

PATTERNS OF DIABETES-RELATED COMPLICATIONS AND CLINICAL OUTCOMES IN GENERAL MEDICINE SETTINGS: A SYSTEMATIC REVIEW WITHOUT META-ANALYSIS

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ABSTRACT

OBJECTIVES

To systematically synthesise recent observational evidence on patterns of diabetes-related complications, clinical outcomes, glycemic-control findings, and factors associated with adverse outcomes in general medicine and related routine-care settings.

METHODOLOGY

PubMed, Web of Science, and Scopus were searched for original studies published from 2020 through 2025. Eligible studies included observational cross-sectional, cohort, retrospective, prospective, multicenter, hospital-based, and community-based studies reporting microvascular or macrovascular complications, glycemic control, multimorbidity, or related clinical outcomes among people with diabetes. Review articles, case reports/series, pilot studies, editorials, opinion articles, and reports with insufficient outcome data were excluded. Owing to substantial heterogeneity in populations, designs, definitions, and outcome reporting, findings were synthesised narratively without statistical pooling. Methodological limitations were appraised across selection, exposure/risk-factor measurement, outcome assessment, confounding, and data-completeness domains.

RESULTS

Twenty studies were included after screening 613 records. The evidence base was predominantly cross-sectional, although large retrospective and prospective cohorts were also represented. Microvascular complications, particularly nephropathy/chronic kidney disease, neuropathy, and retinopathy, were reported more consistently than macrovascular outcomes. Studies that directly assessed both complication categories generally documented an appreciable burden of both small- and large-vessel disease. Across studies, poor glycemic control, longer diabetes duration, hypertension, obesity, dyslipidemia, older age, suboptimal adherence, and irregular follow-up were repeatedly associated with greater complication burden. Most studies were judged to have low-to-moderate methodological concerns, driven mainly by cross-sectional designs, restricted recruitment settings, and incomplete control of confounding.

CONCLUSION

Recent observational evidence indicates a substantial and heterogeneous burden of diabetes-related complications in routine clinical settings. The findings support integrated surveillance of renal, retinal, neurologic, cardiovascular, peripheral vascular, and foot complications alongside sustained glycemic and cardiovascular risk-factor management. Because the included studies were methodologically heterogeneous, the review supports clinical pattern recognition rather than a single pooled prevalence estimate.

KEYWORDS: Diabetes Mellitus, Type 2 Diabetes Mellitus, Diabetic Complications, Microvascular Complications, Macrovascular Complications, Glycemic Control, HbA1c, Clinical Outcomes, Multimorbidity

INTRODUCTION

Diabetes mellitus is a major chronic non-communicable disease and a persistent challenge for general medicine, primary care, and specialist services. Sustained hyperglycemia, together with

coexisting cardiometabolic risk factors, contributes to progressive injury involving the eyes, kidneys, peripheral nerves, heart, brain, and peripheral vasculature.^{1,2,3} The resulting complications account for a substantial share of diabetes-related morbidity, disability, healthcare use, impaired quality of life, and

premature mortality.^{1,4} Diabetes-related complications are commonly classified as microvascular and macrovascular. Microvascular disease includes retinopathy, nephropathy, chronic kidney disease, and peripheral neuropathy, whereas macrovascular disease includes coronary artery disease, cerebrovascular disease, and peripheral arterial disease.³ Diabetic foot disease, infection, impaired wound healing, and multimorbidity add further complexity and often reflect the interaction of neuropathic, vascular, metabolic, and healthcare-related factors. Recent observational studies from diverse healthcare systems have reported considerable variation in complication burden. Studies from Vietnam, Ethiopia, Italy, and India, for example, have documented differing distributions of nephropathy, neuropathy, retinopathy, cardiovascular disease, peripheral vascular disease, and diabetic foot morbidity.^{5,6,7,8} Some complications are already present when type 2 diabetes is first diagnosed, while others accumulate during follow-up, underscoring the importance of early risk assessment and longitudinal surveillance.^{7,9} Across the literature, poor glycemic control, longer disease duration, hypertension, obesity, dyslipidemia, older age, treatment non-adherence, and irregular follow-up recur as factors associated with adverse diabetes outcomes.^{9,10} Multimorbidity is also increasingly recognised as a defining feature of diabetes care rather than an exception, with renal, vascular, neurologic, and cardiometabolic conditions frequently clustering within the same individuals.^{4,11} However, direct comparison across studies is difficult because of differences in study design, population characteristics, healthcare setting, diagnostic criteria, outcome definitions, and methods of glycemic assessment. The objective of this systematic review was therefore to synthesise original studies published from 2019 to 2025 describing patterns of diabetes-related complications and clinical outcomes, with particular emphasis on microvascular and macrovascular disease, glycemic control, multimorbidity, and factors associated with poorer outcomes in general medicine and related routine-care settings.

