Association of peripheral neuropathy with retinopathy in diabetic patients

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Abstract

Introduction: Diabetes mellitus one of the major cause of avoidable blindness where patients with diabetic retinopathy are 25 times more likely to become blind than the non diabetic. Diabetic retinopathy and neuropathy being the major microvascular complications of diabetes, the aim of this study is to determine the association of retinopathy with peripheral neuropathy in diabetic patients in a tertiary care hospital.

Materials and Methods: Study included diabetic patients with age more than 35years of age with a total number of 150 patients attending ophthalmology outpatient department of Saveetha medical college and Hospital. They underwent a detailed ocular examination and fundus examination to know the prevalence and severity of diabetic retinopathy. Peripheral neuropathy was assessed by doing a nerve conduction velocity of peripheral nerves in all patients. The results were evaluated to ascertain the prevalence of diabetic retinopathy and to establish an association with diabetic peripheral neuropathy.

Results: Among the study population the mean age of the patients was 58+/-8.5 and males were affected more than females. The occurrence of complications increased with an increase in HbA 1c values. The prevalence of diabetic neuropathy was 72% and diabetic retinopathy was 44%. The prevalence of diabetic retinopathy in individuals with diabetic peripheral neuropathy was 51% which was 1.75 times more than without diabetic neuropathy (29%). This helps us to know the magnitude of problem of diabetic retinopathy and to timely treat it.

Keywords: Diabetic retinopathy, Diabetic neuropathy, Correlation, Risk factors.

Introduction

Diabetes mellitus is a common disease prevalent globally, presenting with chronic complications and constitute a major risk to the patient.^{1,2} The most commonly encountered microvascular complications of diabetes mellitus are diabetic retinopathy and diabetic peripheral neuropathy and their pathogenesis remain the same. It is found that 27.5% of the patients are detected with microvascular complications only at the time of diagnosis of diabetes mellitus.^{3,4} It is important that regular screening and early detection of complications of diabetes helps us to prevent morbidity and mortality in the patients to a great extent. The aim of this study is to determine the association of peripheral neuropathy with retinopathy in diabetic patients in a tertiary care hospital. This helps to know how prevalent is retinopathy in diabetic patients with coexisting diabetic neuropathy and helps us to take an initiative to redesign our protocols for the management of diabetic retinopathy.

Materials and Methods

The study period was from October 2016 to March 2017, a hospital based prospective study with a total number of 150 patients who attended the outpatient department of Ophthalmology, Saveetha Medical College and Hospital, Chennai and the study was approved by the Institutional Ethics Committee.

The study included diabetic patients with age more than 35 years of age irrespective of symptoms and control of blood sugars. The study excluded patients with gestational diabetes mellitus and those having retinopathy associated with other systemic ailments. And patients with neuropathy associated with other systemic disease (peripheral vascular disease, thyroid dysfunction, alcoholic) were also excluded.

After obtaining an informed consent, a detailed clinical data and history of the patient was obtained. Fundus examination was done using both direct and indirect ophthalmoscope and slit lamp biomicroscope using 90 D lens and retinopathy was graded based on Early Treatment of Diabetic Retinopathy Study classification.⁵

Peripheral neuropathy was evaluated by doing a nerve conduction study of peripheral nerves in the diabetic patients. It is an electrophysiological assessment of peripheral nerves where response of the nerve to an electrical stimulation was studied in the patients.^{6,7} Neuropathies which are not picked on routine clinical examination, nerve conduction study has a better diagnostic value, in which series of surface electrodes are placed at different locations along a specific peripheral nerve. The nerve is stimulated at one site and recorded at a different site to determine if the nerve is conducting appropriately using a Allengers Scorpio electrophysiology test system. Each electrical stimulation is recorded as a waveform on a computer and analyzed by the Neurologist which includes latency (ms), amplitude (μv) and conduction velocity (m/s).



Image 1:

Haematological investigations include fasting and post prandial blood sugars and glycosylated haemoglobin (HbA1c) was done.Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables and SPSS version 22 was used for statistical analysis.

