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Original Research Article

Study of Association between Body Fat & Diabetic Neuropathy in Middle Aged Adults with Type-2 Diabetes Mellitus at SMS Medical College & Attached Hospital Jaipur (Rajasthan)

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Abstract

Background: Diabetes and its complications have a significant impact not only on the individuals' economy but also on their quality of life. Diabetic neuropathy is the most common neuropathy and is associated with a wide range of clinical manifestations. Obesity and increased body fat causes insulin resistance which promotes low-grade inflammation. This inflammation influences endothelial dysfunction and micro-vascular complications. This study evaluated the association of glycemic control and body fat with diabetic peripheral neuropathy in Type 2 Dm patients.

Materials & Methods: After taking necessary permissions, a cross sectional study was conducted at Department of Biochemistry and Department of Endocrinology, SMS Hospital, Jaipur. This study includes 50 Type 2 DM cases having Diabetic neuropathy (DN) aged 20-55 years compared with 50 Type 2 DM cases without Diabetic neuropathy. Samples were analyzed for the measurement of serum glucose by Colorimetric method, body fat mass by bioimpedance analysis and HbA1C measured by latex turbidimetric method.

Results: Results were analyzed statistically by Student's t-test and Pearson correlation coefficient test. mean Body Fat levels for DN Positive cases was 27.60 ± 5.00 % and that for DN Negative Cases was 24.47 ± 2.72 %. Body fat levels were significantly high in DN positive patients. There was statistically highly significant positive correlation between Body fat levels with Fasting blood sugar and HbA1c in diabetic patients.

Conclusion: Obese patients have a higher prevalence of neuropathy in type 2 diabetes cases. The neuropathy in this population is associated with lower quality of life and higher pain scores, indicating that the neuropathy is clinically important. Current clinical practices should concentrate on the management of obesity in cases of diabetes in with neuropathy. Early preventive strategies like life style changes (e.g. healthy diet, regular exercise, maintaining ideal body weight, absolute avoidance of smoking, alcohol) should be adopted.

Keywords: Diabetes Mellitus (DM), Glycated Haemoglobin (HbA1c), Diabetic Neuropathy (DN).

Introduction

In recent years, with change in diet and lifestyle, type 2 diabetes mellitus (T2DM) has gradually become a major public health problem worldwide and one of the main causes of blindness, amputation, heart disease, renal failure, and premature death. Diabetes is one of the non-communicable diseases, the prevalence of which is increasing world-wide.

As per World Health Organization (WHO) global report, the number of adults living with diabetes is 422 million. The International Diabetes Federation estimated the global diabetes prevalence among adults in the age range 18-99 in 2017 to be 451 million, with a projected increase to 693 million in 2045. [1] The prevalence of diabetes in South-East Asian Region (SEAR) is 96 million. [2] With a national DM prevalence of 8.6% and 668,468,800 number of people with DM, India stands second to China in relation to the burden of DM. The burden of diabetes mellitus (DM) is on the rise especially in developing countries like India. [1]

As a result of prolonged hyperglycaemic state along with degenerative changes secondary to ageing, there are injurious effects to the tissues leading to micro vascular and macro vascular complications. The macro-vascular complications include coronary artery disease, peripheral arterial disease and stroke. The micro vascular complications include retinopathy, diabetic nephropathy and peripheral neuropathy. [3] Due to its chronic nature DM tends to cause many debilitating complications and diabetic peripheral neuropathy (DPN) is one of them.

