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GENDER-SPECIFIC RELATIONSHIP BETWEEN SERUM URIC ACID LEVEL AND ASSOCIATED RISK FACTORS IN QUETTA

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Abstract

Uric acid is a natural substance produced endogenously as a purine metabolite and excreted by the kidney. Excessive production or less excretion of uric acid can lead to hyperuricemia, which is associated with number of risk factors, such as gout and metabolic syndromes. The prevalence of cardiovascular disease, diabetes mellitus, gout, kidney and obesity is rapidly increasing. However, the underlying causes of these conditions, including high SUA has been ignored The purpose of the present study was to determine the gender- based relationship between serum uric acid levels and its risk factors in hyperuricemic patients of Quetta city. Since no work has been done in Balochistan related to this topic. so the present research is an attempt to fill this gap. The study was carried out on hyper urecemic patients who received routine medical examinations at Sandeman Provincial Hospital, Quetta. Blood samples were obtained from 100 hyperuricemia patients and analyzed for the identification of serum uric acid levels in laboratory. Clinical, demographical, lifestyle and dietary data of participants were also recorded through a self-designed questionnaire. All the data were evaluated using SPSS version 24. The data was analyzed as the mean ± SD, $\chi 2$ -test, t test and percentages (%). The mean of SUA in both genders was 8.2920 and 7.410 mg /dl in males and females, respectively with a significant association p=0.005<.05. Most of the hyperuricemia patients belonged to age group 45-54. The average age of male and female patients was 48.62 and 43.54 respectively (p=0.016). The study found a non-significant relationship of BMI value in male and female hyperuricemia patients, whereas a non-significant association between the incidence of hyperuricemia and ethnicities was found (p value 0.19 > .05). Patient characteristics including gender, hypertension, renal problems, dairy products intake and sea food intake showed statistical significant association with SUA levels between genders. A non-significant association was found between diabetes, heart disease, kidney disorder and family history with hyperuricemia

This study is a quantitative research and it is significant in many ways. It will highlight the level of serum uric acid in the population of Quetta city. It will also embark upon the prevalence of hyperuricemia in different ethnicities of Quetta City and it is an attempt to identify the risk factors associated with hyperuricemia in male and female adults. ulphate of potash (SOP) levels; and the sweet pepper fertilized with T_4 = SOP = 60 g/kg resulted in highest.

Keywords: *Balochistan, BMI, Diabetes, Hyperuricemia, Metabolic syndrome, SUA*

INTRODUCTION

The elevated level of blood uric acid (SUA) beyond a threshold level (< 7.0 mg/dl, <6.0 mg/dl in males and females) is known hyperuricemia (1). Hyperuricemia is characterized by arthritis of the smaller bones of feet and episodes of acute pain due to increased serum uric acid level caused by defective metabolism (2). A persistant increased level of serum uric acid causes deposition of monosodium urate crystals in the joint and soft tissues resulting clinical manifestation of gout which can happen by dieatary food, medications and alocohol (2-4). A number of urate salts are known to crystallize and deposited within soft tissues leading to gout so hyperuricemia is the root cause of gout, however many individuals with the condition do not produce gout or crystalline uric acid. Additionally, Purine abundant food may also cause uric acid levels to rise (5). The

epidemiological data have shown that HU contribute to the clinical symptoms of diabetes, hypertension, atherosclerosis, chronic kidney disease and atrial fibrillation (AF) (6-8). High blood pressure and cardiovascular disease, are likely brought on by hyperuricemia according to the recent researches (9).

Hyperuricemia, in spite of certain risk factors is also linked to risk of hypertension in the next five years People all over the world are affected by hypertension. Hyperuricemia is discovered to be strongly connected with diastolic hypertension as compare to systolic hypertension. Increased serum uric acid concentration is one of the risk factors and is supposed to be multi-dimensional, yet its particular cause is unidentified. In nearly 90% of juveniles, high levels of uric acid have been noticed with early beginning hypertension. Two recent studies recognized that hyperuricemia was related with a risk of hypertension, and had greater severity in females and young individuals (10).

Pathological researchers have identified a close relation between the elevated level of SUA and the variety of metabolic syndromes along with glucose sensitivity, insulin resistance and obesity. Insulin slows down the renal excretion of uric acid thus the rise in SUA amount in metabolic syndrome found causing Hyperinsulinemia. For early screening, it is necessary to determine the hazardous causes of onset of diabetes (type 2) as SUA is related with the risk of diabetes type 2. SUA and diabetes association is not clear and the results are controversial, probably based on considered gender and ethnicity differences. Some researches stated a direct association between raised SUA and diabetes; however, other studies described no association of SUA to be positively associated with blood glucose level in healthy adults (11).

