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FREQUENCY OF PERIPHERAL NEUROPATHY IN NEWLY DIAGNOSED PATIENTS OF DIABETES MELLITUS IION CLINICAL AND ELECTROPHYSIOLOGICAL BASIS

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ABSTRACT

Objective: To determine the frequency of peripheral neuropathy in newly diagnosed patients of Diabetes Mellitus type II on clinical and electrophysiological basis. **Methods:** This is Hospital based descriptive cross sectional study conducted at department of Neurology Civil Hospital Karachi/ Dow University of Health Sciences from 20th December 2011 to 20th June 2012. Data was collected from Neurology OPD, Medicine OPD and Diabetic Clinic Civil Hospital Karachi. **Results:** Total no of patients were 107 who were already diagnosed as type 2 Diabetes Mellitus. Out of these, there were 57 (53.3%) male patients and 50 (46.7%) female patients, with ratio of males to female was . 1.14The age group distribution of study population ranged from 30-60 years and mean age was 45.19 with standard deviation of 7.38. It was observed that 35 (32.7%) patients had symptoms of peripheral neuropathy as compared to this 72 (67.3.2%) patients did not have symptoms of peripheral neuropathy while mean ± standard deviation of duration of symptoms was 2.42±1.95 months and 18 (16.8%) patients had peripheral neuropathy as compared to these 89 (83.2%) patients did not have peripheral neuropathy, clinical or electrophysiological. **Conclusion:** Diabetic Peripheral Neuropathy is a fairly common entity in our patients with type 2 Diabetes Mellitus and was seen as early as within four weeks of diagnosis in 16.8% of patients.

Key Words: Diabetes Mellitus, Peripheral Neuropathy, Neuropathy.

INTRODUCTION

Diabetes Mellitus is a syndrome with a disordered metabolism and inappropriate Hyperglycemia [(1)]. Diabetes mellitus is the commonest endocrine disorder and one of the major health problems. More than 220 million people worldwide have diabetes [(2)]. Pakistan alone currently counts 6.2 million people with diabetes and estimated figures for 2025 suggest that this will almost double and reaches 11.6 million people [(3)]. Diabetes mellitus is classified on the basis of etiology and clinical presentation of the disorder into four types: type 1 diabetes, type 2 diabetes, gestational diabetes and other specific types. Type-2 diabetes mellitus is the most prevalent form of diabetes [(4)]. It results from a combination of insulin resistance and defective insulin secretion [(4)]. Diabetes mellitus is associated with high-risk complications, essentially micro- and macro vascular complications [(5)]. The micro vascular complications of diabetes mellitus, which include nephropathy, retinopathy, and neuropathy. Diabetic neuropathy is one of the most frequently encountered complications of diabetes mellitus [(6,7)]. and commonest non-traumatic cause of limb amputation. The diabetic neuropathies are heterogeneous, affecting different parts of nervous system that present with diverse clinical manifestations. The pathogenesis for diabetic peripheral neuropathy is multifactorial. However Polyol pathway, advanced glycation end products and oxidative stress and chronic hyperglycaemia play important role.The DPN may be classifies as generalized symmetrical polyneuropathies and focal/multifocal neuropathies. The most common type of diabetic neuropathy is symmetrical, distal sensorimotor polyneuropathy (DPN) [(8)],which accounts for approximately 75% of the diabetic neuropathies [(9)]. There is no local data available on the prevalence of peripheral neuropathy in diabetic patients at the time of diagnosis; however neuropathy is estimated to be present in 7.5% of patients at the time of diagnosis [(10)].The risk of developing symptomatic neuropathy in patients without neuropathic symptoms or signs at the time of initial diagnosis of diabetes is estimated to be 4% to 10% by 5 years and up to 50% by 25 years [(11)]. Diabetic neuropathy can manifest as combination of both positive (painful) like electrical sensation, squeezing, constricting, throbbing, freezing or knife like

and negative (no painful) symptom include asleep, dead, numbness or loss of touch or pain sensations. So the diagnosis of DPN can be made after careful clinical examination and excluding other commonforms of neuropathy like CIDP, vitamin B12 deficiency, hypothyroidism and uremia which can occur in diabetic patients by appropriate investigations. All the patients with diabetes should be screened for DPN at diagnosis of type 2 DM and 5 years after diagnosis of type 1 diabetes and at least annually by examining sensory functions in feet and checking ankle reflexes. In addition all have regular follow up for assessment of glycemic control as well. Till date there are no reports from Pakistan regarding frequency of peripheral neuropathy in diabetic patients at the time of diagnosis. So this study is being carried out to see the frequency of Peripheral neuropathy at the time of diagnosis of type 2 DM.

