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Urine Composition in Type 2 Diabetes: Predisposition to Uric Acid Nephrolithiasis

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Type 2 diabetes is a risk factor for nephrolithiasis in general and has been associated with uric acid stones in particular. The purpose of this study was to identify the metabolic features that place patients with type 2 diabetes at increased risk for uric acid nephrolithiasis. Three groups of individuals were recruited for this outpatient study: Patients who have type 2 diabetes and are not stone formers ($n = 24$), patients who do not have diabetes and are uric acid stone formers (UASF; $n = 8$), and normal volunteers (NV; $n = 59$). Participants provided a fasting blood sample and a single 24-h urine collection for stone risk analysis. Twenty-four-hour urine volume and total uric acid did not differ among the three groups. Patients with type 2 diabetes and UASF had lower 24-h urine pH than NV. Urine pH inversely correlated with both body weight and 24-h urine sulfate in all groups. Urine pH remained significantly lower in patients with type 2 diabetes and UASF than NV after adjustment for weight and urine sulfate ($P < 0.01$). For a given urine sulfate, urine net acid excretion tended to be higher in patients with type 2 diabetes *versus* NV. With increasing urine sulfate, NV and patients with type 2 diabetes had a similar rise in urine ammonium, whereas in UASF, ammonium excretion remained unchanged. The main risk factor for uric acid nephrolithiasis in patients with type 2 diabetes is a low urine pH. Higher body mass and increased acid intake can contribute to but cannot entirely account for the lower urine pH in patients with type 2 diabetes.

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Obesity and type 2 diabetes have reached epidemic proportions worldwide (1,2) and have been implicated as risk factors for nephrolithiasis (3,4). In addition to conferring higher stone risk in general, type 2 diabetes is associated with an increased prevalence of uric acid stones as demonstrated by recent cross-sectional studies(5,6). In one report, uric acid was the main stone constituent in a significantly higher proportion of patients with diabetes than without (5). In another retrospective study, uric acid stones were detected in 33.9% of patients with type 2 diabetes *versus* 6.2% of stone-forming patients without diabetes (6).

This study was conducted to examine the pathophysiologic mechanisms that underlie the strong association between type 2 diabetes and uric acid nephrolithiasis. A low urine pH is the predominant metabolic abnormality in uric acid stone disease (7,8). At a urine pH <5.5, uric acid is sparingly soluble and will precipitate at concentrations >200 mg/L (9). Other urinary abnormalities also predispose to uric acid stone formation, including hyperuricosuria and a low urine volume (10). We therefore evaluated the potential metabolic and biochemical features in patients with type 2 diabetes that predispose them to uric acid stone formation. Uric acid stone formers (UASF) demonstrate features of insulin resistance, a shared characteristic between this group and patients with type 2 diabetes (11). We therefore compared the findings in patients who have type 2 diabetes and are not stone formers with those of normal volunteers (NV) and UASF to determine whether a spectrum of metabolic anomalies exists among these groups.

Materials and Methods

Study Participants

The study was approved by the Institutional Review Board at the University of Texas Southwestern Medical Center (Dallas, TX), and all participants provided informed consent. Three groups were enrolled for this study: NV, patients with type 2 diabetes and without kidney stones, and UASF. Patients with type 2 diabetes and NV were recruited through local advertisements. Patients with type 2 diabetes initially were identified by self-report, and the diagnosis was corroborated by use of oral hypoglycemic agents and/or by fasting blood glucose >126 mg/dl. UASF without type 2 diabetes were serially recruited from the Stone Clinic at the University of Texas Southwestern Medical Center during the same time period as the two other groups. The diagnosis of uric acid stone disease was confirmed by stone analysis.

Individuals were included when they were older than 35 yr. Excluded from the study were pregnant women and individuals with chronic diarrheal illness, creatinine clearance <70 ml/min, or liver disease. An additional exclusion criterion was the use of insulin, thiazolidinediones, or nonsteroidal anti-inflammatory drugs. UASF were instructed to discontinue all medications for treatment of renal stones (allopurinol, potassium citrate) for at least 1 wk before evaluation. Seven patients from the type 2 diabetes group did not take any oral

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hypoglycemic agents, eight took metformin only, two used sulfonylureas alone, and six were taking a combination of a sulfonylurea and metformin.

