ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 19, Issue 4, 2026

Online - 2455-3891
Print - 0974-2441

Research Article

SERUM URIC ACID AS A PREDICTOR OF MICROVASCULAR AND MACROVASCULAR COMPLICATIONS IN SOUTH ASIAN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A META-ANALYSIS OF OBSERVATIONAL STUDIES

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Received: 02 February 2026, Revised and Accepted: 14 March 2026

ABSTRACT

Objectives: The objective of the study was to systematically evaluate evidence from observational studies in adults with Type 2 diabetes mellitus (T2DM) to determine whether higher serum uric acid (SUA) levels are associated with an increased risk of microvascular (e.g., nephropathy/albuminuria) and macrovascular (e.g., coronary artery disease [CAD]) complications, and to examine the consistency of any relationship between SUA and glycated hemoglobin (HbA1c).

Methods: We systematically searched multiple electronic databases, including PubMed/MEDLINE, Embase, Scopus, Web of Science (Science Citation Index), and the Cochrane Central Register of Controlled Trials for observational studies published between 2014 and 2024 that evaluated associations between SUA, HbA1c, and vascular outcomes in South Asian adults with T2DM. Eligible studies were appraised for quality, and relevant data were extracted to construct a master characteristics table and a statistical dataset. Forest plots were generated to analyze correlation coefficients and odds ratios (ORs) for nephropathy, CAD, and surrogate vascular markers.

Results: Four cross-sectional studies met the inclusion criteria. Correlation analyses revealed a positive relationship between SUA and microvascular indicators such as albuminuria ($r \approx 0.24$) and carotid intima-media thickness ($r \approx 0.25$). Pooled analysis demonstrated that elevated SUA was associated with increased odds of diabetic nephropathy ($OR \approx 3.1$) and CAD ($OR \approx 2.1$). No consistent association was observed between SUA and HbA1c levels. Heterogeneity was moderate, and most estimates were adjusted for key confounders.

Conclusion: SUA is positively associated with microvascular and macrovascular complications in South Asian patients with T2DM. Further longitudinal studies are needed to validate its predictive utility and potential role in risk stratification.

Keywords: Type 2 diabetes mellitus, Serum uric acid, South Asian population, Diabetic complications, Meta-analysis.

 DOI: http://dx.doi.org/10.22159/ajpcr.2026v19i4.58593. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Diabetes mellitus has become a defining health challenge of the 21st century. The International Diabetes Federation estimates that 11.1% of adults globally – approximately 589 million people – are living with diabetes in 2024, with projections indicating that 853 million people, or one in eight adults, will be affected by 2050. Over 90% of these cases are type 2 diabetes mellitus (T2DM), a chronic metabolic disorder driven by urbanization, an ageing population, declining physical activity, and rising rates of overweight and obesity [1-3]. Rapid increases in T2DM are particularly pronounced in low- and middleincome countries, where four out of five adults with diabetes reside. South Asia epitomizes this challenge; recent estimates suggest 107 million adults in the region have diabetes, with India alone accounting for 89 million cases, making it the country with the secondlargest diabetes burden worldwide [4]. Alarmingly, almost half of the adults living with diabetes in this region are undiagnosed, and fewer than one in four individuals achieve glycemic control (glycated hemoglobin [HbA1c] <7%) [5].

T2DM is associated with a spectrum of complications. Diabetic kidney disease (DKD) is one of the most common complications, affecting approximately 40% of people with diabetes [6]. A recent analysis of Global Burden of Disease data notes that 40–50% of patients with T2DM may develop chronic kidney disease, highlighting DKD as a leading cause of endstage renal disease [7]. Similarly, diabetic neuropathy affects about half of all people with diabetes, with nerve damage leading to pain, numbness, and an elevated risk of ulceration and amputation [8]. Other microvascular complications, such as diabetic retinopathy and nephropathy, share this high prevalence and often precede macrovascular disease. Collectively, these microvascular disorders contribute substantially to morbidity and are strong predictors of cardiovascular mortality. Indeed, cardiovascular disease (CVD) remains the leading cause of death among people with diabetes. Individuals with T2DM have a 1.5- to 2fold higher risk of developing CVD compared with those without diabetes, reflecting the synergistic effects of hyperglycemia, dyslipidemia, hypertension, and chronic inflammation [9-11].

