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Original Research

Study Of Demographic Characteristics, Risk Factors, And Clinical Profile Of Diabetic Neuropathy In Patients Attending Government Medical College, GGH, Srikakulam

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Abstract

Background: Diabetes mellitus is a metabolic disorder of multiple aetiology, characterised by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.

Objectives: To evaluate the status of distal symmetrical polyneuropathy and painful neuropathy using MNSI scoring system and DN4 questionnaire respectively and cardiac autonomic neuropathy using Bellavere's scoring system in patients of this geographical area.

Materials and Methods: This cross sectional study was conducted among admitted patients presenting to Department of Medicine, Government medical College, GGH, Srikakulam.

Results: Most of the subjects belonged to 6-10 years duration. Based on BMI 13 were underweight,60 were normal, 32 were overweight, 61 were Obese I, 4 were Obese II. 57.05 % of the subjects had abnormal BMI. 36 subjects had normal waist hip ratio. Based on HbA1c levels, most subjects (112) were in range between 6.5-9. Gender vs Neuropathy assessment showed, 16 males and 46 females had neuropathy with P value 0.106, which is statistically not significant, other studies showed neuropathy is more common in males. Age of subject (yrs.) vs neuropathy (P value 0.52) showed non significance,. In my study most of the subjects were diagnosed incidentally and the duration of diabetes based on history may not be the exact duration from which the study subjects were actually suffering from diabetes, hence the duration of diabetes vs neuropathy (p value 0.452) showed no significance. Comparison of Neuropathy vs BMI (p value 0.576) had no statistical significance. Waist hip ratio vs Neuropathy (p value 0.406) also was not significant. Neuropathy was more with subjects with higher values of Fasting blood glucose (Pvalue0.002) which is statistically significant.

Conclusion: Neuropathy was more in subjects with higher of HbA1c. (p value 0.001) which is statistically significant

Keywords : Diabetes, Diabetic Neuropathy, HbA1c.

INTRODUCTION

The long-term effects of diabetes include damage, dysfunction, and failure of various organs. The long-term effects include progressive development of retinopathy with potential blindness,

nephropathy that may lead to renal failure, neuropathy with risk of foot ulcers, amputation, Charcot joints, and features of autonomic dysfunction, including sexual dysfunction. People with diabetes are at increased risk of cardiovascular, peripheral vascular, and cerebrovascular diseases.[1]
Diabetes mellitus (DM) directly and indirectly affects on human vascular tree and these constitute major source of morbidity and mortality in both type 1 and type 2 diabetes. Generally, injurious effects of hyperglycaemia are divided into: (a) macrovascular complications, viz. coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular stroke; and (b) microvascular complications, viz. diabetic nephropathy, neuropathy, and retinopathy Chronic microvascular complications of diabetes mellitus are retinopathy, sensory motor, and autonomic neuropathy and nephropathy. Three-fourth of diabetics develops retinopathy after more than 15 years of diabetes, half of the diabetics have neuropathy, and one-third have nephropathy. Risk of chronic complications in type-1 and type- 2 diabetes result from chronic hyperglycaemia. Large randomised clinical trials of individuals with type-1 or type-2 diabetes have conclusively demonstrated that a reduction in chronic hyper- glycaemia prevents or delays retinopathy, neuropathy, and nephropathy. Diabetic neuropathy occurs in~50% of individuals with long-standing type1 and type 2 DM. It may manifest as polyneuropathy, mononeuropathy, and/or autonomic neuropathy. As with other complications of DM, the development of neuropathy correlates with the duration of diabetes and glycaemic control. Additional risk factors are body mass index (BMI) (the greater the BMI, the greater the risk of neuropathy) and smoking. The presence of CVD, elevated triglycerides, and hypertension is also associated with diabetic peripheral neuropathy. Both myelinated and unmyelinated nerve fibres are lost. Because the clinical features of diabetic neuropathy are similar to those of other neuropathies, the diagnosis of diabetic neuropathy should be made only after other possible aetiologies are excluded [2]

MATERIAL AND METHODS

This cross sectional study was conducted among admitted patients presenting to Department of Medicine, Government medical College, GGH, Srikakulam.

Data was collected from diabetic patients. Ethical approval was obtained from the Institutional Review Board of the Hospital Authority.

DURATION OF STUDY-

This study was conducted July 2022 to July 2023.

STUDY POPULATION-

Diabetic patients with age > 18 years with following inclusion and exclusion criteria.

