

PREVALENCE, FREQUENCY AND SEVERITY OF NEUROPATHIES AND THEIR ASSOCIATED FACTORS IN DIABETIC PATIENTS OF JAMSHORO, SINDH, PAKISTAN

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Abstract:

Objectives: The objective of the research was to examine the prevalence, frequency of neuropathy and its severity in diabetic patients of Jamshoro and common risk factors associated with it like DPN which is a common cause of diabetic foot leading towards amputation and eventually permanent disability or even death. **Methodology:** It was prospective cross-sectional study design conducted in Liaquat University of Medical & Health Sciences Jamshoro among adult diabetic patients. **Results:** Sample size was 300 diabetic patients (type 1 and type 2) diabetes involving 188 (62.66%) females and 112 (37.33%) males admitted in hospital. The majority of the study population had type 2 Diabetes mellitus with larger population with overweight and obesity presented hypertension as well as severe DPN. **Conclusion:** More than half of the study population had neuropathy in severe form. The major risk factors observed were longer period of disease, age, hypertension and obesity.

Key words: Diabetes mellitus, Neuropathy, Diabetic foot, obesity, hypertension

INTRODUCTION

Globally one of the major health issues is Diabetes mellitus (DM) [1]. The prevalence is increasing rapidly among adults and it is expected that this will increase up to 10.4% in 2040 [2]. 90–95% of diabetes cases comprised of elderly peoples [3, 4]. The complications developed by diabetes are becoming the major cause of morbidity as well as mortality in the world. By 2030 it is estimated that the number of diabetes patients will reach approximately 360 million globally. The population of Pakistan is almost 154 million and the rate of DM is observed to be higher than 10%. 3-5 Pakistan is ranked at 6th position among countries encountering highest diabetes burden [5]. Diabetes mellitus is referred as a clinical syndrome involving hyperglycaemia because of insulin deficiency [6]. It is due to endocrine disorder which is most common. Several surveys showed rapidly increase of trend in DM prevalence [7]. DM can contribute towards irreversible and permanent functional alteration in body which eventually leads to different serious complications like neuropathies and retinopathy. Out of all the complications due to DM the two basic complications are diabetic polyneuropathy and leg and foot ulcers. DPN affect almost 30% to 50% of diabetics affecting mainly the lower limbs, legs and feet. The incidence of foot ulcers is approximately 25% [4, 5]. DPN (Diabetic neuropathy) is considered as the utmost risk factor leading to diabetic foot [8] and its prevalence is 50% to 75% of non-traumatic amputations. Approximately 50% of the diabetic patients

experience DPN [9] with 50% diabetics with temperate severity. [10-12]. Globally the variation in frequency of DPN is from 9.6% to 88.7%. This variation in frequency may be because of duration of disease, types of diabetes, sample selection, healthcare facilities, different criteria for diagnostic, and methods used for the physical examination of patients [1, 13-16]. DPN is irreversible so the identification and screening of the associated factors and potentially modifiable risk is critical. The basic known risk factors associated with DPN are long term DM, age, poor control of glycemia, and high body mass index. There is available very scanty data on the risk factors of DPN is scanty, so it became difficult to implement modification, prevention, and treatment. This study was designed to calculate the frequency, prevalence and severity of DPN amongst diabetic patients and the general risk factors related with DPN with the aim to decrease high socioeconomic and healthcare burden.

METHODOLOGY

Study Design: It was a prospective cross-sectional research carried out in a hospital. The research was conducted at Medicine Wards of Liaquat University of Medical & Health Sciences Jamshoro. Clearance letter was granted by Institution Review Board of Liaquat University of Medical & Health Sciences Jamshoro and Ethical Committee before initiation of the research study. Recruitment of the study subjects was also done in different diabetic clinics. The subjects were classified as adolescents aged between 14 years to 22 years, and individuals with age more than 22 years were categorized as adults.

Study population: The sample size consists of 300 diabetic patients. The sampling technique of systemic random sampling was used to recruit subjects. After getting the consent from patients they were further examined and interviewed for data collection

Inclusion and Exclusion criteria: Diabetic patients (Type 1 or Type 2) were included in the study with the ages above 14 years. The patients with co-morbid conditions like tuberculosis, hepatitis, cancer and patients on dialysis were not included in the study.

Data Collection: To collect the data a structured standardized questionnaire was developed including the information related to socio-demographics data, clinical characteristics and associated disease. TCSS (Toronto Clinical Scoring System tool) was used to diagnose neuropathy. The TCSS consists of three portions starting from questions regarding history of disease and the other parts characterizes by assessment made by physical examination which was performed by the expert investigator.

Anthropometric assessment involves measurements of height (m) and weight (kg), which were used to calculate the body mass index (BMI) in kgm^{-2} . Normal weight was assigned the value of BMI ranging from 18.5 kgm^{-2} to 24.9 kgm^{-2} , BMI ranging from 25 kgm^{-2} to 29.9 kgm^{-2} was categorized as overweight and obesity was defined as $\text{BMI} \geq 30 \text{ kgm}^{-2}$. Blood pressure was measured by Mercury sphygmomanometer. JNC 7 guidelines were used to categorize hypertensive state [17].

