

The Burden of Cancer-related Neuropathic Pain: A Multi-centric Cross-sectional Observational Study from North India

Aanchal Satija, Anjum Khan Joad¹, Shiv Pratap Singh Rana², Sushma Bhatnagar

Department of Onco-Anesthesia and Palliative Medicine, Dr B.R. Ambedkar, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, ¹Department of Anesthesia and Palliative Care, Bhagwan Mahaveer Cancer Hospital and Research Centre, Jawahar Lal Nehru Marg, Jaipur, Rajasthan, ²Department of Pain and Palliative Medicine, Fortis Hospital, Noida, Uttar Pradesh, India

Abstract

Introduction: Neuropathic cancer pain is a common consequence of cancer itself and anti-cancer treatments. It is a complex phenomenon, often underdiagnosed by physicians or underreported by patients. Its diagnosis and management are usually more challenging than nociceptive pain. There is a dearth of epidemiological evidence for neuropathic pain in cancer patients in India. Screening questionnaires serve as a quick guide to identify potential cases of neuropathic pain. The aim of the present study was to identify the burden of cancer-related neuropathic pain using the Self-reported version of the Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) pain scale. **Methodology:** This was a cross-sectional, observational, multi-centric study conducted at three hospitals in North India. From January 2017 to October 2017, patients attending pain clinic were screened for participation in the study. Adults aged ≥ 18 years and experiencing the pain of oncologic origin were eligible to participate in the study if they provided informed consent. S-LANSS questionnaire was used to screen patients with neuropathic pain. **Results:** From a total of 261 patients, who were enrolled in the study, 56.7% were male and their mean age was 50.87 (18–80) years. Fifty-four percent patients had pain with predominantly neuropathic component (S-LANSS score ≥ 10). **Conclusion:** High burden of neuropathic cancer pain has been observed in outpatient palliative care settings. Early diagnosis of neuropathic pain through screening questionnaires can serve as a quick guide for physicians in resource-constrained settings. This will allow identification of the neuropathic component of pain in patients suffering with mixed pain.

Keywords: Cancer, India, neuropathic pain, questionnaire, Self-reported Leeds Assessment of Neuropathic Symptoms and Signs

INTRODUCTION

With the advent of newer and efficient diagnostic techniques and therapeutic modalities, the number of people living with cancer are increasing.^[1] Pain is one of the most common symptoms reported by patients during the disease trajectory.^[2] It affects nearly 39%–66% patients during various stages of disease and treatment.^[3] It may be either nociceptive, neuropathic, or mixed.^[4] The International Association for Study of Pain has defined neuropathic pain as “pain caused by a lesion or disease of the somatosensory nervous system.”^[5] Pain (both nociceptive and neuropathic) in cancer patients can have multiple etiologies. It can arise as a result of direct tumor itself, disease metastasis or side-effect of anti-cancer treatment.^[6] Cancer-related neuropathic pain can result from radiculopathies, plexopathies, peripheral neuropathies, spinal cord compressions, leptomeningeal metastasis or cranial

neuralgias. While treatment-related neuropathic pain may be categorized as postsurgery or postradiation syndromes or induced by chemotherapeutic agents.^[7] Identifying the nature and type of pain is the central tenet to provide adequate analgesia to patients.^[4] Treatment for neuropathic pain is often challenging and requires medications and/or interventions distinct from those for managing nociceptive pain.^[8] In addition, this pain has been seen to be associated with poor physical, social and cognitive social functioning; it negatively

Address for correspondence: Dr. Anjum Khan Joad, Department of Anesthesia and Palliative Care, Bhagwan Mahaveer Cancer Hospital and Research Centre, Jawahar Lal Nehru Marg, Jaipur - 302 017, Rajasthan, India.
E-mail: anjumjoad@gmail.com

Submitted: 27-Jul-20 **Accepted:** 02-Oct-20

Published: 17-Feb-21

Access this article online

Quick Response Code:



Website:
www.jpalliativecare.com

DOI:
10.4103/IJPC.IJPC_277_20

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.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Satija A, Joad AK, Rana SP, Bhatnagar S. The burden of cancer-related neuropathic pain: A multi-centric cross-sectional observational study from North India. *Indian J Palliat Care* 2021;27:104-8.

influences patient's treatment outcomes and significantly interferes with daily activities and quality of life.^[4,7,9]

