Mapping the Journey of Patients with Painful Diabetic Peripheral Neuropathy in the Philippines

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ABSTRACT

Objective. Knowing the limited epidemiological studies on painful diabetic peripheral neuropathy (pDPN) in the Philippines, the present review aimed to map the prevalence of pDPN and identify the associated healthcare gaps.

Materials and Methods. A systematic search of MEDLINE, Embase and BIOSIS was conducted using predefined inclusion criteria, and relevant studies published in English between 2004 and 2021 were identified. An unstructured literature search was also conducted on public and government websites with no date restriction. Data combined from all sources were synthesized and presented as a simple mean.

Results. Three studies were considered for final analyses of the 26 articles retrieved from structured and unstructured searches. The sample sizes for the three studies were 103, 172, and 100, respectively. The simple mean prevalence of pDPN was estimated at 26.5%. Awareness of pDPN based on a published study was 89%. According to published studies, screening and diagnosis of pDPN were 65% and 76.7%, respectively. One-third of the patients with pDPN (75%) were treated. No literature is available for adherence and control.

Conclusion. Limited data exist on the different management stages of patients with pDPN in the Philippines. The study analysis will help address the knowledge gaps, improve patient care and pain management, and aid decision-making.

Keywords: diabetes mellitus, painful diabetic peripheral neuropathy, patient journey, Philippines

INTRODUCTION

Diabetes mellitus (DM) is a global health challenge, affecting 463 million adults (aged 20-79 years) and is projected to increase to 700 million by 2045.[1] In the Philippines, 6.3% of the total adult population suffer from diabetes.[2] The direct diabetes-related expenditure per person is estimated at around USD 428, and indirect expenditure at USD1,136 per person in the Philippines, indicating a growing financial burden.[3] Diabetic peripheral neuropathy (DPN) is a frequent microvascular complication of diabetes, resulting in high morbidity and mortality. Oxidative stress caused by AGE (advanced glycation end-products) is responsible for microscopic vascular damage hindering blood supply to the peripheral nerves. Certain pro-inflammatory cytokines, including Interleukin 6 (IL-6) and Tumor Necrosis Factor-alpha (TNF-α), are also increased during hyperglycemia and contribute to nerve cell damage.[4] DPN is associated with prolongation of diabetes, hyperlipidemia,

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and poor glycemic control, affecting up to 60% of patients in the Philippines.[5-7] The common DPN phenotype is painful diabetic neuropathy (pDPN), mainly affecting the lower limbs. While most manifestations are seen in the foot, the upper extremities (fingertips and palms) also seem involved. Furthermore, pDPN affects the quality of life (QoL) and can result in anxiety, depression, and sleep disturbance. This reduces productivity and results in higher healthcare resource utilization and costs.[6,8]

Despite the enormous burden, epidemiological information is sparse. A South Asian community study of 15,000 patients reported painful neuropathy in 34% of patients with diabetes, whereas the prevalence of pDPN in Korea and Japan was said to be 14.4% and 22.1%, respectively.[9-11] Relative to other countries in the South-East region, limited data on the prevalence of patients with pDPN in the Philippines are available. In a large proportion of patients, pDPN remains underdiagnosed and undertreated.[12] Also, the failure of the patients to relate their pain with diabetes results in the under-reporting of pDPN to their clinician.[13,14] Therefore, early screening for symptoms and signs of pDPN is crucial in patients with diabetes to enable intervention.[15] Of commonly deployed screening resources for detecting pDPN in developed countries, a few have been translated from English to local Filipino languages and validated for clinical use.[16] This includes the Filipino version of the MNSI (Michigan Neuropathy Screening Instrument) questionnaire, SigN-PQ_Neuropathic Pain Questionnaire, and Pain-DETECT Questionnaire (PDQ).[16-19] However, there is limited use of the tool on QoL.[20] Also, the perceptual disparity was studied among patients and specialists in a survey from the South Asian countries, where patients believed that primary care providers diagnosed pDPN less often, unlike physicians who thought that primary care physicians (PCPs) had contributed to the majority of the diagnosis of pDPN.[21]

