Assess the Relationship Between Serum Uric Acid and Blood Glucose Concentrations in Individuals with Prediabetes and Type 2 Diabetes at the Son Tra District Medical Center in Da Nang city

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ABSTRACT

Background: Elevated serum uric acid (UA) is implicated in insulin resistance, potentially contributing to the progression of prediabetes and type 2 diabetes (T2D). Understanding the UA-glucose relationship may aid early intervention to prevent complications. ***Methods***: A cross-sectional study was conducted from October 2023 to June 2024 at Son Tra District Medical Center, Da Nang, involving 226 patients (117 prediabetes, 109 T2D). Medical records were reviewed for UA and fasting plasma glucose (FPG) levels. Data were analyzed using SPSS 26.0, with Pearson correlation, t-tests, and ANOVA for associations ($p < 0.05$). ***Results:*** Mean UA was higher in prediabetes (463 ± 84 µmol/L) than T2D (425 ± 91 µmol/L, $p < 0.01$). Hyperuricemia prevalence was 70.6% in prediabetes and 59.2% in T2D. UA levels were higher in males than females in both groups ($p < 0.01$). A moderate positive correlation between UA and FPG was found in prediabetes ($r = 0.383$, $p < 0.001$; $UA = 85.568 \times FPG - 67.694$), but not in T2D ($r = -0.049$, $p = 0.958$). UA increased with FPG levels <7.0 mmol/L ($p < 0.05$) but showed no trend at higher FPG. ***Conclusion:*** Higher UA in prediabetes and its correlation with FPG suggest a role in early insulin resistance. Routine UA screening in prediabetes may facilitate early intervention to mitigate T2D progression and cardiovascular risks.

Keywords: *Uric Acid, Prediabetes, Type 2 Diabetes, Glucose, Insulin Resistance*

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INTRODUCTION

Uric acid (UA) is the end product of purine metabolism, primarily existing as urate anions at physiological pH, with normal serum levels below 6.8 mg/dL (≈404 µmol/L) [1]. Elevated UA, or hyperuricemia, disrupts homeostasis by inducing oxidative stress, endothelial dysfunction, and inflammation, which impair insulin signaling and promote insulin resistance [2]. This contributes to hyperglycemia, a hallmark of prediabetes and type 2 diabetes (T2D) [3]. In Vietnam, hyperuricemia prevalence in T2D ranges from 10–40%, but its role in prediabetes remains underexplored [4,5]. Globally, studies, such as those by Xiong et al. (2019) and Shi et al. (2024), suggest UA influences glucose metabolism differently across glycemic stages, with positive correlations in prediabetes and variable patterns in T2D [6,7].

Prediabetes, characterized by impaired fasting glucose (IFG, 5.6–6.9 mmol/L), impaired glucose tolerance (IGT, 7.8–11.0

mmol/L), or HbA1c 5.7–6.4%, represents an early stage of insulin resistance [8]. T2D, defined by fasting plasma glucose (FPG) ≥7.0 mmol/L, HbA1c ≥6.5%, or post-glucose load ≥11.1 mmol/L, reflects advanced beta-cell dysfunction and chronic hyperglycemia [8]. Hyperuricemia may exacerbate microvascular and macrovascular complications, including nephropathy, retinopathy, and cardiovascular disease, in both conditions [9]. In Vietnam, rapid urbanization and lifestyle changes have increased prediabetes and T2D prevalence, necessitating early biomarkers like UA for risk stratification [10].

This study aims to: (1) determine UA levels in patients with prediabetes and T2D, and (2) investigate the correlation between UA and FPG in these groups at Son Tra District Medical Center, Da Nang. The findings may inform screening strategies to prevent T2D progression and complications in Vietnam.

MATERIALS AND METHOD

Study Design

A cross-sectional study was conducted from October 1, 2023, to June 1, 2024, at Son Tra District Medical Center, Da Nang.

Participants

The study included 226 patients aged ≥18 years: 117 with prediabetes and 109 with T2D, diagnosed per American Diabetes Association (ADA) 2020 criteria [8].

Prediabetes criteria: IFG (FPG 5.6 – 6.9 mmol/L), IGT (2-hour glucose 7.8–11.0 mmol/L post-75g oral glucose tolerance test), or HbA1c 5.7 – 6.4%.

