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Minireview Article

Diabetes Mellitus and Its Neurological Sequelae: A Narrative Review

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Abstract: *Diabetic polyneuropathy (DPN) is among the most common chronic complications of diabetes mellitus (DM), affecting approximately 50% of individuals with the disease. Characterized by progressive damage to peripheral nerves—especially in the lower extremities—DPN leads to significant impairments in motor, sensory, and autonomic function. It is particularly prevalent in industrialized regions and is associated with substantial morbidity, diminished quality of life, and increased socioeconomic burden.* ***Objective:*** *This review aims to synthesize current evidence on the epidemiological patterns, diagnostic complexities, and socioeconomic impacts of diabetic polyneuropathy, with an emphasis on guiding improved clinical and public health strategies.* ***Methods:*** *A comprehensive literature review was performed using electronic databases including PubMed and EMBASE. Studies published in peer-reviewed journals from the past decade were selected based on relevance to DPN epidemiology, diagnostic modalities, and socioeconomic implications. Keywords employed in the search included "diabetes mellitus," "diabetic neuropathy," "polyneuropathy," and "diabetic neuropathic pain (DNP)." Both original research articles and systematic reviews were included in the analysis.* ***Results:*** *DPN is reported in up to 50% of individuals with diabetes, with higher prevalence observed in populations aged over 50 years. Clinical manifestations commonly include burning pain, tingling, numbness, and sleep disturbances. Delayed diagnosis remains a major challenge, often resulting in irreversible complications such as foot ulcers and amputations. Pharmacologic management—comprising serotonin-norepinephrine reuptake inhibitors, sodium channel blockers, and certain antidepressants—provides symptomatic relief but lacks disease-modifying efficacy. Evidence supports that early identification and comprehensive management strategies can mitigate disease progression and improve patient-reported outcomes.* ***Conclusion:*** *Diabetic polyneuropathy constitutes a major public health concern due to its high prevalence, diagnostic challenges, and adverse impact on quality of life and healthcare resources. Enhancing early detection and implementing multidisciplinary management protocols are essential to reducing the individual and systemic burden of the disease.*

Keywords: Diabetes Mellitus; Diabetic Polyneuropathy; Epidemiology; Neuropathic Pain; Diagnostic Delay; Socioeconomic Burden; Peripheral Neuropathy; Quality of Life; Chronic Complications

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from either impaired insulin secretion, insulin resistance, or both. It arises due to the pancreas's inability to produce adequate insulin or the body's ineffective utilization of the insulin it produces (1). Globally, DM represents a major public health burden, affecting both developed and developing countries. As of 2024, an estimated 593 million adults are living with diabetes worldwide, a figure projected to rise to 643 million by 2030 and 783 million by 2045 (2,3). Among all cases, type 2 diabetes mellitus (T2DM) constitutes approximately 90–95%, while the remaining cases are attributed to type 1 diabetes and other specific types (4).

The escalating global prevalence of DM is largely attributed to urbanization, sedentary lifestyles, aging populations, obesity, genetic predisposition, and various socio-environmental determinants (5,6). In addition to its direct metabolic consequences, diabetes significantly increases the risk of chronic complications affecting multiple organ systems, including the kidneys, retina, cardiovascular system, and peripheral nerves (1,7). Common complications include diabetic retinopathy, nephropathy, cardiovascular disease, foot ulcers, and diabetic neuropathy (8).

Among these complications, diabetic polyneuropathy (DPN) is one of the most prevalent and debilitating, with a substantial impact on functional ability and quality of life. It is a disorder of the peripheral nervous system and presents with symptoms such as pain, numbness, burning sensations, and sensory deficits, particularly in the lower limbs (9,10). Despite its high prevalence, estimates of DPN incidence vary considerably across studies due to differences in diagnostic criteria and population characteristics (11). It affects both middle-aged and elderly individuals and is particularly common in obese and poorly controlled diabetic patients (12).

DPN is a leading cause of diabetic foot ulcers and lower limb amputations and contributes significantly to disability and healthcare costs (2,10). Pharmacological interventions—including antidepressants, sodium channel blockers, and serotonin-norepinephrine reuptake inhibitors—can provide symptomatic relief but are not curative (13). Early identification and effective management are critical for preventing progression and reducing complications.

