



Website:

www.jfcmonline.com

DOI:

10.4103/jfcm.jfcm\_79\_21

Department of Family Medicine, International Medical Center Hospital. Salam Home Health Care (Geriatric Care). <sup>2</sup>Advanced Neuro-Musculoskeletal Care Center, Dr. Samir Abbas Hospital, <sup>3</sup>King Abdulaziz University, <sup>4</sup>Upjohn B.V, <sup>1</sup>Department of Diabetes and Endocrine, Dr. Suliaman Alhabib Medical Group, Riyadh, Saudi Arabia, <sup>5</sup>Africa and Middle East Clusters, Upjohn Pfizer Africa and Middle East, Dubai, UAE

### Address for correspondence:

Dr. Said A. Khader,
Department of Diabetes
and Endocrine,
Dr. Suliaman Alhabib
Medical Group, Riyadh
11643, Saudi Arabia.
E-mail: skhader@doctors.
org.uk

Received: 17-02-2021 Revised: 10-07-2021 Accepted: 23-07-2021

Published: 07-09-2021

# Management of neuropathic pain in patients with diabetic peripheral neuropathy and low back pain in Saudi Arabia: Evidence and gaps

Ashraf A. Amir, Said A. Khader<sup>1</sup>, Ziad El Chami<sup>2</sup>, Sami M. Bahlas<sup>3</sup>, Mahmoud Bakir<sup>4</sup>, Shams Arifeen<sup>5</sup>

#### Abstract:

We report existing evidence and gaps in neuropathic pain management in Saudi Arabia, the prevalence and patient management stages in diabetic peripheral neuropathy (DPN) and low back pain (LBP) with a neuropathic component. A semi-systematic approach was adopted to identify data on neuropathic pain. A structured search was conducted through MEDLINE, Embase, and BIOSIS databases to identify articles published in English between January 2010 and December 2019. Unstructured search was conducted through various sources including Google Scholar and Saudi Arabia's Ministry of Health website. Studies including populations ≥18 years and neuropathic pain were included; data gaps were supplemented with anecdotal data from local experts. Weighted or simple means were calculated for overall data; synthesized evidence was represented as an evidence gap map. Of 37 articles retrieved from structured search, none were eligible for final analyses. Thirteen articles from unstructured search and two anecdotal data sources were included for final analyses. The majority of articles included were of cross-sectional design (n = 10) in diabetes patients. The mean (range; number of articles) DPN prevalence was estimated as 33.6% (5.6%–65.3%; n = 8). Data on DPN patient management stages were limited; synthesized evidence indicated that 37.2% (0.41%-80.0%; n=3) of patients had DPN awareness, 17.8% (n=1) underwent screening, 22.4% (18.4%–65.3%; n=2) had DPN diagnosis, and 45.1% (0.0%–62.7%; n=2) received treatment for pain management. Data on LBP with neuropathic component were scarce (prevalence, 41.0% [n = 1]; diagnosis, 54.7% [n = 1]). Data are limited, so more studies are needed to accurately estimate the prevalence and stages of patient management for neuropathic pain in the country.

#### **Keywords:**

Evidence, gap, neuropathic pain, patient management, Saudi Arabia

#### Introduction

Neuropathic pain is defined as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system." [1] It affects approximately 7%–10% of the general population. [2] Neuropathic pain is commonly associated with various disease conditions, including diabetic peripheral

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

 $\textbf{For reprints contact:} WKHLRPMedknow\_reprints@wolterskluwer.com$ 

neuropathy (DPN), postherpetic neuralgia, and low back pain (LBP).<sup>[2,3]</sup>

DPN, a common complication of diabetes, is a major cause of morbidity, mortality, and poor quality of life (QoL) in patients with diabetes. [4] Neuropathic pain in DPN is associated with poorer QoL<sup>[5]</sup> and substantially higher health-care costs compared with diabetic patients without DPN. [6,7] A recent meta-analysis estimated

How to cite this article: Amir AA, Khader SA, El Chami Z, Bahlas SM, Bakir M, Arifeen S. Management of neuropathic pain in patients with diabetic peripheral neuropathy and low back pain in Saudi Arabia: Evidence and gaps. J Fam Community Med 2021;28:155-63.

the pooled prevalence of DPN in patients with diabetes as 30%. [8] In Saudi Arabia, the prevalence of DPN ranges between 29.1% and 40.0% [9,10] and neuropathic pain in DPN, between 33.2% and 34.7%. [11,12] There are multiple risk factors associated with neuropathic pain in DPN, for example, gender, duration of diabetes, and poor glycemic control. [11,12] Despite the high prevalence of DPN in Saudi Arabia, studies evaluating the risk factors and characterizing neuropathic pain management in this population are limited. [9,11-15]

Early identification of high-risk patients is crucial for the modification of risk factors and taking appropriate care of the feet to prevent DPN, and improving prognosis. [14,16] Patient education, a critical factor that drives self-management, is essential to ensure appropriate foot care and prevent secondary complications of DPN such as foot ulcers and amputations. [17] However, studies have demonstrated that awareness among patients and physicians in Middle Eastern countries regarding neuropathy and the risks of developing painful DPN and foot problems is inadequate. This was attributed to the lack of relevant education and specialized centers for the management of DPN. [18,19]