T2D criteria: FPG ≥ 7.0 mmol/L, 2-hour glucose ≥ 11.1 mmol/L, HbA1c ≥ 6.5%, or classic hyperglycemic symptoms with random glucose ≥ 11.1 mmol/L. Diagnosis required two concordant tests (except for symptomatic hyperglycemia).

Inclusion criteria: Complete medical records with UA and FPG data.

Exclusion criteria: Gout treatment, secondary hyperuricemia (e.g., chronic kidney disease with GFR <60 mL/min, hemolysis, tumor lysis syndrome), acute conditions (e.g., heart failure, myocardial infarction), use of UA-altering drugs (e.g., febuxostat, probenecid) within 10 days, dialysis, malignancies (e.g., leukemia, liver cancer), or glucose-altering drugs (e.g., corticosteroids, thiazides).

Sampling method: Convenience sampling, including all eligible patients during the study period.

Sample Size

Sample size was calculated using the formula for comparing means between two groups:

$$n = (Z_{\alpha/2} + Z_{\beta})^2 \times 2 \times \sigma^2/d^2$$

With: $Z_{\alpha/2} = 1.96$) (95% confidence), ($Z_{\beta} = 0.84$) (80% power),

σ (pooled standard deviation) = 100.9 µmol/L, based on Haque et al. [11],

d (expected UA difference) = 48 µmol/L , following Haque et al. [11]).

This yielded n = 117 for prediabetes and n = 109 for T2D.

Data Collection

Medical records provided FPG (mmol/L) and UA (µmol/L) levels, measured using standardized biochemical assays. UA was classified as normal (≤ 420 µmol/L for males, ≤ 360 µmol/L for females) or elevated. Glucose groups were defined in 0.5 mmol/L increments from < 6.0 to ≥ 8.5 mmol/L. Demographic data included age (< 60 or ≥ 60 years) and sex.

Statistical Analysis

Data were analyzed using Microsoft Excel and SPSS 26.0. Descriptive statistics included means ± SD and percentages. T-tests or Mann-Whitney U tests compared

means, ANOVA or Kruskal-Wallis tests compared multiple groups, and Chi-square or Fisher's exact tests compared proportions. Pearson correlation assessed UA-FPG relationships, with r interpreted as: $|r| < 0.3$ (weak), 0.3 – 0.5 (moderate), 0.5 – 0.7 (strong), ≥ 0.7 (very strong). Linear regression modeled UA-FPG in prediabetes. A p-value < 0.05 was significant.

Ethical Issues

The study was conducted according to the Declaration of Helsinki and approved by the Biomedical Ethics Committee of Da Nang University of Medical Technology and Pharmacy (No. 870/BB-HĐĐĐ, November 2023) and the Scientific Council of Son Tra District Medical Center. Patient data were anonymized, and confidentiality was maintained for research purposes only.

RESULTS

Participant Characteristics

Of 226 patients, 91.6% (109/119) of prediabetes and 83.3% (100/120) of T2D patients were male (Table 1). Mean age was 57.9 ± 11.7 years (prediabetes) and 58.8 ± 10.2 years (T2D), with 55.5% (prediabetes) and 60.0% (T2D) aged <60 years (Table 1).

Table 1. *Distribution of sex and age group*

Category	Prediabetes group (No., percentage)	T2D gorup (No., percentage)
Sex		
Male	109 (91.6%)	100 (83.3%)
Female	10 (8.4%)	20 (16.7%)
Age		
<60	66 (55.5%)	72 (60.0%)
≥60	53 (44.5%)	48 (40.0%)
Mean ± SD (years)	*57.9 ± 11.7*	*58.8 ± 10.2*

Uric Acid Levels

Hyperuricemia was present in 70.6% (84/119) of prediabetes and 59.2% (71/120) of T2D patients (Table 2). Most cases were mild (77.4% prediabetes, 87.3% T2D) (Table 2). Mean UA was higher in prediabetes (463 ± 84 µmol/L) than T2D (425 ± 91 µmol/L, $p < 0.01$). Mean FPG was 6.20 ± 0.38 mmol/L (prediabetes) and 7.30 ± 2.38 mmol/L (T2D, $p < 0.01$) (Table 3).