Another physiological condition called chronic kidney disease (CKD) is also associated with hyperuricemia. Heart disorder, bone disease, hyperuricemia, asthma and anemia are issues of the incidence of CKD in a population reached beyond 10%, and it exceeds 50% in high-risk sub populations (12).

There is little data available regarding hyperuricemia and its prevalence in Pakistan. Less than 15 studies were found when hyperuricemia and uric acid were searched for on Pakmedinet.com in contrast to the hypertension that displayed 1543 studies and diabetes had 2140 studies (13). So the aim of the current research was to determine the frequency of increased uric acid level in the population of Quetta and identify the risk factors associated with hyperuricemia in male and female adults.

MATERIALS AND METHODS

STUDY AREA

The study was carried out between November 2019 and February 2021 in Sandeman Provincial Hospital. The participants were the patients who complained joint pains and visited for check-up during the period.

STUDY POPULATION

The study consisted of 100 participants (50 males and 50 females).

EXCLUSION AND INCLUSION CRITERIA

The Individuals who were under 25 years and above 65 years of age were excluded from the study. All individuals from 25 – 65 years of age were included.

ETHICAL CONSIDERATION

Ethical approval was taken from the Head of department of Chemical Pathology of Sandeman Provincial Hospital. Every participant in the study gave their consent after having information about the aims and assurance on the privacy of their personal data.

QUESTIONNAIRE AND ANTHROPOMETRIC MEASUREMENTS

A detailed questionnaire was designed to collect the demographic data while Blood pressure, comprising systolic blood pressure (SBP) and diastolic blood pressure (DBP), was recorded. BMI was calculated after body weight and height measurements as following:

$$\text{BMI (kg/m2)} = \frac{\text{Weight (in kg)}}{(\text{Height in meter})^2}$$

BLOOD SAMPLING AND WORKING REAGENT

For determining the serum uric acid levels, Spin React and Humane reagents were used. First, a swab containing 70% isopropyl alcohol was used to sterilize the skin. Using a disposable syringe (Bec Dickinson Pak), 2cc blood was drawn through venipuncture. After that, Blood was moved to the gel containing SST vacutainer (clot activation). It took fifteen minutes to clot in vertical position. After that, the clotted blood was centrifuged for five to ten minutes using a 500 Vanguard V6500 machine. Before examination, codes were applied to the tubes. A test tube marked as "blank" received 1000µl of reagent. A second test tube with the label "standard" included 1000µl of reagent and 20µl of standard solution. Meanwhile, the third test tube was labeled as a "test" by adding 1000µl reagent and 20µl of serum.

LABORATORY INVESTIGATION

All test tubes were kept in water bath for the duration of ten minutes. The calibration approach was used to set up the uric acid programme in the chemical analyzer (Humalyzer-3500). The Following steps were done while doing the laboratory investigation.

- The machine was used to run the test tube with the code "blank" until the "insert standard" appeared.
- The analyzer was used to run the second test tube, which had the label "standard.
- After displaying the option "insert sample", the sample was applied to the machine.
- The values displayed by the machine were noted down carefully.

STATISTICAL ANALYSIS

All these obtained data were feed and interpreted by using SPSS v. 24 and shown as mean ± SD, $\chi 2$-test and t test. These tests were used to interpret the data. $\chi 2$ -test and to assess the relationship between categorical variables. Mean comparison between two groups were done by t-tests to understand the significance and variability in data.

RESULTS

The reference ranges for both genders (female 2.4 – 5.7 mg/dl, male. 3.4 – 7.0mg/dl) were followed when calculating the mean SUA levels. Male patients had a higher mean value of SUA level than females as were 8.2920 mg/dl and 7.410 mg/dl respectively. .68% of male individuals were diagnosed with 8 mg/dl or above SUA level while 32% individuals of were noted to have SUA level under 8 mg/dl. Similarly, 24% of females had serum uric acid levels of 8 mg/dl and above, however rest of the individuals had SUA level under 8mg/dl. A significant difference was found between SUA level and gender with P value 0.005< .05 showing that males were more hyperuricemic than females. The BMI of the male and female populations were 76.44 and 69.94, respectively. Male patients had higher BMI than female patients and more females fell into the overweight and normal weight categories The mean values of BMI of male and female hyperuricemia patients was 2.7 and 2.5 respectively with nonsignificant association showing that hyperuricemia is not related with body weight and height (Table I).