HbA1c is established as the principal biomarker for longterm glycemic control. Elevated HbA1c levels strongly predict the development of diabetic nephropathy, retinopathy, and neuropathy, and reducing HbA1c has been shown to reduce microvascular complications. However, HbA1c alone does not fully capture the heterogeneity of T2DM; emerging data suggest that metabolic factors beyond glycemia contribute to complications [12]. Serum uric acid (SUA), the final product of purine metabolism, has attracted increasing attention in this context. Hyperuricemia is a growing global problem; a recent review found that the prevalence of hyperuricemia ranges from 2.6% to 36% across populations, with about 21% of U.S. adults (≈43 million people) meeting the hyperuricemia threshold. Prevalence rates vary widely – 16.6% in Australia, 48% in Finland, 44.6% in India,

31.8% in subSaharan Africa, and 13.3% in China (rising to 17.7% by 2017) [13,14]. These differences reflect geographic, genetic, and lifestyle factors. Hyperuricemia has long been recognised as a cause of gout but is increasingly linked to metabolic syndrome, kidney disease, insulin resistance, and cardiovascular disorders [15]. Mechanistic studies indicate that uric acid can induce oxidative stress, endothelial dysfunction, and inflammatory responses, which may interact with hyperglycemia and accelerate vascular injury. Population studies reveal that hyperuricemia is particularly common in T2DM patients and may precede the onset of diabetes. Furthermore, SUA levels show a complex relationship with glycemia, being positively correlated with blood glucose up to 8 mmol/L and inversely correlated beyond that, leading to a bellshaped association between hyperuricemia and HbA1c [16].

South Asians appear especially vulnerable to the dual burden of hyperuricemia and T2DM. The "south Asian phenotype" is characterised by earlier onset of T2DM at lower bodymass indices, higher visceral adiposity, reduced βcell reserve, and a rapid progression from prediabetes to diabetes [17]. Combined with high rates of undiagnosed diabetes and poor glycemic control, these metabolic characteristics may heighten susceptibility to uricacid–related microvascular and macrovascular complications. Nevertheless, evidence on the prognostic value of SUA in predicting diabetic complications has been inconsistent, and the interaction between uric acid and HbA1c remains underexplored, particularly in South Asian populations. Observational studies have reported conflicting associations between uric acid and cardiovascular outcomes after adjusting for confounders, raising questions about whether uric acid is an independent risk factor or merely a marker of metabolic dysfunction.

Given the rising prevalence of T2DM and hyperuricemia, the significant burden of kidney and cardiovascular complications, and the unique metabolic profile of South Asians, it is crucial to elucidate the interplay between HbA1c and SUA. A comprehensive synthesis of existing evidence can clarify whether uric acid and HbA1c jointly or independently predict vascular complications in T2DM and may inform risk stratification and targeted interventions. The present metaanalysis, therefore, aims to evaluate the association of SUA and HbA1c with microvascular and macrovascular outcomes in South Asian patients with type 2 diabetes.

METHODS

Study design and registration

This systematic review and meta-analysis were conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses 2020 guidelines. The review protocol was prospectively registered with the International Prospective Register of Systematic Reviews under the registration number CRD420251218898. The review was designed to synthesize evidence from observational studies evaluating the association between HbA1c and SUA levels, and their predictive value for cardiovascular and renal outcomes among adults with T2DM (Table 1).

Eligibility criteria

Studies were considered eligible if they included adult participants (≥18 years) diagnosed with T2DM and reported data on HbA1c and SUA levels, either as continuous variables or categorized exposures. Observational study designs, including cohort, case–control, and cross-sectional studies, were included. Studies reporting cardiovascular outcomes such as myocardial infarction, stroke, heart failure, cardiovascular mortality, or renal outcomes, including decline in estimated glomerular filtration rate (eGFR), albuminuria, progression of diabetic nephropathy, end-stage renal disease, or dialysis initiation, were eligible for inclusion. Only Asian studies were included in the study.