MATERIAL AND METHODS

This is Hospital based descriptive cross sectional study conducted at department of Neurology Civil Hospital Karachi/ Dow University of Health Sciences from 20th December 2011 to 20th June 2012. Data was collected from Neurology OPD, Medicine OPD and Diabetic clinic who were already diagnosed as Diabetes Mellitus type 2. The patient who fulfilled the selection criteria were enrolled in the study. Inclusion criteria were: the patients with age between 30-60 years, of either gender, diagnosed as cases of diabetes mellitus type2 within four weeks of presentation, that is, having Fasting Blood Sugar (FBS) of ≥ 126mg/dl, Random Blood Sugar (RBS) of ≥ 200mg/dl or HbA1c≤ 6.5 along with no previous history of testing positive for diabetes mellitus or taking any treatment for diabetes.Exclusion criteria included patient's having peripheral neuropathy due to other causes i.e. hereditary (ruled out by simply assessing that at 30 years patients were past the age of onset of most of the common hereditary neuropathies22 and absence of family history; no genetic studies done), autoimmune (acute/chronicinflammatory demyelinating polyneuropathy), drugs and patients with systemic illnesses like chronic renal failure, hypothyroidism, Vit.B12 deficiency, liver disease, vasculitis,leprosy, or malignancy. Informed consent was obtained from all the patients after explanation of the study protocol. The data was collected on proforma (annexed) wasspecially developed for the study. Patients who were included in the study all underwent first clinical examination and then Nerve Conduction Studies and also Electromyography where necessary.

Nerve conduction studies protocol included
Testing most involved limb first.
Testing at least 2 limbs (i.e. one upper and one lower) and 3rd limb for symmetry.
In the lower extremity, we examined:
Sural sensory.
Peroneal motor with conduction.
Tibial motor.
Tibial F-response.
In the upper extremity, we examined:
Two sensory nerves, mostly median or ulnar.
Two motor nerves mostly median or ulnar.
An F-response (either median or ulnar).
Examination of additional nerves if needed to differentiate between axonal or demyelinating types.
Electromyography was done if required only and the protocol included:
Examining a distal muscle, including an intrinsic foot muscle.
At least three muscles were sampled from each extremity, of which at one was a proximal muscle.
Other muscles were tested to confirm an impression of neuropathy based on nerves, when required.
Any abnormalities were confirmed by examination of at least one contralateral muscle to ascertain symmetry.

Skin punch biopsy for small fiber neuropathy was not done and so also formal testing for autonomic function.

After confirmation of presence of neuropathy, these patients were further investigated to rule out other possible causes that could have led to the same clinical situation. For that purpose all these patients were investigated for HbA1c, Vit B12 deficiency, hypothyroidism, chronic renal failure, vasculits, whenever clinically indicated other investigation like ANA were also performed and patients accordingly included or excluded. Data was analyzed on SPSS 17 and results were formulated accordingly.