Although several empirical treatments have been experimented with to slow the disease progression while achieving glycemic goals and providing symptomatic relief in pDPN, poor patient awareness, affordability issues, limited consultation hours, and lower treatment priorities regarding pDPN compared to the other clinical conditions, have been significant barriers.[22] The Philippines has a low physician-to-household ratio, and physicians mainly focus on diseases with associated morbidity and mortality risk, indicating prioritization issues. Although several clinical practice guidelines are available with recommendations for antidepressants, anticonvulsants, opioids, and topical agents to render symptomatic relief of the pain, these have not resulted in significant changes in clinical practice.[5,15,22,23] Physicians consider the diagnosis and treatment of DPN and pDPN as a low priority compared to glycemic control, management of lipid disorders, and complications, including retinopathy and nephropathy.[21]

Despite such a non-linear journey for patients with pDPN, patient journey touchpoints (awareness, screening, diagnosis, treatment, adherence, and control) are less researched and documented in the Philippines, unlike in developed countries. Evidence mapping and corresponding identification of epidemiology and practice gaps benefit healthcare providers and patients and enable patient-centric steps by the government with necessary policy reforms and research and advocacy promotions. This kind of evidence mapping is possible through systematic synthesis and review of the evidence from published literature and actionable real-world insights from local healthcare providers.

The current review aimed to synthesize the knowledge about Philippine-specific epidemiology and patient journey touchpoints for pDPN. It also identified gaps across the patient journey touchpoints that can support decision-making and improve patient outcomes in the Philippines.

MATERIALS AND METHODS

The study used evidence mapping and a systematic data review approach based on a systematic literature search combined with an unstructured search. It is followed by validation, synthesis, and quantitative mapping of the prevalence data and different patient disease journey touchpoints, including disease awareness, screening and diagnosis, treatment, adherence, and control of patients with pDPN in the Philippines (Table 1).[24] Six steps were used to construct the evidence map: a) developing a comprehensive search strategy; b) establishing the inclusion and exclusion criteria; c) screening and shortlisting; d) supplementing with additional and local data; e) data extraction and synthesis; f) evidence mapping.

Quantitative analysis is often associated with numerical analysis, where data is collected, classified, and computed for specific findings using statistical methods. It is concerned with the study of data that cannot be quantified. This type of data is about the understanding and insights into the properties and attributes of objects (participants).[25]

Structured and unstructured literature search

The structured literature search was conducted using the Embase, MEDLINE, and BIOSIS electronic databases using medical subject headings (MeSH) terms and keywords for pDPN in conjunction with search terms related to

Incidence or Prevalence or Occurrence or burden or Epidemiolog* or Screen* or Treat* or Management or Therap* or Aware* or Unaware* or Knowledge or Diagnos* or Undiagnos* or Adheren* or Complian* or nonadheren* or non-adheren* or Control* or uncontrol* or Untreat* AND philippin* OR philipin* OR filipino* OR filippino* OR phillipin* OR fillipino* OR phillippin*patient journey touchpoints. The search was performed for published literature in the English language with full-text and databases filtered for a search time limit of 2004 to 2021 to include all studies related to pDPN conducted in the Philippines. For additional data, the last search was conducted on 23 June 2021.

To address data gaps in structured search, an unstructured literature search was conducted in the Incidence and Prevalence Database (IPD), World Health Organization (WHO), Department of Health Philippines, national clinical practice and treatment guidelines, and Google Scholar with no restrictions on date limits identified in the additional searches. Duplicates or similar data were identified, and the most recent evidence was retained for inclusion in the analysis. In case of a lack of data, the search strategy and evidence sources were adjusted. The complete search strategy is presented in Table 1.

Inclusion and Exclusion Criteria

Studies were eligible for inclusion if they were: i) systematic review or meta-analysis, randomized controlled study, observational study, narrative reviews (full-texts published and conference abstracts), ii) adult populations aged ≥18 years old with neuropathic pain, iii) reporting quantitative epidemiological data from patient journey touchpoints for neuropathic pain, including awareness, screening, diagnosis, treatment, adherence and control iv) studies conducted on patient populations with neuropathic pain, focusing exclusively on pDPN.

