ORIGINAL ARTICLE

FREQUENCY OF SENSORYMOTOR NEUROPATHY IN TYPE 2 DIABETICS

Nadia A. Ather, Rukhsana Abdul Sattar, Jamal Ara.

ABSTARCT:

Objectives: To determine the frequency of sensory motor neuropathy in type 2 diabetics at the time of presentation to the hospital.

Study design: Non interventional, descriptive.

Subjects and methods: The study was conducted at Medical Unit-1, Jinnah Postgraduate Medical Center, Karachi, from November 2005 to April 2006. Patients of different ages and either gender with history of confirmed diabetes for ten years and above, on regular follow up were included. Those with non-diabetic causes of hyperglycemia or neuropathy were excluded. Relevant features like age, gender, treatment, symptoms , signs, nerve conduction study (NCS) results, duration of Diabetes mellitus (DM), fasting blood sugar (FBS) and serum values of glycosylated hemoglobin (HB1Ac) were recorded.

Results: Out of a total of 300 patients, there were 111 female and 189 male patients. Mean age was 58±11.23 years. Mean duration of diabetes was 13.6±5.48 years. One hundred and twenty three patients had symptoms of neuropathy. Clinical examination revealed mixed sensory and motor signs in 135 (45%) patients. Nerve conduction studies revealed abnormalities in 159 (53%) patients. Among patients having an abnormal NCS, the fasting blood glucose (FBS) was <120 mg/dl in 12 (7.5%) patients, while it was > 120mg/dl in 147 (91%) patients. The glycosylated hemoglobin ranged from 4-15% with mean of 8.1% and standard deviation of 2.5%. This showed significant association (p <0.001) of peripheral neuropathy with abnormal FBS, HB1Ac and duration of diabetes.

Conclusion: NCS diagnosed the neuropathy in more than half of the total number of patients, including both symptomatic and asymptomatic patients. Majority of the patients revealed symmetrical and a mixed type (motor and sensory) polyneuropathy. This shows that nerve conduction may not be concordant with the clinical signs and symptoms. NCS detects neuropathy much earlier, before it becomes evident clinically. The neuropathy is associated with abonromal fasting blood sugar, HBIAC and duration of diabetes.

Key words: Diabetes mellitus, neuropathy, blood sugar, glycosylated hemoglobin, nerve conduction study.

INTRODUCTION

Currently, there is a pandemic of diabetes mellitus (DM), with an estimated doubling of the world diabetic population from 110 million in 1994 to 221 million by 2010[1]. This increase makes diabetic complications an obvious public health problem. Estimates of the prevalence of diabetic neuropathy vary widely from 5% to nearly 60% and sometimes 100% if patients with asymptomatic abnormalities of nerve conduction are included[2]. In a study of 4,400 patients with type-2 DM, Pirart found a prevalence of 7.5% at diagnosis,[3] which rose linearly to 50% after 25 years. In a similar study among newly diagnosed diabetics, a prevalence rate of 11.6% was reported[4]. Another population-based study of type-1 and type-2 diabetics in the United States yielded a cumulative incidence of distal symmetrical polyneuropathy of 4% after five years and 15% after 20 years of the diagnosis of DM[4].

The routine investigation worksheet of a common diabetic in the hospital rarely includes nerve conduction studies. Hence the likely hood of detecting the development of and documenting asymptomatic neuropathy is very low.

Department of Medicine, Jinnah Post Graduate Medical Centre, Karachi, Pakistan
Correspondence: Dr. Rukhsana Abdul Sattar, Assistant Professor, Department of Medicine ,Jinnah Post Graduate Medical Centre, Karachi, Pakistan
E-mail: ali316_2001@hotmail.com
Received: December 13, 2007; accepted: March 17, 2008

The aim of this study was to determine the frequency of peripheral neuropathy in a group of diabetics by nerve conduction studies to make quantitative analysis of motor or sensory losses among this group and compare it with the extent of clinically evident neuropathy among the group.

