ORIGINAL RESEARCH PAPER

Biochemistry

THE ASSOCIATION BETWEEN DIABETIC NEUROPATHY AND OSTEOPOROSIS IN PATIENTS WITH TYPE-2 DIABETES

KEY WORDS: Diabetes mellitus, diabetic neuropathy, osteocalcin, osteoporosis.

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ABSTRACT

Objective- The objective of this study was to evaluate the association between osteoporosis and diabetic peripheral neuropathy in patients with type-2 diabetes mellitus (T2DM). **Background-** Diabetic complications and osteoporotic fractures are two of the most important causes of morbidity and mortality in older patients. There is increased fracture rate associated with T2DM, despite these patients having greater bone mineral density. Osteocalcin, one of the bone turn over markers, is a peptide secreted by bone cells and reflect bone formation and consequently indicates bone remodeling status; which is the major mechanism underlying osteoporosis. **Material and methods-** This observational case- control analytical study was done on 60 patients with T2DM. They were classified into two groups. Group A (Neuropathy group) included 30 patients with diabetic neuropathy. Group B (control group) included 30 patients without diabetic neuropathy. Dual-energy X-ray absorptiometry (DEXA) and serum osteocalcin measurement were done for both the studied groups. **Results-** There was no significant difference between the two studied groups in the DEXA scan results; The mean T- score of spine, hip, forearm of the neuropathy group was -0.96, -0.26, 0.98 of the neuropathy group and that of the control group was 1.17(p= 0.421), -0.83 (p=0.072), 0.33 (p=0.107). The mean osteocalcin level of the neuropathy group was 17.88, where as that of the control group was 13.32, showing significant difference the two groups(p= < 0.000). **Conclusion-** Osteoporosis is more prevalent in T2DM with microvascular complications and serum osteocalcin level is better in it's diagnosis than DEXA scan.

INTRODUCTION

As is commonly known, Diabetes Mellitus can impair the function and condition of multiple viscera and systems in the human body[1-6], contributing to a variety of diseases such as coronary artery disease, peripheral vascular disease, and neuropathy[7]. Bone quality could be affected by low bone turnover in T1DM and T2DM; In Type 2 Diabetes Mellitus, bone microarchitecture is compromised through inducing abnormal bone cell function and matrix structure, with increased osteoblast apoptosis, diminishment in its differentiation, and enhanced osteoclast-mediated bone resorption[8]. Osteocalcin (OSN) is an independent predictor for osteoporosis and osteoporotic fractures, and it has been suggested that its production is diminished by negative regulation of osteoblasts in Diabetes condition[8-9]. Diabetic neuropathy is one of the most common comorbidities in patients with T2DM, affecting approximately half of the patients during the course of the disease[10].

Diabetic neuropathies differ in distribution, fiber involvement (size and type), pathophysiology, and clinical course, the most typical type being a length-dependent distal symmetric polyneuropathy with differing degrees of autonomic involvement.

Although the pathogenesis of Osteoporosis in Diabetes are not fully understood, many previous studies have noted that Diabetic neuropathy may play vital roles in the development of Osteoporosis.

In an attempt to resolve these contradictory findings, we performed this observational study to clarify the relationship between Diabetic neuropathy and Osteoporosis.

MATERIAL AND METHODS

This observational case control analytical study was approved from the ethical committee of SMS medical college and attached hospitals jaipur and written consent was taken from the patients. This study was done on 60 patients of T2DM with diabetic neuropathy and without diabetic neuropathy attended the department of endocrinology and department of biochemistry (central lab of immunoassay lab) SMS medical college and hospitals jaipur. The diagnosis of type 2 diabetes was carried out by following the American Diabetes Association criteria (2007), which includes a fasting blood glucose of > 126mg/dl, random (non fasting) blood glucose of > 200mg/dl, a blood glucose more than 200 mg/dl at 2 hrs during a standard oral glucose tolerance test, or hemoglobin A1c more than 6.5%.

Patients were excluded if informed consent was not obtained, they had no diabetes, onset of diabetes was before the age of 40years, or they were on treatment of osteoporosis.

The patients were classified into two groups. Group A(neuropathy group) included 30 patients with diabetic neuropathy of 40-65 years age. Group B (control group) included 30 patients without diabetic neuropathy with the same age group as group A.

