



A STUDY ON THE PREVALENCE OF PERIPHERAL NEUROPATHY AND ITS RISK FACTORS IN PREDIABETICS*

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ABSTRACT

INTRODUCTION: Diabetic Peripheral Neuropathy (DPN) is the commonest symptomatic complication of Diabetes. Prevalence of Diabetic peripheral Neuropathy is 15 to 40 percent in various study groups. It predisposes to foot ulceration and gangrene. In view of poor awareness and lack of regular screening programs, the initial presentation to the physicians is delayed frequently. This may predispose to increased rate of micro vascular complication at onset. There is emerging evidence that Peripheral Neuropathy begins in the early stages of Diabetes pathogenesis.

AIM: 1. To estimate the prevalence of Diabetic Peripheral Neuropathy in subjects with Pre-diabetes. 2. To study the distribution of risk factors for Diabetic Peripheral Neuropathy in Pre-diabetic subjects. **METHOD:** A Cross sectional study on the prevalence of distal sensory peripheral neuropathy in Pre-diabetics and the relation of it with risk factors was done in 216 patients attending Outpatient clinic in Government Vellore Medical College. **RESULTS:** In the study, 61 subjects had peripheral neuropathy according to Michigan Neuropathy Screening Instrument (MNSI) score of ≥ 3 . Out of these 61 patients, 30 were male and 31 were female. Out of 155 pre-diabetics who were not having diabetic peripheral neuropathy, 80 were male and 75 were female. The prevalence of diabetic peripheral neuropathy in the study population was 28.24% { Pearson Chi-Square (X^2) = 0.104 and P value was 0.747 (>0.05)}; hence statistically insignificant. Out of 61 patients with diabetic peripheral neuropathy, 32 patients had systemic hypertension. In 155 subjects without DPN, 33 had systemic hypertension. The prevalence of systemic hypertension in subjects with DPN was 52.5 %. Out of 32 patients, 17 were male and 15 were female. The prevalence of systemic hypertension in subjects without DPN was 21.29 % (X^2 = 20.214 and the P value was 0.001); thus statistically highly significant. 38 out of 61 subjects with DPN were obese and similarly out of 155 subjects without DPN 33 were obese. The prevalence of obesity in subjects with DPN was 62.30 % and that of subjects without DPN was 21.30 % (X^2 = 33.355 and P value was 0.001); hence statistically highly significant. Among subjects with DPN, 3 (4.92%) had HbA_{1c} less than 5.5, 22 (36.07%) had HbA_{1c} levels between 5.6- 6, 36 (59.02%) had HbA_{1c} levels between 6.1-6.4. Most of the subjects with DPN belonged to the group where the HbA_{1c} levels were between 6.1-6.4. The prevalence was 59.02 %. Among subjects without DPN, 53 (34.19%) had HbA_{1c} below 5.5, 71 (45.81%) had HbA_{1c} between 5.6 and 6, 37 (23.87%). The relationship between DPN and HbA_{1c} more than 6.1 was plotted (X^2 = 30.881 and P value was less than 0.001); thus statistically highly significant. The prevalence of hypercholesterolemia (serum cholesterol level of ≥ 200 mg/dl) in patients with Peripheral Neuropathy was 63.9% and patients without DPN had normal serum cholesterol levels were 5.8 %. Mean cholesterol level of the subjects with peripheral neuropathy was 214.75 mg/dl and that of subjects without peripheral neuropathy was 169.61 mg/dl. (X^2 = 85.573 and the P value was <0.001); thus statistically highly significant. Mean triglyceride (TGL) levels in subjects with DPN were 146.95 mg/dl and in subjects without DPN was 130.45 mg/dl. In subjects with Peripheral Neuropathy, 23 out of 61 patients had increased TGL levels. The prevalence of hypertriglyceridemia in peripheral neuropathy was 37.7%. Out of 155 subjects, who did not have peripheral neuropathy, only 8 patients had hypertriglyceridemia . The prevalence was 5.2% (X^2 = 79.489 and P value <0.001). Out of 61 subjects, who had DPN, 39 subjects (63.93%) had dyslipidemia. Out of 155 subjects without DPN, only 11 subjects (7.10%) had dyslipidemia. The prevalence of dyslipidemia in subject with DPN was 63.93 % and the relationship between DPN and dyslipidemia is statistically significant; (X^2 = 79.489 and P value <0.05). In subjects diagnosed to have peripheral neuropathy, 17 were smokers and 44 were non smokers. The prevalence of smokers in DPN was 27.87%. Among subjects without DPN, 18 were smokers and 137 were non smokers. The prevalence of smokers in subjects without DPN was 11.6% (X^2 = 8.519 and the P value was 0.004); thus statistically significant. Out of 61 subjects with DPN, 32 (17 male and 15 female) had abnormal waist circumference. Out of 155 subjects without DPN, 37 had abnormal waist circumference. The prevalence of abnormal waist circumference in subjects with peripheral neuropathy was 52.46 % and the prevalence of abnormal waist circumference in subjects without peripheral neuropathy was 23.87% (X^2 = 12.614 and P value was <0.05); hence there is statistically high significant correlation between abnormal waist circumference and DPN. **CONCLUSION:** Peripheral Neuropathy is equally common in both diabetic and pre-diabetic individuals. It is more prevalent in elderly pre-diabetic individuals of age more than 70 years. Both males and females are equally affected; there is no sex predilection for the occurrence of peripheral neuropathy. Hypertensive individuals are affected more than non hypertensives. There is strong relationship between obesity and peripheral neuropathy in pre-diabetic individuals. Prevalence of dyslipidemia is higher in pre-diabetic people with peripheral neuropathy. People with pre-diabetics who have peripheral neuropathy have higher HbA_{1c} values. Smokers have higher prevalence of peripheral neuropathy among pre-diabetics. Lastly since the prevalence of peripheral neuropathy is high even in pre-diabetic population, the study emphasizes the need for the early diagnosis of peripheral neuropathy in people who are at high risk for developing diabetes and to screen for the possible associated risk factors.