Table 2. *Hyperuricemia Prevalence and Severity of Hyperuricemia*

Category	Prediabetes group (No., (percentage)	T2D gorup (No., (percentage)
UA test outcome		
Normal	35 (29.4%)	49 (40.8%)

Elevated	84 (70.6%)	71 (59.2%)
Severity		
Mild	65 (77.4%)	62 (87.3%)
High	19 (22.6%)	9 (12.7%)

Table 3. *UA and FPG Levels*

Conc. \ Group	Pre-diabetes	T2D	p-value
AU (µmol/L) ($\overline{X}$ ± SD)	463 ± 84	425 ± 91	< 0.01
Glucose (mmol/L) ($\overline{X}$ ± SD)	6.20 ± 0.38	7.30 ± 2.38	< 0.01

UA by Gender

UA was higher in males than females in both groups ($p < 0.05$, Figure 1).

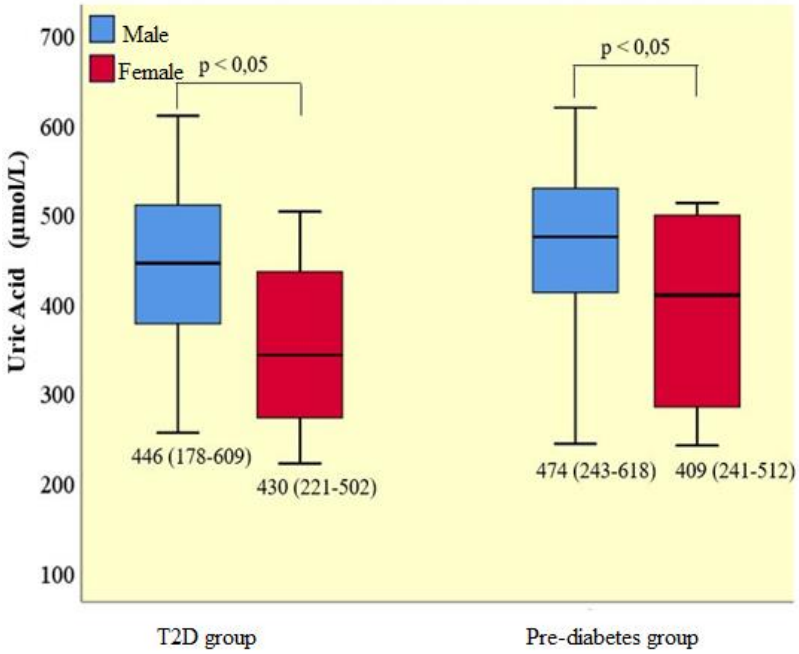

Figure 1. *UA Levels by Sex*

Mean UA was higher in males in both prediabetes and T2D groups ($p < 0.05$, Mann-Whitney U).

UA-FPG Correlation

In prediabetes, a moderate positive correlation was found between UA and FPG ($r = 0.32$, $r^2 = 0.147$, $p < 0.001$; AU = 229.23 × FPG − 589.9) (Figure 2). No correlation was observed in T2D ($r = −0.049$, $p = 0.958$). UA increased with FPG levels <50 mg/dL ($p < 0.05$) but showed no clear trend at FPG ≥70 mg/dL ($p > 0.05$ – not significant).

