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A Meta Analysis

Prevalence of Hyperuricemia Among T2DM Patients in Pakistan: A Meta-Analysis

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ABSTRACT

Background: Hyperuricemia is increasingly recognized as a metabolic dysfunction associated with type 2 diabetes mellitus (T2DM) and its complications. In Pakistan, the incidence of both conditions is rising, yet national data on their co-existence remain limited. Objective: To systematically review the prevalence of hyperuricemia among patients with T2DM in Pakistan. Methods: This systematic review and meta-analysis included nine observational studies conducted in Pakistan from 2014 to 2024. A comprehensive search was performed in PubMed, Google Scholar, and Science Direct using keywords related to hyperuricemia, type 2 diabetes, serum uric acid, and Pakistan. Studies were selected based on predefined inclusion and exclusion criteria, focusing on hospital-based, cross-sectional, or retrospective designs. Extracted data included study characteristics, diagnostic criteria, and reported prevalence of hyperuricemia. Results: From 6,110 records initially identified, 9 studies with a combined total of 1,765 T2DM patients were included. The pooled prevalence of hyperuricemia among these patients was 21.4% (95% CI: 12.9%–31.3%) based on a random-effects model, with prevalence estimates across studies ranging from 6% to 47%. Substantial heterogeneity was observed ($I^2 = 95.37\%$, $p < 0.0001$), while no significant publication bias was detected. Conclusion: The overall prevalence of hyperuricemia among T2DM patients in Pakistan is substantial, but the high degree of heterogeneity suggests these results should be interpreted with caution. Contextual factors such as population characteristics, diagnostic criteria, and comorbidities may significantly influence prevalence estimates.

Keywords: Hyperuricemia, Pakistan, Prevalence, Type 2 Diabetes, Uric Acid

INTRODUCTION

Diabetes mellitus (DM) is increasing all over the world, with current estimates from the International Diabetes Federation (IDF) indicating that 537 million individuals are affected globally, a figure expected to rise to 783 million by 2045 (1). Type 2 diabetes (T2D) is the most prevalent form of DM, accounting for more than 90 percent of cases worldwide (2). In Pakistan, the prevalence of Type 2 DM is approximately 27%, reflecting a significant national burden (3). There is increasing evidence of a connection between hyperinsulinemia, hyperuricemia, and hypouricosuria, highlighting the complex metabolic interplay underlying type 2 diabetes (4). Research has demonstrated that hyperuricemia contributes to impaired fasting glucose levels and serves as an independent risk factor in individuals with T2DM (5). The recognition of hyperuricemia as both a predictive and diagnostic marker in diabetic patients has been suggested, with several studies recommending its use as an additional clinical indicator in the management of T2DM, particularly due to its association with adverse outcomes (6).

Hyperuricemia is associated with multiple negative effects, notably diabetic nephropathy. The underlying mechanisms include endothelial dysfunction, activation of the renin-angiotensin-aldosterone system, stimulation of pro-fibrotic cytokines, and activation of inflammatory pathways, all of which contribute to the development of microvascular disease and subsequent kidney damage in patients with diabetic nephropathy (7). In the United States, data from 2005–2006 reported 47.1 million individuals with hyperuricemia, corresponding to a total prevalence rate of 20.1 percent (8). Prevalence estimates vary internationally, with studies indicating ranges of 11.3–47 percent in the USA, 11.9–25.0 percent in Europe, and 13.1–13.3 percent in China (9). Multiple systematic reviews and meta-analyses have demonstrated a strong association between hyperuricemia and T2DM across different populations. Notably, a recent global meta-analysis showed that the pooled prevalence of diabetes among individuals with hyperuricemia ranged from 16 to 19 percent, depending on the studied population (10, 11).

Despite the high burden of type 2 diabetes in Pakistan and the increasing rates of metabolic syndrome, no systematic review to date has evaluated the prevalence of hyperuricemia among diabetic patients in the Pakistani population. This lack of national data on the co-existence of these conditions represents a critical gap in the literature. Therefore, the present systematic review and meta-analysis aims to synthesize evidence from existing studies conducted in Pakistan to estimate the prevalence of hyperuricemia among patients with type 2 diabetes mellitus.

