The Risk Factors of Diabetic Neuropathy in Type 2 Diabetic Patients Presenting to Services Hospital Lahore

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Abstract

Objective: To investigate the risk factors and to study the effect of these risk factors on the diabetic neuropathy (DN).

Method: The study was a retrospective case-control, hospital-based study and was carried out from18th November 2021 to 20th December 2021 through the questionnaire. Respondents were patients of diabetes mellitus (n=277) who visited the Diabetes Management Center of Services Hospital, Lahore. Binary Logistic regression model was fitted using SPSS 20.0

Result: Sample comprised of 277 subjects and among these, 122 and 155 were cases and controls respectively. Female gender (OR=2.225), duration of diabetes (OR=1.066), blood glucose level in fasting (OR=1.006), and age (OR= 1.042) have a significant effect on the prevalence of diabetic neuropathy.

Conclusion: The risk of Diabetic Neuropathy has been found higher, due to an increase in age, duration of diabetes and uncontrolled glucose level in the blood. Female patients of diabetes mellitus have higher probability of DN as compared to male patients.

Keywords: Type 2 diabetes; Diabetic Neuropathy (DN); Diabetes Mellitus (DM)

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Introduction

Among non-transmissible diseases, diabetes mellitus (DM) has growing economic burden in both developing and developed countries on individuals and on public health care system. In Pakistan, the annual direct and indirect cost estimated to manage diabetes in 2022 was 740.1 USD.[1] Almost 4 out of 5 (79%) adults who had diabetes belonged to "low or middle income countries". Globally, almost 33% of elderly population (65 or older) is diabetic.[2] It is a fact that 50% of diabetic patients remained undiagnosed.[3] In Southeast Asian countries, 80 million population suffered from diabetes and it is forecasted that it can rise to 151 million by 2045.[4] In Pakistan, 11% population had diabetes in 2011 and it is estimated to increase up to 15% till 2030.[4] Another study reported that prevalence of diabetes will be expected to be doubled (7 million to 14 million) by 2040 in Pakistan.[5] Pakistan, stands at 7th number globally regarding prevalence of diabetes mellitus and if it rise at same level it can reach to 4th in ranking.[4] About 48,800 Pakistanis aged 30-69 and 47700 aged >70 died due to diabetes or due to related complications.[5] Health care experts and those who formulate policies have to identify strategies to encounter this situation and take effective interventions to lower down its prevalence rate.[6]

Diabetic neuropathy is one of the common complication of diabetes mellitus. Diabetic Peripheral Neuropathy (DPN) is defined as "It is a symmetrical, length-dependent sensorimotor polyneuropathy attributable to metabolic and micro vessel alterations as a result of chronic hyperglycemia exposure".[7] Globally, 60% to 70% of the diabetic patients suffered from Diabetic Peripheral

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Neuropathy DPN.[8] Diabetic neuropathy creates many complications in different organs of body. It causes harm to nerves, generates sleep and mood disorders and has negative impact on the routine of life. It damages and compromises overall quality of life of the person suffering from this problem. Chances of foot ulcer and charcot joints are more in case of peripheral neuropathy. Peripheral neuropathy may result in morbidity and mortality. Autonomic neuropathy may result in gastric, diarrhea, constipation, bladder, myocardial infraction, arrhythmia, erectile dysfunction and fertility complications.[9] Sometimes it becomes reason of sudden death. Diabetic patients who experience loss of sense, numbness and aches are categorized as suffering from sensorimotor neuropathy.[10]

Age, hyperglycemia, hypertension, duration of DM, smoking, obesity, hyperinsulinemia and dyslipidemia are risk factors of diabetic neuropathy.[11] Progression of diabetic neuropathy can be reduced if controllable risks factors are identified that significantly affect the diabetic patients with particular social and economic background of our region. Early stage screening of diabetic neuropathy curtails the adverse impact of complications. This early screening may be helpful in lowering risk of foot ulcer.[8] In developing countries, health care facilities to look after diabetic neuropathy are either not accessible or affordable. In low resource settings, early identification of diabetic neuropathy and its associated risk factor can be helpful in minimizing the burden of disease.

