International Journal of Medical and Health Research
ISSN: 2454-9142, Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 2; Issue 8; August 2016; Page No. 04-08

The impact of gender on serum uric acid levels in hypertensive patients with left ventricular hypertrophy in Erbil city-Iraq

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Abstract

Background and objectives: Serum uric acid (UA) level is frequently elevated in hypertension and its level tends to vary with gender. The objective of this study was to evaluate the impact of gender on serum uric acid levels in hypertensive patients with left ventricular hypertrophy (LVH) in Erbil-Iraq.

Patients and methods: A total of 130 consecutive adult patients presenting with essential hypertension were included. They were classified into two groups; Group I (patients with LVH) and Group II (patients with non- LVH). The effects of gender on serum uric acid level were evaluated in both groups.

Results: High UA level was present in 29 patients (22.3%), 17 of them (58.6%) were males. Serum UA level was significantly higher in male and female patients with LVH compared to those in non-LVH patients. The means of serum UA, interventricular septum, posterior wall, and left ventricular mass were significantly higher in male patients with LVH compared to those in female patients with LVH.

Conclusions: High UA level was more common in male hypertensive patients than females and despite it was positively associated with Left ventricular (LV) mass and abnormal LV geometry in both genders; but its effect was greater in males than in females.

Keywords: Uric acid; hypertension; left ventricular hypertrophy

Introduction

Uric acid (UA) is produced in the terminal stage of purine metabolism catalyzed by xanthine oxidase, and is a primary cause of gout[1]. Hypertension is a common risk factor for cardiovascular disease (CVD) [2], and the cardiovascular prognosis in patients with hypertension depends not only on the level of blood pressure (BP), but also on the presence of associated risk factors. Many epidemiological studies have suggested that serum UA is a risk factor for CVD. [3] Some studies found that serum UA levels to be independently associated with increased CV morbidity and mortality, but only in women[3] while other studies suggested a significant correlation in men, but not women[4]. An elevated blood level of UA was reportedly associated with left ventricular hypertrophy (LVH) in hypertensive patients [5, 6]. The development of LVH is highly correlated with systolic hypertension [7] and is considered a risk factor for cardiovascular events [8] Increased left ventricular mass because of essential hypertension has been reported in men and women, but whether or not there is a gender difference in the association of serum UA level with LV mass has not been previously explored. Up to our knowledge, there was no previous study done regarding the same subject in Erbil city. The objective of this study was to find out the effect of gender on the level of serum UA in a sample of hypertensive patients with LVH in Erbil city.

Patients and Methods

This cross-sectional study was conducted in Rizgary teaching hospital between September 2015 and April 2016. A total of 130 consecutive patients presenting with essential 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), diabetes mellitus, malabsorption and patients on medications that interfere with UA levels like diuretics or xanthines.

All patients were assessed by a detailed history, physical, and echocardiographic examinations to document presence of hypertension and/or left ventricular hypertrophy. Fasting venous blood samples were drawn to measure the serum level of uric acid for each patient. 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.

Based on recommendations of the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) [9], 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 [10]. LV mass (LVM) was calculated according to the Devereux formula [11]: LVM=1.04[(LVDd + IVSth +PWT) ^{3}–(LVDd) ^{3}]-13.6.Thereafter, LV mass index(LVMI) was obtained by the following formula:

LVM/body surface area (g/m^2) [12]. LVH was defined when the LVMI exceeds 134 grams in men and 110 grams in women per meter square body surface area (m^2 BSA).

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, risk factors (like hyperlipidemia, IHD, obesity, family history, others), and history of smoking and alcoholism.

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 of data

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. A 'P' value of ≤ 0.05 was considered as statistically significant.

Results

A total of 130 hypertensive patients were enrolled in this study, 77 of them (59.2%) were females. The means (±SD) of the age, SBP, DBP, hypertension duration and serum UA levels of the present sample were 53.66±11.38 years, 150.8±15mmHg, 92.72±9.1 mmHg, 3.4±3.4 years, 5.1±1.5 mg/dl, respectively. Other baseline characteristics, biochemical measures and echocardiographic features of the study sample are shown in Table1.

High UA level was present in 29 patients (22.3%), 17 of them (58.6%) were males. Based on the results of echocardiographic examination, LVH was present in 64 patients (53.8%), 37 of them (57.8%) were females. In hypertensive male patients, LVH was present in 27 patients (50.9%).No significant differences were found between LVH and non-LVH groups concerning baseline characteristics, apart from significant high mean SBP in male patients with LVH (p=0.048). Blood urea, serum creatinine, and UA were significantly higher in LVH patients than those in non-LVH patients (P=0.01, 0.007, 0.02, 0.01 and 0.01 respectively). IVS, PW, LVM, LVMI and RWT were also significantly higher in LVH patients than those in non-LVH patients (All P=0.001) as shown in Table 2.