MATERIAL AND METHODS

A comprehensive online search was conducted in PubMed, Google Scholar, and Science Direct to identify studies published between January 2014 and December 2024 relevant to the prevalence of hyperuricemia among patients with type 2 diabetes mellitus in Pakistan. The search strategy combined Medical Subject Headings (MeSH) and free-text terms including "hyperuricemia," "serum uric acid," "type 2 diabetes mellitus," "T2DM," "prevalence," "frequency," and "Pakistan." Additional manual searches of references cited within included articles were performed to capture any potentially overlooked studies. No language restrictions were applied during the search process to minimize the risk of selection bias. Eligibility criteria required studies to be cross-sectional or observational in design, conducted among Pakistani populations, and to report the prevalence or frequency of hyperuricemia among participants with confirmed type 2 diabetes. Study selection proceeded in two stages: initial screening by titles and abstracts, followed by full-text review for final eligibility. Data extraction was independently performed by two reviewers, with discrepancies resolved through consensus. Where consensus could not be achieved, a third reviewer was consulted to arbitrate disagreements.

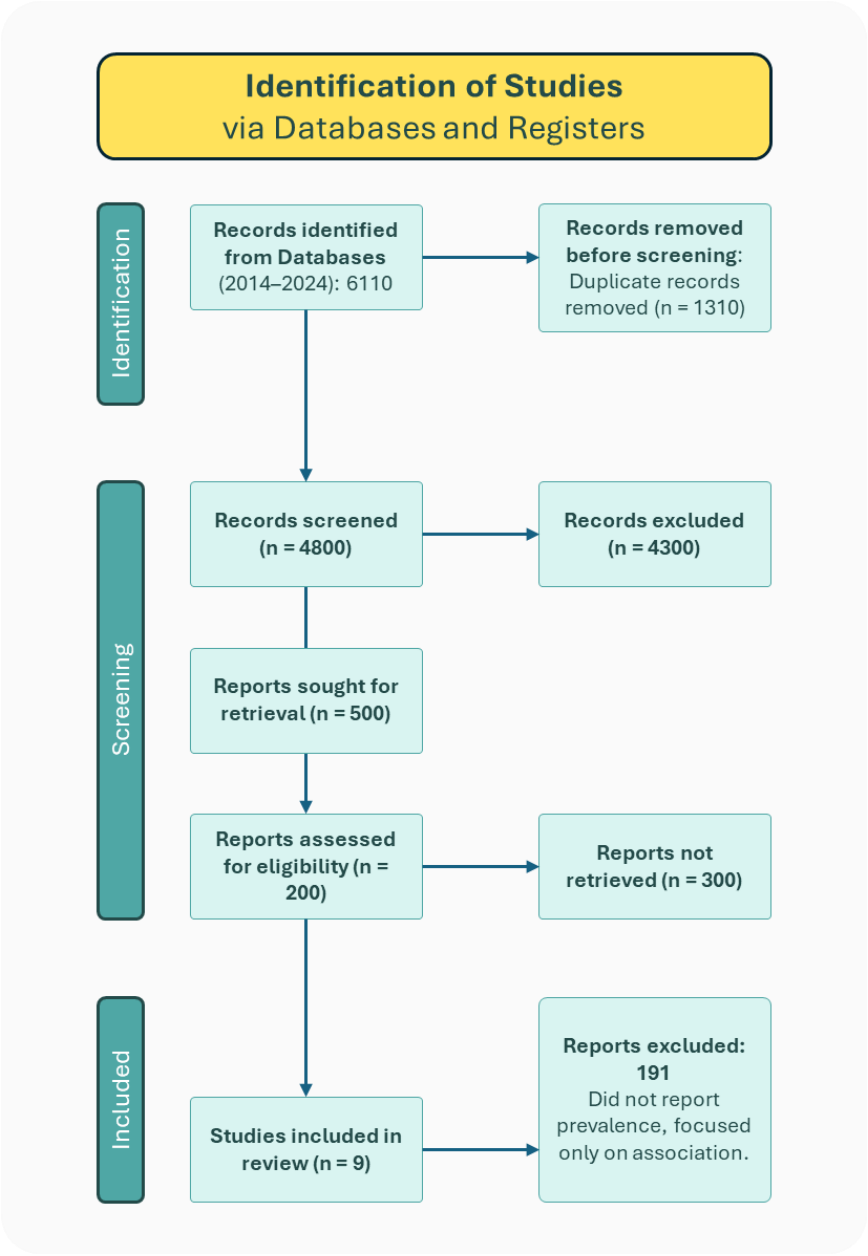

Figure 1 PRISMA Flow Diagram for Inclusion of Studies

Data extracted included first author, publication year, study location, sample size, diagnostic criteria for both type 2 diabetes and hyperuricemia, and reported prevalence rates. All extracted data were tabulated using Microsoft Excel. Statistical analysis was performed using SPSS version 25. Descriptive statistics including means, standard deviations, and proportions were used to summarize key

