Original Article

Association between serum uric acid with diabetes and other biochemical markers

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Abstract

Objective: This study aimed to decipher the association between serum uric acid (UA) and glycated hemoglobin (HbA1c) in the population from the southern region of Saudi Arabia. **Method:** In this retrospective cross-sectional investigation, clinical data obtained from the different commercial laboratories in the Asir region of Saudi Arabia were screened over 2 years. Data were analyzed using standard statistical methods. **Results:** A total of 1984 laboratory investigations with 1215 females (61.2%) and 769 males (38.6%) were included in the data analysis. In our investigation, the prevalence of hyperuricemia in the study population was 53.5% (41.2% females and 12.3% males) and in the diabetic population was 12.7% (9.47% females and 3.23% males), in prediabetics was 12.65% (9.8% females and 2.85% males), respectively. Prediabetic subjects had higher UA levels than people with diabetes or healthy people. Higher UA quartiles were associated with a high level of urea, blood urea nitrogen (BUN) creatinine, HbA1c, fasting blood sugar (FBS), and total cholesterol (TC) ($P < 0.05$). High UA (OR = 1.33 for diabetes; OR = 2.676 for prediabetes), high BUN (OR = 3.05 for diabetes; OR = 2.293 for prediabetes), high TC (OR = 3.75 for diabetes; OR = 1.098 for prediabetes), and high TG (OR = 2.67 for diabetes; OR = 1.943 for prediabetes) parameters are the most influential risk factor in diabetic and prediabetic patients than the people who have normal UA, BUN, TC, and TG value. **Conclusion:** High UA levels are significantly associated with prediabetes as defined by HbA1c criteria, indicating that UA has a significant role in the disturbance of glucose metabolism. A significant positive association was observed between dyslipidemia and serum UA in the study population.

Keywords: Diabetes, dyslipidemia, HbA1c, Saudi Arabia, serum uric acid

Introduction

Serum uric acid (UA) is the end product of purine metabolism and is related to the purine base of nucleic acid.[1] Serum UA is genetically determined but is influenced by a wide range of environmental factors.[1] Globally, the epidemic of hyperuricemia has increased significantly in recent decades. Several ingestions have been carried out in different populations to assess the prevalence of serum UA in different groups and establish whether an association exists between serum UA with various chronic diseases.[2-10] It has been reported that serum UA content >6.57 mg/dL increases the risk of all-cause mortality.[11] It has been reported that elevated serum UA is associated with cardiovascular disease, hypertension, and chronic kidney disease.[11-13] Furthermore, high serum UA level was also associated with metabolic syndrome in both normal subjects and diabetic patients.[6,14,15]

Over the last few decades, substantial economic and environmental development has occurred in the middle east countries, including Saudi Arabia. The traditional lifestyle with its characteristics,

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dietary habits, and exercise pattern has changed to a modernized western lifestyle.[16,17] This change coincided with a significant increase in chronic diseases like hypertension, diabetes, and other degenerative diseases.[17-20] In Saudi Arabia, the overall prevalence of diabetes in adults is 18.3%.[21] A serum UA content >6.57 mg/dL increases the risk of all-cause mortality.[5] Moreover, serum UA levels have been linked to glucose intolerance, obesity, and diabetes.[5] Therefore, we aimed to investigate the association between serum UA with diabetes and other critical biochemical parameters in the Asir region of Saudi Arabia.

Material and Method

This research was planned and carried out according to the Helsinki Declaration standards.[22] Data were properly de-identified, and there was no risk to the study subjects. The research ethics committee at King Khalid University granted approval and granted a waiver of the subject consent requirement (HAPO-06-B-001) (approval number ECM#2021-4405). Neither participant identity nor bioinformation was collected or disclosed. This is a retrospective cross-sectional study; lab reports from different commercial labs were screened over a period of 2 years (July 2018 to June 2020) in the Asir province of Saudi Arabia. Biochemical reports such as UA, urea, blood urea nitrogen (BUN), creatinine, glycosylated hemoglobin (HbA1c), fasting blood sugar (FBS), total cholesterol (TC), low-density lipoprotein (LDL), triglycerides (TG), and high-density lipoprotein (HDL) were recorded from the electronic file system. A total of 2500 lab reports were retrieved from those labs in the Asir region of Saudi Arabia. Laboratory reports were reviewed and excluded for any incomplete biochemical data and those who have liver, kidney, or metabolic diseases; a total of 1984 reports were included in the final study. The screened participant's reports were either from the customer who visited the lab for a routine health check-up or a follow-up of chronic health conditions.

