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Association between Clinical Stage of HIV and Peripheral Sensory Neuropathy

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ABSTRACT

Introduction: Several factors that contributed in the incidence of peripheral sensory neuropathy in HIV patients, including the number of Cluster of Differentiation 4 (CD4) lymphocytes, high HIV viral load, opportunistic infections and clinical stage of HIV.5 The aim of this study was to analyze the association between clinical stage of HIV to peripheral sensory neuropathy.

Method: This research was a descriptive study with a cross-sectional design, conducted in General Hospital of Haji Adam Malik Medan during June to October 2023. Brief Peripheral Neuropathy Screening tool validated by AIDs Clinical trial group was used for screening peripheral sensory neuropathy. The variable to be analyzed in this study was clinical stage of HIV disease. Research data were analyzed using the SPSS (Statistical Product and Science Service) program for Windows, version 26. Univariate, bivariate, and multivariate analyses were conducted. Univariate analysis aimed to obtain the characteristics of the study subjects. The chi square test was used to determine the association between clinical stage of HIV to peripheral sensory neuropathy.

Results: There were 83 subjects eligible for this study, in which 62,7% were males, with the mean age of the patients was 39,4+9,6 years. A total of 47 subjects (56.6%) were stage III and 36 subjects (43.4%) were stage IV. There was a significant association between clinical stage of HIV and peripheral sensory neuropathy in HIV positive patients with p value <0.001.

Conclusion: There was a significant association between clinical stage of HIV to sensory peripheral neuropathy.

Keywords

Human immunodeficiency virus, Sensory peripheral neuropathy, Clinical stage of HIV

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INTRODUCTION

Human Immunodeficiency Virus (HIV) has developed into one of the most important health problems in the world. World Health Organization (WHO) estimates that the total number of people living with HIV/AIDS worldwide is 42 million. Centers for Disease Control and Prevention (CDC) estimates that 40.000 individuals are infected with HIV each year.[1] In 2009, an estimate of 186.000 people in Indonesia is HIV positive. Papua, Jakarta, and Bali are Indonesia's three provinces with the highest new HIV infection cases in 2011.[2]

The neurotoxic effects of HIV on peripheral nerves can occur directly, mediated by Glycoprotein 120, and indirectly through activation of the immune system. Dysregulation in the immune system causes circulating macrophages to be activated. Activated macrophages will infiltrate the Dorsal Root Ganglion, causing the DRG release proinflammatory and pronociceptive cytokines such as TNF α and IL 1β. The release of pro-inflammatory cytokines will cause Axonal Degeneration followed by peripheral sensory neuropathy.[3] Peripheral sensory neuropathy is the most frequent neurological complication of HIV infection that is

characterized by sensation of aching, burning and numbness that present distal symmetrical as well as absence or reduction of deep tendon reflexes or impaired vibration sensation.[4] Several factors that contribute in the incidence of peripheral sensory neuropathy in HIV patients, including the number of Cluster of Differentiation 4 (CD4) lymphocytes, high HIV viral load, opportunistic infections and clinical stage of HIV infection.[5,6] Other factors that play a role in the incidence of peripheral sensory neuropathy include genetics, vitamin deficiencies, and alcohol abuse.[7,8]

Peripheral sensory neuropathy has become one of the major causes of global pain morbidity. Nonetheless, it remains undiagnosed, resulting in inadequate treatment.[2] The absence of neuro-regenerative therapies and ineffectiveness of analgesics treatment of peripheral sensory neuropathy HIV patients, clearly demonstrate the lack of effective treatments and the need for early diagnosis of patients at risk of HIV-SN.[9] Early recognition of signs and symptoms of Peripheral sensory neuropathy is imperative to prevent the progression and to improve patients' quality of life.[2]

METHOD

This research was a descriptive study with a cross-sectional design. The study was conducted in General Hospital of Haji Adam Malik Medan during June to October 2023. The inclusion criteria for this study were HIV patients with sensory neuropathy symptoms, aged ≥18 years and willing to participate in the study. Patients with other risk for peripheral neuropathy such as radiculopathy, diabetes mellitus, chronic kidney disease, chronic liver disease, chemotherapy, radiotherapy, brain lesions, active tuberculosis (TB) and receiving TB treatment during study period, were excluded from the study.