Despite the high disease burden, there remains a lack of comprehensive reviews addressing the epidemiological patterns, diagnostic challenges, therapeutic options, and socioeconomic impact of diabetic polyneuropathy in clinical practice, especially in low- and middle-income countries. Therefore, this review aims to summarize the current literature on the epidemiology, diagnostic approaches, and economic burden of diabetic polyneuropathy to support improved awareness, early detection, and patient-centered care strategies.

Methodology

A comprehensive and systematic narrative review was conducted to explore the epidemiological patterns, diagnostic challenges, and socioeconomic burden associated with diabetic polyneuropathy (DPN). Relevant literature was identified through searches in two major biomedical databases: PubMed and EMBASE. The search strategy incorporated the use of controlled vocabulary and free-text terms,

including the keywords: "diabetes mellitus," "diabetic neuropathy," "polyneuropathy," and "diabetic neuropathic pain (DNP)." Boolean operators such as "AND," "OR," and "NOT" were applied to refine the search and ensure inclusivity while minimizing irrelevant results.

The review was limited to peer-reviewed articles published in the English language between 2014 and 2024 to ensure contemporary relevance. Studies were considered eligible if they met the following inclusion criteria:

1. Research conducted on human subjects;
2. Full-text availability;
3. Studies with clearly defined objectives, robust methodological design, and sufficient sample size;
4. Articles that directly addressed aspects of epidemiology, diagnostic practices, clinical burden, or socioeconomic impact of DPN.

Articles were excluded if they:

- Were published prior to 2014;
- Were not available in full-text;
- Lacked methodological rigor or relevance to the core objectives of the review;
- Were published in languages other than English.

The screening and selection process was performed manually by the author to ensure the accuracy and quality of included studies. Special emphasis was placed on evaluating the methodological soundness of each article, including aspects such as study design, sample population, and statistical validity where applicable.

As this article represents a narrative literature review**,** no meta-analytical or statistical synthesis was conducted. Instead, findings were qualitatively synthesized and discussed to highlight trends, gaps, and implications in the context of diabetic polyneuropathy.

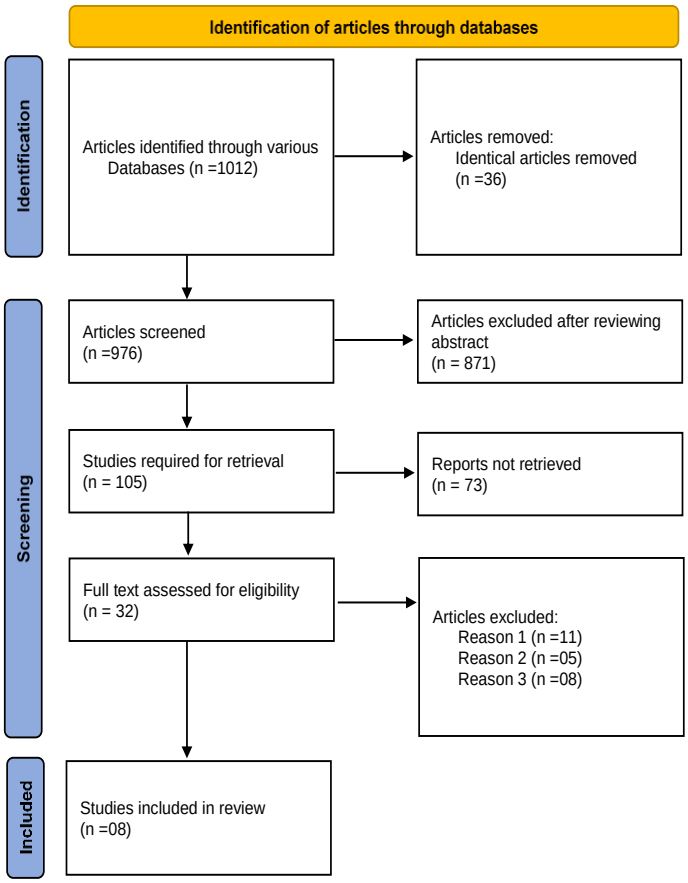

Fig1: PRISMA chart for literature search diabetic neuropathy

Results

During the initial literature search using PubMed and EMBASE, a total of 1,012 articles were identified using the selected keywords. After applying the inclusion and exclusion criteria—based on relevance, methodological rigor, study design, and language—eight studies were finalized and included in this review.

A high degree of heterogeneity was noted among the selected studies with respect to the definition of diabetic neuropathy**,** sample sizes**,** target populations**,** and statistical approaches. Some studies included both diabetic and prediabetic individuals when assessing the prevalence of neuropathy.