METHODOLOGY

This systematic review was designed as a qualitative evidence synthesis without meta-analysis because the included studies differed substantially in population characteristics, study design, clinical setting, definitions of complications, and outcome reporting. The manuscript has been structured using PRISMA 2020 reporting principles and the SWiM reporting guideline for synthesis without meta-analysis.^{12,13} Original research studies published from 2020 through

2025 were eligible if they included people with diabetes mellitus and reported one or more of the following: microvascular complications, macrovascular complications, chronic diabetes-related complications, glycemic-control status, multimorbidity, clinical outcomes, or factors associated with adverse outcomes. Eligible designs included cross-sectional, prospective observational, retrospective cohort, prospective cohort, multicenter, hospital-based, community-based, and other routine-care observational studies. Studies were restricted to English-language full-text reports with sufficient methodological and outcome information for qualitative synthesis. Systematic reviews, meta-analyses, narrative or scoping reviews, case reports, case series, pilot studies, editorials, letters, conference abstracts with insufficient data, and opinion articles were excluded. Reports were also excluded when the study population was not clearly defined, relevant diabetes-related outcomes were not reported, data were duplicated, or the available report did not contain sufficient information for extraction. A structured literature search was undertaken in PubMed, Web of Science, and Scopus. The search covered studies published from January 2019 through 2025. The source review reports the use of Boolean combinations of the following concepts: —type 2 diabetes mellitus,| —diabeti complications,| —microvascular complications,| —macrovascular complications,| —diabetic nephropathy,| —diabeti neuropathy,| —diabetic retinopathy —cardiovascular complications,| —clinical outcomes, —glycemic control,| and —HbA1c. The search identified 613 records: 241 from PubMed, 172 from Web of Science, and 200 from Scopus. Study selection proceeded sequentially. Titles and abstracts were screened to remove clearly irrelevant records, after which potentially eligible reports underwent full-text assessment against the prespecified inclusion and exclusion criteria. Of 613 records identified, 103 were removed before screening, 410 were excluded during title/abstract screening, 8 reports could not be retrieved, and 72 full-text reports were excluded, leaving 20 studies for qualitative synthesis (Figure 1). A structured extraction form was used to record author and year, country or region, study design, sample size, diabetes population, clinical setting, study focus, reported microvascular and macrovascular complications, dominant complication patterns, glycemic-control findings, clinical outcomes, and factors associated with poorer outcomes. The principal outcomes of interest were nephropathy/chronic kidney disease, neuropathy, retinopathy, albuminuria, cardiovascular disease, coronary artery disease, stroke/cerebrovascular disease, peripheral vascular or

arterial disease, diabetic foot complications, glycemic-control status, multimorbidity, healthcare burden, and clinically relevant associated factors. The source review used a qualitative domain-based appraisal informed by Joanna Briggs Institute (JBI) and Newcastle–Ottawa Scale concepts.^{14,15} The recorded domains were participant selection, measurement of exposures or risk factors, outcome assessment, control of confounding, and completeness of data. Each study was categorised as having low, moderate, or low-to-moderate overall concern based on the pattern of domain-level judgments. Because the source extraction did not preserve design-specific item-by-item JBI or NOS scoring, these ratings are presented as an author-defined qualitative appraisal rather than as validated JBI/NOS summary scores. Meta-analysis was not undertaken because outcome definitions, study designs, populations, clinical settings, and reporting metrics were too heterogeneous for defensible statistical pooling. Studies were therefore grouped and compared descriptively by design and setting, complication pattern, glycemic-control findings, associated factors, and reported clinical outcomes. Particular emphasis was placed on recurrent patterns across independent settings rather than on deriving a single pooled prevalence estimate.

RESULTS

Twenty original studies published between 2020 and 2025 were included. The studies represented Asia, Africa, the Middle East, Europe, North America, and South America and included outpatient, primary-care, hospital, referral-centre, community, multicenter, integrated-health-system, and electronic-medical-record settings. Cross-sectional and other observational designs predominated, although the evidence base also included long-term retrospective and prospective cohorts. Sample sizes ranged from 140 participants in smaller hospital-based studies to 496,408 patients in a large electronic-medical-record network analysis. Table 1 summarises the included studies.