KEYWORDS : Diabetes, Diabetic Peripheral Neuropathy (DPN), Michigan Neuropathy Screening Instrument (MNSI) score, systemic hypertension, hypercholesterolemia, dyslipidemia, HbA_{1c} (glycosylated haemoglobin), abnormal waist circumference.

INTRODUCTION

Diabetes Mellitus has become a global epidemic affecting not only Western population, but also the Asian population including those of the Indians. There are currently an estimated number of more than 62,000,000 people suffering from this disease in India. The prevalence of pre-diabetic population is even higher with estimated 77.2 million people in the year 2011 by Indian Council of Medical Research census.¹ By the year 2030 it is estimated that there will be nearly 80 million Indians with Diabetes. It is associated with

more than two fold excess mortality from cardiovascular disease, devastating micro-vascular complication affecting the eyes, kidneys and nerves as well as co-morbidity including cancer, infection and psychosocial stress.

Diabetic Peripheral Neuropathy (DPN) is the commonest symptomatic complication of Diabetes.² Prevalence of Diabetic peripheral Neuropathy is 15 to 40 percent in various study groups.³ It predisposes to foot ulceration and gangrene. Type 2

Diabetes Mellitus is characterized by long asymptomatic phase (4-7 years) between the actual onset of hyperglycemia and clinical diagnosis which may explain the relatively high prevalence of micro-vascular complication in newly diagnosed patients with Type Diabetes Mellitus. In view of poor awareness and lack of regular screening programs, the initial presentation to the physicians is delayed frequently. This may predispose to increased rate of micro-vascular complication at onset. There is emerging evidence that Peripheral Neuropathy begins in the early stages of Diabetes pathogenesis. Hence this study aims to estimate the prevalence of Peripheral neuropathy and its risk factors in pre-diabetic population attending the Outpatient department of Government Vellore Medical College Hospital during the period between September 2015 to August 2016.

MATERIALS AND METHODS:

After prior Institutional Ethical clearance and obtaining written informed consent, the participants satisfying inclusion criteria (Pre-diabetic population of age more than 30 years old) were asked detailed history and clinical examination was performed. 7 ml of venous blood was obtained by venepuncture under aseptic conditions and transferred to Plain and EDTA vacutainers where in Plain sample was centrifuged and the separated serum was used for estimation of fasting blood glucose levels, serum cholesterol and triglycerides and for HbA1C analysis, blood collected in EDTA vacutainer was utilized. Height, weight and waist circumference of the individual patient was measured and BMI was calculated. Presence of peripheral neuropathy was assessed by validated MNSI (Michigan Neuropathy Screening Instrument) scoring system. Patient denying consent, Type 1 Diabetes Mellitus patients, Patients with other known cause of peripheral neuropathy such as Hypothyroidism, Vitamin B12 deficiency, Alcoholism, Uremia, Tuberculosis, HIV, Patients on drugs having peripheral neuropathy as established toxicity. Patients with liver dysfunction, renal dysfunction, neoplastic diseases and on its treatment, also, Pregnant and lactating mothers were excluded from the study.