Another common pain condition associated with neuropathic pain is chronic LBP, which is defined as LBP lasting for  $\geq 3$  months. [20] The prevalence of neuropathic pain in patients with chronic LBP ranges between 41.0% and 54.7% in Saudi Arabia. [21,22] Similar to the literature in DPN, studies characterizing LBP management in Saudi Arabia are limited. A patient-centric approach, which shifts the focus from disease to the needs of the patient, is essential for effective management of the disease and measurement of outcomes. [23] Following the World Health Organization (WHO) recommendation on integrated disease management, the stages of patient journey for DPN can be broadly classified into five touchpoints: awareness, screening, diagnosis, treatment, and adherence, with the integration of palliative care across the care continuum pathway. [24] Consequently, the Mapping the Patient Journey Towards Actionable Beyond the Pill Solutions (MAPS) initiative has been conceptualized by Upjohn– A legacy of Pfizer Research Development and Medical that helps in managing diseases through patient-centric and locally relevant solutions. [25] Quantitative mapping of available evidence and identification of data gaps in terms of disease prevalence and patient management stages would enable the government and health-care authorities to implement relevant health-care policies, fund and prioritize specific research, and sponsor patient awareness programs in Saudi Arabia. This can be achieved through generation of evidence maps that involves evidence synthesis through a systematic search of a large field and identification of gaps in available data

and/or future research needs.<sup>[26]</sup> In instances where a full systematic review is not feasible or may not provide the necessary information, a semi-systematic review approach can be used.<sup>[27]</sup>

The current semi-systematic review was carried out to report the existing evidence and identify gaps in neuropathic pain management in Saudi Arabia. The objectives of this review were to specifically identify data on the prevalence, awareness, screening, diagnosis, treatment, adherence, and control of neuropathic pain in Saudi Arabia, with a focus on DPN and LBP with a neuropathic component. Further, the review provides recommendations on strategies to improve patient awareness and management in Saudi Arabia.

#### **Materials and Methods**

#### Review design

The MAPS methodology followed in our review has been described in detail elsewhere. [24,25] Preliminary literature search for LBP with a neuropathic component in Saudi Arabia yielded only a few articles. Due to the paucity of data, a separate review article on LBP with a neuropathic component was deemed unwarranted. Therefore, a semi-systematic approach was used to identify evidence on neuropathic pain in DPN and chronic LBP with a neuropathic component in Saudi Arabia. Neuropathic pain was defined as pain due to a lesion or disease of the somatosensory system, including DPN and LBP with a neuropathic component. [1]

An electronic structured search of studies published from January 2010 to December 2019 was performed through MEDLINE, Embase, and BIOSIS databases using keywords related to neuropathic pain and different stages of patient management. The comprehensive search was designed to ensure the inclusion of all studies conducted in Saudi Arabia on neuropathic pain in DPN and LBP with a neuropathic component. The full search strategy is detailed in Table 1.

An additional search (unstructured) was also conducted through Google Scholar, the Incidence and Prevalence Database, WHO website, Saudi Arabia Ministry of Health (MOH), and national clinical practice and treatment guidelines to address data gaps in structured search. No date limits were applied to the unstructured search.

#### Inclusion and exclusion criteria

The screening process was limited to articles published in the last 10 years (January 1, 2010–December 20, 2019). Eligible publications were based on: studies on adult populations (aged ≥18 years) on neuropathic pain, specifically DPN and LBP with a neuropathic component, that focused on the

prevalence and epidemiological data from stages of patient management (awareness, screening, diagnosis, treatment, adherence, and control or remission) [Table 2] from systematic reviews, meta-analyses, randomized controlled trials (RCTs), observational studies, and narrative reviews (full-texts published and conference abstracts) in Saudi Arabia.

Case studies, letters to the editor, editorials, and duplicate records were excluded. Studies published prior to 2010, publications in languages other than English, and studies that included specific patient

Table 1: Structured search strategy for neuropathic pain

pain					
Items	Details				
Structured search string	exp neuropathic pain/OR exp neuralgia/OR exp neuropathy/OR neuropath* adj5 pain OR neurogenic adj5 pain OR neuralgia OR nerve pain OR diabet* adj5 neuropath* OR nerve injury OR peripheral neuropath* OR spinal cord injury or post-operative adj5 pain AND				
	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				
	KSA or Saudi Arabia* or Saudi* or Arab*				
Database searched	MEDLINE, Embase, BIOSIS				
Limits applied	Time period: From January 1, 2010, to December 20, 2019				
	Language: English				
	Species: Humans, human				
	Full text available				
Exclusion criteria	No focus on neuropathic pain				
	Data not from representative country				
	Lack of nationally representative population				
	Relevant data on patient management stages not available				
	Not as per inclusion criteria				
	Case studies				

<sup>\*</sup>truncation symbol used in searching

Table 2: Definitions used for screening of articles

Term	Definition
Awareness	Self-reported knowledge or awareness of neuropathic pain
Screening	Proportion of patients screened using standard pain assessment tools or neurological examination
Diagnosis	Patients diagnosed with any type of neuropathic pain
Treatment	Patients taking pharmacological pain medication
Adherence	Proportion of respondents indicating adherence and/ or compliance to the prescribed pharmacological pain medication
Control	An improvement in pain symptoms, quality of life, or disease symptoms (self-reported or using an assessment tool)

subgroups (e.g. patients with comorbidities) were also excluded from the structured search.