Study Protocol

This cross-sectional study was conducted in an outpatient setting. Participants maintained their random home diets. Study participants completed a 24-h urine collection, and a fasting blood sample was obtained. Twenty-four-hour urine was collected under mineral oil and was refrigerated or placed in an ice chest. Urinary measurements included total volume, pH, creatinine, uric acid, citrate, sulfate, ammonium, titratable acidity (TA), and bicarbonate. A fasting blood sample was obtained for the measurement of serum electrolytes, creatinine, uric acid, glucose, and insulin. Body weight and height of the participants were obtained at the time of the blood collection.

Analytical Procedures

Measurements of serum sodium, potassium, chloride, total carbon dioxide, glucose, blood urea nitrogen, uric acid, and creatinine concentrations were obtained as a part of systematic multichannel analysis (using Beckman CX9ALX; Beckman Coulter, Fullerton, CA). Serum insulin was assessed by ELISA (Mercodia Inc., Metuchen, NJ).

Urine pH was measured with a pH electrode. Urinary potassium was assessed by an ion-specific electrode (Beckman Coulter). Uric acid was analyzed by the uricase method using an alkalinized aliquot to prevent precipitation. Urine creatinine and ammonium (NH_4^+) were measured by the picric acid method and the glutamate dehydrogenase method, respectively. Urine sulfate was determined by ion chromatography. Urine TA was measured directly using the automated burette endpoint titration system (Radiometer, Copenhagen, Denmark). Urine citrate was determined enzymatically using reagents from Boehringer-Mannheim Biochemicals (Indianapolis, IN), and milliequivalents of citrate were calculated from urine pH and a pKa of citrate^{2-}/citrate^{3-} of 5.6. Urine bicarbonate (HCO_3^-) was calculated from urine pH and Pco_2.

Endogenous creatinine clearance was calculated from values for creatinine in fasting serum and 24-h urine samples. Urine net acid excretion (NAE) was calculated as (NH_4^+ + TA) − (HCO_3^- + citrate), all in milliequivalents. Net gastrointestinal absorption of alkali (NGIA) was calculated as [Urine ($Na^+ + K^+ + Ca^{2+} + Mg^{2+}$ mEq/d) − (Cl^- mEq/d + 1.8 × PO_4^{3-} mmol/d)], mEq/d as described previously (12). The ratio of urine NAE/sulfate was calculated for all groups.

Statistical Analyses

The demographic characteristics and biochemical features of the three study groups are presented as mean ± SD and were compared using the Kruskal-Wallis test, followed by the Wilcoxon rank sum test. Assessment of correlation between continuous variables was performed using Spearman or Pearson coefficients. Analysis of covariance models were used to adjust for possible confounding factors such as age, weight, gender, creatinine, and sulfate excretion, with data transformations used as needed. Comparison of regression slopes was made with linear models. Because the UASF group contains mostly men, analyses were performed for men only and for the entire group in NV and patients with type 2 diabetes. Because exclusion of women did not alter the results, the data shown throughout this report include both genders. $P \leq 0.05$ was considered significant. Statistical analyses were performed using SAS 9.1 (SAS Institute, Cary, NC).

Results

Demographic Characteristics

Table 1 shows the demographic characteristics of the study participants. A total of 91 individuals participated in this study: 24 in the type 2 diabetes group, 59 in the NV group, and eight in the UASF group. The mean age was not significantly different between NV and patients with type 2 diabetes; however, the UASF were older. The heights were not statistically different among the three groups. Weight and body mass index were significantly greater in patients with type 2 diabetes compared with NV. Weight in UASF was significantly higher than in NV.