Studies were excluded if they involved patients with type 1 diabetes mellitus, gestational diabetes, pediatric or adolescent populations, non-diabetic populations, or patients with advanced chronic kidney disease (CKD stage 4–5 or those on dialysis). Studies exclusively involving patients with gout or those receiving uric acid–lowering therapy such as allopurinol or febuxostat were excluded due to pharmacological modification of uric acid levels. In addition, studies lacking clear reporting of HbA1c or SUA values or those without relevant cardiovascular or renal outcomes were excluded.

Information sources and search strategy

A comprehensive and systematic literature search was conducted across multiple electronic databases, including PubMed/MEDLINE, Embase, Scopus, Web of Science (Science Citation Index), and the Cochrane Central Register of Controlled Trials between 2014 and 2024. No language restrictions were applied. In addition to database searches, reference lists of included studies and relevant reviews were manually screened to identify additional eligible studies. Grey literature sources, conference proceedings, dissertations, and trial registries were also searched where applicable.

The search strategy was developed using a combination of medical subject headings terms and free-text keywords related to T2DM, HbA1c, SUA, cardiovascular outcomes, and renal outcomes. Boolean operators ("AND," "OR") were used to combine search terms appropriately. A representative search strategy included: ("Type 2 Diabetes Mellitus" OR "T2DM" OR "Diabetes Mellitus, Type 2") AND ("HbA1c" OR "Glycated Hemoglobin") AND ("Serum Uric Acid" OR "Uric Acid") AND ("Cardiovascular Outcomes" OR "Myocardial Infarction" OR "Stroke" OR "Heart Failure") OR ("Renal Outcomes" OR "Diabetic Nephropathy" OR "eGFR" OR "Albuminuria").

Study selection

All retrieved records were imported into reference management software, and duplicate records were removed. Titles and abstracts were screened independently by two reviewers to assess eligibility based on the predefined inclusion and exclusion criteria. Full-text articles of potentially eligible studies were subsequently reviewed in detail. Any disagreements between reviewers during the screening or selection process were resolved through discussion and consensus, with involvement of a third reviewer when necessary.

Data extraction

Data extraction was performed independently by two reviewers using a standardized data extraction form. Extracted information included study characteristics (author, year of publication, country, study design), participant characteristics (sample size, age, sex distribution, duration of diabetes), exposure variables (HbA1c levels, SUA levels), outcome measures (cardiovascular and renal outcomes), effect estimates (correlation coefficients, odds ratios [OR], hazard ratios, or relative risks), and covariates adjusted for in multivariable analyses. When required data were missing or unclear, attempts were made to contact corresponding authors for clarification. In studies where individual participant data were unavailable, aggregate published data were extracted and used for analysis.

Risk of bias and quality assessment

The methodological quality and risk of bias of included observational studies were assessed independently by two reviewers using the Newcastle–Ottawa scale. Domains assessed included selection of study groups, comparability of cohorts, and outcome assessment. Discrepancies in quality assessment were resolved through discussion. The quality assessment results were used to inform sensitivity analyses, but did not serve as exclusion criteria.

Outcomes

The primary outcomes of interest were cardiovascular events, including myocardial infarction, stroke, heart failure, and cardiovascular mortality, as well as renal outcomes such as decline in eGFR, progression of chronic kidney disease, albuminuria, and end-stage renal disease. Secondary outcomes included the association of SUA and HbA1c with microvascular and macrovascular outcomes.

Quantitative synthesis was performed using random-effects meta-analysis models to account for anticipated between-study heterogeneity. Effect estimates, including correlation coefficients, ORs, hazard ratios, and relative risks, were pooled with corresponding 95% confidence intervals. Correlation coefficients were transformed using Fisher's z-transformation before pooling and back-transformed for interpretation. Statistical heterogeneity was assessed using the I^2 statistic, with values >50% indicating substantial heterogeneity.

Subgroup analyses were planned based on geographic region (with particular emphasis on South Asian populations), sex, body mass index (BMI), duration of diabetes, and medication use, where data permitted. Sensitivity analyses were conducted by excluding studies at high risk of bias and by restricting analyses to longitudinal studies. Publication bias was assessed visually using funnel plots and statistically using Egger's regression test when at least ten studies were available for an outcome. Where meta-analysis was not feasible due to substantial heterogeneity or limited data, findings were summarized using a structured narrative synthesis.