The publications retrieved from databases were screened based on the eligibility criteria in two phases by two independent reviewers. The first phase included screening of titles and abstracts. The second phase consisted of reviewing the full-text publications. Both data collection and data extraction were conducted by two independent reviewers and any disagreements reconciled. Any identified data gaps were supplemented with anecdotal data from local clinical experts.

#### **Evidence mapping**

The weighted or simple means for the overall data from structured and unstructured searches and anecdotal data were calculated. The data on prevalence and patient management stages were exported into a data extraction grid and verified by more than one local expert to maintain consistency, provide holistic review, and refine data. The synthesized evidence was represented as an evidence gap map. Evidence gap maps are invaluable tools that help in strategic evidence-informed policymaking.<sup>[28]</sup>

#### Results

#### **Study selection**

In total, 37 articles from the structured search were retrieved (accessed through OVID). However, no relevant articles were identified for final analyses after screening the abstracts.

Articles that did not focus on neuropathic pain (n = 25) or were case studies (n = 6) were excluded. Other reasons for the exclusion of articles were nonavailability of data on stages of patient management (n = 4), data not from the representative country (n = 1), and lack of nationally representative population (n = 1).

Thirteen articles from the unstructured search were identified and included for final analyses. To supplement data on DPN-related stages of patient management, two additional data sources (anecdotal data)<sup>[29,30]</sup> were included on the recommendation of local experts. The literature search and study selection process is summarized in Figure 1.

## Literature included for diabetic peripheral neuropathy

Of the articles from unstructured search included, eight studies reported the prevalence of DPN, including neuropathic pain in DPN, ranging from 5.6% to 65.3%, in patients with diabetes in Saudi Arabia [Table 3]. [12,14,31-36] A majority of the articles were of cross-sectional design (n = 10).

Table 3: Description of the included studies

Measure of patient journey	First author, year	Sample size	Study design	Main findings		
DPN						
Prevalence	Ahmed <i>et al.</i> , 2015 <sup>[31]</sup>	350	Cross-sectional	DPN: 47.5% DPN: 19.9% Neuropathic pain in DPN: 34.7% DPN: 20.3%		
	Wang <i>et al.</i> , 2014 <sup>[14]</sup>	552	Cross-sectional			
	Algeffari 2018 <sup>[12]</sup>	242	Cross-sectional			
	Alramadan <i>et al.</i> , 2019[32]	1111	Cross-sectional			
	Alaboud et al., 2016[33]	748	Retrospective	DN: 5.6%		
	Madanat <i>et al.</i> , 2014[34]	351	Cross-sectional	DPN: 22.8%		
	Qadi and Al Zahrani 2011[35]	747	Cross-sectional	DPN: 45.4%		
	Halawa et al., 2010[36]	1039	Cross-sectional	Neuropathic pain in DPN: 65.3%		
Awareness	Algeffari 2018 <sup>[12]</sup>	242	Cross-sectional	Neuropathic pain in DPN: 0.41%		
	Alhashim et al., 2018[37]	329	Retrospective cross-sectional	DN: 56.4%		
	Edison Silvia and Ali 2017[38]	60	Descriptive comparative, cross-sectional	DPN: 80.0%		
	XX <sup>[29]</sup>	NA	NA	DPN: 40.0%		
Screening	Al-Rubeaan <i>et al.</i> , 2015[39]	62,681	Retrospective cross-sectional	DN: 17.8%		
	XX <sup>[29]</sup>	NA	NA	DPN: 75.0%		
	YY <sup>[30]</sup>	NA	NA	DPN: 30.0%		
Diagnosis	Al-Rubeaan <i>et al.</i> , 2015[39]	11,153	Retrospective cross-sectional	DN: 18.4%		
	Halawa et al., 2010[36]	1039	Cross-sectional	Neuropathic pain in DPN: 65.3%		
	YY[30]	NA	NA	DPN: 40.0%		
Treatment	Algeffari 2018 <sup>[12]</sup>	242	Cross-sectional	Neuropathic pain in DPN: 0.0%		
	Halawa et al., 2010[36]	619	Cross-sectional	Neuropathic pain in DPN: 62.7%		
	XX <sup>[29]</sup>	NA	NA	DPN: 50.0%		
	<b>YY</b> [30]	NA	NA	DPN: 20.0%		
Adherence	XX <sup>[29]</sup>	NA	NA	DPN: 80.0%		
	<b>YY</b> [30]	NA	NA	DPN: 50.0%		
Control	XX <sup>[29]</sup>	NA	NA	DPN: 60.0%		
	<b>YY</b> [30]	NA	NA	DPN: 10.0%		
LBP with a neuropathic component						
Prevalence	Hassan et al., 2004[21]	100	Cross-sectional	LBP: 41.0%		
Diagnosis	Kaki <i>et al.</i> , 2005 <sup>[22]</sup>	1169	Prospective	LBP: 54.7%		