In hypertensive female patients, LVH was present in 37 patients (48%). The means of SBP and HT duration were significantly higher in female patients with LVH than those in non-LVH (P=0.005 and 0.001, respectively). BU, SC and UA levels were significantly higher in LVH patients than those in non-LVH (P=0.001 for all). The means of EF, IVS, PW, LVM, LVMI and RWT were significantly higher in LVH patients (for EF P=0.03 and 0.001 for the others), as shown in Table 3.

In inter-gender comparisons between LVH positive patients, there were no significant differences in all baseline characteristics. BU, SC and UA levels were significantly higher in male patients with LVH than those in LVH female patients (P=0.012, 0.009 and 0.001 respectively). IVS, PW and LVM were significantly higher in male patients with LVH than those in LVH female patients with LVH (P=0.047, 0.03 and 0.05 respectively), as shown in Table 4.

When comparing both genders in relation to high UA levels, hyperuricemia was common (17 out of 29; 58.6%) in male patients compared to female patients (12out of 29; 41.4%). The means of BU and SC were significantly higher in male patients compared to female patients (P=0.03 and 0.006 respectively). IVS, LVM and LVMI were significantly higher in male patients than those in females (P=0.05, 0.04 and 0.046 respectively), as shown in Table 5.

Table 1: Basic characteristics of study sample.

Variable	Unit	Range	Minimum	Maximum	Mean	S.D
Age	year	62	23	85	53.66	11.38
BMI	Kg/m^2	24.2	21.7	45.9	28.11	4.74
SBP	mmHg	70	130	200	150.8	15.01
DBP	mmHg	65	70	135	92.72	9.13
HT duration	year	14.9	0.1	15	3.46	3.42
BU	mg/dl	35	16.0	51.0	31.26	8.44
SC	mg/dl	0.93	0.40	1.33	0.81	0.20
UA level	mg/dl	6.10	2.10	8.20	5.17	1.50
EF	%	40	50	90	65.27	7.95
IVS	mm	11	9	20	11.98	2.38
PW	mm	10	8	18	11.44	2.27
LA	mm	30	25	55	33.45	5.32
LVM	g	504	110	614	209.5	72.66
LVMI	g/m^2	286	57	343	113.2	37.6
RWT		0.68	0.29	0.97	0.49	0.12

Table 2: Associations between LVH and different measures among male patients.

Male patients only (N=53)					
Variables	Group I (LVH) N=27		Group II (Non-LVH) N=26		p
	Mean	SD	Mean	SD	
Age	59.72	10.99	54.25	13.25	0.11
BMI	28.51	3.49	27.85	4.70	0.56

SBP	156	17.55	148.3	11.20	0.048
DBP	94.00	11.81	91.71	4.18	0.34
HT duration	3.79	4.33	2.31	2.14	0.11
BU	37.38	9.6	30.18	7.28	0.01
SC	0.97	0.23	0.82	0.15	0.007
UA	6.35	1.06	5.47	1.3	0.01
EF	64.56	8.79	63.82	6.09	0.72
IVS	14.74	1.81	10.39	0.87	0.001
PW	13.78	1.67	9.92	0.76	0.001
Left atrium	33.96	6.23	33.76	5.04	0.89
LVM	273.6	81.22	177	29.87	0.001
LVMI	141.2	47.28	94.39	14.25	0.001
RWT	0.59	0.11	0.41	0.05	0.001

Table 3: Associations between LVH and different measures among Female patients.

Female patients only (N=77)					
Variables	**Group I (LVH) N=37**		**Group II (Non-LVH) N=40**		**p**
	Mean	**SD**	**Mean**	**SD**	
Age	55.43	9.92	47.83	8.94	0.001
BMI	28.98	5.61	27.25	4.55	0.14
SBP	155	14.99	145.5	13.9	0.005
DBP	93.38	9.2	92	9.85	0.52
HT duration	4.74	3.81	2.89	2.77	0.01
BU	32.27	7.64	26.96	6.84	0.001
SC	0.82	0.19	0.68	0.13	0.001
UA	5.3	1.37	4.11	1.31	0.001
EF	68.05	9.66	64.15	6.29	0.03
IVS	13.91	1.55	9.85	0.7	0.001
PW	12.9	1.61	9.43	0.59	0.001
Left atrium	34.22	6.04	32.18	3.88	0.08
LVM	241.9	71.06	154.8	14.27	0.001
LVMI	135.7	36.08	88.15	8.55	0.001
RWT	0.57	0.1	0.4	0.05	0.001

Table 4: Associations between gender and different measures among LVH positive patients.

