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Epidemiology of Gout in Southeast Iran: Unexpected Risk Factor Patterns in a Population-Based Study

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ABSTRACT

Background: Gout is an increasingly recognized public health concern in low- and middle-income regions experiencing rapid socioeconomic change. However, contemporary evidence from southeastern Iran is limited. This study provides the first population-based estimate of gout prevalence in Zahedan and examines its association with demographic, metabolic, and medication-related factors.

Methods: This cross-sectional analysis included 6,322 adults from the Persian Cohort in Zahedan, with a clinically profiled subsample of 2,166 participants aged 35–75 years. Gout diagnosis was based on standardized clinical criteria. Associations with age, sex, body mass index, comorbidities, and medication use were assessed using univariate and multivariable models.

Results: The overall prevalence of gout was 5.7% (95% CI: 5.1–6.3%) in the full cohort and 4.7% (95% CI: 3.8–5.6%) in the subsample. Contrary to global literature, gout was not significantly associated with older age, male sex, obesity, hypertension, or diabetes. Instead, loop diuretic use particularly furosemide demonstrated a strong independent association with gout after adjustment for confounders, whereas other medications, alcohol consumption, and cardiometabolic conditions did not show significant relationships.

Conclusion: Gout affects nearly one in twenty adults in Zahedan, representing a meaningful disease burden. While traditional predictors were not influential, furosemide use emerged as a key modifiable risk factor, emphasizing the need for medication review and gout monitoring among patients receiving loop diuretics. Longitudinal studies incorporating genetic, dietary, and biochemical profiling are warranted to refine prevention and management strategies in this region.

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Introduction

Gout is an ancient crystal-induced metabolic disease that remains a major clinical concern despite centuries of medical recognition (1). It is characterized by persistent hyperuricemia and deposition of monosodium urate crystals within synovial and peri-articular tissues, provoking intense inflammation, severe pain, and joint dysfunction (2, 3). Clinically, gout typically presents as abrupt, severely painful inflammatory attacks of acute arthritis most commonly affecting the first metatarsophalangeal joint although recurrent episodes may progress to chronic, disabling polyarticular disease with tophi and erosive joint damage (4, 5).

Uric acid represents the final product of purine metabolism (6). Excess production or impaired renal excretion responsible for more than 90% of cases leads to pathological accumulation (7). When

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serum urate levels exceed solubility thresholds, crystals precipitate, activate innate immune pathways, and stimulate release of prostaglandins, interleukins, and other cytokines that generate classical features of redness, swelling, and severe pain (8). Nocturnal attacks are common, attributed to venous pooling, lower extremity cooling, and local urate supersaturation (9).

Although gout is one of the best understood and readily treatable forms of arthritis, it continues to be underdiagnosed and undertreated worldwide (10). Its global epidemiological profile has shifted markedly over the past four decades (11). International estimates suggest that 3–6% of adults will develop gout during their lifetime, and large cohort studies show that prevalence has more than doubled in several high-income countries (12, 13). Rising disease burden has been linked to population aging, increasing rates of obesity and metabolic syndrome, shifts in dietary patterns, alcohol consumption, and widespread use of medications such as diuretics, cyclosporine, and calcineurin inhibitors that impair renal urate excretion (14, 15). Despite being highly prevalent in industrialized settings, the distribution of gout is heterogeneous and influenced by socioeconomic, nutritional, ethnic, and environmental factors (16, 17). Large epidemiological studies in the United States, Europe, and East Asia consistently demonstrate upward trends (18); However, data from the Middle East, particularly Iran, remain limited, fragmented, and predominantly clinic-based. Existing estimates vary widely and largely originate from central and northern provinces, leaving southeastern regions without reliable population-based evidence (19, 20).

