

PERIPHERAL NEUROPATHY IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS PATIENTS: AUDIT OF A SINGLE CENTER

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ABSTRACT

Objective: To find out the frequency of peripheral neuropathy in newly diagnosed type 2 diabetic patients.

Material and Methods: This retrospective single center study was carried out in Department of Medicine, Khyber Teaching Hospital (KTH) Peshawar-Pakistan. A total of 151 patients who were either newly diagnosed or diagnosed within 6 months were retrieved from medical records of the Department of Medicine KTH Peshawar from January 2017 to December 2017. Patients with type 1 diabetes or diagnosed later than 6 months were excluded from the study. Both admitted patients and patients seen in OPD were included in the study. Both detailed history and proper neurological examination of the lower limbs were retrieved from medical records and findings were recorded on preformed proforma.

Results: A total of 151 patients either newly diagnosed or diagnosed within 6 months with type 2 diabetes were included in the study. Eighty six were female and 65 were male with female to male ratio of 1.3:1. Age distribution amongst study population ranged between 35-65 years. Mean age of the population was 44.6 ± 8.54 years. Out of 151 patients, 19.2% had peripheral neuropathy on clinical examination.

Conclusion: Diabetic peripheral neuropathy is one of the commonest complications of diabetes mellitus and anyone who develops tingling, numbness or diminished sensations should be thoroughly screened for diabetes mellitus.

Key Words: Diabetes mellitus type 2, peripheral neuropathy, Obesity

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INTRODUCTION

Diabetes Mellitus (DM) is one of the commonest medical illnesses worldwide with enormous morbidity and mortality. Around 387 million adults between the ages 20 and 79 worldwide were suffering from Diabetes Mellitus in 2014 and it is expected to reach 592 million by 2035. Almost 179 million people with type 2 diabetes are undiagnosed. According to International Diabetes Federation (IDF) report 2013, five countries had more than 10 million diabetic population: China, India, USA, Brazil and Russian Federations. In 2013 IDF report, Tokelau (37.5%), Micronesia, Marshall Islands, Kiribati, Cook Islands, Vanuatu, Saudi Arabia, Nauru, Kuwait and Qatar (22.9%) were top 10 countries with highest prevalence of diabetes in adult population. Sixty four percent cases in urban and 36 % in rural is affected

amongst diabetic population worldwide.¹

About 7 million people are suffering from diabetes in Pakistan and acquire 8th position worldwide and is expected to rise to 4th position by the year 2025.² WHO estimates that 10% of male and 9.8% of female population is suffering from diabetes mellitus.³

Diabetes has two main types, type 1 and type 2. Ten percent of diabetic population has type 1 diabetes and 90 percent has type 2 diabetes. Slightly more men are affected than female in general population.^{4,5} Both insulin resistance and defective insulin resistance causes type 2 diabetes mellitus.⁶

Data from various studies consistently show the fact that patients with diabetes mellitus usually develop two main complications, microvascular and macrovascular. Microvascular complications include neuropathy, retinopathy and nephropathy. Amongst these, peripheral neuropathy is the earliest and most frequently observed long term complication of diabetes that causes increased risk of foot ulceration, limb pain with numbness and huge burden on economy. It is also the commonest cause of non-traumatic limb

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amputation.⁷⁻⁹

The most common type of diabetic peripheral neuropathy (DPN) is symmetrical, distal sensorimotor, polyneuropathy, responsible for 75% of all diabetic neuropathies.¹⁰ Diabetic peripheral neuropathy is defined as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes." Peripheral diabetic neuropathy in newly diagnosed diabetics is estimated to be present in 2.4% to 29.2% and in some studies up to 68.1%.¹¹⁻¹⁷ The onset of DPN is usually insidious and typically presents as a painless loss or change of sensation detected by clinical tests. Patients will typically experience numbness, tingling, pain, and/or weakness. These symptoms begin in the lower limbs symmetrically and may eventually spread to the fingers and hands in more severe cases, described as a "stocking-glove" distribution.^{18,19} As this type of neuropathy causes reduced sensations in lower limb and feet, so higher chances of foot ulceration and subsequent amputation.

The primary objective of the study was to determine the frequency of peripheral neuropathy in newly diagnosed diabetics or those who had diabetes for last 6 months. The present study will transfer the message to the population that anyone with peripheral neuropathy must screen himself/herself for diabetes so that other micro and macrovascular complications may be slowed if not totally prevented.