Inclusion criteria

1. Those patients who give valid informed written consent.
2. Patients with Hba1c >6.5.
3. Diagnosed patients of diabetes.
4. Age more than 18years.

Exclusion criteria

1) Neuropathy attributed to causes other than diabetes.
2) Those with limb deformities or loss of limbs.
3) Patients on drugs like beta blockers, tricyclic antidepressants, alpha blockers, ergot alkaloids, parasympathomimetic, anticholinergics, anti-cholinesterase, which interfere with ANS.
4) Patients with obvious intellectual disability.

Sample size Calculation:
The prevalence of diabetic neuropathy in India was observed to be 19.1% (50) The sample size is calculated using the following formula-
$n=Z^2_1 - \alpha PQ/L^2$ where $Z^2_1 - \alpha = 1.96$ Where n is req. Sample size
p = Expected prevalence (0.191) based on previous study from south India. q = 1-p (0.809)
L = Precision = 0.06 Calculated sample size – 168.

Methods of measurement of outcome of interest:
1) The subjects fulfilling inclusion and exclusion criteria were enrolled into the study after obtaining in formed consent.
2) The study subjects were evaluated as below-

DPN (Diabetic Peripheral Neuropathy) will be assessed using the Michigan Neuropathy Screening Instrument (MNSI) which is a validated, 2-component tool designed to facilitate the early diagnosis of DPN. The questionnaire component (MNSIq) comprises 15 questions seeking to characterize sensory disturbance but also peripheral vascular disease and general asthenia. The examination component (MNSIe) comprises a limited foot inspection to identify deformity, skin abnormalities, and ulceration, coupled with an assessment of the vibratory perception and ankle tendon reflexes. For the purpose of this study, DPN is diagnosed if the MNSIe score is >2 and/or MNSIq is ≥7.[(3)(4)]
Painful neuropathy was assessed using DN4 questionnaire. It is a clinician-administered questionnaire consisting of 10 items. Seven items related to pain quality (i.e. sensory and pain descriptors) are based on an interview with the patient and 3 items based on the clinical examination. The DN4 (which stands for Douleur Neuropathique 4) is one of the questionnaires that can be useful in diagnosing neuropathic pain. The total score is calculated as the sum of the 10 items and the cut-off value for the diagnosis of neuropathic pain is a total score of 4/10. [(5)(6)]

The cardiac autonomic neuropathy (CAN) was assessed using a battery of five cardiovascular autonomic reflex tests of Bellavere's score
Heart rate variability in response to deep breathing: The patient is connected to the Electrocardiography (ECG) monitor, lies quietly and breathes deeply at a rate of six breaths per minute, 15 beats per minute difference or more is normal and 10 beats/min or less abnormal.
Heart rate variability in response to standing: The patient is connected to ECG monitor while lying down and then stands to a full upright position. ECG tracings are used to determine the 30:15 ratios, calculated as the ratio of the longest R-R interval during beats 20-40 to the shortest R-R interval during beats 5-25
Heart rate response to Valsalva manoeuvre: The supine patient, connected to an ECG monitor/or clinically, forcibly exhales for 15 seconds against a fixed resistance with an open glottis. The Valsalva ratio is determined from the ECG tracings.
Postural hypotension: Defined as a fall in systolic BP of ≥20 mmHg or diastolic BP of ≥10 mmHg accompanied by symptoms.
BP response to sustained hand grip exercise: The patients is asked to squeeze the handgrip dynamometer to isomeric maximum, and then held at 30% maximum for 5 min. A rise in DBP of ≤16 mmHg in the contralateral arm is considered abnormal. [(29)(27)]
0-1 No autonomic neuropathy 2-4 Early autonomic neuropathy 5-10 Severe autonomic neuropath

RESULTS:

In our study a total of 170 patients were enrolled, demographic distribution as describes below.
age wise distribution of diabetic patients presented to our hospital. 16 were below 40years, 76 were between 41 to 55 and 78 were more than 56 years.
gender wise distribution of diabetic patients presented to our hospital. Males were 57, females were

113. 122 subjects belonged to urban, 48 belonged to rural.
18 subjects (0-5 years), 123 subjects (6-10 years), 24 subjects (11-15 years), 4 subjects (16-20 years), 0 subjects from (21-25 years), 1 subject (26-30 years).

