Frequency of Uric Acid Levels, Symptomatic and Asymptomatic Hyperuricemia among the Pakistani Population

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Abstract

Background: Hyperuricemia is an independent risk factor for cardiovascular disease, cerebrovascular diseases, chronic kidney diseases, diabetes mellitus, hypertension, obesity and dyslipidemia. Its global burden suggests the widest prevalence range in East Asia. No large scale study exists to estimate the prevalence of hyperuricemia across Pakistan. Hence, this study aims to estimate the frequency of hyperuricemia in Pakistan.

Patients and Methods: It was a population-based cross sectional survey conducted in health care facilities across Pakistan. A total of 2,727 complete responses were obtained after taking informed consent. The questionnaire included sociodemographic details and serum uric acid levels of the patients. This study regards hyperuricemia as serum uric acid levels greater than 7 mg/dl in males and greater than 6 mg/dl in females. MultiSure blood glucose/uric acid Monitoring System was used to measure serum uric acid. Data was analysed using SPSS version 23.

Results: With mean age of 43.60 years, 1,320 (48.4%) participants were males while 1,407 (51.6%) were females. Mean uric acid level in male hyperuricemics was 8.11±1.25 mg/dl and in females was 7.44±1.19 mg/dl. The frequency of hyperuricemia was 39% (n=1,061). Frequency of hyperuricemia among males was 27.9% (n=367) and 49.3% (n=694) among females. Of the hyperuricemic population, 90.8% (n=963) were symptomatic. Most common comorbidity was diabetes 35.5% (n=388). Least common comorbidity was Ischemic heart disease 2.1% (n=23). Patients with no comorbidities were more likely to be asymptomatic.

Conclusion: The burden of hyperuricemia together with increasing burden of metabolic syndrome, obesity, ischemic heart disease and chronic kidney disease is becoming alarming. The rising statistics emphasize the dire need to develop proficient prevention and management strategies for hyperuricemia.

Key words: Uric acid, Prevalence, Gout, Hyperuricemia, Pakistan

Introduction

Hyperuricemia (HU), or raised serum uric acid (SUA), is the condition closely associated with gout which is a form of inflammatory arthritis triggered by the crystallization of uric acid within the joints. Gout leads to substantial morbidity and affects 1-2% of the world population. [1]

Hyperuricemia itself evolves from nonfunctioning uricase gene and contributes to increased risk for cardiovascular diseases (CVDs); moreso in women. [2] [3]

Although previous studies didn't identify hyperuricemia as an independent risk factor for CVDs because of the presence of obesity, dyslipidemia, hypertension, use of diuretics and insulin resistance in parallel, [4] recent literature has provided evidence for hyperuricemia to be an independent risk factor for cardiovascular diseases, cerebrovascular diseases, chronic kidney diseases, type II diabetes mellitus, hypertension, obesity and dyslipidemia. [5]

High SUA levels are associated with elevated total serum antioxidant capacity among individuals with atherosclerosis. High SUA levels may cause atherosclerosis through disturbing lipid metabolism, promoting the proliferation of vascular smooth muscle cells, and by activating inflammation. [6] Where insulin resistance plays a potentially key role in the relationship between metabolic syndrome, type 2 Diabetes and hyperuricemia, it is likely that HU and insulin resistance share a bidirectional causal effect. [7] The early appearance of hyperuricemia is a reliable predictor of later development of hypertension, and in adults with essential hypertension the comorbidity of hyperuricemia is very common. [8]

Even with such a crucial influence of uric acid levels on various body systems, it has remained a lesser studied domain. Although, local data exists to support association of hyperuricemia with severe coronary artery disease [9] and metabolic syndrome; [10] no large scale study exists to estimate the prevalence of hyperuricemia across Pakistan. Hence, this multicentre study was conducted with the aims to estimate the prevalence of hyperuricemia in Pakistan.

Patients and Methods

It was a population-based cross sectional survey, conducted from January 1st to December 31st 2016, in different primary care clinics and tertiary care hospitals across Pakistan. A total of 3,000 individuals, of age 18 years and above, were invited to participate in the study. However, after eliminating 145 non-responders and 128 incompletely responded questionnaires, 2,727 genuine and complete responses were obtained in our study. Written informed consent was obtained from the patients. The questionnaire included sociodemographic details (such as age, gender, comorbidity), symptoms of hyperuricemia and uric acid levels of the patients. This study regards hyperuricemia as serum uric acid levels greater than 7 mg/dl in males and greater than 6 mg/dl in females. [11] Comorbidities were taken as per the diagnosis of the treating physician. Where we present our population as symptomatic for HU, we included chronic single/multiple joint pain, urinary stones and tumor lysis syndrome as symptoms of hyperuricemia in this study.