DN: Diabetic neuropathy, DPN: Diabetic peripheral neuropathy, LBP: Lower back pain, NA: Not applicable/available

#### Touchpoints of patient management

## Awareness, screening, and diagnosis of diabetic peripheral neuropathy

Three studies reported on the awareness of DPN, including neuropathic pain in DPN, in patients. [12,37,38] The study conducted by Algeffari [12] revealed that only in 0.41% of patients, neuropathic pain in DPN was recognized by physicians in six primary health-care clinics. One study reported that over half (56.4%) of the patients with diabetes were aware of diabetic neuropathy. [37] Another study reported that 80.0% of patients had a moderate level of awareness of DPN. [38] Anecdotal evidence suggests that 40% of the patients were aware of DPN. [29]

A large retrospective study reported diabetic neuropathy screening in 17.8% of patients. [39] According to anecdotal evidence, approximately 30%–75% of patients underwent screening for DPN. [29,30]

Two studies reported on the diagnosis of DPN, one of which reported the diagnosis of neuropathic pain in DPN in 65.3% of patients.<sup>[36]</sup> Another study reported diabetic neuropathy diagnosis in 18.4% of patients.<sup>[39]</sup> Anecdotal evidence suggests the diagnosis of DPN in 40% of patients.<sup>[30]</sup>

## Treatment, adherence, and control of diabetic peripheral neuropathy

Two studies reported on the use of treatments for neuropathic pain in DPN, one of which revealed the lack of use of medication by patients to manage DPN,<sup>[12]</sup> while the other reported the use of medication by 62.7% of patients.<sup>[36]</sup>

Anecdotal evidence suggests the use of medication by 20%–50% of patients, adherence to treatment by 50%–80% of patients, and DPN control in 10%–60% of patients.<sup>[29,30]</sup>

#### Low back pain

Two articles were included from unstructured searches. [21,22] These studies reported a prevalence of

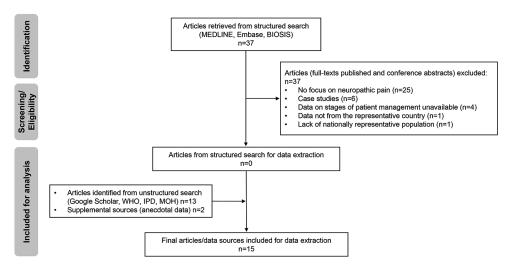


Figure 1: Flowchart of articles included in the study. IPD: Incidence and Prevalence Database, MOH: Ministry of Health, n: number of articles, WHO: World Health Organization

LBP with a neuropathic element in 41.0% of patients<sup>[21]</sup> and a diagnosis in 54.7% of patients.<sup>[22]</sup> Additional study characteristics are presented in Table 3.

#### Mapping the evidence

The data collected on the prevalence and different stages of patient management for neuropathic pain in DPN and LBP with a neuropathic component through semi-systematic review of the literature and anecdotal data are mapped as a proportion of patients against touchpoints of the patient journey [Figure 2].

#### Data extraction and synthesis

The majority of the articles focused on DPN. The weighted mean prevalence of DPN was estimated as 33.6%. The published studies provided limited quantitative evidence on patient awareness, screening, diagnosis, treatment, adherence, and control of DPN. Data on the stages of patient management extracted from the scientific literature and supplemented with anecdotal evidence for DPN in the Saudi Arabian population indicated that less than half of the patients were aware of DPN (weighted mean = 37.2%) and less than a quarter of the patients were screened by means of neurological examination or other pain assessment tools (n = 1; 17.8%) and were diagnosed with DPN (weighted mean = 22.4%). Further, less than half of the patients received treatment for pain management (weighted mean = 45.1%). The articles did not provide any evidence on adherence to treatment and DPN control. Approximately, two-third of the patients were adherent to treatment (simple mean = 65.0%) and based on anecdotal evidence, 35.0% (simple mean) of patients reported an improvement in DPN symptoms or QoL [Table 4].

Data on prevalence and diagnosis of LBP with a neuropathic component were obtained from two articles,

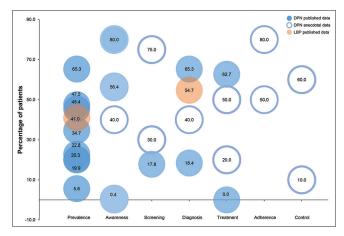


Figure 2: Evidence gap map of individual data points of prevalence and patient management stages across studies and anecdotal evidence on diabetic peripheral neuropathy and low back pain. DPN: Diabetic peripheral neuropathy, LBP: Low back pain. Individual bubbles indicate separate data sources

which did not provide any evidence on the other stages of patient management of LBP with a neuropathic component.

The evidence map highlights data gaps in all the stages of patient management of neuropathic pain in DPN and LBP with a neuropathic component [Figure 3].

