



Prevalence of Hyperuricemia and its Association with Other Cardiovascular Risk Factors in Adult Yemeni People of Sana'a City

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Abstract

Objective: Hyperuricemia is a metabolic problem that has become increasingly common worldwide over the past several decades. Its prevalence is increased in both advanced and developing countries including Yemen. The aim of this cross sectional study was to investigate the prevalence of hyperuricemia in sample of Yemeni adult individual and its relationship to certain cardiovascular risk factors namely obesity, hypertension, serum glucose, total cholesterol, high serum triglyceride, Low High Density Lipoprotein (HDL-C) and high Low Density Lipoprotein (LDL-C).

Methodology: A sample of 600 adult Yemeni people aged equal or over 18 years was randomly chosen to represent the population living in Sana'a City during a period of 16 months from April 2017 to August 2018. All the study groups undergo full clinical history and examination includes measurement of BP and BMI, WC and the following laboratory investigation (FBS, Basal serum uric acid level, total cholesterol, serum TG, HDL and LDL).

Results: The prevalence of hyperuricemia in this study was 8.8% (11.6% male and 6.4% female). The serum uric acid level in this study was significantly correlated with age, Waist Circumference (WC), SBP, DBP, FBS, T-cholesterol, TG and LDL but not with HDL.

Conclusion: There is strong relationship between serum uric acid level and other cardiovascular risk factors.

Keywords: Hyperuricemia, Dyslipidemia, BMI, FBS.

Abbreviations: HDL- High Density Lipoprotein, LDL- Low Density Lipoprotein, WC- Waist Circumference, GBD- Global Burden of Diseases, CDC- Cardiovascular Disease, BMI- Body Mass Index, SUA- Serum Uric Acid, FBS- Fasting Blood Sugar, IFG- Impaired Fasting Glucose, T.Ch- Total Cholesterol, SPSS- Social Package of Statistical Science, NO- Nitric Oxide.

Introduction

Hyperuricemia is metabolic problem that has become increasingly worldwide over the past several decades and it's the most risk factor for gout [1]. Hyperuricemia is defining as serum urate level greater than 6mg/dl in women and 7mg/dl in men, above this concentration serum urate supersaturates in body fluid and is prone to crystallization and subsequent deposition in the tissue [2]. The association of hyperuricemia and gout with other medical condition such as hypertension, chronic kidney diseases, dyslipidemia and other cardiovascular diseases has been recognized for over 100 years [3]. The prevalence of hyperuricemia has been increased in recent years, not only in advanced countries but also in developing countries along with the development with their economics [4]. Published population-based prevalence data of hyperuricemia were reported in 13 of the 21 Global Burden of Diseases (GBD) regions, and a total of 24 countries. In most part of Asia Hyperuricemia is relatively prevalent, but in East Asia it found to be most prevalent. Lowest percentage is seen in Papua New Guinea 1% and in Marshall Islands 85% is seen.

In Japan the high income Asian country Hyperuricemia has increased by five folds in time of two decades. There is no published population-based epidemiological studies on hyperuricemia were identified during the specified systematic review period [5]. Hyperuricemia can be caused by over production of urate which account of less than 10% of the cause such as high cellular turnover, genetic error and tumor lysis syndrome or far more commonly inefficient excretion by the kidney due to renal insufficiency of any cause or medication that impair renal urate clearance [6]. In numerous epidemiological studies since 1950 a positive association has been seen between serum uric acid and cardiovascular diseases such as ischemic heart disease and stroke [7,8]. However whether uric acid is independent risk factor for cardiovascular disease is still disputed as several studies has suggested that hyperuricemia is merely associated with cardiovascular disease because of confounding factors such as obesity, hypertension, dyslipidemia, use of diuretic and insulin resistance [9]. Obesity and central fat distribution were associated with hyperuricemia. Patients with central obesity have greater risk of hyperuricemia [4].

