

ORIGINAL ARTICLE

FREQUENCY OF AUTONOMIC NEUROPATHY IN PATIENTS WITH ERECTILE DYSFUNCTION IN DIABETES MELLITUS

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Background: Among diabetic patients autonomic neuropathy (AN) is one of the most frequent complications. This affects peripheral nervous system and thus results into erectile dysfunction (ED). The main objectives of the study were to determine the frequency of autonomic neuropathy (AN) in diabetic patients with ED and to find out the associated risk factors. **Methods:** In this descriptive case series, a total 200 consecutive patients of Diabetes Mellitus with erectile dysfunction attended the Department of Endocrinology and Metabolism (DEM), Services Hospital Lahore during three months (from June to August 2013), were included. For assessing erectile dysfunction (ED) and autonomic neuropathy (AN) International Index of Erectile Function (IIEF) and Composite Autonomic Scoring System (CASS) were used respectively. Other factors impacting the autonomic functions in diabetes like duration of diabetes, age of patient, body mass index (BMI), and glycaemic control (HbA1c), hypertension and smoking status were recorded. **Results:** Average age of the patients was 57.58 ± 9.53 years (95% C.I. 55.54-59.63). Frequency of autonomic neuropathy (AN) in ED patients was 86 (43%). Duration of diabetes Mellitus and BMI were statistically significantly different among patients with severe, moderate and mild autonomic neuropathy. **Conclusions:** Autonomic neuropathy was very frequent in diabetic patients with erectile dysfunction. The associated risk factors are duration of disease and body mass index.

Keywords: Diabetes Mellitus, Autonomic Neuropathy, Erectile Dysfunction

J Ayub Med Coll Abbottabad 2005;27(3):653-5

INTRODUCTION

Autonomic neuropathy is a common complication of Diabetes and mostly associated with other complications of Diabetes but may be isolated and preceding the other complications of Diabetes. Association of autonomic neuropathy with diabetes mellitus has been well established.^{1,2} In autonomic neuropathy, due to diabetes mellitus, small blood vessels that supply blood to nerves culminates and thus this condition results in to abnormal motor neuron conduction velocity.³ It can affect any part of nervous system.² Most prevalent is peripheral neuropathy.⁴ Prevalence of diabetic autonomic neuropathy is higher in males. It has also been observed that in males the period of developing neuropathy, after diagnosis of diabetes mellitus, is shorter than in females.⁵

Autonomic neuropathy, in long standing diabetes, can blunt the counter regularity hormones like catecholamine causing hypoglycaemic unawareness and severe hypoglycaemia. Autonomic neuropathy is one of the pathogenic factors for impotence.⁶ It has been observed that prevalence of erectile dysfunction is higher in patients with diabetic neuropathy than reported.⁷⁻⁹ Diabetic autonomic neuropathy is mostly asymptomatic, but in symptomatic patients erectile dysfunction is the only symptom in more than 50 per cent cases. Erectile dysfunction when developed in a diabetic patient is an indication of generalized vascular disease. ED is the commonest sexual dysfunction in diabetic males.⁷ ED is defined as the consistent inability

to attain and maintain erection adequate for intercourse. There are many other risk factors of erectile dysfunctions. Among them after diabetes are hypertension, high cholesterol level and peripheral vascular disease.¹⁰ In this study we tried to determine the frequency of autonomic neuropathy in diabetics who had erectile dysfunction (ED) and associated risk factors that is duration of diabetes, BMI, age of patient, glycaemic control, hypertension and smoking.

MATERIAL AND METHODS

This descriptive case series was conducted in the Department of Endocrinology and Metabolism (DEM), Services Hospital, Lahore from June to August 2013. Consecutive sampling technique was used and 200 patients with erectile dysfunction were studied.

A sample of 200 diabetic patients with ED was selected using International Index of Erectile Function (IIEF). Then autonomic neuropathy was assessed using composite autonomic scoring system (CASS). According to CASS, 7-10 score is taken as severe, 4-6 as moderate and 3 score is taken as mild. Patients with CASS score less than 3, i.e., no autonomic neuropathy, Stage 3 hypertension, i.e., $\geq 180/110$ according to Joint National Committee (JNC) and patients using drug which has side effect that results in to autonomic neuropathy were excluded. After fulfilling exclusion criteria 86 patients were selected. Their body mass index (BMI), resting ECG, Blood Pressure (patients with normal BP but taking hypertensive drug were

considered as hypertensive), mean HbA_{1c}%, urea/creatinine and liver function tests (LFTs) were determined. Normally distributed data like age, BMI and duration of diabetes were analysed by one way analysis of variance and not normally distributed data like HbA_{1c} were analysed using Kruskal Wallis H test. To check the association between smoking and diabetes Chi square test and to check the difference between smoking and history of hypertension Mc Nemar test were applied.