Zahedan, the capital of Sistan and Baluchestan Province, represents a unique demographic and cultural region characterized by rapid socioeconomic transition, heterogeneous ethnic composition, and distinctive dietary practices (21). Rapid nutritional shifts, a high burden of cardiometabolic risk factors, and potential genetic influences may give rise to a distinct epidemiological profile of gout in this area .Therefore, this population-based study was conducted to determine the prevalence of gout among residents of Zahedan in 2024 and to examine its demographic, metabolic, and pharmacologic determinants. The findings aim to generate region-specific evidence capable of guiding clinical practice, informing public health policy, and advancing effective management strategies for this southeastern population.

Materials and methods

Study Design and Setting

This population-based cross-sectional study used baseline data from the Zahedan center of the Persian Cohort Study. Although the broader Persian Cohort is longitudinal, the present analysis relied exclusively on the cross-sectional baseline dataset collected in 2024. The Zahedan cohort site enrolls adult residents from diverse socioeconomic backgrounds through systematic population sampling across multiple municipal zones, yielding a broadly representative sample of the city's adult population.

Study Population

All adults registered in the Zahedan Persian Cohort database during the study period were screened for eligibility. A total of 6,322 individuals with complete baseline records and documented informed consent were included in the analysis. Inclusion criteria required (1) residency within the Zahedan city limits, (2) prior enrollment in the Persian Cohort, and (3) completion of demographic, anthropometric, and clinical questionnaires. Individuals with incomplete datasets, missing gout assessment information, or refusal to participate in the clinical interview were excluded.

Sampling and Data Collection Procedures

Participants were selected using systematic random sampling following the standard Persian Cohort protocol, ensuring proportional representation from different urban districts. Data collection consisted of two complementary components: (a) extraction of demographic, lifestyle, and medical history data from the electronic cohort database, and (b) a structured face-to-face interview focused on gout assessment performed by trained health professionals. All interviews were conducted at the Cohort Health Center in Zahedan using standardized procedures to reduce inter-observer variability.

Ascertainment of Gout

Gout status was determined based on a structured diagnostic questionnaire derived from the clinical components of the ACR/EULAR 2015 classification criteria (22). Because synovial fluid analysis is not feasible in large population surveys, epidemiologic case definitions relying on validated clinical patterns were applied. A diagnosis of gout required either (1) self-reported prior physician-diagnosed gout accompanied by typical clinical features (such as sudden onset of severe monoarticular pain, erythema, swelling, maximal pain within 24 hours, and improvement with NSAIDs or colchicine), or (2) a clinical score indicating probable gout based on the standardized questionnaire (23). The presence of acute attacks involving the first metatarsophalangeal joint, recurrent episodes of abrupt inflammatory arthritis, family history of gout, and rapid response to anti-inflammatory therapy were also recorded.

Variables and Measurements

Demographic variables included age (both

continuous and categorized by decade) and sex. Anthropometric measurements were performed according to the cohort protocol, with BMI categorized as underweight, normal weight, overweight, or obese. Behavioral variables included current alcohol consumption, which is uncommon in the region but was assessed due to its known etiological role in gout. Clinical comorbidities including hypertension, diabetes mellitus, and hyperlipidemia were based on self-report and verification through existing cohort medical records. Medication use was documented with a focus on aspirin, thiazide diuretics, and loop diuretics (especially furosemide), which are known to elevate serum urate levels.

Statistical Analysis

All statistical analyses were performed using SPSS version 26. Continuous variables were assessed for normality prior to analysis. Descriptive statistics summarized the demographic and clinical characteristics of the study population. Gout prevalence was calculated as the proportion of individuals meeting the case definition, with associated 95% confidence intervals. Group comparisons between participants with and without gout were conducted using chi-square tests for categorical variables and independent-sample t-tests for continuous variables. To identify independent predictors of gout, binary logistic regression models were constructed, including age, sex, BMI category, cardiometabolic comorbidities, and relevant medications. Statistical significance was defined as a two-sided p-value <0.05.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Zahedan University of Medical Sciences (IR.ZAUMS.REC.1403.337). Written informed consent was obtained from all participants at the time of cohort enrollment and again prior to the gout interview. All data were anonymized prior to analysis.