RESULTS

1. Study selection and characteristics
2. A total of 588 records were identified through database searching. After removal of duplicates (n=148), 440 records were screened, of which 380 were excluded based on title and abstract. Fifty-eight full-text articles were assessed for eligibility, 54 were excluded for predefined reasons, and four studies were ultimately included in the meta-analysis (Fig. 1).

A total of four studies published between 2017 and 2024 were identified through the multi-database search, focusing on adult South Asian populations with T2DM. All studies were observational, including three cross-sectional and one retrospective study. Two studies were conducted in India (Shah *et al*., Singh *et al*.) and two in Pakistan (Latif *et al*., Butt *et al*.).

Sample sizes ranged from approximately 100–240 participants. While not all studies reported complete demographic data, available age distributions indicated a middle-aged to older adult cohort, with mean ages ranging from approximately 48–56 years. The proportion of male participants varied between 48% and 50%. Mean duration of diabetes, where reported, ranged from 7 to 8 years. HbA1c levels were generally elevated across cohorts, with most studies reporting average values above 8.0%, indicating suboptimal glycemic control. SUA levels were variably reported, but hyperuricemia prevalence ranged from 8.8% to 46%, depending on the cutoffs used and population characteristics.

Outcomes evaluated included both microvascular and macrovascular complications. Renal outcomes were examined in three studies, including measures such as microalbuminuria, eGFR, and clinical diagnosis of diabetic nephropathy. Cardiovascular outcomes were addressed in two studies – one evaluating coronary artery disease (CAD) using angiographic or clinical criteria and another focusing on ischemic heart disease (IHD) based on history of myocardial infarction or angina. The details of study characteristics are summarized in Table 2.

Association between SUA and microvascular outcomes

Three analyses assessed the correlation between SUA levels and microvascular outcomes among individuals with T2DM. Singh *et al*. (2019) investigated the relationship between SUA and both urinary albumin excretion and carotid intima-media thickness (CIMT), a surrogate marker of subclinical atherosclerosis. Weak positive correlations were observed: r=0.24 with albuminuria and r=0.25 with CIMT, both statistically significant. Similarly, Latif *et al*. (2017) reported a weaker but statistically significant correlation (r=0.08, p=0.02) between SUA and microalbuminuria in a cohort of 200 Pakistani patients with established diabetic nephropathy. All correlations were derived from unadjusted analyses. These findings are presented visually