After taking a written consent, data such as age, sex, duration of T2DM were obtained clinical examination was done with special emphasis on blood pressure, BMI and foot examination for signs of peripheral neuropathy.

Fasting blood sugar, 2hrs postprandial blood sugar using oral glucose tolerance test, serum creatinine (S. cr), blood urea, dual-energy X-ray absorptiometry (DEXA), and serum osteocalcin(OSN) were done both in the studied groups. Blood sugar was measured by glucose oxidase-peroxidase method on auto analyzer.

Serum creatinine measurement was carried out using Beckman auto analyzer. It is determined by measuring the increase in absorbance at 512 nm. The expected value is 0.7–1.5 mg/dl. Blood urea examination was carried out using the same auto analyzer. It is determined by a kinetic test with urease and glutamate dehydrogenase method.

Urinary albumin–creatinine ratio was calculated by dividing urinary albumin concentration in milligrams by creatinine concentration in urine in grams. Human Osteocalcin ELISA kit (Chongqing Biospes Company, Chongqing, China) was used to measure serum Osteocalcin.

The DEXA Scan (Wipro GE Healthcare Pvt Ltd) , was done by using X-ray equipment and a computer to measure bone density.

Clinical and laboratory data of the cases and controls were tabulated.

Statistical analysis

Data entry, coding, and analysis were conducted using SPSS Statistics for Windows, version 20.0. Description of quantitative variables was in the form of mean ± SD, and description of qualitative variables was by frequency and percentage, P value less than 0.05 was set to be statistically significant.

RESULTS

Table 1: Sex distribution in Diabetes Neuropathy & Diabetes Non-Neuropathy groups in study population P>0.05 NS, *P<0.05 Significant

Characteristics	Diabetes Neuropathy N=30	Diabetes Non-Neuropathy N=30	p-Value
Sex			
Male	13 (43.3)	14 (46.7)	0.793
Female	17 (56.7)	16 (53.3)	

In present study, 22 (73.3%) male and 8 (26.7%) were female participated in neuropathy group while 18 (60%) male and 12 (40%) female in non-neuropathy group were participated. (Table 1 and figure 1)

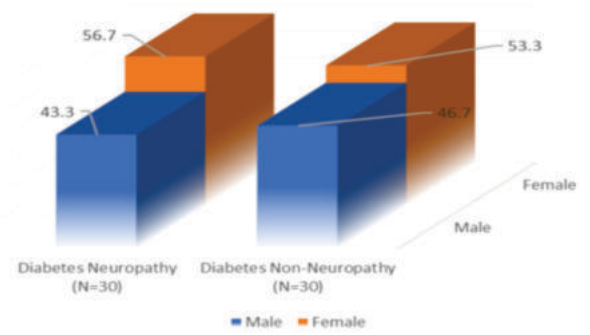

Figure 1: Sex Distribution in Diabetes Neuropathy &Diabetes Non-Neuropathy groups in study population

Table 2: Age distribution in Diabetes Neuropathy & Diabetes Non-Neuropathy groups in study population

Characteristics	Diabetes Neuropathy N=30	Diabetes Non-Neuropathy N=30	Mean Difference (95% CI)	p-Value
Age (Years)	58.28 ± 10.60	55.36 ± 10.63	2.92(-2.57-8.41)	0.291

P>0.05 NS, *P<0.05 Significant

In current study, the mean age of the neuropathy group was 58.28 years, and that of the Diabetes Non-Neuropathy group was 55.36 years, mean difference between these group was 2.92 with no significant difference between the two groups (P = 0.291).(Table 2 and figure 2)

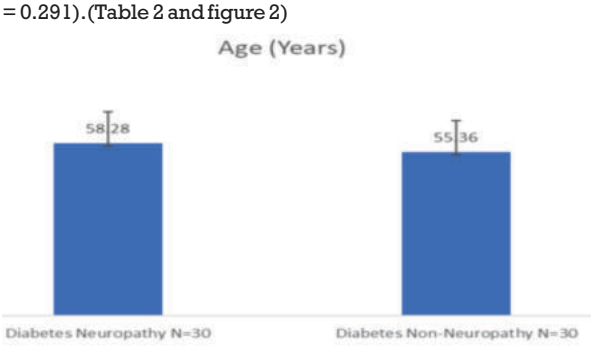

Figure 2: Age distribution in Diabetes Neuropathy & Diabetes Non-Neuropathy groups in study population