Diabetic neuropathies are a group of nerve disorders caused by persistent high blood sugar levels. As a consequence of damage to the nerves the patients develop the inability to perceive important sensations like heat, cold and pain in extremities. As a result of lack of these sensations the patient may not be aware of a sore or an ulcer in the foot. Long-duration diabetes, old age, hyperglycemia, hypertension, dyslipidemia, obesity, alcohol, smoking, and insulin resistance are known risk factors for DPN. [4, 5]

The correlation between obesity and type 2 diabetes mellitus (T2DM) has been constantly proven and reproducibly observed in a wide range of studies across different populations. [6, 7] The World Health Organization (WHO) has defined obesity as a BMI $\geq$ 30 kg/m^2, an epidemic and a disease within itself, which is chronic and progressive in nature with the potential for relapse. [8] The Anglo-Danish-Dutch study of Intensive Treatment of Diabetes in Primary Care (ADDITION) study [9] and Cooperative Health Research in the Region of Augsburg (KORA) study [10] consistently demonstrated that general and central obesity increased the risk of DPN.

In the current study, we aimed to determine risk factors for the development of incident DPN present at the diagnosis of screen-detected type 2 diabetes, with a particular focus placed on components of metabolic syndrome mainly Central Obesity. This study investigated the association between body composition, components of metabolic syndrome, and DPN in middle-aged adults with type 2 diabetes mellitus (T2DM).

Materials and Methods

After taking Necessary permission from the institute ethical committee, Research review Board and Department of endocrinology, the study was conducted at Central Lab, Department of Biochemistry and endocrinology OPD SMS Medical College and hospital, Jaipur. This study was a hospital based comparative Cross sectional study and sampling for the study was done from period of March 2021 to

December 2021. An informed written consent was obtained from the cases and controls. 50 type 2 diabetes patients having Diabetic Neuropathy aged 20-55 years were taken as cases. Age Matched non obese Type 2 DM patients without Diabetic Neuropathy willing to participate in the study giving written consent were taken as controls.

Patients with the following condition: Patients without Diabetes and those with other causes of neuropathy such as heavy alcohol consumption, renal dysfunction (estimated glomerular filtration rate less than 50ml/min/1.73m^2), any history of cancer & exposure to neurotoxic agents were excluded.

Selection of subject was based on inclusion and exclusion criteria; matched controls and cases were included in the present study after obtaining informed consent. A proforma was used to record relevant information and patient's data. 5 mL of venous blood was collected in plain vacutainer, serum glucose was analyzed by Colorimetric method, and 2 mL into EDTA containing vacutainer for Hba1c Assay by turbidimetry. Body fat mass was measured by bioimpedance analysis. Quantitative data analyzed in the form of mean with standard deviation, as & when required suitable test of significance used to infer data. Levels of statistical significance set at a P value<0.05.

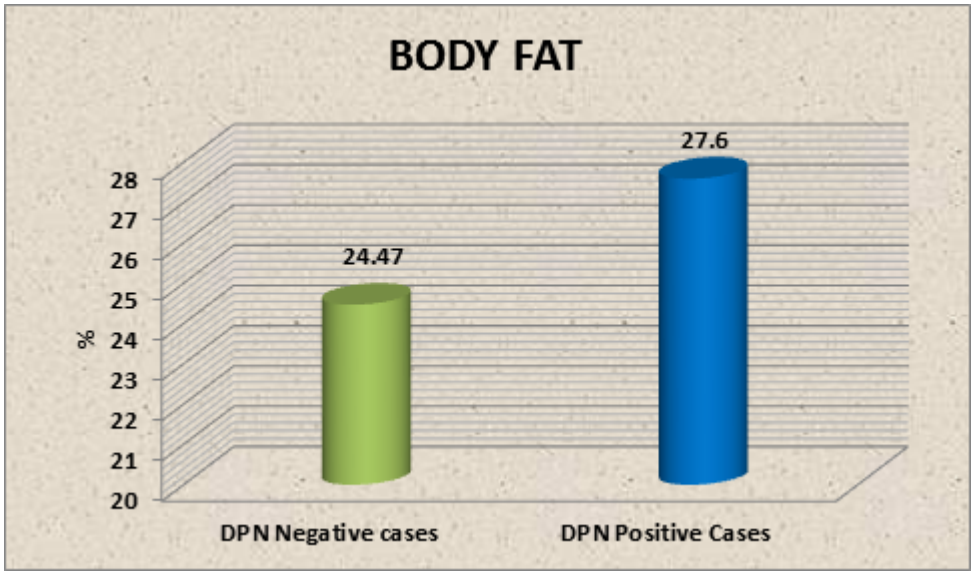
Results

The characteristics of the studied population, including age, the mean levels of blood sugar and HBA1c are shown in Table 1.