Studies published before 2004, non-English language publications, case studies, letters to the editor, editorials, studies including specific patient subgroups, and duplicate records without full text were excluded.

Study selection

An independent reviewer conducted both structured and unstructured searches. The titles and abstracts of the retrieved publications were screened against the inclusion and exclusion criteria. A second independent reviewer assessed these search results based on study title, article citation, author names, year of publication, abstract, study design, study participants, and study setting and excluded the non-relevant publications. Any disagreements were reconciled by discussion among the reviewers. Where nationally representative populations from studies with a sample size of ≥500 were unavailable, data points from studies that included only a population sub-group, single-center experience, or with a sample size of <500 were considered eligible for inclusion. Furthermore, any identified data gaps were supplemented with publications in local languages and anecdotal data from local clinical experts.

Evidence mapping

Due to its heterogeneous nature, proper evidence mapping was impossible to demonstrate the gap between findings from published literature for patient journey touchpoints (Table 1).

RESULTS

Of the 26 articles retrieved, 25 were from the structured search and one from the unstructured search. Finally, three studies met the inclusion criteria after manually screening the available literature. A total of 2 irrelevant studies were excluded by reading the title and abstracts. To supplement data on pDPN-related stages of patient management, one relevant full-text publication on a small population, the UNITE for Diabetes Philippines, was included based on a recommendation from local experts.[7,16,21,26] Another record provided to bridge the data gap included a report from the Food and Nutrition Research Institute (FNRI) on the prevalence of diabetes in the general population, where the value for the majority of DPN in the general population was computed. Data were extracted from a total of three studies for analysis. A detailed study flow diagram with reasons for exclusion is given in Figure 1.

Description of the included studies

All of the included studies were cross-sectional studies. The sample sizes for the three studies were 103, 172, and 100, respectively. All the studies were published in the last five years. While the former research focused on DPN as a whole, the latter study included patients with pDPN as the study population. Table 1 shows the description of the included studies. It is studied from the table that there was a considerable evidence gap in the majority of patient journey touchpoints.

Data extraction and synthesis

The Philippines, with a population of 108,117,000 (108M), has a low health literacy rate of 6%.[13] Analysis of

Table 1. Brief details about Included Studies

First Author	Publication Year	Total Participants	Study Type/ Design	Prevalence	Awareness	Screening	Diagnosis	Treatment	Adherence	Control
Malik RA#	2017	100	Cross-sectional	33%*	89%	65%	–	>75%		
Diabetes Philippines (UNITE for Diabetes)	2008	172	Clinical Practice Guideline	20%*						
Pabellano-Tiongson MLG	2019	103	Cross-sectional				76.7%	–	–	–

** In the diabetic population; # Data pertaining to pDPN*
■ *Data not available* ■ *Data available*

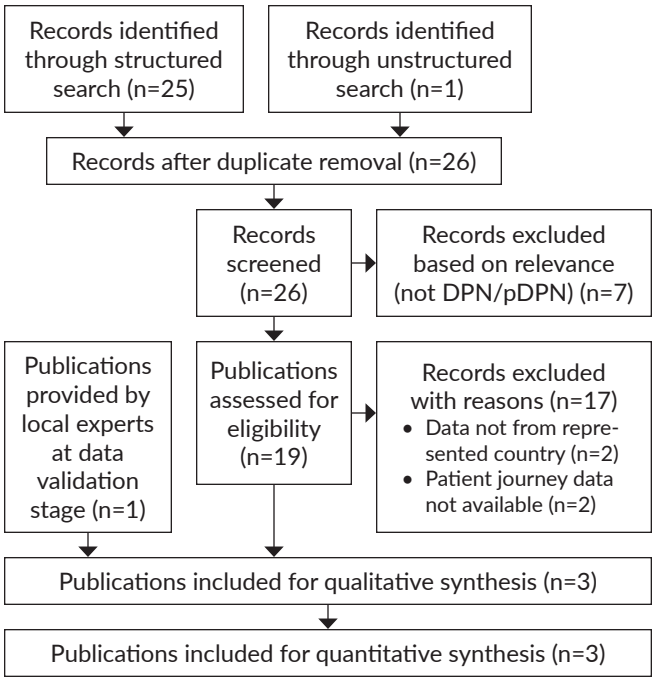

Figure 1. PRISMA Flow Diagram for pDPN studies.

