

FREQUENCY OF HYPERURICEMIA IN PATIENTS WITH HEART DISEASES

Khalid Mehmood¹, Arshad Pervez¹, Munir Hussain¹, Ameer Taj², Shah Sawar³, Muizz Zahoor⁴

ABSTRACT

Introduction: Uric acid is an active organic compound because of its biological role in many body functions. To see the function of uric acid in the pathogenesis of cardiovascular disease has been very difficult. Furthermore the link between cardiovascular diseases and high uric acid levels in blood is not clear. In some studies done earlier the results were contradictory.

To clarify the relationship between cardiovascular diseases and increased serum uric acid levels many studies described several possible mechanisms. On one hand these studies highlighted the injurious role of hyperuricemia on endothelium and on cardiovascular functions. On other hand there is protective role of serum uric acid as an antioxidant, but these possible benefits may be masked by harmful effects in different places.

The effects of changing serum uric acid either raising or lowering, on development of atherosclerosis, endothelial function, and autonomic regulation need research to recognize a possible double action in the cardiovascular system.

Objectives: To see the frequency of hyperuricemia in ischemic and hypertensive heart diseases

Materials and Methods: In this cross sectional study 100 patients with cardiac diseases admitted in cardiac unit of tertiary care hospitals of Peshawar in KPK were selected by non – probability convenient sampling method according to including and excluding criteria. After identifying the study subjects in the hospitals consent was taken, questionnaire was filled and blood sampling was done aseptically. Samples were analyzed in pathology laboratory of HMC by Hitachi chemistry analyzer 902. The collected data was analyzed in SPSS version 22.

Results: The mean age of participants in this study was 62 years with 65 % male and 35% females. The diagnosis was in 48% Ischemic heart diseases, in 30% hypertensive heart diseases and in 22% both ischemic and heart diseases. Hyperuricaemia was more observed in male with ischemic heart diseases while in female with hypertensive heart diseases..

Conclusion: Hyperuricaemia was more observed in males with ischemic heart diseases while in females with hypertensive heart diseases.

Key words: serum uric acid, cardiac diseases, hypertension, myocardial infarction

INTRODUCTION

Considerable discussion has been done in past about the usual link between high serum uric acid level and cardiovascular diseases.¹ Several studies recognized the value of serum uric acid level in populations predicting the cardiovascular events risk like myocardial infarction. Research was directed to the likely trials that might have revealed the effects of uric acid level on cardiovascular system directly or indirectly.

In human beings the purines synthesis is by metabolism of nucleic acids that may be dietary or endogenous. Xanthine oxidase enzyme finally degrades it to

uric acid. As uric acid is a weak acid, it is dispersed as urates of sodium in the extracellular fluid compartment, and its clearance from plasma is through glomerular filtration.² Proximal part of renal tubule is responsible for 90% of reabsorption of uric acid from plasma that is filtered, while overall clearance is done by distal renal tubule through active secretion by an energy dependent mechanism.³

Being a potent antioxidant, uric acid has been considered to safeguard against a few cancers and cardiovascular diseases.⁴ Although uric acid has given protection against cardiovascular diseases due to its antioxidant properties, still research studies have indicated relationships with a greater risk of higher blood pressure, ischemic heart disease, and an adverse cardiovascular risk outlines.⁵⁻¹⁴ Meta-analyses of prospective studies have proved these damaging effects,^{13,14} supporting link of increased serum uric acid with increases in risk for blood pressure and cardiovascular outcomes,^{15,16} in addition to risk factors that are already known.

As we do not have any local data and no such

¹ Department of pathology KGMC Peshawar

² Department of Medicine HMC

³ Department of Cardiology HMC

⁴ TMO Department of Cardiology HMC

Address for correspondence:

Dr. Khalid Mehmood

Department of Pathology KGMC

E-mail: DRKM.2014@gmail.com

Cell: 03339194518

study in past has been done on our local population. To have a clear understanding about the function of increased serum uric acid levels for patients individually and to implement a better approach for therapy regarding the modifications of uric acid level in serum, it is essential to detect means that relates uric acid with the adjustment of cardiovascular system.

AIMS & OBJECTIVES

To see the frequency of hyperuricemia in ischemic and hypertensive heart diseases

MATERIALS AND METHODS

It is a cross sectional study. This study was conducted in Cardiac Care Units of Tertiary Care Hospitals of Peshawar in KPK and laboratory of KGMC & HMC. Study Duration was twelve months. The sample size included 100 patients admitted in cardiac care units of Tertiary Care Hospitals of Peshawar in KPK. Sampling was done by non-probability convenient sampling method.

