The impact of pain intensity on quality of life of postherpetic neuralgia patients

Wizar Putri Mellaratna, Nelva K. Jusuf, Ariyati Yosi

Department of Dermatology and Venereology, School of Medicine, Universitas Sumatera Utara, Medan, Indonesia

ABSTRACT

Aim To investigate the impact of pain intensity of postherpetic neuralgia (PHN) patients.

Methods This cross sectional study included 30 PHN patients attended to the Dermatology and Venereology Department of the School of Medicine of Universitas Sumatera Utara during the period between April 2019 and October 2019. Zoster Brief Pain Inventory questionnaire including the worst pain in 24 hours and the level of interference with seven domains of quality of life (QoL) (general activity, mood, walking ability, working, relationship with other people, sleep and enjoyment of life) were used. Pearson's correlation (r) was categorized as very weak (0.0-<0.2), weak (0.2-<0.4), moderate (0.4-<0.6), strong (0.6-<0.8), and very strong (0.8-1.0).

Results There was a very strong correlation between worst pain intensity and mood disturbance (r=0.846) and working status (r=0.818). Worst pain intensity had a strong correlation with general activity (r=0.673), relationship with other people (r=0.653), sleep (r=0.774) and disturbance of enjoyment of life (r=0.783). Therefore, the correlation between worst pain intensity and walking ability was moderate (r=0.475). The worst pain intensity had a significant correlation with all seven domains of QoL (p<0.05).

Conclusion Pain intensity influences the QoL with directly proportional correlation between pain intensity and disturbance of QoL.

Key words: cross-sectional herpes zoster, pain, questionnaire, survey

Corresponding author:

Wizar Putri Mellaratna Department of Dermatology and Venereology, School of Medicine, Universitas Sumatera Utara JI. Dr. Mansyur No.5 20222 Medan, Indonesia Phone: +62 852 6014 1026; E-mail: mellaratna.iskandar@gmail.com ORCID ID: https://orcid.org/0000-0002-5945-8898

Original submission:

13 December 2019; **Revised submission:** 03 January 2020; **Accepted:** 11 March 2020 doi: 10.17392/1111-20

Med Glas (Zenica) 2020; 17(2): 439-444

INTRODUCTION

Postherpetic neuralgia (PHN) is a long term neuropathic pain experienced commonly within more than three months after onset of herpes zoster (HZ) (1). Based on epidemiological data taken from 13 hospitals in Indonesia from 2011 to 2013, it was found that about 26.5% of the HZ total cases (593) developed into PHN. The risk factors of PHN include an age over 50 years, females, duration of pain during HZ, and psychological stress (2).

Chronic pain of PHN causes sleeping disorders, depression which leads to unsocialised behaviour, anorexia, weight loss, fatigue and disturbances of dressing, shower, general activity, traveling, shopping, cooking and household activities (3). Chen et al. have reported that economic burden caused by PHN was higher than in HZ, and this included medicines costs, consultation, and hospital treatment (4). Deterioration of quality of life (QoL) of PHN patients is assessed with a questionnaire or interview (5), while Zoster Brief Pain Inventory (ZBPI) is one of the questionnaires that assess pain intensity and reflect QoL in the same patients. Thus, an improvement to evaluate the impact of pain intensity on QoL of PHN patients remains a matter of urgency, considering the real impact in disruption of activities of daily living (ADL) (6). Coplan stated that intensity of pain from ZBPI questionnaire strongly correlated with disturbance of quality of life of PHN patients (7). There was no research about the correlation of pain intensity and quality of life of PHN patients in Indonesia.

The aim of this study was to investigate the impact of pain intensity of post herpetic neuralgia (PHN) patients.

