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# LEVELS OF SERUM URIC ACID IN PATIENTS WITH IMPAIRED GLUCOSE TOLERANCE

**[1,2]Shahzad Ali Jiskani*, [1]Lubna Naz, [3]Ali Akbar Pirzado, [4]Dolat Singh, [5]Asadullah Hanif, [6]Razia Bano**

[1]Department of Pathology, Chandka Medical College, SMBBMU, Larkano

[2]Department of Pathology, Indus Medical College Hospital, Tando Muhammad Khan

[3]Department of Community Medicine and Public Health, Chadka Medical College, SMBBMU, Larkana

[4]Department of Medicine, Indus Medical College Hospital, Tando Muhammad Khan

[5]Health Department, Govt. of Sindh

[6]Department of Medicine, Liaquat University of Medical & Health Sciences Jamshoro

***Corresponding Author:** Shahzad Ali Jiskani
Department of Pathology, Chandka Medical College, SMBBMU, Larkano

**ABSTRACT**

**Objective:** The main objective of this study is to see levels of serum uric acid in patients having impaired glucose tolerance as compared to normal glucose tolerant individuals.

**Patients and Methods:** This was prospective study, conducted at Department of Medicine and Department of Pathology, Indus Medical College Hospital, Tando Muhammad Khan for the period of 8 months (March 2019 to October 2019). A total of 140 patients were included in this study. An oral glucose test was performed with load of 75g glucose in patients having impaired glucose in fasting. Both normal glucose tolerance and impaired glucose tolerance individuals were evaluated for their serum uric acid level. Serum glucose levels and serum uric acid levels were performed on COBAS C-111 Chemistry Analyzer ensuring procedures of quality control. Data was entered and analyzed using SPSS 21.0.

**Results:** In patients having impaired glucose tolerance, the frequency of hyperuricemia was 62.35%. Analysis of both groups (patients with normal glucose tolerance and glucose intolerance), association was strong with p-value of <0.001.

**Conclusion:** Majority of patients with impaired glucose tolerance showed hyperuricemia as compared to individuals with normal glucose tolerance. Hyperuricemia should be kept in routine investigation in patients with impaired glucose tolerance as it can reduce the risk of secondary complications of hyperuricemia in patients with pre-diabetes.

**Keywords:** Uric acid, Glucose tolerance test, Impaired fasting glucose, pre-diabetes.

## INTRODUCTION

Diabetes mellitus is chronic metabolic syndrome described by increased level of serum glucose (hyperglycemia) because of relative or absolute deficient production of insulin or its resistance. (1) By 2014, the number of diabetic patients risen up to 422 million. Prevalence of diabetes worldwide among individuals above 18 years of age has increased from 4.7% in 1980 to 8.5% by 2014. (2) By 2011, 38 million cases were reported of pre-diabetes in Pakistan. It has been assumed that Pakistan have became 7$^{th}$ largest country in relation to population of diabetes and will be on 4$^{th}$ largest by 2030. (3)

Many organs can be damaged including heart, kidneys, eyes, nerves and blood vessels in case of inadequately managed diabetes. One death in 6 seconds is due to diabetes, and number of mortalities caused by diabetes is higher than caused by combined tuberculosis, HIV and malaria. (4) Majority of morbidities are related to cardiovascular system. The risk of stroke and ischemic heart disease is 2-4 times higher in patients with diabetes. In females with diabetes, cardiovascular diseases are 23% more prevalent than patients without diabetes. In Pakistani population, the mortality rate was 87,548 in 2014 in patients aged between 20 to 70 years. (5) The pre-diabetes is intermediary state of metabolism between diabetes and normoglycemia. It includes states with impaired glucose tolerance (IGT), increased glycated haemoglobin (HbA1c) or impaired fasting glucose (IFG). (6) There is always increased risk of developing diabetes mellitus type 2 in patients with pre-diabetes. There are also risks inbuilt to state of pre-diabetes such as macrovascular and microvascular diseases. (7)

Over past 40 years, the prevalence rate of hyperuricemia globally has been increased. (8) The uric acid is synthesized by cleavage of purine and via direct production through glutamine and 5-phosphoribosyl pyrophosphate. (9) Level of serum uric acid differs with gender and age. In children normal concentration of serum urate is 180-240 μmol/L. At puberty in males, the levels start to rise; while in females levels are at much lower level until they reach the menopause. The mean levels of serum urate in adult males are females at post-menaupausal stage are 415 μmol/L and 360 μmol/L, respectively. The value in post-menopausal females reaches to that of males. (10) During the period of adulthood, the level slowly raise by

