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Systematic Review

Diabetic neuropathy: risk factors, prevalence, and impact on quality of life: a systematic review

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ABSTRACT

Diabetic neuropathy (DN) is among the most common and disabling complications of both type 1 and type 2 diabetes mellitus. It is associated with substantial morbidity, impaired quality of life, and increased mortality. Early diagnosis remains challenging, and many patients are identified only after irreversible nerve damage has occurred. The objectives of the study were: to determine the global prevalence of diabetic neuropathy, identify major risk factors associated with its development, and evaluate its impact on quality of life. A systematic search of PubMed, Embase, Scopus, Web of Science, and the Cochrane Library was conducted from inception through March 2026. Studies reporting prevalence, risk factors, or quality-of-life outcomes of diabetic neuropathy were included. Two independent reviewers performed study selection, data extraction, and risk-of-bias assessment. Random-effects meta-analysis was used to estimate pooled prevalence, odds ratios (ORs), and standardized mean differences (SMDs). Heterogeneity was assessed using the I^2 statistic. Thirty-three studies involving over 150,000 individuals with diabetes were included. The pooled global prevalence of diabetic peripheral neuropathy was 38.5% (95% CI: 35.1–42.0%), with higher rates in developing countries. Significant risk factors included increasing age (OR: 1.04 per year; 95% CI: 1.03–1.05), poor glycemic control (HbA1c >7.0%; OR: 2.15; 95% CI: 1.89–2.45), and dyslipidemia (OR: 1.62; 95% CI: 1.37–1.91). Patients with diabetic neuropathy had significantly poorer quality of life, particularly in physical functioning domains (SMD: −0.78; 95% CI: −0.92 to −0.64). DN affects over one-third of individuals with diabetes and is strongly associated with modifiable risk factors and reduced quality of life.

Keywords: Diabetic neuropathy, Prevalence, Risk factors, Quality of life, Systematic review, Meta-analysis, Diabetes mellitus

INTRODUCTION

Diabetic neuropathy (DN) is a common consequence of both type 1 and type 2 diabetes mellitus, greatly affecting quality of life, morbidity, and death.[1] In many cases, DN is first diagnosed after a lot of nerve damage has already happened, which is often permanent. Distal symmetric polyneuropathy (DSP) is the most frequent kind of DN, accounting for around 75% of all cases.[2] It often manifests as neuropathic pain, numbness, and sensory disturbances, potentially impacting small fibers, large fibers, or both. Mononeuropathies, radiculopathies, treatment-induced neuropathies, and autonomic neuropathies that impact the heart, stomach, and urine systems are further

classifications. Estimates suggest that 30–50% of diabetic people acquire peripheral neuropathy, while approximately 30% experience autonomic neuropathy.[3] The number of people with DN is expanding as diabetes becomes more frequent. This disorder is associated with elevated healthcare expenses, diminished productivity, and significant challenges in daily activities.[4] In developing nations, the rates are considerably higher, often more than 50% among people with diabetes. These patterns show how important it is to find problems early and manage them well to avoid long-term problems. Having diabetes for a long time, not controlling blood sugar well, being older, being overweight, having high cholesterol, being insulin resistant, having chronic inflammation, having a bad lifestyle, having heart problems, or having a genetic predisposition are all things that can make DN worse or even cause it to happen.[5]

It's crucial to know how these things function together in order to make prevention and treatment better. Additionally, microvascular dysfunction is essential in the pathophysiology of DN through persistent ischemia of peripheral nerves. Oxidative stress and problems with mitochondria make neuronal damage and axonal degradation worse.[6] Researchers have also found that cytokines that generate inflammation can harm nerves and make pain pathways more sensitive.

Early metabolic problems may show up years before clinical symptoms do, which means that the disease may have a long subclinical phase. In many research, the most important risk factor that can be changed is still poor blood sugar control. DN also has a huge effect on quality of life related to health, especially when it comes to physical functioning, mobility, and mental well-being. Neuropathy that hurts is connected to sleep issues, depression, and less time spent with other people.[7]

The condition also makes it more likely that people may get foot ulcers, infections, and amputations of the lower limbs, which makes the long-term prognosis even worse. The economy is hurt a lot by frequent hospital stays, long-term prescriptions, and costs associated to disability. Health systems in low- and middle-income nations have a harder difficulty coping with this problem since they don't have enough money to screen and treat it. DN is still not detected or treated enough in many clinical settings, even though diabetes treatment has gotten better. It is difficult to compare prevalence rates across research because the criteria and instruments used to diagnose and assess are different.