Materials and Methods

The survey-based retrospective study has been conducted in the Diabetes Management Center of Services Hospital, Lahore. The data had been collected from 277 patients who visited the center from 18th November 2021 to 20th December 2021 through the questionnaire. 122 Patients with the manifestation of any type of diabetic neuropathy are taken as cases and the other 155 who did not suffer from neuropathy are considered as control. The main aim of this study is to determine the risk factors of diabetic neuropathy in type 2 diabetes patients. The response variable (diabetic neuropathy) is binary (yes or no). Potential risk factors age, gender, blood sugar level, and blood pressure level are continuous variables and BMI, smoking status, family history, thyroid history, occupation, treatment approach, and physical activity have been taken in the study through extensive literature review on the same research. In this study, SPSS version 20.0 was used for the analysis purpose. BMI is categorized as normal (18.5 to 22.9), over weight (23 to 24.9) and obese (25 or more).[12] Blood sugar level in fasting is taken as low (less than 80), normal (80 to 130) and high (more than 130). Blood sugar level in any time of day(random) is classified as low (less 90), normal (90 to 180) and high (more then 180). Blood pressure (upper/lower) is identified as low (90/60), normal (120/ 80) and high (130/more than 80). The chi-square test is used to test the association between outcome variables i.e. diabetic neuropathy (Yes, No) with different socioeconomic, demographic and clinical factors. The chi-square statistic [11] is computed as:

$$\chi^2 = \Sigma_i \Sigma_j \frac{(n_{ij} - u_{ij})^2}{u_{ij}}$$

Logistic regression is used to study the effect of risk factors on binary dependent variable. In current study diabetic neuropathy is dichotomous (yes, no) that leads to the choice of binary logistic regression model. Model is used to predict the chances of occurrence of an event of interest. The mathematical form of model is given as following:

$$\boldsymbol{Y}_i = \beta\boldsymbol{0} + \beta_i \boldsymbol{X}_i + \varepsilon_i$$

$$P(Y/X) = \frac{e^{\beta_0 + \beta_1 X}}{1+e^{\beta_0 + \beta_1 X}}$$

$$\ln\left(\frac{P(Y \mid X)}{1 - P(Y \mid X)}\right) = \beta_0 + \beta_1 X$$

$$E(Y) = \frac{e^{\beta_0 + \beta_i X_i}}{1+e^{\beta_0 + \beta_i X_i}}$$

Consider the p risk factors denoted by the vector $x_i = (x_1, x_2, x_3 ..., x_p)$. The conditional probability that the outcome of interest is present is given as:

$$\ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + ... + \beta_p X_p$$

$$g(x) = \beta_0 + \beta_1 X_1 + ... + \beta_p X_p$$

Results

In this study, bar charts and percentages are used for data exploration. Results and interpretation of descriptive and analytic section are documented in this section. Among 277 diabetic patients, 44% (122/277*100) suffered from diabetic neuropathy. Retinopathy, nephropathy, stroke, ischemic heart disease, hyperlipidaemia, chronic liver disease, malignancy were found rare in

study participant, where hypertension and intermittent claudication are common complications related to type 2 diabetic patients in this study. None of the patient have been found suffering from pulmonary tuberculosis (TB) and uremia.

Numbness and burning are found very common symptoms of diabetic neuropathy in type 2 patients, where cold, tingling, dull pain, cold pain are rare in patients. Sensitivity is also present in those who have severity of diabetic neuropathy.

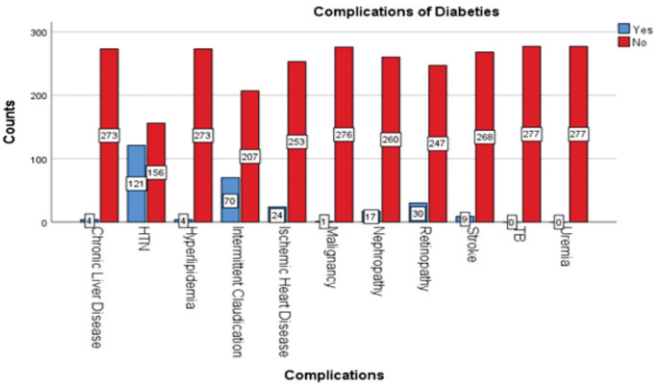

Fig-1: *Prevalence of complications in type 2 Diabetes Patient Other than Diabetic Neuropathy.*