RESULTS

There were 200 patients with erectile dysfunction among which 86 (43%) were diagnosed with autonomic neuropathy. The average ages of patients with severe autonomic neuropathy and moderate autonomic neuropathy were generally higher than those who had mild autonomic neuropathy but this difference was not statistically significant (*p*-value=0.164), whereas the duration of diabetes and body mass index (BMI) were statistically significant (*p*-value=0.010, *p*-value=0.021) (Table-1) The duration of diabetes in patients with severe autonomic neuropathy and moderate autonomic neuropathy was higher (statistically significant) than those who had mild autonomic neuropathy (*p*-value=0.023, *p*-value=0.013) whereas there was no significant difference in the duration of diabetes between patients with severe autonomic neuropathy and moderate autonomic neuropathy (*p*-value=0.889). It shows that the duration of diabetes has significant relationship with the severity of autonomic neuropathy.

Similarly the body mass index (BMI) of patients with severe autonomic neuropathy was higher (statistically significant) than those who had mild autonomic neuropathy (*p*-value=0.018) whereas the mean difference in body mass index of patients with moderate autonomic neuropathy with mild and severe autonomic neuropathy patients was not statistically significant (*p*-value=0.078, *p*-value=0.393). It shows that the BMI is also some significant relationship with the severity of autonomic neuropathy. (Table-2)

The median HbA_{1c} of patients with severe autonomic neuropathy and moderate autonomic neuropathy were generally higher as compared to those patients who had mild autonomic neuropathy but this difference was not statistically significant (*p*-value=0.160). (Table-3) The median history of hypertension in ED patients with severe autonomic neuropathy was generally higher as compare to those patients who had mild and moderate autonomic neuropathy but this difference was not statistically significant (*p*-value=0.095). Among severe autonomic neuropathy and moderate autonomic neuropathy patients, more than 50% were smokers, whereas, in mild autonomic neuropathy patients the smokers were just

33.30%. There was no statistical significant association between smoking and groups (*p*-value 0.312).

Table-1: Comparison of age, duration of diabetes and body mass index among the groups

Variables	Groups			<i>p</i> -value**
	Severe Autonomic Neuropathy Mean±S.D	Moderate Autonomic Neuropathy Mean±S.D	Mild Autonomic Neuropathy Mean±S.D	
Age	58.73±8.84	58.41±9.62	53.33±9.29	0.164
Duration of diabetes in years	10.30±3.23	9.82±3.56	6.80±3.89	0.010*
Body mass index	27.24±2.19	26.18±3.01	24.40±2.37	0.021*

*The mean difference is significant at the 0.05 level, **One way ANOVA

Table-2: Multiple comparisons of age, duration of diabetes and body mass index among the groups

Dependent Variable	(I) Type	(J) Type	Mean Difference (I-J)	Std. Error	<i>p</i> -value
Duration of Diabetes	Severe Autonomic Neuropathy	Moderate Autonomic Neuropathy	.4786	1.0370	0.889
		Mild Autonomic Neuropathy	3.5000	1.3025	0.023*
	Moderate Autonomic Neuropathy	Mild Autonomic Neuropathy	3.0214	1.0370	0.013*
Body Mass Index	Severe Autonomic Neuropathy	Moderate Autonomic Neuropathy	1.06095	.80908	0.393
		Mild Autonomic Neuropathy	2.83667	1.01618	0.018*
	Moderate Autonomic Neuropathy	Mild Autonomic Neuropathy	1.77571	.80908	0.078

*The mean difference is significant at the 0.05 level

Table-3: Comparison of HbA_{1c} among the groups

Groups	HbA _{1c}		<i>p</i> -value
	Mean±S.D	Median (IQR)*	
Severe Autonomic Neuropathy	9.43±5.66	8.00 (6.50–10.00)	0.160
Moderate Autonomic Neuropathy	7.97±1.65	8.00 (6.50–9.00)	
Mild Autonomic Neuropathy	7.12±1.31	6.75 (6.50–8.00)	

*Kruskal Wallis test

DISCUSSION

Men with or without diabetes mellitus are at more risk to develop peripheral neuropathy.¹¹ In patients with diabetes mellitus and peripheral neuropathy, erectile dysfunction is highly prevalent. But due to shyness of health professionals to ask their patients, such a personal question, about erectile dysfunction may lead to many other complications.^{4,8} Studies have shown that ED leads to the manifestation of anxiety and depression.⁹ ED is also a good predictor of cardiovascular neuropathy.¹² In our study frequency of AN among diabetic ED patients was approaching 43%, whereas

globally such prevalence ranges from 27 to 77 percent.^{13,14} Aging factor cannot be denied and in this study the mean age was approximately 58 years and the range was 39–72 years of age. More than fifty per cent patients were above 60 years of age. But there was no statistically difference between ages of patients with severe, moderate or mild autonomic neuropathy. This factor supports the fact that ED is independent of aging.

It has been observed that the severity of neuropathy increases with increase in body mass index and duration of diabetes. In patients with autonomic neuropathy vascular changes could be used to predict as the endothelial and smooth muscle cells increase in ED patients.^{4,15} It is suggested to the researchers that they also consider the BMI before diabetes or inquire the patients about whether they had gain or lose the weight after diabetes mellitus. Diabetic neuropathy affects the neuron, Schwann cells and blood vessels and therefore hypertension may be considered as risk factor.¹⁶ In our study average history of hypertension in years was more in patients with severe AN group than the other groups.

