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PREVALENCE AND CORRELATES OF ASYMPTOMATIC HYPERURICEMIA IN TYPE 2 DIABETES MELLITUS WITHOUT HYPERTENSION OR CHRONIC KIDNEY DISEASE: A CROSS-SECTIONAL STUDY FROM WESTERN RAJASTHAN, INDIA

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ABSTRACT

Background: Hyperuricemia and type 2 diabetes mellitus (T2DM) share insulin resistance as a common mechanism, and raised serum uric acid in diabetes has been linked to nephropathy, cardiovascular disease, and mortality. Most published prevalence estimates, however, come from cohorts that include hypertensive and renally impaired patients, in whom urate retention is already expected. Data from western Rajasthan are scarce. This study determined the prevalence of asymptomatic hyperuricemia, and the factors associated with it, in patients with T2DM of more than two years' duration who were free of hypertension, gout, chronic kidney disease (CKD), and chronic alcohol use.

Materials and Methods: This cross-sectional study enrolled 200 patients aged over 40 years with T2DM of more than two years' duration attending the Department of General Medicine of a tertiary care teaching hospital in Jodhpur, India. Patients with hypertension, past or present gout, CKD, or chronic alcohol use were excluded. Serum uric acid was measured by chemiluminescence immunoassay. Hyperuricemia was defined as >7 mg/dL in men and >6 mg/dL in women, and asymptomatic hyperuricemia as raised urate in the absence of any gout flare. Groups were compared using the chi-square and independent-samples t-tests, and independent predictors were identified by multivariable binary logistic regression.

Results: Mean age was 56.9 ± 9.6 years and 114 patients (57.0%) were men. Asymptomatic hyperuricemia was present in 80 patients (40.0%). Prevalence was 44.2% in women and 36.8% in men (p = 0.294) and rose with age, from 29.6% in those aged 50 years or younger to 55.6% in those above 60 years (p = 0.016); this age gradient was significant in women (19.0% to 66.7%, p = 0.008) but not in men (p = 0.208). Hyperuricemic patients had a longer duration of diabetes (13.42 ± 6.96 vs 5.07 ± 2.03 years), higher HbA1c (8.22 ± 1.12% vs 6.99 ± 0.65%), higher LDL cholesterol, and lower HDL cholesterol (all p < 0.001). Prevalence rose steeply across glycemic strata: 15.4% at HbA1c below 7%, 36.8% at 7–7.9%, and 86.2% at 8% or above. BMI, waist-hip ratio, and smoking showed no association. On multivariable analysis, duration of diabetes (odds ratio [OR]: 1.85 per year, 95% CI: 1.43–2.39), HbA1c (OR: 2.30 per 1%, 95% CI: 1.13–4.67), and HDL cholesterol (OR: 0.91 per mg/dL, 95% CI: 0.84–0.98) were independent predictors.

Conclusion: Two in five patients with T2DM had asymptomatic hyperuricemia despite the exclusion of hypertension, gout, CKD, and alcohol use. Duration of diabetes and glycemic control were the dominant determinants. Serum uric acid

is an inexpensive measurement that may merit routine use in patients with longstanding or poorly controlled type 2 diabetes, before any renal or cardiovascular complication becomes clinically apparent.
Keywords: Asymptomatic hyperuricemia, serum uric acid, type 2 diabetes mellitus, glycated haemoglobin, dyslipidemia, India

INTRODUCTION

Uric acid is the terminal product of purine catabolism in humans. Because humans lack uricase, circulating urate is cleared almost entirely by renal and intestinal excretion rather than further degradation, and the serum level therefore reflects the balance between purine turnover and excretory capacity. Above roughly 6.8 mg/dL, the limit of urate solubility in serum, monosodium urate can deposit in tissue even in people who never develop a clinical gout flare.[1]

The relationship between urate and type 2 diabetes mellitus (T2DM) appears to run in both directions. Insulin reduces the fractional excretion of urate in the proximal tubule, so the compensatory hyperinsulinemia of insulin resistance exerts a sustained antiuricosuric effect on the kidney.[2,3] Urate in turn behaves as an antioxidant at physiological concentrations but as a pro-oxidant once levels rise, generating oxidative stress in insulin-sensitive tissue and promoting vascular smooth muscle proliferation through the local renin-angiotensin system.[4-6] Each process plausibly reinforces the other.