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time and differ with body weight, height, blood pressure, intake of alcohol and function of renal system. [10] Epidemiological studies have demonstrated that hyperuricemia is important factor to be the etiology of medical problems, especially in association with pre-diabetes and diabetes such as kidney diseases, cardiovascular diseases, insulin resistance, chronic inflammation and dysfunction of endothelium. [11]

Meena at al concluded one study regarding presence of hyperuricemia in 40 to 60% patients of impaired tolerance of glucose. [12] In another study, Hong et al, showed the significant association between hyperuricemia and impaired tolerance of glucose in 17.2% patients and risk of development of diabetes mellitus type 2. [13-14] He also showed that increase up to 59.5 µmol/L of levels of serum uric acid signalled risk of development of diabetes mellitus type 2 up to 60%. [13] In one study, Perticon et al, demonstrated that hyperuricemia was significantly related to 1-hour post-glucose levels in population of hypertension regardless of glucose tolerance or diabetes. [15] He also proved strong relationship between hyperuricemia and levels of 2-hour post glucose more in females as compared to males. [16] From these evident, it was obvious that uric acid was major variant of 2-hour post glucose in pre-diabetic patients, indicating the important role of uric acid in deranging metabolism of glucose. The main objective of this study was to prove the significance of increased uric acid levels in glucose metabolism deterioration in patients with pre-diabetes prone to develop type 2 diabetes mellitus and/or its complications.

## PATIENTS AND METHODS

This was prospective study, conducted at Department of Medicine and Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan. The study was carried out for the period of 8 months (March 2019 to October 2019). A total of 175 patients were included for this study. Participants were divided into two groups: Group A included patients with impaired glucose tolerance and group B included individuals with normal glucose tolerance. Method for sampling was non-probability consecutive. Participants included both males and females with age range between 25 years to 55 years. Patients with pregnancy, previously diagnosed diabetes mellitus, hyperlipidemia, disorders of kidney, hypertension and usage of medications such as anti-hypertensive drugs, anti-tuberculosis dugs, oral contraceptives and allopurinol were excluded from the study.

After taking informed consent from participants, medical history and clinical examination was performed. Oral glucose tolerance test was performed for all participants. 75g glucose was dissolved in 300mL water and was given to patients. After exactly 2 hours, blood was drawn using aseptic methods for the determination of serum glucose levels. Group A included the participants whose oral glucose tolerance test at 2-hour post-glucose level was between 7.8 to 11.1 mmol/L; while in Group B, individuals with fasting level of glucose was <5.6 mmol/L and oral glucose tolerance test at 2-hour post-glucose level was <7.8 mmol/L. Both serum plasma levels and serum glucose levels were estimated with the use of COBAS C-111 Chemistry Analyzer.

The data was analyzed using SPSS 24.0. For both groups, means and standard deviations were calculated for quantitative variables. For the comparison of uric acid level, oral glucose tolerance and body mass index (BMI), in relation to included study groups, BMI groups, and gender groups and hyperuricemia, independent sample t-test was performed. To evaluate the association of BMI, gender groups and study groups with hyperuricemia, Chi-square test was performed. The p-value of <0.05 was considered as statistical significant.

## RESULTS

In group A, total of 85 participants were included in the study, out of which 45 were males and 29 were females. Similarly in group B, out of total 90 participants, 55 were males and 35 were females (Figure 1). Mean age in both group A and group B was 41.34 ± 5.91 years and 42.28 ± 6.21 years respectively. Mean serum uric acid level in group A was 389.13 ± 77.31 µmol/L; while in group B, it was 205.41 ± 80.01 µmol/L. The level of p-value was statistically significant (<0.001). Mean body mass index (BMI) in both group A and B was 28.33 ± 2.98 kg/$^2$ and 26.88 ± 3.19 kg/m$^2$ respectively. Mean oral glucose tolerance test value of 2 hours in group A was 9.51 ± 1.12 mmol/L; while in group B the level was 6.82 ± 0.89 mmol/L. The level was statistically significant (<0.001) (Table 1).

Level of serum uric acid was measured in both groups and it revealed that male participants had increased level of serum uric acid level as compared to females (Table 2). The frequency of hyperuricemia was found significantly in group with impaired glucose tolerance (62.35%) as compared to normal glucose tolerance (p<0.001).