In a systematic review conducted by Bennett *et al.*, prevalence of neuropathic cancer pain ranged from 19% to 39%.^[10] However, in a retrospective study conducted at a tertiary cancer center in India, the burden of neuropathic pain was far lower than global data (i.e., 11.8%).^[8] Thus, despite the widespread recognition of cancer-related neuropathy, there is a paucity of multi-centric studies to determine the burden of neuropathic cancer pain in Indian patients. Neuropathic pain is underdiagnosed by physicians and underreported by patients, thereby compounding the complexity of screening and treatment.^[11] Recent controlled studies support that chemotherapy-induced neuropathic pain is significantly underdiagnosed and underreported by physicians as compared to patients.^[12-14] This can be overcome using screening and assessment questionnaires for diagnosis and management of neuropathic cancer pain, respectively.^[15] There is a need for more epidemiological information about cancer-related pain across India.^[16] The aim of the present study was to identify the burden of cancer-related neuropathic pain using a validated screening questionnaire.

METHODOLOGY

This was a cross-sectional, observational, multi-centric study conducted at three hospitals— Department of Onco-anesthesia and Palliative Medicine at Dr B. R. Ambedkar, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi; Department of Anesthesiology and Palliative Medicine, Bhagwan Mahaveer Cancer Hospital and Research Centre, Jaipur; and Department of Anesthesiology, Critical Care and Pain Medicine, Fortis Hospital, Noida. Approval was taken from respective Institute's Ethics Committees before the conduct of the study. Recruitment was carried out from January 2017 to October 2017. Patients attending pain clinic outpatient department were screened for participation in the study. Adults aged ≥ 18 years and experiencing cancer pain were included in the study after obtaining informed consent.

Variables and measures

Demographic data were obtained from the patient, and clinical details were retrieved from patient's medical records. The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale is one of the simpler tools in clinical practice.^[17] The Self-reported version of the LANSS (S-LANSS) pain scale was later developed that eliminated the necessity for clinical examination.^[18] Pain spectrum extends between two mutually exclusive categories—nociceptive or neuropathic; hence, the use of the terms such as “pain of predominant neuropathic” or “pain of predominant nociceptive” types have been proposed.^[18,19] In this study, the S-LANSS questionnaire was used to identify the pain of predominantly neuropathic origin. It is a self-completed or interviewer-completed tool consisting of 7-items with binary response to identify the pain of predominantly neuropathic origin.^[18] Interviews using S-LANSS are reported to be more

reliable than self-completion.^[18,20] Total S-LANSS score is generated by summing up scores of all seven items. The total score range is 0–24, with score ≥ 10 is considered suggestive of the pain of predominantly neuropathic origin for interview format questionnaire administration. It has been validated in a diverse population across the globe and has demonstrated internal consistency (Cronbach's alpha) from 0.6 to 0.74.^[20-22] A palliative care physician cum researcher administered the questionnaire to the eligible patients in the interview format. Adequate internal consistency was demonstrated in the current sample (Cronbach's alpha = 0.67).

Statistical considerations

With 5% precision and 95% level of confidence ($z = 1.96$), minimum sample size required to estimate the burden of neuropathic pain was 261. Descriptive statistics were used to tabulate demographic and clinical characteristics. Patients with S-LANSS score of ≥ 10 were considered to have the pain of neuropathic origin.

RESULTS

A total of 279 patients were screened at three sites, of which, 13 (4.65%) did not qualify the screening criteria, 5 (1.79%) withdrew their consent to participate and 261 (93.54%) were enrolled in the study.

Patients' profile

Mean age of patients was 50.87 (18–80) years and the majority of them i.e., 148 (56.70%) were male, 195 (88.64%) were married, 67 (25.67%) were uneducated and only 48 (18.39%) were employed [Table 1].

Majority of the patients ($n = 70$, 27%) were diagnosed with head-and-neck cancers, followed by nearly equal proportions for lung, gastrointestinal, genitourinary, and breast cancer. Most of the patients ($n = 154$, 59%) had metastatic disease [Table 2].

Neuropathic pain reported by patients included either pain due to cancer or its treatment or both. As per the S-LANSS questionnaire scoring instructions, a cut-off score ≥ 10 indicates pain of mainly neuropathic type. This revealed the burden of neuropathic pain in given clinical settings to be 54.02% [Table 3]. It was reported by 79 (56.03%) male and 62 (43.97%) female patients and included patients with mixed pain but predominantly neuropathic origin.