Results

A total of 6,322 adults were included in the overall analysis, drawn from the Persian Cohort population in Zahedan. The mean age of these participants was 39.91 ± 11.09 years, with an age range spanning 15 to 75 years, reflecting a relatively young adult population. Women were substantially over-represented, constituting 73.5% (n = 3,101) of the cohort, whereas men comprised 26.5% (n = 1,149). The distribution of body mass index indicated that the majority (approximately 69%) had normal BMI values, while 17% were overweight and a smaller but unquantified fraction were categorized as obese. Alcohol consumption was rarely reported, with only 0.6% of the population acknowledging use, which aligns closely with prevailing cultural norms in southeastern Iran. Cardiometabolic conditions such as hypertension, diabetes, and dyslipidemia were present in the sample, although their prevalence did not dominate the cohort landscape.

To provide more clinically detailed profiling, a subsample of 2,166 adults was examined separately. These individuals were slightly older, with a mean age of 49.82 ± 9.19 years (range 35–75 years), and the sex distribution remained female-dominant at 62.5% (n = 1,348). Their BMI profile demonstrated a wider variation, with 4.3% (n = 93) classified as underweight, 30.4% (n = 656) exhibiting normal weight, 38.0% (n = 820) overweight, and 27.3% (n = 588) obese. Within this group, 23.8% had hypertension, 18.4% diabetes, 12.5% thyroid disorders, 0.9% reported prior myocardial infarction, 2.2% chronic kidney disease, and 2.2% alcohol use. These figures suggest a higher burden of metabolic comorbidity in the older subsample compared with the full cohort.

Across the entire sample of 6,322 individuals, 343 cases of gout were identified, yielding an estimated prevalence of 5.7% (95% CI: 5.1–6.3%). In contrast, within the clinically profiled subsample of 2,166 adults, the prevalence was slightly lower at 4.7% (n = 101; 95% CI: 3.8–5.6%). These patterns are further detailed and stratified by demographic and clinical characteristics in Table 1.

Table 1. Distribution of Gout Prevalence According to Demographic and Clinical Characteristics

Variable	Gout Prevalence (%)	p-value
Overall population	5.7%	
Sex		
Male	5.1%	0.488
Female	4.5%	
BMI category		
Underweight	4.3%	
Normal	4.4%	0.612
Overweight	4.8%	
Obese	4.9%	
Other contributors		
Alcohol use	2.1%	0.415
Hypertension	5.1%	0.317
Diabetes	4.5%	0.441
Thyroid disorder	5.9%	0.295
Kidney failure	0.9%	0.998
History of heart attack	2.1%	0.256
Hydrochlorothiazide	1.9%	0.741
Aspirin	14.8%	0.849
Furosemide	0.9%	0.024

Age did not emerge as a strong differentiating factor in either analytic dataset. While participants with gout tended to be somewhat older mean age 57.56 ± 9.6 years among gout cases compared with 49.74 ± 9.1 years among non-cases in the subsample the difference failed to reach statistical significance (p = 0.619). Similarly, the larger cohort analysis did not demonstrate meaningful age-related trends or

gradients in gout prevalence.

Sex-specific differences were also modest. Although men are typically reported to exhibit higher gout risk in most populations, in the Zahedan subsample the prevalence was 5.1% (41/809) among men versus 4.5% (60/1,348) among women. This relative excess did not reach statistical significance (OR: 1.14; 95% CI: 0.76–1.72; p = 0.512), possibly reflecting the disproportionate representation of women and the relatively younger age distribution in this setting, both of which may have limited detection of sex-linked patterns.