Distribution subjects based on BMI, 13 were under weight, 60 were normal, 32 were overweight, 61 were Obese I, 4 were Obese II. This classification based on WHO obesity classifications for Asians.[7]
waist hip ratio distribution among subjects, waist hip ratio of < 0.85 for women and < 0.9 for men was considered normal [8]. 36(21.18%) subjects were in normal range and 134(78.82%) were abnormal.
Out of 170 subjects, 14(8.24%) subjects have nephropathy, based on Revised criteria for the early diagnosis of diabetic nephropathy.[9]
the subjects based on HbA1c levels. 112 (65.88%) subjects were in the range of 6.5-9, 32 (18.82%) subjects were in the range of 9-12, 26 (15.29%) subjects were with HbA1c levels > 12.
31(22.9%) out of 170 subjects were suffering from diabetic peripheral neuropathy. Based on

MICHIGAN NEUROPATHY SCREENING INSTRUMENT (MNSI) [10]

33 subjects had autonomic neuropathy of which 29 had early autonomic neuropathy and 4 individuals were suffering from severe autonomic neuropathy based on Bellavere's scoring system.[11]
42 (24.71%) subjects had painful neuropathy out of 170 subjects. Based on DN4 questionnaire.[5]
62 subjects are had either one type of neuropathy based on Michigan Neuropathy Screening Instrument (MNSI) [3], Bellavere's scoring system.[11], DN4 questionnaire.[5].
DPN (diabetic peripheral neuropathy) in males vs females, 10 out of 57 males, 29 out of 113 females have DPN, With p value according to chi-square test is 0.537 which is statistically not significant.

CAN (Cardiac Autonomic Neuropathy) in males vs females, 8 out of 57 males, 21 out of 113 females have early autonomic neuropathy, 2 males and 2 females have severe autonomic neuropathy with p value 0.612(chi-square test) which is statistically not significant.
Painful neuropathy in male vs female, 13 males and 29 females have painful neuropathy with p value 0.683(chi-square test) which is statistically not significant.

sex vs any Neuropathy (DPN + CAN + Painfull neuropathy), 16 males and 46 females had neuropathy with P value 0.106, which is statistically not significant.
age(yrs.) vs neuropathy. With p value 0.52 (chi-square test) which is statistically not significant.

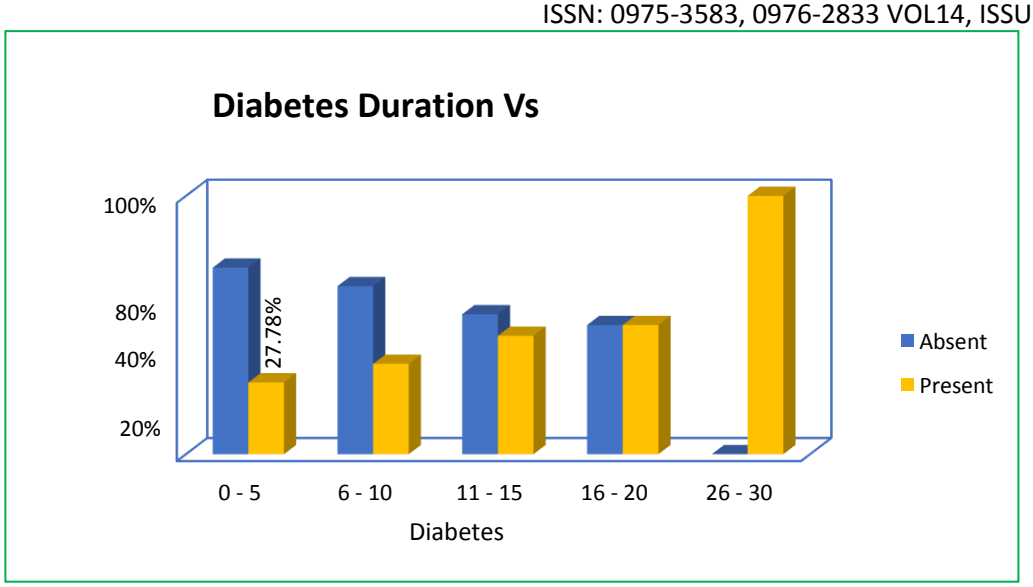

Figure 1 *Diabetes Duration Vs Neuropathy (DPN + CAN + Painful neuropathy)*

Duration of diabetes vs neuropathy, with p value 0.452(chi- square-test), which is statistically not significant.

