Risk Factor of Peripheral Neuropathy among Newly Diagnosed Type 2 Diabetic Patients in Primary Care Clinic

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Abstract

Background: Diabetic foot is one of the most serious complications of diabetes leading to poor quality of life even a higher risk of mortality. Diabetic patients with peripheral neuropathy are at a higher risk of developing foot infection and ulcer. It causes a major source of morbidity, a leading cause of hospital bed occupancy and account for substantial health care, costs and resources.

Objectives: The aim of this study was to identify the risk factors for peripheral neuropathy among newly diagnosed Type 2 diabetic patient in Primary Care Clinic, Kota Bharu, Kelantan, Malaysia.

Methods: This was a part of the cross sectional study to assess the prevalence of peripheral neuropathy among newly diagnosed T2DM patients attending Primary Care Clinic in Kota Bharu district. It involved of 254 patients which were selected from July 2009 until June 2010. A set of case report form consist of socio demographic data, clinical examination and investigation result was used. Diabetic peripheral neuropathy is present if patient unable to feels the monofilament 5.07(10g) to one or more sites tested.

Results: The mean (SD) age of participants was 53.3(9.06) years. About 8.7% of participants were diagnosed to have peripheral neuropathy. The factors that contribute to the development of peripheral neuropathy among newly diagnose type 2 diabetes were age of the patients ($p < 0.001$) and the presence of retinopathy ($p= 0.001$).

Conclusion: The detection of the peripheral neuropathy should be done to all T2DM patients at the diagnosis, so that the preventive measures could be taken to prevent diabetic foot disease. Patients who have retinopathy should also screen for neuropathy.

Keyword: Peripheral neuropathy, Diabetes Mellitus, Primary Care

Background

T2DM is often preceded by a long period of unrecognized metabolic abnormality, the neural dysfunction is likely can be detected at the time when the diabetes is diagnosed.[1] The most common form of diabetic peripheral neuropathy (PN) is distal symmetrical sensory–motor poly neuropathy. Early distal sensory–motor neuropathy is usually asymptomatic and motor involvement occurs later with distal loss of strength[2] but sensory abnormalities may be detectable by neuro-physiological testing such as nerve conduction study and electromyography.[3]

Diabetic PN lead to vulnerability to physical and thermal trauma which increases the risk of foot ulceration by 7-fold[4] and increased 15–20 times risk of amputation if coexist with peripheral vascular disease.[5,6] Foot ulcers are associated with many negative sequences and high costs of treatment. The loss of mobility associated with foot ulcers affects patients' ability to perform simple, everyday tasks and to participate in leisure activities. These often lead to depression and poor quality of life.[7]

The preventive care on diabetic foot can improve survival, reduce ulceration and amputation rate. It is cost effective and can even save on a long term cost when compared to standard care.[3,8] However, Cochrane review on patient education for preventing diabetic foot ulcer appears little evidence available to support it effectiveness.[9] Education should be tailored to the individual need and intervention should be given to those patients according to their risk. Early detection of the PN or loss of protective sensation is important before starting an education and structured treatment plan to prevent lower extremities amputation[10] as it is an important cause of morbidity and mortality in diabetes. The five years mortality rate is up to 55% in patient with leg amputation.[11] This prognosis of lower leg amputation is as bad as cancer survival.

In Malaysia, from Malaysian National Health and Morbidity Survey III (NHMSIII) noted the prevalence of newly diagnosed diabetes has increased from 2.5% in 1996 to 5% in 2006. It is reported about 4.3% of lower limb amputation was a complication of diabetes.[12] Diabetic foot ulcer is a leading cause of morbidity and hospital admission which consumed a substantial amount of health care costs and resources.[13]

Many studies shows the duration of diabetes were associated with the development of diabetic neuropathy.[14,15] However, Malaysia has limited data to look for the risk factors of neuropathy among newly diagnosed diabetes patient. Therefore, it is hope that this study would lay the ground for future effort in controlling this problem.

Methods

Study design

The study was cross sectional study done among 254 newly diagnosed T2DM patients who attended Primary care Clinic in Kota Bharu district of Kelantan from July 2009

until June 2010. Kelantan is one of the states in Malaysia and Kota Bharu district is among the highest number of diabetic registry compared to other nine districts.

The inclusion criteria were age of 18 years and older and newly diagnosed T2DM based on WHO definition criteria. Those who on medication (isoniazide, vincristine, thiazide or gold therapy), working at pesticide and herbicides factories, thyroid disorder, history of stroke affecting the legs**,** pregnant and gestational diabetes mellitus were excluded.