PATIENTS AND METHODS

Patients and study design

This a cross sectional study conducted at the department of Dermatology and Venereology School of Medicine of Universitas Sumatera Utara, Medan, and 30 PHN patients were recruited during the period between April 2019 and October 2019. Data on patients with postherpetic neuralgia diagnosis were collected from medical records of Rumah Sakit Pendidikan Universitas Sumatera Utara, and two local public health centres located in Teladan and Padang Bulan. Postherpetic neuralgia was defined as persisting pain after more than 90 days of herpes zoster rash. The shortest duration of PHN was 3 months, while the longest was 3 years after the HZ onset. Inclusion criteria were patients who had been diagnosed with PHN in the last 5 years (2015-2019), aged over 40 years (40-44, 45-49, 50-54, 55-59, and >60 age groups), who signed informed consent for investigation. Patient demographic data included age, sex, and employment history from medical records.

The research protocol was approved by Ethics Commission in the School of Medicine of Universitas Sumatera Utara and Adam Malik Hospital.

Methods

Demographic data included age, sex, employment record, phone number and patient's address. After being reconfirmed for their willingness to participate in the research, data were collected in the patients' houses. The researcher requested the patients to fill out the ZBPI questionnaire (with permission) (8). The questionnaire evaluated the pain level in 24 hours with Likert scale 0-10 (8): score 0 indicated no pain, up to score 10 which indicated the worst pain felt by the patients. The patients filled out the level of interference with seven domains of quality of life (QoL) questionnaire (8) including general activity, mood, walking ability, working, relationship with other people, sleep and enjoyment of life. The patients responded with a score of 0 to 10 according to the level of disturbance they had experienced. Score 0 indicated no disturbance, up to score 10 indicated worst disturbance in the daily activity.

Statistical analysis

Normality test was performed by using one sample Kolmogorov Smirnov test. Pearson's correlation was used as hypothesis testing. The p<0.05 was considered as statistically significant. This analysis was classified into correlation categories: very weak (r 0.0-< 0.2), weak (r 0.2-< 0.4), moderate (r 0.4-< 0.6), strong (r 0.6-< 0.8), and very strong (r 0.8-1.0) (9). The increase of pain intensity is accompanied by the increase of QoL interference of PHN patients.

RESULTS

This research involved 30 PHN patients, most of them were over the age of 60, 16 (53.3%) and -one (3.3%) was in the 50-54 years age

group. Based on gender, the patients were mostly female, 17 (56.7%), compared with male, 13 (43.3%). Majority of patients worked as private employees and were retired, seven (23.3%) of each, followed by housewives and farmers, six (20.0%) and two (6.7%), respectively (Table 1).

Table 1. Demographic characteristics of 30 patients with postherpetic neuralgia

Variable	No (%) of patients		
Age (years)			
40-44	3 (10.0)		
45-49	4 (13.3)		
50-54	1 (3.3)		
55-59	6 (20.0)		
≥ 60	16 (53.3)		
Gender			
Female	17 (56.7)		
Male	13 (43.3)		
Working status			
Salesman	4 (13.3)		
Farmer	2 (6.7)		
Government employees	4 (13.3)		
Retired	7 (23.3)		
Private employee	7 (23.3)		
Housewife	6 (20.0)		

Majority of patients had worst pain intensity, with score 9 accounted for nine (30.0%) patients, and minority of patients had score, 4 and 5, two (6.7%) patients each. Mean (SD) was 7.17 (2.321) (Table 2).

Table 2. Pain intensity in postherpetic neuralgia patients

Pain intensity	No (%) of patients	Men (SD)
0	0	7.17 (2.321)
1	0	
2	0	
3	4 (13.3)	
4	2 (6.7)	
5	2 (6.7)	
6	0 (0)	
7	6 (20.0)	
8	4 (13.3)	
9	9 (30.0)	
10	3 (10.0)	

There was a very strong correlation between the worst pain intensity and mood disturbance (r=0.846), as well as working status (r=0.818) (p<0.001). The worst pain intensity had a strong correlation with general activity (r=0.673), relationship with other people (r=0.653), sleep (r=0.774), and disturbance on enjoyment of life (r=0.783) (p< 0.001). Therefore, the correlation between worst pain intensity and walking ability was moderate (r=0.475; p<0.05). The worst pain intensity had positive correlation with all seven domains of QoL (Table 3).