Study design: A Cross sectional study on the prevalence of distal sensory peripheral neuropathy in Pre-diabetics and the relation of it with non modifiable risk factors namely age and sex and non-modifiable risk factors namely systemic hypertension(SHT), dyslipidemia with respect to hypercholesterolemia and hypertriglyceridemia, waist circumference , HbA1C and body mass index(BMI) was done in 216 patients attending Outpatient clinic in Government Vellore Medical College.

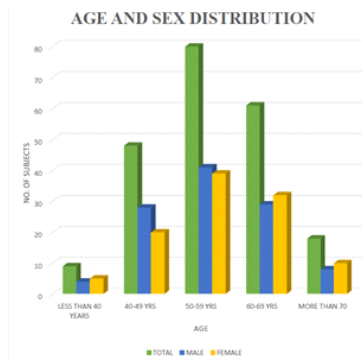
Statistical Methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups.

Statistical software: The Statistical software namely SAS 9.2, SPSS 16, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

STATISTICAL ANALYSIS

I. AGE AND SEX DISTRIBUTION

AGE (IN YRS)	MALE	FEMALE	TOTAL	PERCENTAGE(%)
<40	4	5	9	4.2
40-49	28	20	48	22.2
50-59	41	39	80	37
60-69	29	32	61	28.2
≥70	8	10	18	8.3

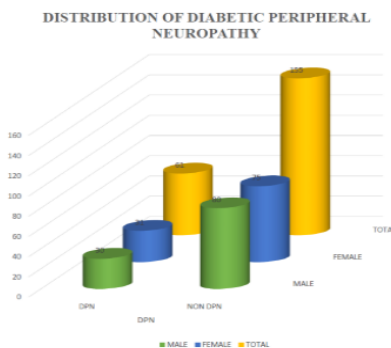


The mean age of the study subjects was 56.3 years. Most of the patients belonged to the age group 50-59 years.

Out of 216 cases, 110 (50.93%) were male and 106 (49.07%) were female. Male to female ratio was 1.04:1.

II. PREVALANCE OF DIABETIC PERIPHERAL NEUROPATHY (DPN)

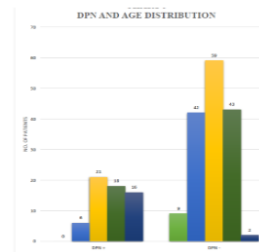
	DPN		TOTAL
	PRESENT	ABSENT	
MALE	30(27.27%)	80	110
FEMALE	31(29.25%)	75	106
TOTAL	61(28.24%)	155	216



In our study, 61 subjects had peripheral neuropathy according to MNSI score of ≥3. Out of these 61 patients 30 were male and 31 were female. Out of 155 pre-diabetics, who were not having diabetic peripheral neuropathy, 80 were male and 75 were female. The prevalence of Diabetic peripheral neuropathy in the study population was 28.24%. From the above X² = 0.104 and P value was 0.747 (<0.05); hence statistically insignificant.

III. DISTRIBUTION OF DPN AND AGE

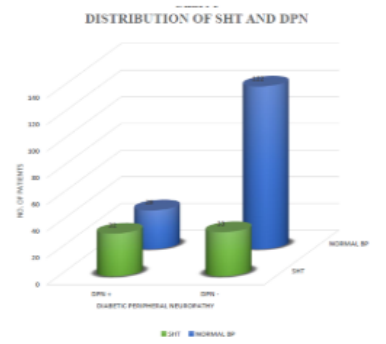
AGE (In years)	DPN		TOTAL
	PRESENT	ABSENT	
<40	0	9	9
40-49	6	42	48
50-59	21	59	80
60-69	18	43	61
≥70	16	2	18
TOTAL	61	155	216



Among subjects who had DPN 6 (9.8%) were in the age group between 40 to 49; 21(34.4%) were between 50-59; 18 (29.5%) were between 60- 69; and 16 (26.2%) were more than 70 years old. Most of the patients belonged to age group between 50 and 59. However the prevalence of peripheral neuropathy in patients aged more than 70 was very high (88.9%). In the above table, the relationship between DPN and Age ≥ 70 years was calculated. Using Pearson Chi-Square test, X^2 was 33.3; P value was <0.05 . Prevalence of DPN in patients aged more than 70 years was statistically significant.