Biochemical Characteristics

Blood Profile. Fasting serum biochemical profiles are shown in Table 2. UASF demonstrated a significantly higher serum uric acid concentration (6.9 ± 1.7 mg/dl) than patients with type 2 diabetes (5.5 ± 1.2 mg/dl) and NV (5.3 ± 1.2 mg/dl). Patients with type 2 diabetes had significantly higher fasting serum glucose compared with the other two groups. Fasting serum insulin was significantly higher in patients with type 2 diabetes (17.3 ± 9.2 mU/L) and UASF (15.2 ± 8.3 mU/L) than in NV (9.1 ± 5.9 mU/L), consistent with greater insulin resistance. Mean serum glycosylated hemoglobin concentration

Table 1. Characteristics of study participants[a]

	Study Group		
	NV	Patients with Type 2 Diabetes	UASF
No. of participants	59	24	8
Gender (M/F)	24/35	10/14	7/1
Race (White/Black/Asian)	38/16/5	16/8/0	7/1/0
Ethnicity (Hispanic/non-Hispanic)	2/57	5/19	0/8
Age (yr)	49 ± 8	52 ± 8	59 ± 6[b,c]
Height (cm)	168 ± 10	169 ± 9	172 ± 9
Weight (kg)	83 ± 20	94 ± 19[d]	96 ± 15[b]
BMI (kg/m^2)	29 ± 6	34 ± 7[d]	33 ± 7

[a]Data are mean ± SD. BMI, body mass index; NV, normal volunteers; UASF, uric acid stone formers.
[b]$P < 0.05$ UASF *versus* NV.
[c]$P < 0.05$ UASF *versus* patients with type 2 diabetes.
[d]$P < 0.05$ patients with type 2 diabetes *versus* NV.

Table 2. Fasting serum profile[a]

	Study Group		
	NV	Patients with Type 2 Diabetes	UASF
Creatinine (mg/dl)	0.9 ± 0.2	0.9 ± 0.2	1.1 ± 0.2[b,c]
Sodium (mEq/L)	139 ± 2	137 ± 2[d]	140 ± 4
Potassium (mEq/L)	4.2 ± 0.3	4.4 ± 0.3[d]	4.6 ± 0.6[b]
Chloride (mEq/L)	107 ± 3	106 ± 3	109 ± 3
Bicarbonate (mEq/L)	27 ± 2	26 ± 2	27 ± 2
Uric acid (mg/dl)	5.3 ± 1.2	5.5 ± 1.2	6.9 ± 1.7[b,c]
Glucose (mg/dl)	94 ± 11	137 ± 42[d]	98 ± 16[c]
Insulin (mU/L)	9.1 ± 5.9	17.3 ± 9.2[d]	15.2 ± 8.3[b]
Glycosylated hemoglobin (%)	5.3 ± 0.5	6.2 ± 0.8[d]	5.1 ± 0.4[c]

[a]Data are mean ± SD.
[b]$P < 0.05$ UASF *versus* NV.
[c]$P < 0.05$ UASF *versus* patients with type 2 diabetes.
[d]$P < 0.05$ patients with type 2 diabetes *versus* NV.

was significantly greater in patients with type 2 diabetes than in NV and UASF (6.2 ± 0.8 *versus* 5.3 ± 0.5 and 5.1 ± 0.4%, respectively). However, the mean glycosylated hemoglobin in patients with type 2 diabetes reflected good glycemic control in most subjects in this group.

Urine Profile. Table 3 shows the 24-h urine profiles for the three groups of subjects in the study. Twenty-four-hour urine volume and uric acid did not differ among the three groups. Twenty-four-hour urine pH in patients with type 2 diabetes (5.66 ± 0.42) and UASF (5.50 ± 0.37) was significantly lower than in NV (6.05 ± 0.42). Because of the low pH, the urinary undissociated uric acid content was significantly higher in patients with type 2 diabetes (193 ± 107 mg/d) and UASF (195 ± 82 mg/d) compared with NV (101 ± 75 mg/d). Similarly, the urine concentration of undissociated uric acid was significantly greater in patients with type 2 diabetes (113 ± 82 mg/L) and

