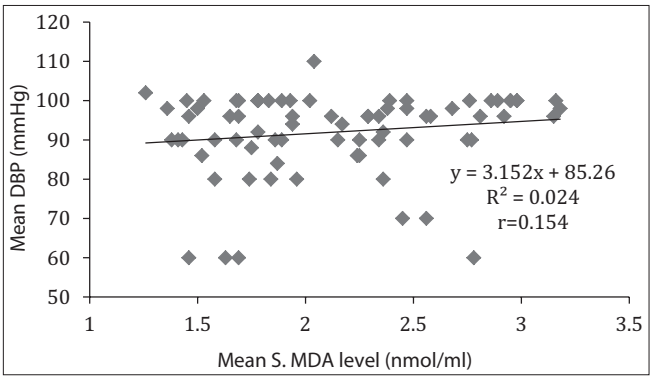

Figure 5: Correlation between serum malondialdehyde levels and diastolic blood pressure (*significant with $P < 0.001$)

with SBP ($r = +0.364$, $P < 0.01$) and SUA level ($r = +0.289$, $P < 0.05$). They found no significant correlation between S. MDA and DBP.[11] Amirkhizi *et al*. assessed the oxidative stress marker related to atherosclerosis in prehypertensive women. Regarding MDA level, they attained that MDA was positively correlated with both SBP ($r = +0.24$, $P < 0.001$) and DBP ($r = +0.18$, $P < 0.001$).[12] Ouppatham *et al*. examined the relationship of hyperuricemia and blood pressure in the Thai army population and observed a significant and positive correlation between both SUA levels and SBP ($r = 0.186$, $P < 0.001$) and same with DBP ($r = 0.255$, $P < 0.001$).[13] However, Teng *et al*. described a contrary result, wherein uric acid was associated with the risk of HT in the elderly.[14]

Hyperuricemia is commonly experienced with essential HT, even untreated HT. Studies in animal models proposed that hyperuricemia may be predominantly important in early HT[15] and likewise studies in humans illustrated that the strongest relationship of hyperuricemia is with premature HT such as discovered in adolescents.[6] Contrary to these findings, a number of studies have recommended that the association between elevated SUA and cardiovascular risk does not carry on after rectifying for other risk factors.

Experimental studies provide a credible physiologic mechanism by which increases in SUA might cause HT. Uric acid enters vascular smooth muscle cells, where it stimulates

mitogen-activated protein kinases, cyclooxygenase-2, and platelet-derived growth factor to stimulate vascular smooth muscle proliferation and preglomerular arteriolopathy.[15,16] Increased SUA further causes an increase in juxtaglomerular renin production and a decrease in macula densa neuronal nitric oxide (NO) synthase expression, leading to renal vasoconstriction and probably increasing blood pressure.[17] If renal vasoconstriction persistent, it may impart to arteriosclerosis and the exploitation of salt-sensitive HT, even if the hyperuricemia is rectified.

In addition, SUA plays a role in the formation of free radicals and may elucidate the link between hyperuricemia and HT.[18] Augmented intracellular uric acid may accelerate oxidative stress directly by raising NADPH oxidase linked ROS or generated by stimulation of xanthine oxidase during the generation of uric acid as well. Oxidative stress may contribute to the generation and/or development of HT through a number of probable mechanisms included (a) curbing of the vasodilator NO by ROS such as superoxide, (b) production of vasoconstrictor lipid peroxidation products, (c) diminution of tetra hydrobiopterin (BH4), an important NO synthase cofactor, (d) structural and functional changes within the vasculature.[19]

Experimentally, by means of which, hyperuricemia results in HT are by way of oxidative stress, endothelial dysfunction, and activation of the renin angiotensin system. The net effect is to provoke renal and systemic vasoconstriction and the progression of HT. Increase in SUA has been demonstrated as an earlier marker of HT, which occurs even before the modification in serum creatinine.[18]

Limitations

As the present study is hospital-based case–control study, so to establish these results to the population of Southern Rajasthan, large sample size should be taken.