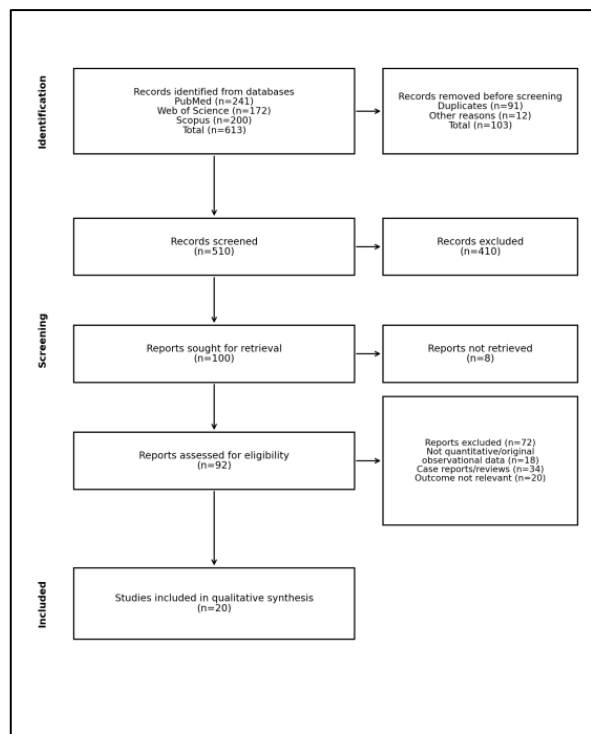


Figure 1: PRISMA-Style Flow Diagram of Study Identification and Selection.

Table 1: Characteristics of Included Studies

Author & Year	Country /Region	Study Design	Sample Size	Diabetes Type/Population	Study Setting	Main Focus
Nguyen et al., 2020 (5)	Vietnam	Observational, non-interventional cross-sectional study	1,631	Type 2 diabetes mellitus	Hospital outpatient diabetes care	Diabetes management, glycemic control, and complications
Sheleme et al., 2020 (6)	Ethiopia	Prospective observational study	400	Diabetes mellitus patients	Mettu Karl Referral Hospital ambulatory clinic	Prevalence, pattern, and predictors of chronic diabetic complications
Bonora et al., 2020 (7)	Italy	Observational study	160	Newly diagnosed type 2 diabetes	Verona Diabetes Clinic	Chronic complications at diagnosis and related clinical features
Venguidesvarane et al., 2020 (8)	India	Hospital-based cross-sectional study	390	Type 2 diabetes mellitus	Rural health and training centre	Microvascular and macrovascular complications and related factors
An et al., 2021 (11)	United States	Retrospective cohort study	135,199	Newly diagnosed type 2 diabetes	Integrated healthcare system	Fifteen-year prevalence and incidence of microvascular and macrovascular complications
Seid et al., 2021(16)	Ethiopia	Cross-sectional study	200	Type 2 diabetes mellitus	Dessie town hospitals	Microvascular complications and predictors among T2DM patients
Hafidh et al., 2022(17)	Middle East and Africa	Baseline cross-sectional analysis of a prospective observational cohort	3,525	Type 2 diabetes starting second-line therapy	Multicountry DISCOVER study	Vascular complications and associated risk factors
Alnaim et al., 2023 (18)	Saudi Arabia	Retrospective cross-sectional study	935	Type 2 diabetes mellitus	Diabetes clinics, National Guard hospitals	Prevalence of microvascular complications
Ewid et al., 2023 (19)	Saudi Arabia	Cross-sectional descriptive study	200	Type 2 diabetes mellitus	Al-Qassim region	Glycemic control and diabetic complications
Dweib et al., 2023 (20)	Palestine	Cross-sectional study	882	Adults with diabetes mellitus	Primary healthcare centres, West Bank	Diabetes-related microvascular complications in primary care
Russo et al., 2023 (21)	Argentina	Observational cross-sectional study	150,725 affiliates ; 12,832 with diabetes	Adults with diabetes	Outpatient/private health system	Diabetes prevalence, epidemiology, comorbidities, and vascular complications
Zhang et al., 2023 (22)	China	Network-based observational study using electronic medical records	496,408	People with type 2 diabetes	Electronic medical records from 35 hospitals in Shanghai	Multimorbidity patterns in T2DM
Shillah et al., 2024 (23)	Tanzania	Cross-sectional analytical hospital-based study	140	Type 2 diabetes mellitus	Singida and Dodoma regional referral hospitals	Predictors of microvascular complications
Merid et al., 2024 (24)	Ethiopia	Institution-based cross-sectional study	378	Type 2 diabetes mellitus	Southern Ethiopia	Microvascular complications and associated factors
Negussie et al., 2024 (25)	Ethiopia	Institution-based cross-sectional study	381	Adult type 2 diabetes patients	Adama, central Ethiopia	Microvascular complications among adults with T2DM
Solela et al., 2024 (26)	Ethiopia	Retrospective study	140	Type 2 diabetes mellitus	Teaching hospital, Addis Ababa	Patterns and determinants of vascular complications
El Aameri et al., 2024 (27)	Morocco	Cross-sectional study	300	Type 2 diabetes mellitus	Clinical/biological assessment setting	Chronic diabetic complications and associated factors
Alrubaiee, 2025(28)	Yemen	Cross-sectional study	222	Follow-up diabetic patients	National Diabetic Referral Centre, Sana'a	Chronic diabetic complications and risk factors
Sreedevi et al., 2025 (29)	India	Observational study	300	Type 2 diabetes mellitus	Clinical/community diabetic population	Prevalence and determinants of neuropathy, retinopathy, and peripheral arterial disease
De Zoysa et al., 2025 (30)	Sri Lanka	Multicenter hospital-based cross-sectional study	2,013	Type 2 diabetes mellitus	Seven tertiary care hospitals	Glycemic control and demographic/behavioral factors linked to clinical outcomes