IV. DISTRIBUTION OF DPN AND SHT

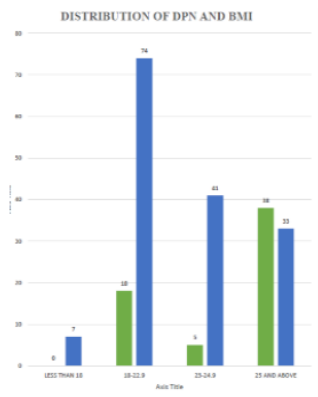
	DPN		TOTAL
	PRESENT	ABSENT	
SYSTEMIC HT	32(52.5%)	33 (21.29%)	65
NORMAL BP	29	122	151
TOTAL	61	155	216



Out of 61 patients with Diabetic Peripheral Neuropathy 32 patients had Systemic Hypertension. In 155 subjects, without DPN 33 had Systemic Hypertension. The prevalence of Systemic Hypertension in subjects with DPN was 52.5 %. Out of 32 patients, 17 were male and 15 were female. The prevalence of systemic hypertension in subjects without DPN was 21.29%. From the above table $X^2 = 20.214$ and the P value was 0.001; thus statistically highly significant.

V. DISTRIBUTION OF DPN AND BMI

BMI	DPN		TOTAL
	PRESENT	ABSENT	
<18	0(0%)	7(4.51%)	7
18-22.9	18(29.5%)	74(47.74%)	92
23-24.9	5(8.20%)	41(26.45%)	46
≥ 25	38(62.30%)	33(21.29%)	71
TOTAL	61	155	216

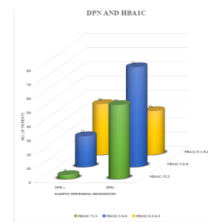


From the above table, 38 out of 61 subjects with DPN were obese and similarly out of 155 subjects without DPN 33 were obese. The prevalence of obesity in subjects with DPN was 62.30 % and that of

subjects without DPN was 21.30 %. $X^2 = 33.355$ and P value was 0.001; hence statistically highly significant.

VI. DISTRIBUTION OF DPN AND HBA1C

HbA1c	DPN		TOTAL
	PRESENT	ABSENT	
≤ 5.5	3(4.92%)	53(34.19%)	56
5.6-6	22(36.07%)	71(45.81%)	93
6.1-6.4	36(59.02%)	37(23.87%)	73
Total	61	155	216

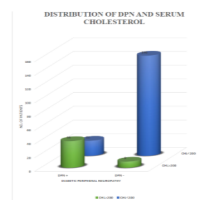


From the above table, among subjects with DPN , 3 (4.92%) had HbA1C less than 5.5, 22 (36.07%) had HbA1C levels between 5.6 to 6, 36 (59.02%) had HbA1C levels between 6.1-6.4 . Most of the subjects with DPN belonged to the group where the HbA1C levels were between 6.1-6.4. The prevalence was 59.02%. Among subjects without DPN, 53 (34.19%) had HbA1C below 5.5, 71 (45.81%) had HbA1C between 5.6 and 37 (23.87%). The relationship between DPN and HbA1C more than

6.1 was plotted. $X^2 = 30.881$ and P value was less than 0.001; thus statistically highly significant.

VII. DISTRIBUTION OF DPN AND SERUM CHOLESTEROL

SERUM CHOLESTEROL (mg/dl)	DIABETIC PERIPHERAL NEUROPATHY		TOTAL
	PRESENT	ABSENT	
≥ 200	39(63.9%)	53(34.1%)	92(73%)
<200	22	146	168
TOTAL	61	155	216

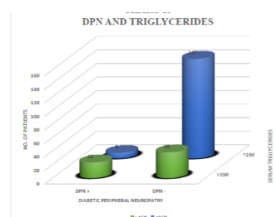


In subjects with DPN, 39 (63.9%) had serum cholesterol level of ≥ 200 mg/dl . The prevalence of hypercholesterolemia in patients with Peripheral Neuropathy was 63.9% and in patients with normal serum cholesterol was 5.8%. Mean cholesterol level of the subjects with peripheral neuropathy was 214.75 mg/dl and that of subjects without peripheral neuropathy was 169.61 mg/dl.