PATIENTS AND METHODS

This non interventional, descriptive study was conducted at Medical Unit 1, J.P.M.C., Karachi, from November 2005 to April 2006. Three hundred patients were included in the study. All indoor and outdoor patients of either gender having type-2 diabetes for a period of ten years or more, irrespective of symptoms of neuropathy were included in this study. Patients having gestational diabetes, impaired glucose tolerance and transient hyperglycemia due to stress/medications were excluded from the study. Patients who had neuropathy due to other causes were also excluded. All patients underwent a complete history including their duration of diabetes, subjective complaints regarding peripheral neuropathy (paresthesias, numbness, decreased sensations, pins-and-needles sensation, deep tendon reflexes etc.) and family history of diabetes. All patients had a detailed systemic examination specially taking into account the central nervous system (sensory system: position sense, vibration sense and pin prick; motor system: power and reflexes: cranial nerves and co-ordination). All patients underwent a fasting and random blood sugar, glycosylated hemoglobin (HBIAC) and nerve conduction studies. Nerve conduction studies determined the conduction velocities of involved nerves in symptomatic patients. While conduction velocities of peripheral nerves of upper (ulnar, median and radial nerves) and lower limbs (sural and posterior tibial) were determined in all asymptomatic patients to detect a sub clinical neuropathy if any. All the features like age, gender, symptoms, signs and NCS, duration of DM, FBS, and HB1Ac were recorded on proforma. According to WHO the normal fasting blood glucose level less than 126 mg/dl is considered normal[5] and taken as the reference range of fasting blood glucose in this study. Consent was taken from institutional ethical committee and from individual patients included in the study.

Statistical software "SPSS-10.0" was used for statistical data analysis. Male to female ratio was computed for gender distribution. Age was presented by mean + SD and histogram of age distribution was made. All qualitative response variables like treatment, symptoms, signs and NCS were presented by frequencies and percentages; chi square test was applied to compare significance of proportions of these variables between normal and patients with neuropathy. Ward funds sponsored the study.

RESULTS

Three hundred patients of type 2 diabetes were evaluated clinically and electro physiologically. Among 300 patients, 189 (63%) were males and 177 (59%) were asymptomatic (Table I). Age ranged from 39-90 years (mean 58±11.2).

Table I: Frequency of neuropathy according to symptoms

Complication	Symptoms		Total
	Present	Absent	
Without neuropathy	0 (0%)	141 (79.7%)	141 (47.0%)
With neuropathy	123* (100.0%)	36 (20.3%)	159 (53.0%)
Total	123 (41.0%)	177 (59.0%)	300

*Significant relationship of symptoms with neuropathy p <0.0001

Table II: Frequency of neuropathy according to clinical examination

Complication	Signs		Total
	Present	Absent	
Without neuropathy	0 (0%)	141 (85.5%)	141 (47.0%)
With neuropathy	135* (100.0%)	24 (14.5%)	159 (53.0%)
Total	135 (45.0%)	165 (55.0%)	300

*Shows significant association of signs with neuropathy p < 0.0001

Duration of diabetes was 10-40 years (mean 13.6 years). Clinical examination revealed mixed sensory and motor signs in 135 (45%) patients (Table II). NCS revealed abnormalities in a total of 159 (53%) patients (Table III). The glycosylated hemoglobin ranged from 4-15% (mean 8.1%, ± 2.5%). This showed significant relationship ($p< 0.05$) of neuropathy with the age, duration of diabetes, symptoms (Table I), signs (Table II) and with NCS abnormalities (Table III).

Among patients having an abnormal NCS, the fasting blood glucose (FBS) was <120 mg/dl in 12 (7.5%) patients,

while it was > 120mg/dl in 147 (91%) patients. The range of glycosylated hemoglobin was 4-15% (8.1% ± 2.5%). This showed significant association of peripheral neuropathy with abnormal FBS, HB1Ac and duration of diabetes (p <0.001, Table IV).

Table III: Frequency of neuropathy according to nerve conduction studies (p=0.661)

Complication	Gender		Total
	Female	Male	
Without neuropathy	54 (48.6%)	141 (79.7%)	141 (47.0%)
With neuropathy	57 (51.4%)	36 (20.3%)	159 (53.0%)
Total	111 (37.0%)	177 (59.0%)	300

Table IV: Relationship of neuropathy with glycemic control and duration of Diabetes

Variables	Patients without neuropathy (n=141)	Patients with neuropathy (n=159)	Significance (P- value)
Fasting blood sugar level	130 ± 10mg /dl	160 ± 10mg /dl	<0.0001
Glycosylated hemoglobin	6.4% ± 1.5	9.6 % ± 2.2	<0.0001
Duration of diabetes in years	13.0 ± 3.2	14.1 ± 5.5	0.031

DISCUSSION

Diabetic neuropathies (DN) are a family of nerve disorders caused by diabetes. People with diabetes can, over time, have damage to nerves throughout the body. The neuropathies are among the most common of the long-term complications of diabetes, affecting up to 50% of patients. Members of an international consensus meeting on the outpatient diagnosis and management of DN agreed on a simple definition of DN as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes " [6]. It was also agreed that neuropathy cannot be diagnosed without a careful clinical examination—absence of symptoms cannot be equated with absence of neuropathy, as asymptomatic neuropathy is common. The importance of excluding nondiabetic causes was emphasized in the Rochester Diabetic Neuropathy Study, in which up to 10% of peripheral neuropathy in diabetic patients was deemed to be of nondiabetic causation[7]. Their clinical features vary immensely, and patients may present to a wide spectrum of specialties, from dermatology to podiatry, for example, or from urology to cardiology. Neuropathies lead to a progressive loss of nerve fibers, which may affect both principle divisions of the peripheral nervous system. There is increasing evidence that measures of neuropathy, such as electrophysiology and quantitative tests, are predictors of not only end points, including foot ulceration, but also of mortality[8]. Neuropathies result in numbness and sometimes pain and weakness in the hands, arms, feet, and legs. Problems may also occur in every organ system, including the digestive tract, heart, and sex organs. Patients with diabetes can develop nerve complication at any time, but the longer the duration of diabetes, the greater the risk.