Table 1: Statistical Indices of the study

Test/ Parameters	DPN Negative Cases (Group 1) (n=50)	DPN Positive Cases (Group 2) (n=50)	P value
Age (years)	44.12 ± 5.40	45.42 ± 5.53	0.136 (NS)
Fasting Blood Glucose (mg/dl)	152.52 ± 18.77	171.38 ± 19.41	< 0.01 (S)
PP Sugar (mg/dl)	209.20 ± 18.36	235.90 ± 29.00	< 0.01 (S)
HBA1c (%)	7.24 ± 0.37	7.81 ± 0.69	< 0.01 (S)
Body Fat (%)	24.47 ± 2.72	27.60 ± 5.00	< 0.01 (S)
Insulin (IU/L)	7.40 ± 2.15	11.31 ± 1.83	< 0.01 (S)

Body Fat (%): The mean Body Fat levels for DPN Positive cases was 27.60 ± 5.00 % and that for DPN Negative Cases was 24.47 ± 2.72 %. The value was statistically significant (p value <0.01) as shown in Table 1 and Graph 1.



Graph 1: Comparison of Mean Body fat levels between DPN Negative Cases (Group 1) and DPN Positive Cases (Group 2)

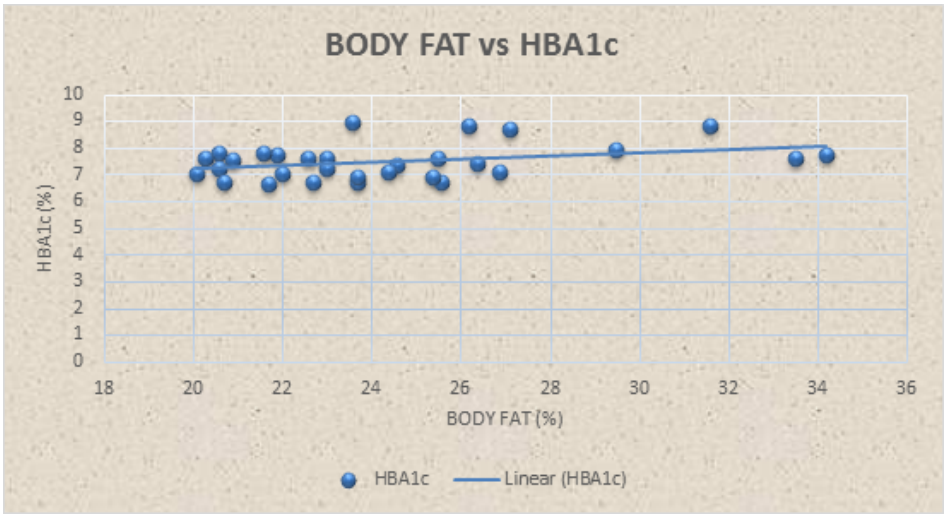
- **Statistical Correlations of Body Fat levels with FBS, HbA1c and Insulin:**