characteristics. Given considerable heterogeneity in study design, participant demographics, and diagnostic methods, both fixed-effects and random-effects meta-analyses were conducted to estimate pooled prevalence rates. The presence of between-study heterogeneity was evaluated using the I^2 statistic and Cochran's Q test, with results informing the choice of the random-effects model for pooled estimates where substantial heterogeneity was present. Publication bias was assessed using Egger's and Begg's tests. Statistical significance was set at a two-sided p value < 0.05 for all analyses.

The review process adhered to PRISMA guidelines for systematic reviews and meta-analyses. As the review utilized previously published data, no ethical approval was required.

RESULTS

This systematic review and meta-analysis included nine observational studies published between 2014 and 2024, conducted in various regions of Pakistan such as Bahawalpur, Peshawar, Lahore, Karachi, Nowshera, and Jamshoro. Across these studies, the prevalence of hyperuricemia among adult patients with type 2 diabetes mellitus (T2DM) was investigated in samples ranging from 85 to 576 participants. All included studies used cross-sectional or descriptive designs and were primarily conducted in hospital-based settings.

As shown in Table 1, the pooled prevalence of hyperuricemia among patients with type II diabetes mellitus varied considerably across studies. The fixed-effect model estimated a pooled prevalence of 24.9% (95% confidence interval [CI]: 22.9% to 27.0%), whereas the random-effects model yielded a slightly lower estimate of 21.4% (95% CI: 12.9% to 31.3%). This difference reflects the substantial heterogeneity observed among the studies included. The reported prevalence ranged from as low as 6.0% in the study by Khattak et al. (2020) to as high as 47.0% in the study by Noor et al. (2023), with intermediate values in studies such as Kumar et al. (2024) at 28.1%, Gulzar et al. (2023) at 36.0%, and Shah et al. (2014) at 25.2%. Studies with smaller sample sizes, including those by Zehra et al. (2024) and Samin et al. (2021), reported lower prevalence rates (9.4% and 12.9%, respectively), contributing proportionately less weight to the overall meta-analysis.

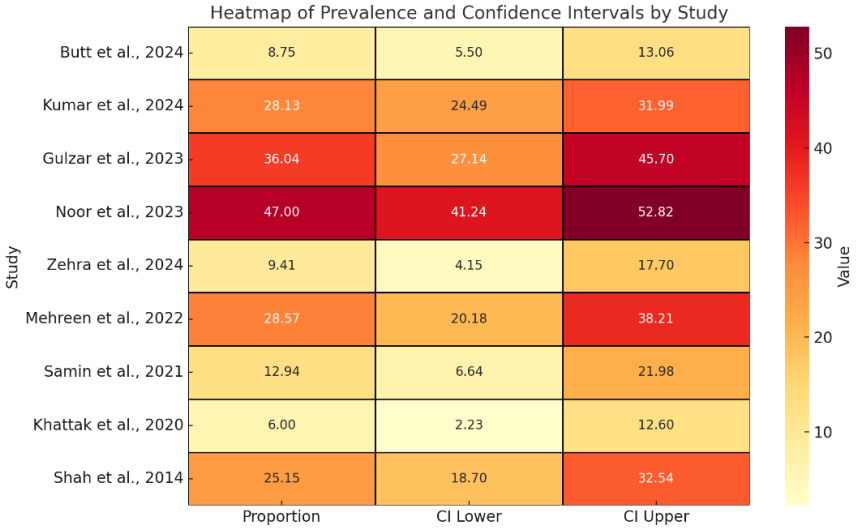

Figure 1 Point Prevalence and 95% Confidence Intervals of Hyperuricemia in Included Studies