#### Discussion

In this semi-systematic review, we compiled and analyzed the evidence and thereby identified gaps in different stages of management of patients in Saudi Arabia with neuropathic pain, with a focus on DPN and LBP. In this evidence gap map on neuropathic pain management in Saudi Arabia, we identified 13 articles through unstructured searches<sup>[12,14,21,22,31-39]</sup> and included two additional data sources (anecdotal data) on DPN.<sup>[29,30]</sup> A major challenge of healthcare evidence

Table 4: Patient management stages estimates from the included studies

Country and population	Literacy	Indications	Prevalence	Awareness	Screening	Diagnosis	Treatment	Adherence	Control
Saudi Arabia	84.4%*[43]	DPN	33.6%*,†	37.2%*,†	17.8%*	22.4%*,†	45.1%* <sup>,†</sup>	65.0%‡,§	35.0%‡,§
343.690.000		LBP	41.0%*	_	_	54.7%*	-	_	-

<sup>\*</sup>Peer-reviewed publication only, \*Weighted mean, ‡Anecdotal data only, \*Simple mean, in instances where published literature was available, anecdotal data were not included in the calculation of the mean values. DPN: Diabetic peripheral neuropathy, LBP: Low back pain

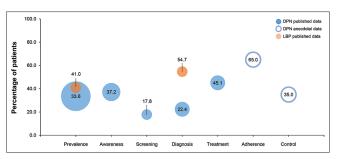


Figure 3: Evidence gap map of weighted or simple means of prevalence and patient management stages across studies and anecdotal evidence on diabetic peripheral neuropathy and low back pain. DPN: Diabetic peripheral neuropathy, LBP: Low back pain. Size of bubble indicates the number of studies/data sources. Data are represented as: Weighted means or single data points for diabetic peripheral neuropathy and low back pain published data; simple means for diabetic peripheral neuropathy anecdotal data

in the Arab countries, including Saudi Arabia is the paucity of research and publications on different medical conditions.<sup>[40]</sup>

#### Gaps in study design

A majority of the studies included in the final analyses were cross-sectional. Although these studies provide valuable information about a population at a specific time point, they lack information on temporality seen in longitudinal observational studies. Further, cross-sectional studies do not provide insights into the causal relationships that RCTs provide. [41] Our study findings indicate the need for longitudinal studies and RCTs on different stages of management of DPN and LBP with a neuropathic component in Saudi Arabia.

#### Prevalence of diabetic peripheral neuropathy

The prevalence of diabetes has been on the rise in Saudi Arabia. [42] Complications associated with diabetes especially neuropathic pain are an increasing concern in several Arab populations. [36]

In this study, the prevalence of DPN after the pooling of data was 33.6% (weighted mean) in Saudi Arabia. A wide variation in the prevalence of DPN, including neuropathic pain in DPN, was reported in the studies (5.6%–65.3%).<sup>[12,14,31-36]</sup>

In fact, the true prevalence of DPN and neuropathic pain in DPN is difficult to estimate owing to the absence of established standard diagnostic criteria and heterogeneity of patient populations.<sup>[18]</sup> More studies that use established diagnostic criteria are needed in Saudi

Arabia to estimate the true prevalence of neuropathic pain in DPN.

## Stages of patient management of diabetic peripheral neuropathy

Very few studies have evaluated awareness, screening, diagnosis, and treatment of DPN in Saudi Arabia. Further, published studies have not provided any evidence on treatment adherence and DPN control. Overall, less than half of the diabetic patients reported awareness of DPN and had treatment to manage DPN pain. Less than a quarter of patients underwent screening for DPN and had a diagnosis of DPN.

Despite high literacy rate in the identified population (84.4%<sup>[43]</sup>), low levels of awareness of DPN indicate the need for robust health education intervention programs for patients and health-care providers (HCPs) in Saudi Arabia. One of the major challenges in identifying DPN is that symptoms often do not reliably indicate the extent of nerve damage.<sup>[4]</sup> Further, there is a lack of effective screening strategy for DPN, which often results in the delay of the diagnosis of DPN until the condition deteriorates and becomes more difficult to treat.<sup>[37]</sup> This further emphasizes the importance of screening and early diagnosis of DPN.

More studies are needed in Saudi Arabia on LBP with a neuropathic component to estimate the true prevalence and patient management stages.

## Expert panel recommendations on neuropathic pain treatment

Expert panel recommendations for neuropathic pain management, especially DPN and chronic LBP with a neuropathic component in the Middle Eastern region, include pharmacological first-line (e.g. pregabalin) and second-line (e.g. tramadol) treatments and nonpharmacological approaches (e.g. stress reduction techniques and physical therapy). [44] Recommendations for physicians in the Middle East and North Africa for neuropathic pain in DPN include screening (at least annually) for symptoms of neuropathic pain using tools (e.g. Doleur Neuropathique en 4 Questions [DN4]), a thorough examination of feet for ulcers in patients with diabetes, and the treatment goal of achieving a clinically meaningful pain reduction using first-line agents. [45]

## Strategies to improve patient awareness and management in Saudi Arabia

Health and educational interventional programs could be implemented along with the establishment of screening and periodic follow-up programs for diabetic patients in Saudi Arabia.<sup>[37]</sup> It would also be beneficial to increase designated screening centers. An educational program for patients and HCPs in Saudi Arabia, to increase awareness of the care of diabetic foot and its complications, has indeed been shown to reduce the amputation rate by 8.1%.<sup>[46]</sup> Thus, training and encouraging HCPs to provide patient education on diabetes and its complications such as neuropathic pain is recommended.