DISCUSSION

The present study revealed a high burden (54%) of neuropathic pain in cancer patients. Roberto's systematic review^[23] of prospective studies reported a pooled prevalence of 31.2%, ranging from 30.0% in oncology settings to 32.4% in palliative care settings. Within the palliative care domain, almost equal prevalence rates were found in different settings, i.e., outpatient— 30.9%, inpatients/hospice — 33.0%, home care — 32.5% and 33.1% in mixed settings. Our prospective study has revealed much higher rates in outpatient settings as compared to previously published literature.^[23]

Table 1: Demographic characteristics of the study population at three sites

Characteristics	Number of patients (%)
Age (in years)	
18- 30	22 (8.42)
31- 45	66 (25.28)
46- 65	136 (52.11)
≥66	37 (14.17)
Sex	
Male	148 (56.70)
Female	113 (43.30)
Marital status	
Unmarried	13 (5.91)
Married	195 (88.64)
Widow	11 (5.00)
Divorced	1 (0.45)
Educational qualifications	
Uneducated	67 (25.67)
Till 5 th standard	59 (22.61)
Till 10 th standard	59 (22.61)
Till 12 th standard	38 (14.56)
Graduate or more	38 (14.56)
Occupation	
Employed	48 (18.39)
Medical leave	1 (0.38)
Resigned	11 (4.21)
Unemployed	92 (35.25)
Homemaker	104 (39.85)
Retired	5 (1.92)

Table 2: Clinical characteristics of the study population at three sites

Characteristics	Number of patients (%)
Primary site of cancer	
Head and neck	70 (26.82)
Lung	41 (15.71)
Gastrointestinal	38 (14.56)
Genitourinary	37 (14.18)
Breast	35 (13.41)
Bone and soft tissue	14 (5.36)
Hematolymphoid	9 (3.45)
Others	17 (6.51)
Metastases	
Yes	154 (59.00)
Bones	57 (21.92)
Liver	37 (14.23)
Lung	35 (13.46)
Lymph node	60 (23.08)
Others	35 (13.46)
No	107 (41.00)

To the best knowledge of the authors, this is the first multi-centric, cross-sectional study conducted in India to screen outpatients in palliative care settings using a screening questionnaire. A retrospective study conducted at a tertiary

cancer care hospital in India showed low prevalence of 11.8%.^[8] Another retrospective study done by Jain *et al.* in similar settings reported a prevalence rate of 39.7% among cancer patients referred for pain management.^[24] In both studies, the diagnosis of neuropathic pain was based on clinical judgment and patient-reported pain characteristics such as burning, shooting, tingling, or pins and needles sensation. A different retrospective study conducted at the pain clinic in a tertiary cancer care center depicted that pain clinicians prescribed anticonvulsants and antidepressants to 72% patients indicating a significant neuropathic component.^[25] A prospective study by Jain *et al.* demonstrated a 10%-point prevalence of neuropathic pain in cancer patients using pain DETECT questionnaire tool, but this was acute postsurgical neuropathic pain.^[26]

The difference in the occurrence of neuropathic cancer pain in the different studies may be attributed to the study design and approach to identify neuropathic pain, i.e., physician's diagnosis or patient-reported pain characteristics or use of screening questionnaires or a combination of these. The higher burden in our patients may be attributed to the higher proportion of patients (almost 60%) that had metastatic disease. Furthermore, all three centers are tertiary referral centers and it is possible that a large proportion of patients that were seen here were a subset of "difficult pain" that were sub-optimally treated by their primary health care providers.

The main purpose of the study was to identify the burden of neuropathic pain in palliative care settings. No consolidated reports of neuropathic pain incidence or prevalence from India are available.^[27] S-LANNS is easy to use and can be quickly completed by the patients.^[15] This offers a practical approach to identify patients with predominant neuropathic cancer pain. This would be particularly effective in Indian settings where public hospitals are overcrowded and understaffed.^[28]

An advantage of the S-LANSS scale is that it can also be used by nonspecialists.^[21] This would also be a solution to underdiagnosis by busy physicians and general practitioners. If screened effectively, patients will not have to visit tertiary cancer hospitals for specialist pain management. An important implication that follows is that with the use of screening questionnaires, neuropathic pain can be detected in patients with mixed pain.