The clinical consequence is that raised urate in diabetes is not an inert laboratory finding. Silent urate deposition has been associated with chronic kidney disease (CKD), cardiovascular disease, and the insulin resistance syndrome,[7] a meta-analysis in T2DM found hyperuricemia to be an independent predictor of vascular complications and mortality,[8] and in a prospective cohort of patients with non-insulin-dependent diabetes, serum uric acid predicted stroke independently of conventional cardiovascular risk factors.[9]

India carries one of the largest absolute burdens of T2DM in the world, driven by a phenotype of greater insulin resistance and central adiposity at lower body mass index than in Western populations.[10] Reported prevalence of hyperuricemia among patients with T2DM nevertheless varies widely, from about 26% in Morocco to 28% in Jordan, and roughly 12% among newly diagnosed Indian patients.[11-13] Part of this spread reflects differing urate cut-offs, but part reflects case mix: most published series include patients with hypertension, CKD, or alcohol use, all of which independently raise urate, so the contribution of diabetes itself is difficult to isolate.

Western Rajasthan has little published data on this question. We therefore measured the prevalence of asymptomatic hyperuricemia, and the factors associated with it, in patients with T2DM of more than two years' duration in whom hypertension, gout, CKD, and chronic alcohol use had been deliberately excluded.

MATERIALS AND METHODS

Study design and setting: This was a hospital-based cross-sectional study conducted in the Department of General Medicine, Dr. Sampurnanand Medical College and Associated Group of Hospitals, Jodhpur, a tertiary care teaching hospital serving western Rajasthan, India. Participants were recruited consecutively from the outpatient department and from medical wards over a two-month period.

Participants: Patients were eligible if they were older than 40 years and had type 2 diabetes mellitus of more than two years' duration, diagnosed according to American Diabetes Association criteria: HbA1c of 6.5% or more; fasting plasma glucose of 126 mg/dL or more after at least eight hours without caloric intake; two-hour plasma glucose of 200 mg/dL or more during a 75 g oral glucose tolerance test; or a random plasma glucose of 200 mg/dL or more in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis.[14]

Patients were excluded if they declined participation, or had any of the following: hypertension, past or present; a past or present diagnosis of gout; chronic kidney disease, past or present; or chronic alcohol use. Blood pressure was measured in the right upper arm in the supine position with a mercury sphygmomanometer, and patients with previously diagnosed hypertension, those receiving antihypertensive treatment, and those with a systolic pressure of 140 mmHg or above or a diastolic pressure of 90 mmHg or above were excluded. Chronic kidney disease was excluded on the basis of renal function tests and ultrasonography of the kidneys, ureters, and bladder; patients with reduced renal size or echotexture changes suggestive of chronic parenchymal disease were not enrolled. Alcohol intake was ascertained from the personal history taken directly from the patient, and those reporting regular ongoing consumption were excluded; no quantitative threshold was applied.

Sample size: Sample size was calculated for a single proportion as $n = Z^2(1-\alpha/2) \times P(1-P) / E^2$, assuming an expected hyperuricemia prevalence of 33% in patients with type 2 diabetes, a 95% confidence level ($Z = 1.96$), and a relative allowable error of 20% (absolute error $E = 0.20 \times 0.33 = 0.066$). This gave $n = 195$, which was rounded up to 200.

Definitions and measurements: Hyperuricemia was defined as a serum uric acid concentration above 7.0 mg/dL in men and above 6.0 mg/dL in women. Asymptomatic hyperuricemia was defined as a raised urate concentration in the absence of any past or present episode of urate crystal-induced inflammation.