Table 1: *Percentage (Frequency) Distribution of Demographic and Clinical Factors of Study Participants*

Variable	Categories	Percentages(n)
Gender	Male	52.5% (145)
	Female	47.7% (132)
Age	<50	47.7% (132)
	50-69	49.5% (137)
	⩾70	2.9% (8)
Sugar Level (Random)	Low	1.1% (3)
	Normal	19.1% (53)
	High	79.8% (221)
Sugar Level (Fasting)	Low	0.7% (2)
	Normal	23.5% (65)
	High	75.8% (210)
Duration of Diabetes (years)	<5	50.2% (139)
	5-11	30.7% (85)
	⩾12	19.1%(53)
BMI	Normal	11.6% (32)
	Over Weight	11.6% (32)
	Obese	76.9% (213)
Blood Pressure (Upper)	Low	1.8% (5)
	Normal	23,1% (64)
	High	75.1%(208)
Blood Pressure (Lower)	Low	1.8% (5)
	Normal	50.2% (139)
	High	48%(133)
Smoking Status	Yes	8.3% (23)
	No	91.7%(254)
No. of Times Sugar Level Checked in Last Month	⩽ 10	57.8% (160)
	11-29	29.2% (81)
	⩾30	13% (36)

Variable	Categories	Percentages(n)
Occupation	Do not Work	56%(155)
	Non Professional	20.9%(58)
	Professional	23.1%(64)
Treatment for Diabetes	Insulin	43.3% (120)
	Oral Hypoglycaemia (OH)	35% (97)
	Both Insulin and OH	13.7% (38)
	No Medicine	7.9% (22)
Working Status	Not Employed	55.2% (153)
	Employed	37.9% (105)
	Retired	6.9% (19)
Visiting Diabetic Centre	Yes	94.9% (263)
	No	5.1% (14)
No. of Visits in Diabetic Centre in a Year	No Visit	5.4% (15)
	1- 3	65.7% (182)
	⩾4	28.9% (80)
Admitted in Hospital Due to Diabetes	Never	84.1% (233)
	1-2	12.6% (35)
	⩾3	3.2% (9)
Drug History	Yes	0.4% (1)
	No	99.6% (276)
Knowledge About Diabetes	Yes	59.6% (165)
	No	40.4%(112)
Family History of Diabetes	Yes	57% (158)
	No	43% (119)
Thyroid (Hyper/Hypo) History	Yes	4% (11)
	No	96% (266)
Physical Activity	Regular	48.0% (133)
	Not Regular	42.6%(188)
	Not any Activity	9.4%(26)

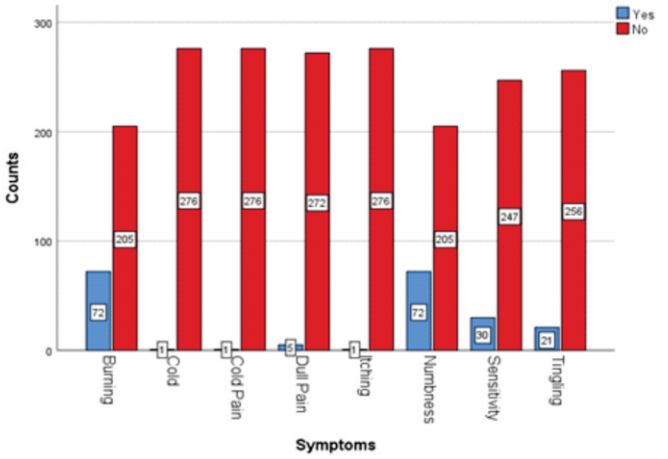

Figure 2: *Symptoms of Diabetic Neuropathy in Type 2 Diabetic Patients*

Gender, age, duration of diabetes, smoking status, occupation, working status, number of visits to doctor/ diabetic clinic in a year, admitted in hospital due to diabetes and physical activity were found significantly associated with diabetic neuropathy **(Table 2)**.