data from the review indicates the occurrence of diabetic complications of neuropathy in over one-fourth of the adult diabetic population in the Philippines. The simple mean prevalence of pDPN after pooling data from the included studies was 26.5% in the adult diabetic population.[21,26] Patient's perspectives regarding who initiates pDPN discussion (awareness) were 89%.[21] Screening for detection of neuropathic symptoms was conducted in 65% of the adult Philippines diabetic population.[21] A total of 79 study participants out of 103 were diagnosed to have neuropathic pain (NP) symptoms (76.7%), which was done via electromyography-nerve conduction velocity (EMG-NCV).[16] Most of the pDPN patients were treated (75%).[21] No relevant literature was obtained for adherence and control touch points. The synthesized findings are shown in Table 2.

DISCUSSION

The present study is part of the Mapping the Patient Journey Towards Actionable Beyond the Pill Solutions (MAPS) initiative, the first systematic, evidence-based study to quantitatively assess and identify gaps associated with the prevalence and different patient journey touchpoints in pDPN in the Philippines. Despite the availability of evidence-based guidelines from the UNITE for Diabetes Philippines and the American Diabetes Association (ADA), DPN and pDPN are under-recognized, and there is a lack of population-based epidemiological data on the prevalence and management. Disparities exist in the perceptions of physicians and patients regarding the disease and symptoms, including awareness, screening, diagnosis, management, and physician-patient dialogue. No Filipino literature is available for adherence and control phases and QoL. Physicians require continuous education to ensure that patients with neuropathic symptoms are diagnosed early and effectively managed. Understanding these touch points in the patient's disease journey can improve the allocation and utilization of healthcare resources and the formulation of public policies in promoting diabetic neuropathy management.

Our literature search retrieved 25 records from structured and one record from unstructured search. Moreover, two reports were considered for inclusion at the data validation stage. However, out of the total 26, only three records met inclusion criteria, suggesting the need for rigorous research in the field of painful diabetic peripheral neuropathy in the Philippines. Also, the clinical practice guidelines were from 2008, thus implying the scope of revision with the latest information before it is fully implemented.

Despite specific initiatives by the government and several health organizations, the health literacy in the Filipino population was found to be very low (6%). This could be attributed to a lack of socio-economic support and poor public health policy in the Philippines.[27]

The prevalence of pDPN ranged from 20% to 33%, which indicates a disparity in reporting the prevalence of pDPN in the Philippines.[21,26] This variation in the prevalence estimates might be attributed to the recruitment methods, diagnostic practices, levels of disease severity, study settings, heterogeneous samples, sample size, time of onset, and definition of neuropathic pain. In the present study, the combined estimates of the pDPN prevalence are 26.5% in the adult diabetic population.

Contrary to the lower health literacy level, our study found a good level of awareness regarding pDPN (89%). The high awareness rate may be attributed to several local disease awareness campaigns. Despite the heightened awareness of Filipinos of the disease and the painful symptoms, there may be poor health-seeking behavior, and reporting of painful

Table 2. Synthesized findings on a patient journey in pDPN

Prevalence	Awareness	Screening	Diagnosis	Treatment	Adherence	Control
26.5% *†a (in diabetics) 2.1% *†a (in the general population)	89%*a	65%*a	76.7%*a	75%*‡b	No data available from peer-reviewed articles or scientific literature	No data available from peer-reviewed articles or scientific literature

** Studies including population sub-groups, single-center studies or samples size <500*
† Weighted Average; ‡ Simple Average
[a] Peer Reviewed Publication; [b] Scientific Literature

symptoms to the treating physicians may be low, resorting to over-the-counter medications for pain relief. Filipinos are also stoic and highly enduring to pain.[27] They consider suffering an opportunity to demonstrate religious virtue and do not report pain symptoms, respond to illness until advanced, or are in severe pain.[28] Hence, there is a need to address beliefs, encourage patients to seek physician consultation to manage their condition appropriately, and educate them on the risks of self-medication.