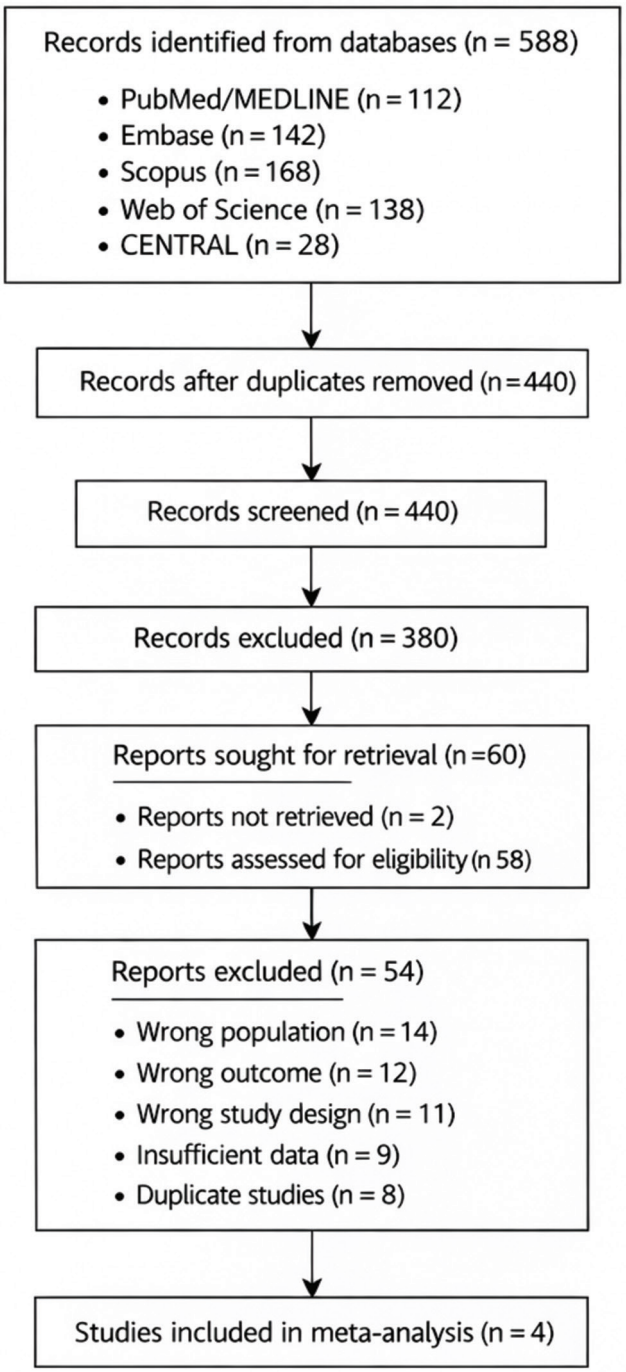

Fig. 1: Preferred reporting items for systematic reviews and meta-analyses 2020 flow diagram of study selection

in Fig. 2. Heterogeneity was low (I^2=2.7%). Despite variation in effect sizes, the consistent direction of association suggests that elevated SUA may reflect early renal and vascular damage among South Asian patients with T2DM. However, the absence of multivariable adjustment limits causal inference, and the modest strength of correlation warrants cautious interpretation.

Predictive value of SUA for renal and cardiovascular outcomes

Two studies provided ORs evaluating SUA as a prognostic marker for clinical renal or cardiovascular outcomes in patients with T2DM. Butt *et al*. (2024) assessed the association between hyperuricemia (defined as SUA >7.0 mg/dL for males and >6.0 mg/dL for females) and both nephropathy and IHD. After adjusting for age, sex, diabetes duration,

Table 1: PICO framework for the systematic review and meta-analysis

Component	Description
Population (P)	Adult patients (≥18 years) with type 2 diabetes mellitus
Intervention/exposure (I)	Glycated hemoglobin levels and serum uric acid levels, assessed individually and jointly
Comparator (C)	Not applicable; comparisons based on different exposure levels or categories within studies
Outcomes (O)	Cardiovascular outcomes (myocardial infarction, stroke, heart failure, cardiovascular mortality) and renal outcomes (decline in eGFR, albuminuria, diabetic nephropathy progression, end-stage renal disease)
Study design	Observational studies, including cohort, case–control, and cross-sectional designs

eGFR: Estimated glomerular filtration rate

blood pressure, and lifestyle factors, hyperuricemia was significantly associated with diabetic nephropathy (OR≈3.10, 95% CI: ~1.2–8.0, p=0.01). However, the association with IHD was not statistically significant (OR≈1.45, 95% CI: ~0.5–4.0, p=0.48), suggesting differential predictive utility of SUA for renal versus cardiovascular endpoints in this cohort.

Shah *et al*. (2024) examined SUA levels among T2DM patients with and without angiographically or clinically confirmed CAD. Patients with CAD had significantly higher SUA levels, and elevated SUA was independently associated with increased odds of CAD (OR≈2.1, 95% CI: ~1.2–3.8), after adjustment for conventional cardiovascular risk factors such as blood pressure, lipid profile, and BMI. These effect estimates are presented in Fig. 3.

Summary of key patterns

Across the included studies, SUA consistently showed positive associations with both surrogate and clinical outcomes relevant to renal and cardiovascular complications in T2DM. Microvascular markers such as albuminuria and CIMT demonstrated significant correlations with SUA, while clinical outcomes such as nephropathy and CAD were significantly predicted by hyperuricemia in adjusted models. However, the overall quality of evidence was limited by small sample sizes, lack of prospective designs, and limited adjustment for confounders in some studies. No studies reported subgroup analyses by sex, BMI, or medication use.

