

Frequency of Demyelinating Pattern on Electrophysiological Study in Patients with Diabetic Peripheral Polyneuropathy

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ABSTRACT

Objective: To determine the frequency of demyelinating pattern on electrophysiological study in patients with diabetic peripheral polyneuropathy.

Study Design: Cross sectional study.

Place and Duration of Study: This study was performed at Department of Neurology, Mayo Hospital, Lahore and Medical Unit II, Allied Hospital, Faisalabad from 01-Jan-2012 to 30-Sep-2012.

Materials and Methods: In this study non-probability purposive sampling technique was used. The calculated sample size was 100 cases. All patients with diabetic peripheral neuropathy and of both gender and age between 15-65 y were included in the study. Whereas Diabetic patients in whom history, clinical examination or medical record showing renal failure, hereditary neuropathies, thyroid disease, alcohol intake and toxic drug intake like anti tuberculous treatment, anti-cancer medicine etc were excluded from the study. Nerve conduction studies and electromyography were performed. Patients were labeled as having demyelinating, axonal or mixed pattern. The collected information was entered into SPSS version 15.

Results: Among the enrolled 100 patients, 56 (56%) patients were male and 44 (44%) patients were female. On electrophysiological examination, demyelinating pattern was found in 18(18%) patients, axonal pattern in 54(54%) patients and mixed pattern in 28(28%) patients. Mean duration of diabetes mellitus was 82 months $\pm$ 56 S.D. The duration of diabetes ranged from 8-264 months.

Conclusion: Our study indicates that there is high frequency of demyelinating neuropathy in patients of diabetic peripheral polyneuropathy in our local population.

Key Words: Peripheral polyneuropathy, Diabetes mellitus, Nerve conduction study.

INTRODUCTION

Diabetic peripheral neuropathies are among the most common long term complications of diabetes mellitus.¹ Prevalence of neuropathy at the time of diagnosis of diabetes mellitus is 7.5% which reaches to 50% after 25 years of diagnosis.² Diabetic neuropathies may be classified into a number of types. Most of these types are of axonal variety. Treatment of this variety of neuropathy is less than satisfactory and includes good glycemic control but patients with diabetic neuropathy having demyelinating pattern show an excellent response to immunomodulatory treatment.^{3, 4} There has been suggestion that chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is more prevalent in patients with diabetes and incidence of demyelinating peripheral neuropathy responsive to immunomodulating treatment is not low in patients with diabetes mellitus.⁵ Usually, there is concomitant cause for this demyelination but diabetics have this type of neuropathy per se as well. Chronic inflammatory demyelinating neuropathy is most common cause of coexisting demyelinating neuropathy. Diabetic

neuropathy with demyelinating pattern which is indistinguishable from idiopathic chronic inflammatory demyelinating polyneuropathy (I-CIDP) has been reported in patients with both type 1 and type 2 DM.⁶ The term DM-CIDP has been used for patients with both these conditions. Many studies have shown that there is increased incidence of CIDP in diabetic patients.^{5,7, 8} These patients usually have atypical features and present with progressive symmetric or asymmetric deficit, progressive sensory neuropathy in spite of optimum diabetic control, short interval between diagnosis of diabetes and onset of neuropathy, early motor deficit, marked asymmetry and generalized areflexia. These clinical features should alert clinician about possibility of demyelinating neuropathy in patient with diabetic neuropathy.^{5,9} Although coexisting demyelinating neuropathy have clinical clues in most of the patients but studies have shown that this is not the rule, and patients of typical diabetic neuropathy clinically may actually have demyelinating neuropathy.¹⁰ Electrophysiological studies are of paramount importance in patients having diabetic neuropathy especially with some atypical features

because even a nerve biopsy is not useful to differentiate demyelinating neuropathies from typical diabetic peripheral polyneuropathy.¹⁰ Studies have shown that segmental demyelination and remyelination, onion bulbs and inflammatory infiltrates which are the histological features of CIPD, were also present in typical diabetic polyneuropathy.¹⁰ Patients with diabetic neuropathy having demyelinating pattern can be treated successfully. Intravenous immunoglobulins (IVIg) are most commonly used and are most effective but oral and injectable steroid can also be used.¹¹ Plasma exchange, azathioprine and cyclophosphamide have also been used.¹² Rituximab may also be effective in chronic inflammatory demyelinating polyradiculoneuropathy (CIPD) patients associated with diabetes.¹³ Some reports have shown that patients who did not respond to or deteriorated on IVIg may do better if started on intravenous methylprednisolone.¹⁴ Vitamin D deficiency is an independent risk factor for diabetic peripheral neuropathy and Vitamin D supplementation could prevent or delay the onset.¹⁵ National data regarding electrophysiological patterns in diabetic neuropathy is very sparse and there are many areas still to be covered. My study highlights the importance of investigating diabetic patients with polyneuropathy in an attempt to identify patients with demyelinating pattern because of the likelihood of benefit in these patients from immunomodulatory therapy.