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There are many researches was conducted to evaluate the relationship between leptin hormone and the cluster of hyperurecemia in order to identify the pathogenic mechanism associating obesity with hyperurecemia. It was suggested that leptin could be a pathogenic factor responsible for hyperurecemia in obese patients [10]. The strong association between hypertension and hyperurecemia has been recognized for more than century. More than one large epidemiological studies published over the past 7 years have found that serum urate level predict later development of hypertension [11,12].

Experimental studies have reported that hyperurecemia induces systemic hypertension and renal injury via activation of renin angiotensin system and direct intery of uric acid into both endothelial and vascular smooth muscle cells, decreased neuronal nitric oxide synthase in the juxtaglomerular apparatus resulting in local inhibition of endothelial nitric oxide level, stimulation of vascular smooth muscle cell proliferation and stimulation of vasoactive and inflammatory mediators [13,14]. There is strong association between hypertriglycemia and hyperurecemia this association could be explained by insulin resistance as hypertriglyceridemia and hyperurecemia are suggested to be associated with insulin resistance syndrome [15].

The association of hypertriglyceridemia and hyperurecemia in patients with insulin resistance syndrome could be explained by accumulation of glycolytic intermediate and release of free fatty acid from adipose tissue [16]. The resemblance of hyperurecemia and the metabolic syndrome has led to the suggestion that the metabolic syndrome can be further expanded to include hyperurecemia [17]. A prospective study in Korea suggested that higher uric acid concentration predicted the incidence of hypertension and the development of metabolic syndrome and hyperurecemia has been considered as component of metabolic syndrome [18,19].

Material and method

This was across sectional population based study conducted in Sana'a city for a period of 16 months from April 2017 to August 2018, a sample of 600 adult Yemeni people (275 male and 325 female aged \geq 18 years) was randomly selected from those attending Al-Kuwait University Hospital and Consultation Clinic. All the participants in this study undergo complete clinical history (regarding their age, occupation, habit, any history of hypertension, diabetes mellitus, dyslipidemia and medication) Anthropometric measurement includes measurement of height, weight, waist circumference and systolic and diastolic blood pressure.

Height was measured with tapeline to the nearest.5cm and weight was measured with beam scale balance. Participants wore light clothing and were asked to remove shoes, heavy outer garments Body Mass Index (BMI: kg/m_2) was calculated from measured weight and height. BMI was classified as underweight ($<18.5 \text{ kg}/\text{m}_2$), normal ($18.5\text{-}25 \text{ kg}/\text{m}_2$), overweight ($25\text{-}30 \text{ kg}/\text{m}_2$) and obese ($>30 \text{ kg}/\text{m}_2$) by WHO criteria [20]. Waist circumference was manually measured on standing subjects with soft tape midway between the lowest rib and the iliac crest. Abdominal obesity was defined as WC \geq 90 cm (male) or WC \geq 80 cm (female) by IDF consensus [21].

Two blood pressure recording were obtained from the right arm of patients with slandered mercury sphygmomanometer in a sitting position after 10 min. of rest measurement were taken in 3-5 minutes interval and the mean values were calculated. Blood pressure was classified as normotensive (SBP $<$ 120 mmHg and DBP $<$ 80 mmHg), pre-hypertensive (SBP: 120-139 mmHg and/or DBP: 80-89 mmHg) and hypertensive (SBP \geq 140 mmHg and/or DBP \geq 90 mmHg) by the Seventh Report of the Joint National Committee on the Prevention,

Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) [22]. The American Diabetes Association criteria was used to classify FBG as normal glucose (FBG $<$ 5.6 mmol/L), Impaired Fasting Glucose (IFG) (FBG \geq 5.6 mmol/L \leq FBG $<$ 7.0 mmol/L), and diabetic (FBG \geq 7.0 mmol/L, Serum uric acid were measured [23]. Hyperurecemia is defined as serum uric acid level greater than 6.0mg/dl in women and 7.0 mg/dl in men. Dyslipidemia was classified according to ATP III, TG: Normal $<$ 1.69 mmol/L, Borderline high 1.69-2.26 mmol/L, High 2.26-5.65 mmol/L, Very high \geq 5.65 mmol/L; TC: Desirable $<$ 5.17 mmol/L, Borderline high 5.17-6.24 mmol/L, High \geq 6.24 mmol/L; HDL-C: High 1.56 mmol/L, Optimal 1.03-1.56 mmol/L, Low $<$ 1.03 mmol/L; LDL-C: Optimal $<$ 2.59 mmol/L, Near optimal 2.59-3.38 mmol/L, Borderline high 3.38-4.16 mmol/L, High 4.16-4.94 mmol/L, Very high \geq 4.94 mmol/L [24].

The results were analyzed by using (Social Package of Statistical Science) SPSS V.15 from LEAD Technologies Inc., USA. Basic characteristics of subjects are presented as mean and slandered deviation for quantities variables and as frequency and percent for qualitative variable. The total participants were divided into two groups according to the sex then there were divided into two mean groups according to serum uric acid level.

The prevalence of cardiovascular diseases risk factors among two groups were calculated and Chi-square test was used to detect the significance /The mean of uric acid in different categories of separated variable were determined and the comparison between the mean was achieved by independent t-test and one way ANOVA test. The relationships between parameters were examined by calculating person's correlation coefficient. For investigating for most effective factors on hyperurecemia such as blood pressure anthropometrical and biochemical (except UC) measurement were considered for Binary logistic regression P-value less than 0.05 was considered statistically significant.

Results

A study sample includes 600 person aged between 18-83 of them 275 (45.4%) were male and 325 (54.6%) were female. The prevalence of high serum uric acid level in the study group was 53 (8.8%) with no significant difference between male and female (**Table 1**) regarding the clinical and laboratory parameters in the study group BMI, WS, serum cholesterol, high TG, low high density lipoprotein, high LDL and high FBS were significantly higher in women than in men (17.2%, 35%, 43.3%, 41.2%, 19.3%, 53.8% and 26.4% vs 13.8%, 14.5%, 27.6%, 27.2%, 8.7%, 38.1% and 19.2% respectively, while the BP was significantly higher in men than women, also there was no significant difference between male and female regarding serum uric acid level.

Discussion

Hyperurecemia is increasingly common medical problem not only in the advanced countries, but also in the developing countries. The incidence of high serum uric acid is increased word wide with average of 20% of population having hyperurecemia and the serum uric acid level is increased with age. It has been described that hyperurecemia is associated with other cardiovascular risk factors such as obesity, dyslipidemia, hyperglycemia and hypertension [1-3]. Elevated serum uric acid levels are commonly seen in association with glucose intolerance, hypertension and dyslipidemia, a cluster of metabolic and hemodynamic disorders which characterize the so-called metabolic syndrome [25-29]. To our knowledge there is no data about the prevalence of hyperurecemia in Yemen so we decided to carry out this research in order to know the prevalence of hyperurecemia and its association with other cardiovascular risk factors in Yemeni population.