A total of 83 patients had been selected using the nonrandom sampling method consecutively. Peripheral sensory neuropathy was determined using Brief Peripheral Neuropathy Screening tool, validated by AIDs Clinical trial group. The brief peripheral neuropathy screen (BPNS) tool assessed both subjective and objective findings consistent with peripheral neuropathy. Patient with neuropathy symptoms such as sensation of burning, pain, aching, and numbness in the distal parts of both limbs accompanied by signs of decrease or absent of Achilles reflexes and or impaired vibration sensibility as assessed using 128 Hz tuning fork was defined as Peripheral sensory neuropathy positive. The variable to be analyzed in this study was clinical stage of HIV disease.

Research data were analyzed using the SPSS (Statistical Product and Science Service) program for Windows, version 26. Univariate, bivariate, and multivariate analyses were conducted. Univariate analysis aimed to obtain the characteristics of the study subjects. The chi square test was used to determine the relationship between clinical stage of HIV and the incidence of peripheral sensory neuropathy.

RESULTS

Based on the characteristics of the 83 research subjects, the mean age of the study subjects was 39,4±9.16 years, in the age range of <40 years for 28 people (33.7%), >40 years for 55 people (66.3%). The mean age of HIV patients with peripheral sensory neuropathy was 43.1+10.3 years and the mean age of HIV patients without peripheral sensory neuropathy was 36.3+8.0 years The gender of the study subjects was mostly male (62.7%). Based on educational background, most patients were high school graduates (69.9%), while based on occupation, most were self-employed (33.7%). The subjects in this study consisted of various tribes and the most common tribe found in this study was the Batak tribe with 53 subjects (63.9%).

Based on the clinical stage of HIV, in the group with peripheral sensory neuropathy positive, 10 subjects (21.3%) were stage III and 26 subjects (72.2%) were stage IV. In the group with peripheral sensory neuropathy negative, 37 subjects (78.7%) were stage III and 10 subjects (27.8%) were stage IV. Research conducted at H. Adam Malik General Hospital found that visits by HIV stage I and II patients every month were less than 1%. This can explain the absence of subjects with complaints of peripheral sensory neuropathy in stages I and II. Bivariate analysis using the Chi square test showed that there was a significant relationship between clinical stage of HIV and peripheral sensory neuropathy in HIV positive patients with p value <0.001.

Table 1. Demographic characteristics of the subject of study

Demographic Charateristics	Total (n = 83)	Peripheral sensory neuropathy positive (n = 36)	Peripheral sensory neuropathy negative (n = 47)
Age (years), mean±SD	39,4 ± 9,6	43,1 ± 10,3	36,3 ± 8,0
Age group, n (%)			
<40 years	28 (33,7)	22 (61,1)	6 (12,8)
>40 years	55 (66,3)	14 (38,9)	41 (87,2)
Gender, n (%)			
Male	52 (62,7)	24 (66,7)	28 (59,6)
Female	31 (37,3)	12 (33,3)	19 (40,4)
Education, n (%)			
SMA	58 (69,9)	28 (77,8)	30 (63,8)
S1	16 (19,3)	6 (16,7)	10 (21,3)
D3	9 (10.8)	2 (5,6)	7 (14,9)
Occupation, n (%)			
Self employed	28 (33,7)	8 (22,2)	19 (40,4)
Housewife	17 (20,5)	10 (27,8)	7 (14,9)
Private employees	13 (15,7)	4 (11,1)	10 (21,3)
Police	5 (6,0)	1 (2,8)	4 (8,5)
Driver	5 (6,0)	4 (11,1)	1 (2,1)
Farmer	5 (6,0)	2 (5,6)	3 (6,4)
Civil servants	4 (4,8)	2 (5,6)	2 (4,3)
Not Working	4 (4,8)	4 (11,1)	0
College Student	2 (2,4)	1 (2,8)	1 (2,1)
Tribe, n (%)			
Batak	53 (63,9)	23 (63,9)	30 (63,8)
Javanese	13 (15,7)	4 (11,1)	9 (19,1)
Chinese	5 (6,0)	4 (11,1)	1 (2,1)
Malay	4 (4,8)	2 (5,6)	2 (4,3)
Minang	4 (4,8)	2 (5,6)	2 (4,3)
Nias	3 (3,6)	0	3 (6,4)
Tamil	1 (1,2)	1 (2,9)	0
Marital Status, n (%)			
Married	55 (66,3)	26 (72,2)	29 (61,7)
Not married	28 (33,7)	10 (27,8)	18 (38,3)