Table 3. 24-hour urine profile[a]

	Study Group		
	NV	Patients with Type 2 Diabetes	UASF
Total volume (L/d)	2.1 ± 1.1	2.2 ± 1.2	1.7 ± 0.6
Total uric acid (mg/d)	500 ± 155	580 ± 224	527 ± 227
pH	6.05 ± 0.42	5.66 ± 0.42[b]	5.50 ± 0.37[c]
Undissociated uric acid (mg/d [median])	101 ± 75 (77)	193 ± 107 (188)[b]	195 ± 82 (178)[c]
Undissociated uric acid concentration (mg/L [median])	63 ± 52 (44)	113 ± 82 (86)[b]	124 ± 50 (136)[c]
Sulfate (mEq/d)	37 ± 13	45 ± 18[b]	39 ± 13
Potassium (mEq/d)	60 ± 22	63 ± 19	65 ± 24
NGIA (mEq/d)	33 ± 21	32 ± 25	28 ± 32
Creatinine clearance (ml/min)	117 ± 26	126 ± 27[b]	113 ± 22
Ammonium (mEq/d)	29 ± 14	36 ± 17	27 ± 17
Titratable acidity (mEq/d)	25 ± 12	34 ± 15[b]	36 ± 13[d]
Citrate (mEq/d)	11 ± 4	11 ± 5	7 ± 3[c,e]
Bicarbonate (mEq/d [median])	4.7 ± 5.5 (2.9)	1.8 ± 3.1 (1.2)[b]	2.2 ± 5.4 (0)[c]
NAE (mEq/d)	39 ± 27	56 ± 29[b]	53 ± 30
NAE/sulfate	1.03 ± 0.59	1.33 ± 0.39[f]	1.50 ± 0.91

[a]Data are mean ± SD, except when otherwise indicated. NAE, net acid excretion; NGIA, net gastrointestinal absorption of alkali.
[b]$P < 0.05$ patients with type 2 diabetes *versus* NV.
[c]$P < 0.05$ UASF *versus* NV.
[d]$P = 0.054$ UASF *versus* NV.
[e]$P < 0.05$ UASF *versus* patients with type 2 diabetes.
[f]$P = 0.09$ patients with type 2 diabetes *versus* NV.

UASF (124 ± 50 mg/L) compared with NV (63 ± 52 mg/L). Twenty-four-hour urine sulfate excretion was higher in patients with type 2 diabetes (45 ± 18 mEq/d) than in NV (37 ± 13 mEq/d), with an intermediate value in the UASF (39 ± 13 mEq/d). Urine potassium and NGIA were not significantly different among the three groups. None of the groups had impaired kidney function.

NAE was significantly higher in patients with type 2 diabetes (56 ± 29 mEq/d) than in NV (39 ± 27 mEq/d; $P \leq 0.05$). The mean 24-h urine ammonium excretion was not different among the groups. Urine TA was significantly greater in patients with type 2 diabetes (34 ± 15 mEq/d) and UASF (36 ± 13 mEq/d) *versus* NV (25 ± 12 mEq/d).

Determinants of Urine pH and NAE

To determine the effect of body weight on urine pH, we plotted these two variables in the three groups (Figure 1). An inverse relationship between body weight and urine pH was observed in all groups. Although the slopes were similar among the three groups, the adjusted means were significantly lower in UASF and patients with type 2 diabetes than in NV. After controlling for body weight, urine pH remained significantly lower in patients with type 2 diabetes and UASF compared with NV ($P = 0.011$).