Educating patients to undergo foot examination at least once a year is recommended. Early detection of DPN helps health-care professionals and patients to take on board preventive measures to avoid major complications. <sup>[9]</sup> There is a need for mandatory awareness programs in hospitals and clinics owing to the lack of formal podiatric educational services. <sup>[47]</sup> Disseminating relevant scientific information through various forums such as social media, brochures, and magazines in both local and English languages is recommended. <sup>[47]</sup> Thus, health authorities are encouraged to provide funding for training and awareness programs for diabetic patients and HCPs. <sup>[40]</sup>

#### Patient-centric approach

There is a need for patient-centric approaches, on the touchpoints of awareness, screening, diagnosis, treatment, adherence, and control, to improve health-care outcomes in patients with chronic neuropathic pain (DPN and LBP) in Saudi Arabia. Physicians could be encouraged to work collaboratively with patients to ensure successful pain management programs. [44] The MOH in Saudi Arabia could follow the approach of "The voice of the patient" used by the Food and Drug Administration in the United States. [48] In this approach, patients and their representatives provided inputs to sponsors in drug development on peripheral neuropathic pain (e.g. symptoms experienced, burden of neuropathic pain, and need for increased awareness).

Nevertheless, several measures have been taken at the national level in Saudi Arabia to bring awareness of diabetes and self-care education to all individuals. [49] The MOH in Saudi Arabia has introduced programs such as the National Executive Plan of Diabetes Control "2010–2020" and the Saudi national program of education against diabetes. The main objectives of these programs are to detect type 2 diabetes in the early stages, reduce the risk of diabetes-related complications, and help patients to control the disease/complications. [49]

The data from the current evidence gap map can be used to guide future research and patient education or awareness programs to generate evidence on neuropathic pain management in Saudi Arabia. Future reviews on patient management stages in LBP with a neuropathic component are warranted as more data evolve.

#### Strengths and limitations

This evidence gap map reported existing evidence and identified gaps using a semi-systematic approach for the management of patients with neuropathic pain in Saudi Arabia. Owing to the limited data available, accurate estimates of awareness, screening, diagnosis, and treatment could not be calculated. Further, adherence and control data for DPN were based solely on anecdotal evidence owing to the lack of relevant published literature. In addition, some studies characterized neuropathic pain in DPN, whereas others mentioned DPN only without characterizing neuropathic pain. Hence, the study results may not be representative of neuropathic pain in DPN and should be given cautious interpretation. In this paper, we neither commented on biases in the studies nor assessed the quality of reporting of findings.

#### Conclusion

There are limited data on the different stages of managing patients with neuropathic pain in DPN and LBP with a neuropathic component in Saudi Arabia. Awareness, screening, and diagnosis of DPN in patients in Saudi Arabia were low, and less than half the patients had treatment for DPN. Published literature on treatment compliance and DPN control was unavailable, and these data were based solely on anecdotal evidence from local experts in Saudi Arabia. More studies are needed to accurately estimate the prevalence and stages of patient management for neuropathic pain in Saudi Arabia.

#### Acknowledgment

We acknowledge the experts who provided insights for bridging the data gaps. The support provided by the independent reviewer, Aditi Karmarkar from Upjohn – A Pfizer division, is deeply acknowledged. We thank Tanaya Bharatan from Upjohn – A Pfizer division for critically reviewing the draft. Medical writing support was provided by Sudha Korwar and Ramu Periyasamy at Indegene and was funded by Upjohn – A legacy Division of Pfizer.

#### Financial support and sponsorship

This project was sponsored by Upjohn – A legacy Pfizer Division.

#### **Conflicts of interest**

Dr. Ashraf A. Amir, Dr. Said A. Khader, Dr. Ziad El Chami, and Dr. Sami M Bahlas have no conflicts of interest to declare. Dr. Mahmoud Bakir is an employee of Upjohn B.V., Saudi Arabia. Dr. Shams Arifeen is an employee of Upjohn, Pfizer AfME (Africa and the Middle East), Dubai, UAE.

