

The Correlation Between HbA1c and Neuropathy Disability Score in Type 2 Diabetes

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Introduction

Based on the International Diabetes Federation, 425 million people would suffer from Diabetes Mellitus (DM) by 2045. In the developing country, including Indonesia it is predicted that 4 out of 5 have Diabetes.¹ According to the Basic Health Research conducted by the Ministry of Health Indonesia in 2013, DM is the 4th most non-communicable disease after cancer in Indonesia. Furthermore, in West Nusa Tenggara, the estimated people having DM is 0.9% of the total population.²

Diabetes is a metabolic disease with an abnormal hyperglycemic index that occurs due to abnormal insulin secretion, insulin action or combined. DM type 2 has several classic symptoms, including polyuria, polydipsia, polyphagia, and weight loss. DM diagnosis requires several laboratory examinations : fasting blood sugar level, 2 hours after post prandial blood sugar level and HbA1c.³ Diabetes Mellitus has several acute and chronic complications that may affect various organs and cause morbidity and mortality. Chronic complications are categorized into vascular (microvascular and macrovascular) and non-vascular complications. Microvascular complications include neuropathy, nephropathy and retinopathy, whereas macrovascular complications include cerebrovascular, coronary heart disease and peripheral arterial disease.⁴

DM neuropathy affects 50% of people with both type 1 and type 2 DM. Diabetic neuropathy can be in the form of polyneuropathy, mononeuropathy, or autonomic neuropathy. The occurrence of neuropathy is related to the duration of DM and control of blood sugar. The most type of neuropathy is distal symmetric polyneuropathy and the most common symptoms are such sensory disorders as hyperesthesia, paresthesia, and dysesthesia.⁴ To identify the complications of neuropathy in diabetes, it is necessary to screen and then stratify for the degree of neuropathy. Screening the occurrence of neuropathy is conducted through a series of questions to patients to find out whether there is neuropathy. If neuropathy is found, an examination is needed to determine the degree of neuropathy so that complications can be prevented. These examinations include pinprick examinations, temperature checks, reflex examinations and vibrations on patients.⁵

Hemoglobin A1c (HbA1c) is glycosylated hemoglobin that is used to monitor the status of sugar levels in the last 2 or 3 months. Recommendation from the American Diabetes Association (ADA), HbA1c levels must be maintained at 7% in all diabetics patients. HbA1c levels above 7% increase the risk of complications, especially

microvascular complications. Koenig and colleagues first reported the relationship between HbA1c and blood sugar control in uncontrolled diabetic patients. Many studies indicate an association between HbA1c and diabetes complications. However, few studies have focused on HbA1c levels with diabetic polyneuropathy.⁶ Early detection of diabetes polyneuropathy can prevent morbidity. Neuropathy Disability Score (NDS) has been widely accepted and validated as an assessment tool to identify the presence of diabetes neuropathy.⁷ The relationship between HbA1c and the severity of diabetic neuropathy is done by electrodiagnostic examination, showing that increased HbA1c levels and age are the main predictors of diabetes neuropathy.⁸ The electrodiagnostic examination is a sophisticated examination and not all hospitals in low resource settings have this device, so that a validated physical testing is needed to establish the severity of the diabetic neuropathy.⁸ For this reason,⁶ research is required in order to explore the correlations between HbA1c with the severity of diabetic neuropathy as assessed by the Neuropathy Disability Score (NDS) among diabetes mellitus patients.

5

Methods

This research is an analytic observational study with the cross-sectional method which was conducted in March to August 2019 with criteria of type 2 diabetes mellitus who experienced neuropathy symptoms selected by examining neuropathy symptom scores. Patients were recruited from the internal medicine outpatients ward of West Nusa Tenggara General Hospital. Patients who experience symptoms of neuropathy were examined for neuropathy disability scores and hemoglobin A1c levels.

In this study, a minimum sample of 51 patients was determined and sampling was carried out by the method according to the case that came sequentially (sampling from consecutive admission) until predetermined sample size was reached. Data was analyzed through Pearson correlation test or Spearman if the requirements for Pearson correlation test was not obtained.¹⁰ All data were analyzed using SPSS version 22.0.

Results

As many as 56 research subjects met the criteria for this study. Demographic data including age, sex, duration of DM, DM therapy, Neuropathy Symptoms Score (NSS), Neuropathy Disability Score (NDS) and HbA1c values are presented in Table 1. The mean age of the study subjects was 59.55 ± 9.48 years. The youngest patient is 43 years old and the oldest is 79 years old. Demographic data of research subjects based on age are set out in table 4.1.