Table I. Mean of SUA level, age and BMI in male and female

	Mean		
	Male	**Female**	**p- value**
UA level	8.2920	7.412	0.005<.05
Age	48.62	43.54	0.016
BMI	2.7400	2.5200	0.342

The data of age of study patients is split into five age groups, with the 45-54 age groups accounting for the majority of hyperuricemia patients.

For most of the female participants in the study, hyperuricemia is present at age 35 and up, for male participants, this range is 45 and above. The data of age group showed a non-significant association within age groups with P value of 0.069>0.05 and chi square test also described least variation within data (Table II).

Table II. Distribution of hyperuricemia across different age groups and gender

Variable	Total	Gender		Chi – Square	p-value
		Women	Men		
Age Groups					
25-34	15	11	04	8.717	0.069<0.05 Non-Significant
35-44	29	17	12		
44-54	32	15	17		
55-64	19	05	14		
65-74	05	2	03		
Total	100	50	50		

The demographic data of patients was also collected through a designed questionnaire. The academic data of patients indicated that the higher percentage of patients were illiterate. The educational percentage in males was greater, 56% of male patients had a matriculation or higher. In 17% females the educational level was either matric or higher than it, 28.88% individuals were in the primary level whereas 44% were uneducated. A significant association was found between serum uric acid level and education status with p-value 0.03<0.05 (Table III).

Table III. Distribution of hyperuricemia across education levels in male and female patients

Variable	Total	Gender		Chi – Square	p-value
		Women	Men		
Education				8.9	0.03<0.05 Significant
>BS	17	5 (10%)	12 (12%)		
Matric	24	9 (18%)	15 (30%)		
Primary	27	14 (28%)	13 (26%)		
Nil	32	22 (44%)	10 (20%)		
Total	100	-	-		

Furthermore, from the obtained data of ethnicity of 100 patients, 38 individuals were Pathan, 30 patients were form Baloch Tribe, and 15 patients belonged to Persian community while settlers were 17. It was concluded that the most of the patients from pashtoon tribe were suffering from hyperuricemia and a non-significant association between prevalence of hyperuricemia and ethnic group was found with P value 0.194 > .05 (Table IV).

Table IV. Prevalence of hyperuricemia across different ethnic groups: A Non-significant association

Uric acid level categories		Ethnicity				Total	p-value
		Pathan	Baloch	Persian	Others		
6.0 - 6.9	Count	10	6	1	4	21	0.194> .05
	%	26.3%	20.0%	6.7%	23.5%	21.0%	
7.0 - 7.9	Count	16	9	4	7	36	
	%	42.1%	30.0%	26.7%	41.2%	36.0%	
8.0 - 8.9	Count	10	12	6	2	30	
	%	26.3%	40.0%	40.0%	11.8%	30.0%	

9.0 - 9.9	Count	2	3	4	4	13
	%	5.3%	10.0%	26.7%	23.5%	13.0%
Total	Count	38	30	15	17	100
	%	100.0%	100.0%	100.0%	100.0%	100.0%

The study also included the clinical data from patients with hyperuricemia. Clinical data included the factors like diabetes, kidney problems, use of medication, heart disease and hypertension, of which medicine intake and hypertension were significantly related with gender difference and other factors did not. The number of diabetic patients was 36% male and 38% female. Additionally, there were 30 % of female kidney patients and 48 % of male kidney patients in the study. The ratio of medicine intake was higher in female patients as 64% were on medication while in males; only 30% were taking medicines. Moreover, hypertensive patients were higher as 62% in females while only 38% were hypertensive patients in male category. Patients with a family history of elevated uric acid comprised 24% of male and 32% of the female patients (Table V).

Table V. Association of clinical factors with gender in hyperuricemic patients: A comparative analysis

Variables	Total	Gender		Chi – Square	p- value
		Women	Men		
Diabetic patients	37	19 (38%)	18 (36%)	0.043	0.836 >0.05 non- significant
Kidney Problem	39	15 (30%)	24 (48%)	0.065	0.1>0.05 non- significant
Medicine intake	47	32 (64%)	15 (30%)-	11.60	0.001 < 0.05 significant
Family History	28	16 (32%)	12 (24%)	0.504	0.37>0.05 non- significant
Heart diseases	6	4 (8%)	2 (4%)	0.709	0.4 >0.05 non- significant
Hypertensive	56	31 (62%)	25 (50%)	1.461	0.006<0.05 significant

The dietary characteristics included meat consumption, dairy product intake, sea food consumption, use of beverages and vegetable consumption. Seafood consumption and dairy product intake of hyperuricemia patients showed a significant association with gender having p value 0.001<.05 for both. The beverages, use of vegetables and meat intake did not show significant relationship with gender showing p values as 0.192, 0.06 and 0.84 respectively. The data showed that meat was consumed by both genders, 54% and 50% of female and male patients took meat mostly and 50% took meat sometimes. Ratio of beverages intake was lower in female patients and higher in male patients like 90% in male patients and 76% in female patients.