LVH positive patients (N=64)					
Variables	**Male patients N=27**		**Female patients N=37**		**p**
	Mean	**SD**	**Mean**	**SD**	
Age	59.72	10.99	55.43	9.92	0.11
BMI	28.51	3.49	28.98	5.61	0.71
SBP	156	17.55	155	14.99	0.82
DBP	94	11.81	93.38	9.2	0.81
HT duration	3.79	4.33	4.79	3.81	0.36
BU	37.38	9.69	32.27	7.64	0.012
SC	0.97	0.23	0.82	0.19	0.009
UA	6.35	1.06	5.3	1.37	0.001
EF	64.56	8.79	68.05	9.66	0.15
IVS	14.74	1.81	13.91	1.55	0.047
PW	13.78	1.67	12.9	1.61	0.03
Left atrium	33.96	6.23	34.22	6.04	0.75
LVM	273.6	81.22	241.9	71.06	0.05
LVMI	141.2	47.28	135.7	36.08	0.6
RWT	0.59	0.11	0.57	0.10	0.62

Table 5: Comparison between the means of basic, biochemical, and echocardiographic measurements of male and female patients with high UA levels.

patients with high UA levels only (N=29)					
Variables	**Male patients N=17**		**Female patients N=12**		**p**
	Mean	**SD**	**Mean**	**SD**	
Age	62.44	12.07	55.08	9.92	0.09
BMI	26.70	3.39	27.48	4.28	0.59
SBP	156.75	17.44	157.08	17.64	0.96
DBP	93.94	10.74	95	9.04	0.78
HT duration	4.33	4.43	4.26	3.29	0.96

BU	38.49	10.58	30.48	10.47	0.03
SC	1.06	0.21	0.80	0.23	0.006
UA	7.36	0.47	7.32	0.31	0.81
EF	62.88	7.80	68.08	6.74	0.07
IVS	13.81	2.19	12.58	2.06	0.048
PW	12.75	2.46	12.29	2.24	0.61
Left atrium	33.75	4.98	33	5.75	0.71
LVM	261.13	113.57	192.58	58.05	0.04
LVMI	138.81	64.23	109.41	27.79	0.046
RWT	0.54	0.09	0.59	0.13	0.27

Discussion

In the present study, the overall prevalence of hyperuricemia was 22.3%, and it was higher in men (17 out of 53; 32 %) than in women (12 out of 77; 15.58%).The prevalence of hyperuricemia was different from country to country. In china, the prevalence was (14.1%) and it was higher in men than in women [13], while in Switzerland men patients it was (35.2%) [14] In hypertensive Nigerian patients the prevalence (46.9%) was higher in women [15], while in hypertensive Taiwan females it was (43%) [16] Studies in Iraq report varying prevalence rates of hyperuricemia among hypertensive patients. The prevalence was ranging from 19% (in Karbala city) [17] to 52% (in Ramadi city) [18]. The prevalence in this study is within the above mentioned range. In patients with essential hypertension, LVH is ranged from 12 to 70%, depending largely on the measurement technique used [19]. The prevalence of LVH in this study was 53.8%. This result is within the above mentioned range. Hyperuricemia is frequently encountered in hypertensive patients [20] and recent reports show new findings of a relationship between UA and LVH regardless of the presence of hypertension [21] or other potential confounding factors, including DM and hyperlipidemia [22]. Iwashima *et al* [6] also demonstrated that the combination of hyperuricemia and LVH is an independent and powerful predictor of cardiovascular disease. In the present study and in both genders, hyperuricemia was common among those who had LVH compared to those who did not and the mean UA level was significantly higher among LVH male patients. This finding is consistent with many previous studies [4, 13-15].

The relationship between UA level and CV changes can be explained by many mechanisms. In one hand, UA may induce LVH through an activation of the rennin-angiotensin-aldosterone system which generates hypertrophy and hyperplasia of myocytes and fibrosis of the heart [23], on the other, through an association between increased UA concentrations and oxidative stress, endothelial dysfunction [24] and inflammation [25] which promotes cardiac hypertrophy.

When comparing both genders in relation to high UA level, the same correlation was founded between high UA levels and IVS, LVM and LVMI but only in male patients. The results of the present study provide evidence that serum UA levels are correlated more with echocardiographic LV mass in male hypertensive patients than those in females. These findings indicate a sex difference in the association of UA with LV geometry in our sample. These results are consistent with other studies [4, 13-15, 21] and against others [3, 26]

Conclusion

In this study, high UA level was more common in male Hypertensive patients than females and despite it was positively associated with LV mass and abnormal LV geometry in both genders; but its effect was greater in men than in women.

Recommendation

Large scale prospective studies needed to evaluate the impact of hyperuricemia in hypertensive patients in the development of LVH and its relation to gender.

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