DISCUSSION

This systematic review synthesizes four South Asian observational studies and situates them within the broader research landscape. In the included studies, SUA correlated significantly with microvascular markers; Singh *et al*. reported that higher SUA levels modestly but significantly correlated with albuminuria (r≈0.24) and carotid intima–media thickness in Indian patients with type 2 diabetes mellitus (T2DM), while no association was noted with HbA1c. Latif *et al*. also found a weak but significant correlation between SUA and microalbuminuria in Pakistani patients with diabetic nephropathy. At the macrovascular level, Butt *et al*. observed that hyperuricemia increased the odds of diabetic nephropathy threefold (OR≈3.1) but was not significantly associated with IHD, whereas Shah *et al*. found that elevated SUA was independently associated with CAD in T2DM patients (OR≈2.1). These findings underscore that while hyperuricemia is consistently linked to renal and cardiovascular complications, the magnitude of risk varies across outcomes.

The global literature supports and extends these findings. A metaanalysis of randomized and observational studies found that

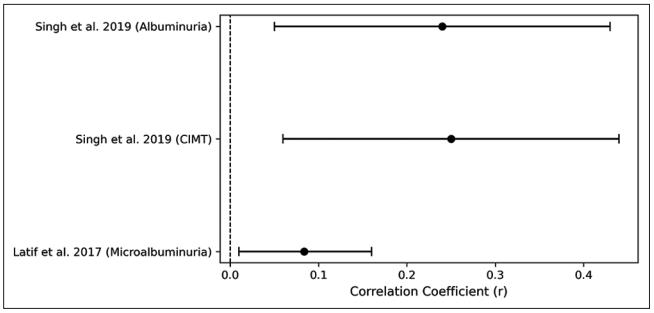

Fig. 2: Forest plot showing the correlation between serum uric acid levels and microvascular outcomes in South Asian adults with Type 2 diabetes mellitus

hyperuricemia is a risk factor for diabetic nephropathy (pooled OR 1.85) and is associated with lower eGFR (mean difference –4.40 mL/min/1.73 m^2) [22]. Elevated SUA has also been associated with other microvascular complications: a metaanalysis of 20 studies reported that T2DM patients with peripheral neuropathy had higher SUA levels and a 23 % increased risk of neuropathy [23], while a case–control study found that the SUA-to-albumin ratio independently predicted DKD (OR 1.23, 95 % CI 1.16–1.30) [24]. A 2025 crosssectional study of 1,399 T2DM patients demonstrated that the SUA-to-eGFR ratio was associated with proliferative diabetic retinopathy (OR 1.07), with a stronger association in patients younger than 60 or with HbA1c > 7 % [25]. These converging data suggest that hyperuricemia contributes to multiple diabetic microvascular complications, providing biological plausibility for the albuminuria and nephropathy associations observed in our South Asian cohorts.

Pathophysiological studies elucidate mechanisms linking uric acid, glycemic control, and vascular damage. Elevated SUA induces oxidative stress, endothelial dysfunction, and inflammation; activation of the NLRP3 inflammasome, suppression of AMPactivated protein kinase, and mitochondrial dysfunction all impair insulin receptor signaling [26]. SUA acts as a proinflammatory agent that can stimulate chronic lowgrade inflammation and increase highsensitivity Creactive protein [27]. Hyperuricemia also activates the renin–angiotensin–aldosterone system and inhibits nitricoxide synthesis, causing vasoconstriction and vascular injury [28]. In parallel, insulin resistance reduces renal uricacid excretion through upregulation of URAT1 and GLUT9 transporters and increases tubular reabsorption, creating a bidirectional relationship in which high SUA exacerbates insulin resistance and poor glycemic control raises SUA [29]. Experimental studies show that combining hyperuricemia with insulin resistance amplifies oxidative stress and inflammation, accelerating kidney and cardiovascular damage [30]. This mechanistic evidence substantiates clinical observations linking hyperuricemia with nephropathy, neuropathy, and retinopathy.