Assessment of heterogeneity, as detailed in Table 2, demonstrated a very high level of inconsistency among studies, with an I^2 statistic of 95.37% (95% CI: 93.03% to 96.92%) and a highly significant Cochran's Q statistic ($Q = 172.72$, degrees of freedom = 8, $p < 0.0001$). The I^2 statistic quantifies the percentage of total variation across studies attributable to heterogeneity rather than chance, supporting the use of a random-effects model for pooled estimation. Figures 1 and 2 illustrate the point prevalence and confidence intervals for each study, as well as the forest plot for pooled prevalence estimates, with all axes, study names, and effect size bars clearly labeled. Figures and plots were generated using SPSS version 25.

Table 1. Prevalence of Hyperuricemia in Type II Diabetes Mellitus

Study	Sample Size	Proportion (%)	95% CI	Weight (%) Fixed	Weight (%) Random
Butt et al., 2024	240	8.75	5.50 – 13.06	13.59	11.41
Kumar et al., 2024	576	28.13	24.49 – 31.99	32.53	11.65
Gulzar et al., 2023	111	36.04	27.14 – 45.70	6.31	10.96
Noor et al., 2023	300	47.00	41.24 – 52.82	16.97	11.49
Zehra et al., 2024	85	9.41	4.15 – 17.70	4.85	10.73
Mehreen et al., 2022	105	28.57	20.18 – 38.21	5.98	10.92
Samin et al., 2021	85	12.94	6.64 – 21.98	4.85	10.73
Khattak et al., 2020	100	6.00	2.23 – 12.60	5.69	10.88
Shah et al., 2014	163	25.15	18.70 – 32.54	9.24	11.23
Total (fixed effects)	1765	24.94	22.94 – 27.02	100.00	100.00

Total (random effects)	1765	21.38	12.91 – 31.32	100.00	100.00

Table 2. Test of Heterogeneity and Publication Bias

Test for Heterogeneity	Value	Publication Bias	Value
Cochran's Q	172.72	Egger's Intercept	–5.32
Degrees of Freedom (DF)	8	95% CI	–16.10 to 5.47
Significance Level (Q)	$p < 0.0001$	Significance Level	$p = 0.2819$
I^2 (inconsistency)	95.37%	Begg's Kendall's Tau	–0.3099
95% CI for I^2	93.03–96.92	Significance	$p = 0.2448$

The assessment of potential publication bias was performed using Egger's and Begg's tests. Egger's test produced an intercept of –5.32 (95% CI: –16.10 to 5.47, $p = 0.2819$), and Begg's test yielded a Kendall's Tau of –0.3099 ($p = 0.2448$), as shown in Table 2. Both results suggest no statistically significant evidence of publication bias.