We also evaluated the effect of dietary acid intake on urine pH (Figure 2). In all groups, an inverse relationship was demonstrated between urine pH and urine sulfate, an indirect measure of dietary acid load. For any given urine sulfate, urine pH was lowest in UASF, highest in NV, and intermediate in patients with type 2 diabetes (Figure 2). When adjusted for urine sulfate, urine pH in patients with type 2 diabetes and UASF

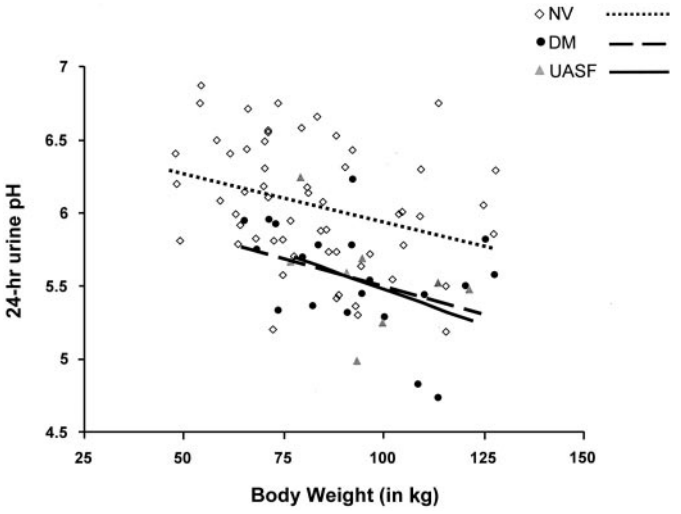

Figure 1. Twenty-four-hour urine pH *versus* body weight. An inverse relationship between body weight and urine pH was observed in all groups. Urine pH was significantly lower in patients with type 2 diabetes (DM; ●) and uric acid stone formers (UASF; ▲) compared with normal volunteers (NV; ◇) after controlling for body weight using analysis of covariance models ($P < 0.01$). Individual data points are shown as symbols with regression lines for each group.

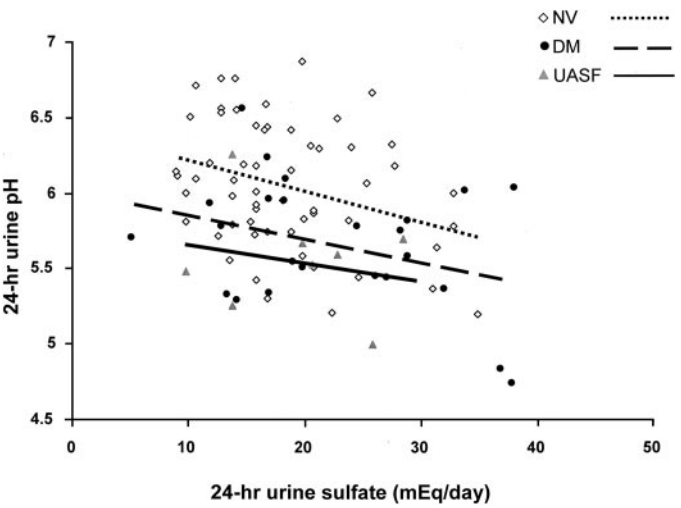

Figure 2. Twenty-four-hour urine pH *versus* 24-h urine sulfate. An inverse relationship between urine sulfate and urine pH was observed in all groups. Urine pH remained significantly lower in patients with type 2 diabetes (●) and UASF (▲) compared with NV (◇) after controlling for urine sulfate using analysis of covariance models ($P < 0.005$). Individual data points are shown as symbols with regression lines for each group.

was significantly lower than that in NV ($P = 0.0026$ and $P = 0.0023$, respectively). In multivariable analysis, urine pH remained significantly lower in patients with type 2 diabetes and UASF than in NV after adjustment for differences in weight, creatinine clearance, and urine sulfate ($P < 0.05$). In addition to variation in body weight, renal function, and dietary acid intake, other factors may be responsible for differences in urine pH among the three groups. We therefore compared urine NAE and its components with respect to dietary acid load. The ratio of NAE/sulfate tended to be higher in patients with type 2 diabetes (1.33 ± 0.39) and UASF (1.50 ± 0.91) compared with NV (1.03 ± 0.59; Table 3).

