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Prevalence of nephropathy among diabetic patients in North American region

A systematic review and meta-analysis

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Abstract

Background: Nephropathy is one of the most common microvascular impediments of diabetes mellitus. In this study, we aimed to estimate the prevalence of nephropathy in diabetic patients across the North American region.

Methods: Eligible studies were screened out from 3 electronic databases, for example, PubMed, Google Scholar, and ScienceDirect using specific search keywords based on the eligibility criteria. Extracting the data from the included studies publication bias, quality assessment, outlier investigation, and meta-analysis was done followed by the subgroup analysis. A total of 11 studies met the study inclusion criteria. Meta-analysis was performed with the extracted data.

Results: Pooled prevalence of 28.2% (95% confidence interval [CI]: 19.7–36.7) with a high rate of heterogeneity (I^2 = 100%) was identified. The pooled prevalence of nephropathy among diabetic patients in the United States of America, Canada, and Mexico was 24.2% (95% CI: 13.8–34.5), 31.2% (95% CI: 25.8–36.5), and 31.1% (95% CI: 20.8–41.5), respectively.

Conclusion: The prevalence of nephropathy among diabetic patients was found lower in the United States of America as compared to Canada and Mexico. Besides, the pooled prevalence of the North American region was found to be lower as compared to the African, European, and Asian regions. Minimizing the pathogenic factors, sufficient diagnostic, healthcare facilities, and awareness are recommended to improve the situation.

Abbreviations: CI = confidence interval, CKD = chronic kidney disease, DM = diabetes mellitus, ESRD = end-stage renal disease, USA = United States of America.

Keywords: diabetes, epidemiology, frequency, kidney, nephropathy

1. Introduction

Diabetes mellitus (DM), commonly known as diabetes refers to a group of chronic systemic noncommunicable diseases characterized by abnormally high blood glucose levels termed as hyperglycemia caused due to the resistance and lack of insulin production, or uncontrolled glucagon secretion.[1–3] Being one of the top 10 causes of global mortality, diabetes has turned into a global epidemic and a massive threat to public health with an estimated number of 451 million adult patients worldwide in 2017 which may rise to 693 million by 2045 if no worthwhile preventive actions are taken immediately.[4,5] According

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The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The research included data from online sources; no human subjects, human data, tissue, or animals were used. Hence ethical approval was not required from the ethical committee.

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Key points

- The overall pooled prevalence of nephropathy among diabetes patients in the United States of America, Canada, and Mexico is 28.2%, with higher rates in Canada and Mexico than in the United States of America.
- To lower the prevalence of nephropathy, public awareness, proper management practices, and advanced healthcare facilities are necessary.

to National Diabetes Statistics Report, 2022, more than 37 million United States adults are currently living with diabetes and 1 in every 5 of them are unaware of having it.[6] Diabetes is the eighth leading cause of mortality and the leading cause of end-stage renal disease (ESRD) and renal failure, lower-limb amputations, and adult blindness in the United States of America (USA).[7]

Type 1 and type 2 are the 2 most common types of DM although some other categories including maturity-onset diabetes of the young, gestational diabetes mellitus, neonatal diabetes, and secondary diabetes resulting from endocrine disease or hereditary diseases or medications such as corticosteroids, thiazide diuretics, beta-blockers, antipsychotics, statins, etc.[8–10] Type 1 DM, also known as juvenile diabetes or insulin-dependent diabetes mellitus is caused due to insulin deficiency resulting from the death of pancreatic beta-cells and type 2 DM or non-insulin-dependent diabetes mellitus, which is far more prevalent, is largely the result of gradually poor glucose regulation caused by a combination of malfunctioning pancreatic beta cells and insulin resistance.[11,12] Type 1 DM is expected to afflict children and adolescents, but type 2 DM is thought to affect middle-aged and older individuals who have chronic hyperglycemia as a result of poor lifestyle and nutritional factors.[13,14] Persistent hyperglycemia due to type 1 and type 2 DM affects the vascular system and induces diabetic vascular complications including microvascular complications such as diabetic nephropathy, neuropathy, and retinopathy as well as macrovascular complications such as ischemic heart disease, coronary artery disease, peripheral vascular disease, and cerebrovascular disease leading to organ damage and failure in approximately one third to one-half of people living with diabetes.[15–17]

Nephropathy is a serious consequence of DM that has a substantial impact on communities worldwide.[18] It is a disorder characterized by chronic albuminuria, decline in glomerular filtration rate, and elevated arterial blood pressure leading to progressive decline of kidney function and increased cardiovascular morbidity and mortality among 20% to 40% of people with type 1 and type 2 DM.[19–21] The occurrence of nephropathy has increased along with the prevalence of diabetes.[22] The association between hemodynamic and metabolic pathways, that are commonly disrupted in the setting of diabetes, are likely to have a role in the initiation and progression of nephropathy.[23] Nephropathy is a significant microvascular consequence of diabetes along with a high prevalence, mortality, and treatment expense, yet it is poorly understood and treated. The primary cause of the problem is a lack of early detection and effective treatment therapy and strategy.[24] Also, the pathophysiological development of nephropathy is significantly influenced by poor glycemic management, hyperlipidemia, smoking, oxidative stress, accumulation of advanced glycation end products, and environmental, genetic, and epigenetic variables.[25] Effective measures to reduce the risks of nephropathy or to slow down the progression include proper monitoring and control of blood glucose levels and hypertension either by doing physical exercise and maintaining a healthy diet and lifestyle or by taking blood glucose-lowering agents for glycemic control and antihypertensive drugs.[26]

Nephropathy among diabetic patients is the leading cause of dialysis in many nations, including, Western regions, Asians, and Caucasians.[17] Diabetic complications, particularly renal disease, significantly raise the chance of severe illness and death among diabetic patients. The number of cases of nephropathy in diabetic patients continues to rise significantly along with its associated mortality and cardiovascular consequences.[27] Diabetes-associated nephropathy, the primary cause of chronic kidney disease has been found to be increased in overall Europe and countries of the other continents such as Japan and Nigeria as well.[28,29] Nephropathy-associated end-stage renal failure poses a significant health problem for the people living with diabetes besides their families and healthcare systems in both high and middle-income nations due to the uprising prevalence of diabetes worldwide.[23]

The epidemiology of nephropathy among diabetic patients has not yet been well examined, and its variance has not yet been described, limiting our capacity to recognize its severity and characteristics. To properly understand the disease burden and establish further research ambitions, it is essential to first study the prevalence of nephropathy in diabetic patients. This systematic review and meta-analysis targeted to investigate the pooled and individual prevalence of nephropathy among diabetic patients within 3 major North American countries, that is, the USA, Canada, and Mexico.

2. Materials and methods

2.1. Study guideline, screening and inclusion criteria

This systematic review and meta-analysis were targeted to determine the prevalence of nephropathy among diabetes patients residing in the North American region. We maintained the PRISMA guideline for this study.[30–32] Only the original articles that are published in peer-reviewed journals and completely relevant to the prevalence, frequency, or incidence of nephropathy among diabetes patients in North American countries were decided to be selected for inclusion. Comprehensive/narrative review, systematic review, mini-reviews, meta-analyses, book chapters, editorials, correspondence, short communications, press releases, blogs, news, conference info, website data, or any content other than the peer-reviewed original articles regarding the study topic were decided to be screened out as ineligible contents. Only the English-language-written articles were considered eligible and thus included in this systematic review and meta-analysis.

2.2. Literature search strategy

As the sole purpose of this systematic review and meta-analysis is to find out the pooled prevalence of nephropathy among North American diabetes patients, relevant search keywords, for example, "prevalence," "frequency," "diabetes," "nephropathy," "kidney" were searched along with selected study types, for example, "case–control," "cohort," "cross-sectional" and names of the North American countries, for example, "USA', "Canada" and "Mexico" in 3 electronic databases, Google Scholar, ScienceDirect, and PubMed. The keywords were adjusted by using appropriate Boolean operators during searches in the databases. Studies were searched in advanced search options by applying "Title and abstract" as well as "Title, abstract or author-specified keywords" filters in PubMed and ScienceDirect respectively whereas the term "allintitle" was used prior to the search keywords during searches in Google Scholar. Year restriction was not applied during searches in any database. Duplicate content generated due to searches in different databases was checked and managed using EndNote software.