From the above $X^2 = 85.573$ and the P value was <0.001 ; thus statistically highly significant.

VIII. DISTRIBUTION OF DPN AND SERUM TRIGLYCERIDES (TGL)

TRIGLYCERIDES (mg/dl)	DIABETIC PERIPHERAL NEUROPATHY		TOTAL
	PRESENT	ABSENT	
≥ 150	23(37.7%)	8 (5.2%)	31(14.4%)
<150	38	147	185
TOTAL	61	155	216

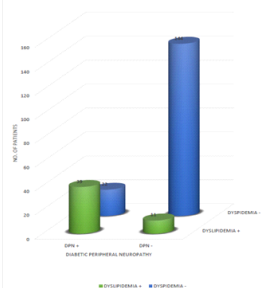


Mean TGL levels in subjects with DPN was 146.95 mg/dl and in subjects without DPN was 130.45 mg/dl. In subjects with Peripheral Neuropathy, 23 out of 61 patient had increased TGL levels. The prevalence of hypertriglyceridemia in peripheral neuropathy was 37.7%. Out of 155 subjects who did not have peripheral neuropathy, only 8 patients had hypertriglyceridemia. The prevalence was 5.2%. From the above table, $X^2 = 79.489$ and P value was less than 0.001; thus statistically highly significant.

IX. DISTRIBUTION OF DYSLIPIDEMIA AND DPN

DYSLIPIDEMIA	DIABETIC PERIPHERAL NEUROPATHY		TOTAL
	PRESENT	ABSENT	
PRESENT	39(63.93%)	11(7.10%)	50(23.26%)
ABSENT	22	144	166
TOTAL	61	155	216

DISTRIBUTION OF DPN AND DYSLIPIDEMIA



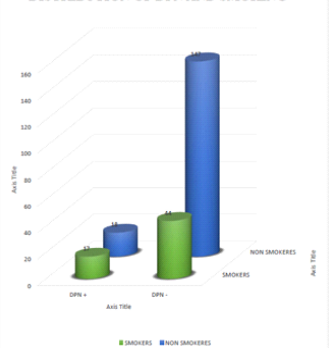
From this table $X^2 = 79.489$ and P value was less than 0.05; thus statistically highly significant.

Out of 61 subjects who had DPN, 39 subjects (63.93%) had dyslipidemia. Out of 155 subjects without DPN, only 11 subjects (7.10%) had dyslipidemia. The prevalence of Dyslipidemia in subject with DPN was 63.93 % and the relationship between DPN and Dyslipidemia is statistically significant.

X. DISTRIBUTION OF SMOKING AND DPN

SMOKING	DIABETIC PERIPHERAL NEUROPATHY		TOTAL
	PRESENT	ABSENT	
YES	17(27.87%)	18(11.6%)	35(16.2%)
NO	44	137	181
TOTAL	61	155	216

DISTRIBUTION OF DPN AND SMOKING

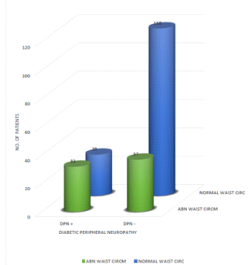


In subjects diagnosed to have peripheral neuropathy 17 were smokers and 44 were non smokers. The prevalence of smokers in DPN was 27.87%. Among subjects without DPN 18 were smokers and 137 were non smokers. The prevalence of smoke in subjects without DPN was 11.6%. From the above table, $X^2 = 8.519$ and the P value was 0.004; thus statistically significant.

XI. DISTRIBUTION OF WAIST CIRCUMFERENCE AND DPN

ABNORMAL WAIST CIRCUMFERENCE	DIABETIC PERIPHERAL NEUROPATHY		TOTAL
	PRESENT	ABSENT	
YES	32(52.46%)	37(23.87%)	69(31.84%)
NO	29	118	147
TOTAL	61	155	216

DPN AND WAIST CIRCUMFERENCE



Out of 61 subjects with DPN, 32 (17 male and 15 female) had abnormal waist circumference. Out of 155 subjects without DPN, 37 had abnormal waist circumference. The prevalence of abnormal waist circumference in subjects with peripheral neuropathy was 52.46% and the prevalence of abnormal waist circumference in subjects without peripheral neuropathy was 23.87%. From the above table, $X^2 = 12.614$ and P value was <0.05; hence statistically highly significant correlation between abnormal waist circumference and DPN.