We defined it as hyperuricemia if serum UA concentration is >7 mg/dL in men and >6 mg/dL in women.[2,23-26] HbA1c was defined as normal if <5.7%, prediabetes if 5.7% to 6.4%, and diabetes if >6.5%.[27] The reference range for TC were set as normal (<200 mg/d), borderline high (200–239 mg/dL), and high (≥240 mg/dL), respectively.[28,29] The reference range for LDL was set as optimal (<100 mg/dL), near optimal (100–129 mg/dL), borderline high (130–159 mg/dL), high (160–189 mg/dL), and very high (≥ 190 mg/dL), respectively.[28,29] For TG, normal (<150 mg/dL), borderline high (150–199 mg/dL), high (200–499 mg/dL), and very high (≥500 mg/dL), respectively.[28,29] The cutoff points used for lipid profile parameters for TC was 200 mg/dL, TG was 150 mg/dL, LDL was 130 mg/dL, and HDL was 40 mg/dL, respectively.

Statistical analysis

Data analysis was done using IBM-SPSS version 26 (SPSS Inc., Chicago, IL, USA). Chi-Square was used to analyze categorical variables and expressed as a percentage ± standard deviation (SD). T-test was used to assess the difference between group means of parametric variables, while Mann–Whitney and Kruskal–Wallis tests were used to compare groups of independent nonparametric variables.[16,17] Logistic regression analysis and receiver operator characteristics (ROCs) curves were used to analyze biochemical parameters against the risk of diabetes in the study population.[30-31] The significance level was set at $P < 0.05$.

Results

General characteristics

In total, our study included 1984 lab reports with 1215 females (61.2%) and 769 males (38.6%). The mean age ± SD (years) was 41.86 ± 14.15 ranging from 20 to 93 years, and the most represented age group was 31 to 40 years (36.1%). There was no significant difference ($P = 0.086$) in the mean age between the females (40.95 ± 13.90 years) and males (43.30 ± 14.41 years). Age range of the study population stratified by gender is presented in Table 1.

The median ± IQR level of UA in the study population was 6.4 ± 1.30 mg/dL with minimum value of 1.0 mg/dL and maximum value of 13.60 mg/dL ($P > 0.05$). The median ± IQR level of urea in the study subject was 27.0 ± 12.0 mg/dL with a minimum value of 6.0 and a maximum value of 220 mg/dL ($P > 0.05$). The median ± IQR level of BUN in the study population was 12.61 ± 5.61 mg/dL with a minimum value of 2.80 and maximum value of 102.80 mg/dL ($P > 0.05$). The median ± IQR level of creatinine in the study population was 0.84 ± 0.29 mg/dL with minimum value of 0.20 mg/dL and maximum value of 14.50 mg/dL ($P > 0.05$). The median ± IQR level of the BUN/creatinine ratio of the study population was 15.37 ± 6.29 mg/dL with a minimum value of 18.70 mg/dL and maximum value of 80.76 mg/dL ($P > 0.05$). The median ± IQR level of HbA1c in the study population was 5.50 ± 0.90%, with a minimum value of 4.2% and a maximum value of 13.40% ($P > 0.05$). The median ± IQR level of FBS in the study population was 101.0 ± 16.0 mg/dL with minimum value of 62.0 mg/dL and maximum value of 423.0 mg/dL ($P > 0.05$). The median ± IQR level of TC in the study population was 192.0 ± 55.0 mg/dL with minimum value of 85.0 mg/dL and maximum value of 743.0 mg/dL ($P > 0.05$). The median ± IQR