In order to assess uric acid levels, MultiSure blood glucose/uric acid Monitoring System was used in this study. MultiSure is a portable, hand-held device with advanced biosensor technology to accurately assess blood uric acid levels. With a sample volume of 3 µL, MultiSure has a measuring range of 3 - 20 mg/dL (1.1 ~ 33.3 mmol/L) and a measuring time of 30 seconds. [12]

Data was entered and descriptive analysis was performed with SPSS software version 23. Frequency of patients with HU was calculated. Mean age and SUA levels were calculated. Stratification with respect to gender and symptomatic or asymptomatic was done and relation with morbidity and symptoms of hyperuricemia was calculated via cross tabulation and was presented in tabular form.

Results

A total of 2,727 patients participated. With a mean ± SD age of 43.60 ± 12.19 years, 1,320 (48.4%) were males while 1,407 (51.6%) were females. Comorbidities were present in 1,154 (42.3%) patients which are shown in detail in Table 1.

Mean uric acid (MUA) levels of the entire sample were 6.11 ± 1.7 mg/dl. MUA level of males was 6.19 ± 1.65 mg/dl and that of females was 6.04 ± 1.75 mg/dl. The prevalence of hyperuricemia in our study was 39% (n=1,061). Frequency of hyperuricemia among males was 27.9% (n=367) and 49.3% (n=694) among females.

Of patients with HU, 9.2% (n=98) were asymptomatic at the time of study while 90.8% (n=963) presented with symptoms of hyperuricemia. MUA level of clinically symptomatic population was 7.67±1.24 mg/dl and of asymptomatic was 7.68±1.37 mg/dl. The proportion of patients with HU presenting with various comorbidities and their MUA levels are shown in Table 2.

As seen in Table 3, comorbidities were more common in patients with hyperuricemia; only 32.9% were without any comorbidity. The most common comorbidity was diabetes; 36.6% (n=388). Although IHD was the least commonly witnessed comorbidity in our HU patients 2.2% (n=23); it was seen that 100% of IHD patients were symptomatic (Table 3).

Table 1: Characteristics of the subjects included in the study

CHARACTERISTICS	n=2727 n (%)
Age (Mean ± SD)	43.60 ±12.19
Gender	
Male	1320 (48.4)
Female	1407 (51.6)
Comorbidity	
Nil	1573 (57.9)
Diabetes	783 (28.7)
Hypertension	675 (24.8)
CKD	104 (3.8)
IHD	62 (2.3)
Obesity	456 (16.7)
Other	157 (5.8)

Table 2: Uric Acid Level in different populations (mg/dl)

	TOTAL SUBJECTS n (%)	ALL (Mean ± SD)	MALES (Mean ± SD)	FEMALES (Mean ± SD)	p value*
All subjects	2727 (100)	6.11±1.71	6.19±1.65	6.04±1.75	0.006*
Hyperuricemia subjects[$]	1061 (39)	7.67±1.26	8.11±1.25	7.44±1.19	<0.01*
Asymptomatic	98 (9.2)	7.68±1.37	7.93±0.80	7.18±1.74	0.07
Symptomatic	963 (90.8)	7.67±1.24	8.13±1.31	7.44±1.14	<0.01*
Diabetics	388 (35.56)	7.71±1.15	8.07±1.09	7.50±1.13	<0.01*
Hypertensives	350 (32.98)	7.88±1.29	8.17±1.14	7.75±1.33	0.005*
With Chronic kidney disease	57 (5.37)	8.15±1.46	8.38±1.31	7.97±1.56	0.29
With Ischemic heart disease	23 (2.16)	7.90±1.21	7.97±1.11	7.87±1.30	0.84
With obesity	198(18.66)	7.56±1.26	8.19±1.36	7.32±1.14	<0.01*

$Males with uric acid levels greater than 7 mg/dl and females greater than 6 mg/dl were classified as Hyperuricemia.
* Independent sample t test applied

Table 3: Asymptomatic and symptomatic Hyperuricemia among different comorbid populations

