IJCRR
Vol 05 issue 12
Section: Healthcare
Category: Research
Received on: 09/05/13
Revised on: 23/05/13
Accepted on: 18/06/13

EVALUATION OF DIABETIC PERIPHERAL NEUROPATHY IN KNOWN CASES OF TYPE 2 DIABETES IN URBAN AND RURAL POPULATION

Lakshmana Kumar N.[1], Mallikarjuna Rao K.V.N.[1], Srinivas Ch[2], Kishore K.[1], Kiran Deedi M. [1], Lakshmana Rao N. [3]

[1]Department of Biochemistry, GSL Medical College, Rajahmundry, AP, India
[2]Department of Physiology, GSL Medical College, Rajahmundry, AP, India
[3]Department of Community Medicine, RIMS, Ongole, India

E-mail of Corresponding Author: luckylakshman@yahoo.com

ABSTRACT

Background: Diabetic Peripheral Neuropathy (DPN) is one of the microvascular complications of diabetes, and is responsible for most of the amputations in diabetes. Measurement of Vibration Perception Threshold (VPT) is useful in assessment of peripheral neuropathy. The aim of the study is to study the role and correlation of age, duration of diabetes, fasting plasma glucose, HbA1C, and microalbumin:creatinine ratio with diabetic peripheral neuropathy in known cases of type 2 diabetes mellitus in urban and rural population of Rajahmundry, Andhra Pradesh, India.

Methods: Study was done on two groups comprising of 30 cases with normal VPT and 30 cases with abnormal VPT in type 2 diabetes. Age, duration of diabetes, body mass index, fasting plasma glucose, HbA1C, and microalbumin:creatinine ratio were recorded and analyzed.

Results: Significant difference in age, duration of diabetes, fasting plasma glucose, HbA1C, and microalbumin:creatinine ratio is observed between groups ($P < 0.05$). There is significant correlation of age, duration of diabetes, fasting plasma glucose, HbA1C, and microalbumin:creatinine ratio with VPT ($P < 0.05$) in all cases. Among the correlating parameters multiple regression analysis revealed that age and HbA1C are good predictors of VPT ($P < 0.05$).

Conclusion: Age, duration of diabetes, fasting plasma glucose, HbA1C, and microalbuminuria were associated with DPN in urban and rural population. However age and HbA1C are strong predictors of changes in VPT. There is need to study the prevalence of and other risk factors associated with DPN with a larger sample size in this area.

Keywords: Diabetes, Peripheral neuropathy, Vibration perception threshold, Risk factors.

INTRODUCTION

Type 2 Diabetes mellitus is one of the most common forms of chronic disease.[1] With the change in life style and urbanization, the number of individuals with diabetes are increasing and the age of diagnosis is decreasing.[1] Longer periods of exposure to hyperglycaemia have increased the risk of developing complications related to diabetes.[1] The real burden of diabetes is due to its micro and macro vascular complications which may present even at the time of diagnosis.[2] Diabetic Peripheral Neuropathy (DPN) is one of the microvascular complication of diabetes, and affects approximately 30% of people with diabetes.[3] More than 80% of amputations occur after ulceration or injury, which can result from diabetic neuropathy.[4] Diabetic patients are 15 times more likely to have an amputation than non diabetic patients.[5] Early

identification of DPN prevents the morbidity and mortality due to diabetic neuropathy. [5]

Assessment of Vibration Perception Threshold (VPT) is one of the recommended standardised quantitative sensory testing methods employed in the diagnosis of DPN.[6] Elevated VPT is an effective predictor of neuropathic foot ulceration, one of the most common causes for hospital admission and lower limb amputations among patients with diabetes.[7] Along with markers of microangiopathy such as microalbuminuria, VPT may also predict mortality in people with diabetes.[8]

Most of the available studies in India on DPN were either hospital based or done in metro populations.[9,10] There are geographical variations of prevalence and risk factors associated with DPN.[10,11,12] Further research is required in small urban and rural population of India to study DPN. The present work was taken up to evaluate the association of age, duration of diabetes, body mass index (BMI), fasting plasma glucose (FPG), glycated haemoglobin (HbA1C), and microalbuminuria in known cases of type 2 diabetes mellitus in urban & rural population of Rajahmundry, Andhra Pradesh, India.