The prevalence of diabetic neuropathy varied widely across studies. For example, one study reported a prevalence rate of 25.8%**,** while another reported a significantly lower rate of **11.2%** (14). Similarly, the prevalence of neuropathic pain among diabetic patients ranged from **8.7% to 14%** across various studies (15).

The impact of diabetic polyneuropathy on quality of life was consistently reported as negative, with affected patients experiencing decreased mobility, increased pain, and emotional distress (16). Prevalence rates were notably lower in non-diabetic individuals as compared to those with diabetes (17).

A significant difference in prevalence was also observed between Type 1 and Type 2 diabetes mellitus. One study reported a prevalence of 7% among Type 1 diabetic patients and 22% in those with Type 2 diabetes (18). Furthermore, approximately 43% of patients reported symptoms such as anxiety, sleep disturbances, and social disconnection due to diabetic neuropathy (19).

The risk of falling in elderly patients with diabetic neuropathy was alarmingly high, estimated at 69.5% in one study (20). Several metabolic and lifestyle-related risk factors were consistently associated with the development and progression of diabetic polyneuropathy, including poor glycemic control (elevated HbA1c), obesity, smoking, high LDL cholesterol, and elevated triglycerides (21, 22). Lowering triglyceride and cholesterol levels was shown to significantly reduce the progression of neuropathy in affected individuals (23).

Annual screening and early diagnosis were emphasized across multiple studies. Patients with Type 2 diabetes mellitus are advised to undergo annual screening for neuropathy even in the absence of symptoms. When symptoms such as burning feet, numbness, tingling, or muscle **weakness** are present, immediate clinical evaluation is recommended (24).

The Diabetic Neuropathy Study Group classified diabetic neuropathy into three categories based on severity and symptomatology:

- **Confirmed neuropathy** (evident on nerve conduction studies),
- **Probable neuropathy** (decreased or altered sensation), and
- **Possible neuropathy** (subjective symptoms such as burning, aching, or sleep disturbances).

Regarding socio-demographic patterns, diabetic neuropathy showed a higher prevalence in males (60%) compared to females (40%)**,** yielding a male-to-female ratio of 1.5:1 in one health survey (25). The condition was more prevalent in industrialized countries, particularly among individuals over 50 years of age, and more frequently observed in **overweight and obese** patients.

Discussion

Diabetic polyneuropathy (DPN) remains one of the most frequent and This review highlights the widespread and multifactorial burden of diabetic polyneuropathy (DPN), underscoring the need for comprehensive screening, prevention, and management strategies. The marked variation in reported prevalence rates **(**11.2% to 25.8%) across studies may be due to inconsistencies in diagnostic criteria, population characteristics, and methodological approaches (14,15). This heterogeneity emphasizes the need for standardization in defining and diagnosing DPN in both clinical and research settings.

One critical observation is that neuropathy is significantly more prevalent in patients with Type 2 diabetes compared to those with Type 1, with reported rates of 22% vs. 7%, respectively (18). This may be attributable to the longer asymptomatic duration and often-late diagnosis of Type 2 diabetes, allowing complications like neuropathy to develop unnoticed.

In addition to its sensory and motor complications, diabetic neuropathy profoundly impacts emotional well-being**.** Affected individuals commonly report anxiety, poor sleep, and social withdrawal (19), factors that further impair quality of life and functional independence. The observed 69.5% fall risk among elderly patients with DPN (20) illustrates the disabling nature of this complication and the importance of fall prevention measures in clinical care.

This review further confirms that metabolic control plays a pivotal role in the development of neuropathy. Studies identifying elevated HbA1c, LDL cholesterol, and triglycerides as risk factors (21,22) support the hypothesis that better glycemic and lipid management may mitigate neuropathic complications. Lifestyle modifications such as weight reduction and smoking cessation are also shown to be beneficial and should be integral to preventive strategies.

The review also identified a clear lack of consensus regarding diagnostic thresholds**.** While expert guidelines recommend annual screening for all Type 2 diabetes patients, many individuals remain undiagnosed until complications arise (24). There is an urgent need for standardized protocols for early diagnosis, ideally incorporating both clinical examination and objective tests such as nerve conduction studies and validated symptom scores.