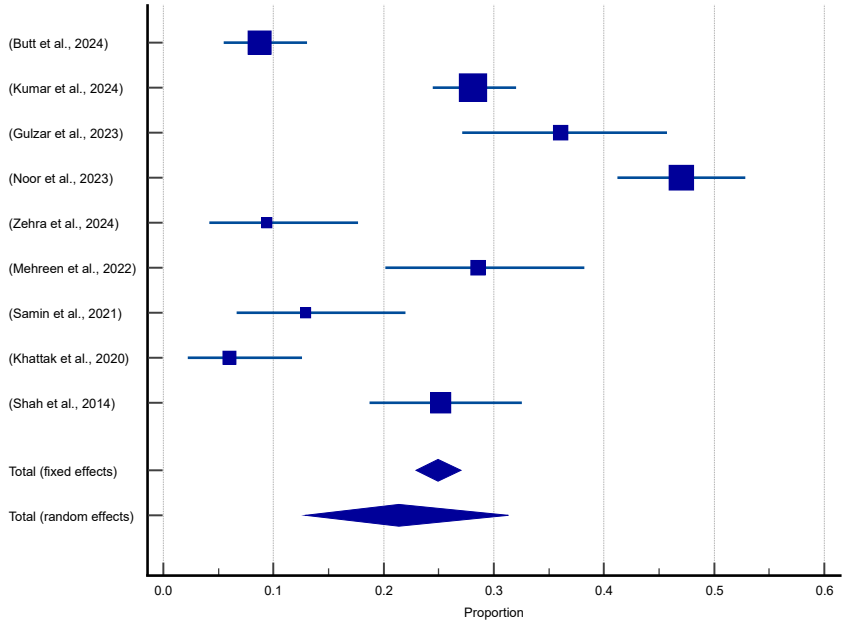

Figure 2 Forest Plot of the Prevalence of Hyperuricemia Among Patients with Type 2 Diabetes Mellitus

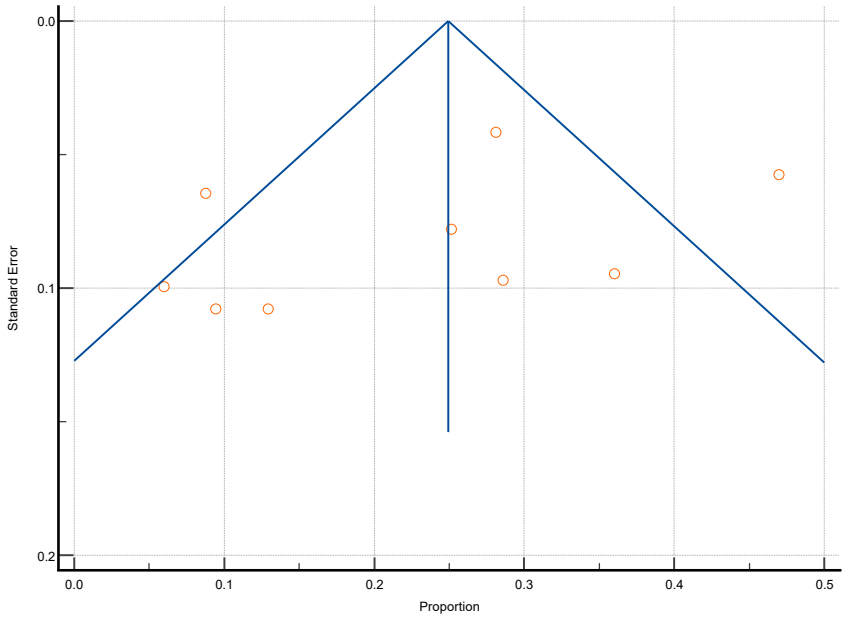

Figure 3 Funnel Plot Assessing Publication Bias for Prevalence of Hyperuricemia in Type 2 Diabetes Mellitus

However, given the small number of included studies, the power to detect publication bias is inherently limited and results should be interpreted with caution. The funnel plot for prevalence estimates (Figure 3) provides a visual assessment of publication bias and further supports these findings.

DISCUSSION

The present systematic review and meta-analysis provides valuable insights into the burden of hyperuricemia among patients with type 2 diabetes mellitus (T2DM) in Pakistan. Pooled prevalence estimates were 24.9% (95% CI: 22.9% to 27.0%) under a fixed-effects model and 21.4% (95% CI: 12.9% to 31.3%) under a random-effects model, with the broader confidence interval in the latter reflecting substantial heterogeneity across studies. The wide range of reported prevalence values, from 6% to 47%, highlights significant variability in the populations and methodologies included.