Results

Among the study population of 150 diabetic patients there were 95 males and 55 females (Table 1). All the patients were in the mean age of 58+/-8.5 with a range between 35-75 years. In our study, 120 patients were diagnosed with diabetic retinopathy and peripheral neuropathy, males (77 patients) were more affected than females (43 patients). (Fig. 1)

Table 1: Descriptive analysis of Gender distributionin the total study population



Fig.1: Gender distribution of microvascular complications (diabetic retinopathy and peripheral neuropathy) among the study group

Considering the level of glyocsylated hemoglobin, patients with HbA1c of <7%, 32 patients had microvascular complications and moderate (HbA1c7-10%) and severe derangement (HbA1c>10%) of blood sugars 58 and 30 patients presented with microvascular complications. (Fig. 2)



Fig. 2: Effect of level of glycosylated hemoglobin on complications of diabetes (diabetic retinopathy and peripheral neuropathy)

Of the total 150 patients included in the study, 108 patients had diabetic neuropathy and 42 patients had no diabetic neuropathy. Prevalance of retinopathy was more among the patients with diabetic neuropathy. (Chart 1 and Table 2)

Chart 1: Association of Diabetic retinopathy and Diabetic peripheral neuropathy



	comparison of severity of diabetic recinopatity with the diabetic peripheral neuropatity					
	Diabetic peripheral	Diabetic peripheral				
	neuropathy present (No=108)	neuropathy absent (No=42)				
Total number of patients with diabetic	55 (51%)	12 (28.57%)				
retinopathy						
Mild non proliferative diabetic retinopathy	12 (21.81%)	3 (25.0%)				
Moderate non proliferative diabetic	15(27.27%)	2 (16.66%)				
retinopathy						
Severe non proliferative diabetic retinopathy	8(14.54%)	2 (16.66%)				
Very severe non proliferative diabetic	9 (16.36%)	1 (8.33%)				
retinopathy						
Early proliferative diabetic retinopathy	5 (9.09%)	3 (25.0%)				
High risk proliferative diabetic retinopathy	6 (10.90%)	1 (8.33%)				

Table 2: Comparison of severity of diabetic retinopathy with the diabetic peripheral neuropathy

Diabetic peripheral neuropathy was diagnosed based on the values which was recorded as a waveform in the nerve conduction study. Latency is prolonged, amplitude and nerve conduction velocity along the peripheral nerves is decreased in patients with diabetic peripheral neuropathy. (Fig. 3)

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Fig. 3: Nerve conduction study

Table 3: Prevalence of diabetic retinopathy andneuropathy in the study population (N=150)

Diabetic	Frequency	95% CI						
Retinopathy								
Yes	67(44.67%)	36.95%-52.66%						
No	83 (55.33%)	47.34%-63.05%						
Neuropathy								
Yes	108 (72%)	64.33%-78.57%						
No	42 (28%)	21.43%-35.67%						

Among the study population, 67 (44.67%) had retinopathy (95% CI 36.95% - 52.66%), and 108 (72%) had neuropathy (95% CI 64.33% - 78.57%) in the diabetic group. (Table 3)

Prevalence of diabetic retinopathy in individuals with diabetic peripheral neuropathy was studied to establish the relation between the two. The prevalence of diabetic retinopathy in cases with diabetic peripheral neuropathy was 51% which is 1.75 times more than in patients without diabetic peripheral neuropathy (29%).(Fig. 4)





Table 4:	Comparison	of retinopath	v with neurop	athy of study	population (N=150)
Lable 1.	Comparison	or remoputing	y with neurop	amy or study	population (11-100)

Nouvonathy	Retinop	athy	Chiaguana	P-value	
Neuropathy	Positive	Negative	Chi square		
Positive (N=108)	55 (50.92%)	53 (49.07%)	6 1 1 4	0.013	
Negative (N=42)	12(28.57%)	30(71.43%)	0.114		

Out of 108 people with neuropathy, 55 patients (50.92%) had retinopathy and 53 patients (49.07%) had no retinopathy. The difference in the proportion of retinopathy in patients with and without neuropathy was statistically significant (P value 0.013) (Table. 4)