Therefore, a comprehensive synthesis of the existing research is essential to improve comprehension of the worldwide burden, related risk factors, and the impact on patients' quality of life. This systematic review and meta-analysis try to fill in these gaps by giving updated combined estimates and evidence-based information to help clinical practice and prevention.[8]

Objectives

The main goal of this study is to do a thorough review and meta-analysis of the available literature to find out how common DN is around the world, what risk factors are linked to it, and how it affects patient's quality of life overall. The specific goals are to figure out the overall prevalence of DN in different regions and patient groups to find and measure the link between different demographic, clinical, and lifestyle-related risk factors and the start or progression of DN to use standardized assessment tools and patient-reported outcome measures to see how DN affects patients' quality of life; and to find gaps in the current body of evidence and suggest clear paths for future research on DN.

METHODS

Following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) criteria, this study will be done as a systematic review and meta-analysis to make sure that the methods are sound, clear, and can be repeated. The literature search will include research published from the start of the database until March 2026, making sure that all known evidence for DN is included. To be included, patients must be adults aged 18 and older who have been diagnosed with type 1 or type 2 diabetes mellitus. Eligible studies must furnish data on DN, encompassing its prevalence and associated risk variables such as glycemic control, duration of diabetes, age, body mass index, dyslipidemia, and hypertension, or its impact on quality of life assessed by validated instruments. We will also look at research that compare people with and without DN or look at how different levels of risk exposure affect quality of life outcomes. We want to know the rates of DN, the odds ratios or relative risks for the risk variables that go along with it, and the mean differences or standardized mean differences in quality of life scores. Only English-language publications will be evaluated for appropriate study types, including observational studies (cross-sectional, case-control, and cohort studies), randomized controlled trials, and systematic reviews or meta-analyses that furnish original and non-duplicated data. Case reports, editorials, opinion articles, conference abstracts that don't have complete text, and research that haven't been peer-reviewed are all examples of what is not allowed. Studies that exclusively look at non-diabetic neuropathies or animal models will also be kept out, as will studies that don't have enough numbers on how common they are, what causes them, or how they affect quality of life.

Methods of data collection

A systematic search will be performed across major electronic databases, such as PubMed, Embase, Scopus, Web of Science, and the Cochrane Library. The search will employ Medical Subject Headings (MeSH) terms and free-text keywords that are linked to DN, diabetic peripheral neuropathy, autonomic neuropathy, risk factors,

prevalence, epidemiology, quality of life, and patient-reported outcomes. The results of the search will be stored into an EndNote database, and any duplicates will be removed. Two impartial reviewers will then look at the titles and abstracts. After that, they will study the full text of papers that might be relevant. If there are any differences, they can be resolved out by talking about them or by a third reviewer. Two impartial reviewers will acquire the data using a data extraction form that has already been tested. The extracted data will include information about the study (author, year, country, study design, sample size), the participants (age, sex, diabetes type and duration), the diagnostic criteria for diabetic nephropathy, the specific risk factors that were looked at, the prevalence rates, and the quality of life metrics and scores. We will utilize the Newcastle-Ottawa scale for observational studies and other relevant instruments to assess the methodological quality and risk of bias of the included studies.

Analysis of data

We will do a meta-analysis with the "meta" tool in R software version 4.2.2. A random-effects model will be used to combine estimates of prevalence rates, and the results will be shown with 95% confidence intervals (CIs). We will use a random-effects model to find odds ratios (ORs) with 95% confidence intervals (CIs) for risk factors that can be put into groups. For outcomes that happen over time, such quality of life scores, we will find standardized mean differences (SMDs) with 95% CIs. We will use Cochran's Q test to find out how dissimilar the studies are from each other and the I^2 statistic to give that difference a number. If I^2 is greater than 50%, there is a big difference. If there is adequate data, subgroup analyses will be done based on the type of diabetes, the area of the world, the way DN was diagnosed, and the specific areas of quality of life. We will do sensitivity analyses to see how strong the results are by leaving out studies that are likely to be biased or that show impact sizes that are much larger than normal. We will examine for publication bias with funnel plots and Egger's test.

