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Research Article
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Hyperuricemia in Libyan Patients with Cardiovascular Diseases

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ABSTRACT

Hyperuricemia is a metabolic disorder characterized by elevation of uric acid (UA) in the blood. It is associated with a range of commodities including gout, cardiovascular diseases (CVDs), kidney disorders, metabolic syndrome, and diabetes, among others.

The goal of the study is to look into possible risk factors for hyperuricemia, specifically the possible impacts of age, gender, body mass index (BMI), diabetes, and the use of various antihypertensive drugs on the incidence of hyperuricemia in Libyan patients who also have cardiovascular disease.

In all, 59 patients with various CVDs were involved in the study. Each participant's sociodemographic and health-related lifestyle factors were recorded (age, BMI, diabetes, smoking, alcohol consumption). Serum urea, uric acid, triglycerides, serum creatinine, low density lipoprotein were all measured. Patient's complaint of hyperuricemia (urinary stones, arthalgia, arthritis, or asymptomatic) was also recorded.

Thirty-three women (54.9%) and twenty-six men (41.1%) with hyperuricemia and cardiovascular disease, ages 28–86, were recruited for the research. In 59.3% of cases, hypertension was the most prevalent cardiovascular illness, followed by hypertension/heart failure with 13.6%.

Hypertension was the most common cardiovascular disease (59.3%), followed by hypertension/heart failure (13.6%). The majority of patients with hyperuricemia (93.2%) had no complaints (asymptomatic), and kidney stones were recorded in only 6.8%. Unknown cause of hyperuricemia was reported in 49.2%, drug-induced in 45.8%, and renal causes in only 8.5%. The most frequently used drugs in these patients were thiazide diuretics, loop diuretics, and calcium channel blockers (23.7%, 22%, and 18.6%, respectively).This study adds to the growing body of research on the relationship between cardiovascular disease and hyperuricemia. Our results regarding the asymptomatic nature of hyperuricemia, the prevalence of diabetes and hypertension, and gender differences are consistent with previous studies. Our findings highlight the importance of regularly testing uric acid levels in patients with cardiovascular disease to avoid complications, even in the absence of symptoms.

Key words- *Hyperuricemia; Cardiovascular diseases; Uric acid.*

INTRODUCTION

Hyperuricemia (HU), characterized by elevated serum uric acid (SUA) levels, is a significant factor in the development of gout and is associated with various health conditions, including metabolic syndrome, diabetes, kidney stones, hypertension and other cardiovascular diseases. UA is the final result of purine metabolism. The kidneys primarily remove UA from the urine in order to maintain normal blood levels of UA. Therefore, metabolic disorders that lead to a decrease in renal excretion or an increase in purine synthesis may be the cause of the accumulation of UA in the blood.[1]

Serum uric acid (SUA) levels greater than 7 mg/dL are typically considered to indicate HU, with a lower limit of ≥5.7 mg/dL for women.[2]

According to Dalbeth et al. (2016), pathological HU brought on by a diet high in purines and fructose, genetic or environmental factors, excess production from hepatic metabolism and cell turnover, and renal or extra-renal under excretion that results in crystal precipitation in the kidneys, joints, soft tissues, and other organs.[3]

A growing body of research suggests that elevated UA levels may be an etiologic factor or an indicative marker in the pathophysiology of cardiovascular risk factors and diseases, including heart failure (HF), coronary artery disease (CAD), atrial fibrillation (AF), hypertension, and cardiovascular death.[4-6]

Evidence from the European study on cardiovascular risk prevention and management in daily practice (EURIKA) study suggests that, SUA levels are positively associated with 10-year risk of cardiovascular mortality in patients without evidence of cardiovascular disease but with at least one cardiovascular risk factor (i.e. dyslipidemia, hypertension, smoking, diabetes or obesity).[7] Even SUA

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levels within the upper normal range have been attributed to increase cardiovascular risk.[8,9]

Furthermore, recent research has found that HU is an independent risk factor for major cardiovascular events (MACE) including stroke and ischemic heart disease.[10,11]

Numerous factors, including endothelial dysfunction[12], renninangiotensin system activation[13], and inflammation[12,14], are involved in the complex relationship between HU and cardiovascular health.