The clinical tests including physical examination for TCSS were carried out using following parameters. 10gm monofilament was used to examine pressure sensation. The sensation of pressure was assessed at ten different standard sites of feet sole, Pin-prick was used to assess pain sensation, Tuning fork (128 Hz) was used to examine sense of vibration at bony area of the toe, Cold and warm cylinders were used to test temperature sensation by placing it on foot dorsum. Reflex hammer was used to test tendon reflex by striking the quadriceps and a chillestendons.

Blood sampling and Analysis: Blood samples were taken from the patient and were sent to the pathological lab for analysis of, hemoglobin level, cholesterol, low-density lipoproteins cholesterol, and creatinine levels. Blood glucose levels including fasting and random glucose levels were analyzed using Glucometer.

Assessment of peripheral neuropathy: The peripheral neuropathy in lower-extremity was assessed by expert using TCSS score (maximal score of 19) consisting of 6 major clinical symptoms including five sensory tests and examination of reflexes of lower limbs. The classification of peripheral neuropathy was based on its severity on the basis of which scoring was done. 0 to 5 = no neuropathy, 6 to 8 = mild neuropathy, 9 to 11 = moderate neuropathy and ≥ 12 = severe neuropathy. Tests were applied initially on the hand and then the foot was examined.

Statistical Analysis

Analysis of data was done using software IBM SPSS Statistics 20. Univariable analysis was applied for calculation of distribution and outliers. Descriptive analysis of quantitative data was done for calculating means, range, standard deviations, and inter quartile and for categorical data, distribution of frequency was calculated. Student's t-test and Chi-Square test was used to compare means. 95% confidence intervals and p values= 0.05 or less was taken to be statistically significant.

RESULTS

Total 300 patients were enrolled in research out of which 188 (62.66%) were females and 112 (37.33%) were males. 58.4 years (SD ± 15.2 years) was calculated to be the mean age of subjects included in study. The majority of the study population had DM type 2 (70.3%), with 55% urban, >60 years age were presented by 53%, with 40% overweight, 30% obese and 80.7% hypertensive patients (Tables 1). The duration of the disease was found to short (1 year to 6 years) in 35%. The individuals taking oral hypoglycemic drugs accounted for 73.3% and 26.7% were using insulin (Tables 2)

Table 1: Demographics of study population

Characteristics	N	%
Gender		
Male	112	37.33
Female	188	62.66
Age (Years) Mean = 58.4 years		
15-40	36	12
40-60	105	35
>60	159	53
Residence		
Rural	135	45
Urban	165	55
BMIkgm⁻²		
BMI<18.5 Underweight	12	4
18.5 - 24.9 Normal	78	26
25 - 29.9 Overweight	120	40
≥ 30 Obese	90	30
Diabetes Mellitus		
Type 1	89	29.6
Type 2	211	70.3
Duration of disease (Years)		
1-6	104	35
7-12	78	26
13-18	60	20
19-24	18	6
25-32	12	4
33-40	6	2

The prevalence of DPN was calculated to be 73 % found in 219patients, with 68% (n=76) males, and 76% (n=143) females respectively. Patients with age more than 60 years showed high prevalence 87% with p value<0.001), overweight 75% and obesity 85% with p vale of <0.001. Among them the subjects using hypoglycemic agents were 73.3% (p=<0.005). Additionally the DPN prevalence was also found to be high in hypertensive 80.3% (p=<0.001) and with longer duration (>6 years) of DM accounted for 67.4% (p=<0.012). The results of laboratory test revealed that87.3% of subjects had higher level of Hb and 76.0% had highcholesterol level and 7.3% of the patients had elevated levels of creatinine (Tables 2).

Table 2: Medical and DPN profiling of diabetic patients

Characteristics	N	%
Treatment		
Oral Hypoglycemic agents	220	73.3
Insulin	80	26.6
Hypertension		
Yes	241	80.3
No	59	19.6
Diabetic Foot		
Yes	11	3.66
No	289	96.3
Hb Level		
Normal	38	12.6
Elevated	262	87.3
Creatinine		
Normal	276	92.7
Elevated	24	7.3
LDL-C		
Normal	72	24
Abnormal	228	76
Dyslipidemia (TC)		
Normal	180	60
Abnormal	120	40
DPN Patterns		
Severe	123	41
Moderate	47	15.6
Mild	63	21
None	74	24.6

The majority of patients 78.5% with type 2 DM and DPN were using oral treatment, among them 78.9% were using oral drugs for glycemic control for more than 10 years ($p \Rightarrow 0.009$). The statistics revealed that type 2 DM patients using oral agents for >ten years had more risk of developing peripheral neuropathy as compared to the patients with DM type 1 (Table 3).