Serum uric acid was estimated by chemiluminescence immunoassay on a fully automated analyser in the institutional biochemistry laboratory. Blood urea was estimated by the diacetyl monoxime method and serum creatinine by the modified Jaffe method. HbA1c and a fasting lipid profile were obtained for every participant. Height and weight were measured and body mass index calculated as weight in kilograms divided by height in metres squared, with participants grouped as underweight (<18.5 kg/m²), normal (18.5–24.9 kg/m²), or overweight and above (≥25 kg/m²). Waist and hip circumferences were measured and the waist-hip ratio derived. Smoking status was recorded as current or never. Dyslipidemia was defined according to the International Diabetes Federation criteria as a serum triglyceride concentration above 150 mg/dL, or an HDL cholesterol below 40 mg/dL in men or below 50 mg/dL in women, or specific treatment for either lipid abnormality.[15] A low HDL cholesterol was defined by the same sex-specific thresholds.

Statistical analysis: Data were analysed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). Categorical variables are presented as frequencies and percentages and compared with the chi-square test. Continuous variables are presented as mean ± standard deviation and compared between hyperuricemic and normouricemic patients with the independent-samples t-test. Correlation between variables was assessed with Kendall's tau-b. Variables were entered into a multivariable binary logistic regression model with the presence of hyperuricemia as the dependent variable and age, body mass index, waist-hip ratio, LDL cholesterol, HDL cholesterol, HbA1c, and duration of diabetes as covariates. Odds ratios are reported with 95% confidence intervals. A two-sided p value below 0.05 was taken as significant.

Ethical considerations: The study was approved by the Institutional Ethics Committee of Dr. S.N. Medical College, Jodhpur [SNMC/IEC/2022/Plan/679 Date 16.11.2022]. Written informed consent was obtained from every participant in a language they understood, and participation was voluntary with the right to withdraw at any time.

RESULTS

Baseline characteristics: Two hundred patients were enrolled. Mean age was 56.9 ± 9.6 years, with a median of 60 years (Q1–Q3: 50–63), and 114 patients (57.0%) were men. Mean duration of diabetes was 8.41 ± 6.21 years and mean HbA1c was 7.48 ± 1.06%. Most patients were not obese: mean body mass index was 22.95 ± 3.59 kg/m² and only 57 patients (28.5%) had a body mass index of 25 kg/m² or above [Table 1].

Table 1: Baseline characteristics of the study population (n = 200)

Characteristic	Value
Age, years (mean ± SD)	56.9 ± 9.6
Age, years (median, Q1–Q3)	60 (50–63)
≤50 years, n (%)	54 (27.0)
51–60 years, n (%)	92 (46.0)
>60 years, n (%)	54 (27.0)
Men, n (%)	114 (57.0)
Women, n (%)	86 (43.0)
Duration of diabetes, years (mean ± SD)	8.41 ± 6.21
Body mass index, kg/m² (mean ± SD)	22.95 ± 3.59
<18.5 kg/m², n (%)	6 (3.0)
18.5–24.9 kg/m², n (%)	137 (68.5)
≥25 kg/m², n (%)	57 (28.5)
Waist-hip ratio (mean ± SD)	0.92 ± 0.29
Current smoker, n (%)	73 (36.5)
HbA1c, % (mean ± SD)	7.48 ± 1.06
<7%, n (%)	104 (52.0)
7–7.9%, n (%)	38 (19.0)
≥8%, n (%)	58 (29.0)
LDL cholesterol, mg/dL (mean ± SD)	121.87 ± 42.26
HDL cholesterol, mg/dL (mean ± SD)	48.54 ± 11.03
Dyslipidemia, n (%)	54 (27.0)

SD: standard deviation; HbA1c: glycated hemoglobin; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

Prevalence of asymptomatic hyperuricemia: Asymptomatic hyperuricemia was present in 80 of 200 patients, a prevalence of 40.0%. Prevalence was higher in women than in men, 44.2% versus 36.8%, but the difference was not significant (p = 0.294); mean serum uric acid ran in the opposite direction, 6.54 ± 1.75 mg/dL in men versus 6.37 ± 1.76 mg/dL in women (p = 0.391), a discordance that follows from the sex-specific diagnostic thresholds.