Table 3. C	Correlation	between	pain	intensity	and QoL
------------	-------------	---------	------	-----------	---------

The worst pain intensity in category	Correlation coefficient (No of patients)	р
General activity	r = 0.673 (30)	< 0.001
Mood	r = 0.846 (30)	< 0.001
Walking ability	r = 0.475 (30)	0.008
Working ability	r = 0.818 (30)	< 0.001
Relationship with other people	r = 0.653 (30)	< 0.001
Sleep	r = 0.774 (30)	< 0.001
Enjoyment of life	r = 0.783 (30)	< 0.001

DISCUSSION

The worst pain intensity had a very strong correlation with increasing interference of QoL and it affected all seven domains of ADL in ZBPI with significant impact on mood, sleep and general activity (10). In this research, PHN was mostly found in the age group over 60 years. Munoz-Quiles et al. reported the increasing risk of PHN was two times higher in age group 60-69 years, three times higher in the age group 70-79 years, and 3.67 higher in the age group over 80 years (11).Weaver reported that incidence of PHN was the highest at the age of 70 (73%), and it was followed by the age 55 years (27%) (12).

Incidence of PHN mostly involved females compared with the males because females have a low pain threshold. Whilst curiosity about pain for females is greater than that in males, and women have lower sensitization to sensory stimulus (13). In this research, it is shown that the female proportion was greater than male. Schmidt-Ot et al. and Nahm et al. reported that about 63% and 62.65% of PHN patients were female (14,15). Majority of patients had already retired because generally PHN involved older patients. Postherpetic neuralgia was caused by the economic burden due to the high absenteeism rate at work (16). In this research, majority of patients worked as private employee and already retired. This corresponds to Nakamura et al. that proposed the highest occurrence of PHN patients in retired conditions (39.6%), housewives (33.7%) and those still actively working (23%) (17). Johnson et al. also stated the same that 51.9% of PHN patients were already retired, those with full-time employment status (16%), housewives (13.7%), part-time employment status (11.4%), and the employed (6.9%) (18).

From the dimension of pain intensity items, pain at its worst has the highest internal validity compared with others (Cronbach's alpha 0.77-0.85), and also has the strongest correlation with disturbance of ADL (Cronbanch's alpha 0.76-0.85) (19). Worst pain intensity was also recommended by Food and Drugs Administration (FDA) to assess patient reported outcomes (PRO) (20). Our research indicated that most of PHN patients had a worst pain intensity score of 9. This is in accordance with Wyrwich et al. who reported mean (SD) worst pain intensity score from the ZBPI questionnaire was 6.8 (2) (21). Van Seventer et al. reported that mean (SD) in placebo group (who have not yet received pregabalin) was 6.86 (1.49) with median (minimum-maximum) 7 (1.71-10) (10).

This research indicated that worst pain intensity was very strongly correlated with mood disturbance. This is different from Coplan et al. who stated that worst pain intensity was strongly correlated with mood disturbance (7). This research is in accordance with Schelereth et al. who mentioned Pain Rating Index (PRI) had a positive correlation with allodynia and Hospital Anxiety and Depression Scale (HADS) for anxiety and depression (22). Saxena et al. reported a negative correlation between Brain Derived Neurotropic Factor (BDNF) and pain intensity in PHN patients, where an increase in pain intensity is followed by a decrease in BDNF level, and vice versa (23). Chen et al. also has reported that PHN/HZ was related to depression through a mechanism mediated by cellular immunity (24).

This research showed that there was a very strong correlation between worst pain intensity and working interference. Aunhachoke et al. mentioned that pain intensity was moderately correlated with work (25). Coplan et al. also mentioned strongly correlated occurrence between worst pain intensity and work disturbance (7). Meanwhile, Serpel et al. reported a decrease in effectiveness in their work in PHN patients who were still actively working (6).

This research indicated there was a strong correlation between worst pain intensity and general activity. Laurent et al. stated the disturbance of general activity including ability to dress (54%), move (47%), and wash (26%) (26). This is different from Coplan et al. research that reported a very strong correlation between worst pain intensity and general activity (7). Nevertheless, the results of our research correspond with Oster et al. reporting moderate to strong impact of pain intensity value (with mean SD) on general activity ($40\% \pm 3.7$ -3.1) (27).