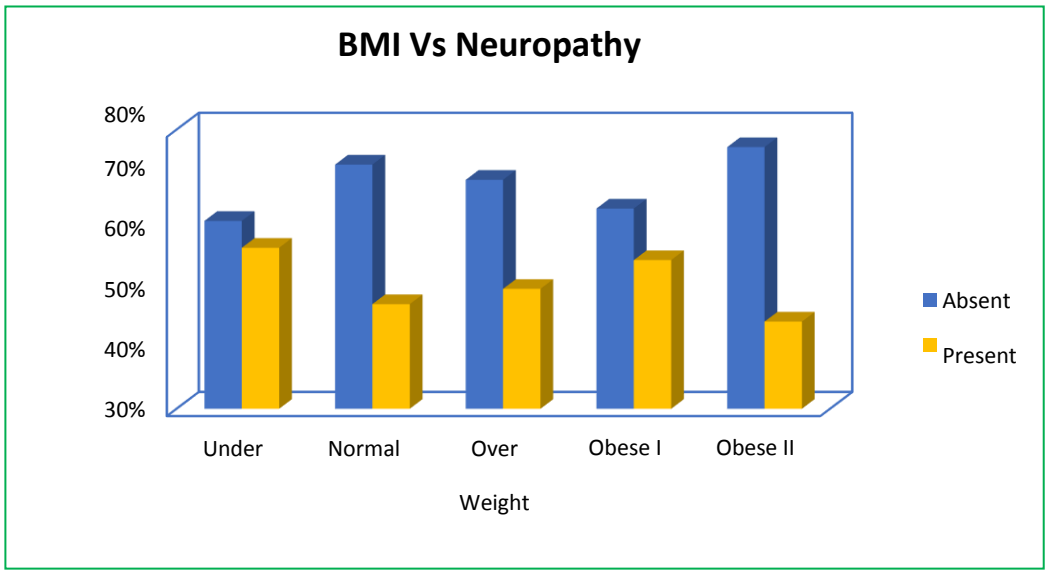

Figure 2 *Diabetes duration Vs Neuropathy (DPN + CAN + Painful neuropathy)*

Diabetes duration vs neuropathy with BMI with p value 0.576 which is statistically not significant

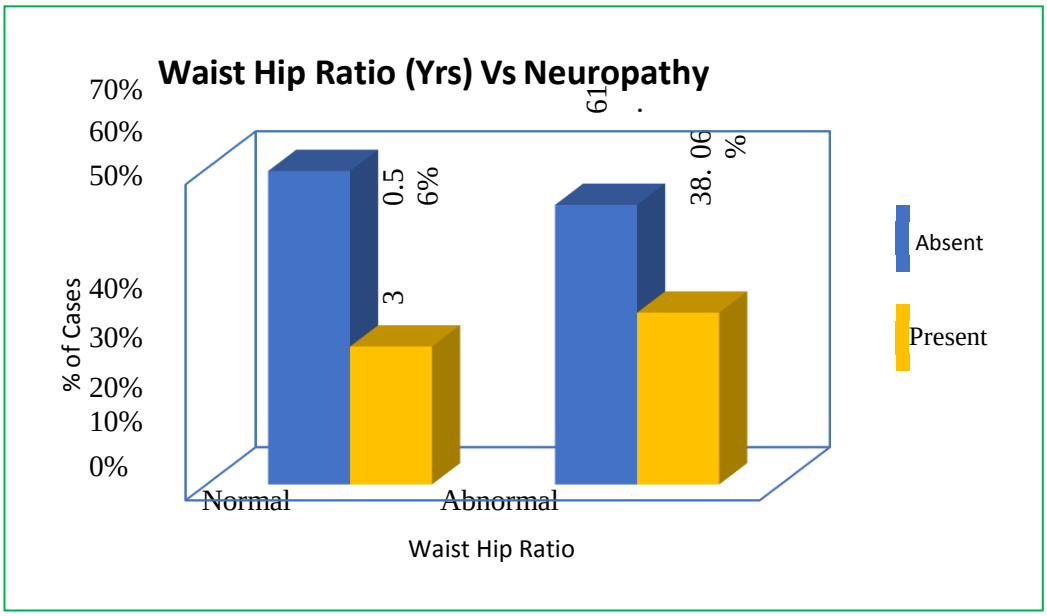

Figure 3 *Waist hip ratio Vs Neuropathy (DPN + CAN + Painful neuropathy)*

waist hip ratio vs Neuropathy (DPN + CAN + Painful neuropathy) with p value 0.406 which is statistically not significant.