A major inference of this study is that neuropathic pain is experienced by a significant number of cancer patients. All health-care professionals treating cancer need to have a high index of suspicion about neuropathic pain and its predominance in mixed pain. In India, cancer pain is underassessed and undertreated even in tertiary hospitals. The adequacy of cancer pain management varies at different hospitals for both outpatient and inpatient services, ranging from 54% to 90%.^[29] One of the main reasons for suboptimal treatment of cancer pain is inadequate assessment.^[30] Impeccable assessment is the first step to address a large number of cancer patients with pain in our country. Using

Table 3: S-LANSS score for the study population

S-LANSS score	Number of patients (%)
<10	120 (45.98)
≥10	141 (54.02)
Total patients	261 (100)

S-LANSS: Self-reported version of the Leeds Assessment of Neuropathic Symptoms and Signs

S-LANNS to screen can help to zero in on patients with predominantly neuropathic pain.

Nonetheless, screening questionnaires are associated with limitation of overdiagnosis or underdiagnosis.^[15] Clinical diagnosis by the physician is considered as the gold standard for identifying neuropathic pain.^[31] Concordance between screening tool outcome and physician's diagnosis is necessary for identifying accurate rates of neuropathic pain. In this study, the S-LANNS was administered by a palliative care clinician. However, a limitation of this study was that the interpretation of the S-LANSS questionnaire was not confirmed by another physician. An independent clinical diagnosis by a blinded palliative care physician would have strengthened this study. For future studies, we recommend cross-examination of questionnaire's outcomes with physician's clinical experience. This will validate the applicability of the S-LANSS questionnaire as a screening tool for neuropathic pain in cancer patients. The present study was conducted at three tertiary care hospitals in North India and may not be applicable to all settings. We intend to conduct larger multi-centric studies for the vast and diverse Indian population.

CONCLUSION

This study reports a high burden of neuropathic pain in cancer patients. It recommends the use of S-LANNS to identify neuropathic cancer pain in outpatient clinics. Quick screening with these questionnaires can prevent both underreporting by patients and under-recognition by physicians. It further emphasizes the need to accurately diagnose and manage neuropathic pain and thus reducing its incapacitating impact on patient's quality of life.

Acknowledgments

This study is supported by a grant from Janssen (Pharmaceutical division of Johnson and Johnson Private Limited), Mumbai. We extend our thanks to all patients who participated in the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Satija A, Bhatnagar S. Complementary therapies for symptom management in cancer patients. *Indian J Palliat Care* 2017;23:468-79.
- Goyal A, Bhatnagar S. Neuropathic pain in cancer. *Ann Palliat Med* 2014;3:1-3.
- van den Beuken-van Everdingen MH, Hochstenbach LM, Joosten EA, Tjan-Heijnen VC, Janssen DJ. Update on prevalence of pain in patients with cancer: Systematic review and meta-analysis. *J Pain Symptom Manage* 2016;51:1070-90.e9.
- Garzón-Rodríguez C, Lyras L, Gayoso LO, Sepúlveda JM, Samantas E, Pelzer U, *et al.* Cancer-related neuropathic pain in out-patient oncology clinics: A European survey. *BMC Palliat Care* 2013;12:41.
- International Association for the Study of Pain. IASP Terminology. Available from: <https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698#Neuropathicpain>. [Last accessed on 2020 Jun 22].
- Satija A, Ahmed SM, Gupta R, Ahmed A, Rana SP, Singh SP, *et al.* Breast cancer pain management-a review of current & novel therapies. *Indian J Med Res* 2014;139:216-25.
- Yoon SY, Oh J. Neuropathic cancer pain: Prevalence, pathophysiology, and management. *Korean J Intern Med* 2018;33:1058-69.
- Bhatnagar S, Mishra S, Roshni S, Gogia V, Khanna S. Neuropathic pain in cancer patients--Prevalence and management in a tertiary care anesthesia-run referral clinic based in urban India. *J Palliat Med* 2010;13:819-24.
- Lema MJ, Foley KM, Hausheer FH. Types and epidemiology of cancer-related neuropathic pain: The intersection of cancer pain and neuropathic pain. *Oncologist* 2010;15 Suppl 2:3-8.
- Bennett MI, Rayment C, Hjermsstad M, Aass N, Caraceni A, Kaasa S. Prevalence and aetiology of neuropathic pain in cancer patients: A systematic review. *Pain* 2012;153:359-65.
- Esin E, Yalcin S. Neuropathic cancer pain: What we are dealing with? How to manage it? *Onco Targets Ther* 2014;7:599-618.
- Kuroi K, Shimozuma K, Ohashi Y, Takeuchi A, Aranishi T, Morita S, *et al.* A questionnaire survey of physicians' perspectives regarding the assessment of chemotherapy-induced peripheral neuropathy in patients with breast cancer. *Jpn J Clin Oncol* 2008;38:748-54.
- Kuroi K, Shimozuma K, Ohashi Y, Hisamatsu K, Masuda N, Takeuchi A, *et al.* Prospective assessment of chemotherapy-induced peripheral neuropathy due to weekly paclitaxel in patients with advanced or metastatic breast cancer (CSP-HOR 02 study). *Support Care Cancer* 2009;17:1071-80.
- Shimozuma K, Ohashi Y, Takeuchi A, Aranishi T, Morita S, Kuroi K, *et al.* Feasibility and validity of the Patient Neurotoxicity Questionnaire during taxane chemotherapy in a phase III randomized trial in patients with breast cancer: N-SAS BC 02. *Support Care Cancer* 2009;17:1483-91.
- Attal N, Bouhassira D, Baron R. Diagnosis and assessment of neuropathic pain through questionnaires. *Lancet Neurol* 2018;17:456-66.
- Patrick DL, Ferketich SL, Frame PS, Harris JJ, Hendricks CB, Levin B, *et al.* National Institutes of Health State-of-the-Science conference statement: Symptom management in cancer: Pain, depression, and fatigue, July 15-17, 2002. *J Natl Cancer Inst* 2003;95:1110-7.
- Bennett M. The LANSS Pain Scale: The Leeds assessment of neuropathic symptoms and signs. *Pain* 2001;92:147-57.
- Bennett MI, Smith BH, Torrance N, Potter J. The S-LANSS score for identifying pain of predominantly neuropathic origin: Validation for use in clinical and postal research. *J Pain* 2005;6:149-58.
- Bennett MI, Smith BH, Torrance N, Lee AJ. Can pain can be more or less neuropathic? Comparison of symptom assessment tools with ratings of certainty by clinicians. *Pain* 2006;122:289-94.
- Koc R, Erdemoglu AK. Validity and reliability of the Turkish Self-administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire. *Pain Med* 2010;11:1107-14.
- Batistaki C, Lyrakos G, Drachtidi K, Stamatiou G, Kitsou MC, Kostopanagiotou G. Translation, Cultural Adaptation, and Validation of Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) and Self-Complete Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) Questionnaires into the Greek Language. *Pain Pract* 2016;16:552-64.
- Gudala K, Bansal D, Ghai B. Cross-cultural validation of four commonly used symptoms based questionnaires to assess neuropathic pain in patients with chronic pain. *Value Health* 2016;19:A71.
- Roberto A, Deandrea S, Greco MT, Corli O, Negri E, Pizzuto M, *et al.*