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Variable	Men=275	Women=325	Total=600	p-value
BM				
Lean	27 (9.8%)	36 (11%)	63 (10.5%)	0.05
Normal	125 (45.4%)	148 (45.5%)	273 (44.5%)	
Overweight	85 (30.9)	85 (26.1%)	170 (28.3%)	
Obese	38 (13.8%)	56 (17.2%)	94 (15.6%)	
WC				
Normal	235 (85.4%)	211 (64.9%)	446 (74.3%)	0
Obese	40 (14.5%)	114 (35%)	154 (25.6%)	
BP mm/Hg				
Normal	225 (81.8%)	231 (71%)	456 (76%)	0.003
High	50 (18.1%)	94 (15.5%)	144 (24%)	
SUA				
Normal	243 (88.3%)	304 (93.5%)	547 (91.1%)	0.185
High	32 (11.6%)	21 (6.4%)	53 (8.8%)	
FBS; mg/dl				
Normal	221 (80.3%)	239 (73.5%)	460 (85.7%)	0.05
IFG	28 (10.1%)	16 (4.9%)	44 (7.3%)	
Diabetes	26 (9.1%)	70 (21.5%)	96 (15.8%)	
T.Ch; mg/dl				
Normal	199 (72.3%)	184 (56.6%)	383 (63.8%)	0
High	76 (27.6%)	141 (43.3%)	217 (36.1%)	
TG; mg/dl				
Normal	200 (72.7%)	191 (58.7%)	391 (65.1%)	0
High	75 (27.2%)	134 (41.2%)	209 (34.8%)	
HDL; mg/dl				
Normal	251 (91.2%)	262 (80.6%)	513 (85.5%)	0
High	24 (8.7%)	63 (19.3%)	87 (12.8%)	
LDL; mg/dl				
Normal	170 (61.8%)	150 (46.8%)	320 (53.3%)	0.04
High	105 (38.1%)	175 (53.8%)	280 (46.6%)	

Note: SUA-Serum Uric Acid, FBS- Fasting Blood Sugar, IFG- Impaired Fasting Glucose, T.Ch- Total Cholesterol, TG- Triglyceride, HDL- High Density Lipoprotein, LDL- Low Density Lipoprotein.

Table 1: Shows the clinical and laboratory characteristics of the study group.

Variable	Hyperurecemic subject Mean ± SD	Normal subject Mean ± SD	P-value
Age	41.2 ± 11.6	38.4 ± 11.5	0.034
Systolic blood press	118.8 ± 11.2	114.8 ± 14.2	0.016
Diastolic blood press	79.9 ± 7.5	78.2 ± 8.6	0.091
BMI	25.4 ± 3.9	24.7 ± 5.4	0.207
WC	88.5 ± 13.4	84.4 ± 12.7	0.009
FBS (mg/dl)	113.2 ± 64.4	92.7 ± 38.7	0
T.Ch (mg/dl)	227.0 ± 52.0	184.1 ± 42.8	0
TG (mg/dl)	243.8 ± 116.7	131.2 ± 73.1	0
HDL (mg/dl)	58.5 ± 19.0	59.6 ± 19.4	0.605
LDL (mg/dl)	119.8 ± 48.9	98.6 ± 39.8	0

Note: Table 2 present comparing the mean of selected study parameters in relation to the uric acid level, it shows the mean of age, SBP, WS, fasting blood glucose, total cholesterol, TG and LDL were significantly higher within hyperurecemic study population in comparing to those with normal serum uric acid level, there were no significant difference in DBP, BMI and HDL between the two groups.

Table 2: The prevalence of both clinical and laboratory character of person with high and normal serum uric acid.

		Age	SBP	DBP	BMI	WS	FBS	T.CH	TG	HDL	LDL
SUA	Personal correlation	0.158**	0.138**	0.092*	0.097*	0.110*	0.159**	0.269**	0.392**	-0.035	0.146**
	Sig-(2-tailed)	0	0.001	0.03	0.021	0.017	0	0	0	0.411	0.001

*correlation is significant at the 0.05 level (2-tailed). **correlation is significant at the 0.01 level (2-tailed).

Note: Table 3 shows the simple correlation coefficients between serum uric acid levels and the various cardiovascular risk factors in the population. Uric acid was significantly positively correlated with age, SBP, FBS, TG, total cholesterol, LDL (P-value ≤ 0.01) and weak positive correlated with DBP, BMI and WC (P-value ≤ 0.05) while it was insignificantly correlated with HDL (P-value 0.411).

Table 3: Shows the correlation between the serum uric acid level and different cardiovascular risk factors.

The mean observations of the present study are the following; firstly the prevalence of hyperurecemia present in a good proportion in Yemeni peoples and it was insignificantly high in women than in men. Secondly significant correlation between serum uric acid the various cardiovascular risk factors were found.