Since there are not many local studies that show this relationship, we looked into the possible risk factors for HU, the effects of gender, age, BMI, diabetes, and the relationship between the use of various antihypertensive medications and the occurrence of HU in a group of Libyan patients with cardiovascular diseases and HU.

MATERIALS AND METHODS

2.1 *Study population and data collection*

In this study patients with cardiovascular diseases (CVDs) such as: hypertension, ischemic heart disease, arrhythmia, heart failure, and heart valve disease, and with HU (male; female), attending Al-Masarra Clinic in Tripoli for follow up and treatment were selected. We defined HU as >7.0 mg/Dl in men[2] and >6 mg/dL in women. A total of 59 patients were included in the study. We obtained the history of CVDs from all participants (age, body mass index, diabetes, smoking, alcohol consumption, complain, drugs used to treat CVDs, and treatment of HU). The World Health Organization (WHO) BMI classification was used to categorize patients into three groups: normal weight (BMI < 25.0 kg/m2), overweight (25.0 ≤ BMI < 30.0 kg/m^2), and obese (BMI ≥ 30.0 kg/m^2).

2.2 *Statistical analysis*

All data collected were statistically analyzed using descriptive statistics and inferential statistics were primarily used for the analysis.

Means and standard deviation were used for parametric and median quantitative variables with interquartile ranges for quantitative non parametric ranges. Qualitative variables were expressed as percentages. To compare qualitative variables χ^2 was used, whilst quantitative variables were compared with the Student›s *t*-test or the Mann–Whitney *U* test, depending on the normality of the variables.

Multiple linear regression analysis was calculated to predict the effect of age, gender, diabetes mellitus, triglycerides, LDL, BMI, serum creatinine, serum urate, cardiovascular disease, complain (symptomatic or asymptomatic), drugs used to treat cardiovascular disease, and probable causes of HU on serum uric acid levels.

Statistical analysis was performed with the SPSS version 22, and statistical significance was determined as $P<.05$. Excel Microsoft was used to generate graphs and tables.

RESULTS

A total of 59 patients with cardiovascular diseases and HU aged between 28- 86 years were enrolled in the study including 26 (41.1%) males and 33 (55.9%) females.

The mean age of the patients was (62.27 ± 13.08 years), with no significant difference between males and

females (62.15 ± 15.18 years and 62.36 ± 11.39 years, respectively; P= 0.952). Males and females did not significantly vary in terms of BMI, serum urea, serum uric acid, LDL, triglycerides, or HbA1c. Serum creatinine levels were the only significant variation between the sexes (Table 1).

Table 1: Characteristics of subjects included in the study

Variable	Male	Female	P-value
Age (years)	62.15 ± 15.18	62.36 ± 11.39	0.952
BMI (kg/m^2)	29.67 ± 5.82	31.53 ± 6.24	0.247
Serum uric acid (mg/dl)	7.8 (7.3-8.2)	7.4 (6.7-8.4)	0.138
Serum urea (mg/dl)	42.5 (35-68)	35.0 (29.0- 48.0)	0.069
Serum creatinine (mg/dl)	1.2٥ (1.0-1.6)	91 (0.8-1.2)	0.01
Triglycerides (mg/dl)	142 (126.8-181.8)	161 (133.5-207)	0.116
Low density lipoprotein (mg/dl)	94.81 ± 27.86	108.85 ± 34.27	0.096
HbA1c (%)	6.45 (5.8-7.8)	6.0 (5.6-8.0)	0.309

The study found that 20.3% of patients had normal BMI, 27.1% were overweight, and 52.6% were obese, with female patients being more likely to be obese.

Based on serum uric acid values, we categorized patients into three groups (≤7.0 mg/dL, 7.1-8.0 mg/dL, and ≥8.1 mg/dL). 100% males *vs* 60.61% females had significantly higher uric acid levels (P <0.001) at 7.1 to ≥8.1 mg/dL, indicating a gender difference (Table 2).