Table 2: Statistical Correlations of Body Fat levels with FBS, HbA1c and Insulin

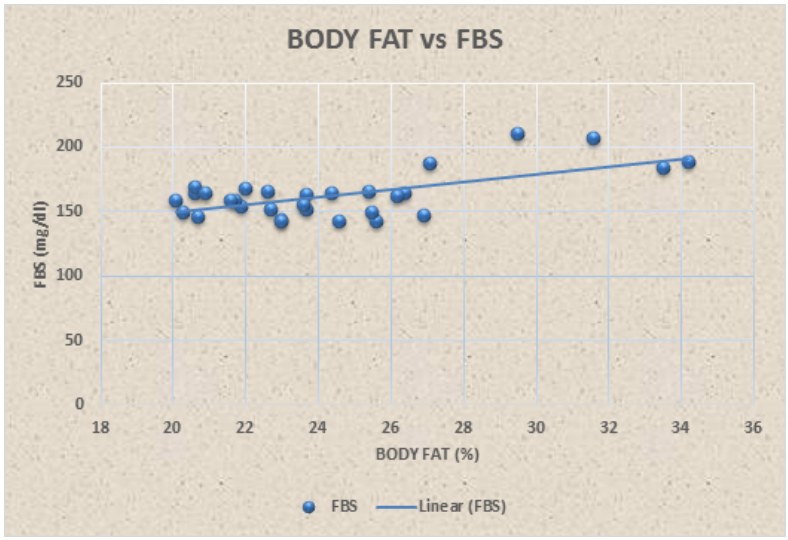
Parameter	P value	R Score	R^2	Significance
Body fat vs HBA1C	<0.001	0.6086	0.3704	S
Body fat vs FBS	<0.001	0.6909	0.4773	S
Body fat vs Insulin	<0.001	0.597	0.3564	S

*Data analysis using Pearson correlation analysis

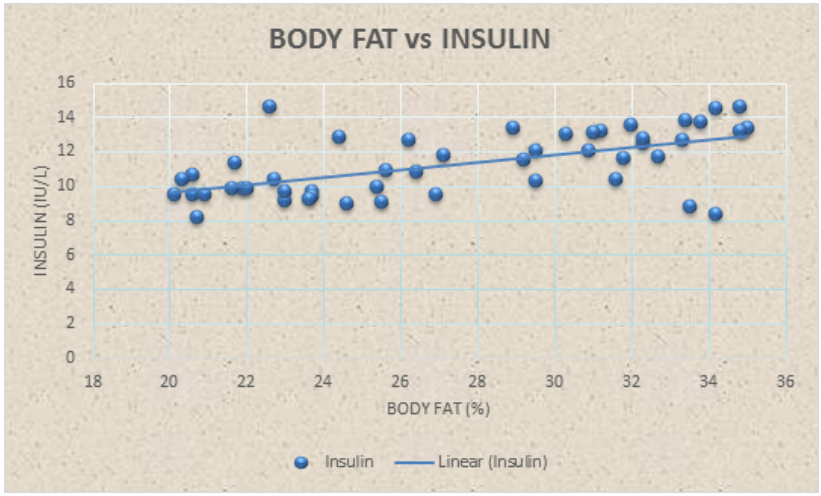
Above table shows statistically significant Positive correlation between Body Fat and HBA1c (r = 0.6086) (Graph 2). It also shows correlation between Body Fat and FBS which is positive (r score = 0.6909) and statistically significant (p value <0.001) (Graph 3) and also a positive correlation between Body Fat and Insulin (r score = 0.597). (Graph 4)



Graph 2: Pearson correlation between Body Fat & HBA1c in DPN Positive Patients



Graph 3: Pearson correlation between Body Fat & FBS in DPN Positive Patients



Graph 4: Pearson Correlation between Body Fat & Insulin in DPN Positive Patients

Discussion

Diabetes and its complications have a significant impact not only on the individuals' economy but also on their quality of life. As the disease progresses, it can involve multiple organs, and the complications can be broadly divided into macrovascular and microvascular. One of the microvascular complications is diabetic peripheral neuropathy. Proper management of diabetes and screening of complications will have a potential impact on the quality of life of these patients.

Diabetic neuropathy is the most common neuropathy and is associated with a wide range of clinical manifestations. The pathogenesis of sensorimotor neuropathy in diabetes mellitus type 2 is multifactorial and related metabolic disturbances, such as hyperglycemia, dyslipidemia, oxidative and nitrosative stress, and growth factor deficiency all contribute to the development of this complication.