Discussion

Diabetes mellitus, which is known to cause dreaded microvascular complications, occur due to target organ damage. Early recognition of chronic complications of diabetes mellitus is important, as most of the patients are asymptomatic at the time of diagnosis.²⁻⁴ The pathogenesis of diabetic retinopathy and neuropathy remain the same and the severity of the disease is reflected through the occurrence of any of these complications.^{8,10} In our study we found that males were affected more than females. In contrast, Katulanda P et al¹⁴ and Narendran et al¹⁵ found that incidence of microvascular complications were almost the same in both the sex. Our study found that poor glycemic control which is based on HbA1c values correlated with a consistent increase in occurrence of retinopathy and neuropathy, which is in accordance to CURES study,¹⁶ were elevated HbA1C values increases the risk of diabetic retinopathy. Salwa and Ayman et al¹⁹ also concluded that HbA1c as a modifiable risk factor for diabetic neuropathy. According to the study $(Vikendra et al)^{20}$ the prevalence of diabetic peripheral neuropathy was 56% and 27% and in our study the prevalence of diabetic neruropathy was 72% and retinopathy was 44%. The association of prevalence of diabetic retinopathy in individuals with and without diabetic neuropathy was studied which revealed that prevalence of diabetic retinopathy in individuals with diabetic peripheral neuropathy (51%) was 1.75 times more than without diabetic neuropathy (29%), whereas in the study Gavin Tan et al ²² it was 2 times more. Ji et al²³ proved that retinopathy was an independent risk factor for diabetic neuropathy. In a study to detect prevalence of neuropathy, Ashok et al.,²⁴ compared incidence of retinopathy in patients with and without neuropathy and found a higher incidence in those with neuropathy Thus this study provide us with a further insight into the known complications of diabetes. This will help us to formulate advanced strategies for screening and management of population with diabetes mellitus.

The limitation of this study is that the sample size is small and the study period may be expanded to obtain an extended correlation.

Conclusion

It was concluded that prevalence of retinopathy was more in patients with diabetic neuropathy and its progression is associated with a decrease in the nerve conduction velocity as interpreted in the nerve conduction studies. Therefore the Physician, Neurologist and Ophthalmologist together play a vital role in creating awareness among patients about diabetes and its complications and thereby timely treating it. This stresses upon the importance of a multidisciplinary approach to improve the quality of life and to prevent vision loss in diabetic patients.