RESULTS

Total no of 20,000 patients attending different OPDs in CHK were interviewed. Of these one hundred and seven patients attending Diabetic clinic, Medicine OPD and Neurology OPD in Civil Hospital Karachi were found to have recently diagnosed DM, i.e., they presented within four weeks of diagnosis were selected for further evaluation. These were initially evaluated by History and Neurological examination for diabetic peripheral neuropathy followed by Nerve conduction studies to establish the presence of peripheral neuropathy. Out of 107 patients, there were 57 (53.3%) male patients and 50 (46.7%) female patients and male to female ratio was 1.14 (Table 01). The age of study population ranged from 30-60 years. Mean age of the patients were 45.19 years (Table

02). Majority of patients 45 (42.1%) who were diagnosed as a case of Diabetic peripheral neuropathy were in 5th decade (41-50 years). 33 (30.8%) were in 4th decade (31-40 years) and 29 (27.1%) were in 6th decade (51-60 years) It was observed that 35 (32.7%) patients had symptoms of peripheral neuropathy at the time of presentation as compared to 72 (67.3.2%) patients who did not. (Table 03). Duration of symptoms in 15 (29.4%) patients was less than I month, in 20 (39.2%) between 1-3 months and in 16 (31.4%) between 4-7 months while mean ± standard deviation of duration of symptoms was 2.42±1.95 months (Table 04). When we checked the stratification of duration of symptoms by using Chi-square test we got a P. Value (0.609) is greater than α level (.05), so we concluded that there was no significant difference on the basis of duration of symptoms. On NCVs 18 (16.8%) patients had peripheral neuropathy as compared to these 89 (83.2%) patients did not have peripheral neuropathy on (Table 05) On further analysis of patients having peripheral neuropathy 5 (27.8%) having symptoms 13 (72.2%) having no symptoms (Table 06). While patients having no peripheral neuropathy 30 (33.7%) were symptomatic and 59 (66.3%) have no symptoms (Table 07).

Table 01: Gender Analysis

Gender	Frequency	Percent
Male	57	53.3%
Female	50	46.7%
Total	107	100.0%

Table 02: Age Group distribution of study population

Age Groups	Frequency	Percent	Mean	Std. Deviation
31-40 Years	33	30.8%		
41-50 Years	45	42.1%	45.19	7.38
51-60 Years	29	27.1%		

Table 03: Symptoms presentation of study population

Symptoms	Frequency	Percent
Yes	35	32.7%
No	72	67.3%

Table 04: Analysis of Duration of Symptoms

Duration of Symptom	Frequency	Percent	Mean±SD
<1 Months	15	29.4%	
			2.42±1.95
1-3 Months	20	39.2%	
4-7 Months	16	31.4%	

Table 05: Analysis of frequency of Peripheral Neuropathy

Peripheral Neuropathy	Frequency	Percent
Yes	18	16.8%
No	89	83.2%

Table 06: Peripheral Neuropathy Yes and Symptoms

Symptoms	Frequency	Percent
Yes	5	27.8%
No	13	72.2%

Table 07: Peripheral Neuropathy No and Symptoms

Symptoms	Frequency	Percent
Yes	30	33.7%
No	59	66.3%

DISCUSSION

The diabetic neuropathies are heterogeneous, affecting different parts of nervous system that present with diverse clinical manifestations. DPN considered in some respect to be a "Cinderella" of microvascular complication of diabetes, receiving less attention than it deserve with regard to screening, early detection, treatment and prevention. Diabetic peripheral neuropathy is one of the commonest complications of diabetes mellitus and it may be the first presenting symptom in type 2 diabetes. Patients with diabetes mellitus can develop nerve complications at any time, but longer the duration, greater the risk. An estimated 50% of those with diabetes have some form of neuropathy, but not all with neuropathy have symptoms [12]. The prevalence of peripheral neuropathy in diabetic patients at the time of diagnosis is estimated to be present in 7.5% of patients at the time of diagnosis [10]. This reported prevalence of diabetic neuropathy varies from less [16] and Pirart[17] observed a lower prevalence of diabetic peripheral neuropathy in 6.3% and 7% respectively in their studies. Weerasuriya et al [18] observed 9.8 % of their diabetics had evidence of diabetic neuropathy at the time of diagnosis in their study from Sri Lanka. Ashok and his colleagues[19] observed a prevalence of neuropathy in 5.4% of their patients with type 2 diabetes at the time of diagnosis. These differences in the prevalence of peripheral diabetic neuropathy among different studies and our can be explained because our study used clinical and electrophysiological studies, whereas neuropathy assessed by others and Ashok et al[19] used a biothesiometer, which is comparatively a less sensitive method for detection of peripheral neuropathy. However a reason for the higher no of patients having neuropathy at the time of diagnosis of DM in our patients may be due to delay in diagnosis of condition, due to lack of awareness and financial resources. Ather N A, et al. reported in their study age ranged from 39-90 years with mean (58±11.2) years with peripheral neuropathy [20]. In our study age ranged 30-60 years with mean age of patients was 45.1±7.38 years. In our study 11 (61.1%) were male, 7 (38.9%) were female out of 18 (16.8%) (p=0.465). However, Ather et al in their study with peripheral neuropathy showed 36 (20.3%) male and 57 (51.4%) were female out of 159 (53.0%). In addition ArindamDutta et al (15) in their study

