The frequency of hyperuricemia with left ventricular hypertrophy in patient with primary hypertension in Erbil city-Iraq

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Abstract

Background: High serum uric acid level is common in hypertension and it may be correlated with left ventricular hypertrophy. The frequency of hyperuricemia is not previously well investigated in Erbil city. **Objectives:** The objective of this study was to investigate the frequency of hyperuricemia and the association between serum uric acid levels and left ventricular hypertrophy in a group of hypertensive patients in Erbil-Iraq. **Patients and methods:** A cross-sectional study was conducted in Rizgary teaching hospital between September 2015 and September 2016. A total of 150 consecutive adult patients presenting with primary hypertension were included. Based on the results of the echocardiography, the patients were classified into two groups; Group I (patients with left ventricular hypertrophy) and Group II (patients with non- left ventricular hypertrophy). The effects of high serum uric acid level on left ventricular mass and geometry were evaluated in both groups. **Results:** High serum uric acid level was present in 38 patients (25.3%). Based on the results of echocardiographic examination, left ventricular hypertrophy was present in 78 patients (52%), 25 of them (32 %) had hyperuricemia. The mean of serum uric acid level, means of age, systolic blood pressure, diastolic blood pressure and lipid profile significantly higher in group I patients compared to those in group II patients. Regarding echocardiographic parameters, There were significantly higher in hyperuricemic patients compared to patients without hyperuricemia the means of interventricular septal thickness, left atrium and left ventricular mass. **Conclusions:** In this study, high serum uric acid level was common in hypertensive patients and it was positively associated with left ventricular hypertrophy and dyslipidemia.

Keywords: Uric acid; hypertension; left ventricular hypertrophy.

Introduction

Hypertension is a global health problem (1). It is estimated that over 30% of all adults across the world have hypertension (2). The incidence of hypertension is growing among women and adolescents as well as the older adults. According to the 2006 Iraqi national survey for chronic disease risk factors, 40 % of the Iraqi adult populations have elevated blood pressure (3). The development of left ventricular hypertrophy (LVH) is highly correlated with systolic hypertension and is considered as a marker of target cardiac damage in hypertension (4) .Uric acid (UA) is produced as a terminal stage of purine metabolism (5). Hyperuricemia is a condition that results from increased production of uric acid, decreased excretion or a combination of both. Elevated serum uric acid levels are commonly seen in association with glucose intolerance, hypertension, dyslipidemia and other cardiovascular diseases (CVDs) (6). An elevated blood level of UA was reportedly associated with left ventricular hypertrophy (LVH) in hypertensive patients (7). Some studies suggested that lower serum uric acid level in hypertensive patients with LVH is associated with better prognosis (8). Understanding this issue of association with cardiovascular disease risk factors, hyperuricemia deserves special attention regarding the progressive prevalence of cardiovascular disease throughout the world. The aim of the present study is to investigate the association of UA with LVH and other variables in patients with essential hypertension in Erbil city.

Patients and Methods

This cross-sectional study was conducted in Rizgary teaching hospital between September 2015 and September 2016. A total of 150 consecutive patients presenting with primary hypertension, aged ≥18 years were enrolled in the study. The exclusion criteria were patients with secondary hypertension diabetic nephropathy, polycystic kidney disease, renovascular hypertension, cushing syndrome, chronic renal failure, malabsorption and patients on medications that interfere with UA levels like diuretics or xanthines. All patients were assessed by a detailed history, physical examination, and echocardiographic study to document presence of hypertension and/or left ventricular hypertrophy. Fasting venous blood samples were drawn to measure blood sugar , blood urea (BU), serum creatinine (SC), total cholesterol (TC), triglyceride (TG), and serum uric acid for each patient according to standard methods. Uric acid was analyzed by the uricase-peroxidase method. Normal serum UA level in our laboratory was 1.5-7 mg/dl for both genders. BMI (Body Mass Index, weight kg/height^2 ^{m2}) was calculated according to a standard definition (12). Based on recommendations of the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) (13), hypertension is defined as systolic blood pressure (SBP) ≥140 mmHg and diastolic blood pressure (DBP) ≥ 90 mmHg for adults aged 18 years and less than 60 years, and systolic blood pressure ≥ 150 or diastolic ≥ 90 in general population ≥ 60 years. Blood pressure measurements were taken with a mercury