Prevalence rose across age groups, from 29.6% in patients aged 50 years or younger to 37.0% at 51–60 years and 55.6% above 60 years (p = 0.016), and mean serum uric acid rose in parallel (p < 0.001). Stratified by sex, this age gradient was significant in women, where prevalence climbed from 19.0% to 66.7% (p = 0.008), but not in men (p = 0.208) [Table 2, Figure 1].

Table 2: Prevalence of asymptomatic hyperuricemia and mean serum uric acid by sex and age group

Subgroup	n	Hyperuricemia, n (%)	Serum uric acid, mg/dL (mean ± SD)	p
All patients	200	80 (40.0)	—	—
Men	114	42 (36.8)	6.54 ± 1.75	0.294
Women	86	38 (44.2)	6.37 ± 1.76	
≤50 years	54	16 (29.6)	6.08 ± 1.50	0.016
51–60 years	92	34 (37.0)	6.35 ± 1.70	
>60 years	54	30 (55.6)	7.04 ± 1.92	
Men, ≤50 years	33	12 (36.4)	6.35 ± 1.65	0.208
Men, 51–60 years	48	14 (29.2)	6.22 ± 1.63	
Men, >60 years	33	16 (48.5)	6.54 ± 1.83	
Women, ≤50 years	21	4 (19.0)	5.67 ± 1.12	0.008
Women, 51–60 years	44	20 (45.5)	6.35 ± 1.69	
Women, >60 years	21	14 (66.7)	6.63 ± 1.79	

p values are for the comparison of prevalence within each stratification, by chi-square test. SD: standard deviation.

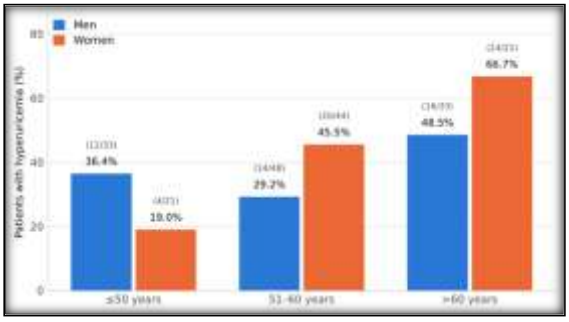

Figure 1: Prevalence of asymptomatic hyperuricemia by age group and sex.

Denominators are shown in parentheses. Prevalence rose significantly with age in women (p = 0.008) but not in men (p = 0.208); the two sexes cross between the youngest and middle age bands.

Comparison of hyperuricemic and normouricemic patients: Patients with hyperuricemia had had diabetes for more than twice as long as those without (13.42 ± 6.96 versus 5.07 ± 2.03 years, p < 0.001) and were substantially less well controlled (HbA1c 8.22 ± 1.12% versus 6.99 ± 0.65%, p < 0.001). LDL cholesterol was higher and HDL cholesterol lower in the hyperuricemic group (both p < 0.001). Body mass index, waist-hip ratio, and smoking did not differ significantly between the groups [Table 3].

The gradient across glycemic strata was steep: hyperuricemia was present in 16 of 104 patients (15.4%) with HbA1c below 7%, 14 of 38 (36.8%) at 7–7.9%, and 50 of 58 (86.2%) at 8% or above [Figure 2]. The association with lipids was of similar magnitude. Of the 54 patients with dyslipidemia, 50 (92.6%) were hyperuricemic, against 30 of 146 (20.5%) without dyslipidemia; among the 45 patients with a low HDL cholesterol, 38 (84.4%) were hyperuricemic, against 42 of 155 (27.1%) with a normal HDL.