The present research indicated worst pain intensity strongly correlated with relationship with others. Coplan et al. research reported that worst pain intensity moderately correlated with relation with others (7). Deshpande et al. also stated that there was a decline on QoL from relationship with others (using SF-36 questionnaire) with score 70.3 (24.2) in PHN patients with VAS score 5 (2.1), while in the control group normative values were obtained for relationship with other people at around 88.3 (18.6) (28).

Our results indicated that worst pain intensity strongly correlated with sleep disturbance, which corresponds with Coplan et al. study (7). Vinik et al. found that in PHN patients who receive no treatment with 6.64 of mean pain score intensity, a disturbance of sleep at the level of severe (43.3%), moderate (38.1%) and mild (18.6%) was experienced; relationship between pain intensity and sleep interference can occur in two directions, improvement and derivation of one component which can affect others. Vinik et al. also mentioned that by using pregabalin in PHN patients, pain intensity decreased, which can improve the sleep quality. It is because pregabalin works in the pathways responsible for pain response and sleep (29). Cao et al. reported that chronic pain in PHN caused sleep disturbance, based on an analysis of brain regional activities discovering a limbic system disturbance, which regulates sleep activity, otherwise it caused persistent chronic pain in PHN patients (30).

This research indicated that worst pain intensity strongly correlated with enjoyment of life which is consistent with Coplan et al. research (7). Oster reported that in PHN patients mean (SD) score of worst pain intensity was 6 (2.4), about 48% experienced impaired ability to enjoy life with moderate to severe level (27).

We reported that worst pain intensity moderately correlated with walking ability. Aunhachoke et al. reported that correlation between pain intensity and walking ability was low/moderate (25). This is different from Coplan et al. who mentioned the presence of strong correlation between worst pain intensity and walking ability (7).

Laurent et al. reported that impact of pain intensity in PHN was significant to general activity, mood and enjoyment of life (26). This is also relevant to Freeman's research that reported significant impact in pain intensity score with mean value of 7.3 on disturbance of sleep, enjoyment of life and mood (31). Correlation test analysis results in this study indicated the influence of worst pain intensity in PHN patients to their QoL. An increase in pain intensity followed by an increase in QoL interference, with significant impact on mood, work, general activity, relationship with others, sleep and enjoyment of life were found.

This study has some limitations including no exclusion of patients who were currently using analgesics and the wide range of persisted pain after HZ rash (3 months-3 years), which might influence the study results. Pain in PHN patients was normally intense in 3 months after HZ onset and reduced gradually in several years after (32). In conclusion, the pain intensity influences the QoL, with directly proportional correlation

between pain intensity and disturbance on QoL.

REFERENCES

- Schmader KE, Dworkin RH. The epidemiology and natural history of herpes zoster and post herpetic neuralgia. In: Watson CPN, Gershon AA, Oxman MN. Herpes Zoster: Post Herpetic Neuralgia and other Complications. Switzerland: Springer, 2017. https:// www.springer.com/gp/book/9783319443461// (10 February 2018).
- Pusponegoro E, Nilasari H, Lumintang H, Niode NJ, Daili SF, Djauzi S. Buku Panduan Herpes Zoster di Indonesia (Indonesia Shingles Book Guide) [in Indonesian]. Jakarta: BP FKUI, 2014.
- Schmader KE, Oxman MN. Varicella and Herpes Zoster. In: Goldsmith LA, Katz SI, Gilchrest, Paller AS, Leffell DJ, Wolff K. Fitzpatrick's Dermatology in General Medicine. 8th Ed. New York: The Mc Graw Hill Company Inc., 2012:2393-8.
- Chen Q, Hsu TY, Chan R, Kawai K, Acosta CJ, Walia A, Pan JY. Clinical and economic burden of herpes zoster and postherpetic neuralgia in patients from the national skin center, Singapore. Dermatol Sin 2015; 33:201-5.
- Lukas K, Edte A, Bertrand I. The impact of herpes zoster and post herpetic neuralgia on quality of life: patient-reported outcomes in six European countries. Z Gesundh Wiss 2012; 20:441-51.