Table 1: Demographic characteristics of the study population

Age range	Gender name		Total
	Female	Male	
20-30	13.9% (275)	6.9% (137)	20.8% (412)
	13.9%	6.9%	20.8%
31-40	22.9% (455)	13.2% (261)	36.1% (716)
	22.9%	13.2%	36.1%
41-50	11% (219)	8.5% (168)	19.5% (387)
	11.0%	8.5%	19.5%
Above 50	13.4% (266)	10.2% (203)	23.6% (469)
	13.4%	10.2%	23.6%
	61.2% (1215)	38.5% (769)	100% (1984)

level of LDL in the study population was 128.0 ± 49.0 mg/dL with minimum value of 38.0 mg/dL and maximum value of 436.0 mg/dL ($P > 0.05$). The median ± IQR level of TG in the study population was 125.0 ± 65.0mg/dL with minimum value of 34.0 mg/dL and maximum value of 1313 mg/dL ($P > 0.05$). The median ± IQR level of HDL in the study population was 45.0 ± 14.0 mg/dL with minimum value of 12.0 mg/dL and maximum value of 103.0 mg/dL ($P > 0.05$). As presented in Table 2, the higher UA quartiles were associated with the high level of urea, BUN creatinine, HbA1c, FBS, and TC ($P < 0.05$), but the lower level of BUN/creatinine ratio, LDL, TG, and HDL ($P < 0.05$) among females and males throughout the quartiles.

Prevalence of hyperuricemia and other biochemical parameters

A significantly high prevalence ($P = 0.033$) of hyperuricemia (53.5%) was observed in our study population. Among them, there were 41.2% females and 12.3% males. The overall prevalence of high BUN in the study population was only 10.8%, with 7.1% females and 3.7% males ($P = 0.267$). The prevalence of elevated creatinine in the study population was 13.8%, among which there were 8.6% females and 5.2% males ($P = 0.090$). The study population's overall prevalence of BUN/creatinine ratio was 20.4%, with 12.9% females and 3.9% males ($P = 0.049$). The overall prevalence of prediabetic patients in our study population was 19.9%, with 12.8% females and 7.2% males ($P = 0.039$). The overall prevalence of diabetic patients in our study population was 21.4%, with 13.0% females and 8.4% males ($P = 0.041$). The prevalence of high TC among the study population was 13.1%, with 8.5% females and 4.6% males ($P = 0.005$). The prevalence of high LDL in the study population was 13.4%, with 7.9% females and 5.5% males ($P = 0.143$). The prevalence of high TG among the study population was 14.4%, with 8.7% females and 5.7% males ($P = 0.215$). A significantly increased prevalence of low HDL was observed in the study population with 18.6% females and 12.1% males ($P = 0.046$). Similarly, the prevalence of optimal HDL was significantly high (57.4%) with 34.8% females and 22.6% males ($P = 0.001$). The overall prevalence of hyperuricemia, BUN/creatinine ratio, prediabetes and diabetes, TC, and LDL was significantly higher in the female ($P < 0.05$) population in comparison to the male study population [Table 3]. Furthermore, the prevalence of hyperuricemia was significantly lower in the diabetes and prediabetes groups than in the normal group ($P = 0.000$) [Table 4]. However, the prevalence of high lipid profiles (TC, TG, and LDL) was significantly high in the diabetic and prediabetes group ($P < 0.05$) [Table 4]. Similarly, the prevalence of low HDL was relatively high in diabetes and prediabetes groups ($P < 0.05$) [Table 4]. The general characteristic of the diabetic and prediabetic population stratified by gender is presented in Table 5.