Across the included evidence, microvascular complications were reported more consistently than macrovascular outcomes. Nephropathy/chronic kidney disease, neuropathy, and retinopathy were the most recurrent microvascular conditions, while cardiovascular disease, cerebrovascular disease, peripheral vascular/arterial disease, and diabetic foot complications represented the main macrovascular or mixed clinical outcomes. Importantly —more frequently reported— does not necessarily indicate a higher pooled prevalence because not all studies assessed both complication categories using comparable methods. Where both categories were directly evaluated, an appreciable burden of microvascular and macrovascular disease was evident. Venguidesvarane et al. reported microvascular complications in 52.1% and macrovascular complications in 29.7% of a rural Indian sample.⁸ In

the DISCOVER Middle East and Africa cohort, crude prevalence was 17.7% for microvascular and 10.7% for macrovascular complications among 3,525 patients initiating second-line therapy.¹³ In the US retrospective cohort, chronic kidney disease was the most prevalent complication at diagnosis (12.3%), and new complications accumulated over long-term follow-up.¹¹ Several studies also demonstrated substantial complication burden within primary or referral care. Dweib et al. reported at least one microvascular complication in 34.4% of 882 participants in the West Bank, while studies from Tanzania, Ethiopia, Morocco, and Yemen documented varying but clinically meaningful prevalences of retinopathy, neuropathy, nephropathy, and chronic complications.^{16,19,20,21,22,23,24} Table 2 summarises study-level complication patterns.

Table 2: Patterns of Diabetes-Related Complications Reported In Included Studies

Author & Year	Microvascular Complications Reported	Macrovascular / Other Complications Reported	Most Common / Main Reported Pattern	Key Finding
Nguyen et al., 2020 (5)	Retinopathy, nephropathy, neuropathy	Cardiovascular and other diabetes-related complications	Mixed diabetic complications	The study described glycemic control and diabetes-related complications among Vietnamese patients with type 2 diabetes.
Sheleme et al., 2020 (6)	Retinopathy, neuropathy, nephropathy	Cardiovascular disease and diabetic foot-related complications	Chronic diabetic complications	Nearly two-fifths of patients had chronic complications, with poor glycemic control and hypertension contributing to higher risk.
Bonora et al., 2020 (7)	Neuropathy, retinopathy, albuminuria, chronic kidney disease	Cardiovascular disease	Complications already present at diagnosis	Chronic complications were observed even among newly diagnosed type 2 diabetes patients, showing the need for early screening.
Venguidesvarane et al., 2020 (8)	Neuropathy, nephropathy, retinopathy	Coronary artery disease and peripheral vascular disease	Microvascular complications were more frequent	Microvascular complications were reported in 52.1%, while macrovascular complications were found in 29.7% of patients.
An et al., 2021 (11)	Chronic kidney disease, retinopathy, neuropathy	Cardiovascular disease, cerebrovascular disease, peripheral vascular disease	Chronic kidney disease was prominent	At diagnosis, chronic kidney disease was the most prevalent complication (12.3%); incident complications accumulated during follow-up.
Seid et al., 2021(16)	Retinopathy, neuropathy, nephropathy	Not the main focus	Microvascular complications	The study focused on microvascular complications and showed that these complications remained common among type 2 diabetes patients.
Hafidh et al., 2022(17)	Neuropathy, nephropathy, retinopathy	Cardiovascular disease, stroke, peripheral arterial disease	Microvascular complications more prevalent than macrovascular complications	In the DISCOVER Middle East/Africa cohort, crude prevalence was 17.7% for microvascular and 10.7% for macrovascular complications.
Alnaim et al., 2023 (18)	Nephropathy, retinopathy, neuropathy	Not the main focus	Nephropathy was the leading complication	Nephropathy was the most commonly reported microvascular complication, followed by retinopathy and neuropathy.
Ewid et al., 2023 (19)	Diabetes related microvascular complications	Diabetes related macrovascular complications	Complications linked with poor glycemic control	Suboptimal glycemic control was an important clinical issue and was associated with diabetes-related complications.