#### References

- Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, et al. Neuropathic pain: Redefinition and a grading system for clinical and research purposes. Neurology 2008;70:1630-5.
- van Hecke O, Austin SK, Khan RA, Smith BH, Torrance N. Neuropathic pain in the general population: A systematic review of epidemiological studies. Pain 2014;155:654-62.
- Freynhagen R, Baron R. The evaluation of neuropathic components in low back pain. Curr Pain Headache Rep 2009;13:185-90.
- Tesfaye S, Selvarajah D. Advances in the epidemiology, pathogenesis and management of diabetic peripheral neuropathy. Diabetes Metab Res Rev 2012;28 Suppl 1:8-14.
- Girach A, Julian TH, Varrassi G, Paladini A, Vadalouka A, Zis P. Quality of life in painful peripheral neuropathies: A systematic review. Pain Res Manag 2019;2019:2091960.
- Dworkin RH, Malone DC, Panarites CJ, Armstrong EP, Pham SV. Impact of postherpetic neuralgia and painful diabetic peripheral neuropathy on health care costs. J Pain 2010;11:360-8.
- Kiyani M, Yang Z, Charalambous LT, Adil SM, Lee HJ, Yang S, et al. Painful diabetic peripheral neuropathy: Health care costs and complications from 2010 to 2015. Neurol Clin Pract 2020;10:47-57.
- Sun J, Wang Y, Zhang X, Zhu S, He H. Prevalence of peripheral neuropathy in patients with diabetes: A systematic review and meta-analysis. Prim Care Diabetes 2020;14:435-44.
- Sendi R, Mahrus A, Saeed R, Mohammed M, Al-Dubai SR. Diabetic peripheral neuropathy among Saudi diabetic patients: A multicenter cross-sectional study at primary health care setting. J Fam Med Prim Care 2020;9:197.
- 10. Alshaya AK, Alsayegh AK, Alshaya HK, Almutlaq BA, Alenazi NS, Rasheedi AH, *et al*. The common complications and comorbidities among Saudi diabetic patients in Northern Saudi Arabia. Open J Endocr Metab Dis 2017;07:151-61.
- AlSufyani MH, Alzahrani AM, Allah AA, Abdullah RI, Alzhrani SH, Alsaab AA. Prevalence of painful diabetic peripheral neuropathy and its impact on quality of life among diabetic patients in Western region, Saudi Arabia. J Family Med Prim Care 2020;9:4897-903.
- Algeffari MA. Painful diabetic peripheral neuropathy among Saudi diabetic patients is common but under-recognized: Multicenter cross-sectional study at primary health care setting. J Family Community Med 2018;25:43-7.
- Almohisen AA, Almuhaysen LM, Alhatlany KK, Alghalth RH, Almutairi AM, Almarzogy FA, et al. Prevalence and risk factors of diabetic neuropathy in Qassim, Saudi Arabia. Majmaah J Heal Sci 2020;8:23-31.
- Wang DD, Bakhotmah BA, Hu FB, Alzahrani HA. Prevalence and correlates of diabetic peripheral neuropathy in a Saudi Arabic population: A cross-sectional study. PLoS One 2014;9:e106935.
- 15. AlQuliti K. Predictors of painful diabetic neuropathy in Saudi Patients with type 2 diabetes: A case-control study. J Pain Relief 2015;4:181.
- Pop-Busui R, Boulton AJ, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic neuropathy: A position statement by the American diabetes association. Diabetes Care 2017;40:136-54.
- 17. Şen HM, Şen H, Aşık M, Özkan A, Binnetoglu E, Erbağ G, *et al.* The importance of education in diabetic foot care of patients with diabetic neuropathy. Exp Clin Endocrinol Diabetes 2015;123:178-81.

- 18. Petropoulos IN, Javed S, Azmi S, Khan A, Ponirakis G, Malik RA. Diabetic neuropathy and painful diabetic neuropathy in the Middle East and North Africa (MENA) region: Much work needs to be done. J Taibah Univ Med Sci 2016;11:284-94.
- Karahan AY, Kucuksarac S, Soran N, Ordahan B, Tekin L, Basaran A. Nurse's knowledge of neuropathic pain. Neurol Int 2014;6:5492.
- El Sissi W, Arnaout A, Chaarani MW, Fouad M, El Assuity W, Zalzala M, et al. Prevalence of neuropathic pain among patients with chronic low-back pain in the Arabian Gulf Region assessed using the Leeds assessment of neuropathic symptoms and signs pain scale. J Int Med Res 2010;38:2135-45.
- Hassan AE, Saleh HA, Baroudy YM, Abdul-Rahman KI, Najjar MW, Kazi MS, et al. Prevalence of neuropathic pain among patients suffering from chronic low back pain in Saudi Arabia. Saudi Med J 2004;25:1986-90.
- 22. Kaki AM, El-Yaski AZ, Youseif E. Identifying neuropathic pain among patients with chronic low-back pain: Use of the Leeds Assessment of Neuropathic Symptoms and Signs pain scale. Reg Anesth Pain Med 2005;30:422-8.
- 23. Hwang S, van Nooten F, Wells T, Ryan A, Crawford B, Evans C, et al. Neuropathic pain: A patient-centred approach to measuring outcomes. Health Expect 2018;21:774-86.
- Devi R, Kanitkar K, Narendhar R, Sehmi K, Subramaniam K. A narrative review of the patient journey through the lens of non-communicable diseases in low- and middle-income countries. Adv Ther 2020;37:4808-30.
- 25. Bharatan T, Devi R, Huang PH, Javed A, Jeffers B, Lansberg P, *et al*. A methodology for mapping the patient journey for noncommunicable diseases in low- and middle-income countries. J Healthc Leadersh 2021;13:35-46.
- Miake-Lye IM, Hempel S, Shanman R, Shekelle PG. What is an evidence map? A systematic review of published evidence maps and their definitions, methods, and products. Syst Rev 2016;5:28.
- 27. Snyder H. Literature review as a research methodology: An overview and guidelines. J Bus Res 2019;104:333-9.
- 28. Snilstveit B, Vojtkova M, Bhavsar A, Stevenson J, Gaarder M. Evidence and Gap Maps: A tool for promoting evidence informed policy and strategic research agendas. J Clin Epidemiol 2016;79:120-9.
- Amir A. Anecdotal Evidence by Dr. Ashraf Amir (Neuropathic Pain MOH Guidelines Author & Chief Medical Officer of International Medical Center [MAYO Clinic Network], Jeddah).
- 30. Khader S. Anecdotal Evidence by Dr. Said Khader (Consultant Endocrinology, Sulaiman Al-Habib Hospital, Riyadh).
- Ahmed AA, Algamdi SA, Alzahrani AM. Surveillance of risk factors for diabetic foot ulceration with particular concern to local practice. Diabetes Metab Syndr 2015;9:310-5.
- 32. Alramadan MJ, Magliano DJ, Alhamrani HA, Alramadan AJ, Alameer SM, Amin GM, et al. Lifestyle factors and macro- and micro-vascular complications among people with type 2 diabetes in Saudi Arabia. Diabetes Metab Syndr 2019;13:484-91.
- 33. Alaboud AF, Tourkmani AM, Alharbi TJ, Alobikan AH, Abdelhay O, Al Batal SM, et al. Microvascular and macrovascular complications of type 2 diabetic mellitus in Central, Kingdom of Saudi Arabia. Saudi Med J 2016;37:1408-11.
- 34. Madanat A, Sheshah E, Badawy El-B, Abbas A, Al-Bakheet A. Utilizing the Ipswich Touch Test to simplify screening methods for identifying the risk of foot ulceration among diabetics: The Saudi experience. Prim Care Diabetes 2015;9:304-6.
- 35. Qadi M, Al Zahrani H. Foot care knowledge and practice among diabetic patients attending primary health care centers in Jeddah City. J King Abdulaziz Univ Sci 2011;18:55-71.
- Halawa MR, Karawagh A, Zeidan A, Mahmoud AE, Sakr M, Hegazy A. Prevalence of painful diabetic peripheral neuropathy among patients suffering from diabetes mellitus in Saudi Arabia. Curr Med Res Opin 2010;26:337-43.