Table 2; Serum uric acid levels according to gender

mg/dl 7≥ mg/dl 7.1-8			Serum uric acid levels			Total
			mg/dl 8.1≤			
Gender	Male	Count	0	17	9	26
	Female	Count	13	10	10	33
Total		Count	13	**27**	**19**	59

A history of hypertension was present in 59.32% of the population, heart failure in 8.47%, and cardiac arrhythmia in 5.08%. Other prevalent issues were diabetes (49.15%), renal disease (6.77%), hypertension plus heart failure (13.56%), and hypertension plus valvular heart disease (VHD) (3.39%). 45.76% of instances of HU were drug-induced, 8.47% had a renal origin, and 49.15% had an unexplained etiology (Figure 1).

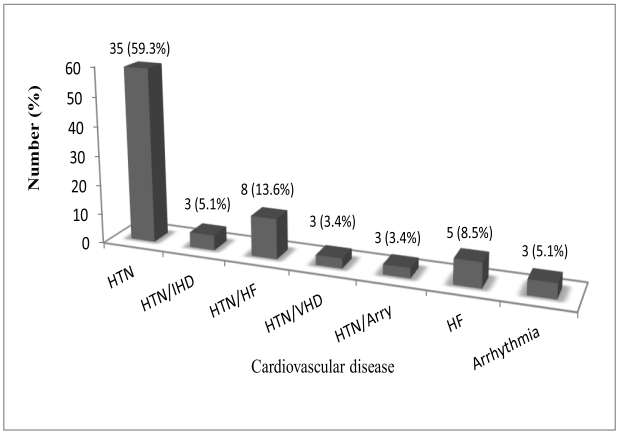

Figure 1: Prevalence of cardiac diseases in patients with hyperuricemia.

HTN: hypertension; IDH: ischemic heart disease; HF: heart failure; Arry: arrhythmia; VHD: valvular heart disease.

Thiazides, loop diuretics, beta blockers, calcium channel blockers (CCBs), angiotensin receptor blockers (ARBs), angiotensin converting enzyme inhibitors (ACEIs), and beta blockers were taken by 23.73%, 22%, 18.64%, and 6.78% of patients with HU and hypertension, respectively (Figure 2).

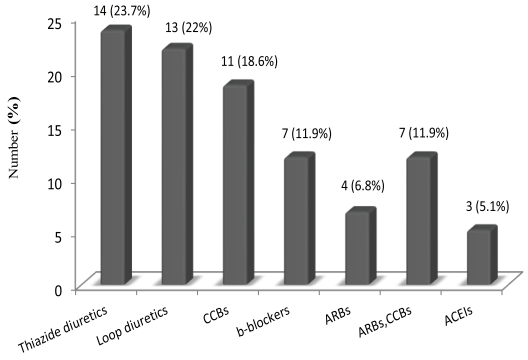

Figure 2: Drugs used to treat hypertension/cardiovascular disease

CCB: calcium channel blockers; b-blocers: beta-blockers; ARBs: angiotensin receptor blockers, ACEIs: angiotensin converting enzyme inhibitors.

The variability explained by the model of multiple linear

Table 3: Model summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change
1	.602[a]	.362	.160	.9556	.362	1.787	14	44	.072

regression test was 36.2% using the predictors (age, gender, BMI, complaint, diabetes, serum triglycerides, LDL, serum creatinine, HbA1c) and uric acid levels as the dependent variable (Table 3).