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Dweib et al., 2023 (20)	Retinopathy, neuropathy, nephropathy	Not the main focus	At least one microvascular complication	At least one microvascular complication was reported in 34.4% of participants; retinopathy was the most frequent individual complication.
Russo et al., 2023 (21)	Microvascular complications	Vascular and cardiometabolic complications	Vascular complications with comorbid burden	The study described diabetes prevalence, comorbidities, and vascular complications in a large outpatient population.
Zhang et al., 2023 (22)	Diabetic kidney disease, retinopathy, neuropathy within multimorbidity patterns	Cardiovascular and metabolic comorbidities	Multimorbidity clustering	Large-scale electronic medical records showed multimorbidity clustering among people with type 2 diabetes.
Shillah et al., 2024 (23)	Retinopathy, neuropathy, nephropathy	Not the main focus	Retinopathy was the most frequent microvascular complication	Microvascular complications were present in 57.6% of patients, with retinopathy being the most common reported complication.
Merid et al., 2024 (24)	Neuropathy, nephropathy, retinopathy	Not the main focus	Neuropathy was the leading complication	Microvascular complications were found in 26.5% of patients; neuropathy was most common, followed by nephropathy and retinopathy.
Negussie et al., 2024 (25)	Neuropathy, retinopathy, nephropathy	Not the main focus	Microvascular complications	More than one-fifth of adults with type 2 diabetes had microvascular complications, mainly related to poor glycemic control and hypertension.
Solela et al., 2024 (26)	Neuropathy, nephropathy, retinopathy	Coronary artery disease and other vascular complications	Both microvascular and macrovascular complications	Overall vascular complications were reported in 39%; microvascular complications were 23.5% and macrovascular complications were 21%.
El Aameri et al., 2024 (27)	Retinopathy, nephropathy, neuropathy	Cardiovascular disease	Combined chronic complications	The study assessed chronic complications among Moroccan type 2 diabetes patients and emphasised both microvascular and cardiovascular involvement.
Alrubaiee, 2025(28)	Nephropathy, retinopathy, neuropathy	Diabetic foot and other chronic complications	High overall complication burden	Chronic diabetic complications were reported in 62.6% of patients; non-adherence, obesity, uncontrolled hypertension, and irregular follow-up were major risk factors.
Sreedevi et al., 2025 (29)	Peripheral neuropathy, diabetic retinopathy	Peripheral arterial disease	Peripheral neuropathy and peripheral arterial disease were common	Peripheral neuropathy, diabetic retinopathy, and peripheral arterial disease were common, showing a combined microvascular and peripheral vascular burden.
De Zoysa et al., 2025 (30)	Complications considered in relation to glycemic control	Clinical outcomes related to diabetes control	Glycemic control-related outcome pattern	The study highlighted behavioural and demographic factors associated with optimal glycemic control among type 2 diabetes patients.

Poor glycemic control was the most consistent modifiable factor associated with complication burden. Across studies, higher or uncontrolled HbA1c, longer diabetes duration, hypertension, obesity, dyslipidemia, older age, suboptimal treatment adherence, and irregular clinical follow-up recurred as factors associated with adverse outcomes. Because most included studies were cross-sectional, these factors are described primarily as associations rather than causal predictors. The outcome spectrum extended beyond

the presence of individual complications. Studies described long-term incident vascular disease, renal impairment, multimorbidity, diabetic foot morbidity, and poorer overall clinical stability among patients with uncontrolled or inadequately monitored diabetes. Large electronic-health-record data also demonstrated complex clustering of cardiometabolic, vascular, renal, and other chronic conditions among people with type 2 diabetes.¹⁸ Table 3 summarises the main clinical outcomes and associated factors.