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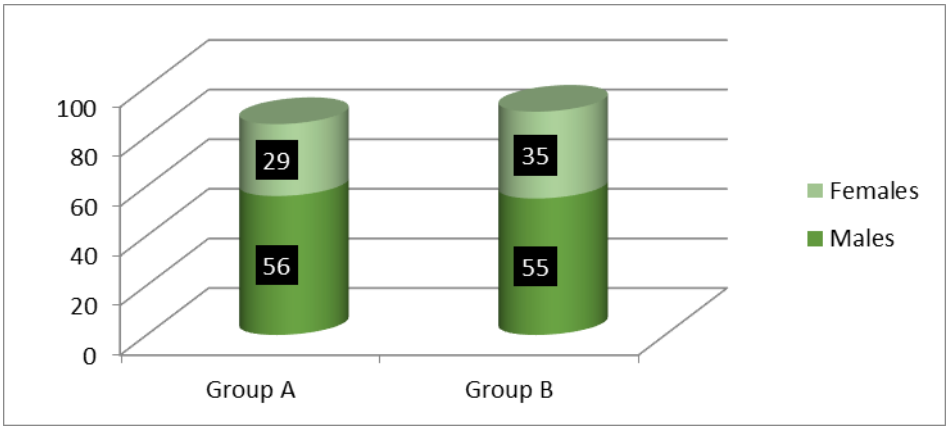


**Figure 1: Gender Distribution in Both Groups (n=175)**

**Table 1: Demographic data and characteristics of patients in both groups (n=175)**

| Number of Patients | Group A | Group B | P – value |
|---|---|---|---|
| | 85 | 90 | |
| **Mean age (years)** | 41.34 ± 5.91 | 42.28 ± 6.21 | 0.09 |
| **Mean level of serum uric acid (µmol/L)** | 389.13 ± 77.31 | 205.41 ± 80.01 | <0.001 |
| **Mean body mass index (kg/m$^2$)** | 28.33 ± 2.98 | 26.88 ± 3.19 | 0.06 |
| **Mean OGTT test value (2 hours) (mmol/L)** | 9.51 ± 1.12 | 6.82 ± 0.89 | <0.001 |

**Table 2: Distribution of hyperuricemia in both groups in relation to gender (n=175)**

| Gender | | Hyperuricemia | | P – value |
|---|---|---|---|---|
| | | Yes | No | |
| **Males** | Group A | 37 | 19 | <0.001 |
| | Group B | 14 | 41 | |
| **Females** | Group A | 16 | 13 | <0.001 |
| | Group B | 04 | 31 | |

**Table 3: Association of hyperuricemia in both groups (n=175)**

| Study Group | Hyperuricemia | | P-value | Odd ratio with 95% Coefficient Interval |
|---|---|---|---|---|
| | Yes | No | | |
| **Group A** | 53 (62.35%) | 32 (37.64%) | <0.001 | 7.1 |
| **Group B** | 18 (20%) | 72 (80%) | | |

## DISCUSSION

In our study, it was concluded that 62.35% of patients having impaired glucose tolerance were having hyperuricemia; while in normal glucose tolerance group, the frequency was 20%. These findings were in similar pattern as of other studies including Feig et al and Meena et al who demonstrated that hyperuricemia was present in 40 to 60% patients with impaired glucose tolerance. [3,12] This study also postulated that level of serum uric acid was significantly higher in patients with impaired tolerance of glucose as compared to normal glucose tolerant individuals. Similar finding was also revealed by Rao et al who reported higher frequency of hyperuricemia in pre-diabetic patients. [10]

In gender analysis in our study, it was observed that males in both groups were having higher levels of serum uric acid as compared to females. Meena et al presented the study with same findings. [12] Rahman et al in study showed that 21% of males and 15.1% of females with metabolic disorder had hyperuricemia. [7] In the development of diabetic states, body mass index (BMI) serves as important factor. In our study, it was evident that level of serum uric acid was higher in participants having BMI >30 kg/m$^2$ as compared to those having BMI <30 kg/m$^2$. This suggests that patients having higher body mass index (BMI)

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had higher levels of serum uric acid which may be one of the factors for derangement of glucose tolerance. These findings are also supported by study performed by Rahman et al. [13]

Fan Hong Qi et al reported that high level of serum uric acid were related significantly with oral glucose tolerance test (OGTT) of 2-hour plasma glucose level and also wit risk of developing diabetes mellitus type 2. [17-18] There were few limitations of our study. It was single-centred study. Study including large population and including multiple demographic areas should be included to achieve stronger correlation between the parameters.

**CONCLUSION:**

In patients with impaired glucose tolerance (IGT), the level of serum uric acid was significantly higher as compared to those with normal glucose tolerance. Multiple factors should be evaluated by clinicians in patients with pre-diabetes to adequately and timely management of the patients.

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