An estimated 50 percent of those with diabetes have some form of neuropathy, but not all with neuropathy have symptoms[9]. In recent study conducted by Rana and co-workers has estimated a prevalence of 2.2% in a sample of Pakistani population where they have found the prevalence to be the same in Kasur District as in the rest of Pakistan[10]. Shaukat et al. in another prevalence study have found the prevalence of Diabetes mellitus to be 5.33% in Bahwalpur area [11]. Yousaf and Chaudary in found the prevalence of Diabetes mellitus among Pakistani Hajj pilgrims to be very high (14.7 percent)[12] as compared to prevalence rates found among average Pakistani population reported by others [11, 13]. This wide difference has emerged due to the difference in the screening methods.

This study showed the similar showed neuropathy in 53% patients of NIDDM. Forty one percent were symptomatic and 45% showed clinical signs. Another study conducted by Fedele et al. showed the prevalence of diabetic neuropathy in up to 32.3% patients of DM in Italy[14]. This difference reflects the higher prevalence of DM in Pakistan and lack of early diagnosis of DM resulting in higher frequency of its complications. The reason behind their not seeking medical attention is the poor quality of life among our patients, lack of awareness and poor follow up and health care facilities. The highest rates of neuropathy are among people who have had the disease for at least 25 years[15]. Neuropathy was consistently related to diabetes duration in a number of studies [16, 17]. Decrease in sensory thresholds have been found to be related to the degree of hyperglycemia [18] in both cross-sectional and follow-up studies. In the WESDR, the development of symptoms of the loss of tactile and temperature sensation tended to be related to HbA1c [19].

In this study those patients were included who were diabetic for at least 10 years, which is another reason for the higher frequency of neuropathy in the population of this study.

Whole nerve electrophysiological procedures (e.g., NCV, F-waves, sensory, and/or motor amplitudes) have emerged as an important method of tracing the onset and progression of distal peripheral neuropathy[20]. Multiple consensus panels have recommended the inclusion of electrophysiology in the evaluation of distal peripheral neuropathy, as well as the use of these procedures as surrogate measures in multicenter clinical trials[21].

Nerve conduction studies detect neuropathy not only at an earlier stage but are also highly specific and sensitive tool[22]. Mard et al. reported that 29% of their childhood or adolescent patients had a neurophysiological polyneuropathy specially involving the legs, while only 10% had clinical neuropathy[23]. Similar results were documented in a study conducted over 112 newly diagnosed type 2 patients to determine the prevalence of peripheral neuropathy[24]. He showed that 9.8% at diagnosis had neuropathy confirmed by NCS while only 7.1% had clinical signs[24]. Same results were obtained in the present series with more patients having neurophysiological neuropathy (53%) as compared to those who had clinical polyneuropathy (45%). This shows that signs and symptoms of neuropathy are a less reliable marker of diabetic neuropathy than NCS. NCS has to be advocated as an important tool for early detection of diabetic polyneuropathy, in measuring the course of diabetic polyneuropathy and in taking measures against progression of polyneuropathy which deteriorates the quality of life of patients[25].

This highlights yet again the need of developing a more integrated health care system with staged referral policy. There is a need to stress more on the preventive aspect of the complications and patient education. Every diabetic patient, regardless of type, should undergo a careful clinical examination of the lower extremities and feet at least once a year[26].

Medical science stands poised to take a very aggressive approach to diabetic neuropathy; preventing it, diagnosing it, controlling its secondary complications and symptoms, and possibly even reversing it. Early recognition and surveillance with adequate tests and glycemic control is the key to prevent this complication and its aftermath.

CONCLUSION

This study showed that majority of asymptomatic diabetics had the neuropathy determined by nerve conduction study. Majority had symmetrical and a mixed (motor and sensory) polyneuropathy. Thus there is a need to evaluate, each diabetic patient both clinically and electrophysiologically.

REFERENCES

1. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: Estimates and projections to the year 2010. Diabet Med 1997;14 (suppl 5):S1-S85.