Table 3: Clinical Outcomes and Factors Associated with Adverse Outcomes

Author & Year	Main Clinical Outcomes Reported	Glycemic Control / HbA1c-Related Findings	Factors associated with adverse outcomes	Overall Interpretation
Nguyen et al., 2020 (5)	Diabetes control status, treatment pattern, and presence of complications	Poor glycemic control was common among patients with type 2 diabetes	Longer diabetes duration, suboptimal treatment adherence, and inadequate metabolic control	Uncontrolled diabetes was associated with a greater burden of diabetes-related complications.
Sheleme et al., 2020 (6)	Chronic diabetic complications and related morbidity	Poor glycemic control increased the likelihood of chronic complications	Hypertension, long disease duration, poor glycemic control, and irregular follow-up	Patients with uncontrolled diabetes and coexisting hypertension were more likely to develop chronic complications.
Bonora et al., 2020 (7)	Chronic complications at the time of diabetes diagnosis	Newly diagnosed patients already showed metabolic and clinical risk burden	Older age, obesity, hypertension, dyslipidemia, and metabolic abnormalities	Complications may begin before formal diagnosis, supporting early screening and risk assessment.
Venguidesvarane et al., 2020 (8)	Microvascular and macrovascular complications	Poor glycemic control was linked with higher complication frequency	Increasing age, longer diabetes duration, hypertension, and poor glucose control	Both microvascular and macrovascular complications were clinically important in rural type 2 diabetes patients.
An et al., 2021 (11)	Long term incidence of microvascular and macrovascular complications	Baseline and follow-up metabolic control influenced complication development	Older age, baseline comorbidities, renal impairment, and duration of diabetes	New complications continued to develop over time, showing the need for long-term surveillance.
Seid et al., 2021 (16)	Microvascular complications among type 2 diabetes patients	Poor glucose control contributed to microvascular disease	Longer duration of diabetes, hypertension, and uncontrolled blood glucose	Microvascular outcomes were associated with chronic exposure to poor metabolic control.
Hafidh et al., 2022 (17)	Vascular complications in patients receiving second-line therapy	Uncontrolled diabetes remained an important background factor	Older age, longer diabetes duration, hypertension, dyslipidemia, and obesity	Patients requiring treatment intensification had a meaningful vascular complication burden.
Alnaim et al., 2023 (18)	Nephropathy, retinopathy, neuropathy, and other microvascular outcomes	Glycemic control was relevant to microvascular complication occurrence	Longer diabetes duration, elevated HbA1c, hypertension, and age	Microvascular complications were common, particularly among patients with poor long-term diabetes control.
Ewid et al., 2023 (19)	Diabetes complications and metabolic control status	Poor HbA1c control was frequently observed	Poor adherence, inadequate glycemic control, obesity, and comorbid disease	Complication risk was greater when diabetes remained uncontrolled or poorly monitored.
Dweib et al., 2023 (20)	Microvascular complications in primary healthcare patients	Glycemic status influenced the occurrence of microvascular outcomes	Older age, longer disease duration, hypertension, and poor diabetes control	Primary care diabetic patients showed substantial microvascular morbidity, requiring routine screening.
Russo et al., 2023 (21)	Vascular complications and comorbid conditions	Diabetes control was evaluated with clinical and epidemiological factors	Older age, cardiovascular risk factors, hypertension, and associated comorbidities	Diabetes was associated with a high cardiometabolic and vascular disease burden.
Zhang et al., 2023 (22)	Multimorbidity patterns among people with type 2 diabetes	Glycemic control contributed to disease clustering but was not the only factor	Age, obesity, hypertension, dyslipidemia, and multiple chronic conditions	Type 2 diabetes frequently occurred with multimorbidity, increasing the complexity of clinical management.
Shillah et al., 2024 (23)	Microvascular complications in hospital-based patients	Poor glycemic control was linked to microvascular complications	Older age, long duration of diabetes, hypertension, and poor glucose control	Retinopathy and other microvascular outcomes were important indicators of disease progression.
Merid et al., 2024 (24)	Neuropathy, nephropathy, and retinopathy	Inadequate glycemic control increased microvascular risk	Long diabetes duration, hypertension, poor glycemic control, and treatment-related factors	Microvascular disease remained a major outcome among type 2 diabetes patients in Southern Ethiopia.
Negussie et al., 2024 (25)	Microvascular complications among adults with type 2 diabetes	Poor glucose control was associated with higher complication risk	Hypertension, uncontrolled diabetes, older age, and longer disease duration	The study emphasised the importance of early identification of high-risk patients.

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Solela et al., 2024 (26)	Overall vascular complications, including microvascular and macrovascular disease	Glycemic status contributed to vascular risk	Age, hypertension, diabetes duration, lipid abnormality, and poor glycemic control	Both small-vessel and large-vessel complications contributed to the overall outcome burden.
El Aameri et al., 2024 (27)	Chronic complications and associated clinical factors	Poor control was related to chronic complication development	Longer diabetes duration, hypertension, obesity, and poor metabolic control	Chronic complications were common and reflected delayed control of modifiable risk factors.
Alrubaiee, 2025(28)	Chronic complications, diabetic foot, and follow-up-related outcomes	Uncontrolled diabetes increased chronic complication risk	Non-adherence, obesity, uncontrolled hypertension, irregular follow-up, and poor glucose control	Complications were frequent among patients with poor adherence and inadequate disease monitoring.
Sreedevi et al., 2025 (29)	Neuropathy, retinopathy, and peripheral arterial disease	Glycemic control was relevant to complication development	Age, diabetes duration, hypertension, poor glycemic control, and vascular risk factors	The study showed combined microvascular and peripheral vascular disease burden among type 2 diabetes patients.
De Zoysa et al., 2025 (30)	Optimal glycemic control and related clinical outcomes	Optimal glycemic control was associated with behavioural and demographic factors	Lifestyle behaviour, demographic profile, treatment adherence, and clinical monitoring	Better glycemic control was linked with modifiable behavioural and healthcare-related factors.