- Prevalence of neuropathic pain in cancer Patients: Pooled estimates from a systematic review of published literature and results from a survey conducted in 50 Italian palliative care centers. *J Pain Symptom Manage* 2016;51:1091-1102.e4.
24. Jain PN, Chatterjee A, Choudhary AH, Sareen R. Prevalence, etiology, and management of neuropathic pain in an Indian cancer hospital. *J Pain Palliat Care Pharmacother* 2009;23:114-9.
 25. Jain PN, Pai K, Chatterjee AS. The prevalence of severe pain, its etiopathological characteristics and treatment profile of patients referred to a tertiary cancer care pain clinic. *Indian J Palliat Care* 2015;21:148-51.
 26. Jain P, Padole D, Bakshi S. Prevalence of acute neuropathic pain after cancer surgery: A prospective study. *Indian J Anaesth* 2014;58:36-42.
 27. Saxena AK, Jain P, Dureja GP, Venkitachalam A, Goswami S, Usmani H, *et al.* Pharmacological management of neuropathic pain in India: A consensus statement from Indian experts. *Indian J Pain* 2018;32:132-44.
 28. Bajpai V. The challenges confronting public hospitals in India, their origins, and possible solutions. *Adv Public Health* 2014;2014:27.
 29. Doyle KE, El Nakib SK, Rajagopal MR, Babu S, Joshi G, Kumarasamy V, *et al.* Predictors and prevalence of pain and its management in four regional cancer hospitals in India. *J Glob Oncol* 2018;4:1-9.
 30. Von Roenn JH, Cleeland CS, Gonin R, Hatfield AK, Pandya KJ. Physician attitudes and practice in cancer pain management. A survey from the Eastern Cooperative Oncology Group. *Ann Intern Med* 1993;119:121-6.
 31. Anzar S, Koshy C, Abraham KM. Validation of the Malayalam Version of Leeds assessment of neuropathic symptoms and signs pain scale in cancer patients in the regional cancer centre, Thiruvananthapuram, Kerala, India. *Indian J Palliat Care* 2017;23:293-9.