METHODS

This cross-sectional observation study was carried out in Rajahmundry urban and rural population in the month of April 2013. Rajahmundry is a coastal town with a population of 3,43,903 which was divided into 50 municipal wards. The surrounding rural population of five villages (Bommuru, Dowleswaram, Hukumpet, Katheru and Morampudi) under Rajahmundry metro area is 1,34,296. The study group is comprised of 300 known cases of Type-2 Diabetes mellitus. 200 cases were recruited from five wards of Rajahmundry city and 100 cases were recruited from surrounding five villages by systematic random sampling as a part of ongoing Rajahmundry Integrated Diabetes Evaluation and Research (RIDER) study. Study was approved by institutional Ethics committee. Written and informed consent was obtained from all the participants.

Known cases of neuropathy due to other causes like chronic inflammatory polyneuropathy, hypothyroidism, B_6, B_{12} deficiency and uraemia were excluded from the present study. Study population was screened using VPT assessment by biothesiometer. VPT below 10 volts was considered as normal and above 10 volts was considered as abnormal with loss of vibratory perception. 30 cases with normal VPT and 30 cases with abnormal VPT (Twenty cases from urban population as four from each ward and ten cases from rural population as two from each village) were selected by systematic random sampling and were recruited for the present study for further anthropometric and biochemical evaluation.

VPT was measured using digital biothesiometer (Diabetik foot care India) at six different places (First toe, 1^{st}, 3^{rd}, 5^{th} metatarsal head, instep and heal) on both feet. Average of the twelve readings was taken as final value. Fasting whole blood sample was collected. First morning midstream urine was collected in a sterile urine container. Age, Height and weight were recorded. BMI was calculated from height and weight by the formula Wt. in Kg/Ht. in m^2. HbA1C was measured with whole blood using NGSP (National Glycohemoglobin Standardisation Programme) certified Biorad in2it analyser. Plasma glucose was measured by glucose oxidase and peroxidase method. Microalbumin was measured by immuno turbidimetry and urinary creatinine by Jaffe's method. Microalbumin: creatinine ratio was calculated.

Statistical Analysis

Data was analyzed using Microsoft excel 2007 and SPSS trial version 16.0. Continuous variables were expressed as mean ± standard deviation. Student ' t ' test was used to compare means of the two groups. Karl Pearson method was used to observe the correlation of variables. Multiple

regression analysis was used to study the prediction of dependant variable by correlating variables. Probability (*P*) value less than 0.05 was regarded as statistically significant.

RESULTS

There is significant difference of mean of all variables except BMI between cases with normal VPT and abnormal VPT (Table -1, 2). Correlation analysis was done in all cases. Age, duration of diabetes, FPG, HbA1C, and microalbumin:creatinine correlates significantly with VPT in type 2 diabetes (Table -3). Microalbuminuria is present in all cases with abnormal VPT. Multiple regression analysis was done to assess the predictability of VPT by correlating variables. Age and HbA1C are good predictors of changes in VPT (Table -4).

Discussion

In the present study, there is significant difference in age and duration of diabetes between groups, and correlation of age and duration of diabetes with VPT. DPN increases with both age and duration of diabetes, and 50% cases of type 2 diabetes cases aged over 60 years have DPN.[13] There is progression of polyneuropathy with advancing age with a decline in sensory and motor action potentials.[14] Significant difference in FPG and HbA1C between groups, and correlation of FPG and HbA1C with VPT suggests that impaired glycaemic control plays definite role in development of DPN. Micro vascular complications are caused by prolonged exposure to hyperglycaemia, which damages tissues by polyol pathway, increased advanced glycation end products (AGE), and induction of super oxide production in mitochondria.[15] Significant difference in microalbumin;creatinine ratio between groups and correlation of microalbumin:creatinine with VPT supports the concept of coexistence of other microvascular complications like nephropathy and retinopathy in cases of neuropathy.[9] All the cases with abnormal VPT have microalbumnuria in the present study. This may be due to the higher prevalence of microalbuminuria in this geographical area.[16] The degree of coexistence and prevalence of microvascular complications are associated with differences in individual susceptibility, which is linked with polymorphism of genes like super oxide dismutase (SOD).[17] Though some studies have reported negative correlation of BMI with neuropathy, there is no statistically significant difference and correlation of BMI with VPT in the present study. [9]

The limitation of the present study is that age wise, gender wise, within the group analysis was not donebecause of small sample size. Evaluation of other parameters like lipid profile, blood pressure, ankle brachial index may help in more detailed evaluation. This study will serve as pilot study for further research in this area.