Correlation of biochemicals parameters

Spearman correlation was used to determine the correlation of urea, BUN, creatinine, BUN/creatinine ratio, HbA1c, and lipid profile to

Table 2: General characteristic of the study population stratified by UA quartiles

	Female					Male				
	Q1	Q2	Q3	Q4	*P*	Q1	Q2	Q3	Q4	*P*
Age (mean±SD years)	40.47±13.68	41.42±13.84	41.0±14.22	40.88±13.86	0.878†	42.06±14.41	44.28±15.0	44.61±14.82	42.03±13.46	0.145†
Urea (Median±IQR) mg/dL	24.0±11.0	27.0±11.0	29.0±11.50	30.0±12.0	0.000‡	24.0±11.0	27.0±10.50	27.50±9.0	30.0±12.0	0.000‡
BUN (Median±IQR) mg/dL	11.21±5.14	12.61±5.14	13.55±5.37	14.01±5.61	0.000‡	11.21±5.14	12.61±4.91	12.85±4.21	14.01±5.61	0.000‡
Creatinine (Median±IQR) mg/dL	0.7±0.27	0.82±0.28	0.88±0.22	0.94±0.26	0.000‡	0.70±0.26	0.80±0.25	0.89±0.23	0.93±0.27	0.000‡
BUN/Creatinine ratio (Median±IQR)	16.36±7.75	15.84±6.29	15.18±6.24	14.81±5.72	0.001‡	15.67±6.85	15.39±6.71	14.24±5.83	14.89±6.72	0.008‡
HbA1c% (Median±IQR)	5.30±0.60	6.6±0.80	5.94±0.95	5.60±1.10	0.000‡	5.20±0.50	6.55±1.20	5.6±0.80	5.7±1.20	0.000‡
FBS (Median±IQR) mg/dL	101.0±2.0	116.8±25.50	115.2±22.75	112.25±22.0	0.025‡	101.0±2.0	117.40±26.0	111.06±17.50	108±19.25	0.047‡
TC (Median±IQR) mg/dL	182.0±54.0	192.0±54.50	189.0±50.50	199.50±61.0	0.012‡	189.50±49.50	192.0±48.25	206.50±59.75	223.7.50±46.25	0.008‡
LDL (mean±SD) mg/dL	117.98±35.95	132.03±38.69	129.50±35.51	128.27±35.60	0.000†	128.50±42.0	133.0±53.0	131.0±46.25	129.21±46.0	0.044‡
TG (Median±IQR) mg/dL	102.0±71.0	136.0±68.0	130.0±59.50	124.50±61.75	0.000‡	107.0±66.50	140.0±71.25	133.50±59.50	123.0±75.25	0.000‡
HDL (Median±IQR) mg/dL	48.0±14.50	39.0±13.0	44.0±15.50	43.0±15.0	0.000‡	46.0±14.75	46.0±14.0	43.50±13.0	43.0±12.50	0.000‡

†Analyzed by one-way ANOVA, ‡Analyzed by Kruskal-Wallis Test. UA quartiles: <5.9 mg/dL, 5.9-6.4 mg/dL, 6.4-7.2 mg/dL, and <7.2 mg/dL

Table 3: Prevalence (%) of different biochemical parameters in the study populationstratified by gender

	Total% (*n*)	Female	Male	*P*†
Hyperuricemia	53.5% (1061)	41.2% (817)	12.3% (244)	0.033
High BUN	215 (10.8%)	7.1% (141)	3.7% (74)	0.267
High creatinine	13.8% (273)	8.6% (170)	5.2% (103)	0.090
High BUN/Creatinine	20.4% (405)	12.9% (255)	3.9% (77)	0.049
HbA1c (5.7-6.4)	19.9% (395)	12.8% (253)	7.2% (142)	0.039
HbA1c (≥6.5)	21.4% (425)	13% (258)	8.4% (167)	0.041
FBS (100 mg/dL-125 mg/dL)	51% (1011)	30.6% (608)	20.3% (403)	0.016
FBS (≥126 mg/dL)	17.2% (341)	10.8% (215)	6.4% (126)	0.005
Borderline high TC	29.,9% (593	17.3% (342)	12.7% (251)	0.075
High TC	13.1% (261)	8.5% (169)	4.6% (92)	0.005
Borderline high LDL	582 (29.2%)	17.5% (348)	11.8% (234)	0.015
High LDL	13.4% (266)	7.9% (156)	5.5% (110)	0.143
Very high LDL	5.3% (105)	3.3% (66)	2.0% (39)	0.157
Borderline High TG	19.2% (380)	11.5% (228)	7.7% (152)	0.210
High TG	14.4% (285)	8.7% (172)	5.7% (113)	0.215
Very High TG	0.6% (12)	0.4% (7)	0.3% (5)	0.494
Low HDL	30.7% (608)	18.6% (368)	12.1% (240)	0.046
Good HDL	237 (12%	7.9% (157)	4.0% (80)	0.563
Optimal HDL	57.4% (1137)	34.8% (690)	22.6% (447)	0.001