MATERIAL AND METHODS

This retrospective single center study was conducted in Medicine Department of Khyber Teaching Hospital, a tertiary care hospital from medical records of patients from January, 2017 to December, 2017. Newly diagnosed diabetic patients are defined as those patients who are either newly diagnosed or diagnosed within last 6 months. The total sample size was 151, keeping 8% margin of error and 95% confidence interval, using WHO sample size calculator. Both admitted patients and seen in OPD with age range 35-65 years were included in the study. Patients with type 1 diabetes, patients with gestational diabetes or other type of diabetes, patients whose duration of diabetes was more than 6 months, patients with peripheral vascular disease, patients with foot ulcers or any critical illness, unconscious patients, patients with altered sensorium or dementia or patients with secondary causes of neuropathy like uremia or vitamin B12 deficiency were excluded from the study. Informed consent was obtained from all patients. After getting approval from hospital ethical committee to conduct the study, data of patients was retrieved for all patient who visited either OPD or admitted in ward and who were either newly

diagnosed diabetics or had diabetes for last 6 months.

Peripheral neuropathy was diagnosed from their medical records of detailed neurological assessment at the time of admission. The main variables recorded were numbness, tingling sensations, paresthesias, burning sensations, lower limb weakness and clinical examination using tests such as pin prick sensations, 10gm monofilament for touch sensations at planter surface of both great toes and metatarsal joints, 128 Hz tuning fork for vibration sensations and ankle reflex. All relevant investigations like renal function tests, liver function tests, peripheral blood smears, X Ray Chest, ECG, random blood sugar, daily fasting blood sugar and HbA1c were recorded too on designated proforma. All the informations and other demographic data like name, age, sex, BMI and address was also recorded on this proforma. Data was analyzed using SPSS version 20. All the results were presented as tables and graphs.

RESULTS

Mean age of the population was 46.6 ± 8.54 years. Eighty six (57%) were female in our population and 65 (43%) were male as shown in graph no. 1. Female to male ratio was 1.3:1. The mean age of the male was 48.4 ± 7.5 years while those of female were 44.8 ± 9.5 . Stratification of patients into different age groups is shown in table 1.

The mean HbA1c was 9.2 ± 2.0 SD. It was more deranged in female patients (Mean = 9.8 ± 1.8 SD) as compared to male patients (Mean = 8.6 ± 2.2 SD). These results are shown in table 2. In our study, 33 (38.4%) female participants were obese (BMI >30), 39 (45.3%) were overweight (BMI 25-29.9) while only 14 (16.3%) had normal weight (BMI 18.5-24.9). Amongst male patients, 20 (30.7%) were obese (BMI >30), 30 (46.1%) were overweight (BMI 25-29.9) while only 15 (23.1%) had normal weight (BMI 18.5-24.9). The results are shown in table 3.

In our study, out of 151 patients, 29 patients (19.2%) had developed peripheral neuropathy when they visited our department. Out of these 29 patients, 19 were female and 10 were male. Out of these 19 female patients, 9 were obese, 9 were overweight and only 1 had normal BMI. Out of 10 male patients, 4 were obese, 3 were overweight and 2 had normal BMI. The results are shown in fig no. 2 and table 4. The frequency of signs and symptoms of peripheral neuropathy is shown in fig. 3 and 4 respectively.

DISCUSSION

Poorly managed diabetes mellitus is associated with a lot of serious complications including cardiovascular, neurological, locomotor, visual, renal, dermato-