Table 1. Baseline Characteristic (n : 56)

<i>Characteristic</i>	<i>Value</i>	<i>p value</i>
Age (years)	59.55 ± 9.48	0.757
Sex		0.396
Male	24	
Female	32	
Type Of Therapy		
Medical	36	
Insulin	15	
Others	5	
Length of Diabetes	6.95 ± 5.07	0.238
NDS value	6.77 ± 2.55	
HbA1c value	9.13 ± 2.36	

The correlation between NDS values and HbA1c levels was tested with the Spearman correlation test because the data were not normally distributed even though the data transformation was done. From the Spearman correlation test results obtained a correlation coefficient of 0.487 with a value of $p = 0.000$ (Table 2)

Table 2 Correlation of HbA1c with NDS

Variabel	Coeffition Correlation	p	n
NDS vs HbA1c	+ 0.487	0,000	56

Spearman correlation test

Discussion

Research subjects were predominately female. This was similar to previous study in China that has shown show the prevalence of DM in women is mostly found in rural and male urban areas.⁹ Based on age, the mean age of study subjects was 59.55 ± 9.48 years. The CDC (*Centers for Disease Control and Prevention*) report shows the average age of DM sufferers was 53.8 years in 1997 and 54.2 years in 2011. Furthermore, previous studies report also reported the average age of DM in Hong Kong was 52 years and in China 40-59 years.⁹

Patients with DM fore more than five years have a higher risk of neuropathy. The results of this study indicate that the median duration of DM is 5.5 years. Reports in the United Kingdom (UK), DM neuropathy, occurs in 36% of people with diabetes for more than ten years compared with people with diabetes less than five years and nerve denervation damage increases with the length of DM.¹⁰

Various scores were developed to assess the degree of neuropathy in people with DM; one of the scores that are often used is NDS (*Neuropathy Disability Score*). The median value of NDS in the study was 7.5. NDS assesses foot reflexes, vibration sensations, prick pin tests and temperature sensations on both feet with a maximum score of 10 where a score of 6 or more indicates a severe degree of neuropathy. Data reports in the UK show that 50% of people with DM show neuropathy symptoms and 7% have diabetic foot after 1 year.¹¹

This study aims to find the relationship between DM neuropathy severity by measuring the NDS scale with HbA1c levels. Spearman correlation analysis results show there is a significant relationship between HbA1c and NDS. This indicates that the higher the HbA1c value in patients with type 2 DM, the higher the NDS value was. In other words, the higher the HbA1c level, the higher the severity of the neuropathy. Zilliox *et al* (2015) research showed that NDS values in DM neuropathies were 6.26 ± 0.34 . The electrodiagnostic examination found in patients with large fiber neuropathy showed a heavier NDS value compared to patients with small fiber neuropathy (7.23 ± 0.91 vs 4.77 ± 0.53).¹² The research of Stem *et al* (2016) shows that complications of DM (neuropathy, retinopathy or nephropathy) occur in patients with HbA1c 8.5 ± 1.5 . The higher levels of HbA1c will further accelerate and worsen the complications of neuropathy. Control of glucose levels is very important to prevent and decrease the complications from DM. High levels of HbA1c are associated with high microvascular complications in people with DM.¹³ Limitations of this study was HbA1c was only

evaluated once and electrodiagnostic examination was not performed as a gold standard to determine severity of neuropathy.

Conclusion

HbA1c levels are related to the ⁹ severity of neuropathy in patients with type 2 diabetes. The higher the HbA1c value, the higher the Neuropathy Disability Scale. This study emphasize the importance of regular HbA1c levels monitoring to prevent further complications of DM both in the nervous system and in other organs.

The screenshot shows the website for Acta Medica Indonesiana, The Indonesian Journal of Internal Medicine. The page is viewed from the author's perspective, as indicated by the URL www.actamedindones.org/index.php/ijim/author. The journal is an open access publication of The Indonesian Society of Internal Medicine, with eISSN: 2338-2732 and pISSN: 0125-9326. The main navigation menu includes Home, About, Editorial Team, Issue, Submissions, Announcements, and Contact. The user is logged in as 'itsahunafi' and is viewing the 'Active Submissions' page. The page features a search bar, search scope options, and a list of active submissions. The submission table includes columns for ID, Submitted Authors, Title, and Status. The current submission is ID 1572-09-16, submitted by Hinafi, Agustriadi, Asmara, and Budyono, with the title 'Correlation of Hemoglobin A1c with Neuropathy Disability...'. The status is 'In Review: Revisions Required'. The page also includes a 'Start a New Submission' button and a 'Refbacks' section. The footer shows the journal's logo, a COVID-19 notice, and the HP logo.

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