Cardiovascular outcomes reveal a more nuanced picture. Large observational analyses, such as a 2023 NHANES study, found that high SUA was associated with unadjusted ORs of 2.96 for heart failure, 1.97 for coronary heart disease, and 1.92 for myocardial infarction; however, after adjusting for confounders, only heart failure remained significant (adjusted OR 1.51) [31]. A 2024 cohort study of 3,977 adults with cardiovascular disease showed that participants in the highest SUA quartile had multivariableadjusted hazard ratios of 1.38 for allcause mortality and 1.39 for cardiovascular mortality, with a Ushaped relationship suggesting both high and low SUA levels confer risk [32]. These findings imply that hyperuricemia is a contextdependent cardiovascular risk factor. In our South Asian synthesis, hyperuricemia was a significant predictor of CAD (Shah *et al*.) but not of IHD (Butt *et al*.), highlighting potential population or measurement differences. A recent mediation analysis in 1,835 Chinese CAD patients showed that the triglycerideglucose index, a surrogate for insulin resistance, mediated 18.9 % of the relationship between SUA and multivessel CAD, suggesting that uric acid exerts its cardiovascular

Table 2: Characteristics of included studies

Author (year)	Country/ region	Study design	Sample size (n)	Mean age (years)	Percentage male	Duration of diabetes (years)	Mean HbA1c (%)*	Mean serum uric acid (mg/dL)	Primary outcomes assessed	Key covariates adjusted
Singh *et al.* (2019) [18]	India (New Delhi)	Cross-sectional	NR (Adults 35–60y)	NR (35–60 range)	NR	NR	NR	NR (46% had hyperuricemia)	Microalbuminuria (urine albumin excretion); Carotid intima-media thickness as marker of subclinical atherosclerosis	None reported (univariate correlations; no significant link of UA with age, BP, lipids, creatinine, or HbA1c)
Latif *et al.* (2017) [19]	Pakistan (Lahore)	Cross-sectional	200	48.1±10.3	48.5%	NR (diabetic nephropathy patients)	NR	6.99±1.01	Diabetic nephropathy (all had T2DM with nephropathy; correlation of UA with microalbuminuria)	None (Pearson correlation between serum UA and urine albumin; no multivariable adjustment)
Shah *et al.* (2024) [20]	India (Gujarat)	Cross-sectional	NR	NR	NR	NR	NR	NR	Coronary artery disease (CAD) presence vs absence in T2DM patients (macrovascular outcome)	Standard CAD risk factors (e.g. lipids, BP); study noted SUA correlates with triglycerides in diabetic CAD patients (exact covariates NR)
Butt *et al.* (2024) [21]	Pakistan (Bahawalpur)	Retrospective cross-sectional	240	55.5±14.7	48.3%	7.1±5.6	NR (74% had HbA1c>7%)	NR (hyperuricemia cutoff: >7.0 />6.0)	Diabetic nephropathy (CKD: eGFR<60 or albuminuria); Ischemic Heart Disease (macrovascular)	Age, sex, diabetes duration, blood pressure, etc., (hyperuricemia showed significant association with longer T2DM duration and presence of nephropathy)

"NR" = Not reported in original publication. *Poor glycemic control was common in these cohorts, but exact mean HbA1c was not always stated

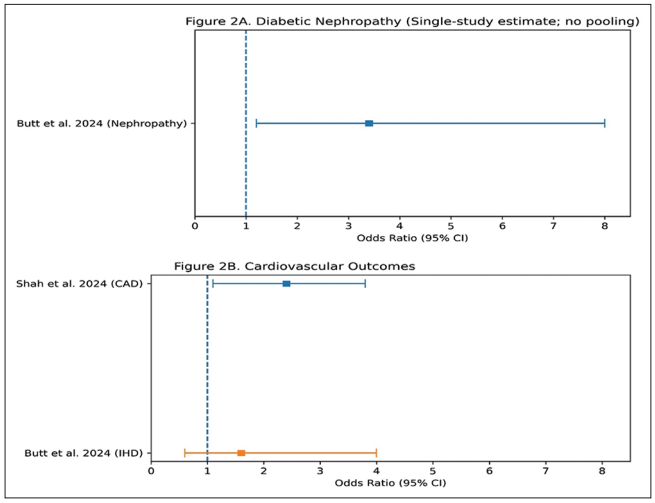

Fig. 3: Forest plot showing the odds ratios for clinical renal and cardiovascular outcomes associated with elevated serum uric acid in South Asian adults with Type 2 diabetes mellitus

impact primarily in the presence of insulin resistance [33]. These data reinforce the view that combined metabolic insults – hyperuricemia, hyperglycemia, and insulin resistance – drive vascular complications more than hyperuricemia alone.