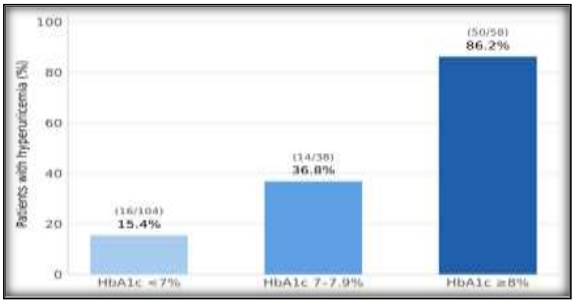

Figure 2. Prevalence of asymptomatic hyperuricemia by glycemic stratum.

Denominators are shown in parentheses. Prevalence rose from 15.4% at an HbA1c below 7% to 86.2% at 8% or above (p < 0.001). HbA1c: glycated hemoglobin.

Table 3: Clinical and biochemical characteristics by hyperuricemia status

Variable	Hyperuricemia (n = 80)	No hyperuricemia (n = 120)	p
Duration of diabetes, years	13.42 ± 6.96	5.07 ± 2.03	<0.001
HbA1c, %	8.22 ± 1.12	6.99 ± 0.65	<0.001
LDL cholesterol, mg/dL	153.44 ± 44.13	100.82 ± 23.89	<0.001
HDL cholesterol, mg/dL	40.50 ± 11.86	53.44 ± 6.96	<0.001
Body mass index, kg/m²	23.29 ± 3.61	22.73 ± 3.57	0.228
Waist-hip ratio	0.941 ± 0.277	0.913 ± 0.307	0.054
HbA1c <7%, n (%)	16 (20.0)	88 (73.3)	<0.001
HbA1c 7–7.9%, n (%)	14 (17.5)	24 (20.0)	
HbA1c ≥8%, n (%)	50 (62.5)	8 (6.7)	
Dyslipidemia, n (%)	50 (62.5)	4 (3.3)	<0.001
LDL cholesterol ≥100 mg/dL, n (%)	63 (78.8)	47 (39.2)	<0.001
Low HDL cholesterol, n (%)	38 (47.5)	7 (5.8)	<0.001
Body mass index ≥25 kg/m², n (%)	28 (35.0)	29 (24.2)	0.197
Current smoker, n (%)	34 (42.5)	39 (32.5)	0.151

Values are mean ± SD unless stated otherwise. Continuous variables compared by independent-samples t-test, categorical variables by chi-square test. HbA1c: glycated hemoglobin; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

Correlates of hyperuricemia and of serum uric acid: Duration of diabetes showed the strongest correlation with serum uric acid (Kendall's tau-b = 0.740, $p < 0.001$), followed by dyslipidemia, HbA1c, LDL cholesterol, and, inversely, HDL cholesterol. Age correlated weakly but significantly. Sex, body mass index, waist-hip ratio, and smoking showed no significant correlation with either hyperuricemia or serum uric acid [Table 4].

Table 4: Correlation of study variables with hyperuricemia and with serum uric acid (Kendall's tau-b)

Variable	τ (hyperuricemia)	p	τ (serum uric acid)	p
Duration of diabetes	0.642	<0.001	0.740	<0.001
Dyslipidemia	0.653	<0.001	0.491	<0.001
HbA1c	0.491	<0.001	0.467	<0.001
LDL cholesterol	0.440	<0.001	0.346	<0.001
HDL cholesterol	−0.407	<0.001	−0.329	<0.001
Age	0.219	<0.001	0.172	<0.001
Waist-hip ratio	0.116	0.054	0.077	0.125
Smoking	0.102	0.151	0.045	0.437
Body mass index	0.072	0.228	0.024	0.630
Sex	−0.074	0.295	0.050	0.391

τ: Kendall's tau-b correlation coefficient. HbA1c: glycated hemoglobin; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

Independent predictors of hyperuricemia: In the multivariable logistic regression model, three variables remained independently associated with hyperuricemia: duration of diabetes, HbA1c, and HDL cholesterol. Each additional year of diabetes raised the odds of hyperuricemia by 85%, each one percentage point of HbA1c more than doubled them, and each 1 mg/dL increase in HDL cholesterol reduced them by about 9%. Age, body mass index, waist-hip ratio, and LDL cholesterol were not independent predictors. The model explained a large share of the variance (Nagelkerke $R^2 = 0.778$) [Table 5, Figure 3].