- + Suggestive significance (P value: 0.05 < P < 0.10)
- * Moderately significant (P value: 0.01 < P < 0.05)
- ** Strongly significant (P value: P < 0.01)

DISCUSSION
GENERAL CHARACTERISTICS

This study involved a total of 216 subjects of which 110(50.93%) were males and 106(49.07%) were females. Most of the subjects were in the age group 50-59 years. The mean age of the study population was 56.3 years.

PREVALENCE OF DIABETIC PERIPHERAL NEUROPATHY

Among the study population 61 subjects had DPN. The prevalence of DPN in the study population was 28.24%. Out of these 61 subjects 30 were male and 31 were female. Though the prevalence of DPN is slightly higher in female subjects, it was not statistically not significant ($X^2 = 0.104$ and P value 0.747). Hence according to our study there is no sex difference in the prevalence of DPN in pre-diabetic subjects.

Among subjects with DPN most of them belonged to the age group 50-59 (34.4%). However the prevalence of the DPN in the age group >70 years was very high (88.9%) and statistically significant ($X^2 = 33.3$ and P value was <0.05)

In a study conducted by Dan Ziegler et al, the prevalence of peripheral neuropathy was 28.0% in diabetic subjects, 13% in those with IGT, 11.3% in those with IFG.⁴

In a similar study conducted by Papanas et al it was estimated that the prevalence of neuropathy in Pre-diabetics was around 11-25%.⁵ In another similar study conducted by Lee CC et al the prevalence of DPN in pre-diabetics was 49% which was high compared to our study.⁶

In the Indian population, a study was conducted by Meena et al which concluded that the prevalence was 32.8% among subjects with impaired glucose tolerance.⁷

DYSLIPIDEMIA

In this study, the prevalence of dyslipidemia was 23.26%. It was higher in subjects with DPN (63.93%) than in subjects without DPN

(7.10%). P value was < 0.05.

Mean total serum cholesterol was 214.75 mg/dl in subjects with DPN and 169.61 mg/dl in subjects without DPN. Prevalence of hypercholesterolemia was significantly higher in subjects with DPN (63.93%) than in subjects without DPN (5.8%).

The prevalence of TGL in the study population was 14.4%. Mean TGL value in subjects with DPN was 146.95 mg/dl and in subjects without DPN was 130.45 mg/dl. Prevalence of hypertriglyceridemia was significantly higher in subjects with DPN (37.7%). P value < 0.001.

In a similar study conducted by KATULANDA et al, the average total cholesterol level was 217.4 mg/dl in subjects with DPN and 217.1 mg/dl in subjects without DPN which was statistically insignificant, similarly mean TGL levels in subjects with DPN was 162.1 and in subjects without DPN was 138.2 which was statistically significant. (p < 0.05)

HYPERTENSION

The prevalence of systemic hypertension in the study population was 30.1%. Mean systolic and diastolic BP were 128 mm Hg and 81 mm Hg respectively. The prevalence of Systemic hypertension in subjects with DPN (52.5%) was significantly higher than in subjects without DPN (21.29%). The P value was < 0.05.

According to a study conducted by Fargol Booya et al, the prevalence of Systemic hypertension in patients with DPN was 41.8% which was little higher than our study.

SMOKING

Among the study subjects, 35 people (16.2%) were smokers and 181 (83.77%) were non smokers. The prevalence of smokers was significantly higher in subjects with DPN (27.87%) than in subjects without DPN (11.6%). The P value was 0.004

(< 0.05).

In a similar study conducted by Dipika Bansal et al which was on prevalence of DPN in a cohort of diabetic subjects, the prevalence of smoking in patients with DPN (12.4%) was statistically insignificant than in patients without DPN (13.3%) (p < 0.05).¹⁰

HBA1C

The average HbA1c of the study population was 5.8%. The average HbA1c values of the subjects with DPN were 6.10%. The prevalence of subjects whose HbA1c more than 6.0 was significantly higher in DPN subjects (59.02%) than in NON DPN (23.87%) subjects. p value was less than 0.005.