†Analyzed by Chi-square test

Table 4: Prevalence of high biochemical parameters is study population stratified by diabetes, prediabetes, and normal group

	HbA1c range			*P*†
	Diabetes	Prediabetes	Normal	
Hyperuricemia	12.7% (252)	12.65% (251)	28.1% (558)	0.000
High BUN	5.8% (116)	1.9% (38)	3.1% (61)	0.000
High Creatinine	4.9% (98)	2.8% (55)	6.0% (120)	0.000
High BUN/creatinine	7.9% (156)	3.8% (76)	8.7% (73)	0.000
High TC	24.8% (491)	9.8% (195)	8.5% (168)	0.012
High LDL	27.8% (552)	10.7% (213)	9.5% (188)	0.017
High TG	17.6% (350)	7.6% (150)	8.9% 177)	0.000
Low HDL	18.6% (368)	9.1% (181)	6.9% (137)	0.000

†Analyzed by Chi-square test

the UA. A significant ($P < 0.05$) positive correlation was observed among urea, BUN, HbA1c, TC, LDL, and TG with UA [Table 6]. This study demonstrates that the increase in urea, BUN, creatinine, HbA1c, TC, LDL, and TG is associated with a high UA value. However, a significant inverse correlation was observed between the BUN/creatinine ratio and HDL with UA level. This finding suggests an increase in the BUN/creatinine ratio value, and HDL values will tend to experience a decrease in UA value.

Predictive model and biochemical markers for diabetes

Prediction models were performed by ROC analysis on biochemical parameters to the risk of diabetes as the outcomes of this study [Figure 1].

UA, urea, BUN, creatinine, BUN/creatinine ratio, and TG may be used as a predictive model because they have an area under the curve >0.5 [Table 7]. UA has a sensitivity value of 71.1% and specificity of 61.5%, with a cut-off value of 6.15; urea has a sensitivity value of 74.8% and specificity value of 54.8%, with a cut-off value of 2.31. BUN has a sensitivity value of 52.2% and specificity of 25.7%, with a cut-off value of 14.70, while creatinine has a sensitivity of 42.4% and specificity of 33.6%, with a cut-off value of 0.915. BUN/creatinine ratio has a sensitivity value of 60.7% and specificity value of 34.9%, with a cut-off value of 16.42. TG has a sensitivity of 79.3% and specificity of 71.3%, with a cut-off value of 102.5%. The value of biochemical parameters exceeding the cut-off point will be classified as high level, and the value equal to or below the cut-off point will be considered a normal level. Multinomial regression analysis found that

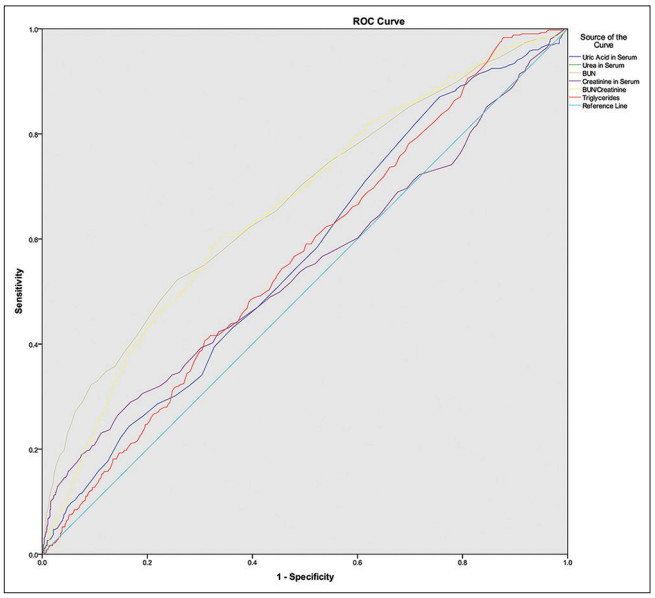

Figure 1: ROC analysis of different biochemical parameters predictive marker for diabetes

