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Research Article

**ANALYSIS OF FREQUENCY OF HYPERURICEMIA IN
PATIENTS WITH PRE-DIABETES****¹Dr Saira Bano, ²Dr Shazia Zammurad, ³Dr Alam Zeb, ⁴Dr Sufiyan Khan, ⁵Dr Uzma
Rasheed, ⁶Dr Wajahat Aziz**¹Department of Rheumatology, PIMS Hospital Islamabad.**Article Received:** July 2019**Accepted:** August 2019**Published:** September 2019**Abstract:**

Introduction Several prospective studies have found an association between higher levels of serum uric acid and an increased risk of developing type 2 diabetes.

Objective: To determine the frequency of Hyperuricemia in patients with pre-diabetes.

Material and methods: This cross sectional study was conducted in PIMS Hospital, Islamabad during 14-09-2018 to 15-03-2019. A total of one hundred and fifty one (n =151) patients either gender, aged between 40-55 years. Serum uric acid & fasting blood sugar levels were measured in each patient. Stratification was performed among age, gender and fasting blood sugar levels to see the effect modifications.

Results: Hyperuricemia was found in 55.6% (n=84) patients. It was found in 52.0% of patients with age between 40-47 years and in 59.2% of patients with age between 48-55 years ($P > 0.05$), in 63.6% of males and 44.4% of females ($P < 0.05$) and in 36.6% of patients who had fasting sugar levels < 110 mg/dl and in 62.78% of patients who had fasting sugar levels > 110 mg/dl ($P < 0.05$).

Conclusions: Hyperuricemia was found in significant percentage of patients with pre-diabetes. No significant association was found with age. However, significant association was observed with gender and fasting blood sugar levels.

Key Words: Hyperuricemia, Prediabetes, Risk factor.

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INTRODUCTION:

Hyperuricemia as a cause of gout is discovered in early 1800s and a large no of studies have recognized a link between elevated concentration of serum uric acid (SUA) to hypertension, diabetes, cardiovascular diseases (CVD) and kidney disease in subsequent years. A positive correlation of raised concentration of serum uric acid (SUA) and increased mortality has been found in the patients with myocardial infarction, heart failure, and stroke [1].

Jasna Vucak et al has reported that prevalence of Hyperuricemia was 10.7% (15.4% male, 7.8% female) in their study. Experimental models have demonstrated that Hyperuricemia increases blood pressure without affecting the morphology of the kidney and by lowering uric acid concentration can normalize blood pressure [2]. In addition to this association of Hyperuricemia with hypertension, many authors have confirmed the correlation between serum uric acid (SUA) and diabetes.

This positive association between uric acid concentration and diabetes which may be explained by following potential mechanisms; First, As metabolic syndrome is a precursor of diabetes induces high oxidative stress and causing hyperinsulinemia which is basis of type 2 DM, that is worsened by the accompanying hyperuricemia [3]. Second, Increased serum uric acid concentration decrease renal perfusion via stimulation of afferent arteriolar vascular smooth muscle proliferation, and decrease endothelial nitric oxide production. This induces endothelial dysfunction, glomerular hypertension and insulin resistance [4].

Among diabetic patients, microalbuminuria is a main marker of diabetic nephropathy. The results showed that every increase of serum uric acid by 59.5 $\mu\text{mol/L}$ results in a 60% increase in risk for developing diabetes [5]. Consequently, if Hyperuricemia contributes to diabetes, the assumption is that it should also contribute to prediabetes (PreDM). While Hyperuricemia's relationship with hypertension and diabetes has been well studied, but only few studies dealt with the relationship between hyperuricemia and prediabetes (Pre DM). One study showing Hyperuricemia 32.5% in prediabetics [6].

Objectives of the study

The main objective of this study was to determine the frequency of Hyperuricemia in patients with prediabetes (Pre DM).

MATERIAL AND METHODS:

This cross sectional study was conducted in PIMS Hospital, Islamabad during 14-09-2018 to 15-03-2019. Non-probability purposive sampling technique was used for this purpose.

INCLUSION CRITERIA:

- Aged ≥ 40 years to 55 years
- Either gender
- Newly diagnosed PreDM (as defined in operational definitions)

EXCLUSION CRITERIA:

Patients having other risk factors for cardiovascular disease such as pre-existing diabetes mellitus, use of thiazide diuretics, any malignancy & pre-eclampsia will be excluded.

Data collection:

The study was conducted after approval from Hospital Ethical Committee. Samples were collected from both indoor and outdoor patients. Informed consent was taken from patients. Blood samples were drawn in vacutainers by phlebotomist and these samples were centrifuged to separate serum and analyzed for serum uric acid & fasting blood sugar at hospital central laboratory. Automated results of serum uric acid and fasting blood sugar were generated and finalized by consultant hematologist.

Statistical analysis:

Statistical Package for Social Sciences (SPSS) Version 10.0 was used for data processing purpose. Categorical variables, such as gender and hyperuricemia were expressed in frequencies and percentages, whereas numerical variables such as age, fasting blood sugar & serum uric acid level were expressed in mean and standard deviation.