Table 5: Multivariable logistic regression for the presence of asymptomatic hyperuricemia

Variable	Odds ratio	95% CI	p
Duration of diabetes, per year	1.85	1.43–2.39	<0.001
HbA1c, per 1%	2.30	1.13–4.67	0.021
HDL cholesterol, per mg/dL	0.91	0.84–0.98	0.019
Age, per year	1.01	0.95–1.07	0.796
Body mass index, per kg/m²	0.93	0.69–1.26	0.639
LDL cholesterol, per mg/dL	1.01	0.98–1.03	0.624
Waist-hip ratio, per unit	1.76	0.05–62.50	0.756

Nagelkerke $R^2 = 0.778$; Cox and Snell $R^2 = 0.575$; McFadden $R^2 = 0.636$. CI: confidence interval; HbA1c: glycated hemoglobin; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

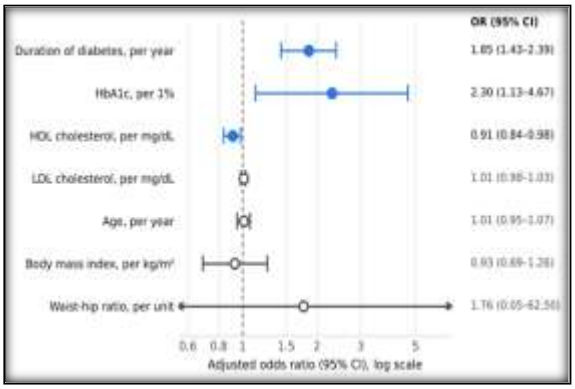

Figure 3: Adjusted odds ratios for asymptomatic hyperuricemia.

Filled markers denote statistically significant predictors, open markers non-significant ones; the dashed line marks an odds ratio of 1. The confidence interval for waist-hip ratio extends beyond the plotted range and is truncated with arrowheads; its full interval is given in Table 5. CI: confidence interval; HbA1c: glycated hemoglobin; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

DISCUSSION

Two in five patients in this cohort had asymptomatic hyperuricemia, and they had it despite the exclusion of hypertension, gout, chronic kidney disease, and chronic alcohol use — the four conditions that most reliably raise serum urate. Duration of diabetes and glycemic control accounted for most of the variation.

Prevalence in context: The 40.0% prevalence observed here is higher than most published series in type 2 diabetes: 26.5% in a Moroccan cohort,[11] and 28.1% in Jordan.[12] In a Saudi cohort it was 28.8% in women and 20.5% in men,[16] and in newly diagnosed Indian diabetic patients only 12.13%.[17] It is also well above the prevalence of roughly 21% reported for United States adults in the general population, where 21.2% of men and 21.6% of women were hyperuricemic.[18] The largest Indian dataset, drawn from hyperuricemia screening camps, reports an overall rate of 24.7%, but that figure covers all attendees with hypertension, diabetes, or both, and is not a diabetes-specific prevalence.[13]

That this cohort sits at the top of that range while excluding the usual contributors is the central observation of the study. Three features of the sample explain part of it. First, entry required diabetes of more than two years' duration, and the mean duration was 8.4 years, so the sample is weighted towards exactly the exposure that proved to be the dominant predictor. Second, recruitment was from a tertiary referral hospital, and 29.0% of patients had an HbA1c of 8% or above. Third, the sex-specific thresholds used here classify women at 6.0 mg/dL, which is lower than the 6.8 mg/dL solubility limit sometimes applied uniformly, and so detects more women.