Figure 3 depicts the relationships of urine NAE and its components to dietary acid intake. For a given urine sulfate, urine NAE tended to be higher in patients with type 2 diabetes *versus* NV ($P = 0.07$ and $P = 0.04$ when adjusted for gender; Figure 3A). Urine ammonium was virtually identical between patients with type 2 diabetes and NV (Figure 3B). However, in UASF, urine ammonium excretion was not increased by higher dietary acid load, indicating a different pattern of renal NH_4^+ excretory response compared with patients with type 2 diabetes and NV (Figure 3B). More of the excreted acid appeared in the form of TA in UASF and patients with type 2 diabetes (Figure 3C). Controlling for urine sulfate excretion, urine TA was higher in UASF than in NV ($P = 0.006$). The regression slopes of the three groups were not statistically different (Figure 3C).

Discussion

The goal of this investigation was to evaluate which abnormalities place patients with type 2 diabetes at greater risk for uric acid nephrolithiasis. To our knowledge, this is the only

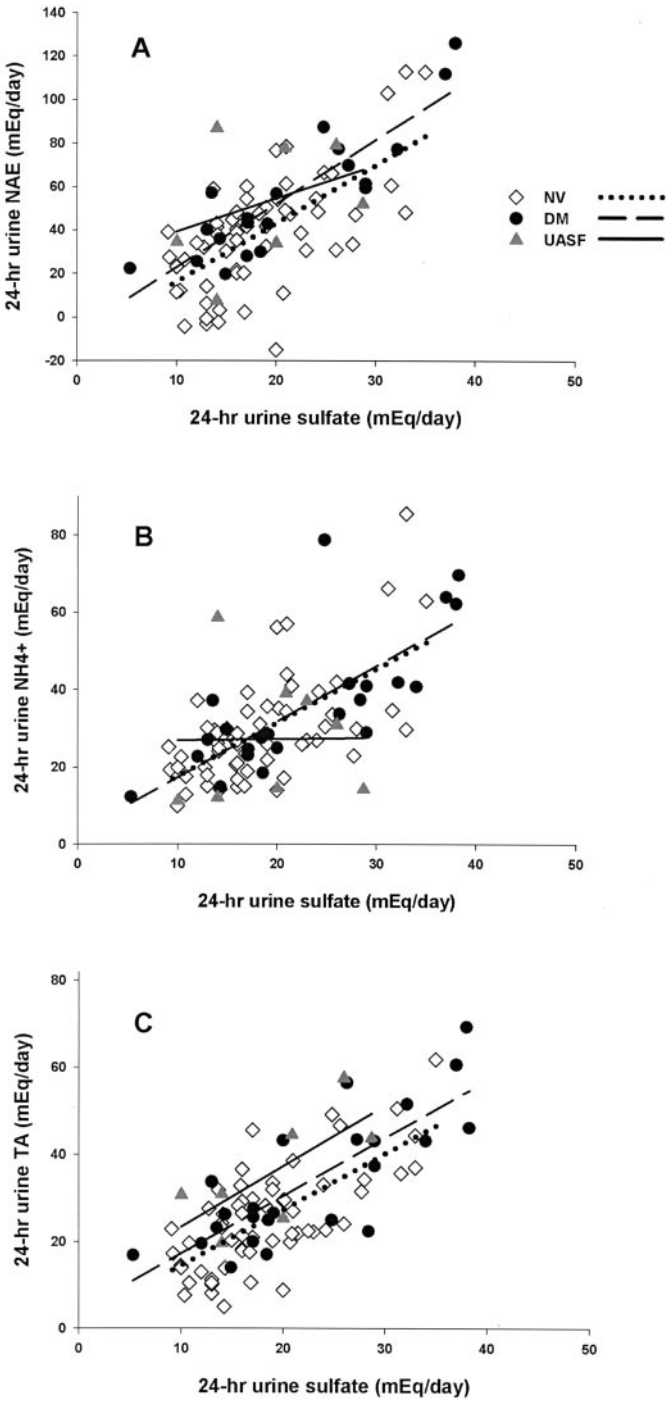

Figure 3. Twenty-four-hour urine net acid excretion (NAE; A) ammonium (B), and titratable acidity (TA; C) *versus* 24-hour urine sulfate. For a given urine sulfate, urine NAE tended to be higher in patients with type 2 diabetes *versus* NV (A). Urine ammonium was virtually identical between patients with type 2 diabetes and NV. In UASF, urine ammonium excretion was not altered by higher dietary acid load (B). More of the excreted acid appeared in the form of TA in UASF and patients with type 2 diabetes (C). Controlling for urine sulfate excretion, urine TA was higher in UASF than in NV ($P = 0.006$) using analysis of covariance models. In C, the regression slopes of the three groups were not statistically different when compared using linear models. Individual data points are shown as symbols with regression lines for each group.

study to examine urinary biochemical characteristics in non–stone-forming patients with type 2 diabetes. The primary risk factor identified in patients with type 2 diabetes was a low urine pH, a typical finding in uric acid nephrolithiasis (7). This feature seems to be shared between UASF and some patients with type 2 diabetes, suggesting a common underlying pathophysiologic abnormality. In addition, both UASF and patients with type 2 diabetes demonstrated obesity and hyperinsulinemia, which are characteristics of insulin resistance and the metabolic syndrome. When compared with individuals without diabetes, the acidic urine was not entirely explained by differences in body weight, kidney function, or dietary acid intake.

A low urine pH (≤5.5) is the single most important and invariant finding in patients with idiopathic uric acid stone disease (10). This acidic urinary environment promotes the precipitation of poorly soluble uric acid, leading to stone formation. The two other risk factors that predispose to uric acid nephrolithiasis are low urine volume and hyperuricosuria, although the latter is an uncommon finding in idiopathic UASF (7). The urine volume and uric acid excretion in patients with type 2 diabetes did not differ from NV, but urine pH was markedly lower. As a result of this more acidic urine, patients with type 2 diabetes had a significantly greater urinary content and concentration of undissociated uric acid, approaching the levels seen in UASF (Table 3).