sphygmomanometer. Measurements were made to the nearest 2mmHg, in the sitting position with the arm supported, and repeated after 5 minutes' rest if the first recording is high. Two measurements at each visit were taken. Transthoracic echocardiographic examination was performed by an expert cardiologist in the left lateral position. Standard M-mode, 2-Dimensional and Doppler Echocardiograph were performed using (GE brand, Vivid E9, model 2012) echocardiography machine. All diameters were measured according to established standards of the American Society of Echocardiography (14) .Based on the results of the echocardiographic examination, the study sample was classified into two groups; Group I (patients with LVH) and Group II (patients with non-LVH). Hemodynamic, biochemical and echocardiographic parameters were measured in both groups. The data were collected by interviewing the patients using a questionnaire designed by the researchers. The questionnaire included information about socio-demographic data, hypertension and some risk factors (like hyperlipidemia, IHD, and obesity).

Ethical considerations

The study protocol was approved by the ethics committee of the College of Medicine of Hawler Medical University. This study was conducted by using an informed verbal consent from the patients prior to participation in the study. The purpose of the study was carefully explained to each patient.

Statistical analysis

Data were analyzed using the statistical package for social sciences (SPSS, version 19). Student's t test for two independent samples was used to compare means. Correlation coefficient (r) was obtained to demonstrate the correlations between variables. A 'P' value of ≤ 0.05 was considered as statistically significant.

Results

A total of 150 hypertensive patients were enrolled in this study, 80 of them (53.3%) were females. High UA level was presented in 38 patients. The frequency of hyperuricemia in this study was 25.3 %. Based on the results of echocardiographic examination, LVH was present in 78 patients (52%), 25 of them (32 %) had hyperuricemia. Many significant differences were found between LVH and non-LVH groups concerning basic characteristics and biochemical measures. The means of age, SBP, DBP, BU, SC, TC and serum UA levels were significantly higher in LVH patients than those in non-LVH patients (P= 0.007,0.001, 0.024, <0.001, 0.012,0.009 and< 0.001 respectively), as shown in Table 1.

Table (1):- Comparisons between the means of the two study groups regarding basic characteristics and clinical variables

Total patients (N=150)					
Variables	**Group I (LVH) patients N=78**		**Group II (non-LVH) patients N=72**		**p**
	Mean	**SD**	**Mean**	**SD**	
Age (year)	54.6	10.1	50.5	11.4	**0.007**
BMI (kg/m2)	28.42	4.17	26.8	4.59	0.369
SBP (mmHg)	158.2	43.9	140.7	17.11	**0.001**
DBP (mmHg)	95.6	9.9	91.4	9.3	**0.024**
HT duration	5.2	3.1	4.7	3.8	**<0.001**
BU (mg/dl)	37.38	9.69	32.27	7.64	**0.012**
SC (mg/dl)	0.97	0.23	0.82	0.19	**0.009**
Cholesterol(mg/dl)	198.73	33	190.5	45	**<0.001**
TG (mg/dl)	162.5	113.7	156.6	106.8	0.78
UA (mg/dl)	6.15	1.06	5	1.37	**0.001**
Patients with hyperuricemia %	25 (32%)		13 (18%)		**<0.001**

Regarding echocardiographic parameters, the means of IVS thickness, PW thickness, LVM, LVMI and relative wall thickness (RWT) were also significantly higher in LVH patients than those in non-LVH patients (All P=0.001) as shown in Table 2.

Table (2):- Comparison between the means of the two study groups regarding echocardiographic parameters.

Total patients (N=150)					
Variables	**Group I (LVH) patients N=78**		**Group II (non-LVH) patients N=72**		**P value**
	Mean	**SD**	**Mean**	**SD**	
IVS: mm	13.77	1.43	9.82	0.78	**<0.0001**
PW: mm	13.09	1.51	9.37	0.62	**<0.0001**
Left atrium: mm	33.68	4.99	31.6	3.81	**0.027**
LVM: gm	250.35	52.16	166.22	26.87	**<0.0001**
LVMI: gm	135.3	29.05	91.6	12.11	**<0.0001**
RWT:	0.56	0.08	0.38	0.05	**<0.0001**

When comparing both groups in relation to serum UA levels, many significant differences were found. The means of age, SBP, DBP, BU, SC and lipid profile were significantly higher in hyperuricemic patients compared to patients without hyperuricemia (P= 0.001, 0.001, 0.01, 0.001, <0.001 , 0.001 and < 0.001 respectively), as shown in table 3.