Table 5: General characteristics of diabetic and prediabetic population stratified by gender

	Female		Male		*P*
	Diabetes	Prediabetes	Diabetes	Prediabetes	
Age (mean±SD years)	42.29±13.90	40.87±14.06	43.49±14.54	43.62±13.78	0.000†
Uric acid (Median±IQR) mg/dL	6.60±1.25	7.90±1.10	6.70±1.23	7.6±1.0	0.000‡
Urea (Median±IQR) mg/dL	40.00±12.0	29.90±12	31.0±19.00	27.50±9.25	0.000‡
BUN (Median±IQR) mg/dL	18.69±5.61	13.55±5.61	14.48±8.88	12.85±4.32	0.001‡
Creatinine (Median±IQR) mg/dL	1.89±0.26	0.85±0.26	0.93±0.27	0.85±0.26	0.001‡
BUN/Creatinine ratio (Median±IQR)	17.67±7.46	15.57±5.79	17.74±8.50	14.74±5.73	0.000‡
FBS (Median±IQR) mg/dL	150.50±65.50	102.0±16.50	141.0±59.0	104.0±15.0	0.000‡
TC (Median±IQR) mg/dL	207.0±66.50	197.0±59.50	223.0±68	201.50±48.25	0.004‡
LDL (Median±IQR) mg/dL	133.0±50.50	130.0±51.0	134.0±50.25	131.0±43.0	0.002‡
TG (Median±IQR) mg/dL	135±65.0	127.0±66.0	140.50±74.0	137.0±76.0	0.000‡
HDL (Median±IQR) mg/dL	39.0±14.0	45.0±13.0	38.0±15.0	43.0±13.50	0.000‡

†Analyzed by independent sample *t*-test, ‡analyzed by Mann-Whitney test

Table 6: Spearman correlation between uric acid and other biochemicals parameters

	Uric acid	
	r (correlation coefficient)	*P*
Urea	0.242	0.000
BUN	0.242	0.000
Creatinine	0.444	0.000
BUN/Creatinine ratio	−0.099	0.000
HbA1c	0.211	0.000
TC	0.058	0.010
LDL	0.704	0.000
TG	0.629	0.000
HDL	−0.166	0.000

UA (OR = 1.33; CI = 1.04–1.7; *P* = 0.023), creatinine (OR = 1.65, CI = 1.14–2.4; *P* = 0.007), BUN (OR = 3.05, CI = 1.98–4.68; *P* = 0.000), BUN/creatinine (OR = 2.63; CI = 1.91–3.63; *P* = 0.000), TC (OR = 3.75; CI = 0.73–1.57; *P* = 0.011), TG (OR = 2.67;CI = 1.30–2.14; *P* = 0.000), and low HDL (OR = 1.53; CI = 1.19–1.95; *P* = 0.001) are associated with high level of HA1C and could be a risk factor for the occurrence of diabetes. High UA, BUN, TC, and TG parameters are the most influential risk factors in diabetic and prediabetic patients than those with normal UA, BUN, TC, and TG values [Table 8].