Relationship of severity of neuropathy with smoking is always controversial, whereas with alcohol it is well recognized.¹⁰ The frequency of the smokers was greater in severe and moderates AN group. Our study is also supported by Cho DY *et al.*¹⁷ In this study average HbA_{1c} was higher in severe AN group. It was observed on total records of HbA_{1c} (mean of total available HbA_{1c} was taken in each patient) but in many subjects detail previous HbA_{1c} record was not available.

CONCLUSIONS

Autonomic neuropathy is frequent in diabetic patients with erectile dysfunction. The associated risk factors are duration of disease and body mass index.

AUTHOR'S CONTRIBUTION

All the authors contributed equally in manuscript writing, data collection and data analysis

REFERENCES

1. Foss-Freitas MC, Marques Junior W, Foss MC. [Autonomic neuropathy: a high risk complication for type 1 Foss-Freitas MC, Marques Junior W, Foss MC. [Autonomic neuropathy: a high risk complication for type 1 diabetes mellitus]. *Arq Bras Endocrinol Metabol* 2008;52(2):398–406.
2. Bruna J, Navarro X. [Autonomic neuropathy in diabetes mellitus]. *Rev Neurol* 2005;40(2):102–10.
3. Millan-Guerrero RO, Vasquez C, Isais-Millan S, Trujillo-

- Hernandez B, Caballero-Hoyos R. [Association between neuropathy and peripheral vascular insufficiency in patients with diabetes mellitus type 2]. *Rev Invest Clin* 2011;63(6):621–9.
4. Valles-Antuna C, Fernandez-Gomez J, Fernandez-Gonzalez F. Peripheral neuropathy: an underdiagnosed cause of erectile dysfunction. *BJU Int* 2011;108(11):1855–9.
5. Kamenov ZA, Parapunova RA, Georgieva RT. Earlier development of diabetic neuropathy in men than in women with type 2 diabetes mellitus. *Gend Med* 2010;7(6):600–15.
6. Kamenov ZA. Comparison of the first intake of vardenafil and tadalafil in patients with diabetic neuropathy and diabetic erectile dysfunction. *J Sex Med* 2011;8(3):851–64.
7. Ravaglia S, Marchioni E, Costa A, Maurelli M, Moglia A. Erectile dysfunction as a sentinel symptom of cardiovascular autonomic neuropathy in heavy drinkers. *J Peripher Nerv Sys* 2004;9(4):209–14.
8. Grant PS, Lipscomb D. How often do we ask about erectile dysfunction in the diabetes review clinic? Development of a neuropathy screening tool. *Acta Diabetol* 2009;46(4):285–90.
9. Mehtiyev TV. [Stress, anxiety, depression and erectile dysfunction in patients with diabetes mellitus]. *Georgian Med News* 2013;(220-221):77–81.
10. Martin-Morales A, Sanchez-Cruz JJ, Saenz de Tejada I, Rodriguez-Vela L, Jimenez-Cruz JF, Burgos-Rodriguez R. Prevalence and independent risk factors for erectile dysfunction in Spain: results of the Epidemiologia de la Disfuncion Erectil Masculina Study. *J Urol* 2001;166(2):569–74.
11. Tata S, Morewitz S, Tan KH, Clark J. Demographic characteristics of individuals with diabetes mellitus and peripheral neuropathy. *J Am Podiatr Med Assoc* 2013;103(5):355–60.
12. Debono M, Cachia E, Cassar A, Calleja N, Mallia M, Vassallo J. Is erectile dysfunction a sentinel symptom for cardiovascular autonomic neuropathy in patients with type 2 diabetes? *Andrologia* 2008;40(1):1–6.
13. Suder NC, Wukich DK. Prevalence of diabetic neuropathy in patients undergoing foot and ankle surgery. *Foot Ankle Spec* 2012;5(2):97–101.
14. Hasani N, Khosrawi S, Hashemipour M, Haghghatiyan M, Javdan Z, Taheri MH, *et al.* Prevalence and related risk-factors of peripheral neuropathy in children with insulin-dependent diabetes mellitus. *J Res Med Sci* 2013;18(2):132–6.
15. Liu QZ, Hu LQ. [Advances in etiology of diabetes mellitus and erectile dysfunction]. *Zhonghua Nan ke Xue* 2002;8(3):215–7.
16. Gregory JA, Jolivald CG, Goor J, Mizisin AP, Calcutt NA. Hypertension-induced peripheral neuropathy and the combined effects of hypertension and diabetes on nerve structure and function in rats. *Acta Neuropathol* 2012;124(4):561–73.
17. Cho DY, Mold JW, Roberts M. Further investigation of the negative association between hypertension and peripheral neuropathy in the elderly: an Oklahoma Physicians Resource/Research Network (OKPRN) Study. *J Am Board Fam Med* 2006;19(3):240–50.

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