Most included studies were categorised as having low, low-to-moderate, or moderate methodological. Common strengths included clearly described clinical populations, direct clinical or record-based outcome ascertainment, and, in several studies, large samples or multicenter recruitment. Recurrent limitations

included cross-sectional design, single-centre or referral-centre sampling, limited temporal information, incomplete adjustment for confounding, and inconsistent reporting of glycemic-control or complication-screening methods.

Table 4: Domain-Based Methodological Appraisal of Included Studies

Author & Year	Selection Bias	Measurement of Exposure / Risk Factors	Outcome Assessment	Control of Confounding	Completeness of Data	Overall Risk of Bias	Main Reason for Judgment
Nguyen et al., 2020 (5)	Low	Low	Low	Moderate	Low	Low to Moderate	Large sample and clear clinical assessment, but observational design limited causal interpretation.
Sheleme et al., 2020 (6)	Moderate	Low	Low	Moderate	Moderate	Moderate	Prospective design was useful, but some confounding factors may not have been fully controlled.
Bonora et al., 2020 (7)	Low	Low	Low	Low	Low	Low	Newly diagnosed diabetic patients were systematically assessed with good reporting of clinical features.
Venguidesvarane et al., 2020 (8)	Moderate	Low	Low	Moderate	Low	Moderate	Hospital/rural health-centre recruitment may limit generalizability, although complication assessment was clearly reported.
An et al., 2021 (11)	Low	Low	Low	Low	Low	Low	Large retrospective cohort with long follow-up and clear reporting of microvascular and macrovascular outcomes.
Seid et al., 2021(16)	Moderate	Low	Low	Moderate	Moderate	Moderate	Cross-sectional design restricted temporality, and residual confounding remained possible.
Hafidh et al., 2022(17)	Low	Low	Low	Low	Low	Low	Multicountry prospective cohort design strengthened external validity and complication reporting.

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Alnaim et al., 2023 (18)	Moderate	Low	Low	Moderate	Low	Moderate	Retrospective cross-sectional design was appropriate for prevalence estimation but limited causal inference.
Ewid et al., 2023 (19)	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Descriptive design and modest sample size increased the possibility of selection and confounding bias.
Dweib et al., 2023 (20)	Moderate	Low	Low	Moderate	Low	Moderate	Primary-care-based design improved relevance, but cross-sectional data limited interpretation of predictors.
Russo et al., 2023 (21)	Low	Low	Low	Moderate	Low	Low to Moderate	Very large population improved precision, but observational design and database-based assessment may have introduced residual confounding.
Zhang et al., 2023 (22)	Low	Low	Low	Moderate	Low	Low to Moderate	Network-based analysis provided broad multimorbidity information, but clinical detail for individual complications may have varied.
Shillah et al., 2024 (23)	Moderate	Low	Low	Moderate	Low	Moderate	Hospital-based cross-sectional design may have overrepresented patients with more advanced disease.
Merid et al., 2024 (24)	Moderate	Low	Low	Moderate	Low	Moderate	Institution-based design and cross-sectional analysis limited generalizability and temporal conclusions.
Negussie et al., 2024 (25)	Moderate	Low	Low	Moderate	Low	Moderate	Adequate complication assessment was reported, but selection from a limited geographic area may reduce external validity.
Solela et al., 2024 (26)	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Retrospective records may have incomplete information on exposures, follow-up, and confounders.
El Aameri et al., 2024 (27)	Moderate	Low	Low	Moderate	Low	Moderate	Cross-sectional design was suitable for estimating chronic complications but could not establish direction of association.
Alrubaiee, 2025(28)	Moderate	Low	Low	Moderate	Low	Moderate	Referral-center sampling may have included patients with more severe disease, affecting representativeness.
Sreedevi et al., 2025 (29)	Moderate	Low	Low	Moderate	Low	Moderate	Community screening improved detection, but observational design limited causal interpretation of determinants.
De Zoysa et al., 2025 (30)	Low	Low	Low	Moderate	Low	Low to Moderate	Multicenter design and large sample strengthened reliability, although residual confounding could not be excluded.