Conclusion

This study in urban an rural population shows that age, duration of diabetes, fasting plasma glucose, glycated haemoglobin (HbA1C), microalbumin:creatinine ratio were high in cases with abnormal vibration perception threshold, and correlate with vibration perception threshold in known cases of type2 diabetes mellitus. Body mass index has no association with vibration perception threshold. Age and HbA1C are good predictors of vibration perception threshold in type 2 diabetes. Detailed evaluation with a larger sample size is required to assess the prevalence of and risk factors of diabetic peripheral neuropathy in urban and rural population.

Source of funding: Authors have not received any grant for the present study.

Conflicts of interest: There are no conflicts of interest in the present study.

ACKNOWLEDGEMENTS

Authors wish to acknowledge Dr.Y.N.Rao, Professor and Head, Department of Biochemistry, GSL Medical College, Rajahmundry for his

support and guidance and all the participants of RIDER study for their cooperation. Authors acknowledge the great help received from the scholars whose articles cited and included in references of this manuscript. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed. Authors are grateful to IJCRR editorial board members and IJCRR team of reviewers who have helped to bring quality to this manuscript.

REFERENCES

1. Ronald C.W. Ma, Petr C.Y. Tong. Epidemiology of Type 2 Diabetes. In: Richard I.G. Holt, Clive S. Cockram, Allan Flyvbjerg, Barry J. Goldstein, editors. Text book of Diabetes. 4th ed. 20 West Sussex (UK): Wiley –Blackwell; pp.45-46.
2. Shashank R Joshi, AK Das, VJ Vijay, V Mohan. Challenges in Diabetes Care in India: Sheer Numbers, Lack of Awareness and Inadequate Control. J Assoc Physicians India 2008;56: 443-50.
3. Shaw JE, Zimmet PZ, Gries FA, Ziegler D. Epidemiology of diabetic neuropathy. In: Gries FA, Cameron NE, Low PA, Ziegler D, editors. Textbook of Diabetic Neuropathy. Stuttgart/Newyork: Thieme, 2003;64-82.
4. Boulton AJM, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R, *et al*. Diabetic neuropathies: a statement by the American Diabetes Association. Diabetes Care 2005;28:956-962.
5. Bild DE, Selby JV, Sinnock P, Browner WS, Braveman P, Showstack JA. Lower extremity amputation in people with diabetes: epidemiology and prevention. Diabetes Care 1989;12:24-31.
6. Consensus Development Conference on Standardised Measures in Diabetic Neuropathy. Proceedings of a consensus development conference on standardised measures in diabetic neuropathy. Diabetes Care 1992;15(3):1080-1107.
7. Abbott CA, Vileikyte L, Willimason S, Carrington AL, Boulton AJM. Multicenter study of the incidence of and predictive risk factors for diabetic neuropathic foot ulceration. Diabetes Care 1998;21:1071-1075.
8. Coppini DV, Bowtell PA, Weng C, Young MJ, Sonksen PH. Showing neuropathy is related to increased mortality in diabetic patients: a survival analysis using an accelerated failu re time model. J Clin Epidemiol 2000.;53:519-523.
9. Hari KVS Kumar, SK Kota, A Basile, KD Modi. Profile of Microvascular Disease in Type 2 Diabetes in a tertiary Health Care Hospital in India. Ann Med Health Sci Res 2012;2(2):103-108.
10. Rani PK, Raman R, Rachapalli SR, Pal SS, Kulothungan V, Sharma T. Prevalence and risk factors for severity of diabetic neuropathy in type 2 diabetes mellitus. Indian J Med Sci 2010;64:51-57.
11. Pradeepa R, Rema M, Vignesh J, Deepa M, Deepa R, Mohan V. Prevalence and risk factors of Diabetic neuropathy in an Urban south Indian population: The Chennai Urban Rural Epidemilogy Study (CURES-55). Diabet Med 2008;25:407-12.
12. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, *et al*. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population based cohort: The Rochestor Diabetic Neuropathy Study. Neurology 1993;43:817-824.
13. Young MJ, Boulton AJM, Macleod AF, Willims DRR, Sonksen PH. A multicentre study of diabetic peripheral neuropathy in the United Kingdom hospital clinic population. Diabetologia 1993;36(2):150-154.
14. Partanen J, Niskanen L, Lehtinen J, Mervaala E, Siitonen O, Uusitupa M. Natural history of