Discussion

Our investigation focused on assessing HbA1c, serum UA levels, and other important biochemical parameters among the general adult population from the Asir province of Saudi Arabia in this population-based cross-sectional study. UA is an end product of purine catabolism.[32] Hyperuricemia has been demonstrated as a potential risk factor for metabolic syndrome, hypertension, stroke, cardiovascular disease, atherosclerosis, and chronic renal disease.[2,14] HbA1c level is commonly used as a clinical indicator for glycemic control and is used as a tool to diagnose people with unidentified diabetes or who are at risk.[17] The relationship between UA levels and impaired glucose metabolism has long been a hot research topic. A large number of studies have demonstrated the "bell" fit association between UA and plasma glucose level. UA levels tend to fall after their initial rise, accompanied by increased blood glucose concentration.[33,34] This study demonstrated that the prevalence of hyperuricemia in the whole study population was 53.5% (41.2% females, 12.3% males), in the diabetic population was 12.7% (9.47% females, 3.23% males), and in prediabetics was 12.65% (9.8% females, 2.85% males), respectively. Wei *et al*.[14] reported that the prevalence of hyperuricemia among diabetic patients was 17.25% (14.86% men, 20.06% female) and was more frequent in women in Tianjin, China. Some researchers have suggested that this gender difference could result from the uricosuric effects of estrogen.[7,9] Male and female have a metabolic differential in serum UA, which may be due to the variation in sex hormones.[35] Also, this speculation was further reinforced by hormonal replacement therapy to reduce the incidence of hyperuricemia and associated consequences.[36] Furthermore, these gender-specific associations of UA were also observed in other studies.[4,9,10,37] Dyslipidemia (elevated LDL, elevated TG, and low level of HDL) and HbA1c were highly correlated with UA. Our data support other recent reports on the UA levels in Saudi females with diabetes.[38]

One of the most severe consequences of hyperuricemia is gout and renal disease, which are recognized as risk factors for developing metabolic syndrome, cardiovascular disease, and hypertension, known as complications of longstanding diabetes.[2,8,9,23-25] So far, there have been few investigations on the relationship between UA and glucose metabolism disorders, and even the available data are conflicting. Certain studies suggest a positive correlation between elevated serum UA levels and diabetes, whereas other reports are neutral or negative correlations.[1,5,6,39] We observed a statistically significant increment of HbA1c and FBS across the serum UA quartiles. In our study population, the prediabetic group had the maximum UA levels followed by the non-diabetic and diabetic group, which may indicate that the high UA levels may accelerate the development of diabetes or the high UA level has a role in the pathogenesis of diabetes. Earlier studies also reported similar findings.[15,40,41] Vučak *et al*.[41] reported the positive association between hyperuricemia and prediabetes (OR 1.66, 95% CI 1.09–2.53).

Table 7: Area under the curve (AUC), cutoff value, sensitivity, and specificity of biochemical parameters

Parameters	AUC	*P*	Cut-off value	95% CI	Sensitivity	Specificity
UA	0.564	0.000	6.15	0.533-0.594	71.1	61.5
Urea	0.671	0.000	25.5	0.641-0.701	74.8	54.8
BUN	0.671	0.000	14.70	0.641-0.701	52.2	25.7
Creatinine	0.545	0.005	0.915	0.511-0.578	42.4	33.6
BUN/creatinine ratio	0.659	0.000	16.42	0.630-0.688	60.7	34.9
TG	0.564	0.000	102.5	0.534-0.594	79.3	71.3

Table 8: Risk analysis of different biochemical parameters in diabetes and prediabetes

Parameters	Diabetes				Prediabetes			
	Sig.	OR	95% Confidence Interval for OR		Sig.	OR	95% Confidence Interval for OR	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
High Uric acid	0.023	1.33	1.041	1.707	0.000	2.676	1.314	3.138
High Creatinine	0.007	1.65	1.146	2.400	0.037	1.207	0.822	1.773
High BUN	0.000	3.05	1.983	4.680	0.022	2.293	0.777	3.150
BUN/creatinine ratio	0.000	2.63	1.912	3.633	0.013	1.552	1.095	2.198
TC	0.011	3.75	0.733	4.578	0.072	1.098	0.893	1.888
LDL	0.032	1.88	0.206	1.995	0.077	0.994	0.683	1.447
TG	0.000	2.67	1.305	2.840	0.018	1.943	1.052	2.714
Low HDL	0.001	1.527	1.194	1.954	0.046	1.094	0.854	1.401