2.3. Study selection and quality assessment

Pooled search contents were screened thoroughly by title, abstract, and full-text evaluation to find out the eligible studies based on the inclusion criteria. To ensure and justify the quality of the included studies, among the studies we searched the answers to a set of different questions selected from the Study Quality Assessment Tools, National Institutes of Health, and Systematic Reviews: Step 6: Assess Quality of Included Studies, University of North Carolina.[33,34] For this systematic review and meta-analysis, 10 different questions were selected which could be answered in Yes, No, Unclear, Not Reported, or Not Applicable. Later, these answers were converted into numerical scores, that is, 1 for the answer Yes, 0 for No and Unclear answers, and no score for Not Reported and Not Applicable, and then the scores were summed up to obtain the overall score for an individual study. The overall score thus obtained was divided by the number of questions applied for that particular study and then converted into a percentage value which determines the quality as well as the validity of that included study. Studies are classified as high-scoring, moderate-scoring, and low-scoring if the obtained overall score is ≥80%, 60% to 70% and ≤50%, respectively following the previous study.[35]

2.4. Data extraction and analysis

Major characteristics dataset included information about the included studies, for example, study ID, study location and study type, demographics of the participants, for example, number of total participants, percentages of male and female participants, participants' average age as well as body mass index, and different methods used for diabetes and nephropathy measurement after extracting the data from each of the included studies respectively. The study ID consisted of the last name of the primary author and the publication year of any respective study. In case of unresolved discrepancy or lack of clarification, the corresponding author of that study was contacted for clarification and additional data. Data were collected solely from the included peer-reviewed published articles without the involvement of patients, healthcare institutions, or third parties in any aspect.

RStudio software (version 4.3.0) and the "metafor" package (version 4.2-0) of R software was used by the authors to perform meta-analysis. Pooled prevalence was analyzed using a random-effects model with 95% confidence intervals (CIs) method and heterogeneity of the included studies was determined by using I^2 statistics. Values of I^2 represented the levels of heterogeneity, for example, values ranging from 25% to 50% indicated a low degree of heterogeneity, 51% to 75% indicated moderate heterogeneity, and more than 75% indicated a high degree of heterogeneity.

2.5. Publication bias and sensitivity analysis

Potential sources of publication bias were determined by assessing the quality of the included studies. High-scoring studies have a low risk of bias whereas the low-scoring studies are more prone to publication bias and subsequent asymmetry. Besides quality assessment, a funnel plot, a Galbraith plot and a radial plot were constructed by the authors using RStudio software (version 4.3.0) and the "metafor" package (version 4.2-0) of R to facilitate visual identification and confirmation of the studies with plausible publication bias as outliers. The impact of the heterogeneity of each outlier study on the overall effect size was assessed by conducting a sensitivity analysis. This analysis was performed following our previous study by excluding the plausible outlier study and replicating the analysis using both the random and fixed-effects model respectively.[36,37]

3. Results

3.1. Search outcomes and inclusion of studies

Initially, a total of 229 search contents were found from the 3 electronic databases (Google Scholar: 45, ScienceDirect: 71, and PubMed: 113) based on the combinations of search keywords, different filters, and search strategies applied in the database searching. Two hundred one studies were directly excluded as ineligible since they did not match the eligibility criteria of this study. The remaining 28 full-length peer-reviewed studies proceeded to the eligibility assessment step. After excluding 2 studies due to duplication, 26 studies were carefully evaluated to screen out the eligible studies. After rigorous evaluation and validation, 15 studies were eliminated due to not fulfilling the inclusion criteria stated in 2.1 leaving 11 studies that were decided to be included in this study by the authors (Fig. 1). Initial database searching, study screening, eligibility assessment, study evaluation, and final inclusion—each step was carefully performed and validated by the authors according to the procedure described in section 2.3.

3.2. Quality appraisement

To assess the quality of the selected studies, each study was asked a set of 10 different questions and scored accordingly (Table 1). Among the 11 included studies, 10 scored ≥80% and passed as high-quality studies whereas Bello-Chavolla 2017 scored 70% and identified as moderate quality study.[38] Zenteno-Castillo 2015 and Bai 2007 had the maximum and minimum scores of 100% and 80% whereas the other 8 high-quality studies equally scored 90%[39,40] (Table 1).

3.3. Study characteristics

Among the 11 studies that were identified as eligible for this study, 5 were from USA[41–45] and 3 from both Canada[40,46,47] and Mexico.[38,39,48] The included studies were mainly of 2 types: cohort (4 studies) and cross-sectional (7 studies). The total number of participants, and their demographics including the numbers of male and female, age as well as body mass index of the participants was investigated. Besides, the diabetes and nephropathy measurement tools that were used by the studies were mentioned in detail in Table 2.

3.4. Outcomes of meta-analysis

A total of 1411,706 diabetes patients from 11 studies were found in this study among whom 225,921 patients reported nephropathy. Five studies were conducted in the USA which comprised the largest study population of 1,144,762 (about 81.1% of the total population) whereas the 3 studies conducted in Mexico included the least number of study population of 546 diabetes patients (about 0.038% of the total study population). The remaining 3 studies which were conducted in Canada included 266,398 diabetes patients which comprised about 18.87% of the total study population. The overall pooled prevalence of nephropathy among diabetes patients is 28.2% with 95% CI of 19.7 to 36.7. The highest prevalence of 63.1% (95% CI: 60.6–65.6) was reported in Yu 2015 whereas both Fried 2023 and Sauder 2019 reported the lowest prevalence of <4.0% with 95% CI of 3.6 to 3.7 and 2.9 to 5.0, respectively. Hundred percent heterogeneity was found among the included studies in I^2 statistics with a 95% CI of 2.9 to 65.6 and a P-value of zero. Subgroup analysis in this study comprised the individual pooled prevalence of nephropathy among diabetes patients in the USA, Canada, and Mexico. The highest pooled prevalence of approximately 31.1% was reported in both Canada and Mexico with a 95% CI of 25.8 to 36.5 and 20.8 to 41.5, respectively, whereas the lowest pooled prevalence

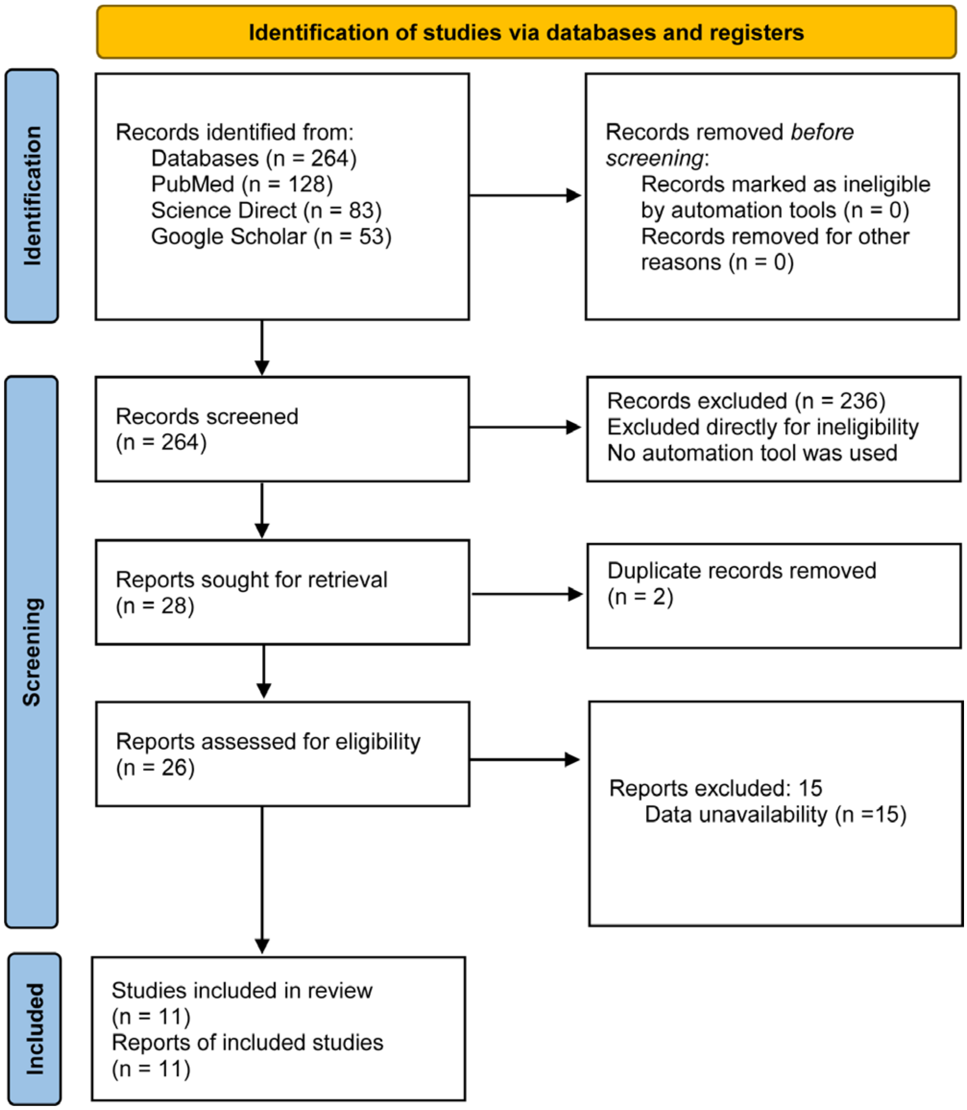

Figure 1. PRISMA flow diagram. PRISMA = the preferred reporting items for systematic reviews and meta-analyses.

