INTRODUCTION

Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycemia. Poor glycemic control along with metabolic abnormalities in diabetes may lead to macro and microvascular complications effecting multiple systems like cardiovascular, renal and neurological. 1 Uric acid is the metabolic end product of purine bases, normally excreted through kidneys. At normal concentration Uric acid acts as a potent antioxidant and reducing agent. The normal range of serum uric acid in plasma is 1.5-6 mg /dl in females’ and. 2.5-8 mg in males. Hyperuricemia is a common condition estimated to occur in about 8.9 to 24.4 % of population. 2 Raised serum uric acid in diabetes leads to oxidative stress which activates Renin angiotensin system causing different pathological changes like inflammation, vascular dysfunction, high intraglomerular pressure. These pathological changes may lead to cardiovascular and renal complications. 3 Previous studies highlighted the close relationship of hyperuricemia with multiple health conditions such as obesity, metabolic syndrome, insulin resistance, diabetes mellitus, essential hypertension, cardiovascular disease and renal disease. 4 Increased level of serum uric acid has a toxic effect which causes precipitation of uric acid crystals in the tissues and joints ultimately leading to complications such as gout, nephrolithiasis and chronic nephropathy. 5

The association between diabetes mellitus and serum uric acid is controversial. Previous clinical trials have found a positive relationship between diabetes and serum uric acid, while some studies
have reported no association of uric acid with diabetes or inverse association was present. A meta-analysis found a positive association of serum uric acid with diabetes. Hyperuricemic patients have more tendencies for development of diabetes mellitus type 2. i. Hyperuricemia is believed to interfere with glucose homeostasis and insulin sensitivity leading to diabetes mellitus. Elevated Serum uric acid levels in diabetes causes metabolic syndrome, hypertension and cardiovascular disease. Cortese et al have reported a powerful association between serum uric acid and cardiovascular diseases, he reported the elevated serum uric acid causes hypertension, atherosclerotic cardiovascular diseases, atrial fibrillation and heart failure through different pathologic processes. De Pergola et al demonstrated that hyperuricemia may predict the risk of metabolic syndrome.

The objective of this study is to determine the serum uric acid level in prediabetics and diabetics so as to guide clinicians about importance of serum uric acid level in these patients in order to avoid hyperuricemia and its related complications.

MATERIAL & METHODS
A cross sectional study was carried out in Chemical section department of pathology, Sheikh Zayed Medical college/Hospital Rahim Yar Khan from 1st December 2022 to 31st may 2023 after approval from Ethical Review committee (674/IRB/SZMC/SZH).

After informed consent 144 study subjects of both genders aged 20 to-70 years were included using consecutive sampling technique. Patients with renal, liver and cardiovascular disease were excluded on the basis of history. Pregnant and lactating females and patients taking antihyperuricemic drugs were also excluded. Data was collected from patients who came to lab for their HbA1C test. Samples for serum uric acid and HbA1C were collected in gel tube and EDTA tube respectively. Serum uric acid and HbA1C were performed on Atellica CH 930 fully automated clinical chemistry analyzer. Based on the HbA1C results patients were categorized as euglycemic (HbA1C 4%-5.6%) prediabetic (HbA1C 5.7%-6.4%) and diabetic (HbA1C > 6.5%) according to criteria of American Diabetic Association. Demographic characteristics and test results were documented on a predesigned performa. Data was entered and analyzed on SPSS 22 version. Qualitative data was given in frequency and percentage while mean and SD was calculated for quantitative data. ANOVA was applied to access significance of difference of serum uric acid between euglycemic, prediabetic and diabetic groups. A significant p value was taken as < 0.05.

RESULTS
Among 144 patients 68(47.2%) were females while 76(52.7%) were males. Mean age of the participants was 50.69 ±12.5% years. Mean HbA1c and serum uric acid were 7.65 ±2.41% and 5.72 ±1.35 mg/dl respectively. The mean uric acid of the male and female patients was 5.193mg/dl and 4.987mg/dl respectively. The age and gender distribution of mean uric acid level and HbA1c is shown in Table-I. Glycemic status of participants showed that Serum uric acid was higher in prediabetics as compared to diabetics and euglycemics and difference of serum uric acid between these 3 groups was statistically significant with p value 0.001 as shown in Table (II).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subgroups</th>
<th>Frequency (%)</th>
<th>Serum Uric Acid (mg/dl)</th>
<th>HbA1c (%)</th>
</tr>
</thead>
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<tr>
<td>Age (Years)</td>
<td>20-50</td>
<td>79(54.86%)</td>
<td>4.959±1.357</td>
<td>7.600±2.576</td>
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<td>&gt;50</td>
<td>65(45.13%)</td>
<td>5.262±1.509</td>
<td>7.702±2.223</td>
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<tr>
<td>Gender</td>
<td>Male</td>
<td>76(52.77%)</td>
<td>5.193±1.583</td>
<td>7.529±2.400</td>
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<tr>
<td></td>
<td>Female</td>
<td>68(47.22%)</td>
<td>4.987±1.241</td>
<td>7.776±2.443</td>
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</table>