Table 3: Prevalence of peripheral neuropathy

Characteristics	DPN Presence		
	No	Yes	P value
Gender			
Male	32%	68%	0.41
Female	24%	76%	0.032
Age (Years)			
15-40	70%	30%	0.013
40-60	31%	69%	0.001*
>60	13%	87%	0.017
Residence			
Rural	30%	70%	0.82
Urban	31%	69%	0.21
BMIkgm⁻²			
Underweight (<18.5)	80.2%	19.8%	0.52
Normal (18.5 - 24.9)	45.6%	54.4%	0.001*
Overweight (25 - 29.9)	25%	75%	0.49
Obese (≥ 30)	15%	85%	0.198
Diabetic Foot			
Yes	-	3.6%	0.0407
No	30%	70%	0.034
Treatment			
Oral	42%	58%	0.0039
Insulin	25%	75%	0.013*
Both	52%	48%	0.029
Hb level			
<7	23%	77%	0.242
>7	29.4%	69.6%	0.31
Hypertension			
Yes	20.1%	79.9%	0.019
No	64%	36%	0.001*
Duration of DM (Years)			
1-6	40%	60%	0.029
7-12	43%	67%	0.037
13-18	17%	82%	0.020
19-24	14%	86%	0.012*
25-32	23%	77%	0.036
33-40	1.1%	98.9%	0.082

The presence and severity of peripheral neuropathy were categorized by scores of TCSS. Total 230 patients diabetic patients had neuropathy, severe in 51%, moderate in 20%, and mild in 29% subjects. The risks linked with neuropathy are presented in table 4 which showed the increase in age was one of the major factor regarding the severity of neuropathy ($p < 0.001$), the older the patient high will be the severity. The high BMI ($p < 0.001$), and longer period of diabetes with more than 6 years ($p < 0.005$) was also found to be the contributing factors towards severe DPN. The association of high Hb with DPN was not significant ($p = 0.710$). The patients having ages between 40 to 60 years and with dyslipidemia showed the highest risk for DPN. HbA was found not to be associated with DPN.

DISCUSSION

Overall high prevalence of DPN was found amongst diabetic patients of Jamshoro population. The duration of DM is considered as the major factor contributing towards development of retinopathy. According to researches there are found higher chances of proliferative diabetic retinopathy after 20 years of diabetes accounting 60 % of diabetes type 1, and 40% of DM type 2. These findings support the results of our research that the incidence of neuropathy was higher in individuals with longer DM duration as compared to shorter duration. This research also showed high comorbidities associated with diabetes in obese and overweight patients including hypertension, and hyperlipidemia, along renal impairment and ulcer or diabetic foot. These are the major complications leading towards vascular disease as well as peripheral neuropathy. High level of Hb level and hyperglycemia was also evidenced in this research. Various studies also showed similar results, including study conducted in Ethiopia [18] and Turkey [19] showing 60% DPN in diabetics, the results also in consistent with the results of this research and prevalence of 56.2% was reported in Yemen [20]. The diabetic foot and ulcers were the skin disorder which was observed in 4% of the population and was more prevalent in men compared to women. The studies also reported the prevalence of foot complications including diabetic foot and leg ulcer to be 30% and 46.7% of the population [21, 22] but our research showed lower prevalence of diabetic foot which may be due to better care of the foot. Mahmood [23] and Zafer [24] also described that foot abnormalities were more common prevalent in men. Ali [25] reported that females having high BMI showed development of diabetic foot and ulceration.

High degree of DPN was found in our research which was way too high as compared to the other reported studies in developed countries South Africa [26], Uganda [27], Germany [28] and UK. This may be due to different tools, settings, or the genetics of the study population. The main factor of this difference can be the study setting as this research was conducted tertiary hospital where patients take too long to be diagnosed with disease as well as presents diverse complications [17–21]. The severity of DPN was high in more than half of the study population which was majorly associated with duration of DM, age and BMI. Higher Hb showed no relation with the severity of DPN in our study. No correlation was also reported by [29] who demonstrated that higher glucose level will develop neuropathy but not necessarily linear correlation can be found among these factors [30-32].

There have been reported a large number of issues related to diabetes and neuropathy which needs to be prevented by identifying the risk factors. Initiating of early diabetic treatment, control of glycaemia and maintenance of low blood glucose level can help in the prevention of macro vascular as well as microvascular complications. Blood pressure and serum cholesterol, along with the modifications in lifestyle can also be the major factors [33, 34]. The main hindrance in effectiveness interventions in population are the undiagnosed diabetes and no adherence and non-compliance to treatment.

CONCLUSION

Diabetic patients have DPN which was observed to be highly prevalent in our research accounting more than half of the study population experiencing severe DPN. The factors which are mainly associated with DPN in diabetic subjects are age, high BMI, longer DM duration, hypertension, and high cholesterol level. Interventions are needed to educate the patients about the associated factors involved in developing DPN, glycemic control, foot care blood pressure control as well as healthy lifestyle to prevent and control the frequency and severity of diabetic neuropathies.

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