In our study, the mean age in DPN Negative case group 44.12 ± 5.40 years was slightly lower than DPN Positive cases (45.42 ± 5.53 years). This difference was statistically non-significant (p value =0.136). Our study showed non-significant relation between age group of cases with and without Diabetic neuropathy. However, A study by Vibha et al. [11] in Udupi in 2015 had shown significant association with advancing age, low socioeconomic status, sedentary physical

activity, longer duration of DM and DPN. Similarly, A study by Begum et al. [12] done at Puducherry in 2017 had shown significant association with advancing age, smoking and longer duration of the disease and DPN. The three main alterations that are involved in the pathogenesis of DPN are inflammation, oxidative stress and mitochondrial dysfunction. [13] All these three alterations are related to the process of ageing. [14]

The mean Body Fat levels for DPN Positive cases was 27.60 ± 5.00 % and that for DPN Negative Cases was 24.47 ± 2.72 % (Table 1 and Graph 1). The mean Insulin levels for DPN Positive cases 11.31 ± 1.83 IU/L and that for DPN Negative Cases was 7.40 ± 2.15 IU/L. The value was statistically significant (p value <0.01). Statistically significant Positive correlation is also seen between Body Fat and FBS, HbA1c and Insulin.

As per our study, poor glycemic control and higher insulin resistance was seen in the Cases developing diabetic neuropathy. The United Kingdom Prospective Diabetes Study (UKPDS) showed that the intense glucose control group had a 25% reduction in the risk of microvascular complications endpoints. Furthermore, UKPDS showed that keeping HbA1c at a mean of 7% over 10 years significantly reduced the risk of microvascular complications. [15] These studies also recommend a target HbA1c as close to normal as possible, which provides improved outcomes. [16]

Similar to the present study, a study by Battula et al. [17] in 2017 at Kurnool had shown a significant association between obesity and DPN. Obesity causes insulin resistance which promotes low-grade inflammation. This inflammation influences endothelial dysfunction and micro-vascular complications. [5] The same patho-physiology holds for a sedentary life-style which increases the likelihood of obesity.

Central obesity has been the most important risk factor for DPN in subjects with diabetes. Numerous studies have demonstrated that obesity, especially visceral adiposity, plays an important role in the onset and development of DPN. [18, 19] Visceral adiposity, commonly assessed by WC, could contribute to IR, hyperglycaemia, dyslipidemia, hypertension, chronic inflammation and oxidative stress, [20, 21] and has been reported to be associated with damaged nerve conduction velocity and higher DPN risk. [22]

Oh et al showed that VFA level was higher in middle-aged T2DM patients with DPN than those without DPN, and VFA level was associated with a 2.6% increase in likelihood of DPN.5 On the contrary, another study of 90 Japanese patients with T2DM conducted by Tayama et al demonstrated that levels of preperitoneal fat determined by ultrasonography, an indicator of visceral fat deposition, were positively correlated with motor or sensory nerve conduction velocity. [23]

It has been well established that visceral adipose tissue can overproduce several bioactive pro-inflammatory cytokines and adipocytokines that lead to IR, metabolic disorders, chronic inflammation, oxidative stress, endothelial dysfunction, and atherosclerotic vascular damage, subsequently resulting in nerve ischemia and direct axonal injury. [24] Body fat, measured by the bioelectrical impedance analysis (BIA), has been recognized as a noninvasive, relatively accurate, and low-cost method of quantifying visceral adipose tissue. [25,26]

Conclusion

The present study was designed to determine the relationship between the relationship between glycemic variability focusing on Body fat and diabetic peripheral neuropathy in type 2 diabetes. Type 2 DM cases with Neuropathy were associated with significantly higher body

fat percentage. Obese patients have a higher prevalence of neuropathy in type 2 diabetes cases. The neuropathy in this population is associated with lower quality of life and higher pain scores, indicating that the neuropathy is clinically important. Current clinical practice concentrates on the management of diabetes in those with neuropathy. Obesity and dyslipidemia can be modified either by proper life style changes or medical management or by the combination of the both. This study suggests that type 2 DM patients with Diabetic neuropathy need measurement of glycemic control measures at regular interval to prevent further complications.

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