Table 1

Quality assessment of the included studies.

Study ID	1	2	3	4	5	6	7	8	9	10	Overall score (%)
Tonelli 2019	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	90%
Yu 2015	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	90%
Huang 2014	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	90%
Bae 2022	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	90%
Sauder 2019	Y	Y	Y	U	Y	Y	Y	Y	Y	Y	90%
Fried 2023	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	90%
Bello-Chavolla 2017	Y	Y	Y	U	Y	Y	Y	N	N	Y	70%
García-Tejeda 2018	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	90%
Nouraei 2021	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	90%
Zenteno-Castillo 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100%
Bai 2017	Y	Y	Y	U	Y	Y	Y	Y	U	Y	80%

Here, 1. Was the research question appropriate? 2. Is the target/study population clearly defined? 3. Were any inclusion and/or exclusion criteria mentioned? 4. Was any time frame mentioned? 5. Is the response rate ≥ 70%? 6. Is the sample representative of the target population? 7. Were data collection methods standardized? 8. Were valid criteria used to assess diabetes? (that is, any of the following-diagnostic tools/kit/survey, etc) 9. Was the nephropathy measuring kit/tool validated? 10. Did the authors use statistical analyses? Y = Yes, N = No, U = Unclear.

of 24.2 was found in the USA with a 95% CI of 13.8 to 34.5. I2 statistics revealed a high degree of heterogeneity among the studies conducted in all 3 countries ranging from 100% ($P = 0$) among the USA studies to 83% ($P < .01$) among the Mexican studies whereas the Canadian studies reported 98% ($P < .01$) heterogeneity (Figs. 2, 3, and 4).

Table 2

Characteristics of the included studies.

Study ID	Location	Study type	Male (%)	Female (%)	Total participants	Age (mean/ mean ± SD)	BMI	Types of diabetes in the study participants	Diabetes measurement method	Nephropathy measurement method	References
Tonelli 2019	Canada	Cross-Sectional	53.6%	44.4%	260,903	64	≥35 kg/m^2	Type 2	HbA1c	eGFR	[46]
Yu 2015	USA	Cohort	48%	52%	1464	61.45 ± 13	NR	Type 1, Type 2	Self-reported or medication observation	Serum creatinine level, eGFR	[41]
Huang 2014	USA	Cross-sectional	47.5%	52.5%	356	69 ± 8	NR	Type 2	NR	Serum creatinine level, eGFR	[42]
Bae 2022	USA	Cohort study	55.67%	44.33%	580,741	64	NR	Type 2	HbA1c	NR	[43]
Sauder 2019	USA	Cohort study	NR	NR	1327	18	NR	Type 1	Self-reported or medication observation	NR	[44]
Fried 2023	USA	Cohort	46.4%	53.6%	560,874	72	NR	Type 2	HbA1c	eGFR UACR	[45]
Bello-Chavolla 2017	Mexico	Cross-sectional	45.9%	54.1%	135	77.7 ± 5.8	26.3 ± 4.4	Type 2	Self-reported or medication observation	NR	[38]
Garcia-Tejeda 2018	Mexico	Cross-sectional	32%	68%	76	60.67	28.71	Type 2	NR	Measurement of albumin excretion. Creatinine level	[48]
Nouraei 2021	Canada	Cross - sectional	46.5%	53.5%	5172	71	30.5 ± 6.8	Type 2	Random plasma glucose Fasting plasma glucose HbA1c	eGFR	[47]
Zenteno-Castillo 2015	Mexico	Cross-sectional	NR	NR	335	62	NR	Type 2	Serum Glucose Level HbA1c	Creatinine Level, eGFR	[39]
Bai 2017	Canada	Cross-sectional cohort study	43.8%	56.2%	323	65.5 ± 8.5	NR	Type 1	HbA1c	Creatinine Level, eGFR	[40]

BMI = body mass index, NR = not reported, USA = United States of America.

3.5. Study biasness and sensitivity identification

The funnel plot was constructed to find out the possible sources of heterogeneity and publication bias detected the presence of outliers (Fig. 5). For definitive identification of outliers, a Galbraith plot was constructed which detected Sauder 2019 and Fried 2023 as outliers (Fig. 6). To assess the impacts of the outliers on the overall sample size, first, the outliers were excluded from the analysis and a forest plot was constructed in the random effects model which showed an overall pooled prevalence of 0.34% (95% CI: 0.27; 0.40) although the I^2 statistics showed indifferent heterogeneity (100%) (Fig. 7). Then a forest plot was reconstructed in the fixed effects model without the 2 outliers which showed an overall pooled prevalence of 0.23% (95% CI: 0.23; 0.23) although the heterogeneity level remained unchanged (Fig. 8).

4. Discussion

Nephropathy, being one of the most serious and life-threatening microvascular complications of DM accounts for 31.1% increase in mortality risk among the people living with diabetes.[49] Approximately, 1 in every 3 people living with DM are suffering from chronic kidney disease (CKD) with an estimated 2 million deaths worldwide in 2019.[50,51] The International Diabetes Federation says diabetes is one of the leading causes of CKD and together with hypertension causes 80% of ESRD cases worldwide. Around 40% of people living with DM develop kidney diseases in their lifetime.[52] Generally, enhanced excretion of urinary albumin, increased levels of glucose, dyslipidemia, glomerular hyperfiltration, obesity, smoking, age, oxidative stress, inflammation, and genetics are regarded as the risk factors of diabetic nephropathy.[53] Due to the increased morbidity and mortality of the population having CKD besides diabetes healthcare costs enhanced significantly. For instance, in the United States, overall medical costs were reported to be 50% higher for people having both diabetes and CKD as compared to those who only have diabetes without CKD. Moreover, complications such as kidney failure, dialysis, and kidney transplants make the situation even worse.[54] Increased morbidity, mortality, and associated increase in healthcare expenditure along with enormous humanistic, societal, and economic crises in the North American region indicate the significance of proper estimation and understanding of the prevalence of nephropathy leading to ESRD and kidney failure among the people living with diabetes.

The current study, as per our concern, is the first meta-analysis to assess the pooled prevalence of nephropathy in patients with DM in the North American region, and interestingly, we observed a variation while comparing our analysis with the previous reports of the other countries and continents.

Significantly higher prevalences of nephropathy within diabetic patients were reported previously across different regions of Africa. For instance, Wagnew et al reported a pooled

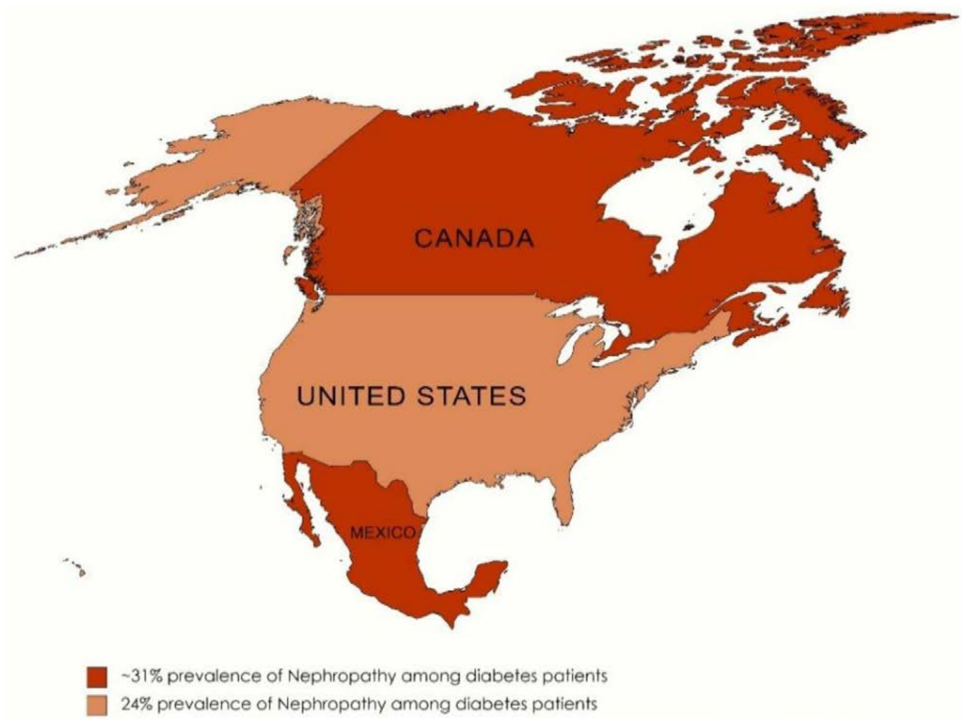

Figure 2. Geographical presentation of the prevalence of nephropathy among diabetes patients in the North American region.