DISCUSSION

This systematic review synthesises recent observational evidence showing that diabetes-related complications remain common across general medicine and routine-care settings. The most persistent pattern was the repeated documentation of microvascular disease particularly nephropathy/chronic kidney disease, neuropathy, and retinopathy alongside clinically important macrovascular and peripheral vascular outcomes. The evidence also indicates that complications frequently coexist, supporting a multisystem rather than organ-isolated view of diabetes morbidity. The review should not be interpreted as demonstrating a universal prevalence hierarchy between microvascular and macrovascular complications. Studies differed substantially in which complications they actively screened for, how outcomes were defined, and whether ascertainment relied on clinical examination, laboratory data, patient records, or administrative coding. Among studies that evaluated both categories, microvascular complications were often numerically more common, while macrovascular disease remained a major source of morbidity and long-term risk. Poor glycemic control was the most recurrent modifiable correlate of complication burden. This finding is consistent with external evidence showing that inadequate glycemic control is common in type 2 diabetes and is associated with a broad range of clinical and behavioural factors.^{31,32} The reviewed studies also repeatedly implicated hypertension, obesity, dyslipidemia, and longer diabetes duration, emphasising that complication prevention depends on comprehensive cardiometabolic risk management rather than glucose control alone. The temporal dimension is also clinically important. The large US cohort demonstrated that a substantial proportion of patients already had complications at the time of type 2 diabetes diagnosis and that new complications developed within only a few years.¹¹ Similarly, Bonora et al. documented chronic complications among newly diagnosed patients.⁷ These findings support early screening at diagnosis and sustained surveillance thereafter. Diabetes-related complications rarely occur in isolation. Large-scale network data and clinical cohorts demonstrate clustering of kidney disease, neuropathy, retinopathy, cardiovascular disease, hypertension, obesity, dyslipidemia, and peripheral vascular disease.^{18,33,34,35} Pető et al. reported relationships between distal sensorimotor polyneuropathy and age, HbA1c, albuminuria, retinopathy, and cardiovascular complications (), while Roostaei et al. described interrelationships among neuropathy, retinopathy, and nephropathy.^{33,34} These patterns support integrated risk stratification and

coordinated care pathways rather than sequential, organ-specific management. Peripheral arterial disease and diabetic foot morbidity were less consistently reported than nephropathy, neuropathy, and retinopathy, but they remain clinically consequential. External evidence indicates that at-risk diabetic foot status is associated with higher all-cause and cardiovascular mortality, and that deep or infected diabetes-related foot ulcers are associated with increased major adverse cardiovascular-event risk.^{36,37} Neuropathy may be present early in type 2 diabetes and can contribute to loss of protective sensation, ulceration, infection, and disability.³⁸ These findings reinforce the value of routine foot examination, neuropathy assessment, vascular evaluation, and prompt management of high-risk lesions. The synthesis supports a pragmatic, integrated surveillance model in which glycemic assessment is combined with periodic renal, retinal, neurologic, cardiovascular, peripheral vascular, and foot evaluation. Blood-pressure management, lipid control, weight management, medication adherence, smoking-risk reduction where relevant, and regular follow-up should be considered alongside glucose-lowering therapy. The evidence also supports multidisciplinary coordination across primary care, internal medicine, endocrinology, nephrology, ophthalmology, cardiology, vascular/foot services, diabetes education, and other disciplines according to the patient's risk profile. Future studies should use standardised definitions for microvascular and macrovascular outcomes, report complication-screening methods explicitly, provide comparable HbA1c and cardiometabolic-risk data, and distinguish prevalent from incident complications. Prospective multicenter cohorts are particularly important for establishing temporality and quantifying progression. Future systematic reviews would benefit from protocol registration, reproducible database-specific search strategies, independent duplicate screening and extraction, design-specific risk-of-bias tools, and meta-analysis where clinically and methodologically appropriate.

LIMITATIONS

Several limitations require consideration. Most included studies were observational, and many were cross-sectional, limiting temporal and causal inference. Study populations, screening practices, diagnostic definitions, HbA1c thresholds, and outcome measures were heterogeneous, precluding defensible meta-analysis and direct prevalence comparison. Many studies used hospital or referral-centre samples, which may overrepresent patients with more advanced disease. Residual confounding was common, and the

source review used a qualitative composite appraisal rather than consistently applying design-specific risk-of-bias tools item by item. No formal certainty-of-evidence framework was applied, so conclusions should be interpreted as a structured qualitative synthesis rather than a graded estimate of effect or prevalence.

CONCLUSIONS

Diabetes-related complications remain a substantial and heterogeneous clinical burden in general medicine and routine-care settings. Nephropathy/chronic kidney disease, neuropathy, and retinopathy were the most consistently reported microvascular complications, while cardiovascular disease, cerebrovascular disease, peripheral vascular disease, and diabetic foot morbidity contributed important macrovascular and mixed outcomes. Poor glycemic control, longer diabetes duration, hypertension, obesity, dyslipidemia, older age, suboptimal adherence, and irregular follow-up were recurrently associated with greater complication burden. The evidence supports early and repeated multisystem screening together with sustained control of modifiable metabolic and cardiovascular risk factors. Because of marked heterogeneity across the included studies, these findings should guide clinical pattern recognition and risk-based surveillance rather than be interpreted as a single pooled estimate of complication prevalence.

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The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.



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