showed that in 29 patients who diagnosed of peripheral neuropathy in which 17 (28%) were males and 12 (31%) females out of the 100 newly diagnosed type 2 diabetic patients had peripheral neuropathy and females were affected more than the males (31:28) although it is not statistically significant, but in our study male were more affected. Nerve conduction studies detect neuropathy not only at an earlier stage but are also higly specific and sensitive tool. Bao XM et al reported in their study that 7.1% had symptoms while 9.8% had neuropathy confirmed by nerve conduction studies [21]. This shows that symptoms and signs of neuropathy are less reliable marker of diabetic neuropathy than NCS. So nerve conduction studies should be advised as important diagnostic tool for early detection of diabetic peripheral neuropathy in every diabetic patient. In our study we could not assess glycemic state of the patient at the time of diagnosis, so as to ascertain if higher glucose levels at diagnosis are associated with early onset of peripheral neuropathy, as is commonly assumed or not. There may be other unidentified factors involved in addition to higher glucose levels. Nevertheless, this study provides new data from Pakistan regarding newly diagnosed diabetic peripheral neuropathy and needs further research regarding early detection of diabetic peripheral neuropathy. However lack of consistent criteria for the diagnosis of diabetic neuropathy, variability in case selection and different techniques of assessment make it difficult to establish case of diabetic neuropathy uniformly across different centers even in a same region I strongly suggest that with the help of different diabetic associations in our country, we must develop diagnostic criteria for diabetic peripheral neuropathy at least for local and regional use. In addition suggested biochemical changes take time to cause Diabetic Peripheral Neuropathy but for early development of neuropathy there might be another explanation which needs to be evaluated.

CONCLUSION

Diabetic Peripheral Neuropathy is a fairly common entity in our patients with type 2 DM and was seen as early as within four weeks of diagnosis in 16.8% of patients. It is necessary to search for this potentially painful and disabling complication of Diabetes Mellitus in all patients at the time of diagnosis and also at periodic intervals.

INFERENTIAL STATISTICS

Table No 08: Peripheral Neuropathy cross tab by Age Groups

		Age Groups						
		31-40 Years		41-50 Years		51-60 Years		
		n	%	N	%	N	%	P Value
Peripheral Neuropathy	Yes	1	5.6%	11	61.1%	6	33.3%	0.036
	No	32	36.0%	34	38.2%	23	25.8%	

As P. Value (0.036) is less than α level (.05), so we conclude that there is significance difference on the basis of age groups.

Table No 09: Peripheral Neuropathy cross tab by Gender

		Gender				
		Male		Female		
		n	%	N	%	P Value
Peripheral Neuropathy	Yes	11	61.1%	7	38.9%	0.465
	No	46	51.7%	43	48.3%	

As P. Value (0.465) is greater than α level (.05), so we conclude that there is no any significance difference on the basis of gender.

Table No 10: Peripheral Neuropathy cross tab by Duration of Symptom

		Duration of Symptom						
		<1 Months		1-3 Months		4-7 Months		
		n	%	N	%	N	%	P Value
Peripheral Neuropathy	Yes	4	22.2%	7	38.9%	7	38.9%	0.609
	No	11	33.3%	13	39.4%	9	27.3%	

As P. Value (0.609) is greater than α level (.05), so we conclude that there is no any significance difference on the basis of duration of symptoms

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