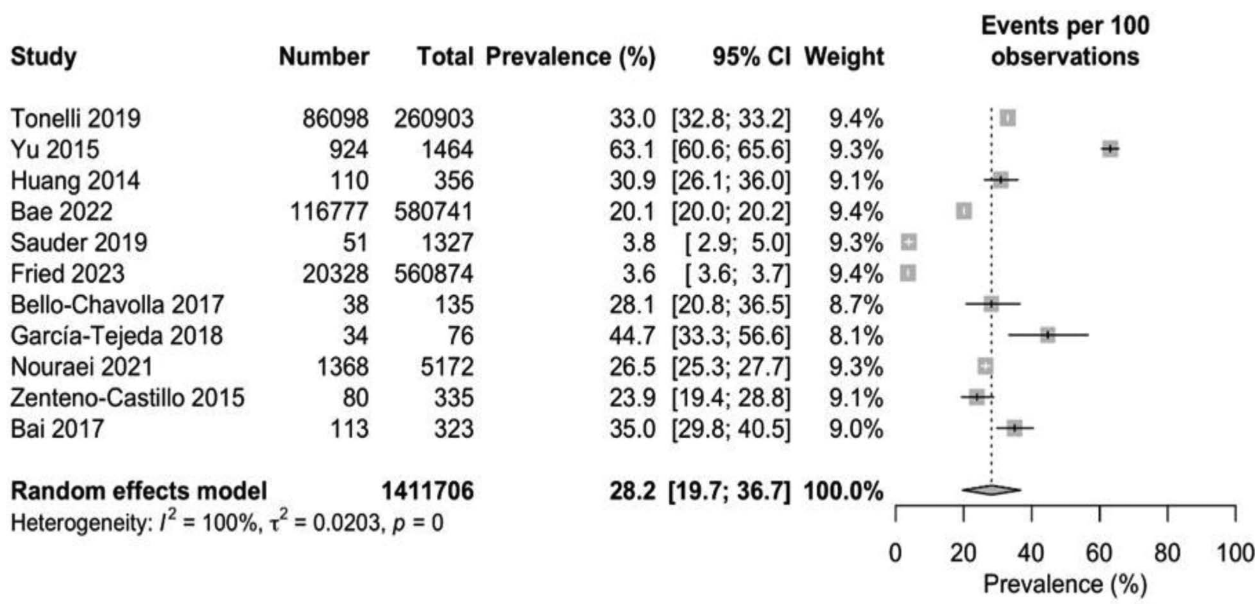

Figure 3. Forest plot of the pooled prevalence of nephropathy among diabetes patients.

prevalence of 40.4% (95% CI: 24.1–56.7) and 40.2% (95% CI: 33.3–47.21) of nephropathy among diabetic patients in Southern and Western Africa whereas the Eastern and Central Africa showed a comparatively lower prevalence rate of 29.7% (95% CI: 14.3–45.1) and 35.3% (95% CI: 27.46–43.14), respectively. Diabetes-associated nephropathy was reported to be more prevalent among type 2 diabetes patients in these regions with a pooled prevalence of 41.39% (95% CI: 32.2–50.58%) compared to type 1 diabetes with 29.3% (95% CI: 20.3–38.25) of pooled prevalence. A significant increase in the frequency of nephropathy was reported among diabetic patients with hypertension in this meta-analysis.[55] However, in a systematic review, El Hafeez et al reported the highest pooled prevalence of nephropathy among diabetic patients in Eastern Africa ranging from 18% to 84% with a pooled prevalence of 46.9%. Nevertheless, Central, West, South, and North Africa showed the pooled prevalence to be 40.8%, 27.7%, 23.0%, and 18.9%, respectively.[56] Wide varieties of factors including delayed diagnosis, paucity of diagnostic facilities and screening, variations in the definitions of CKD and diagnostic methods, inadequate treatment facilities at an early stage along with poor lifestyle and blood sugar control might be responsible for this alarmingly higher prevalence of nephropathy in diabetic patients and variations of findings among different studies conducted across Africa as compared to the developed countries.[29,57,58]

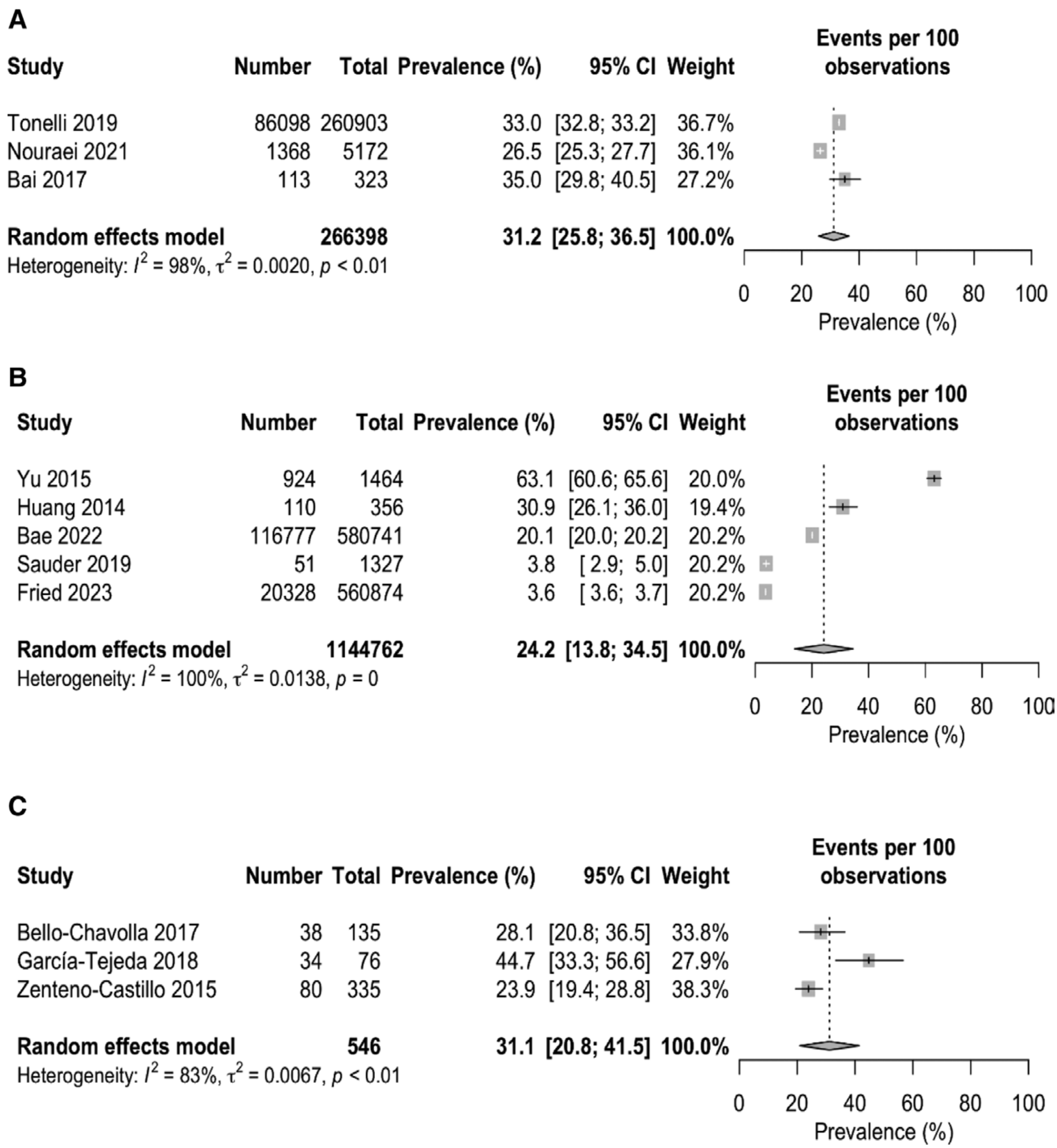

Figure 4. Forest plot of the prevalence of nephropathy among diabetes patients in (A) Canada, (B) USA, and (C) Mexico. USA = United States of America.