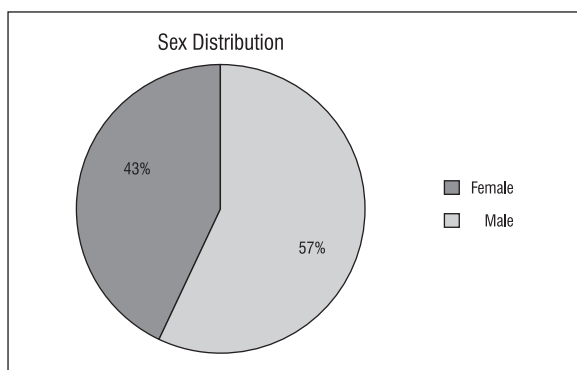


Fig. No. 1

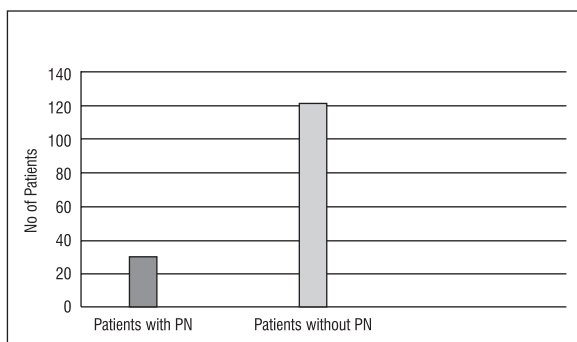


Fig. No. 2

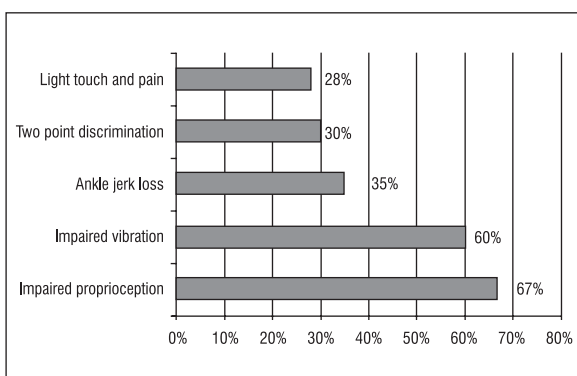


Fig. No. 3

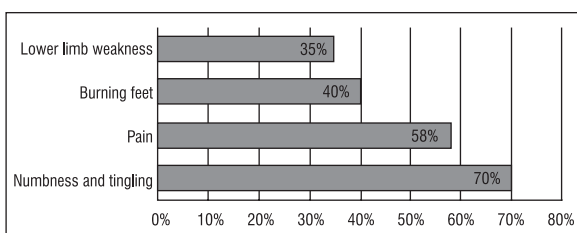


Fig. No. 4

Table 1: Age Distribution (n=151)

| Age (Years) | Frequency (Percentage) |
|-------------|------------------------|
| 35-45 | 58 (38.4%) |
| 46-55 | 64 (42.4%) |
| 56-65 | 29 (19.2%) |
| TOTAL | 151 (100%) |

Table 2: Stratification of Participants according to HbA1c (n=151)

| Gender | No. of Patients | HbA1C |
|--------|-----------------|---------|
| Female | 86 | 9.8±1.8 |
| Male | 65 | 8.6±2.2 |
| Total | 151 | 9.2±2.0 |

Table 3: Stratification of Participants According to Bmi (n=151)

| BMI | Male | Female |
|----------------------|------|--------|
| Obesity (>30) | 20 | 33 |
| Overweight (25-29.9) | 30 | 39 |
| Normal (18.5-24.9) | 15 | 14 |
| Total | 65 | 86 |

Table 4: Gender and Bmi Wise Stratification of Patients with Peripheral Neropathy

| BMI | Male Patients | | Female Patients | |
|------------|-------------------------|-----|-------------------------|-------|
| | Total No (Percentage %) | | Total No (Percentage %) | |
| Obese | 4 | 40 | 9 | 47.37 |
| Overweight | 4 | 40 | 9 | 47.37 |
| Normal | 2 | 40 | 1 | 05.26 |
| Total n=29 | 10 | 100 | 19 | 100 |

logical, depression and even limb amputation leading to minor and major disability and premature mortality. It also puts a substantial financial burden on the economy of the country. Good diabetic management substantially reduces the risk of all these complications.²⁰

Half of the patients show signs of complication even at the time of diagnosis of type 2 diabetes mellitus.²¹ Patients may start developing complications even five to six years before diagnosis and it may take more than 10 years before clinical diagnosis of diabetes.²²

Our present study is more focused on neurological complications developed either in newly diagnosed type 2 diabetic patients or who presented within 6 months of their diagnosis.

Our study comprised of 151 individuals, 86 (57%)

female and 65 (43%) male. Gender analysis in two other local studies showed male predominance as compared to our study.^{23,24} This may be due to different geographic distribution, early visits to tertiary care hospital by females, more severe diabetes complications amongst female patients, more prevalent obesity amongst our female population or it may be an accidental finding.

Mean age in our study population was 46.6 ± 8.5 years. Nearly the same mean age (45.19 years) was reported in other studies.^{23,24} It was reported high in studies conducted in Iran (52.7 ± 9.9 years) and India (49 years).^{25,26} Diabetes was poorly controlled in all of the participants with mean HbA1c 9.2 ± 2.0 . It was more deranged in female as compared to male (9.8 ± 1.8 vs. 8.6 ± 2.2 respectively). HbA1c level more than 7 was reported in half of study population in another study conducted by Roman-Pintos LM, while Sheesha E reported 9.5 ± 2.4 ; so both these studies favours my high HbA1c value.^{24,27}

In majority of our population, BMI was >24.9 . Thirty three female and 20 male were obese (BMI >30) while 39 female and 30 male were overweight (BMI $>25-29.9$). Rest of the population had normal BMI. A study conducted by Chandrashekar N, showed BMI of 29.93 ± 10.23 which is nearly comparable to our study.²⁸