Urine pH correlates inversely with body weight in a cross-sectional study of kidney stone formers (13). Higher body weight is also linked to insulin resistance (14), which may be responsible for the more acidic urine in heavier individuals (11). However, the association between body weight and urine pH has not been reported in non–stone-forming individuals. Our evaluation found a similar relationship in NV and patients with type 2 diabetes as well as in UASF (Figure 1), further indicating the importance of body weight as a determinant of urine pH. However, using covariate analysis, we found urine pH in patients with type 2 diabetes and UASF to be significantly more acidic than in NV after controlling for body weight. This suggests that factors other than body weight account for the lower urine pH in patients with type 2 diabetes and UASF.

Additional factors that are associated with low urine pH include older age, impaired renal function, and greater dietary acid intake (15–18). Age was not different between patients with type 2 diabetes and NV. Although creatinine clearance was significantly higher in patients with type 2 diabetes than in NV, no relationship was seen between creatinine clearance and urine pH in either group. In addition, the difference in urine pH between patients with type 2 diabetes and NV remained significant when adjusted for creatinine clearance. At this time, the implications of the higher creatinine clearance on urine acidification are unknown and require further investigation.

To determine the impact of dietary factors on urine pH, we measured urine potassium and calculated NGIA as indicators of dietary alkali. These two variables did not differ among the three groups; therefore, it is unlikely that the higher pH in NV is secondary to greater dietary alkali intake. We also measured urine sulfate, an indicator of dietary acid load. On the basis of

a random outpatient diet, patients with type 2 diabetes seem to consume more dietary acid, which can account partially for the lower urinary pH. To determine whether low urine pH in patients with type 2 diabetes is due to the differential effect of animal protein intake, we controlled for urine sulfate (Figure 2). Urine pH adjusted for urine sulfate remained significantly lower in patients with type 2 diabetes compared with NV. A multivariate analysis was performed to evaluate the combined effect of known determinants on urine pH. After controlling for body weight, creatinine clearance, urine sulfate, and age, urine pH still was significantly lower in patients with type 2 diabetes than in NV (5.65 *versus* 6.01; $P = 0.001$). Neither body weight nor dietary acid load in isolation or in combination can account completely for the lower urinary pH in patients with type 2 diabetes and UASF.