Higher prevalence of nephropathy along with considerable variations in the findings of different studies were also found across different regions and countries of Europe. Substantial differences in the prevalence of CKD stage 1 to 5 among diabetic patients across the European general population were reported in a study by Brück et al Across the 6 different European countries included in this study, the minimum and maximum prevalence rates were reported in the Netherlands (15.4%) and Germany (41.5%) respectively, whereas 23.9%, 24.6%, 27.0%, and 28.4% prevalence were reported in Spain, Ireland, Italy, and Norway respectively.[59] However, a study conducted by Griffin et al in Northern Europe reported an overall DKD prevalence of 42.0% with 23.4% and 47.9% between patients with type 1 and 2 diabetes, respectively.[60] Three different studies investigated the prevalence of kidney diseases in type 2 diabetic patients in England, Spain, and France reported 30%, 35%, and 40% pooled prevalence rates, respectively.[61–63]

Seemingly identical variations in the prevalence of diabetes-associated nephropathy across different Asian regions and countries were reported in different meta-analysis and separate prevalence studies. For example, a study conducted among type 2 diabetic patients in a total of 103 centers in 10 Asian countries or regions found the pooled prevalence of microalbuminuria and macroalbuminuria of 39.8% (95% CI: 39.2–40.5) and 18.8% (95% CI: 18.2–19.3), respectively. The highest prevalence of microalbuminuria was observed in Korea (56.5%) and the lowest in Pakistan (24.2%).[64] A meta-analysis of observational studies of type 2 diabetes patients in China reported an estimated pooled prevalence of 21.8% (95% CI: 18.5–25.4) with the highest prevalence of 41.3% in

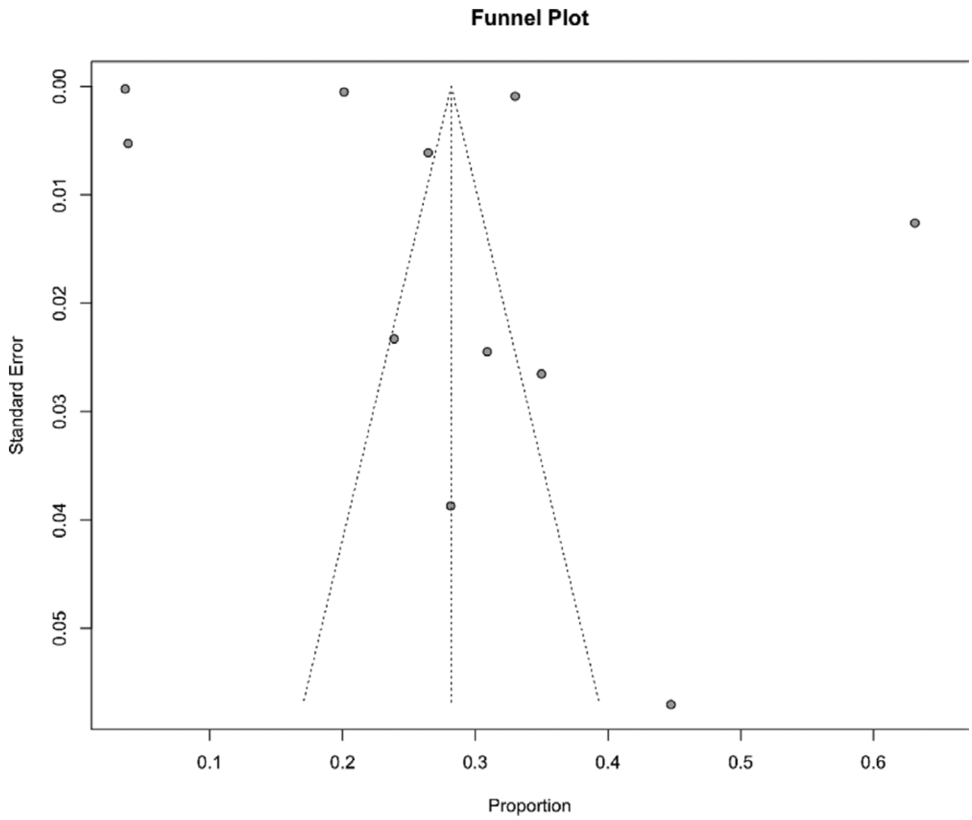

Figure 5. Funnel plot assessing publication bias.

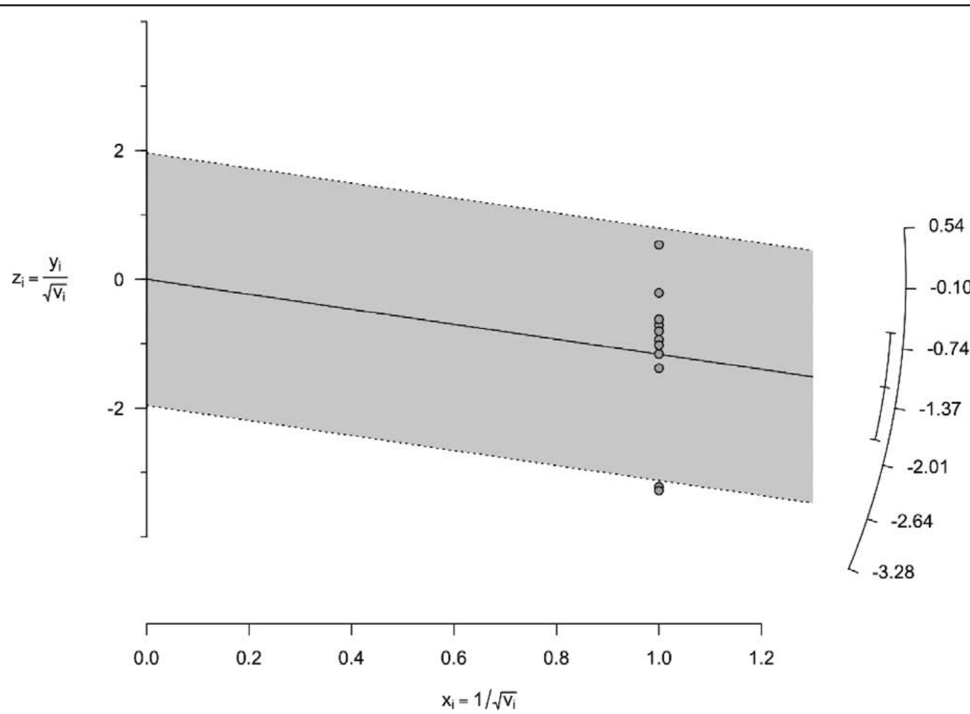

Figure 6. Galbraith plot indicating outlier studies.

the western part followed by the eastern province with 22.3% and northeastern province with 20.7%.[65] In an Indian study conducted in an urban south Indian population, 26.1% overall pooled prevalence of diabetic nephropathy along with significant association between age, diabetes duration and glycated hemoglobin were reported.[66]

The decrease in the pooled prevalence of nephropathy in the USA (24.2%) among diabetic patients as compared to Canada (31.2%) and Mexico (31.1%) perhaps resulted from the increasing trends in controlling the modifiable factors of diabetes such as blood glucose level, lipid level, and hypertension along with increased practices of aerobic exercise, resistance training, and