Odd ratios computed from binary logistic regression model have been reported in Table 3 using backward elimination method for selection of significant predictors. Gender, duration of diabetes, age and blood sugar level (in fasting) has shown significant relationship with diabetic neuropathy in type 2 diabetic patients. The probability of diabetic neuropathy is increased by 4.2% (OR=1.042; CI= 1.238, 3.998) for per year increase in the age of type 2 diabetic patient. Per year increase in the duration of diabetes increased the risk of occurrence of diabetic neuropathy by 6.6% (OR= 1.066; CI=1.0616, 1.116). The chances of diabetic

Table 2: *Percentage Distribution of Risk Factors × Diabetic Neuropathy*

Risk Factors	Categories	Neuropathy		χ^2
		Yes	No	
Gender	Male	31.1%	68.9%	17.246*
	Female	55.9%	44.1%	(0.000)
Age	< 50	36.4%	63.6%	6.664*
	50-69	51.8%	48.2%	(0.036)
	>70	44.0%	56.0%	
BMI	Normal	37.5%	62.5%	2.282
	Over weight	34.4%	65.6%	(0.319)
	Obese	46.5%	53.5%	
Duration of Diabetes (years)	<5	30.9%	69.1%	18.493*
	5-11	58.8%	41.2%	(0.000)
	⩾12	54.7%	45.3%	
Sugar Level (Fasting)	Low	0%	100%	-
	Normal	33.8%	66.2%	
	High	47.6%	52.4%	
Knowledge about Diabetes	Yes	40.2%	59.8%	1.140
	No	46.7%	53.3%	(0.286)
Smoking Status	Yes	17.4%	82.6%	7.229*
	No	46.5%	53.5%	(0.007)
Sugar Level (Random)	Low	0%	100%	-
	Normal	30.2%	69.8%	
	High	48.5%	52/0%	
Blood Pressure (Upper)	Low	___	___	0.203
	Normal	46.4%	53.6%	(0.652)
	High	43.3%	56.7%	
Blood Pressure (Lower)	Low	80.0%	20.0%	2.677
	Normal	43.2%	56.8%	(0.262)
	High	43.6%	56.4%	
Visiting a Diabetic Centre	Yes	44.1%	55.9%	0.008
	No	42.9%	57.1%	(0.927)

Risk Factors	Categories	Neuropathy		χ^2
		Yes	No	
Drug History	Yes	100%	0%	-
	No	43.8%	56.2%	
Occupation	Do not work	56.1%	43.9%	21.104*
	Non Professional	26.6%	73.4%	(0.000)
	Professional	31.0%	69.0%	
Working Status	Not Employed	53.6%	46.4%	18.636*
	Employed	27.6%	72.4%	(0.000)
	Retired	57.9%	42.1%	
Treatment for Diabetes	Insulin	46.7%	53.3%	3.517
	Oral Hypoglycaemia OH)	42.3%	57.7%	(0.319)
	Both (Insulin and OH)	50.0%	50.0%	
	No Medicine	27.3%	72.7%	
Family History of Diabetes	Yes	41.1%	58.9%	1.259
	No	47.9%	52.1%	(0.262)
History of Thyroid (Hyper/Hypo)	Yes	36.4%	63.6%	0.274
	No	44.4%	55.6%	(0.601)
No. of Times Sugar Level Checked in Last Month	⩽10	40.6%	59.4%	1.843
	11-29	49.4%	50.6%	(0.398)
	⩾30	47.2%	52.85	
No. of Visits in Diabetic Centre in a Year	No Visit	40.0%	60.0%	7.163*
	1-3	40.5%	59.5%	(0.028)
	⩾4	61.7%	38.3%	
Admitted in Hospital due to Diabetes	Never	40.8%	59.2%	7.604*
	1-2	57.1%	42.9%	(0.022)
	⩾3	77.8%	22.2%	
Physical Activity	Regular	43.6%	56.4%	7.929*
	Not Regular	39.6%	61.0%	(0.019)
	No Activity	69.2%	30.8	

– is used in Table 2 as chi square is not computed if any cell frequency is "0", * significant at 5%

neuropathy is increased by 0.6% for per unit increase in blood glucose level in fasting. Females have almost a twice risk of having diabetic neuropathy as compared to the male type 2 diabetic patient (OR=2.225 CI= 1.238, 3.998).