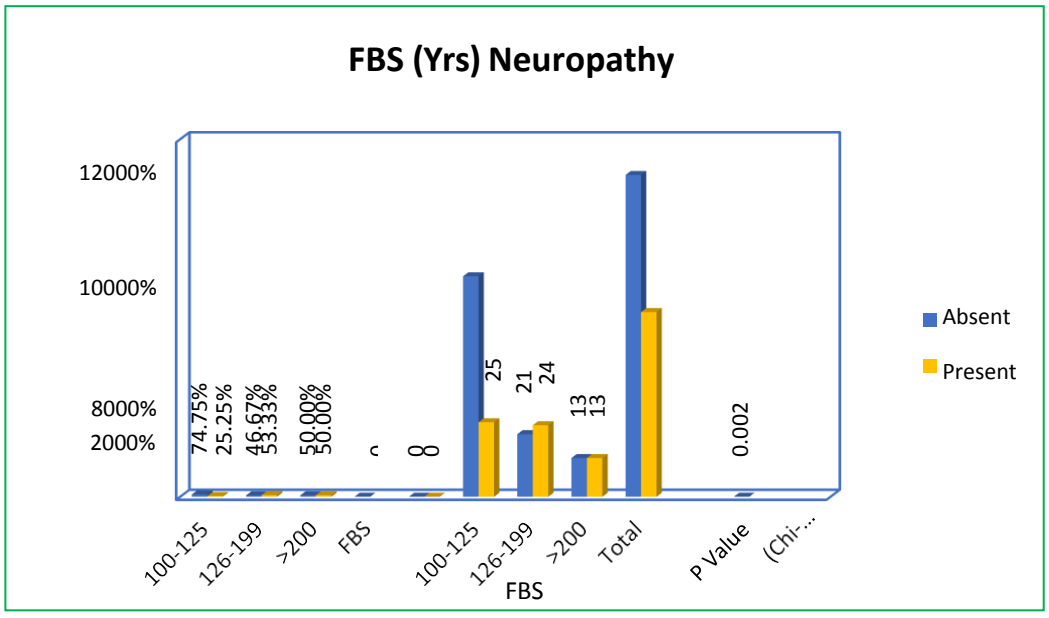

Figure 4 *FBS (fasting blood sugar) Vs Neuropathy (DPN + CAN + Painful neuropathy)*

FBS (fasting blood sugar) Vs Neuropathy (DPN + CAN + Painful neuropathy) in which neuropathy is more with subjects with higher values of Fasting blood glucose values with p value 0.002 (chi-square test) which is statistically significant.

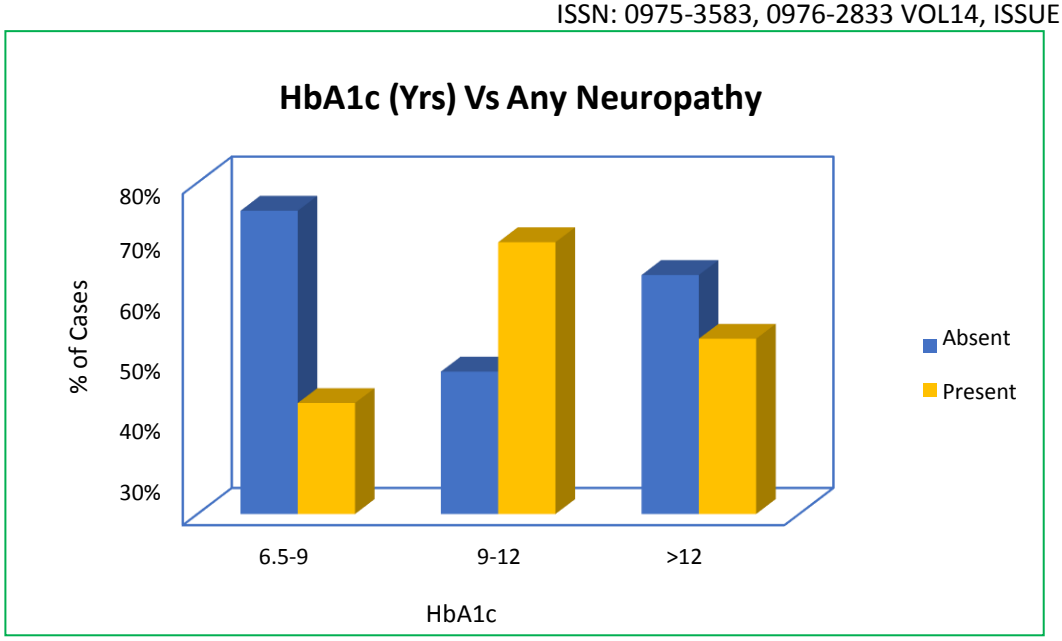

Figure 5 *HbA1c Vs Neuropathy (DPN + CAN + Painful neuropathy).*

HbA1c vs Neuropathy, Neuropathy is more with subjects with higher values of HbA1c. with p value 0.001 which is statistically significant.