Data collection

The participants were chosen by non probability sampling method and those who meet the criteria were explained about the study and informed consent was obtained. Those who agreed were interview on demographic data and medical history were reviewed from medical record.

Patient's parameter such as blood pressure, heart rate, height and weight was taken by the assistant nurse at the triage counter. Measurement of blood pressure using mercury column sphygmomanometer after patient had adequately rest and seated. Hypertension was defined as blood pressure of more than 140/90 mmHg or ongoing treatment with hypertensive medication. Weight and height was taken without shoes and sock using SECA measuring scale and body mass index (BMI) was calculated based on patient weight in kilograms divided by square of height in m^2.

Fasting blood sample were taken to assess for blood sugar, HBA1c, lipid profile and cretinine level. Estimated glomerular filtration rate was calculated using Cockcroft-Gault method and nephropathy is defined if calculated GFR less than 60mL/min/1.73m^2. Dyslipidemia was considered if total cholesterol was > 5.6 mmol/L and/ot triglyceride >2.1 mmpl/L and or LDL >3.4 mmol/L and or HDL < 0.9 mmol/L.

A standard 12 lead ECG was recorded and ischemic heart disease was defined when presence of ischemic changes in ST segment, T waves or present of Q wave in the reciprocal lead or history of previous myocardial infarction, angina or history of coronary-artery bypass. Fundus picture was taken with fundus camera kowa non Myd 10 Mega 7 by trained staff. Retinopathy is defined base on fundus pictures including background retinopathy, maculopathy, preproliferative and proliferative retinopathy.

PN was assessed with Nylon Semmes-Weinstein Monofilament (SWM) as it is the most commonly used for detecting neuropathy in which the pressure was given till the monofilament band buckled. The monofilament 5.07(10g) correlated best with the presence or history of foot ulcer and identifying patients at risk for foot ulceration.[16,17] Based on Smieja et al, four plantar sites[18] were tested to diagnosed peripheral neuropathy in this study. With eyes closed, monofilament will be applied (up to 3 times) for one second to the dorsum of the first toe, first, third and fifth metatarsal head. The participants will indicate when the touch occurred and results were classified as neuropathy when they were unable to feels the pressure to one or more sites.

Statistical analysis

Data was entered and analyzed using Statistical Program for Social Sciences (SPSS) version 18.0. Descriptive analysis was presented as the frequency and percentage for the categorical variable. Numerical variable was presented as mean and standard deviation (SD) for normally distributed data or as median and inter quartile range (IQR) for not normality distributed data. The dependent variable was neuropathy and the independent variables were includes age, sex, race, BMI, SBP, DBP, triglyceride, LDL-C, HDL-C, total cholesterol level, smoking status, retinopathy, nephropathy and ischemic heart disease.

Simple logistic regression was used to determine the associated factors for diabetic peripheral neuropathy. Multiple logistic regression was used to determine the associated factors while controlling for other confounders in the model.

Results

Socio-demographic and medical characteristic of participants

Of all the 254 participants, 147 were female (58%) and 107 were male (42%) with majority of them were Malays (86.2%). The mean (SD) age of the participants was 53.3± 9.06 years with 81.5% of them were hypertensive and majority of them were non smoker (82.7%). Retinopathy (14.6%) was the highest complication, followed by nephropathy (11%), neuropathy (8.7%) and ischemic heart disease (6.7%). Fasting blood sugar more than 7.0mmol/l was observed in 60.2% of the participants and 56.2% had HBA1c more than 8.0% at the diagnosis.

High total cholesterol of more than 5.2mmol/l was present in 88.6% of participants, 46.1% had HDL-C less than 1mmol/l, 53.1% had TG more than 1.7mmol/l and 86.6% had LDL-C more than 2.6mmol/l. (Table 1)

Factors associated with peripheral neuropathy

The prevalence of diabetic peripheral neuropathy in this study was 8.3% (95% CI: 5.23 - 12.17). The factors associated with diabetic peripheral neuropathy using simple logistic regression were age (p= 0.001), weight (p= 0.041) and retinopathy ($p < 0.001$).