Table (3):- Comparisons between the means of the basic characteristics and clinical variables of hypertensive patients with and without hyperuricemia.

Total patients (N=150)					
Variables	**With Hyperuricemia N=38**		**Without hyperuricemia N=112**		**p**
	Mean	**SD**	**Mean**	**SD**	
Age (year)	54.7	11.1	50.9	9.4	**0.001**
BMI (kg/m2)	28.2	3.7	27.3	4.5	0.69
SBP (mmHg)	156.9	17.5	144.3	17.11	**0.001**
DBP (mmHg)	94.4	9.9	92.6	9.3	**0.01**
HT duration (year)	5.2	4.4	4.7	3.8	**0.0001**
BU: mg/dl	38.48	10.69	31.2	7.64	**<0.001**
SC: mg/dl	1.06	0.3	0.79	0.2	**<0.001**
Cholesterol: mg/dl	200.3	33	188.6	45	**<0.001**
TG: mg/dl	160.19	56.3	155.6	36.8	**0.001**
UA: mg/dl	7.64	0.3	4.46	1.27	**<0.001**

Regarding echocardiographic parameters, the means of IVS thickness, LA, LVM, LVMI and RWT were significantly higher in hyperuricemic patients than those without hyperuricemia (P= <0.0001,<0.0001, 0.004 and <0.0001 respectively), as shown in Table 4.

Table (4):- Comparisons between the means of the echocardiographic parameters of hypertensive patients with and without hyperuricemia

Total patients (N=150)					
Variables	**With Hyperuricemia N=38**		**Without hyperuricemia N=112**		**P value**
	Mean	**SD**	**Mean**	**SD**	
IVS: mm	12.41	2.19	11.09	0.78	**<0.0001**
PW: mm	11.44	1.8	11	1.6	**<0.0001**
Left atrium: mm	33.75	4.98	31.45	5.1	**0.004**
LVM: gm	230.5	32.6	185.4	52.87	**<0.0001**
LVMI: gm	125.4	40.05	104.6	22.11	**<0.0001**
RWT: mm	0.50	0.09	0.44	0.05	**<0.0001**

Discussion

In the present study, the frequency of hyperuricemia was 25.3%, and it was significantly higher in group I [patients with LVH, 25 out of 78; 30 %] than in group II [patients without LVH, 13 out of 72; 18%]. The prevalence of hyperuricemia was different from country to another. In china, the prevalence was 14.1% (15), while in Switzerland it was 35.2% (16) .In hypertensive Nigerian patients the prevalence was 46.9% (17), while in hypertensive Taiwan patients it was 43% (18). Studies in Iraq report varying prevalence rates of hyperuricemia among hypertensive patients. The prevalence was ranging from 19% in Karbala city (19) to 52% in Ramadi city (20).The frequency of hyperuricemia in this study was within the above mentioned range. In patients with primary hypertension, LVH is ranged from 12 to 70%, depending largely on the cut-off values used to determine LVH and the patient selected criteria (21). The frequency of LVH in the current study was 52 %. This result was similar to other studies. Hyperuricemia is frequently encountered in hypertensive patients (22) and recent reports show new findings of a relationship between UA and LVH regardless of the presence of hypertension (23) or other potential confounding factors, including DM and dyslipidemia (24). Iwashima et al (7) also demonstrated that the combination of hyperuricemia and LVH is an independent and powerful predictor of cardiovascular disease. High serum uric acid (SUA) is linked with dyslipidemia (25, 30). Dyslipidemia and hypertension co-exist, and they had an additive effect on the cardiovascular system (26). In this study, patients with hyperuricemia had higher