Table-I. Distribution of mean serum uric acid level and HbA1c in study subjects with respect to age and gender
DISCUSSION
We have conducted this study to determine the level of serum uric acid in diabetes, prediabetes patients and compare them with euglycemic control. We found a higher serum uric acid level in prediabetes patients as compared to diabetics and euglycemic control with a statistically significant difference of serum uric acid between these three groups (p=0.001). Our study comprised of a total 144 patients among which 68 (47.2%) were females while 76 (52.7%) were males. The mean age of the study participants was 50.69±12.5 years. Among 144 study subjects 79(54.8%) were between 20-50 years and had serum uric acid 4.95 ±1.357mg/dl while 65(45.13%) were more than 50 years and had serum uric acid 5.262±1.509 mg/dl. A study conducted on 3200 residents of North Italy by Bombelli et al.\textsuperscript{10} concluded that raised serum uric acid may lead to increased chances of impaired fasting glucose (IFG), metabolic syndrome and diabetes. Shani et al. reported an increased risk of diabetes in women with serum uric acid in normal range as compared to women with low normal values of serum uric acid.\textsuperscript{11} Study conducted by Chang et al. showed that older adults between 75-84 years have increased chance to develop metabolic syndrome and type 2 diabetes mellitus.\textsuperscript{12} Our study included 74(51.4%) diabetics, 35(24.3%) prediabetics and 35(24.3%) euglycemics. Mean age of diabetics, prediabetics and euglycemics was 51.08±12 years, 55.03±9.81 years and 44.54±14.70 years respectively while mean Serum Uric Acid level among diabetics, prediabetics and euglycemics was 5.01±1.61mg/dl, 6.07±1.04mg/dl and 5.59±1.16mg/dl respectively. Study conducted by Seraj et al. reported statistically significant difference of serum uric acid among diabetics, prediabetics and euglycemics (p=0.010) with mean serum uric acid level of 7.50±2.24 among diabetics, 7.25±2.15 among prediabetics and 6.44±2.06mg/dl in euglycemics.\textsuperscript{13} In this study a higher level of serum uric acid in diabetics was observed, while in our study higher level of uric acid was observed in prediabetics. Study conducted by Alqahtani et al. showed 53.5% incidence of hyperuricemia in whole study population (p=0.033) while in diabetic and prediabetic patients it was 12.7% and 12.65% respectively.\textsuperscript{14} Previous studies have shown a positive correlation of hyperuricemia and Diabetes, whereas others have demonstrated neutral or negative association.\textsuperscript{15} Zhang et al. demonstrated a strong and positive correlation between mean serum uric acid value and prediabetes risk, with mean serum uric acid value having a better predictive ability for prediabetes while baseline serum uric acid had a positive relation with prediabetes when HbA1c was used for diagnosis of prediabetes. They also concluded that serum uric acid may serve as a novel predictor and potential therapeutic target for prediabetes.\textsuperscript{16} Vučak et al. also reported the positive association of raised uric acid levels and prediabetes.\textsuperscript{17} Similarly, Xue et al.\textsuperscript{18} reported that patients with prediabetes had a higher serum uric acid levels than those with euglycemic states. Haque and colleagues have reported high mean uric acid level (338.2mmol/L) in prediabetics as compared to diabetics (290.9mmol/L) in their study.\textsuperscript{6} Shrestha J et al. conducted a comparative study in Nepal and documented serum uric acid levels did not vary significantly among non-diabetics, pre-diabetics and diabetics.\textsuperscript{19} In 2019, another study investigated the positive association of serum uric acid with cardiovascular diseases in diabetes patients.\textsuperscript{20} Similarly, Sui et al.\textsuperscript{21} reported that the elevated uric acid level are associated with a risk of metabolic syndrome in diabetic patients. Our study reported a significant difference in serum uric acid level in diabetics, prediabetics, and euglycemic study subjects.

<table>
<thead>
<tr>
<th>Glycemic Status</th>
<th>Frequency</th>
<th>%</th>
<th>Serum Uric acid (mg/dl)</th>
<th>P-Value</th>
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<tr>
<td>Euglycemic</td>
<td>35</td>
<td>24.3%</td>
<td>5.59±1.16</td>
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<td>Prediabetic</td>
<td>35</td>
<td>24.3%</td>
<td>6.07±1.04</td>
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<tr>
<td>Diabetic</td>
<td>74</td>
<td>51.4%</td>
<td>5.01±1.61</td>
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</table>

Table-II. Significance of difference of mean serum uric acid level in study subjects with respect to glycemic status

One way ANOVA: P<0.05 is set as significant.
CONCLUSION
It is concluded that prediabetics are more prone to have higher serum uric acid levels and its related complications as compared to euglycemic and diabetic patients. Regular assessment of serum uric acid should be done in these patients to avoid hyperuricemia related complications.

REFERENCES


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**AUTHORSHIP AND CONTRIBUTION DECLARATION**

<table>
<thead>
<tr>
<th>No.</th>
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<th>Contribution to the paper</th>
<th>Author(s) Signature</th>
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<tr>
<td>1</td>
<td>Ume Farwa</td>
<td>Manuscript writing, Data collection, Data analysis and methodology.</td>
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<tr>
<td>2</td>
<td>Syeda Sabahat Haider</td>
<td>Proof reading and results.</td>
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</tr>
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<td>3</td>
<td>Mehwish Sana</td>
<td>Manuscript writing, data collection, Data analysis and methodology.</td>
<td></td>
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