- 37. Alhashim BN, Zaher A, Albujays DS, Alhashim J, Ali SI. Study of the level of awareness of diabetic neuropathy among diabetic patients in Al-Ahsa region, Kingdom of Saudi Arabia: A cross-sectional study. Int J Sci Study 2018;5:11-4.
- Edison Silvia J, Ali LA. Awareness on risk factors for diabetic mellitus and diabetic peripheral neuropathy among the nationalities of Egypt and Saudi Arabia. Int J Med Sci Clin Invent 2017;4:3317-21.
- Al-Rubeaan K, Al Derwish M, Ouizi S, Youssef AM, Subhani SN, Ibrahim HM, et al. Diabetic foot complications and their risk factors from a large retrospective cohort study. PLoS One 2015;10:e0124446.
- 40. Ahmed AA, Elsharief E, Alsharief A. The diabetic foot in the Arab world. J Diabet Foot Complicat 2011;3:55-61.
- 41. Cartwright N. What are randomised controlled trials good for? Philos Stud 2010;147:59-70.
- 42. Alkhier Ahmed A. Epidemiology of diabetes mellitus diabetic foot problems in Saudi Arabia. Av Diabetol 2010;26:29-35.
- Alkhaldi TM, Al-Jumaili AA, Alnemer KA, Alharbi K, Al-Akeel ES, Alharbi MM, et al. Measuring the health literacy level of Arabic speaking population in Saudi Arabia using translated health literacy instruments. Pharm Pract (Granada) 2018;16:1223.
- 44. Bohlega S, Alsaadi T, Amir A, Hosny H, Karawagh AM, Moulin D,

- *et al.* Guidelines for the pharmacological treatment of peripheral neuropathic pain: Expert panel recommendations for the middle East region. J Int Med Res 2010;38:295-317.
- 45. Aizarani C, Amir AA, Benchouk Z, Abu Al-Samen MA, Farghaly M, Kandil A, et al. The dos and don'ts of painful diabetic peripheral neuropathy: Primary care guidelines for the Middle East and North Africa. Middle East J Fam Med 2017;15:4-18.
- Al-Wahbi AM. Impact of a diabetic foot care education program on lower limb amputation rate. Vasc Health Risk Manag 2010;6:923-34.
- Al Odhayani AA, Al Sayed Tayel S, Al-Madi F. Foot care practices of diabetic patients in Saudi Arabia. Saudi J Biol Sci 2017;24:1667-71.
- FDA. The voice of the patient. Neuropathic pain associated with peripheral neuropathy. [Internet]. Available from: https://www. fda.gov/files/about fda/published/The-Voice-of-the-Patient--Neuropathic-Pain-Associated-with-Peripheral-Neuropathy.pd. [Last accessed on 2020 Aug 31].
- 49. Ministry of Health. Vision 2030. Kingdom of Saudi Arabia. MOH Publications. Available from: https://www.moh.gov.sa/en/Ministry/MediaCenter/Publications/Pages/Publications-2013-06-09-004.aspx. [Last accessed on 2020 Aug 31; Last updated on 2013 Jun 09].