Neuropathies are a common long term complication of diabetes affecting almost 50% of diabetic population.¹⁸ Diabetic peripheral neuropathy was recorded in 19.2% of our study population. Impaired proprioception was the most common abnormality followed by loss of vibration sense, loss of ankle jerk then two point discrimination, light touch and pin prick. Numbness and tingling was the most common symptom followed by burning feet and pain, and lower limb weakness. Incidence and prevalence of peripheral neuropathy varies greatly but most studies report prevalence in at least 10-15% of newly diagnosed diabetic patients.²⁹ Peripheral neuropathy is the most common cause of foot ulceration leading to charcot neuroarthropathy.¹⁸ Study conducted by Dutta A, 29% of the participant had peripheral diabetic neuropathy.³¹ In another study conducted by Shukla V in India reported prevalence of peripheral neuropathy as 23% which is nearly correlating my study.²⁶ In few studies, quite low prevalence has been noted (approximately 10%).^{32,33} A local study conducted by Alia A-in Lahore showed prevalence of peripheral neuropathy in 68 of patients which is higher than our study.¹⁵ Another local study conducted in Karachi showed a prevalence of 16.8% which is nearly correlating my study.²³ A study conducted in India showed a prevalence of 15.9% which is nearly co-inciding my study.²⁸

As this is a retrospective, single center study and the population under study is also small, so the results can't be applied on large population. To be applied on large population, multi centered, prospective, randomized controlled large sample size trial is required. Moreover nerve conduction studies were not performed on patients due to financial restrains.

CONCLUSION

Peripheral neuropathy is a very common microvascular complication of diabetes mellitus and poor glycemic control is the main culprit. Moreover anyone who presents to us with signs and symptoms of peripheral neuropathy must be evaluated for diabetes mellitus and thus many serious complications of diabetes like diabetic foot ulcers which is the leading cause of limb amputation and charcot arthropathy can be prevented.

REFERENCES

1. International Diabetes Federation (2014). Diabetes atlas, sixth edition: (www.diabetesatlas.org)
2. Basit A, Hydrie, Ahmed K, Hakeem R. Prevalence of diabetes, impaired glucose and associated risk factors in a rural area of Baluchistan province according to new ADA criteria. J Pak Med Assoc. 2002; 52: 357–60.
3. World Health Organization – Diabetes country profiles, 2016.
4. HSCIC: National Diabetes Audit 2012/13: Report 1: Care Processes and Treatment Targets.
5. Scottish Diabetes Survey 2016. Scottish Diabetes Survey Monitoring Group.
6. Kim SM, Lee JS, Lee J, Na JK, Han JH, Yoon DK, et al. Prevalence of diabetes and impaired fasting glucose in Korea: Korean National Health and Nutrition Survey 2001. Diabetes Care. 2006; 29:226-31
7. AJ Scheen. Diabetes mellitus: from clinical knowledge to public health concern. J Soc Biol. 2007; 201: 133–40.
8. Vinik AI, Freeman R, Erbas T. Diabetic autonomic neuropathy. Semi Neurol. 2003; 23: 365–72.
9. Jasik M. Therapy of diabetic neuropathy. Przegl Lek. 2003; 60: 167–9.
10. Boulton AJ, Cavanagh PR, Rayman G. The foot in diabetes. 4th ed. John Wiley & Sons Ltd; 2006.
11. Ambizas EM, Maniara B. Diabetic Peripheral Neuropathy: How Can We Help Our Patients? US Pharm. 2016; 41(3): 8-15.
12. Kostev K, Jockwig A, Hallwachs A, Rathmann W. Prevalence and risk factors of neuropathy in newly diagnosed type 2 diabetes in primary care practices: a retrospective database analysis in Germany and UK. Prim Care Diabetes 2014; 8(3): 250-55
13. Gill HK, Yadav SB, Ramesh V, Bhatia E. Prospective study of prevalence and association of peripheral neuropathy in Indian patients with newly diagnosed type 2 diabetes mellitus. J Postgrad Med 2014; 60(3): 270-75.