Worst pain intensity had a very strong correlation to mood and work, and a strong correlation to general activity, relationship with other people, sleep and enjoyment of life, but it has moderate correlation with walking ability.

Intensity of pain level in PHN patients has a significant impact of the QoL, so the authors recommend to treat the PHN patients adequately based on patient's characteristic, routine monitoring of the treatment outcomes and prevention of PHN complication after onset of HZ by administering vaccination.

ACKNOWLEDGEMENT

We would like to express our gratitude to Rumah Sakit Pendidikan Universitas Sumatera Utara, and two local public health centres located in Teladan and Padang Bulan, Medan for permitting the use of patients' data from medical records.

FUNDING

No specific funding was received for this study.

TRANSPARENCY DECLARATION

Conflicts of interest: None to declare.

- Serpell M, Gater A, Carrol S, Abetz-Webb L, Mannan A, Johnson R. Burden of post-herpetic neuralgia in a sample of UK residents aged 50 years or older: findings from the Zoster Quality of Life (ZQOL) study. Health Qual Life Outcomes 2014; 12:92.
- Coplan PM, Schmader K, Nikas A, Chan IS, Choo P, Levin MJ, Johnson G, Bauer M, Williams HM, Kaplan KM, Guess HA, Oxman MN. Development of a measure of the burden of pain due to herpes zoster and postherpetic neuralgia for prevention trials: adaptation of the brief pain inventory. J Pain 2004; 5: 344-56.
- Cleeland CS. The Brief Pain Inventory User Guide. Texas: The University of Texas MD Anderson Cancer Center; 2009 (05 May 2018) https://www.mdanderson.org/research/departments-labs-institutes/ departments-divisions/symptom-research/symptomassessment-tools/brief-pain-inventory.html
- Dahlan MS. Statistik untuk kedokteran dan kesehatan (Statistic for Medicine and Health). [in Indonesian] 6th Ed. Jakarta: Salemba Medika, 2014.
- Van Seventer R, Sadosky A, Lucero M, Dukes E. A cross-sectional survey of health state impairment and treatment patterns in patients with postherpetic neuralgia. Age Ageing 2006; 35:132-7.

- Muñoz-Quiles C, López-Lacort M, Orrico-Sánchez A, Díez-Domingo J. Impact of postherpetic neuralgia: A six year population-based analysis on people aged 50 years or older. J Infect 2018; 77:131-6.
- Weaver BA. The burden of herpes zoster and postherpetic neuralgia in the United States. J Am Osteopath Assoc 2007; 107:S2-7.
- 13. Belfer I. Pain in women. Agri Pain 2017; 29:51-4.
- Schmidt-Ott R, Schutter U, Simon J, Nautrup BP, Von Krempelhuber AV, Gopala K, Anastassopoulou A, Guignard A, Curran D, Matthews S, Espie E. Incidence and costs of herpes zoster and postherpetic neuralgia in German adults aged ≥ 50 years: a prospective study. J Infect 2018; 76:475-82.
- Nahm FS, Kim SH, Kim HS, Shin JW, Yoo SH, Yoon MH, Lee DI, Lee YW, Lee JH, Jeon YH, Jo DH. Survey on the treatment of postherpetic neuralgia in Korea; multicenter study of 1.414 Patients. Korean J Pain 2013; 26:21-6.
- 16. Vinik A, Emir B, Cheung R, Whalen E. Relationship between pain relief and improvements in patient function/quality of life in patients with painful diabetic peripheral neuropathy or postherpetic neuralgia treated with pregabalin. Clin ther 2013: 35:612-22.
- 17. Nakamura H, Mizukami A, Adachi K, Matthews S, Holl K, Asano K, Watanabe A, Adachi R, Kiuchi M, Kobayashi K, Sato K, Matsuki T, Kaise T, Curran D. Economic burden of herpes zoster and postherpetic neuralgia in adults 60 years of age or older: results from a prospective, physician practice-based cohort study in Kushiro, Japan. Drugs Real World Outcomes 2017; 4:187-98.
- Johnson RW, Wasner G, Saddier P, Baron R. Postherpetic neuralgia: epidemiology, pathophysiology and management. Expert Rev Neurother 2014; 7:1581-95.
- Atkinson TM, Mendoza TR, Sit L, Passik S, Scher HI, Cleeland C, Basch E. The brief pain inventory and its "pain at its worst in the last 24 hours" item: clinical trial endpoint considerations. Pain Med 2010; 11:337-46.
- U.S. Food and Drug Administration. FDA Draft Guidance for Industry. Analgesic Indications: Developing Drugs and Biological Products (05 May 2018). https://www.policymed. com/2014/02/fda-draft-guidance-analgesic-indications-developing-drug-and-biological-products.html
- Wyrwich KW, Kawata AK, Thompson C, Holmstrom S, Stoker M, Wiklund I. Validation of the self-assessment of treatment questionnaire among patients with postherpetic neuralgia. Pain Res Treat 2012; 621619.