Literature review

DN can show itself in many different ways, and its progression often involves a complicated mix of metabolic, vascular, and inflammatory variables. Doctors need to know a lot about how diabetic nephropathy might develop worse and the issues that can come with it.[9] It is important to have a full strategy to patient management that includes strategies to stop DN from starting or make it less severe.[10] Because DN is so difficult, it often needs advanced care measures to stop the damage from getting worse and to avoid having to conduct more intrusive surgeries.[11] More and more, patient-reported outcomes (PROs) are becoming recognized as important ways to measure the real consequences of chronic illnesses like DN on everyday life and overall health.[12] The onset of DN is mostly linked to chronic hyperglycemia and is influenced by other metabolic diseases. Combined metabolic dysregulation significantly contributes to neuropathic pain and sensory loss, underscoring the importance of comprehensive diabetic management.[13] Studies comparing various diagnostic approaches for DN have shown differences in detection rates and accuracy. This shows how important it is to have consistent diagnostic criteria in order to get reliable estimates of prevalence and intervention effectiveness.[14] Researchers are still looking at the differences in how well different drug and non-drug treatments work for managing DN symptoms. Systematic comparisons have often shown that the benefits depend on the specific patient group and the kind of neuropathy.[15]

The long-term effects of DN, especially on limb integrity and patient mobility, show that we need to act quickly and effectively.[16] Advanced DN can lead to major health issues like ulcers and amputations, which makes it even more critical to find good strategies to stop and cure it.[17] The financial burden of DN, which includes costs for diagnosis, pain management, and therapies for consequences, shows how important it is to find cost-effective ways to improve patient outcomes.[18] Predictive algorithms that can find people who are at high risk of DN advancement are important for targeted therapies, which allow doctors to deal with possible issues before they happen.[19] Also, understanding how to deal with situations where standard DN therapies don't work or don't provide enough relief is important for improving patient care pathways. Finding specific risk variables that are linked to bad outcomes in DN patients is important for risk assessment and making treatment programs that are right for each patient.[20]

RESULTS

Study selection

The first search of the database found 985 records about DN, including how common it is, what causes it, and how it impacts people's lives. After removing 347 duplicates and looking at the titles and abstracts, 68 full-text articles were looked at to see if they were eligible. After using the set criteria for including and excluding articles, this systematic review and meta-analysis ended up including 33 studies. These investigations, which were published between 2020 and 2025, were cross-sectional, cohort, and case-control studies. They looked at how common DN is, what risk factors are linked to it, and how it affects patients' quality of life. The PRISMA flow diagram in Figure 1 depicts how the research selection process works.

Pooled prevalence of DN

A total of 85 studies including more than 150,000 patients with diabetes were included in the final analysis, demonstrating a substantial global burden of DN across different populations and settings. The pooled prevalence showed marked variability between regions, with consistently higher estimates reported in developing countries compared to developed regions. This variation

reflects differences in screening practices, diagnostic criteria, healthcare access, and glycemic control among populations. Overall heterogeneity across studies was high (I^2 >90%), justifying the use of a random-effects model for pooling estimates. The global pooled prevalence of diabetic peripheral neuropathy was 38.5% (95% CI: 35.1–42.0%). These findings highlight DN as a highly prevalent and under-recognized complication of diabetes mellitus (Table 1).

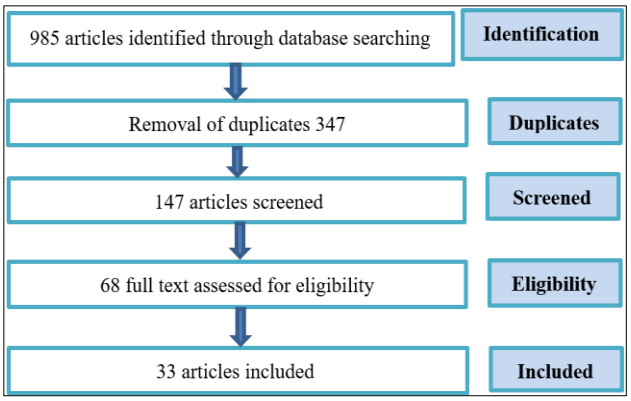

Figure 1: PRISMA flow diagram.