RESULTS:

One hundred and fifty one (n =151) patients of either gender, aged between 40-55 years who were included in the study. Patients who had Patients having other risk factors for cardiovascular disease such as pre-existing diabetes mellitus, use of thiazide diuretics, any malignancy & pre-eclampsia were excluded. All patients were subjected to detailed history and clinical examination. Blood samples were drawn in vacutainers by phlebotomist and these samples were centrifuged to separate serum and analyzed for serum uric acid & fasting blood sugar at hospital central laboratory.

Table 01: Demographic Profile of the study Population

	Number	Mean Age \pm SD (years)
Males	88 (58.3 %)	45.9 \pm 11.7
Females	63 (41.7%)	49.8 \pm 14.1
Total	151 (100%)	47.6 \pm 12.8

Table 02: Fasting Blood sugar of the study Population

GROUPS	NUMBER (PERCENTAGE)
< 110 mg/dl	41 (27.2%)
> 110 mg/dl	110 (72.8%)
TOTAL	151 (100.0%)

Automated results of serum uric acid and fasting blood sugar were generated and finalized by consultant hematologist. This study was funded by PAEC General Hospital, Islamabad and results were collected on standardized performa. Out of total 151 (100%) patients, 88 patients (58.3 %) were males with the mean age of 45.9 years \pm 11.7 Standard Deviation (SD) and 63 (41.7%) were females with mean age of 49.8 \pm 14.1 SD.

In the overall study population, there were 84 (55.6%) patients who had hyperuricemia as per our operational definition (serum uric acid levels of > 6 mg/dl). Stratification was performed among age, gender and fasting blood sugar levels to see the effect modifications. Age groups stratifications showed that hyperuricemia was found in 52.0% (n=39) of patients with age between 40-47 years and in 59.2% (n=45) of patients with age between 48-55 years.

Table 03: Association of hyperuricemia with different age groups

AGE GROUPS	SERUM URIC ACID		TOTAL	P-value
	< 6 mg/dl	> 6 mg/dl		
40-47 Years	36 (48.0%*)	39 (52.0%)	75 (100%)	0.373 (>0.05)
48-55 Years	31 (40.8%)	45 (59.2%)	76 (100%)	
Total	67 (100%)	84 (100%)	151(100%)	

*Percentages are rows wise

Table 14: Association of hyperuricemia with fasting blood sugar

BSF	SERUM URIC ACID		TOTAL	P-value
	< 6 mg/dl	> 6 mg/dl		
< 110 mg/dl	26 (63.4%*)	15 (36.6%)	41 (100%)	0.004 (<0.05)
> 110 mg/dl	41 (37.3%)	69 (62.7%)	110 (100%)	
Total	67 (100%)	84 (100%)	151(100%)	

*Percentages are rows wise

DISCUSSION:

The implications of hyperuricemia may be broadly regarded as those related to urate or uric acid crystal deposition and as those emerging from crystal deposition-unrelated associations of hyperuricemia with important disorders, including hypertension, chronic kidney disease, cardiovascular disease, and the insulin resistance syndrome [7]. Primary hyperuricemia in men frequently begins at puberty, when the lower serum urate levels characteristic of children rise into the adult male range [8]. Normal adult male values exceed those in women of reproductive age due to enhancement by estrogenic compounds of renal urate clearance, an effect that is probably mediated by inhibition of renal urate reabsorption by organic anion transporters [9]. Thus, hyperuricemia in women is usually delayed until after menopause; at that point, serum urate values in normal women increase and approximate those in normal men of corresponding age. There is a lesser rise in urate levels in postmenopausal women treated with hormone replacement therapy. The clinical manifestations of hyperuricemia in both men and women occur, on average, about two decades later than the initial physiologic increase in serum urate concentration [10]. Type 2 diabetes mellitus is characterized by hyperglycemia, insulin resistance, and relative impairment in insulin secretion. Its pathogenesis is poorly understood, but is heterogeneous and both genetic factors affecting insulin release and responsiveness and environmental factors, such as obesity [11], are important. Several prospective studies have found an association between higher levels of serum uric acid and an increased risk of developing type 2 diabetes. After controlling for other diabetes risk factors (e.g. BMI, alcohol consumption, smoking, physical activity) the relative risk was attenuated but remained significant [12]. Proposed mechanisms for such an increase in risk include development of endothelial dysfunction, oxidative stress, and insulin resistance. This positive association between uric acid concentration and diabetes which may be due to the fact that metabolic syndrome is a precursor of diabetes induces high oxidative stress and causing hyperinsulinemia which is basis of type 2 DM [13], that is worsened by the accompanying hyperuricemia and increased serum uric acid concentration decrease renal perfusion via stimulation of afferent arteriolar vascular smooth muscle proliferation, and decrease endothelial nitric oxide production. This induces endothelial dysfunction, glomerular hypertension and insulin resistance [14-15].

CONCLUSIONS:

Hyperuricemia was found in significant percentage of patients with pre-diabetes. No significant association was found with age. However, there was significant association with gender and fasting blood sugar levels with males and patients with higher fasting levels showed higher percentages of hyperuricemia.

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