Similarly, Xue *et al*.[15] reported that patients with prediabetes had higher UA levels than those with normal glucose tolerance. Recently, Haque *et al*.[6] reported that prediabetic individuals had a higher mean level of UA (338.2 μmol/L) compared with diabetic individuals (290.9μmole/L). On the other side, National Health and Nutrition Examination Survey (NHANES III), USA, reported a significantly low prevalence of hypouricemia among diabetic patients compared with healthy individuals.[42] In 2019, another study investigated the relationship between serum UA levels and clinical and biochemical markers in diabetic individuals. They reported that serum UA was positively associated with CVD incidence in diabetes patients.[20] Similarly, Sui *et al*. [23] reported that the high levels of serum UA in diabetic patients are strongly associated with the risk of metabolic syndrome. Our result is consistent with the above studies. However, some research has revealed contradictory findings.[1,5]

Stratified by gender, we observed a significantly high prevalence of diabetes and prediabetes among hyperuricemic females (9.47% and 9.8%) in comparison to hyperuricemic males (3.23% and 2.85%). This finding was consistent with earlier cohort studies. Chou *et al*.[43] reported that the association of serum UA level to insulin resistance and plasma glucose levels is more substantial in females than in males. According to Meisinger *et al*.,[44] UA is related to the development of diabetes in women (HR = 2.05 for each 1 mmol/L increase). Yamada *et al*.[45] reported the statistically significant correlation between serum UA and the probability of developing diabetes and impaired fasting glucose in women. Similarly, Kivity *et al*.[46] demonstrated that UA is associated with diabetes outcomes in females (HR 1.57, 95% CI 1.32–1.86) but not in males (HR 1.08, 95% CI 0.99–1.17).

The molecular mechanisms underlying the association between serum UA in glucose metabolism and the development of diabetes are still debatable. The activation of the NF-kB signaling pathway, which is related to the generation of renal inflammatory markers and vascular alterations, is maybe one plausible mechanism for these changes to occur.[47] Hyperuricemia can influence endothelial dysfunction, which stimulates the renin-angiotensin system while suppressing the neuronal nitric oxide system, resulting in a dysregulation of the glucose uptake system.[48] Hyperuricemia results in mitochondrial oxidative stress, which increases fat storage without high caloric intake.[49] Furthermore, insulin resistance can develop due to the mitochondrial oxidative stress in islet cells and the encouragement of fatty liver production.[49] Again, reverse transport of UA and glucose in renal tubules may account for the association between serum UA and the incidence of prediabetes, followed by diabetes.[14] This condition is implicated in the underlying mechanism of hyperuricemia and the occurrence of diabetes, and it plays a crucial role in the pathogenesis of diabetes.[8,50-55] This finding supports the hypothesis that serum UA might be involved in the early stages of impaired glucose metabolism leading to prediabetes and accelerating the development of diabetes.

This study has a few strengths. To the best of our knowledge, this is the first kind of advanced population-based study in Saudi Arabia to demonstrate the association between serum UA level and diabetic patients and other biochemical parameters. This population-based design has a comparatively large sample size, including healthy, prediabetic, and diabetic populations. However, there are a few limitations that need to be considered. A cross-sectional study precludes any causality analysis. Furthermore, our study was a single-center study; thus,

it is unclear whether or not our findings apply to other parts of Saudi Arabia. In addition, this study was unable to assess lifestyle variables from the study sample.

Conclusion

Serum UA was substantially higher in prediabetic individuals, but a decreasing trend was observed in non-diabetic followed by diabetic individuals. Our study population observed a positive correlation between serum UA and dyslipidemia (high TC, high LDL, and high TG); however, it was relatively weak after controlling for urea, BUN, and creatinine. In the prediabetic and diabetic group, dyslipidemia did not contribute independently to the serum UA, serum creatinine, BUN, and urea were the strongest predictor of serum UA in our study population.

Keypoint

- Hyperuricemia is associated with prediabetes
- Positive correlation between UA and dyslipidemia

Declaration of patient consent

The study protocol and study subject consent waiver were approved by the research Ethics Committee at King Khalid University (HAPO-06-B-001). The research was conducted by using de-identified data. Neither personal identification nor bio-information was disclosed. Hence patients concent approval was waived by the ethical approval committee because as the procedure does not involve any risk to the participants.

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Conflicts of interest

There are no conflicts of interest.

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