What remains after those allowances is a substantial burden of urate elevation attributable to longstanding, poorly controlled diabetes on its own. The comparison most often made in the literature — that hyperuricemia is commonest when diabetes and hypertension coexist,[13] — may have obscured how much of the signal diabetes carries by itself.

Sex and age: Prevalence was higher in women while mean serum uric acid was higher in men. These are not contradictory: the female diagnostic threshold is 1 mg/dL lower, so a given population of women crosses it more readily. The same pattern of female predominance in prevalence has been reported from Morocco, where 76% of hyperuricemic diabetic patients were women,[11] and from Saudi Arabia.[16]

The more informative finding is the interaction between sex and age. Prevalence in women rose from 19.0% below 50 years to 66.7% above 60 years, whereas in men it did not change significantly. Estrogen is uricosuric, and its withdrawal at menopause removes that effect, so women accumulate urate across the sixth and seventh decades while men, whose levels are already higher from early adulthood, change less. Sex- and age-dependent differences in the relationship between serum urate and metabolic abnormalities have been described previously.[19] The implication for practice is that a woman with longstanding type 2 diabetes in her seventh decade is at least as likely to be hyperuricemic as a man of the same age, which is not the intuition most clinicians carry.

Duration of diabetes: Duration of diabetes was the strongest correlate of serum uric acid in this study ($\tau = 0.740$) and the strongest independent predictor of hyperuricemia (OR 1.85 per year). A comparable positive gradient has been described, with mean urate rising from 6.80 ± 0.89 mg/dL at two to six years of diabetes to 7.72 ± 2.90 mg/dL at seven to ten years,[20] and prevalence of hyperuricemia increasing with disease duration in hypertensive and diabetic patients from western Uttar Pradesh.[21]

The largest Indian dataset, however, points the other way: among nearly 200,000 subjects screened across 592 locations, hyperuricemia was commoner at two to five years of disease than beyond five years.[13] Several differences may reconcile this. That study drew on screening-camp attendees rather than a hospital population and combined diabetes with hypertension; it did not exclude renal impairment; and in an unselected long-duration population, patients who develop chronic kidney disease are precisely those in whom urate rises further, yet they are also those most likely to be on treatment that alters it. Our cohort, screened free of renal disease and hypertension, isolates a cleaner duration effect. The discrepancy nevertheless deserves testing in a larger, prospectively followed Indian sample.

Glycemic control: The gradient across glycemic strata was steep and monotonic: 15.4%, 36.8%, and 86.2% of patients were hyperuricemic at HbA1c below 7%, 7–7.9%, and 8% or above. A positive association between urate and HbA1c has been reported previously.[22,23]

This is not, however, a settled literature. Several studies have found serum uric acid to be lower in patients with diabetes than in those with prediabetes or normal glucose tolerance, and to fall as fasting glucose rises.[24,25] The likely explanation is that the relationship is not monotonic across the whole glycemic range. Hyperuricemia and hypouricemia have been described as two distinct phenotypes within type 2 diabetes,[26] at moderate hyperglycemia, hyperinsulinemia reduces renal urate clearance and urate rises, whereas once glycosuria becomes marked, glucose in the proximal tubule competes with urate reabsorption and produces a uricosuria that drives urate down. Our cohort had a mean HbA1c of 7.48% and excluded renal impairment, placing almost all patients on the ascending limb of that curve. Studies reporting an inverse association have generally included patients with far higher glucose levels. Framing the two bodies of evidence this way, rather than as a straightforward disagreement, is probably closer to the physiology.