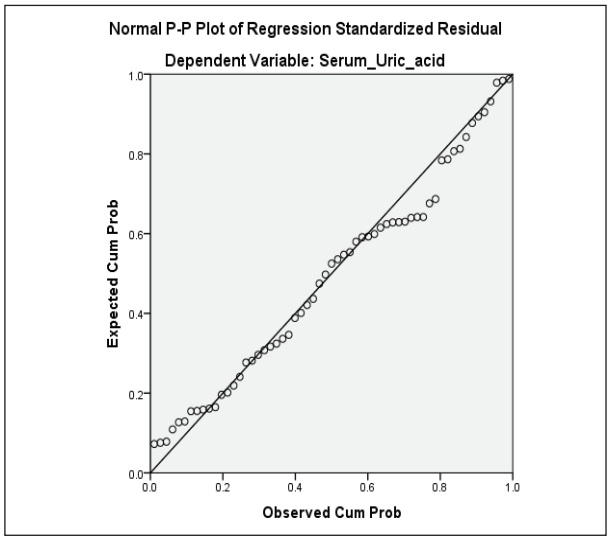

Figure 3: Normal P-P plot of regression standardized residual

DISCUSSION

Our study focused on gender differences, the existence of diabetes, and the effects of elevated blood uric acid levels in patients with a variety of cardiovascular conditions, such as hypertension, heart failure, arrhythmia, ischemic heart disease, and valvular heart disease.

Serum creatinine levels were significantly higher in males (41.1% of the study's participants were men) than in women (55.9%). This is because creatinine excretion is known to be greater in men due to gender variations in muscle mass.[15] This is consistent with results from other research that show variations in renal function and uric acid levels by gender. Increased serum creatinine levels, a sign of compromised renal function, have been linked to elevated serum urate levels. HU may cause renal function to rapidly deteriorate in persons with chronic kidney disease.[16]

The participants' age range (28–86 years) and BMI category distribution (20.3% normal, 27.1% overweight, and 52.6% obese) are consistent with findings from prior research. Obesity is a substantial risk factor for high uric acid levels, especially in women, according to a study looking at the connection between HU and cardiovascular disease.[17]

Our observation of higher obesity rates in females, although statistically insignificant, is noteworthy and aligns with existing literature that suggests a higher prevalence of obesity among women with HU.[18]

In terms of cardiovascular disorders, our patient sample had a significant prevalence of hypertension (59.3%), which is in agreement with earlier research showing a strong correlation between hypertension and HU.

For instance, a meta-analysis revealed that a considerable percentage of individuals with hypertension also had increased uric acid levels, indicating that HU is an independent risk factor for hypertension.[17,18]

Our results, which showed that 50.8% of individuals had diabetes, are consistent with research showing that a substantial percentage of patients with HU also have diabetes. The cardiovascular risk profile of these patients is further complicated by research showing that excessive uric acid levels are linked to an increased risk of type 2 diabetes.[18]

Our study found that whereas 49.2% of patients had an unclear cause for their elevated uric acid levels, 45.8% of patients had drug-induced explanations. This is consistent with findings from other research that highlights the challenge of identifying the source of HU, especially when it comes to polypharmacy in older persons with cardiovascular conditions.[18,19]

It is noteworthy that 93.2% of the participants in our study had no symptoms. According to other research, a large number of people with HU do not show any symptoms, which may result in an under diagnosis and under treatment of the illness.[19] The fact that only 6.8% of patients had kidney stones is also consistent with research showing that kidney stones are a less frequent consequence of HU than other issues.[17]

It is questionable if urate-lowering drugs are suitable for those with asymptomatic hyperuricemia due to their adverse effects. Some specialists recommend pharmaceutical treatment to delay any decline in kidney function[20, 21], whereas others disagree.[22]

A recent systematic review found evidence that asymptomatic hyperuricemia should only be treated in three specific situations: first, when urinary excretion of uric acid exceeds 11 mg/dL daily; second, when patients have persistent SUA levels greater than 13 mg/dL for men or 10 mg/dL for women; and third, prior to the start of radiation or chemotherapy.[23]

CONCLUSION

The results about gender differences, the prevalence of diabetes and hypertension, and the asymptomatic nature of HU are in line with previous research, and they strengthen the case for routinely monitoring uric acid levels in patients with cardiovascular conditions, even when symptoms are absent, in order to prevent potential complications. Pharmacological management may be initiated in patients with more than one risk factor, for instance history of diabetes, kidney function abnormalities and obesity. The study adds to the expanding body of literature on the association between HU and cardiovascular diseases.

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