DISCUSSION:

16 (9.4%) were below 40years, 76 (44.7%) were between 41 to 55 and 78(45.9) were more than 56 years. Similar distribution observed in publication of *Sarah Wild et al (2004) in Edinburgh* [(12)]

18 (10.6%) subjects had diabetes for 0-5 years, 123(72.4%) subjects had diabetes for 6-10 years, 24(14.1%)subjects for11-15years,4(2.4%) subjects(16-20years),0 subjects from21- 25 years, 1 subject for 26-30 years. Most of the subjects were belongs to 6-10 years duration.
13(7.6%) were underweight, 60(35.3%) were normal,32(18.8%) were overweight,61(35.9%) were Obese I, 4(2.4%) were Obese II. This classification based on who obesity classifications for Asians.(53)' 57.05 % of the subjects have abnormal BMI. Similar study conducted by *H E Resnick et al (1971-1992)* (57) in USA showed similar results.
Waist hip ratio of < 0.85 for women and < 0.9 for men was considered normal [(8).] In which 36 (21.2%) subjects were in normal range and 134(78.4%) were abnormal, similar findings were observed in a study conducted by *Maria Inés Schmidt et al (1992) in Brazil.*[(13)]
112(65.9%) subjects were in the range of 6.5-9, 32(18.8%) subjects were in the range of 9-12, 26(15.3%) subjects were with HbA1c levels > 12. More subjects were distributed in the range between 6.5-9.
Sex vs any Neuropathy (DPN + CAN + Painfull neuropathy), 16 males and 46 females have neuropathy with P value 0.106, which is statistically not significant. Study conducted by *Aaberg ML et al (2007*) Cleveland, demonstrates that the males in the study population developed neuropathy earlier than did the females [(14)]
Age(yrs.) vs neuropathy. With P value 0.52 (chi-square test) which is **statistically not significant**. In a study conducted by patients *Simona Popescu et al (2016)* Timisoara showed the severity of DN was significantly and positively correlated with age and with the HbA1c value. No significant correlations were observed between the severity of DN and diabetes duration, BMI, or the number of centimetres exceeding the normal waist circumference. Age influenced the presence of DN, independent of other risk factors.[(15)]
Duration of diabetes vs neuropathy, with P value 0.452(chi- square-test), which is **statistically not significant**. *Muhammad Umer Nisar et al (2015)* Rawalpindi, Pakistan showed significant

association with duration of diabetes.[16] in my study most of the subjects were diagnosed incidentally and the duration of diabetes based on history may not be the exact duration from which the study subjects were actually suffering from diabetes.

BMI vs neuropathy with P value 0.576 **which is statistically not significant**. A similar study by *Tae Jung Oh et al (2019)* Korea showed BMI was higher in subjects with DPN than in subjects without DPN (26.5±4.3 kg/m^2 vs. 24.1±3.2 kg/m^2, P=0.011). SBP tended to be higher in the DPN(+).[17]

waist hip ratio vs Neuropathy (DPN + CAN + Painful neuropathy) with P value 0.406 which is **statistically not significant**. Similar study conducted by *Schmidt MI et al (1992)* North Carolina showed Central obesity, as measured by the WHR, is importantly and independently associated with NIDDM [13].

FBS (fasting blood sugar) Vs Neuropathy (DPN + CAN + Painful neuropathy) in which neuropathy is more with subjects with higher values of Fasting blood glucose values with P value 0.002 (chi-square test) which is **statistically significant**. A study conducted by *Tabatabaei Malazy et al (2011)* in Tehran/Iran showed similar results.[18]

HbA1c vs Neuropathy, Neuropathy is more with subjects with higher values of HbA1c. with P value 0.001 which is **statistically significant**. Study conducted by *Jian-bin Su et al (2018)* in Nantong showed similar results.[19]

CONCLUSION:

Neuropathy was more in subjects with higher of HbA1c. (p value 0.001) which is statistically significant. Neuropathy was observed more among taller subjects (p value 0.133), but it is statistically not significant. In the study it was observed that high fasting sugar levels, high HbA1c are independent risk factors for diabetic neuropathy.

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