Inclusion Criteria: Cases diagnosed as ischemic, hypertensive heart diseases and residents of KPK admitted in cardiac care unit of tertiary care hospitals of Peshawar in KPK were included in the study. Only consenting patients were included. **Exclusion Criteria:** Patients with ischemic, hypertensive heart diseases not admitted in cardiac care unit were excluded.

Data Collection Procedure: Methods After identifying the study subject in a hospital, consent was taken from all of them and the questionnaire was filled. Then under aseptic condition blood was taken and the syringes containing samples were labeled. Then stratification for different cardiac diseases and factors like age and gender were done.

The determination of serum uric acid was done by Hitachi 902 chemistry analyzer (Japan) 1993 version. The reference ranges for serum uric acid were in male 2.5 – 7.2 and in female 2.5 – 6.0. Uricase method was used by process of automation through single run. It is based on the principle that uric acid is oxidized in the presence of enzyme Uricase to allantoin and hydrogen peroxide. The hydrogen peroxide was then measured by means of catalase peroxidase linked reactions.

The collected data were recorded and analyzed in SPSS version 22.0 for windows. Mean + SD were calculated for numerical variables like age. Frequency and Percentages were calculated for categorical variables like gender. All results were presented in the form of tables and graphs.

RESULTS

The mean age of participants in this study was 62 years with standard deviation of 11.4. All the female participants were above 50 years while most of the male

participants were above 50 years. (Table no. 1)

There were 65% male and 35% female in the study. Majority of the males and females suffered from ischemic heart diseases. (Graph no. 1)

The diagnosis was in 48% Ischemic heart diseases, in 30% hypertensive heart diseases and in 22% both ischemic and hypertensive heart diseases. (Graph no. 2)

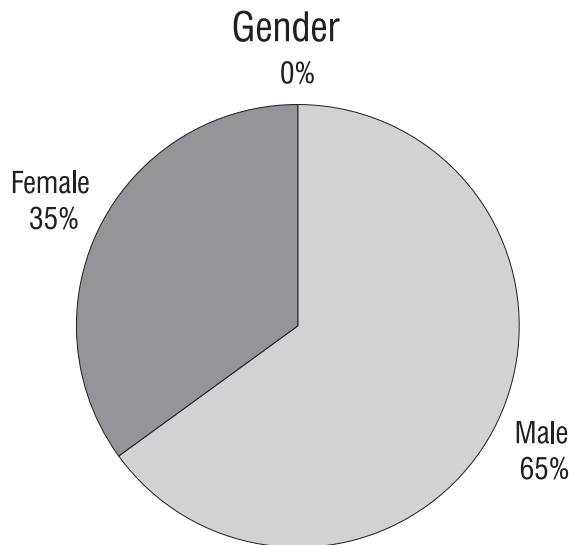


Figure 1: Gender Distribution of the Participants

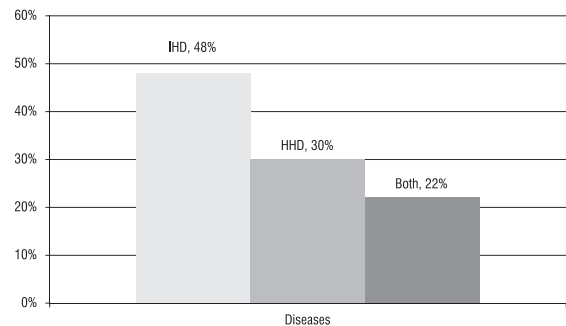


Figure 2: Disease Distribution

IHD = Ischemic Heart Diseases

HHD = Hypertensive Heart Diseases

Table 1: Age Groups of the Participants

Age groups	Male	Female	Total
Less than 50 years	08	---	08
50 – 80 years	54	35	89
More than 80 years	03	---	03
Total	65	35	100

Table 2: Serum Uric Acid Levels With Gender

Gender	Serum Uric Acid Level			Total
	More than 7.22 mgs/dl	7.22 – 2.5 mgs /dl	Less than 2.5 mgs/dl	
Male	17 (26 %)	48	----	65
Female	12 (34 %)	23	----	35
Total	29	71	-----	100

Table 3: Serum Uric Acid Levels With Diseases

Diseases	Serum Uric Acid Level			Total
	10 - 7.22 mgs/dl	7.22 - 2.5 mgs/dl	Less than 2.5 mgs/dl	
Ischemic heart diseases	17	31	---	48
Hypertensive heart disease	11	19	---	30
Both	01	21	---	22
Total	29	71	---	100

The average value of serum uric acid was 7.22 mgs /dl with SD of 1.98. Hyperuricaemia was seen in 29% of participants with 26% in male participants while in female participants the percentage was 34. Hyperuricaemia was more observed in male with ischemic heart diseases while in female with hypertensive heart diseases. (Table no. 2 & 3.)