2. England JD, Gronseth GS, Franklin G et al. Distal symmetric polyneuropathy: a definition for clinical research: report of the American Academy of Neurology, and the American Association of Electrodiagnostic Medical and the American Academy of Physical Medicine and Rehabilitation. Neurology 2005;64:199-204.

3. Pirart J. Diabetes mellitus and its degenerative complications: a prospective study of 4,400 patients observed between 1947 and 1973. Diabetes Metab 1977;3:245-56.

4. Dyck PJ, Melton LJ. Epidemiology. In: Dyck PJ, Thomas PK, Asbury AK (edi). Diabetic neuropathy. Philadelphia: WB Saunders; 1987;1-27.

5. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of Diabetes mellitus and its complications Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO Consultation Diabetic Medicine, 1998; 15: 539- 53

6. Boulton AJ, Gries FA, Jervell JA. Guidelines for the diagnosis and outpatient management of diabetic peripheral neuropathy. Diabet Med 1998;15:508-14.

7. Dyck PJ, Kratz KM, Karnes JL et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. Neurology 1993;43:817-24.

8. Carrington AL, Shaw JE, Van Schie CH et al. Can motor nerve conduction velocity predict foot problems

in diabetic subjects over a 6-year outcome period? Diabetes Care 2002;25:2010-5.

9. Wunderlich RP, Peters EJ, Bosma J et al. Pathophysiology and treatment of painful diabetic neuropathy of the lower extremity. South Med J 1998; 91:894-8.

10. Rana MI, Shamim-ul-Haq, Yahya M. Prevalence of diabetes mellitus in practice: A study conducted in three private clinics in two districts of central rural Punjab. Med Channel 1998; 4:22.

11. Shaukat A, Arain TM, Mahmud R et al. The prevalence of diabetes mellitus in the general population of Bahawalpur City. J Coll Physicians Surg Pak 1988; 8:167-9.

12. Yousuf M, Chaudhry SA. Profile of Diabetes mellitus among haj pilgrims visiting Madinah Al Munawarah. Specialist 1998; 15:1-5.

13. Khurshid R, Farooq S, Begum M et al. A retrospective study of diabetes mellitus in Lahore (Pakistan): an etiologic perspective. Prof Med J 2000;7:70-4.

14. Fedele D, Comi G, Coscelli C et al. A multicenter study on the prevalence of diabetic neuropathy in Italy. Italian Diabetic Neuropathy Committee. Diabetes Care 1997;20:836-43.

15. Dyck PJ, Giannini C. Pathologic alterations in the diabetic neuropathies of humans: a review. J Neuropathol Exp Neurol 1996;55:1181-93.

16. Sorensen L, Molyneaux L, Yue DK. Insensate versus painful diabetic neuropathy: the effects of height, gender, ethnicity and glycaemic control. Diabetes Res Clin Pract 2002;57:45-51.

17. Sosenko JM, Gadia MT, Fournier AM et al. Body stature as a risk factor for diabetic sensory neuropathy. Am J Med 1986;80:1031-4.

18. Coppini DV, Wellmer A, Weng C et al. The natural history of diabetic peripheral neuropathy determined by a 12 year prospective study using vibration perception thresholds. J Clin Neurosci 2001;8:520-4.

19. Klein R. Hyperglycemia and microvascular and macrovascular disease in diabetes. Diabetes Care 1995;18:258-68.

20. Bril V. Electrophysiologic testing. In: Gries FA, Cameron NE, Low PA, Ziegler D, (edi). Textbook of diabetic neuropathy. New York: Thieme, Stuttgart, 2002: 177–84.

21. Peters AL, Davidson MB, Schriger DL et al. A clinical approach for the diagnosis of diabetes mellitus: an analysis using glycosylated hemoglobin levels. Meta-analysis Research Group on the Diagnosis of Diabetes using glycated hemoglobin levels. JAMA 1996; 276:1246-52.

22. Solders G, Thalme B, Aguirre-Aquino M et al. Nerve conduction and autonomic nerve function in diabetic children: a 10-year follow-up study. Acta Paediatr 1997; 86:361-6.

23. Bahri-Ben MF, Gouider R, Fredj M et al. Childhood diabetic neuropathy: a clinical and electrophysiological study. Funct Neurol 2000;15:35-40.

24. Bao XH, Wong V, Wang Q et al. Prevalence of peripheral neuropathy with insulin-dependent Diabetes mellitus. Pediatr Neurol 1999; 20:204-9.

25. Argoff CE, Backonja MM, Belgrade MJ et al. Consensus guidelines: treatment planning and options. Diabetic peripheral neuropathic pain. Mayo Clin Proc 2006;81(4 Suppl):S12-25.

26. Spruce MC, Potter J, Coppini DV. The pathogenesis and management of painful diabetic neuropathy: a review. Diabet Med 2003;20:88-98.