The highest prevalence was reported by Noor et al. (2023), where 47% of overweight diabetic patients (BMI >23 kg/m²) had hyperuricemia, and this subgroup also showed strong correlations between hyperuricemia, hypertension, elevated HbA1c, and higher BMI, suggesting that poor metabolic control and increased adiposity may be important risk factors (15). Conversely, the lowest prevalence (6%) was observed in Khattak et al. (2020), where only 23% of participants had diabetes, and the proportion of hyperuricemia was actually higher among non-diabetics than diabetics. This finding contrasts with the overall trend of the review and may be attributed to sampling bias, under-representation of diabetic patients, or unmeasured confounding factors (19). Moderate prevalence rates, such as those reported by Kumar et al. (2024) at 28.1%, further support the overall pooled estimate and underscore the relevance of smoking as a confounding variable influencing oxidative stress and serum uric acid levels (13). Gulzar et al. (2023) demonstrated a prevalence of 36%, with significant associations between hyperuricemia, diabetic nephropathy, fasting glucose, HbA1c, and the albumin-creatinine ratio (14). Similarly, Shah et al. (2014) reported a prevalence of 25.1% and found that hyperuricemia was present in half of patients with diabetic nephropathy compared to 19% in those without nephropathy (20).

Lower prevalence values in studies with smaller sample sizes, such as Zehra et al. (2024) and Samin et al. (2021) at 9.4% and 12.9%, respectively, may reflect limited statistical power. The inclusion of healthy controls in Samin et al. was particularly informative, revealing that no non-diabetic control had elevated uric acid levels, which strengthens the evidence for a potential association between diabetes and hyperuricemia. Furthermore, Samin et al. observed that uric acid levels increased with diabetes duration, suggesting a possible progressive relationship (18). Butt et al. (2024) reported a relatively low prevalence (8.8%) but noted significant associations with nephropathy and longer diabetes duration (12). Mehreen et al. (2022) found a prevalence of 28.6%, reinforcing the frequent co-occurrence of hyperuricemia in diabetics (17). The very high degree of heterogeneity observed ($I^2 = 95.37\%$) may be attributed to differences in sample sizes, regional, demographic, and lifestyle factors, as well as varying inclusion criteria and diagnostic definitions. While formal assessment found no statistically significant evidence of publication bias, it is important to recognize that the small number of included studies limits the power of such tests and the ability to detect bias. The results of this review are therefore best interpreted with caution. Comparing these findings to global data, the pooled prevalence of hyperuricemia in T2DM patients in Pakistan appears to be similar or slightly higher than estimates reported in meta-analyses from other populations, which typically range from 16% to 19% (10, 11). This highlights the significance of hyperuricemia as a public health concern in the Pakistani diabetic population, where rising rates of metabolic syndrome may further exacerbate disease burden.

Several limitations must be acknowledged. Most included studies were cross-sectional, hospital-based, and single-center, which restricts the ability to draw causal inferences and limits generalizability. Heterogeneity in diagnostic criteria, participant demographics (e.g. gender, comorbidities, BMI cut-offs), and methodological quality further complicate interpretation. The small number of studies included also precluded meaningful subgroup analyses to explore factors such as gender, age, obesity, hypertension, or medication use. Additionally, few studies adequately adjusted for potential confounding variables, including smoking, medications, or dietary factors, and regional data may not be nationally representative. Despite these limitations, the findings underscore the need for clinicians to consider routine screening for hyperuricemia in patients with T2DM, particularly those with poor glycemic control, obesity, or established nephropathy. Public health initiatives targeting lifestyle modification and metabolic risk factors may help reduce both the prevalence and adverse outcomes associated with hyperuricemia in this population. Future research should focus on large, multi-center, prospective studies that standardize diagnostic criteria, adjust for key confounders, and investigate the interplay of metabolic, genetic, and lifestyle factors in the development of hyperuricemia among patients with type 2 diabetes.

CONCLUSION

In conclusion, the overall prevalence of hyperuricemia among patients with type 2 diabetes mellitus (T2DM) in Pakistan is substantial, with pooled estimates ranging from 21% to 25%. However, considerable heterogeneity across studies warrants cautious interpretation of these findings. Contextual factors such as patient BMI, hypertension, glycemic control, and the presence of diabetic nephropathy, as well as differences in diagnostic criteria, may significantly influence prevalence estimates. Future research should focus on addressing these variables to provide a more accurate national picture and guide targeted interventions.

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