DISCUSSION

The part of increased serum urate being a distinct risk factor for ischemic heart diseases has got significance recently with several views indicated in several editorials and reviews.¹⁷⁻¹⁹ The correlation of hyperuricaemia with myocardial infarction may be defensive as an antioxidant because increase in serum urate may attempt to prevent peroxidation of lipids and thus play a defending role against the process of atherosclerosis.^{20,21} On the other hand it is shown that serum urate can raise peroxidation of lipids along with oxygenation of cholesterol and low density lipoproteins. Hyperuricaemia can lead to endothelial injury and enhance the chance of myocardial infarction through the formation and release of free radicals that is due to change in the surface receptors and cell adhesions molecules expression in cardiac cells. Research must be directed to know the real function of increase serum urate in this setting whether it can help to identify the people that are at risk for myocardial infarction to develop.

Increased serum uric acid became the main important risk factor in patients with high blood pressure as it highlights the progression of hypertension in population generally.²² A close relationship of high serum uric acid with elevated blood pressure in cardiac patients has been observed that is not dependant on kidney function, medication for hypertension or increased weight by many observational, clinical and epidemiological studies.²³ Hyperuricaemia has been observed in 25% hypertensive patients while in cardiac patients with malignant hypertension it reaches to 75%.²⁴

The causal role of high serum uric acid levels on high blood pressure has been shown by studies done on animals. For example in rats hyperuricaemia developed when uricase inhibitor was given to them. In these rats hypertension developed after taking uricase inhibitor for three weeks but hypertension did not develop in the control group of rats.^{25, 26} And there was reversal of induced hypertension in experimental rats when they were treated with antihypertensive medicine like enalapril.

As serum uric acid level being a cheap and easily available test, can be easily modified and may identify people with hyperuricaemia that can be further investigated for the obesity and its related complications. It is also important to note that hyperuricaemia in people with normal blood pressure may lead to increase protective actions to prevent the development of hypertension in future.

Although the current study has indicated some positive link between hyperuricaemia and ischemic / hypertensive heart diseases as seen by observational studies⁵⁻¹² done earlier and proved by meta-analysis of prospective studies^{13,14} but it may show a doable role in the pathology of cardiac diseases.^{27, 28}

So it is essential to make plans so that the people understand about the importance to alter their eating habits and to assume active life styles instead of lazy life styles particularly aiming on sizes of waist line.^{29,30}

CONCLUSION

Hyperuricaemia was more observed in male with ischemic heart diseases while in female with hypertensive heart diseases.