High proportions of patients feel difficulty or hesitation in describing their pain. For a chronic and debilitating complication like pDPN, the patient-physician dialogue is critical for a timely and accurate diagnosis. Difficulty expressing and reluctance to discuss the symptoms with physicians are significant communication barriers. There is a considerable gap in patient-physician communication due to the patient's belief that physicians must start communication regarding pain and symptoms. Many patients also do not consider pDPN as a serious health concern. Similarly, the majority of treatment providers do not consider pDPN management as a top priority.[21]

Screening efforts were reported, with 65% of the diabetic population being screened and 78.7% being diagnosed in the Philippines. Screening depends on the physician's practice and the index of suspicion. Although clinical guidelines recommend screening for all diabetic patients,[14] may be poorly implemented locally. Primary care centers may also be unaware of how to screen patients with neuropathic pain conditions such as pDPN, and screening tools may not be available in these facilities. Several neuropathic pain questionnaires are also available, which have been localized and validated; however, this may be poorly utilized in the clinical setting.[18-20] The high cost of diagnostic tools, such as EMG-NCV and their limited availability, restricts their utilization. However, diagnosis can be made with history and physical exam alone,[29] even without diagnostic tools, especially for remote areas or when the cost is an issue.

The majority of the patients with pDPN (75%) received treatment.[7,11,21] Despite the high treatment rate, about 70% of medications used for neuropathic pain conditions are agents that lack evidence-based efficacy data.[5] Hence, physician education must be strengthened on properly managing neuropathic pain conditions such as pDPN.

Filipino patients also have limited and incomplete information and understanding of the type of medication, dosage, and the importance of treatment compliance. The Philippines' healthcare and national insurance system do not allow comprehensive coverage of disease management. Patients need to make out-of-pocket expenses for laboratory procedures and medications. They fear potential additional costs of treatment and avoid taking medications.[30] Filipinos are afraid of taking pain medications, fearing that this might affect their kidneys or liver and that they may become addicted. There is also a misconception that all vitamins and herbal medicines are safe, without side effects. Therefore, a need to correct and address these misconceptions to avoid inappropriate intake of medications/supplements or premature discontinuation of prescribed medications.

CONCLUSION

Based on the results from the current study, we recommend future studies and research to obtain local Filipino information for adherence, control, and QoL. We further recommend continuous education to healthcare professionals, including PCPs and specialists, to enhance screening in both the public and private sectors. In the hope of reducing the social and economic costs of the disease and its complications in the future, we recommend that a program to screen for diabetes and pre-diabetic states needs to be initiated. Public health and disease awareness campaigns should be undertaken for the high-risk patient population regarding diabetes and related complications to enable a better approach and dialogue with their physicians, encourage early medical consultation for proper diagnosis and management, and address misconceptions. Similar educational programs to be undertaken for pharmacists and diabetic educators, for patient counseling, self-medication, and over-the-counter (OTC) products for disease and pain management, as well as programs to build capabilities of PCPs in the diagnosis and management of DPN and pDPN in association with societies such as the Philippine Society of Endocrinology, Diabetes and Metabolism (PSEDM) and the Philippine Neurological Association (PNA).

Study limitations

Major problems: The study undertaken has few associated limitations. Language bias was introduced by the inclusion of only English language studies, although effects were minimized with the inclusion of local publications during the data validation step. Publication bias was introduced by the inclusion of foremost full-text journals and the exclusion of non-clinical study types. Data has been extracted from limited literature, only three small population-based studies, and from using information from evidence-based guidelines and survey results.

Minor problems: A few minor issues are also associated with this manuscript: the use of non-conventional terms such as "semi-systematic review" and patient journey touchpoints.

Statement of Authorship

All authors participated in the data collection and analysis and approved the final version submitted.

Author Disclosure

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