MATERIALS AND METHODS

In this study non-probability purposive sampling technique was used. The calculated sample size was 100 cases. All patients with diabetic peripheral neuropathy and of both gender and age between 15-65 y were included in the study. Whereas Diabetic patients in whom history, clinical examination or medical record showing renal failure, hereditary neuropathies, thyroid disease, alcohol intake and toxic drug intake like anti tuberculous treatment, anti-cancer medicine etc were excluded from the study. Nerve conduction studies and electromyography were performed. Patients were labeled as having demyelinating, axonal or mixed pattern.

Data Analysis: The collected information was entered into SPSS version 11.0. Quantitative variables like age and duration of diabetes mellitus were analyzed as mean and standard deviation. Qualitative variables including presence or absence of demyelinating pattern and gender were described as frequencies and percentages. As it was a descriptive study, no test of significance was applied

RESULTS

Among the enrolled 100 patients, 56 (56%) patients were male and 44 (44%) patients were female with age ranging from 23 to 65 years and mean age was 52.65

years $\pm$ 10.73 S.D. The age of patients were divided into three groups, i.e. < 36 years, 36 to 55 years and > 55 years. The duration of diabetes mellitus before the diagnosis of neuropathy was also divided in three groups. i.e. < 3 of diabetes, 3-7 years of diabetes and > 7 years of diabetes mellitus for ease in interpretation. On electrophysiological examination, demyelinating pattern was found in 18(18%) patients, axonal pattern in 54(54%) patients and mixed pattern in 28(28%) patients. Mean duration of diabetes mellitus was 82 months $\pm$ 56 S.D. The duration of diabetes ranged from 8-264 months. We also analyzed the electrophysiological patterns with respect to different age groups. Among the 6 patients below 36 years of age, mixed pattern was found in 5 (83%) patients and axonal pattern in 1 (17%) patient but there was no patient with demyelinating pattern. Similarly among 54 patients in age group of 36-55 years, demyelinating pattern was found in 16 (29.6%) patients, axonal pattern in 21(38.8%) patients and mixed pattern in 17(31.6%) patients. In 40 (40%) patients of > 55 years of age group, demyelinating pattern was found in 2 (5%) patients, axonal pattern in 32 (80%) and mixed pattern in 6 (15%) patients (table 1). Among the 18 patients with demyelinating pattern, 16 (88.8%) patients were from age group of 36-55, 2(11.2%) patients were from > 55 years age group and there was no patient from < 36 years age group. Most of these patients had shorter duration of disease. Average age among the patients with demyelinating pattern was found to be 48.7 years with mean duration of diabetes mellitus of 39 months (just over three years). Similarly on further analysis of patients with respect to duration of diabetes mellitus, we found that 10(55.5%) patients were having diabetes mellitus for less than 3 years, 7(38.8%) patients for 3 to 7 years and 1(5.7%) patient for more than 7 years (table 1). Among the 54 patients who were having axonal pattern, only 2 (3.7%) was from age group of < 36 years, 20(37.1%) were from age group of 36-55 years and 32 (59.2%) were from > 55 years age group. Most of these patients had longer disease duration. Average age among the patients with axonal pattern was 58.12 years which is higher than demyelinating and mixed patterns. Mean duration of diabetes in this pattern was 114.9 months (eleven and a half year) which is quite longer than the patients of demyelinating and mixed pattern. On analysis of patient with respect to duration of diabetes mellitus, we found that 33(61.2%) had diabetes mellitus for > 7 years, 19 (35.1%) had diabetes mellitus for 3-7 years and only 2(3.7%) was having diabetes mellitus for less than 3 years. There were 20 patients with duration of diabetes less than 3 years. Demyelinating pattern was the most common pattern and was present in 11 (55%), axonal pattern was seen in 2(10%) and mixed pattern in 7(35%). Forty two patients had diabetes mellitus from 3 to 7 years, among these demyelination was seen in 6(14.2%), axonal

pattern in 21(50 %) and mixed pattern in 15(35.8%). Thirty eight patients had diabetes mellitus for > 7 years; among these, axonal pattern was predominant and was

found in 31(81.5%) patients, demyelinating pattern in 1(2.6%) patients and mixed pattern in 6(15.9%) patients (Table 1).