REFERENCES

1. Dobson A. Is raised serum uric acid a cause of cardiovascular disease or death? *Lancet*.1999;

- 354:1578.
2. Emmerson BT. The management of gout. *N Engl J Med.* 1996; 334: 445–51.
 3. Steele TH. Hyperuricemic nephropathies. *Nephron.* 1999; 81 (Suppl. 1): 45–9.
 4. Ames BN, Cathcart R, Schwiers E, Hochstein P. Uric acid provides an antioxidant defense in humans against oxidant- and radical-caused aging and cancer: a hypothesis. *Proc Natl Acad Sci U S A.* 1981; 78: 6858-62.
 5. Liese AD, Hense HW, Lowel H, Doring A, Tietze M, Keil U. Association of serum uric acid with all-cause and cardiovascular disease mortality and incident myocardial infarction in the MONICA Augsburg cohort. *Epidemiology.* 1999; 10: 391-7.
 6. Alderman M, Aiyer KJV. Uric acid: role in cardiovascular disease and effects of losartan. *Curr Med Res Opin.* 2004; 20:369-79.
 7. Sundstrom J, Sullivan L, D'Agostino RB, Levy D, Kannel WB, Vasan RS. Relations of serum uric acid to longitudinal blood pressure tracking and hypertension incidence. *Hypertension.* 2005; 45:28-33.
 8. Perlstein TS, Gumieniak O, Williams GH, Sparrow D, Vokonas PS, Gaziano M, et al. Uric acid and the development of hypertension. *Hypertension.* 2006; 48:1031-6.
 9. Bos MJ, Koudstaal PJ, Hofman A, Witteman JCM, Breteler MMB. Uric acid is a risk factor for myocardial infarction and stroke: the Rotterdam study. *Stroke.* 2006; 37:1503-7.
 10. Deveci OS, Kabakci G, Okutucu S, Tulumen E, Aksoy H, Kaya EB, et al. The association between serum uric acid level and coronary artery disease. *Int J Clin Pract.* 2010; 64: 900-7.
 11. Fang J, Alderman MH. Serum uric acid and cardiovascular mortality: the NHANES I epidemiologic follow-up study, 1971-1992. *JAMA.* 2000; 283: 2404-10.
 12. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and risk of stroke: a systematic review and meta-analysis. *Arthritis Care Res.* 2009; 61: 885-92.
 13. Meisinger C, Koenig W, Baumert J, Doring A. Uric acid levels are associated with all-cause and cardiovascular disease mortality independent of systemic inflammation in men from the general population: the MONICA/KORA cohort study. *Arterioscler Thromb Vasc Biol.* 2008; 28:1186-92.
 14. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and coronary heart disease: a systematic review and meta-analysis. *Arthritis Care Res.* 2010; 62:170-80.
 15. Strasak AM, Kelleher CC, Brant LJ, et al. VHM&PP study group. Serum uric acid is an independent predictor for all major forms of cardiovascular death in 28,613 elderly women: a prospective 21-year follow-up study. *Int J Cardiol.* 2008; 125: 232-9.
 16. Thanassoulis G, Brophy JM, Richard H, Pilote L. Gout, allopurinol use, and heart failure outcomes. *Arch Intern Med.* 2010; 170: 1358-64.
 17. Kivity S, Kopel E, Maor E, Abu-Bachar F, Segev S, Sidi Y and Olchovsky D. Association of serum uric acid and cardiovascular disease in healthy adults. *Am J Cardiol.* 2013; 111: 1146-1151.
 18. Chiquete E, Ruiz-Sandoval JL, Murillo-Bonilla LM, Arauz A, Orozco-Valera DR, Ochoa-Guzmán A, Villarreal-Careaga J, León-Jiménez, Barina-garmenteria F, Ramos-Moreno A and Cantú-Brito C. Serum Uric Acid and Outcome after Acute Ischemic Stroke-PREMIER Study. *Cerebrovasc Dis.* 2013; 35:168-174.
 19. Rosendorff C and Jogendra MRD. Uric Acid: Where Are We? *The Journal of Clinical Hypertension.* 2013; 15.
 20. Davies KJ, Sevanian A, Muakkassah-Kelly SF and Hochstein P. Uric acid iron ion complexes. A new aspect of the antioxidant functions of uric acid. *Biochem J.* 1986; 235: 747–754.
 21. Nieto FJ, Iribarren C, Gross MD, Comstock GW and Cutler RG. Uric acid and serum antioxidant capacity: a reaction to atherosclerosis? *Atherosclerosis.* 2000; 148: 131–9.
 22. Jossa F, Farinaro E, Panico S, Krogh V, Celentano E, Galasso R, Mancini M and Trevisan M. Serum uric acid and hypertension: the Olivetti heart study. *J Hum Hypertens.* 1994; 8:668-77.
 23. Heinig M and Johnson RJ. Role of uric acid in hypertension, renal disease and metabolic syndrome. *Cleve Clin J Med.* 2006; 73: 1059-63.
 24. Johnson RJ, Kang DH, Feig D et al. Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? *Hypertens.* 2003; 41:1183–90.
 25. Mazzali M, Hughes J, Kim YG, et al. Elevated uric acid increases blood pressure in the rat by a novel crystal-independent mechanism. *Hypertension.* 2001; 38:1101–1106.
 26. Hsu PF, Chuang SY, Yu WC, Leu HB, Chan WL and Chen CH. The Impacts of Serum Uric Acid on arterial hemodynamics and Cardiovascular Risks. *Acta Cardiol Sin.* 2013; 29:142-50.
 27. Brodov Y, Chouraqui P, Goldenberg I, Boyko V, Mandelzweig L, Behar S. Serum uric acid for risk stratification of patients with coronary artery disease. *Cardiology.* 2009; 114(4): 300-5.
 28. Wiik BP, Larstorp AC, Høiegggen A, Kjeldsen SE, Olsen MH, Ibsen H, et al. Serum uric acid is associated with new-onset diabetes in hypertensive patients with left ventricular hypertrophy: The LIFE Study. *Am J Hypertens.* 2010; 23 (8): 845-51.
 29. Rodrigues SL, Baldo MP, Sá Cunha R, Angelo LC, Pereira AC, Krieger JE, et al. Anthropometric measures of increased central and overall adiposity in association with echocardiographic left ventricular hypertrophy. *Hypertens Res.* 2010; 33 (1): 83-7.
 30. Rodrigues SL, Baldo MP, Mill JG. Association of waist-stature ratio with hypertension and metabolic syndrome: population-based study. *Arq Bras Cardiol.* 2010; 95 (2): 186-91.