With respect to adiposity, BMI was not significantly associated with gout. The proportion of individuals with gout across BMI strata was nearly identical 4.3% in underweight, 4.4% in normal weight, 4.8% in overweight, and 4.9% among obese participants, with no p-value below 0.05 for any category. Likewise, in the larger dataset, overweight and obese adults did not demonstrate higher odds of gout relative to normal weight individuals, suggesting that excess weight did not emerge as a dominant risk determinant in this population.

Evaluation of comorbid and behavioral variables further supported these findings (Table 2). In univariate assessments, gout did not show significant relationships with hypertension (OR: 1.11; p = 0.644), diabetes (OR: 0.96; p = 0.960), thyroid disorders (OR: 1.24; p = 0.295), myocardial infarction, chronic kidney disease, or alcohol consumption (OR: 0.44; p = 0.415). Similar null trends were observed in the larger dataset for cardiometabolic diseases, indicating that conventional gout-related comorbidities did not independently predict disease presence in this community.

Table 2. Multivariable logistic regression analysis of predictors of gout

Variable	Adjusted OR	95% CI	p-value
Age	1.01	0.99–1.02	0.270
Male sex	1.08	0.87–1.33	0.488
BMI	1.02	0.97–1.07	0.603
Hypertension	1.14	0.89–1.46	0.317
Diabetes mellitus	1.10	0.82–1.46	0.441
Hyperlipidemia	1.12	0.87–1.45	0.348
Furosemide use	2.10	1.42–3.11	0.01
Aspirin use	1.02	0.80–1.30	0.549

In contrast, medication use particularly loop diuretic exposure showed a pronounced and consistent association. Among gout-positive individuals in the subsample, 14.8% (15/101) reported current furosemide use compared with 5.9% (122/2,065) among gout-negative individuals, representing a statistically significant difference (p = 0.024). The association persisted in multivariable logistic regression within the full cohort analysis, remaining independent of age, sex, BMI, and metabolic comorbidities. This suggests that impaired renal urate excretion induced by loop diuretics is a major contributor to gout risk in this population. By contrast, use of hydrochlorothiazide (p = 0.741) and aspirin (p = 0.849) did not display significant independent associations.

Discussion

This large population-based study provides the first contemporary estimate of gout prevalence in Zahedan, southeastern Iran, showing that approximately one in twenty adults is affected. The prevalence of 5.7% places Zahedan at the higher end of rates reported in several Middle Eastern and some East Asian populations, and is comparable to, though in some surveys slightly below, estimates from high income settings such as the United States and parts of Europe (24, 25). These findings are consistent with recent international evidence demonstrating wide geographic variation in gout prevalence and an overall increasing trend driven by demographic transitions and rising cardiometabolic exposures (25). The prevalence observed here also exceeds earlier clinic based estimates from Iran, underscoring the importance of community based sampling when assessing chronic disease burden (26).

International studies consistently identify older age, male sex, higher BMI, hypertension, kidney dysfunction, and diabetes as established correlates of gout (26, 27). In contrast, these associations were not observed in our dataset, and this divergence warrants cautious interpretation. Several non-mutually exclusive explanations are plausible. First, the study population is relatively young (mean age <40 years), which may limit the cumulative exposure to metabolic factors that typically lead to hyperuricemia and clinical gout later in life (28). Second, Sistan Baluchestan is an ethnically distinct region, and population specific variation in urate transporter polymorphisms (e.g., SLC2A9, ABCG2) may influence urate handling and modify associations that are well established in other populations (29). Third, although dietary habits are changing, regional differences in traditional diet, alcohol consumption, and fructose intake may attenuate associations commonly reported in Western cohorts (30). Fourth, underdiagnosis of comorbidities such as hypertension or diabetes, potentially related to healthcare seeking behaviors or access, could bias associations toward the null in cross sectional analyses (26, 30). Given the cross-sectional design, residual confounding and the possibility of reverse causation for example, weight loss or medication changes following gout diagnosis cannot be excluded. Despite these complexities, a clear association emerged between furosemide use and gout. This is consistent with numerous population based studies demonstrating that loop and thiazide diuretics are associated with elevated serum urate levels and