Finally, the gender differences and regional disparities in prevalence (25) suggest that socio-cultural and healthcare access factors may influence disease outcomes. Male predominance and higher rates in developed countries may reflect a combination **of** lifestyle factors, health-seeking behavior, and diagnostic resources**.**

This review also acknowledges several limitations. Only studies published in English were included, potentially omitting valuable insights from non-English literature. The review was restricted to a limited number of databases, and no meta-analysis or pooled statistical synthesis was conducted. Additionally, interventional trials (e.g., RCTs) were not the primary focus and should be addressed in future systematic reviews. Being a single-author review, the potential for subjective bias in article selection and interpretation exists.

Conclusion

Diabetic polyneuropathy (DPN) remains one of the most frequent and disabling complications of diabetes mellitus, contributing significantly to reduced quality of life, increased morbidity, and long-term healthcare costs. Despite its high prevalence—affecting nearly half of all diabetic individuals—DPN is frequently underdiagnosed or misdiagnosed, particularly in the early stages when symptoms such as burning sensations or mild paresthesia may be overlooked. If left unrecognized, DPN can progress to complete sensory loss, motor impairment, and serious outcomes such as foot ulcers and amputations.

Currently, tight glycemic control remains the cornerstone of both prevention and progression delay in diabetic neuropathy, as there is no definitive curative therapy available. However, the burden of DPN highlights the urgent need for standardized diagnostic criteria, improved screening protocols, and the integration of multidisciplinary care to identify high-risk patients early and implement tailored interventions.

Future research should prioritize high-quality randomized controlled trials to evaluate pharmacological and non-pharmacological interventions, explore biomarkers for early detection, and assess cost-effective screening tools. Expanding literature searches to include multiple languages and databases will strengthen future reviews and improve the generalizability of findings.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned.

Consent for publication

Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

MN (Medical Practitioner)

Study design, manuscript review, and critical input.

Conception of Study, Development of Research Methodology Design, and manuscript preparation

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

References

1. Farmaki P, Damaskos C, Garmpis N, Garmpi A, Savvanis S, Diamantis E. Complications of the Type 2 Diabetes Mellitus. Curr Cardiol Rev. 2021;16(4):249–51. https://doi.org/10.2174/1573403X1604201229115531
2. Cancelliere P. A Review of the Pathophysiology and Clinical Sequelae of Diabetic Polyneuropathy in the Feet. J Diabetes, Metab Disord Control. 2016;3(2):21–4. https://doi.org/10.15406/jdmdc.2016.03.00062
3. Syed O, Jancic P, Knezevic NN. A Review of Recent Pharmacological Advances in the Management of Diabetes-Associated Peripheral Neuropathy. Pharmaceuticals (Basel). 2023 May;16(6). https://doi.org/10.3390/ph16060801
4. Xu G, Liu B, Sun Y, Du Y, Snetselaar LG, Hu FB, et al. Prevalence of diagnosed type 1 and type 2 diabetes among US adults in 2016 and 2017: population based study. BMJ. 2018 Sep;362:k1497. https://doi.org/10.1136/bmj.k1497
5. Taylor R. Understanding the cause of type 2 diabetes. Lancet Diabetes Endocrinol [Internet]. 2024 Sep 1;12(9):664–73. Available from: https://doi.org/10.1016/S2213-8587(24)00157-8 https://doi.org/10.1016/S2213-8587(24)00157-8
6. Suja. T, Appavu S, Sasikala. D. Prevalence of Peripheral Neuropathy: A Cross Sectional Study among Diabetic Patients. Res Rev Int J Multidiscip [Internet]. 2025;10(2):283–292. Available from: https://doi.org/10.31305/rrijm.2025.v10.n2.031
7. Gregg EW, Buckley J, Ali MK, Davies J, Flood D, Mehta R, et al. Improving health outcomes of people with diabetes: target setting for the WHO Global Diabetes Compact. Lancet. 2023;401(10384):1302–12. https://doi.org/10.1016/s0140-6736(23)00001-6
8. Naik DA. Drug utilisation study of oral Anti Diabetic drugs in a Tertiary care hospital in semi urban region of western Maharashtra htra" (Doctoral dissertation). https://mitmimer-ir.tiss.co.in/jspui/bitstream/123456789/51/1/Dr.Alisha%20Naik%20-Pharmacology%202018-21%2040.pdf
9. Callaghan BC, Reynolds E, Banerjee M, Chant E, Villegas-Umana E, Feldman EL. Central Obesity is Associated With Neuropathy in the Severely Obese. Mayo Clin Proc. 2020;95(7):1342–53. https://doi.org/10.1016/j.mayocp.2020.03.025
10. Perveen W, Ahsan H, Rameen Shahzad, Fayyaz S, Zaif A, Paracha MA, et al. Prevalence of peripheral neuropathy, amputation, and quality of life in patients with diabetes mellitus. Sci Rep [Internet]. 2024;14(1):1–10. Available from: https://doi.org/10.1038/s41598-024-