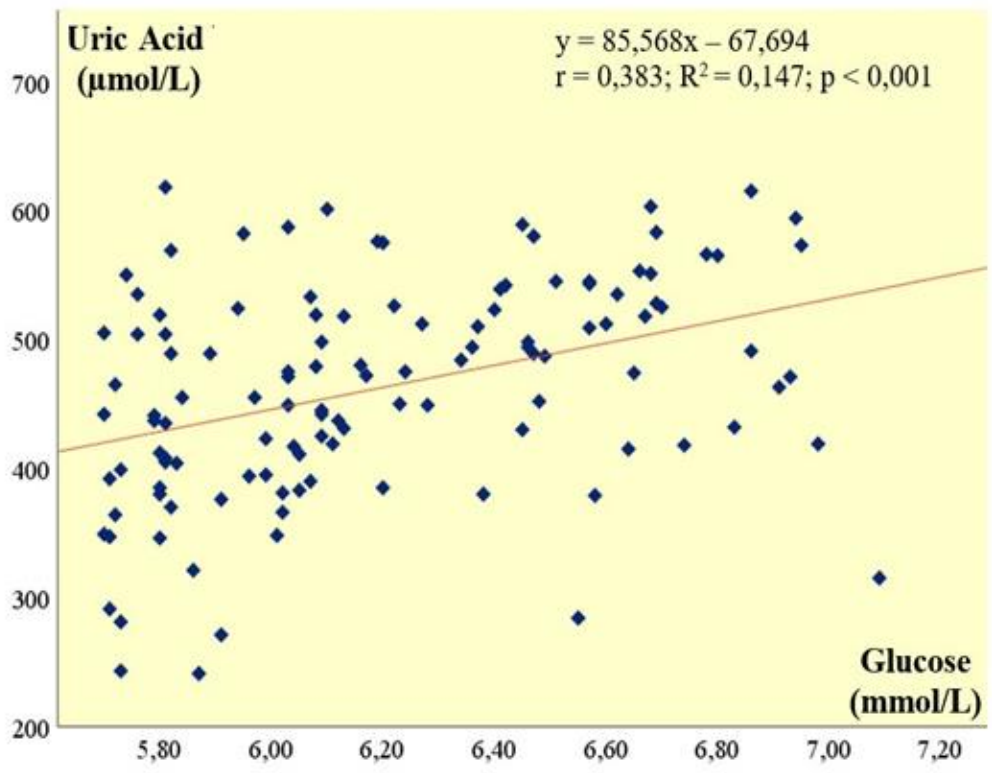

Figure 2. UA vs. FPG in Prediabetes

Linear regression in prediabetes: AU = 229.23 × FPG − 589.9, r = 0.32, p < 0.001.

DISCUSSION

This study found higher UA levels in prediabetes (463 ± 84 µmol/L) than T2D (425 ± 91 µmol/L), with a moderate positive correlation between UA and FPG in prediabetes (r = 0.32, p < 0.001) but not in T2D. Hyperuricemia was prevalent (70.6% prediabetes, 43% T2D), particularly in males. These findings suggest UA's role in early insulin resistance, with implications for screening in Vietnam.

UA Levels and Hyperuricemia Prevalence

The higher UA in prediabetes aligns with Haque et al. (2019), who reported 338.2 ± 101.6 µmol/L in prediabetes vs. 290.9 ± 98.2 µmol/L in T2D [11]. Similarly, Rabari et al. (2018) found elevated UA in prediabetes, attributing it to insulin-mediated UA reabsorption in the kidneys [12]. The 70.6% hyperuricemia prevalence in prediabetes is higher than Park et al.'s (2019) 45% in a Korean population, possibly due to dietary factors in Vietnam, such as high-purine foods or fructose consumption [13]. The lower UA in T2D may reflect increased renal UA excretion due to chronic hyperglycemia, as described by Ruggenenti et al. (2012), where glomerular hyperfiltration enhances urate clearance [14].

Hyperuricemia's predominance in males ($p < 0.05$) is consistent with Liu et al. (2018), who noted testosterone-driven purine metabolism and reduced renal UA clearance in men, while estrogen enhances UA excretion in women [15]. The mild severity (77.4–87.3%) suggests early-stage metabolic changes, supporting early intervention to prevent gout or cardiovascular complications [16].

UA-FPG Correlation in Prediabetes

The moderate positive correlation in prediabetes ($r = 0.32$, $p < 0.001$) is comparable to Zhang et al.'s (2021) stronger correlation ($r = 0.589$) in a Chinese cohort [17]. Facchini et al. (1991) suggest insulin resistance increases renal UA reabsorption via urate transporter 1 (URAT1), elevating serum UA as FPG rises [18]. The linear equation ($AU = 229.23 \times FPG - 589.9$) indicates a 59 µmol/L UA increase per 0.1 mmol/L FPG rise, highlighting UA's sensitivity to early glycemic changes. This aligns with van der Schaft et al.'s (2017) Rotterdam Study, which linked hyperuricemia to prediabetes incidence, suggesting UA as a biomarker for insulin resistance [19].

The UA-FPG correlation diminishes at FPG ≥70 mg/dL, consistent with Shi et al.'s (2024) finding of an inverted U-shaped relationship, with UA peaking at FPG 6.5 mmol/L in men and 8.8 mmol/L in women [7]. This shift may reflect compensatory insulin hypersecretion in prediabetes, which upregulates URAT1, versus beta-cell failure in T2D, reducing insulin's effect on UA reabsorption [20].