All of the male patients consumed dairy products so the intake of dairy product was found to be higher in men. However, 96% of females took dairy products. 12% of females drank milk only once a week, compared to 88% of females took who did so regularly. On the other hand, 76% of male patients took it on daily basis and 24% took it on weekly basis (Table VI).

DISCUSSION

Hyperurecemia is caused by increase synthesis and a decrease in excretion of uric acid (14). It is a chemical process in which the conversion of hypoxanthine into xanthine and then into uric acid leads to UA production catalyzed by xanthine oxidase. The range of Uric acid level in the blood must be 6.5 to 7 mg/dl for men and 6 to 6.5 mg/dl for women (15). Hyperuricemia can lead to deposition of uric acid crystals in joints of body that can cause joint irritation and inflammation resulting joint pain and swelling as a clinical symptom of gout. Most people with hyperuricemia have not necessarily gout, it is estimated that 21% of general population had hyperuricemia but 45% of them have gout (16). Increased SUA level was found to vary between genders. Comparatively, males have higher average SUA level than females. In the present study the values of females mean uric acid levels were lower than males in accordance with previous study where the highest level SUA level in male patients was 9.90 mg/dl while in female patients; it was 9.60 mg/dL (17). A survey found that among males aged 65 to 90; the rise in hyperuricemia was only 6%. On the other hand, the ratio for women was higher as it doubled, going from 15.3% for those over 65 as compare to 34.4% for those over 90 (18). The prevalence of hyperuricemia is not significantly affected by age in males as

compare to females. Females have higher risk of HUA after 50 years of age while males are at the risk of HUA before age 70, the phenomenon might be related with different levels of sex hormones (19). The subjects in this study ranged in age from 25 to 74. In the current study, the frequency of hyperuricemia was found to be higher in the elderly population in both genders, it has been discovered that the risk factors connected to an elevated SUA level also increase with age. There are more HU males over 50 years of age in present data . A significant association has been found between increasing age and hyperuricemia in a study which could be explained due to age related factor like change in renal function (20).

Table VI. Dietary habits of hyperuricemic patients: A gender-stratified analysis

Variables	Total	Gender		Chi – Square	p-value
		Women	Men		
Organ Meat Consumption	100	-	-	0.689	0.841 >0.05 non- significant
Sometimes	48	23 (46%)	25 (50%)		
Mostly	52	27 (54%)	25 (50%)		
Sea food intake	100	-	-	14.16	0.001 < 0.05 significant
Yes	88	38 (76%)	50 (100%)		
No	12	12 (24%)	0		
Beverages	100	-	-	2.439	0.192 >0.05 non- significant
Yes	82	37 (74%)	45 (90%)		
No	18	13 (26%)	5 (10%)		
Dairy products Intake	100	-	-	19.2	0.001< 0.05 significant
Sometimes	28	23 (46%)	5 (10%)		
Daily	70	25 (50%)	45 (90%)		
Never	02	2 (4%)	0 (0%)		
Vegetables consumption	100	-	-	4.336	0.066> 0.05 non-significant
Weekly	18	6 (12%)	12 (24%)		
Daily	82	44 (88%)	38 (76%)		

It is important to remember that uric acid tolerance is influenced by ethnic characteristics. Four ethnic groups living in the area are pathans, balochs, persians and others (settlers) had higher SUA levels. Each of them had a different elevated SUA level. Our observations show that pathan and baloch had more patients with elevated SUA levels than other casts in a random sample of 100 patients, however a non-significant association was found between SUA level and ethnicity. A study of variable SUA level also showed difference in proportion of gout patients among New Zealand Europeans and New Zealand Maori population (21).

The present study also included the clinical data from hyperurecemic patients comprising diabetes, kidney problems, use of medication, heart disease and hypertension. The values of factors like medicine intake, family history, heart disease and hypertension were higher in female gender as compare to males. Hypertension is significantly related with hyperuricemia in both the genders. A cross sectional study also revealed that hypertension is directly linked with hyperuricemia by the mechanism including renin angiotensin system activation, oxidative stress and endothelial inflammation (22, 23). Another report from Pakistan also showed that SUA levels were raised in hypertensive patients than those without hypertension (24)

Patients with renal illness, heart disease, hypertension, increases body mass index, a family history of kidney disease had higher SUA levels. In addition, a significant correlation has been found between hyperuricemia and Kidney disease and risk factors related to cardiovascular disease (CVD), particularly in women (25). In another study Borghi *et al.* found a relationship between elevated SUA levels and cardiovascular risk. There are many factors that mediate the long-lasting relationship between elevated SUA levels and CVDs (26). Numerous animal studies and human epidemiological data have shown that uric acid lowering therapy is beneficial for CVDs. The study participants also suffered heart problem. According to MacIsaac RL, one of the main risk factors for cardiovascular disease is an elevated SUA level (27).