Study	Number	Total	Prevalence (%)	95% CI	Weight
Tonelli 2019	86098	260903	33.0	[32.8; 33.2]	12.0%
Yu 2015	924	1464	63.1	[60.6; 65.6]	11.8%
Huang 2014	110	356	30.9	[26.1; 36.0]	11.2%
Bae 2022	116777	580741	20.1	[20.0; 20.2]	12.0%
Bello-Chavolla 2017	38	135	28.1	[20.8; 36.5]	10.2%
García-Tejeda 2018	34	76	44.7	[33.3; 56.6]	8.7%
Nouraei 2021	1368	5172	26.5	[25.3; 27.7]	11.9%
Zenteno-Castillo 2015	80	335	23.9	[19.4; 28.8]	11.3%
Bai 2017	113	323	35.0	[29.8; 40.5]	11.1%
Random effects model		**849505**	**33.7**	**[27.4; 40.0]**	**100.0%**

Heterogeneity: $I^2 = 100\%$, $\tau^2 = 0.0086$, $p = 0$

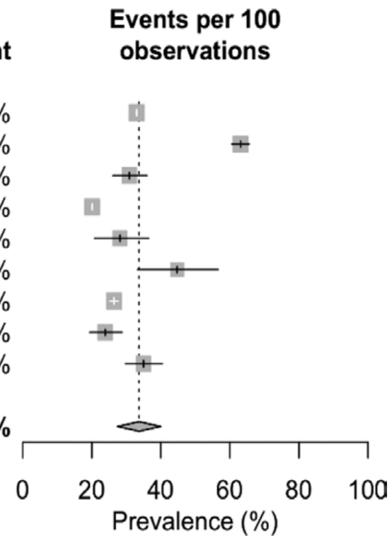

Figure 7. Forest plot of the prevalence of nephropathy among diabetes patients using random effect model (excluding outlier studies).

Study	Number	Total	Prevalence (%)	95% CI	Weight
Tonelli 2019	86098	260903	33.0	[32.8; 33.2]	12.0%
Yu 2015	924	1464	63.1	[60.6; 65.6]	11.8%
Huang 2014	110	356	30.9	[26.1; 36.0]	11.2%
Bae 2022	116777	580741	20.1	[20.0; 20.2]	12.0%
Bello-Chavolla 2017	38	135	28.1	[20.8; 36.5]	10.2%
García-Tejeda 2018	34	76	44.7	[33.3; 56.6]	8.7%
Nouraei 2021	1368	5172	26.5	[25.3; 27.7]	11.9%
Zenteno-Castillo 2015	80	335	23.9	[19.4; 28.8]	11.3%
Bai 2017	113	323	35.0	[29.8; 40.5]	11.1%
Common effect model		**849505**	**23.4**	**[23.3; 23.4]**	**--**

Heterogeneity: $I^2 = 100\%$, $\tau^2 = 0.0086$, $p = 0$

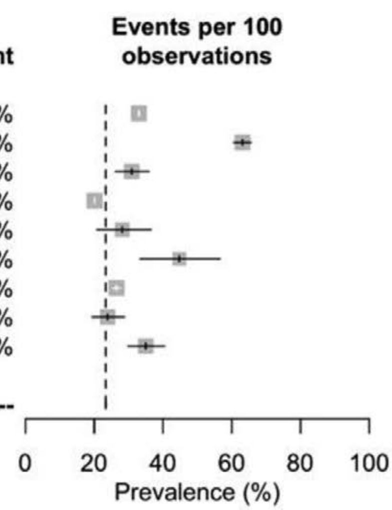

Figure 8. Forest plot of the prevalence of nephropathy among diabetes patients using fixed effect model (excluding outlier studies).

preventive practices among the diabetic population of USA over the last 2 decades.[67,68] An increase in the uptake of antidiabetic and antihypertensive medications among diabetic patients in the USA might also play a crucial role in controlling diabetes and the subsequent progression of nephropathy.[69,70] Besides, the improvements in diabetes screening and diagnosis, increased attitudes to receiving diabetes self-management education as well as different campaigns and training programs of centers for disease control and prevention, for example, the National Diabetes Prevention Program, Diabetes Self-Management Education and Training program, etc also plausibly contributed to minimizing in the prevalence of diabetes along with the risk of diabetes associated nephropathy in the USA.[71–73]

On the other hand, a variety of reasons e.g., poor attitudes and practices towards glycemic control, poor dietary habits, inadequate physical activity, obesity etc among the general population might be responsible for the higher prevalence of nephropathy among diabetic patients in Canada.[74,75] Failure to achieve the glycemic target, high morbidity load among diabetic patients, insufficient early treatment measures, poor knowledge, and performance of physicians in glycemic control and microvascular complication screening and providing vascular protection to the patients might also lead to higher prevalence of diabetes as well as the microvascular complication including nephropathy among the Canadian populations.[75–77]

Similarly higher prevalence of nephropathy among diabetic patients in Mexico was found in our current meta-analysis which might have resulted from the increasing childhood and adult obesity and metabolic syndrome, inadequate diabetic prevention and control practices, lack of public awareness as well as suboptimal glycemic control, and outpatient care in health-care centers and inadequate screening and diagnostic facilitates of diabetes among the Mexican population.[78–81]

All the included studies in our study focused on the frequency of nephropathy within adult diabetic patients except the study by Sauder et al in which young adults and adolescents living with diabetes type 1 are included and it was found that the prevalence of nephropathy is significantly low (3.8%) in this young population than the adult diabetic population included in other studies. This finding agrees with the lower prevalence (5.6%) reported in the diabetes incidence study conducted in Sweden with young adults living with type 1 diabetes.[82] Variations found in the overall prevalence of nephropathy in diabetic patients in the USA, Canada, and Mexico might also be caused due to several other reasons e.g. different study types, wide varieties of diabetes and nephropathy measurement methods, differences in study years and follow-up times, variations in the definition of diabetes associated nephropathy, associated comorbidities as well as the socio-demographics of the participants which were also mentioned in 2 systematic review and meta-analysis of diabetic kidney disease in conducted in Africa.[56,83]

Development and progression of nephropathy among the diabetic population can be prevented or reduced through strict control of modifiable and non-modifiable factors that are associated with the pathogenesis of the modifiable factors including high blood sugar level, hypertension, dyslipidemia, metabolic syndrome e.g. obesity, salt intake, poor dietary control, advanced glycation end products, smoking, low physical activity, and exercise, etc whereas the non-modifiable factors include genetic factors, duration of diabetes, advanced age, gender and family history of diabetic kidney disease, insulin resistance, hypertension, and DM.[84,85]

The overall prevalence of nephropathy in diabetes patients found in this study is in proximity with the frequency of other common microvascular complications of diabetes. For instance, the global prevalence of diabetic retinopathy is 22.27% (95% CI: 19.73–25.03) with a prevalence of 33.30% in North American and the Caribbean regions whereas the global prevalence of diabetic peripheral neuropathy is 30% (95% CI: 25–34).[86,87] A high level of heterogeneity was determined in the studies which might have been generated from the wide variations in the numbers of diabetic patients with nephropathy and the total diabetic patients included in the studies as well as the variations in study types and diagnostic methods.

5. Conclusion

In this study, we found that the overall prevalence of nephropathy among diabetic patients in the USA, Canada, and Mexico is lower than most of the regions and countries in Africa, Asia, and Europe. The pooled prevalence of diabetic nephropathy is much lower in the USA compared to Canada and Mexico. Wide varieties of factors including glycemic control, dyslipidemia, hypertension management, metabolic syndrome, genetic and demographic factors, smoking and alcohol consumption, uptake of antidiabetic and antihypertensive drugs, dietary habits, practices of exercise along with timely diagnosis, knowledge and performances of the physician and healthcare facilities lead to the variations in the prevalence of nephropathy among diabetic patients across different counties, regions, and continents. Improvement in public awareness regarding diabetes, diabetic nephropathy and associated risk factors, proper management practices of diabetes and hypertension as well as advancement in diagnostic and healthcare facilities are recommended to reduce the prevalence of nephropathy among the people living with diabetes.