- 22. Schlereth T, Heiland A, Breimhorst M, Féchir M, Kern U, Magerl W, Birklein F. Association between pain, central sensitization and anxiety in postherpetic neuralgia. Eur J Pain 2014; 19:193-201.
- Saxena AK, Lakshman K, Sharma T, Gupta N, Banerjee BD, Singal A. Modulation of serum BDNF levels in postherpetic neuralgia following pulsed radiofrequency of intercostal nerve and pregabalin. Pain Manag 2016; 6:217-27.
- 24. Chen MH, Wei HT, Su TP, Li CT, Lin WC, Chang WH, Chen TJ, Bai YM. Risk of depressive disorder among patients with herpes zoster: a nationwide population-based prospective study. Psychosom Med 2014; 76:285-91.
- 25. Aunhachoke K, Bussaratid V, Chirachanakul P, Chua-Intra B, Dhitavat J, Jaisathaporn K, Kaewkungwai J, Kampirapap K, Khuhaprema T, Pairayayutakui K, Pitisuttihum P, Sindhvananda J, Thaipisuttikul Y. Measuring herpes zoster, zosterassociated pain, post-herpetic neuralgia-associated loss of quality of life, and healthcare utilization and costs in Thailand. Int. J. Dermatol 2011; 50:428-35.
- Laurent B, Vicaut E, Leplège A, Bloch K, Leutenegger E. Prevalence and impact on quality of life of post-herpetic neuralgia in French medical centers specialized in chronic pain management: The ZOCAD study. Med Mal Infect 2014; 44:515-24.
- 27. Oster G, Harding G, Dukes E, Edelsberg J, Cleary PD. Pain, Medication use, and health-related quality of life in older persons with postherpetic neuralgia: results from a population-based survey. J Pain 2005; 6:356-63.
- Deshpande MA, Holden RR, Gilron I. The impact of therapy on quality of life and mood in neuropathic pain: what is the effect of pain reduction?. Anesth Analg 2006; 102:1473-9.
- 29. Vinik A, Emir B, Parsons B, Cheung R. Prediction of pregabalin-mediated pain response by severity of sleep disturbance in patients with painful diabetic neuropathy and postherpetic neuralgia. Pain Med 2014; 15:661-70.
- Cao S, Song G, Zhang Y, Xie P, Tu Y, Li Y, Yu T, Yu B. Abnormal local brain activity beyond the pain matrix in postherpetic neuralgia patients: a restingstate functional MRI Study. Pain Physician 2017; 20:E303-14.
- Freeman R, Wallace MS, Sweeney M, Backonja MM. Relationships among pain quality, pain impact, and overall improvement in patients with postherpetic neuralgia treated with gastroretentive gabapentin. Pain Med 2015; 16:2000-11.
- 32. Mick G, Hans G. Postherpetic neuralgia in Europe: the scale of the problem and outlook for the future. J. Clin. Gerontol Geriatr 2013; 4:102-8.