systolic and diastolic BP measurements, higher TC and TG levels than patients with normal SUA level. These results are consistent with other studies. Todd et al (2006) showed the same results (27). Another study observed that high SUA level was associated with high TC, triglyceride, LDL and carotid intima media thickness in hypertensive patients compared to healthy control subjects (28).These results suggest that higher SUA levels are associated with atherogenesis. These studies conclude that high SUA level is a sensitive marker of risk for CVD. The close relationship between uric acid and left ventricular geometry (represented by LVM, LVMI and RWT) in the present study was observed by many other studies, in Japan (3, 7, 29) ,china (15) and Italy (31) .While these studies showed a significant correlation between SUA and echocardiographic LV mass in hypertensive male patients ,other studies, in contrast, didn't show such association, or the association was observed only in females and not in both genders. These studies mentioned that age and sex might affect the SUA levels in hypertensive patients .They assumed that postmenopausal women had higher SUA than premenopausal women. Ofori and Akpa (2015) from Nigeria found that the association between SUA and LV geometry was stronger in women than in men (17). Same results were found by Rodrigues et al (2011) in Brazil (32) and in The LIFE study (33).

Conclusion

In this study, high SUA level was common in hypertensive patients and it was positively associated with left ventricular hypertrophy and dyslipidemia.

Recommendations

Large scale prospective studies in the future are needed to evaluate whether lowering uric acid among hypertensive patients will be beneficial in regressing LVH in this group.

Conflicts of interest: The author report no conflicts of interest

References

1.Global Atlas on Cardiovascular Disease Prevention and Control. Mendis S, Puska P, Norrving B editors. World Health Organization (in collaboration with the World Heart Federation and World Stroke Organization), Geneva 2011.

2. Global Disparities of Hypertension Prevalence and Control A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation. 2016;134:441–450.

3-. World Health Organization: World Health Statistics 2012. Part II ، Highlighted Topics. In Geneva: WHO Press; 2012:34.

4- Bombelli M, Facchetti R, Carugo S, Madotto F, Arenare F, Qurati-Trevano F, et al. Left ventricular hypertrophy increases cardiovascular risk independently of in-office and out-of-office blood pressure values. J hypertens. 2009; 27:2458-64.

5- Choi HK, Mount DB, Reginato AM. Pathogenesis of gout. Annals of Internal Medicine 2005; 143(7):499-516.

6- Conen D, Wietlisbach V, Bovet P, Shamlaye C, Riesen W, Paccaud F, et al.Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country .BMC public health,2004;4:9.

7- Iwashima Y, Horio T, Kamide K, Rakugi H, Ogihara T, Kawano Y. Uric acid, left ventricular mass index, and risk of cardiovascular disease in essential hypertension. Hypertension 2006; 47:195-202.

8- Dahlof B, Devereux R, de Faire U, Fhyrquist F, Hender T, Ibsen H, et al. The losartan intervention for Endpoint reduction (LIFE) in hypertension study: Rationale,

design, and methods. The LIFE study Group. Am J Hypertens 1997;10:705-13.

9- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010;33(suppl 1):S62–S69.

10- Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum serum creatinine. Nephron 1976;16:31-41.

11- Nader Rifai and G. Russell Warnick. Lipids, lipoproteins, apolipoproteins and other cardiovascular risk factors. Teitz text book of clinical chemistry. 2006.4th Edition. Section IV. Chapter 26. Pages 943-48.

12- National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults- the evidence report. Obes Res 1998; 6 suppl 2:51-209.

13- Paul AJ, Suzanne O, Barry LC, William CC, Cheryl DH, Joel H, et al. Evidence-Based Guideline for the Management of High Blood Pressure in Adults. Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014; 311(5):507- 20. International Journal of Medical and Health Research 8

14- lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, Developed in conjunction with the European Association of Echocardiography, a branch of The European Society of Cardiology. J Am Soc Echocardiogr. 2005; 18:1440-63.

15- Fan XH, Sun K, Wang YB, Dang AM, Zhou XL, Zhang HM, et al. Prevalence and associated risk factors of hyperuricemia in rural hypertensive patients. Zhonghua Yi Xue Za Zhi 2009; 89(38):266-70..