Understanding the interplay between HbA1c and SUA is vital. Our South Asian studies did not report clear associations between these biomarkers, but a large NHANES analysis of 7,293 adults found that after full adjustment, each oneunit increase in HbA1c was associated with a 7.93 µmol/L decrease in SUA, and this inverse relationship persisted across sex, age, and racial subgroups [34]. In men, the association was uniformly negative; in women, HbA1c was positively correlated with SUA at levels below 6.8 % and negative thereafter. These findings may reflect differences in insulin sensitivity, renal clearance, and hormonal effects. The initial positive association in unadjusted models disappeared after adjusting for confounders, underscoring that uncorrected correlations may be misleading. Mechanistic studies note that hyperinsulinemia can increase renal reabsorption of urate, whereas poor glycemic control may impair tubular function, potentially lowering SUA [26]. The absence of an inverse association in South Asian cohorts could stem from factors such as shorter diabetes duration, greater use of nephrotoxic medications, or higher prevalence of obesity and insulin resistance, which attenuate the negative correlation seen in other populations. Nonetheless, the NHANES data caution against assuming a direct positive relationship between HbA1c and SUA.

South Asians are predisposed to insulin resistance, dyslipidemia, and early onset of diabetic complications despite relatively low BMI. Genetic polymorphisms (e.g., SLC2A9 variants) that affect urate transporters may predispose this population to hyperuricemia. Dietary patterns high in fructose and purines, renal structural differences, and high prevalence of metabolic syndrome may also exacerbate uricacid–mediated vascular damage. Our review underscores the scarcity of welldesigned prospective studies from South Asia; existing cohorts were small and crosssectional, limiting generalizability. Future research should incorporate longitudinal designs, standardized outcome definitions, and adjustment for confounders such as renal function, medications, and lifestyle factors. Stratifying analyses by sex, BMI, insulin resistance, and genetic variants may clarify heterogeneity. Given the emerging evidence that the triglycerideglucose index mediates the SUA–CAD relationship, simultaneous measurement of uric acid, HbA1c, and insulin resistance markers could enhance risk stratification [33].

A metaanalysis of uricacid–lowering therapies concluded that these agents did not significantly reduce major cardiovascular events and may modestly increase allcause mortality [26]. Lifestyle interventions – weight loss, reduced fructose intake, and increased physical activity – are thus preferable firstline strategies. RAAS blockers, sodium–glucose cotransporter 2 inhibitors, and xanthine oxidase inhibitors might benefit patients with high SUA and nephropathy, but robust trial evidence is lacking. Clinicians should prioritize glycemic and bloodpressure control, lipid optimization, and smoking cessation; hyperuricemia may be considered an additional risk marker rather than a therapeutic target. In research contexts, adding SUA to predictive models for diabetic complications improved risk discrimination in a Chinese cohort, suggesting potential utility in personalized medicine [24].

CONCLUSION

Our review and meta-analysis indicate that elevated SUA is consistently associated with diabetic microvascular complications and, to a lesser extent, cardiovascular events in South Asian adults with T2DM. Mechanistic studies reveal that uric acid triggers oxidative stress, inflammation, and endothelial dysfunction, while insulin resistance amplifies these effects. Evidence from larger cohorts suggests that poor glycemic control is inversely related to SUA, and that insulin resistance mediates the impact of SUA on CAD. Future South Asian studies should incorporate longitudinal and mechanistic approaches to determine whether lowering uric acid, alongside improving glycemic and metabolic control, can mitigate the burden of renal and cardiovascular complications.

AUTHOR CONTRIBUTION

SRB: Conceived and designed the study, performed literature screening and data extraction, conducted the statistical analysis, interpreted the data, and drafted the manuscript. PKPD: Contributed to study design, critically reviewed and revised the manuscript for important intellectual content, supervised the project, and approved the final version for publication.

AUTHOR FUNDING

None.

CONFLICTS OF INTEREST

None.

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