14. Sosale A, Prasanna KM, Sadikot SM, Nigam A, Bajaj S. Chronic complications in newly diagnosed patients with Type 2 diabetes mellitus in India. *Indian J EndocrinolMetab* 2014; 18(3): 355-60
15. Ali A, Iqbal F, Taj A, Iqbal Z, Amin MJ. Prevalence of microvascular complications in newly diagnosed patients with type 2 diabetes. *Pak J Med Sci* 2013; 29(4): 899-902.
16. Harzallah F, Ncibi N, Alberti H, Ben Brahim A, Smadhi H. Clinical and metabolic characteristics of newly diagnosed diabetes patients: experience of a university hospital in Tunis. *Diabetes Metab* 2006; 32(6): 632-5.
17. Spijkerman AM, Dekker JM, Nijples G, Adriaanse MC, Kostense PJ. Microvascular complications at time of diagnosis of Type 2 Diabetes are similar among diabetic patients detected by targeted screening and patients newly diagnosed in general practice. The Hoorn Screening Study. *Diabetes Care* 26(9): 2604-8.
18. Boulton AJ. Management of diabetic peripheral neuropathy. *Clin Diabetes*. 2005; 23(1): 9-15.
19. Callaghan BC, Cheng H, Stables CL. Diabetic neuropathy: clinical manifestations and current treatments. *Lancet Neurol*. 2012; 11(6):521-534.
20. Stratton IM, Adler AI, Neil HAW. Association of glycaemia with macrovascular and microvascular complications of Type 2 diabetes (UKPDS 35): prospective observational study. *Br Med J* 2000; 321: 405-12
21. UKPDS Group: UK Prospective Diabetes Study VIII: study design, progress and performance. *Diabetologia* 1991; 34: 877-90.
22. Harris MI, Klein R, Welborn TA. Onset of NIDDM occurs at least 4-7 years before clinical diagnosis. *Diabetes Care* 1992; 15 (7): 815-819
23. Lakhiar MA, Shahbaz NN, Bughio AH, Prakash J. Frequency Of Peripheral Neuropathy In Newly Diagnosed Patients Of Diabetes Mellitus on Clinical And Electrophysiological Basis. "Pakistan Journal of Neurological Sciences (PJNS) 2014 ; 9 (4): 31-35
24. Sheshah E, Algreeshah F, Al-Madani K, Al-Qaisi D, Madanat A. Diabetic Peripheral Neuropathy and Sudomotor Dysfunction in Saudi Patients with Newly Diagnosed Type 2 Diabetes Mellitus. *J Diabetes MetabDisord Control* 2017; 4(2): 00108.
25. Janghorbani M, Rezvanian H, Kachooei A, Ghorbani A, Chitsaz A, Izadi F, et al. Peripheral neuropathy in type 2 diabetes mellitus in Isfahan, Iran: Prevalence and risk factors. *Int J Diabetes & Metabolism* 2006; 14: 126-133
26. Shukla V, Karoli R, Chandra A. A Study of Newly Diagnosed Type 2 Diabetes Mellitus Patients from Rural Areas. *JAPI* 2014; 62: 682-4
27. Román-Pintos LM, Villegas-Rivera G, Rodríguez-Carrizalez AD, Miranda-Díaz AG, Cardona-Muñoz EG. Diabetic Polyneuropathy in Type 2 Diabetes Mellitus: Inflammation, Oxidative Stress, and Mitochondrial Function. *J Diabetes Res*. 2016; 3425617.
28. Chandrashekar N, Maity N, Kalra P. Profile of Microvascular Complications in Newly Diagnosed Type 2 Diabetics and its Association with Correlates of Metabolic Syndrome in a Tertiary Hospital: An Observational Study. *Journal of Pharmaceutical Research* 2017; 16 (2): 120-25.
29. Young MJ, Boulton AJ, MacLeod AF, Williams DR, Sonksen PH. A multicentre study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population. *Diabetologia* 1993; 36: 150-54
30. Boulton AJ. The pathway to foot ulceration in diabetes. *Med Clin North Am* 2013; 97: 775-90
31. Dutta A, Naorem S, Singh TP, Wangjam K. Prevalence Of Peripheral Neuropathy In Newly Diagnosed Type 2 Diabetics. *Int. J. Diab. Dev. Countries* 2005; 2: 30-33.
32. Boulton A. J. M., Malik R. A., Arezzo J. C., Sosenko J. M. Diabetic somatic neuropathies. *Diabetes Care*. 2004; 27(6):1458-86
33. Raman R., Gupta A., Krishna S., Kulothungan V, Sharma T. Prevalence and risk factors for diabetic microvascular complications in newly diagnosed type II diabetes mellitus. SankaraNethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS, report 27) *Journal of Diabetes and Its Complications*. 2012; 26(2): 123-8.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Khan Z: Conception and design, Acquisition of data, drafting the manuscript

Khan I: Collection of data and computer work.

Khan WM: Analysis and interpretation of data. Final proof reading.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.