16- Ofori SN, Apaka M. Relationship between uric acid and left ventricular mass and geometry in Nigerian patients with untreated essential hypertension. Nigerian Journal of cardiology 2015;Vol 12;2:129-135.

17- Lin CS, Lee WL, Hung YJ, Lee DY, Chen KF, Chi WC, et al. Prevalence of hyperuricemia and its association with antihypertensive treatment in hypertensive patients in Taiwan. Int J Cardiol. 2012; 156(1):41-6.

18- El-Yassen HD, Al-sharifi ZA, Al-Jebuori S. Prevalence of hyperuricemia and its correlation with cardiovascular risk factors in Iraqi subjects of Karbala city. Fac Med Baghdad 2012; 54:1.

19- Atia MM. Hyperuricemia, is it a cause or an effect of hypertension? A study in Ramadi city, Iraq. Al-Anbar Medical Journal. 3(1).

20- Okin PM, Devereux RB, Jern S, Kjeldsen SE, Julius S, Nieminen MS, et al.: Losartan Intervention for Endpoint reduction in hypertension Study Investigations. Regression of electrocardiographic left ventricular hypertrophy by losartan versus atenolol: The Losartan Intervention for Endpoint reduction in Hypertension (LIFE) Study. Circulation 2003; 108:684-90.

21- Johnson RJ, Feig DI, Herrera-Acosta J, Kang DH. Resurrection of uric acid as a causal risk factor in essential hypertension. Hypertension 2005; 45:18-20.

22- Mitsuhashi H, Yatsuya H, Matsushita K, Zhang H, Otsuka R, Muramatsu T, et al. Uric acid and left ventricular hypertrophy in Japanese men. Circ J. 2009; 73: 667-72.

23- Ichihara Y, Sugino M, Hattori R, Anno T, Mizuno Y, Yokoi M, et al. Relation of electrocardiographic left ventricular hypertrophy with and without T-wave changes to systemic blood pressure, body mass, serum lipids and blood glucose levels in Japanese men. Am J Cardiol. 1997; 15(80):730-35.

24-.Maxwell AJ, Bruinsma KA. Uric acid is closely linked to vascular nitric oxide activity: Evidence for mechanism of

association with cardiovascular disease. J Am Coll. Cardiol. 2001;38:1850-58.

25- Vancea C, Serban C, Mozos I, Susan L,Pacurari A, Romosan I. Lipid metabolism parametersand renal function in hypertensive elderly patients. Annals of RSCB 2008;14;2:226-230.

26- Todd SP, Gumieniak O, Williams GH, Sparrow A, Vokonas PS, Gaziano M, et al. Uric acid and the development of hypertension. Hypertension American Heart Association 2006;48:1031.

27-Modagan P, Dr.Meera,Dr. Suntharavadivelu. Uric acid as a mediator of endothelial dysfunction in hypertension. IJRPBS 2013;vol 4(1):106-112.

28.Yoshimura A, Adachi H, Hirai Y, Enomoto M,Fukami A,Kumagai E, et al. Serum uric acid is associated with left ventricular mass index in males of a general population. Int Heart J 2014.

29-Nan H, Qiao Q, Dong Y, Gao W, Tang B, Qian R, et al. The prevalence of hyperuricemia in a population of the coastal city of Qingdao, China. J Rheumatol 2006;33(7):1346-50.

30- Rinadi ER, Bentivenga C, Cosentino E, Corvaglia S, Rosticci M, Magnani L, et al. Correlation between serum uric acid and left ventricular mass in essential hypertension. Ann Rheum Dis 2015;74:773-774.

31- Rodrigues SL, Baldo MP, Capingana DP, Magalhaes P, Dantas EM, Molina M del C, et al. Gender distribution of serum uric acid and cardiovascular risk factors: Population based study. Arq Bras Cardiol 2012;98(1):13-21.

32- kjeldsen SE, Dahlof B, Devereux RB,Julius S, Aurup P, Edelman J, et al. LIFE (Losartan Intervention for Endpoint Reduction) study group. Effects of losartan on cardiovascular morbidity and mortality in patients with isolated systolic hypertension and left ventricular hypertrophy: A Losartan Intervention for Endpoint Reduction (LIFE) sub-study. JAMA 2002;288:1491-8.