Lack of UA-FPG Correlation in T2D

The absence of correlation in T2D ($r = -0.049$, $p = 0.958$) aligns with Nguyen Long Hai et al. (2022) in Vietnam and Farwa et al. (2023) in India, who reported no or inverse UA-FPG relationships in T2D [5,21]. This contrasts with Le Xuan Truong et al. (2016), who found a positive correlation, possibly due to differences in disease duration or treatment regimens [4]. Chronic hyperglycemia in T2D increases osmotic diuresis, enhancing UA excretion, as noted by Golik et al. (1993) [22]. Additionally, pancreatic beta-cell dysfunction reduces insulin levels, downregulating URAT1 and lowering UA, as described by Nan et al. (2010) [23]. Variations in findings may stem from genetic, dietary, or treatment factors, such as metformin's potential to lower UA [24].

Gender and Age Trends

The male predominance (83.3–91.6%) contrasts with some studies, for example the publised one of Ton That Thanh et al. (2019), reporting higher female T2D prevalence in Da Nang [25]. This may reflect sampling bias or male-dominated clinic attendance. The mean age (57.9–58.8 years) and higher prevalence in those <60 years align with Vietnam's trend of younger T2D onset due to urbanization and lifestyle changes [26]. Haque et al. (2019) reported a younger prediabetes cohort (39.4 ± 17.6 years), suggesting regional differences in disease onset [11].

Vietnam's rising prediabetes and T2D burden, driven by dietary shifts and obesity, underscores the need for early biomarkers [27]. The high hyperuricemia prevalence in prediabetes and its FPG correlation support routine UA screening to identify at-risk individuals. Interventions, such as low-purine diets or allopurinol for severe hyperuricemia, could mitigate cardiovascular and renal risks [28]. The lack of UA-FPG correlation in T2D suggests UA's utility is stage-specific, with greater relevance in prediabetes. Public health campaigns in Vietnam should emphasize lifestyle modification to address hyperuricemia and insulin resistance concurrently.

Compared to Shi et al.'s (2024) large-scale Chinese study (n = 10,217), our findings confirm an inverted U-shaped UA-FPG relationship, but our smaller sample (n = 226) and narrower FPG range limit trend detection at higher glucose levels [7]. Ali et al.'s (2018) Bangladeshi study reported

lower hyperuricemia prevalence (≈30%), possibly due to dietary or genetic differences [29]. The Rotterdam Study's prospective design contrasts with our cross-sectional approach, highlighting the need for longitudinal data to establish causality [19]. These comparisons underscore the influence of ethnicity, diet, and study design on UA-glucose dynamics.

The study's cross-sectional design precludes causality assessment. Convenience sampling and male predominance may introduce bias, limiting generalizability. The small female sample (8.4–16.7%) restricts gender-specific analyses. Unmeasured confounders, such as diet, BMI, or medication adherence, may affect results. Future studies should employ longitudinal designs, larger samples, and adjust for confounders to validate findings.

CONCLUSION

To concludes serum UA is higher in prediabetes (463 ± 84 µmol/L) than T2D (425 ± 91 µmol/L), with hyperuricemia prevalent in 70.6% and 59.2% of patients, respectively. A moderate positive UA-FPG correlation exists in prediabetes ($r = 0.32$, $p < 0.001$), but not in T2D. UA increases with FPG <50 mg/dL, reflecting early insulin resistance. Routine UA screening in prediabetes could enhance early intervention to prevent T2D and complications in Vietnam.

Supplementary Materials

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Author Contributions

Study concept and design: TTL, NTHL; data acquisition: GNN, KTN, TMV, NTN; data analysis and interpretation: NTN, LTN; manuscript drafting: LTN, GNN; statistical analysis: NTQN; manucripts revising: TTL.

Institutional Review Board Statement

The study was conducted according to the Declaration of Helsinki and approved by the Ethics Committee of Da Nang University of Medical Technology and Pharmacy (No. 870/BB-HĐĐĐ, November 2023)and Son Tra District Medical Center.

Informed Consent Statement

Patient data were anonymized, and consent was waived due to retrospective record review.

Data Availability Statement

Data are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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