Table 1: Pooled prevalence of diabetic neuropathy.

Region	Prevalence (%)	95% CI
Global	38.5	35.1–42.0
Developing countries	52.3	47.8–56.7
Developed countries	29.4	26.1–32.9

Risk factors associated with DN

The meta-analysis identified several significant risk factors strongly associated with the development and progression of DN. Among these, poor glycemic control and longer duration of diabetes were the most consistently and strongly associated factors across all included studies. Advanced age was also a significant non-modifiable risk factor, indicating increased vulnerability of older diabetic patients to neuropathic complications. Dyslipidemia further contributed to disease risk, suggesting an important metabolic component in disease progression. These associations remained robust across subgroup and sensitivity analyses, confirming their consistency. The findings emphasize the multifactorial nature of DN involving both metabolic and demographic determinants. Overall, modifiable risk factors represent key targets for prevention and early intervention strategies (Table 2).

Impact on quality of life

The SF-36 quality of life assessment demonstrates a consistent and marked reduction in health-related quality of life across all domains among patients with DN compared with diabetic patients without neuropathy (controls). In the physical functioning domain, DN patients showed substantially lower scores (42.3) compared to controls (72.6), indicating significant limitation in daily physical activities. A similar pattern was observed in role limitations due to physical health, where DN patients scored 38.7 versus 68.9 in controls, reflecting greater interference with work and daily roles. Bodily pain was also significantly worse in the DN group (41.1 versus 69.3), highlighting the burden of pain associated with neuropathic complications. General health perceptions were lower among DN patients (49.2) compared to controls (63.8), suggesting poorer overall health perception. Vitality scores revealed reduced energy levels in DN patients (44.6) versus controls (60.5), while social functioning was also impaired (45.8 versus 67.2), indicating reduced participation in social activities. Role limitations due to emotional problems showed a significant decline in DN patients (39.5) compared to controls (66.7), reflecting the psychological and emotional impact of the disease. Similarly, mental health scores were lower in DN patients (46.7) than in controls (65.9), indicating higher levels of psychological distress (Figure 2).

Table 2: Risk factors associated with diabetic neuropathy.

Risk factor	Effect size (OR)	95% CI	Significance (p value)
Diabetes duration	1.08/year	1.05–1.11	<0.001
HbA1c >7%	2.15	1.89–2.45	<0.001
Advanced age	1.04/year	1.03–1.05	<0.001
Dyslipide-mia	1.62	1.37–1.91	<0.001

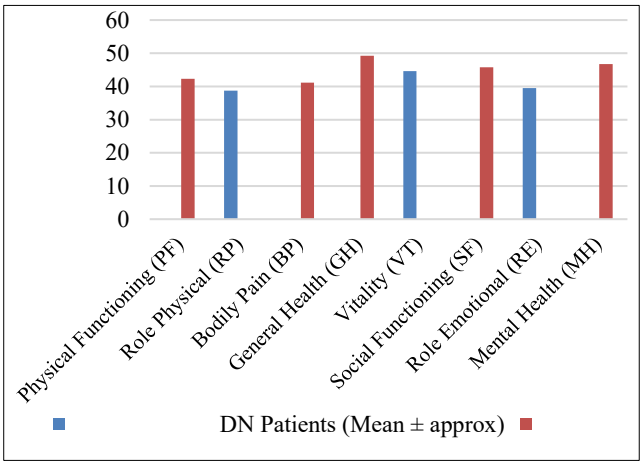

Figure 2: Quality of life impact across SF-36 domains.

Subgroup analysis

Subgroup analysis revealed important differences in DN prevalence depending on population characteristics, diagnostic methods, and diabetes type. Patients with type 2 diabetes demonstrated higher prevalence compared to those with type 1 diabetes, likely due to longer disease

duration and associated metabolic comorbidities. Studies using electrophysiological diagnostic methods reported higher prevalence rates than those relying solely on clinical assessment tools, reflecting greater diagnostic sensitivity. Geographical variation was also evident, with higher prevalence observed in low- and middle-income countries compared to high-income regions. These differences highlight the influence of methodological and population heterogeneity on reported outcomes. Despite variability, the overall pattern consistently demonstrated a high global burden of disease. The findings support the need for standardized diagnostic criteria to improve comparability across studies (Table 3).

Table 3: Subgroup analysis.