The Multiple Logistic Regression with backward stepwise procedure were used for selection of variable shows that peripheral neuropathy were associated with age ($p < 0.001$) and retinopathy (p= 0.001). Those who had retinopathy were 5.51 times at odds of having neuropathy compared to those without retinopathy and for every 1 year increase in age, there will be 1.11 times at odds of having neuropathy compared to non neuropathy.

Discussion

In this study, the associated factors of the peripheral neuropathy were age, weight and retinopathy. However, when all the associated factors were adjusted in the multivariate analysis, the significant associated factors of peripheral neuropathy among newly diagnosed T2DM in this study were age and presence of retinopathy. Like this study, other studies[19-22] shows age is one of the factors associated with neuropathy.

The neuropathy was increased with age and for every 1 year increase in age, there will be 1.11 times at odds of having neuropathy compared to non neuropathy. Other studies by Sosenko J and Franklin et al also support the finding in which they found increasing age was 1.74 (95% CI 1.40, 2.16)[20] and 1.3 (95% CI 1.1, 1.6)[22] risk for neuropathy respectively. However these studies were done among long standing T2DM patient. The possibility of our patient had preclinical diabetes and poor glycaemic control at diagnosis.

Those who had retinopathy were 5.51 times at odds of having neuropathy compared to those without retinopathy. This finding was supported by Franklin et al in which they investigated the risk factors for distal (sensory) neuropathy among T2DM in a population-based study in Southern Colorado. They found that the odd of having neuropathy was 3 times (CI = 1.2, 7.7) in participant with retinopathy.[22] Among IDDM also shows the similar finding in which the relative risk of having neuropathy was 2.0 (95% CI 1.5, 2.8) in the background retinopathy and 5.4 (95% CI 3.4,8.6) in the proliferative retinopathy respectively.[19] This was because they shared the microangiopathy complication of the disease. Another study in China by Fang Liu et al were noted those with diabetic retinopathy has 6.06 times risk of having peripheral neuropathy. Their risk was higher because of the prevalence of PN was 17.2% and they include known case of diabetic in the study population.[23]

Franklin et al also found, the increased glycohemoglobin percentage and insulin used were associated with neuropathy. All the above factors were not associated to neuropathy in this study since this study was done among the newly diagnosed diabetic population.[22]

In this study we did not find positive correlation between lipids profile and neuropathy. This finding was supported by Agrawal et al among 4067 participants with T2DM in Northwest India.[24] However, the results were inconsistent with studies by Tesfaye et al among T1DM in which they found that all types of lipoproteins were significant for diabetic peripheral neuropathy. Perhaps further study needs to be done to find the relationship between peripheral neuropathy and the lipid profile among newly diagnosed T2DM.

Other factors such as duration of diabetes and height were associated with neuropathy[19,20] among long standing T2DM and was not observed in this study population as it was done in newly diagnosed patient.

Conclusions

From this study, the prevalence of peripheral neuropathy among newly diagnosed T2DM was 8.3%. Factors contribute to the risk of getting peripheral neuropathy were age with odd ratio 1.11(95% CI 1.05, 1.18) and retinopathy with odd ratio 5.51(95% CI 2.07, 14.69).

Conflict of Interest: None

Authors' contributions

Azura M.S: Conception and design, Data collection and analysis, drafting article and final approval
Adibah H I: Conception and design of the study, interpretation and final approval
Juwita S: Conception and design of the study, interpretation, drafting and final approval

Acknowledgements

We would like to acknowledge the Ethical committee of Universiti Sains Malaysia for allowing us to conduct this study on 7th July 2009 [USMKK/PPP/JEPeM 214.3. (2)]. We also greatly acknowledge and appreciate the cooperation of all participants and clinic staff for their assistant in this study.

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Table 1: Socio demographic medical characteristic of 254 participants

Variable n=254	Mean ± SD[a]	n(%)
Age (years)	53.5 ± 9.06	
Race		
Malay		219(86.2)
Non Malay		35 (13.8)
Occupation		
Government servant		78(30.7)
Private sector		32(12.6)
Self employed		37(14.6)
Unemployed		71(27.9)
Pensioner		36(14.2)
Gender		
Female		147(57.9)
Male		107(42.1)
Smoking status		
Smoker		44(17.3)
Non Smoker		210(82.7)
BMI(kg/m^2)	26.70(4.17)	
SBP(mmHg)	140.9(21.52)	
DBP(mmHg)	84.5(11.07)	
HBA1c (%)		
>8		140(56.2)
7-8		63(25.3)
<7		46(18.5)
FBS(mmol/L)		
> 7.8		153(60.2)
6.7 - 7.8		44(17.3)
< 6.7		57(22.4)
TC(mmol/L)		
≥5.2		225(88.6)
< 5.2		29(11.4)
HDL-C(mmol/L)		
<1		117(46.1)
≥1		134(52.8)
LDL-C(mmol/L)		
≥2.6		220(86.6)
<2.6		24(9.4)
TG(mmol/L)		
≥1.7		135(53.1)
<1.7		119(46.9)
Retinopathy		
Yes		37(16.6)
No		217(85.4)
Nephropathy		
Yes		28(11.0)
No		226(89.0)
Neuropathy		
Yes		21(8.3)
No		233(91.7)
Hypertension		
Yes		185(27.2)
No		47(72.8)
IHD		
Yes		17(6.7)
No		236(92.9)