The primary buffer in the urine is ammonium; other buffers, including phosphate and various organic anions, are collectively referred to as titratable acids. The low urine pH in UASF has been attributed to relative ammonium deficiency. When UASF were studied in a highly controlled inpatient setting, they demonstrated a lower NH_4^+/NAE ratio and a much blunted ammoniagenic response to an acute oral acid load (8). Our outpatient study confirmed these findings in UASF who were on random *ad libitum* diets and demonstrated blunted urine NH_4^+ excretion in response to higher dietary acid intake (Figure 3B). In contrast, urine NH_4^+ for a given sulfate did not differ between patients with type 2 diabetes and NV (Figure 3B). This result suggests that patients with type 2 diabetes, unlike UASF, are able to augment their NH_4^+ excretion in the face of a greater dietary acid load. A previous study demonstrated that an acute insulin infusion increased urine ammonium excretion in normal individuals but not in UASF (11). These results suggest that impaired NH_4^+ excretion is a renal manifestation of insulin resistance. In our current study, urine NH_4^+ increased in relation to sulfate and NAE to a similar degree in insulin-sensitive (NV) and -resistant (patients with type 2 diabetes) non–stone formers. Although seemingly contradictory, the results from these two studies cannot be compared directly because the NH_4^+ response to an acute insulin infusion was not evaluated in this study. No available studies have examined differences in renal acidification response to acute *versus* chronic hyperinsulinemia.

In addition to the lower urine pH, patients with type 2 diabetes and UASF had greater NAE than NV. Furthermore, they exhibited a higher ratio of NAE/sulfate (Table 3), suggesting greater acid excretion that is independent of diet. This higher NAE in patients with type 2 diabetes and UASF can be attributed partially to increased TA excretion seen over a wide range of urine sulfate (Table 3, Figure 3C). Greater TA in UASF was described in previous reports (8,11). Mechanisms that are responsible for increased TA and NAE in patients with type 2 diabetes and UASF are unknown. However, it is conceivable that insulin resistance accounts for increased production of organic acids. Plasma lactate has been reported to be higher in patients with type 2 diabetes (19), likely as a result of altered glucose metabolism causing increased lactate production (20). Therefore, urinary lactate may contribute to the greater TA in UASF and patients with type 2 diabetes. Moreover, there may be other, unidentified anions in the urine of these two groups that contribute to their acidic urine.

This study evaluated individuals in an outpatient setting, while they consumed their home diets. Although this method precludes elimination of dietary confounders, it reflects patients with type 2 diabetes in their usual environment and indicates which factors may be responsible for their increased risk for uric acid nephrolithiasis. These results should be confirmed in a controlled setting with fixed dietary sulfate and where a discrete dietary acid load can be provided. A limitation of this report was the small number of UASF included. However, the biochemical characteristics of UASF from this study are consistent with findings from previous reports (7,8,11).

In this study, the urinary content of undissociated uric acid was similar in patients with type 2 diabetes and UASF (Table 3), although the majority of patients with type 2 diabetes do not form kidney stones. The additional risk of stone formation in UASF remains to be defined, although it may be due to differences in urinary inhibitors such as glycosaminoglycans (21) and/or crystal adhesion (22). Such factors were not evaluated specifically in this report.

Conclusion

This study demonstrates that, in patients with type 2 diabetes, the main risk factor for uric acid nephrolithiasis is a low urine pH. This acidic urine may be due, in part, to higher body weight and higher acid intake. However, the lower urine pH in patients with type 2 diabetes persists after correction for age, body weight, creatinine clearance, and dietary factors. In contrast to UASF, impaired ammonium excretion alone does not explain the acidic urine in patients with type 2 diabetes. These findings suggest that other factors that are associated with type 2 diabetes or insulin resistance account for the low urine pH in this population.

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