	HYPERURICEMIA n (%)	ASYMPTOMATIC n (%)	SYMPTOMATIC n (%)	p-value
All subjects	1061 (39)	98(9.2)	963(90.8)	<0.01*
All subjects without comorbidity	349(32.9)	42(12)	307(88)	<0.01*
Diabetic	388(36.6)	22(5.7)	366(94.3)	<0.01*
Hypertensive	350(33)	22(6.3)	328(93.7)	<0.01*
Chronic kidney disease	57(5.4)	12(21.1)	45(78.9)	<0.01*
Ischemic heart disease	23(2.2)	Nil	23(100)	N.A
Obesity	198(18.7)	20(10.1)	178(89.9)	<0.01*

* Chi2 test applied between the groups

Discussion

We reported a hyperuricemia prevalence of 39% in the Pakistani population with a mean uric acid (MUA) level of 6.11 ± 1.7 mg/dl among all subjects while 7.67±1.26 mg/dl MUA level among hyperuricemic subjects. HU was found to be more prevalent in women than in men (49.3% vs. 27.9%). The proportion of clinically asymptomatic HU was 9.2%. Most of our HU sample had one or more comorbidities and was symptomatic. Most common comorbidity in our patients with HU was Diabetes Mellitus. Although Ischemic Heart Disease was the least common comorbidity, all patients of IHD were symptomatic. Except for chronic kidney disease and IHD, all other comorbidities were significantly related to SUA levels in our study.

This is the first report of hyperuricemia prevalence from Pakistan and helps determine the burden of this condition in the population. These latest prevalence estimates help determine the burden of the condition on the Pakistani healthcare system. As per our knowledge, no other study has been conducted on such a large sample including population from various cities of Pakistan. However, we have not utilized laboratory methods to measure uric acids levels which would have been more accurate but also expensive, and only utilized portable MultiSure kit (a validated test).[12]

Attempts have been made to assess the global burden of hyperuricemia and findings suggested widest range of prevalence in East Asia with Chinese prevalence of 6-25%, Taiwanese 10-52% and Indonesian prevalence of 18%. [1] Even in an Indian obese population, HU prevalence is 44.6%, however they report more hyperuricemic males. [13] Furthermore, as per The National Health and Nutrition Examination Survey 2007–2008, the prevalence of HU in the United States general population is 21.4%. [14] In a local study involving a relatively smaller sample, the frequency of elevated SUA levels was 47%. [15]

Consistent with our findings, prevalence of metabolic syndrome and its components increased significantly according to SUA concentration in both sexes in a Korean study. [16] Hyperuricemia has been studied to be somehow responsible for the proinflammatory endocrine imbalance in the adipose tissue, which is an underlying mechanism of inflammation and consequent insulin resistance. [17] UA levels have also been regarded as a metabolic biomarker in older adults for early detection and prevention of Metabolic Syndrome. [18]

A meta-analysis of 13 studies showed 1.3% incidence of ischemic heart disease in individuals with HU and an overall risk of IHD death increased by 12% for each increase of 1 mg/dl of serum uric acid level. [19] Another five year long Japanese cohort concluded asymptomatic HU to possess a significant risk for developing hypertension, dyslipidemia, obesity and chronic renal disease. [20]

As far as the studies on recent trend of chronic kidney diseases are concerned, it has been seen that both elevated SUA levels and metabolic syndrome are associated with increase in the prevalence of CKD. [21, 22] In a longitudinal cohort, the incidence of CKD was influenced by the presence of hyperuricemia, but not by that of metabolic syndrome. However, if complicated by metabolic syndrome, HU had an even detrimental effect. [23]

In view of the crucial role of HU and its incapacitating impacts on essential bodily systems and functions, it becomes vital to first assess its burden, recognize the targeted population and then make endeavours in bringing about relevant management strategies to detect hyperuricemia at an early stage and prevent its consequent complications. This study has taken the first step in this region. With such a high prevalence of hyperuricemia in Pakistan, this study leads other researchers to investigate more of this alarming issue.

Conclusion

The burden of hyperuricemia together with increasing burden of metabolic syndrome, obesity, ischemic heart disease and chronic kidney disease is becoming alarming. Hyperuricemia plays a pivotal role in initiating the vicious cycle of debilitating involvement of almost all vital body systems. The rising statistics further emphasize the significance and dire need for the development of proficient prevention and management strategies for hyperuricemia.

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