65495-2
11. Gylfadottir SS, Christensen DH, Nicolaisen SK, Andersen H, Callaghan BC, Itani M, et al. Diabetic polyneuropathy and pain, prevalence, and patient characteristics: A cross-sectional questionnaire study of 5,514 patients with recently diagnosed type 2 diabetes. Vol. 161, Pain. 2020. 574–583 p. https://doi.org/10.1097/j.pain.0000000000001744
12. Cheng Y, Cao W, Zhang J, Wang J, Liu X, Wu Q, et al. Determinants of Diabetic Peripheral Neuropathy and Their Clinical Significance: A Retrospective Cohort Study. Front Endocrinol (Lausanne). 2022;13(July):1–8. https://doi.org/10.3389/fendo.2022.934020
13. Jang HN, Oh TJ. Pharmacological and Nonpharmacological Treatments for Painful Diabetic Peripheral Neuropathy. Diabetes Metab J. 2023;47(6):743–56. DOI: https://doi.org/10.4093/dmj.2023.0018
14. Iqbal Z, Azmi S, Yadav R, Ferdousi M, Kumar M, Cuthbertson DJ, et al. Diabetic Peripheral Neuropathy: Epidemiology, Diagnosis, and Pharmacotherapy. Clin Ther [Internet]. 2018;40(6):828–49. Available from: http://dx.doi.org/10.1016/j.clinthera.2018.04.001
15. Pop-Busui R. Diagnosis and treatment of painful diabetic peripheral neuropathy. Am Diabetes Assoc. 2022;1–32. https://doi.org/10.2337/db2022-01
16. Vileikyte L. Quality of life of persons with painful diabetic neuropathy: How can we improve it? Diabetes Res Clin Pract [Internet]. 2023;206(S1):110756. Available from: https://doi.org/10.1016/j.diabres.2023.110756
17. Ogretmen B. 乳鼠心肌提取 HHS Public Access. Physiol. Behav. 2019;176(3):139-48.
18. Sempere-Bigorra M, Julián-Rochina I, Cauli O. Differences and similarities in neuropathy in type 1 and 2 diabetes: A systematic review. J Pers Med. 2021;11(3):NA. https://doi.org/10.3390/jpm11030230
19. Perveen W, Ahsan H, Shahzad R, Fayyaz S, Zaif A, Paracha MA, et al. Prevalence of peripheral neuropathy, amputation, and quality of life in patients with diabetes mellitus. Sci Rep [Internet]. 2024;14(1):14430. Available from: https://doi.org/10.1038/s41598-024-65495-2
20. Maria, Khan A, Rahat A, Haleem F, Khalid Z, Gulalai. Frequency of Fall Risk in Patients with Diabetic Peripheral Neuropathy and its Impact on Quality of Life. J Heal Rehabil Res. 2024;4(1):825–30. https://doi.org/10.61919/jhrr.v4i1.504
21. Alam U, Fawwad A, Shaheen F, Tahir B, Basit A, Malik RA. Improvement in Neuropathy Specific Quality of Life in Patients with Diabetes after Vitamin D Supplementation. J Diabetes Res. 2017;2017. https://doi.org/10.1155/2017/7928083
22. Srinivasan S, Singh P, Kulothungan V, Sharma T, Raman R. Relationship between triglyceride glucose index, retinopathy and nephropathy in Type 2 diabetes. Endocrinol Diabetes Metab. 2021;4(1):1–8. https://doi.org/10.1002/edm2.151
23. Smith S, Normahani P, Lane T, Hohenschurz-Schmidt D, Oliver N, Davies AH. Prevention and Management Strategies for Diabetic Neuropathy. Life. 2022;12(8):1–28. https://doi.org/10.3390/life12081185
24. Yang Z, Zhang Y, Chen R, Huang Y, Ji L, Sun F, et al. Simple tests to screen for diabetic peripheral neuropathy. Cochrane Database Syst Rev. 2018;2018(7):2–5. https://doi.org/10.1002/14651858.CD010975
25. Richards SE, Wijeweera C, Wijeweera A. Lifestyle and socioeconomic determinants of diabetes: Evidence from country-level data. PLoS One [Internet]. 2022;17(7 July):1–20. Available from: http://dx.doi.org/10.1371/journal.pone.0270476