References

- Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.
- Mohan V, Shah S, Saboo B, Current glycemic status and diabetes related complications among type 2 diabetes patients in India: data from the A1chieve study, J Assoc Physicians India. 2013 Jan;61(1 Suppl):12-5.
- Abbate M, Cravedi P, Iliev I, Remuzzi G, Ruggenenti P. Prevention and treatment of diabetic retinopathy: Evidence from clinical trials and perspectives. Curr Diabetes Rev 2011;7:190-200.
- Williams R, Airey M, Baxter H. Epidemiology of diabetic retinopathy and macular edema: A systematic review. Eye 2004;18:963-83.
- 5. Early treatment of diabetic retinopathy study design and baseline characteristics, Ophthalmology, Volume 98,issue 5,741-756)
- 6. Role of neurophysiologic evaluation in diagnosis. J Am Acad Orthop Surg. 2000 May-Jun;8(3):190-9.
- Kimura J. Facts, fallacies, and fancies of nerve conduction studies: twenty-first annual Edward H. Lambert Lecture. Muscle Nerve. 1997 Jul;20(7):777–787.
- Boulton AJ, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R, Malik RA, Maser RE, Sosenko JM, Ziegler D; Diabetic neuropathies: a statement by the American Diabetes Association. Diabetes Care. 2005;28(4):956-62.
- Malone JI, Morrison AD, Pavan PR, Cuthbertson DD. Diabetic Control and Complications Trial: Prevalence and significance of retinopathy in subjects with type 1 diabetes of less than 5 years duration screened for the diabetes control and complications trial. Diabetes Care 200;124:522-6.
- Klein R, Klein BEK, Moss SE. Visual impairment in diabetes. Ophthalmology 1984;91:1-9.
- Raman R, Rani PK, Reddi Rachepalle S, Gnanamoorthy P, Uthra S, Kumaramanickavel G, et al. Prevalence of diabetic retinopathy in India: Sankara Nethralaya diabetic retinopathy epidemiology and molecular genetics study report 2. Ophthalmology 2009;116:311-8.
- 12. Irfan gul, Shujat Gul, Manzoor Ahmad DarPrevalence Of Peripheral Neuropathy And Pattern Of Involvement On Nerve Conduction Study In Patients Of Type 2 Diabetes Mellitus With Clinical Symptoms Of Peripheral Neuropathy In Kashmiri Population A Hospital Based Study. Imperial Journal of Interdisciplinary Research (IJIR) Vol-3, Issue-2, 2017.
- Won JC, Kwon HS, Kim CH, Lee JH, Park TS, Ko KS, et al. Prevalence and clinical characteristics of diabetic peripheral neuropathy in hospital patients with Type 2 diabetes in Korea. Diabet Med 2012;29:e290-6.
- 14. Katulanda P, Ranasinghe P, Jayawardena R, Constantine GR, Sheriff MH, Matthews DR. The prevalence, patterns and predictors of diabetic peripheral neuropathy in a developing country. Diabetol Metab Syndr 2012;4:21.
- Narendran V, John RK, Raghuram A, Ravindran RD, Nirmalan PK, Thulasiraj RD. Diabetic retinopathy among selfreported diabetics in southern India: A population based assessment. Br J Ophthalmol 2002;86:1014-8.
- Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of diabetic retinopathy in urban India: The Chennai Urban Rural Epidemiology Study (CURES) eye study, I. Invest Ophthalmol Vis Sci 2005;46:2328-33.
- H.A. VanLeiden, J.M. Dekker, A. C. Moll et al., "Riskfactors for incident retinopathy in a diabetic and nondiabetic population: the Hoorn study," Archives of Ophthalmology, vol. 121, no. 2, pp. 245–251,2003.

- Dowse GK, Humphrey AR, Collins VR, et al. Prevalence and risk factors for diabetic retinopathy in the multiethnic population of Mauritius. Am J Epidemiol. 1998;47:448– 457.
- Salwa SI, Ayman SA. Explorative study on diabetic neuropathy among type 2 diabetic patients in university Sains Malaysia Hospital. Diabet Metab Syndr Clin Res Rev 2012;6:167-72.
- Vikrendra K. Sharma, Mita V. Joshi, Avijit A. Vishnoi, Interrelation of retinopathy with peripheral neuropathy in diabetes mellitus, J Clin Ophthalmol Res 2016;4:83-7.
- American Diabetic Association. Standerdised measures in diabetic neuropathy. Diabetes Care 1996;19(1S):72S-92S.
- 22. Gavin Tan, the relationship between peripheral Neuropathy and Diabetic Retinopathy in an Asian Population. Singapore Malay Eye Study, Ophthalmology 2008.
- 23. JiN, Zhang N, RenZJ, JiaKB, WangL, NiJX, et al. Risk factors and pain status due to diabetic neuropathy in chronic long-term diabetic patients in a Chinese urban population. Chin Med J (Engl) 2012;125:4190-6.
- Ashok S, Ramu M, Deepa R, Mohan V. Prevalence of neuropathy in type 2 diabetic patients attending a diabetes centre in South India. J Assoc Physicians India 2002;50:546-50.
- 25. H.A. VanLeiden, J.M. Dekker, A. C. Moll et al., "Risk factors for incident retinopathy in a diabetic and nondiabetic population: the Hoorn study," Archives of Ophthalmology, vol. 121, no. 2, pp. 245–251,2003.
- Giloyan A, Harutyunyan T, Petrosyan V. The prevalence of and major risk factors associated with diabetic retinopathy in Gegharkunik province of Armenia: Cross-sectional study. BMC Ophthalmol 2015;15:46.
- 27. Guidelines for the Comprehensive Management of Diabetic Retinopathy in India. A vision 2020 the right to sight India Publication; July, 2008.