According to a study conducted by Solomon et al³⁷, the subjects without diabetic peripheral neuropathy had good glycemic control than in subjects with peripheral neuropathy.

BODY MASS INDEX

The average BMI of the study population was 24.2. out of 216 subjects 71 were obese. The average BMI of the subjects with DPN was 26.8%. The prevalence of obesity in the study subject was 33%. Among subjects with DPN 38 were obese (BMI ≥ 25). The prevalence of obesity in subjects with DPN (62.30%) was significantly higher than in subjects without DPN (p < 0.05).

In a similar study conducted by Christine Lee et al in PROMISE cohort, the average BMI of subjects with DPN was 30.7 and without DPN was 30.4 (P value > 0.05). A prospective study on the prevalence and association of Peripheral Neuropathy in Indian Diabetic patients by H.K Gill et al. did not find a statistical significant correlation between obesity and peripheral neuropathy.³⁸

WAIST CIRCUMFERENCE

The mean waist circumference of the study population was 82.58 cms. The mean waist circumference of the males was higher

than in females. The prevalence of patients with increased waist circumference was significantly higher in subjects with DPN than in patients without DPN (P value < 0.005).

CONCLUSION

1. Peripheral Neuropathy is equally common in both diabetic and prediabetic individuals.

2. It is more prevalent in elderly pre-diabetic individuals of age more than 70 years. Both males and females are equally affected; there is no sex predilection for the occurrence of peripheral neuropathy.

3. Hypertensive individuals are affected more than non hypertensives.

4. There is strong relationship between obesity and peripheral neuropathy in pre-diabetic individuals.

5. Prevalence of dyslipidemia is higher in pre-diabetic people with peripheral neuropathy.

6. People with pre-diabetics who have peripheral neuropathy have higher HbA1c values.

7. Smokers have higher prevalence of peripheral neuropathy among pre-diabetics.

Lastly since the prevalence of peripheral neuropathy is high even in pre-diabetic population, my study emphasizes the need for the early diagnosis of peripheral neuropathy in people who are at high risk for developing diabetes and to screen for the possible associated risk factors.

REFERENCES

1. Anjana, R.M., Pradeepa, R., Deepa M. et al. Prevalence of Diabetes and Prediabetes in urban and rural India. *Diabetologia* (2011).
2. Boulton AJ, Malik RA. Diabetic neuropathy. *Med Clin North Am.* 1998 Jul.
3. Young, M.J., Boulton, A.J.M., Macleod, A.F. et al. A multicentre study on the prevalence of Diabetic neuropathy *Diabetologia* (1993).
4. Dan Ziegler et al. "Prevalence of Polyneuropathy in Pre-Diabetes and Diabetes Is Associated With Abdominal Obesity and Macroangiopathy". KORA study group.
5. Papanas N1, Vinik AI, Ziegler D. "Neuropathy in prediabetes: does the clock start ticking early?". *Nat Rev Endocrinol.* 2011.
6. Lee CC, Perkins BA, Kayaniyl S, Harris SB, Retnakaran R, Gerstein HC, Zinman B, Hanley AJ. "Peripheral Neuropathy and Nerve Dysfunction in Individuals at High Risk for Type 2 Diabetes: The PROMISE Cohort".
7. Meena A Kannan, Sailaja Sarva, Rukmini Mridula Kandadai et al. "Prevalence of neuropathy in patients with impaired glucose tolerance using various electrophysiological tests." *Diabetes Care.* 2015 May
8. Prasad Katulanda et al. "the prevalence, patterns and predictors of diabetic peripheral neuropathy in a developing country". *DMS journal* 2012.
9. Fargol Booya et al. "Potential risk factors for diabetic neuropathy: a case control study". *Biomedcentral* 2005.
10. Dipika Bansal et al. "Prevalence and risk factors of development of peripheral diabetic neuropathy in type 2 diabetes in a tertiary care setting." *Journal of Diabetic Investigation* 2014
11. Solomon et al. "The association between Body Mass Index and Diabetic Peripheral Neuropathy." *Hungarian Medical Journal* march 2008.
12. H.K Gill, SB Yadav et al. "A prospective study of prevalence and association of peripheral neuropathy in Indian patients with newly diagnosed type 2 diabetes mellitus.