Table 3: *Odd Ratios of Significant Factors of Diabetic Neuropathy using Binary Logistic Regression Model*

Risk Factors	OR	P-value	95%CI	
			Lower	Upper
Gender (ref. male)	—	—	—	—
Female	2.225	0.008	1.238	3.998
Duration of diabetes	1.066	0.009	1.0616	1.116
Age	1.042	0.001	1.016	1.068
Blood sugar level (fasting)	1.006	0.002	1.002	1.010

Discussion

Knowledge about risk factors of diabetic neuropathy (DP) helps to control its prevalence. Diabetic neuropathy (DN) has different types like diabetic peripheral neuropathy (DPN), proximal neuropathy, autonomic neuropathy, and sensorimotor neuropathy. This study was conducted to determine the risk factors of diabetic neuropathy and investigated its effect on developing DN. Age, gender, duration of diabetes, and unbalanced glucose level in fasting has shown significant association in developing diabetic neuropathy in type 2 diabetic patients. It is widely accepted that older age, long-duration diabetes, and poor glycemic control are important risk factors in DN development.[13] In this study, the age group 50 to 69 has a large number of people suffering from DN. Another study conducted in Lahore had shown that this particular age group has a large number of diabetic peripheral neuropathy patients and age had also shown a significant association with DPN.[14] The cross-sectional study, previously conducted at the Diabetic Management Center (DMC) of Services Hospital Lahore indicated that age had a significant effect on sensorimotor neuropathy.[15] In the research conducted in India, it has been also shown that the age wise prevalence of diabetic neuropathy for age groups 50 to 59 and 60 to 69 was found at 43.6% and 52.9% respectively.[16]

It is also observed in current study that as the duration of diabetes increases the prevalence of diabetic neuropathy also increases. Similar results were found in some other studies in which peripheral neuropathy and sensorimotor neuropathy showed positive significance in duration of diabetes.[14,15] In a recent study unbalanced glucose level in fasting has a positive significant effect on prevalence of diabetic neuropathy. These results are in line with previous research in which uncontrolled glucose level in fasting is significantly associated with sensorimotor neuropathy.[15] A study conducted in 14 countries on diabetic peripheral neuropathy had shown that the risk of DPN is increased due to poor glycemic control.[17] The current study revealed that the female type 2 diabetes patient (n=132) has 55.9% diabetic neuropathy cases present while male type 2 diabetic patient (n=145) has 31.1% diabetic neuropathy cases found. The probability of DN is twice as higher in female type 2 diabetic patients as compared to the male type 2 diabetic patients The Cross-Sectional study conducted in Services Institute of Medical Sciences, Lahore, indicated that 21.25% of males with type 2 diabetic patients (n=80) suffered from DPN and 20% of type 2 diabetic females (n=70) faced problem of DPN.[18] In research, males have a large number of cases of DPN but carpal tunnel syndrome (CTS) in females is more frequent.[19] CTS may become the cause of numbness and pain in the finger. These symptoms of DN are found very common in current study so that might be the cause of the significantly higher risk of DN in females.

Conclusion

Risk of diabetic neuropathy significantly increased due to increase in age, duration of diabetes, uncontrolled glucose level in the blood. The chances of diabetic neuropathy is found twice for female diabetic patients as compared to male diabetic patients. Studies should be conducted to reduce burden of diabetic neuropathy by creating awareness among female and aged patients to control their glucose level.

Conflict of interest *None*

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Authors Contribution

AK, MI: Conceptualization of Project
SA, MI, KM: Data Collection
SA, AK: Literature Search
AK, SA, AS: Statistical Analysis
AK, SA, AK, MI, KM: Drafting, Revision
AK, SA, AK, AS : Writing of Manuscript