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References

[1] Blair M. Diabetes mellitus review. Urol Nurs. 2016;36:27–36.
[2] Egan AM, Dinneen SF. What is diabetes? Medicine (Baltimore). 2019;42:679–81.
[3] Savitha A. The need for patient follow-up strategies to confirm diabetes mellitus in large scale opportunistic screening. J Clin Diagnostic Res. 2016;10:LE01.
[4] Lin X, Xu Y, Pan X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep. 2020;10:14790.
[5] Cho NH, Shaw JE, Karuranga S, et al. IDF diabetes atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271–81.
[6] CDC. National Diabetes Statistics Report. 2022 [cited November 01, 2023]. Available at: https://www.cdc.gov/diabetes/php/data-research/index.html. Accessed November 1, 2023.
[7] CDC. What is Diabetes? 2023 [cited November 01, 2023]. Available at: https://www.cdc.gov/diabetes/about/?CDC_AAref_Val=https://www.cdc.gov/diabetes/basics/diabetes.html. Accessed November 10, 2023.
[8] WHO. Classification of Diabetes Mellitus. 2019. Available at: www.who.int/publications/i/item/classification-of-diabetes-mellitus. Accessed November 7, 2023.
[9] Nomiyama T, Yanase T. Secondary diabetes. Nihon rinsho. Japanese J Clin Med. 2015;73:2008–12.
[10] Repaske DR. Medication-induced diabetes mellitus. Pediatr Diabetes. 2016;17:392–7.
[11] Roep BO, Thomaidou S, van Tienhoven R, Zaldumbide A. Type 1 diabetes mellitus as a disease of the β-cell (do not blame the immune system?). Nat Rev Endocrinol. 2021;17:150–61.
[12] Galicia-Garcia U, Benito-Vicente A, Jebari S, et al. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci . 2020;21:6275.
[13] Katsarou A, Gudbjörnsdottir S, Rawshani A, et al. Type 1 diabetes mellitus. Nat Rev Dis Primers. 2017;3:1–17.
[14] Waly MI, Essa MM, Ali, A. The global burden of type 2 diabetes: a review. Int J Biol Med Res. 2010;1:326–9.
[15] Fowler MJ. Microvascular and macrovascular complications of diabetes. Clinical Diabetes. 2011;26:77–82.
[16] Chawla A, Chawla R, Jaggi S. Microvasular and macrovascular complications in diabetes mellitus: distinct or continuum? Indian J Endocrinol Metab. 2016;20:546–51.
[17] Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. Diabetologia. 2019;62:3–16.
[18] Giglio RV, Patti AM, Rizvi AA, et al. Advances in the pharmacological management of diabetic nephropathy: a 2022 International Update. Biomedicines. 2023;11:291.
[19] Thomas MC, Brownlee M, Susztak K, et al. Diabetic kidney disease. Nat Rev Dis Primers. 2015;1:1–20.
[20] Rossing P, Persson F, Frimodt-Møller M. Prognosis and treatment of diabetic nephropathy: recent advances and perspectives. Nephrologie Therapeutique, 2018. 14: S31–S37.
[21] Hahr AJME, Molitch ME. Management of diabetes mellitus in patients with chronic kidney disease. Molitch Clin Diabetes Endocrinol. 2015;1:1–9.
[22] Abu-Farha M, Iizuka K, Yabe D, Al-Mulla F, Abubaker J. Advances in the research of diabetic nephropathy. Front Endocrinol. 2023;13:1116188.
[23] Dronavalli S, Duka I, Bakris GL. The pathogenesis of diabetic nephropathy. Nature Clin Pract Endocrinol Metab. 2008;4: 444–452.
[24] Jiang W, Wang J, Shen X, et al. Establishment and validation of a risk prediction model for early diabetic kidney disease based on a systematic review and meta-analysis of 20 cohorts. Diabetes Care. 2020;43:925–33.
[25] Papadopoulou-Marketou N, Paschou SA, Marketos N, Adamidi S, Adamidis S, Kanaka-Gantenbein C. Diabetic nephropathy in type 1 diabetes. Minerva Med. 2017;109:218–28.
[26] Lim AKh. Diabetic nephropathy—complications and treatment. Int J Nephrol Renovasc Dis. 2014;7:361–81.
[27] Satirapoj B, Adler SG. Prevalence and management of diabetic nephropathy in western countries. Kidney Diseases (Basel, Switzerland). 2015;1:61–70.
[28] Liyanage T, Toyama T, Hockham C, et al. Prevalence of chronic kidney disease in Asia: a systematic review and analysis. BMJ Global Health. 2022;7:e007525.
[29] Badro DA. Chronic kidney disease management in developing countries. In: Al-Worafi YM, ed. Handbook of Medical and Health Sciences in Developing Countries: Education, Practice, and Research. Springer, Cham; 2023:1–146.
[30] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.

[31] Khandker SS, Godman B, Jawad MI, et al. A systematic review on COVID-19 vaccine strategies, their effectiveness, and issues. Vaccines. 2021;9:1387.

[32] PRISMA Flow Diagram. 2020. Available at: https://www.prisma-statement.org/prisma-2020-flow-diagram. Accessed December 10, 2023.

[33] NIH. Study Quality Assessment Tools. 2021. Available at: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools. Accessed December 10, 2023.

[34] UNC. Systematic Reviews: Step 6: Assess Quality of Included Studies. 2023. Available at: https://guides.lib.unc.edu/systematic-reviews/assess-quality. Accessed November 29, 2023.

[35] Khandker SS, Jannat N, Sarkar D, et al. Association between glomerular filtration rate and β-Thalassemia major: a systematic review and meta-analysis. Thalassemia Reports. 2023;13:195–205.

[36] Islam MA, Khandker SS, Alam SS, Kotyla P, Hassan R. Vitamin D status in patients with systemic lupus erythematosus (SLE): a systematic review and meta-analysis. Autoimmun Rev. 2019;18:102392.

[37] Khandker SS, Nik Hashim NHH, Deris ZZ, Shueb RH, Islam MA. Diagnostic accuracy of rapid antigen test kits for detecting SARS-CoV-2: a systematic review and meta-analysis of 17,171 suspected COVID-19 patients. J Clin Med. 2021;10:3493.

[38] Bello-Chavolla OY, Aguilar-Salinas CA, Avila-Funes JA. Geriatric syndromes and not cardiovascular risk factors are associated with cognitive impairment among Mexican community-dwelling elderly with type 2 diabetes. Revista de investigacion clinica; organo del Hospital de Enfermedades de la Nutricion. 2017;69:166–72.

[39] Zenteno-Castillo P, Muñoz-López DB, Merino-Reyes B, et al. Prevalence of diabetic nephropathy in Type 2 Diabetes Mellitus in rural communities of Guanajuato, Mexico. Effect after 6 months of Telmisartan treatment. J Clin Translat Endocrinol. 2015;2:125–8.

[40] Bai J-W, Lovblom LE, Cardinez M, et al. Neuropathy and presence of emotional distress and depression in longstanding diabetes: results from the Canadian study of longevity in type 1 diabetes. J Diabetes Complications. 2017;31:1318–24.

[41] Yu MK, Katon W, Young BA. Associations between sex and incident chronic kidney disease in a prospective diabetic cohort. Nephrology (Carlton, Vic.). 2015;20:451–8.

[42] Huang DL, Abrass IB, Young BA. Medication safety and chronic kidney disease in older adults prescribed metformin: a cross-sectional analysis. BMC Nephrol. 2014;15:1–7.

[43] Bae JP, Kadziola ZA, Liu D, Chinthammit C, Boye KS, Mather KJ. An early assessment of the real-world treatment patterns of type 2 diabetes: a comparison to the 2018 ADA/EASD Consensus Report Recommendations. Diabetes Ther. 2022;13:1499–510.

[44] Sauder KA, Stafford JM, Mayer-Davis EJ, et al. Co-occurrence of early diabetes-related complications in adolescents and young adults with type 1 diabetes: an observational cohort study. Lancet Child Adolescent Health. 2019;3:35–43.

[45] Fried L, Schmedt N, Folkerts K, et al. High unmet treatment needs in patients with chronic kidney disease and type 2 diabetes: real-world evidence from a US claims database. Nephrol Dialysis Transplant. 2023;38:630–43.

[46] Tonelli M, Wiebe N, Richard J-F, Klarenbach SW, Hemmelgarn BR. Characteristics of adults with type 2 diabetes mellitus by category of chronic kidney disease and presence of cardiovascular disease in Alberta Canada: a cross-sectional study. Can J Kidney Health Dis. 2019;6:2054358119854113.

[47] Nouraei H, Leiter LA, Tan MK, et al. Glycemic control and cardiovascular risk factor management in adults with type 2 diabetes with and without chronic kidney disease before sodium-glucose cotransporter protein 2 inhibitors: insights from the Diabetes Mellitus Status in Canada survey. Can J Diabetes. 2021;45:743–9.

[48] García-Tejeda AU, Sampieri CL, Suárez-Torres I, et al. Association of urinary activity of MMP-9 with renal impairment in Mexican patients with type 2 diabetes mellitus. PeerJ. 2018;6:e6067.

[49] Afkarian M, Sachs MC, Kestenbaum B, et al. Kidney disease and increased mortality risk in type 2 diabetes. J Am Soc Nephrol. 2013;24:302–8.