Lipids: Dyslipidemia showed the strongest categorical association in the study: 92.6% of dyslipidemic patients were hyperuricemic against 20.5% of the rest. HDL cholesterol remained independently protective after adjustment (OR 0.91 per mg/dL), while LDL cholesterol did not, which suggests the relevant axis is the insulin-resistant lipid phenotype of low HDL rather than LDL burden. An inverse relationship between serum urate and HDL cholesterol has been documented in large population samples.[27]

Mechanistic interpretation: The findings fit the insulin resistance model. Compensatory hyperinsulinemia reduces the fractional excretion of urate in the proximal tubule, exerting a sustained antiuricosuric pressure on the kidney.[2,3] Raised urate then acts as a pro-oxidant, generating oxidative stress in insulin-sensitive tissue and further impairing insulin signalling,[4,5] and urate has been shown prospectively to predict incident type 2 diabetes.[28] Longer disease duration and worse control represent a longer and heavier exposure to that loop, which is consistent with duration and HbA1c emerging as the two dominant predictors here.

Clinical implications: Serum uric acid is among the cheapest tests available in Indian practice. In patients with type 2 diabetes it has been shown to predict

vascular complications and mortality,[8] and, independently of conventional risk factors, stroke.[9] On the evidence here, a patient with diabetes of more than five years' duration and an HbA1c of 8% or above has a high prior probability of asymptomatic hyperuricemia, and measuring urate in that group is inexpensive and simple.

It does not follow that urate should be lowered pharmacologically. Trials of urate-lowering therapy in asymptomatic hyperuricemia have not demonstrated renal or cardiovascular benefit, and nothing in a cross-sectional study of this kind can support treatment. The finding argues for recognition and for tighter glycemic control, not for allopurinol.

Limitations

This study has several limitations. It is cross-sectional, so the associations described cannot establish whether hyperuricemia follows longstanding diabetes or contributes to its progression; the direction of the duration effect is inferred from biological plausibility, not from the data. Recruitment was from a single tertiary care centre, which selects for longer disease duration and poorer control than a community sample, and the prevalence reported here should not be read as a population estimate.

The most important residual confounder is medication. Metformin, pioglitazone, sodium-glucose cotransporter-2 inhibitors, losartan, aspirin, and diuretics all alter serum urate, and treatment data were not analysed. Renal function was used only as an exclusion criterion; estimated glomerular filtration rate was not reported, so variation in renal urate handling within the normal range is unaccounted for. Serum uric acid was measured once, without control of dietary purine intake, and single measurements are subject to intra-individual variation.

The sample size was calculated to estimate a prevalence, not to compare subgroups, so the non-significant comparisons — by sex, body mass index, waist-hip ratio, and smoking — may reflect type II error rather than absence of association. Waist-hip ratio values showed unusually wide dispersion and should be interpreted with caution. Menopausal status was not recorded, so the age-sex interaction is consistent with a menopausal mechanism but does not demonstrate one. Finally, there was no non-diabetic control group, so the prevalence observed cannot be compared against a contemporaneous local reference population.

The deliberate exclusion of hypertension, chronic kidney disease, gout, and alcohol use is both the design strength of this study and a limit on its reach: it isolates the contribution of diabetes, but the resulting cohort is not the typical patient seen in a diabetes clinic, where hypertension is common.

CONCLUSION

Asymptomatic hyperuricemia was present in 40% of patients with type 2 diabetes mellitus of more than two years' duration, despite the exclusion of hypertension, gout, chronic kidney disease, and chronic alcohol use. Prevalence rose with age, and the age gradient was confined to women, consistent with loss of the uricosuric effect of estrogen after menopause. Duration of diabetes, HbA1c, and HDL cholesterol were independent predictors; body mass index, waist-hip ratio, and smoking were not.

These findings suggest that longstanding and poorly controlled type 2 diabetes raises serum urate substantially on its own, without the contribution of the comorbidities usually held responsible. Serum uric acid is inexpensive and may be worth measuring in patients with diabetes of long duration or poor glycemic control. Prospective studies with medication and renal function data are needed to determine whether this asymptomatic elevation carries prognostic weight in such patients, and randomised evidence would be required before any recommendation to treat it.

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