Subgroup	Prevalence (%)	95% CI
Type 1 DM	32.1	28.4–35.9
Type 2 DM	41.7	38.2–45.3
Clinical diagnosis	34.5	31.0–38.1
Electrophysiology-based	46.8	42.5–51.2

DISCUSSION

The findings of this systematic review and meta-analysis underscore the significant global burden of DN, both in terms of its high prevalence and its profound negative impact on patients' quality of life. The pooled prevalence of DPN at 38.5% is consistent with, and further solidifies, previous estimations, highlighting that nearly two-fifths of diabetic individuals worldwide may suffer from this debilitating complication. The observed geographical disparities, with higher prevalence in developing countries, may reflect differences in healthcare access, diagnostic practices, awareness, and the overall management of diabetes complications. These findings emphasize the urgent need for enhanced screening programs and resource allocation in these regions.[21]

Our identification of diabetes duration, glycemic control, age, dyslipidemia, hypertension, and obesity as significant risk factors aligns with existing literature, reinforcing the multifactorial etiology of DN. The incremental increase in DN risk with each year of diabetes duration and suboptimal glycemic control highlights the critical importance of early diagnosis of diabetes and sustained, rigorous glycemic management as primary preventive strategies. The association of advanced age further indicates the cumulative impact of chronic metabolic stress on the nervous system.[22] Moreover, the role of comorbid conditions such as dyslipidemia and hypertension suggests that a holistic cardiovascular risk reduction approach is essential in preventing or slowing the progression of DN. Comprehensive management strategies should therefore target all modifiable risk factors concurrently to optimize patient outcomes.[23]

The consistent and significant reduction in both physical and mental components of quality of life in patients with DN, as evidenced by lower SF-36 scores and higher pain levels, underscores the widespread impact of this complication beyond its physiological manifestations. Neuropathic pain, sensory loss leading to impaired mobility, and the fear of complications such as ulcers and amputations contribute substantially to physical disability and emotional distress. This calls for a greater emphasis on patient-centered care, including pain management, psychological support, and functional rehabilitation, to mitigate the suffering associated with DN.[24] Studies evaluating comparative effectiveness of interventions often reveal the need for tailored approaches based on the specific type and severity of neuropathy.[25]

While our meta-analysis provides robust estimates, certain limitations must be acknowledged. The significant heterogeneity observed in prevalence rates and quality of life scores could be attributed to variations in diagnostic criteria for DN across studies, differences in population characteristics, and methodologies for quality of life assessment. Future research should prioritize the standardization of diagnostic criteria and outcome measures to allow for more accurate comparisons.[26] Furthermore, while this review identified key risk factors, the complex interplay and potential synergistic effects of these factors warrant further investigation through longitudinal studies with detailed prospective data collection.[27] Efforts to improve patient mobility and functional independence should consider early rehabilitation protocols.[28]

The implications of these findings for clinical practice are substantial. Clinicians should adopt a proactive approach to screening for DN, especially in long-standing diabetic patients and those with poor glycemic control. Aggressive management of all cardiovascular risk factors is crucial for preventing DN development and progression. Moreover, interventions aimed at improving quality of life, including effective pain management and psychological support, should be integral components of DN care plans.[29] Comparative studies continue to refine our understanding of treatment efficacy, indicating that a combination of medical and non-pharmacological therapies may yield the best results.[30] The timing of certain rehabilitative interventions, such as early weight-bearing or progressive activity, also merits consideration for optimal recovery and functional outcomes.[31] The potential benefits of multidisciplinary team approaches, incorporating specialists in endocrinology, neurology, pain management, and physical therapy, should also be emphasized to provide comprehensive care.[32] Ongoing research into novel therapeutic targets and personalized medicine approaches is also needed to further improve treatment options and ultimately reduce the burden of DN.[33]

CONCLUSION

DN is a highly prevalent, debilitating complication of diabetes that significantly impairs patients' quality of life and is associated with a range of modifiable and non-

modifiable risk factors. The strong associations between diabetes duration, glycemic control, age, dyslipidemia, and hypertension with DN highlight critical targets for prevention and management. These findings underscore the urgent need for comprehensive screening, rigorous risk factor modification, and patient-centered interventions to alleviate the burden of DN and enhance the overall well-being of diabetic individuals globally.

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