increased gout risk (28, 31). The biological mechanism reduced renal urate excretion is well established and supported by multiple observational cohorts (32, 33). Given the rising prevalence of cardiovascular and renal diseases requiring diuretic therapy, careful medication review and consideration of alternative antihypertensive agents e.g., losartan or calcium channel blockers may be warranted to reduce gout risk (34, 35). While the cross-sectional design prevents assessment of temporal sequence, the strength of the association and its consistency with external literature highlight the importance of medication related exposures in this region. Moreover, gene by diuretic interaction studies suggest that individuals genetically predisposed to higher urate levels may experience disproportionate increases in gout risk when exposed to loop diuretics (29). This may be relevant in ethnically distinct populations such as Zahedan, although genetic data were not available to assess this directly.

Because loop diuretics are frequently prescribed for cardiovascular and renal conditions, the observed association has clinical relevance. In contexts where diuretics are widely used, careful medication review and the use of alternative antihypertensive agents with neutral or uricosuric properties such as losartan or calcium channel blockers may help reduce treatment related risk. Observational studies have suggested that these agents may mitigate diuretic associated increases in serum urate or gout risk (36). At a population level, and particularly in regions experiencing growth in cardiometabolic disease and cardiovascular medication use, medication exposures may constitute an important and potentially modifiable contributor to the burden of gout (18, 27).

The strengths of this study include its large sample size, population based sampling, and standardized data collection procedures within the Persian Cohort framework. Several limitations merit emphasis. The cross-sectional design does not allow evaluation of temporality or directional relationships, and reverse causation is possible—for instance, patients with known gout may have altered diet or medications, influencing observed associations. Causal inference is therefore not possible, and all findings should be interpreted strictly as associations. Gout diagnosis relied on clinical criteria rather than crystal confirmation, introducing potential misclassification. Serum urate measurements were not available, limiting assessment of hyperuricemia as an intermediate phenotype. Finally, the relatively young population and low prevalence of alcohol use may have reduced the ability to detect associations typically observed in older or higher risk groups.

Overall, the findings suggest that in Zahedan, the pattern of factors associated with gout may differ from patterns seen in many international cohorts, potentially reflecting unique demographic, genetic, cultural, and prescribing contexts. These results highlight the importance of contextualized public health strategies, including careful medication review and culturally appropriate lifestyle interventions, to address the evolving burden of gout in southeastern Iran.

Conclusion

Gout is a common condition in Zahedan, affecting more than 5% of adults, a relatively high prevalence for a young population. Unlike patterns observed in many international studies, classical metabolic and demographic factors were not associated with gout in this cohort, whereas furosemide use showed a strong association. These findings emphasize the need for attention to medication-related exposures and region-specific prevention strategies. Longitudinal follow-up of this cohort will be important to clarify temporal relationships and to monitor changes in risk patterns as demographic and lifestyle factors evolve.

Ethics Approval and Consent to Participate

The study protocol was approved by the Ethics Committee of Zahedan University of Medical Sciences (IR.ZAUMS.REC.1403.337). Written informed consent was obtained from all participants at the time of Persian Cohort enrollment and again prior to the gout assessment interview. All data were anonymized prior to analysis.

Consent for Publication

Written informed consent was obtained from all participants. No identifiable data are presented.

Availability of Data and Materials

The datasets generated and analyzed during the current study are not publicly available due to institutional restrictions and participant confidentiality.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

MN: Conceptualization, study design, data analysis, manuscript drafting.

AD: Data collection, supervision of fieldwork, critical manuscript revision.

MM: Statistical analysis, interpretation of findings, manuscript editing.

SN: Literature review, drafting of the Discussion, manuscript revisions.

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Portions of the manuscript text were revised using AI-assisted language editing (ChatGPT-5.2, OpenAI). All analyses, interpretations, and final decisions regarding manuscript content were made by the authors.

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