Table 2 Association between clinical stage of HIV and peripheral sensory neuropathy

Clinical Stage of HIV	Neuropathy postive		Neuropathy negative		Total	p
	n	%	n	%		
Stadium IV	26	72,2 %	10	27,8 %	36	< 0,001
Stadium III	10	21,3 %	37	78,7 %	47	
Total	36	43,4 %	47	56,6 %	83	

**Chi square test*

DISCUSSION

The number of HIV patients with peripheral sensory neuropathy in this study was 83 subjects, with the mean age was 39.4+9.6. This is relevant with the research by Deivy et al (2018) which stated that the 20-40 year age group was the group with the highest percentage of HIV patients.[5] A total of 22 subjects (61.1%) with peripheral sensory neuropathy positive were over 40 years old. This is relevant with the research by Kedir et al (2019) which stated that there was a two-fold increased risk of experiencing peripheral sensory neuropathy in HIV patients aged over 40 years.[9] Age was a factor related to the incidence of neuropathy. Peripheral nerve regeneration ability decreased due to aging.[5]

In this study, most of the subjects were male (62.7%) and followed by female (37.3%). These results are relevant to research conducted by Joko et al (2020) where HIV patients with peripheral sensory neuropathy symptoms were mostly found in male (57.14%) followed by female (42.86%).[1] Another study by Deivy et

al (2018) also stated that the majority of peripheral sensory neuropathy cases were found in male HIV patients. This is relevant with statistical data on the ratio of men to women for HIV/AIDS cases in Indonesia until March 2016 as much as 1.7:1.[5]

In this study, it was found that 28 subjects (77.8%) with peripheral sensory neuropathy positive had a high school education level. This is relevant to research by Luh et al (2013) which stated that the highest level of education was high school (51.6%). Level of education was positively correlated with the level of awareness toward healthy lifestyles as well as compliance toward treatments.[10]

This study found a significant association between clinical stage of HIV and peripheral sensory neuropathy positive in HIV patients with a p value <0.001. This is relevant to research by I Putu et al (2017) which stated that there was a significant correlation between clinical stage of HIV and peripheral sensory neuropathy positive (r = 0.358).[11] Peripheral sensory neuropathy occurred more frequently in HIV patients in clinical stages 3 and 4, associated with the increased in viral replication. An increase in viral replication was followed by a decrease in the number of CD4 T lymphocyte cells, which were the main target of the HIV virus, since the beginning of infection.[5,6,12] A decrease in the number of CD4 T lymphocyte cells caused immune dysregulation which was followed by the increase of macrophage activation and the release of pro-inflammatory cytokines (TNF α, IL-1, IL-6). Excessive inflammatory cytokines would accelerate the process of neuron apoptosis in sensory nerve fibers and caused peripheral sensory neuropathy.[13,14] Research by Desti et al (2020) stated that there was a significant relationship between CD4 count and nerve conduction speed (p = 0.038, OR = 4.636, CI 1.023-21.004). Patients with a CD4 count < 185 cells/mm3 had a 4.6 times risk of decreased nerve conduction speed compared to patients with a CD4 count > 185 cells/mm3.14 Furthermore, HIV patients in advanced clinical stages of HIV had a risk of experiencing nutritional and vitamin deficiencies which were predisposing factors of peripheral sensory neuropathy.[15]

CONCLUSION

This study concluded that there was a significant association between clinical stage of HIV to sensory peripheral neuropathy. This relationship was explained by an increase in viral replication followed by neuronal apoptosis in sensory nerves.

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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