CONCLUSION

From the above discussion, it can be concluded that increased serum MDA in hypertensive indicates an association between increased oxidative stress and HT. SUA through lipid peroxidation might be processing toward the etiopathogenesis of essential HT even in its former stages, and its serum level may be a modifiable factor for progression of the disease. Measuring these biomarkers in clinical practice may identify high-risk individuals. Further, the maintenance of the oxidative balance and SUA in hypertensive patients would be helpful in preventing the CVD and other diseases associated with HT.

REFERENCES

1. Kinsey D, Walther R, Sise HS, Whitelaw G, Smithwick R. Incidence of hyperuricemia in 400 hypertensive patients. Circulation 1961;24:972-6.
2. Kahn HA, Medalie JH, Neufeld HN, Riss E, Goldbourt U. The incidence of hypertension and associated factors: The Israel ischemic heart disease study. Am Heart J 1972;84:171-82.
3. Jawed S, Khawaja TF, Sultan MA, Ahmed S. The effect of essential hypertension on serum uric acid level. Biomedica 2005;21:98-102.
4. Fauci AS, Harrison TR. Harrison's Principles of Internal Medicine. 17th ed. New York, USA: McGraw-Hill Medical; 2008.
5. Alderman MH, Cohen H, Madhavan S, Kivlighn S. Serum uric acid and cardiovascular events in successfully treated hypertensive patients. Hypertension 1999;34:144-50.
6. Feig DI, Johnson RJ. Hyperuricemia in childhood primary hypertension. Hypertension 2003;42:247-52.
7. McIntyre M, Bohr DF, Dominiczak AF. Endothelial function in hypertension: The role of superoxide anion. Hypertension 1999;34:539-45.
8. Trinder P. Quantitative determination of uric acid in human serum. J Clin Pathol 1949;22:246-50.
9. Buege JA, Aust SD. The thiobarbituric acid assay methods. Enzymol 1978;52:306.
10. Masuo K, Kawaguchi H, Mikami H, Ogihara T, Tuck ML. Serum uric acid and plasma norepinephrine concentrations predict subsequent weight gain and blood pressure elevation. Hypertension 2003;42:474-80.
11. Acharya V, Mishra PK. Hyperuricemia and oxidative stress in borderline hypertension. Biomedicine 2007;21:19-22.
12. Amirkhizi F, Siassi F, Djalali M, Minaie S, Dorosty AR. Assessment of oxidative stress markers related to atherosclerosis in pre-hypertensive women. J Teh Univ Heart Cent 2007;3:137-43.
13. Ouppatham S, Bancha S, Choovichian P. The relationship of hyperuricemia and blood pressure in the Thai army population. J Postgrad Med 2008;54:259-62.
14. Teng F, Zhu R, Zou C, Xue Y, Yang M, Song H, *et al.* Interaction between serum uric acid and triglycerides in relation to blood pressure. J Hum Hypertens 2011;25:686-91.
15. Watanabe S, Kang DH, Feng L, Nakagawa T, Kanellis J, Lan H, *et al.* Uric acid, hominoid evolution, and the pathogenesis of salt-sensitivity. Hypertension 2002;40:355-60.
16. Mazzali M, Kanellis J, Han L, Feng L, Xia YY, Chen Q, *et al.* Hyperuricemia induces a primary renal arteriolopathy in rats by a blood pressure-independent mechanism. Am J Physiol Renal Physiol 2002;282:F991-7.
17. Mazzali M, Hughes J, Kim YG, Jefferson JA, Kang DH, Gordon KL, *et al.* Elevated uric acid increases blood pressure in the rat by a novel crystal-independent mechanism. Hypertension 2001;38:1101-6.
18. Alderman MH. Serum uric acid as a cardiovascular risk factor for heart disease. Curr Hypertens Rep 2001;8:12-7.
19. Grossman E. Does increased oxidative stress cause hypertension? Diabetes Care 2008;31 Suppl 2:S185-9.

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