The prevalence of hyperurecemia in the present study was 8.8%, which is mainly near to that reported in Saudi Arabia (9.3%), Iran (8%), Thailand (9-11%), Mexico (11%) and in Turkish (12%) which may be reflected to similar race and environmental factors. while it's lower than that found in Columbia (26.3%).

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Indian (25.8%), Taiwan (30.4%) and USA (21-22%) which may be attributed to the high economic state of these countries. Hyperuricemia was insignificantly higher in women (7.9%) than men (6.3%) which may be explained by high prevalence of obesity in women (BMI and WC was 17.2%, 35% in women VS 13.8% and 14.1% in men respectively). This finding was supported by study done in Saudi Arabia and but other studies are against this observation. Comparing hyperuricemic subject with those with normal serum uric acid level, those with hyperuricemia are older centrally obese, had high systolic blood pressure, high FBS, total cholesterol, triglyceride, and LDL [30-36] (Table 2).

In this study, multiple logistic regression results have further confirmed the association between metabolic abnormalities and high serum uric acid, and have conducted further stratified analysis on each metabolic abnormality-related indicator. Table 3 shows the simple correlation coefficients between serum uric acid levels and the various cardiovascular risk factors in the population. Our results have shown that high serum uric acid was significantly positively correlated with age, SBP, FBS, TG, total cholesterol, LDL (P-value ≤ 0.01) and weak positive correlated with DBP, BMI and WC (P-value ≤ 0.05) while it was insignificantly correlated with HDL (P-value 0.411) [35].

Elevation of the serum uric acid level has been known associated with major cardiovascular risk factors, such as hypertension, insulin resistance, dyslipidemia and obesity, which are hallmarks of metabolic syndrome [36-39]. Similar to other studies, in this study, individuals with hyperuricemia had higher prevalence of major cardiovascular risk factors, including dyslipidemia, hypertension and overweight. Uric Acid (UA) is a known endogenous scavenger, which provides a major part of the antioxidant capacity against oxidative and radical injury. However, at high levels, UA can shift from an antioxidant to a pro-oxidant factor (shuttle capacity), depending on the characteristic of the surrounding microenvironment (e.g., UA levels, acidity, depletion of other antioxidants, reduced Nitric Oxide (NO), availability) [40,41].

Accordingly, high UA values have been associated with metabolic syndrome, Cardiovascular Disease (CVD), and renal dysfunction, involving mechanisms that favor oxidative stress, inflammation, and endothelial dysfunction. The result of this study showed significant positive correlation were found between serum uric acid and several component of the metabolic syndrome such as higher WS, BP, TG and FBS (p-value ≤ 0.005) but there was insignificant negative correlation with HDL. Several possible pathophysiological mechanisms have been evoked to explain these associations including insulin resistance, the use of diuretics or impaired renal function accompanying hypertension [42-49].

Indeed the kidney seems to play an important role in the development of the metabolic syndrome. Insulin-resistant individuals secrete larger amounts of insulin in order to maintain an adequate glucose metabolism. The kidney which is not insulin-resistant responds to these high insulin levels by decreasing uric acid clearance, probably linked to insulin-induced urinary sodium retention. Insulin resistance may increase blood pressure directly via enhanced proximal tubular sodium reabsorption or indirectly by the sympatho-adrenal system [43-45]. Thereby, the kidney has been implicated as the potential link between muscle insulin resistance and compensatory hyperinsulinemia and the development of hyperuricemia and eventually hypertension.

Conclusion

Our study demonstrates an alarming high prevalence of hyperuricemia among Yemeni patients that increases the burden on overstrained Yemeni health system with uprising CVDs and other hyperuricemia related health problems e.g. hypertension, dyslipidemia DM.

There is also an urgent need to develop strategies for prevention, detection, and treatment of hyperuricemia that could contribute to decreasing the incidence of grave consequences such cardiovascular disease and chronic renal diseases.

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