Table No.1: Electrophysiological patterns compared with age groups and duration of diabetes

Electro-physiological pattern	No. of patients	Age groups (years)			Duration of diabetes(Y)		
		< 36	36-55	> 55	<3	3-7	>7
Demyelinating	18	0(0%)	16(88.8%)	2(11.2%)	11(55.5%)	6(38.8%)	1(5.7%)
Axonal	54	2(3.7%)	20(37.1%)	32(59.2%)	2(3.7%)	21(35.2%)	31(61.1%)
Mixed	28	5(17.8%)	17(60.7%)	6(21.4%)	7(25%)	15(53.5%)	6(21.4%)
Total	100	6	54	40	20	42	38

DISCUSSION

We enrolled a total of 100 patients in period of 9months. Standard electrophysiological studies were done to diagnose demyelinating, axonal or mixed pattern. There were 56(56%) males and 44(44%) females in our study with male to female ratio of 1.27 : 1. There was slight male predominance in our study which is similar to studies done by Miyasaki H and colleagues ⁷ (males 56.5%, females 43.5%), Sharma KR and colleagues ¹⁶ (males 61.6%, females 38.4%) and Kiziltam ME and colleagues ¹⁶ (males 60%, females 40%) but studies done by Akbar DH ¹⁷ (males 39%, females 61%), Karagoz E and colleagues ¹⁸ (males 36.7%, females 63.3%) and Asad A and colleagues ¹⁹ (males 43.3%, females 56.7%) reported female predominance in patients of diabetic neuropathy. Mean age in our study was 52.65 ± 10.73 years which is slightly less than studies done by Sharma KR and colleagues ²⁰ (57 ± 11.4 years), Karagoz E and colleagues ¹⁸ (57.8 years), Akbar DH ¹⁷ (56.20 years) but more than the study done by Pastore C and colleagues ²¹ (39.8 years). Average duration of diabetes mellitus in our patient was 82 months (6.83 years) which is almost equal to study done by Karagoz E and colleagues ¹⁸ (6.3 years) but less than the studies done by Sharma KR and colleagues ⁶ (10.5 years), Pastore C and colleagues ²¹ (10.6 years) and Akbar DH ¹⁷ (12.49 years). Eighteen (18%) patients were found to have predominantly demyelinating pattern which is more than that described by Miyasaki H and colleagues ⁷ who studied the incidence of neuropathy which fulfills the electrophysiological criteria of CIDP in patients of diabetic polyneuropathy. He reported that 11.3% had demyelinating pattern severe enough to fulfill criteria for CIDP. Frequency of demyelinating pattern in our study was also more than that described by Sharma KR and colleagues ⁶ who found demyelinating pattern in 16.9% patients of diabetic peripheral neuropathy. It is also higher in comparison to results of Kiziltam ME and colleagues ¹⁶ who did electrophysiological studies in diabetic patients with neuropathic foot ulcers and reported demyelinating pattern in 10% of patients. In our study, out of 18 patients with demyelinating pattern,

10(55.6%) were male and 8(44.4%) were female. This is almost similar to gender distribution of our study population which means that there is no particular predisposition for demyelinating pattern based upon gender. A similar pattern of gender distribution was also seen in axonal type of neuropathy (59.1% males and 40.9% females). Mean age in group of patients having demyelination was 48.69 years which is quiet less than patients having axonal pattern (58.12 years) but almost similar to patients having mixed pattern (46.32 years). This shows that younger patients are more predisposed to develop demyelination and mixed pattern and older patients tend to develop axonal type of diabetic neuropathy. Mean duration of diabetes in patients having demyelinating pattern was 39.08 months (3.25 years) which is much shorter than in patients having axonal (114.95 months or 9.58 years) and mixed pattern (46.32 months or 3.86 years). This clearly shows that duration of diabetes before the onset of neuropathy does have great impact on type or pattern of neuropathy. In our study 20 patients had duration of diabetes less than 3 years before onset of neuropathy. Among these 11 (55%) had predominant demyelination, 7 (35%) had mixed pattern and only 2 (10%) had axonal pattern. Thus a patient who develops neuropathy after short period of diagnosis of diabetes is at high risk of demyelinating neuropathy and has a potentially treatable cause. Thirty eight patients had duration of diabetes for more than 7 years before onset of neuropathy. Among these 31 (81.5%) had axonal pattern, 6 (15.7%) had mixed pattern and only 1 (2.6%) had demyelinating pattern. This shows that axonal type of neuropathy becomes more common as duration of diabetes increases. Our study has clearly shown that frequency of demyelinating neuropathy is very high in patients of diabetic peripheral polyneuropathy. Electrophysiological studies are the corner stone for evaluation of neuropathy. Data collection from two tertiary care hospitals was a study limitation and a larger study is needed to assess the true incidence of demyelinating neuropathy in patients of diabetic peripheral polyneuropathy. Frequency of demyelination may have been overestimated in our study probably because those patients who had atypical features were

referred to us more frequently than those who had typical features of diabetic neuropathy. Our study highlights the importance of more frequent use of electrophysiological studies in evaluation of diabetic neuropathy.

CONCLUSION

Our study indicates that there is high frequency of demyelinating neuropathy in patients of diabetic peripheral polyneuropathy in our local population. Patients of diabetic neuropathy should be assessed regularly and electrophysiological studies should be done in all patients so that patients of demyelinating neuropathy can be diagnosed early in order to provide benefits of immunomodulatory therapy.

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