[50] WHO. Diabetes 2023. Available at: https://www.who.int/news-room/fact-sheets/detail/diabetes. Accessed November 28, 2023.

[51] CDC. Diabetes and Chronic Kidney Disease. 2022 . Available at: https://www.cdc.gov/diabetes/diabetes-complications/diabetes-and-chronic-kidney-disease.html?CDC_AAref_Val=https://www.cdc.gov/diabetes/managing/diabetes-kidney-disease.html. Accessed December 3, 2023.

[52] Europe, I. Chronic Kidney Disease. Available at: https://idf.org/europe/life-with-diabetes/diabetes-related-complications/chronic-kidney-disease/. Accessed November 30, 2023.

[53] Tziomalos K, Athyros VG. Diabetic nephropathy: new risk factors and improvements in diagnosis. Rev Diabet Stud. 2015;12:110–8.

[54] Li R, Bilik D, Brown MB, et al. Medical costs associated with type 2 diabetes complications and comorbidities. Am J Manag Care. 2013;19:421–30.

[55] Wagnew F, Eshetie S, Kibret GD, et al. Diabetic nephropathy and hypertension in diabetes patients of sub-Saharan countries: a systematic review and meta-analysis. BMC Research Notes. 2018;11:1–7.

[56] Abd ElHafeez S, Bolignano D, D'Arrigo G, Dounousi E, Tripepi G, Zoccali C. Prevalence and burden of chronic kidney disease among the general population and high-risk groups in Africa: a systematic review. BMJ Open. 2018;8:e015069.

[57] Noubiap JJ, Naidoo J, Kengne AP. Diabetic nephropathy in Africa: a systematic review. World J Diabetes. 2015;6:759–73.

[58] Zimmermann M, Bunn C, Namadingo H, Gray CM, Lwanda J. Experiences of type 2 diabetes in sub-Saharan Africa: a scoping review. Global Health Res Policy. 2018;3:1–13.

[59] Brück K, Stel VS, Gambaro G, et al. CKD prevalence varies across the European general population. J Am Soc Nephrol. 2016;27:2135–47.

[60] Griffin TP, O'Shea PM, Smyth A, et al. Burden of chronic kidney disease and rapid decline in renal function among adults attending a hospital-based diabetes center in Northern Europe. BMJ Open Diabetes Res Care. 2021;9:e002125.

[61] Cook S, Schmedt N, Broughton J, Kalra PA, Tomlinson LA, Quint JK. Characterising the burden of chronic kidney disease among people with type 2 diabetes in England: a cohort study using the clinical practice research datalink. BMJ Open. 2023;13:e065927.

[62] Detournay B, Simon D, Guillausseau P-J, et al. Chronic kidney disease in type 2 diabetes patients in France: prevalence, influence of glycaemic control and implications for the pharmacological management of diabetes. Diabetes Metab. 2012;38:102–12.

[63] Coll-de-Tuero G, Mata-Cases M, Rodriguez-Poncelas A, et al. Chronic kidney disease in the type 2 diabetic patients: prevalence and associated variables in a random sample of 2642 patients of a Mediterranean area. BMC Nephrol. 2012;13:1–9.

[64] Wu A, Kong NCT, de Leon FA, et al. An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: the MicroAlbuminuria Prevalence (MAP) Study. Diabetologia. 2005;48:17–26.

[65] Zhang XX, Kong J, Yun K. Prevalence of diabetic nephropathy among patients with type 2 diabetes mellitus in China: a meta-analysis of observational studies. J Diabetes Res. 2020;2020:2315607.

[66] Pradeepa R, Rema M, Vignesh J, Deepa M, Deepa R, Mohan V. Prevalence and risk factors for diabetic neuropathy in an urban south Indian population: the Chennai Urban Rural Epidemiology Study (CURES-55). Diabetic Med. 2008;25:407–12.

[67] Fang M, Wang D, Coresh J, Selvin E. Trends in diabetes treatment and control in US adults, 1999–2018. N Engl J Med. 2021;384:2219–28.

[68] Fang M. Trends in diabetes management among US adults: 1999–2016. J Gen Intern Med. 2020;35:1427–34.

[69] Hampp C, Borders-Hemphill V, Moeny DG, Wysowski DK. Use of antidiabetic drugs in the US, 2003–2012. Diabetes Care. 2014;37:1367–74.

[70] Derington CG, Bress AP, Herrick JS, et al. Antihypertensive medication regimens used by US adults with hypertension and the potential for fixed-dose combination products: the national health and nutrition examination surveys 2015 to 2020. J Am Heart Assoc. 2023;12:e028573.

[71] Selvin E, Parrinello CM, Sacks DB, Coresh J. Trends in prevalence and control of diabetes in the United States, 1988–1994 and 1999–2010. Ann Intern Med. 2014;160:517–25.

[72] Li R, Shrestha SS, Lipman R, et al. Diabetes self-management education and training among privately insured persons with newly diagnosed diabetes—United States, 2011–2012. Morb Mortal Wkly Rep. 2014;63:1045.

[73] Adjei Boakye E, Varble A, Rojek R, et al. Sociodemographic factors associated with engagement in diabetes self-management education among people with diabetes in the United States. Public Health Reports (Washington, DC: 1974). 2018;133:685–91.

[74] Smith KJ, Pagé V, Gariépy G, Béland M, Badawi G, Schmitz N. Self-rated diabetes control in a Canadian population with type 2 diabetes: associations with health behaviours and outcomes. Diabetes Res Clin Pract. 2012;95:162–8.

[75] Coons MJ, Greiver M, Aliarzadeh B, et al. Is glycemia control in Canadians with diabetes individualized? A cross-sectional observational study. BMJ Open Diabetes Res Care. 2017;5:e000316.

[76] Agarwal G, Kaczorowski J, Hanna S. Care for patients with type 2 diabetes in a random sample of community family practices in Ontario, Canada. Int J Family Med. 2012;2012:734202.
[77] Leiter LA, Berard L, Bowering CK, et al. Type 2 diabetes mellitus management in Canada: is it improving? Can J Diabetes. 2013;37:82–9.
[78] Barquera S, Campos-Nonato I, Aguilar-Salinas C, Lopez-Ridaura R, Arredondo A, Rivera-Dommarco J. Diabetes in Mexico: cost and management of diabetes and its complications and challenges for health policy. Globalization Health. 2013;9:1–9.
[79] Barquera S, Hernández-Alcaraz C, Jáuregui A, et al. Diabetes awareness, treatment, and control among Mexico City residents. Diabetology. 2021;2:16–30.
[80] Flores-Hernández S, Saturno-Hernández PJ, Reyes-Morales H, Barrientos-Gutiérrez T, Villalpando S, Hernández-Ávila M. Quality of diabetes care: the challenges of an increasing epidemic in Mexico. Results from two national health surveys (2006 and 2012). PLoS One. 2015;10:e0133958.
[81] Basto-Abreu A, López-Olmedo N, Rojas-Martínez R, et al. Prevalence of diabetes and glycemic control in Mexico: national results from 2018 and 2020. salud pública de méxico. 2021;63:725–33.
[82] Svensson M, Sundkvist G, Arnqvist HJ, et al. Signs of nephropathy may occur early in young adults with diabetes despite modern diabetes management: results from the nationwide population-based Diabetes Incidence Study in Sweden (DISS). Diabetes Care. 2003;26:2903–9.
[83] Azeez TA, Efuntoye O, Abiola BI, Adeyemo SP, Adewale BA. The burden of diabetic kidney disease in Nigeria– systematic review and meta-analysis. J Egypt Soc Nephrol Transplant. 2021;21:194–202.
[84] Harjutsalo V, Groop P-H. Epidemiology and risk factors for diabetic kidney disease. Adv Chronic Kidney Dis. 2014;21:260–6.
[85] Hu F, Zhang T. Study on risk factors of diabetic nephropathy in obese patients with type 2 diabetes mellitus. Int J Gen Med. 2020;13:351–60.
[86] Teo ZL, Tham Y-C, Yu M, et al. Global prevalence of diabetic retinopathy and projection of burden through 2045: systematic review and meta-analysis. Ophthalmology. 2021;128:1580–91.
[87] Sun J, Wang Y, Zhang X, Zhu S, He H. Prevalence of peripheral neuropathy in patients with diabetes: a systematic review and meta-analysis. Primary Care Diabetes. 2020;14:435–44.