[a] standard deviation

Table 2: Factors associated with peripheral neuropathy in newly diagnosed T2DM using Simple Logistic Regression

Variables	Neuropathy		Crude OR[a]	(95%CI[b])	*Wald stat*[c]	*P* value
	Yes n(%)	No n(%)				
Age (year)			1.12	(1.05,1.12)	14.49	0.001
Race						
Non Malay	16(7.3)	203(92.7)	1.00			
Malay	6(17.1)	29(82.9)	0.38	(0.14,1.05)	3.47	0.063
Gender						
Female	15(10.2)	132(89.8)	1.00			
Male	7(6.5)	100(93.5)	0.62	(0.24,1.57)	1.03	0.309
Smoking status						
Non smoker	18(8.6)	192(91.4)	1.00			
Smoker	4(9.1)	40(90.9)	1.07	(0.34,3.32)	0.01	0.911
BMI			0.93	(0.84,1.04)	1.60	0.210
Height(meters)			0.02	(0.00,3.66)	2.23	0.136
Weight(kg)			0.04	(0.96,1.00)	4.17	0.041
FBS (mmol/l)						
> 7.8	15(9.8)	138(90.2)	1.44	(0.46,4.54)	0.388	0.533
6.7 - 7.8	30(93.8)	2(6.3)	0.97	(0.205,4.57)	0.002	0.969
< 6.7	37(92.5)	3(7.5)	1.00			
HBA1c (%)						
>8	10(7.1)	130(92.9)	0.63	(0.20,1.95)	0.639	0.424
7-8	7(11.1)	56(88.9)	1.03	(0.30,3.46)	0.002	0.968
≤7	5(10.9)	41(89.1)	1.00			
TC(mmol/l)						
≥5.2	20(8.9)	205(91.1)	1.32	(0.29,5.95)	0.13	0.720
<5.2	2(6.9)	27(93.1)	1.00			
HDL-C(mmol/l)						
<1	10(8.5)	107(91.5)	0.95	(0.40,2.29)	0.01	0.950
≥1	12(9.0)	122(91.0)	1.00			
LDL-C(mmol/l)						
≥2.6	21(9.5)	199(90.5)	2.43	(0.312,18.89)	0.72	0.397
<2.6	1(4.2)	23(95.8)	1.00			
TG(mmol/l)						
≥1.7	14(10.4)	121(89.6)	1.61	(0.65,3.97)	1.05	0.306
<1.7	8(6.7)	111(93.3)	1.00			
Retinopathy						
No	12(5.5)	205(94.5)	1.00			
Yes	10(27)	27 (73.0)	6.33	(2.50,16.04)	15.11	<0.001
Nephropathy						
No	17(7.5)	209(92.5)	1.00			
Yes	5(17.9)	23(82.1)	2.67	(0.90,7.92)	3.15	0.076
Hypertension						
No	4 (5.8)	65(92.4)	1.00			
Yes	165(89.2)	20(10.8)	2.53	(0.90,7.10)	3.12	0.077
IHD						
No	20(8.5)	216(91.5)	1.00			
Yes	2(11.8)	15(91.5)	1.44	(0.31,6.75)	0.21	0.644

[a] crude odd ratio [b] confidence interval [c] wald statistic

Table 3: Associated factors for peripheral neuropathy among newly diagnosed T2DM

Variables	Adjusted OR[a]	(95% CI[b])	Wald statistic	*P* value
Age (year)	1.11	1.05,1.18	12.42	<0.001
Retinopathy				
No	1.00			
Yes	5.51	2.07,14.69	13.04	0.001

[a] adjusted odd ratio [b]confidence interval