peripheral neuropathy in patients with NIDDM. N Engl J Med 1995;333(2):89-94.

15. Ferdinando Giacco, Michael Brownlee. Pathogenesis of Microvascular Complications. In: Richard I.G. Holt, Clive S. Cockram, Allan Flyvbjerg, Barry J. Goldstein, editors. Text book of Diabetes. 4th ed. 20 West Sussex (UK): Wiley –Blackwell; pp.555-574.
16. Lakshmana Kumar N, Mallikarjuna Rao KVN, Kishore K, Priyadarsini DVS, Kiran Deedi M, Laxman Rao N. Awareness of Diabetes and its relation to prevalence of microalbuminuria in known cases of Type 2 Diabetes. Indian Journal of Public Health Research and Development. In press 2013.
17. Al-Kateb H, Boright AP, Mirea L, Xie X, Sutradhar R, Mowjoodi A, *et al*. Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Multiple super oxide dismutase 1/splicing factor serine alanine 15 variants are associated with the development and progression of diabetic nephropathy:the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Genetics study. Diabetes 2008;57:218-228.

Table -1: Mean and S.D. of variables in two different groups

	Normal VPT (N=30) Mean ± S.D.	Abnormal VPT (N=30) Mean ± S.D.
VPT volts	4.0 ± 2.0	18.6 ± 8.3
Age (years)	47.8 ± 7.1	55.4 ± 10.5
Duration of diabetes (years)	6.6 ± 3.7	12.9 ± 7.0
BMI (Kg/m^2)	27.0 ± 3.1	26.6 ± 4.2
FPG (mg/dL)	131 ± 31	182 ± 60
HbA1C (%)	6.9 ± 0.8	9.2 ± 1.7
Microalbumin (µg/mg creatinine)	22.5 ± 13.0	74.6 ± 65.3

Table –2: Comparison of means of groups by student ' t ' test

	Levene's Test for Equality of Variances		t-test for Equality of Means		
	F	Sig.	t	df	Sig. (*P*) (2-tailed)
Age (years)	6.012	.017	3.288	58	.002*
Duration of diabetes (years)	12.868	.001	4.355	58	.000*
BMI (Kg/m^2)	.747	.391	-.472	58	.639
FPG (mg/dL)	9.434	.003	3.972	58	.000*
HbA1C (%)	8.009	.006	6.927	58	.000*
Microalbumin (µg/mg creatinine)	14.799	.000	4.287	58	.000*

* $P < 0.05$.

Table -3: Correlation of variables with VPT

	Pearson correlation	Sig. (*P*) (2-tailed
Age (years)	0.405	0.001*
Duration of diabetes (years)	0.431	0.001*
BMI (Kg/m^2)	0.130	0.321
FPG (mg/dL)	0.389	0.002*
HbA1C (%)	0.522	< 0.001*
Microalbumin (µg/mg creatinine)	0.308	0.017*

* $P < 0.05$.

Table -4: Multiple regression analysis for prediction of dependent variable VPT by independent variables

	Un standardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	Sig.
(Constant)	-31.032	8.080		-3.841	.000
Age (years)	.360	.126	.366	2.855	.006*
Duration of diabetes (years)	.080	.211	.053	.376	.708
FPG (mg/dL)	.038	.022	.224	1.713	.093
HbA1C (%)	2.261	.788	.420	2.871	.006*
Microalbumin (µg/mg creatinine)	-.024	.025	-.137	-.987	.328

R square = 0.435

* $P < 0.05$.