It was discovered that renal disease was an additional risk factor for elevated SUA levels. Increased SUA level and newly diagnosed chronic kidney disease (CKD) are positively correlated, per a literature review and meta-analysis study. A distinct marker of new-onset CKD was found to be hyperuricemia (28). As people age, chronic kidney disease (CKD) becomes more common. Hyperuricemia may be one of the most powerful risk factors for CKD in the elderly population. Elderly people have higher SUA levels and a higher risk of developing CKD (29). The study patients also had renal disorder and males had higher proportion than females. One study showed a substantial correlation between the elevated level of SUA and the rising incidence of renal disorders.. Patients with elevated SUA levels were found to have higher rates of risk factors, such as renal illness, suggesting a connection between elevated SUA levels and kidney illness (24, 30).

There is no association between diabetes and hyperuricemia according to certain studies, while Sluijs et al., research have found no significant relationship of increased uric acid with a greater risk of diabetes (31). Diabetic patients were found to have a lower SUA level than non-diabetic patients in our study, and there was no significant association between increased SUA level and diabetes. On the other hand, male patients with diabetes outnumbered females. Males had greater increased SUA level, which might be attributable to obesity, hypertension, or another illness. As a result, it was difficult to determine whether diabetes mellitus was a risk factor or not.

An additional risk factor associated to a higher SUA is BMI associated with obesity. Studies conducted in China, Japan, India, Pakistan, Iraq, and the United States revealed a strong positive correlation between rising SUA and obesity (32). The current study found that mean value of BMI is higher in female patients as compare to males

A person's genetic vulnerability to hyperuricemia may interact with dietary circumstances, functioning either alone or jointly. According to several researches, eating meals like red meat, fish and beverages can raise uric acid amount in blood (33)28. The correlation of carbohydrate fizz drinks and hyperuricemia indicated similar outcomes. The present research discovered a link between red meat and drinks that caused elevated plasma UA level. It was found that the patients, who consumed a large amount of red meat and soft drink, had higher SUA level. On the other hand, a significant difference was found between dairy products intake and sea food with gender in study hyperuricemia patients. There is an increased proportion of patients who had frequent intake of dairy products. This is in accordance with the previous studies where urinary excretion of uric acid was increased following ingestion of dairy products (34). SUA levels were higher in patients who consumed more dairy products, drinks and organ meat. The other factors included a poor family financial background, a poor diet, and Ignorance of the illness (25). In population of Quetta, an elevated serum uric acid level was caused by an unbalanced lifestyle, a poor diet, and low socioeconomic status. In addition, patients lacked any prior clinical information.

CONCLUSIONS

The present study investigated the hyperuricemia patients in different aspects. Most of the hyperuricemia patients belonged to age group 45-54. The mean of SUA was higher in male patients in comparison of female patients. The study found a non-significant association between the incidence of hyperuricemia and ethnicities. Patient demographical features like gender, hypertension, renal problems, dairy products intake and sea food intake showed statistical significant association with SUA levels. A non-significant association was found between diabetes, heart disease, kidney disorder and family history with

hyperuricemia. There was no relationship of SUA Level with ethnicity as it showed non-significant value but overall SUA Level were higher in Pathan community as compared to others. The implications of the research could be significant for the medical field, as it suggests a potential gender-specific relationship between these factors. The findings could help healthcare professionals can further contribute to several important implications, it also highlights the need for gender-specific approaches in diagnosing and managing conditions related to SUA. Healthcare professionals can consider these factors when assessing the risk of developing conditions. The research underscores the importance of addressing diabetes in males as potential contributors to elevated SUA levels. This information can guide interventions and treatment strategies aimed at reducing the risk of associated health complications. Overall, this research provides valuable insights into the gender-specific relationship between serum uric acid levels and its risk factors, offering opportunities to enhance medical understanding and improve patient's health.

Study Limitations:

The study has compared the risk factors associated with hyperuricemia in male and female adults of Quetta. Like other researchers, our study also has certain limitations. The sample size can be increased and the data could be compared with data of healthy people that can be seen as control group. More features can be included in data.

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