Table3: Dual energy X-ray absorptiometry scan results of the studied groups

Site of T-Score	Diabetes Neuropathy N=30	Diabetes Non-Neuropathy N=30	Mean Difference (95% CI)	p-value
T-score of spine	-0.96±1.4	1.17±0.24	0.21(-0.31-0.73)	0.421
T-score of hip	-0.26±1.3	-0.83±1.10	0.57(-0.05-1.19)	0.072
T-score of forearm	0.98±0.97	0.33±1.95	-0.65(-1.45-0.15)	0.107

P>0.05 NS, *P<0.05 Significant

The DEXA Scan results showed no significant difference between the studied groups. The mean T-score of the spine of the neuropathy group was −0.96 and that of the Diabetes Non-Neuropathy was 1.17 with mean difference was 0.21 (P = 0.421). The mean T-score of the hip of the neuropathy group was −0.26 and that of the Diabetes Non-Neuropathy was −0.83 with mean difference between group was 0.57(P = 0.072) and mean T-score of the forearm of the neuropathy group was 0.98 and that of the Diabetes Non-Neuropathy was 0.33 with mean difference was 0.65(P = 0.107) (Table3 & figure3).

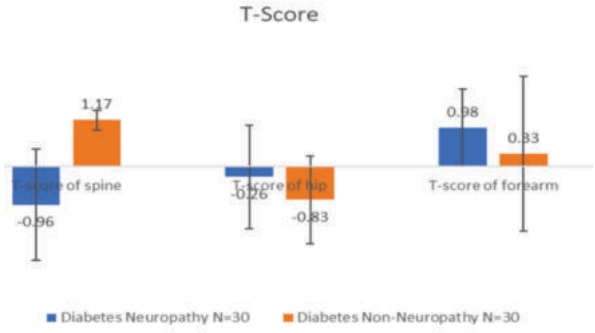

Figure 3: Dual energy X-ray absorptiometry scan results of the studied groups

According to DEXA scan, in the neuropathy group, there were seven (23.3%) patients with normal bone density, 20 (66.67%) patients with osteopenia, and three (10%) patients with osteoporosis, whereas in the Diabetes Non-Neuropathy, there were 10 (33.3%) patients with normal bone density, 18 (60%) patients with osteopenia, and three (6.67%) patient with osteoporosis, with no significant difference between the two groups (P =0.659) (Table4 and Fig.4).

Table 4: Bone condition of the studied groups

Bone condition	Diabetes Neuropathy N=30	Diabetes Non-Neuropathy N=30	p-value
Normal	7 (23.3)	10 (33.3)	0.659
Osteopenia	20 (66.67)	18(60.0)	
Osteoporosis	3 (10.0)	2 (6.67)	

P>0.05 NS, *P<0.05 Significant

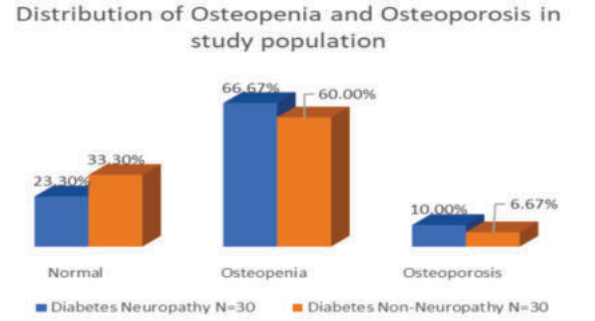

Figure 4: Bone condition of the studied groups

Table 5: Serum Osteocalcin level in Diabetes Neuropathy & Diabetes Non-Neuropathy groups in study population

Characteristics	Diabetes Neuropathy N=30	Diabetes Non-Neuropathy N=30	Mean Difference (95% CI)	p-Value
Osteocalcin (ng/dl)	17.88 ± 0.19	13.32 ± 0.16	4.56(4.46-4.65)	<0.000*

P>0.05 NS, *P<0.05 Significant

The mean Osteocalcin level of the neuropathy group was 17.88, whereas that of the Diabetes Non-Neuropathy was 13.32, with mean difference between group was 4.56 ng/dl showing significant difference between the two groups (P = 0.000) (Table 5 and Fig. 5).

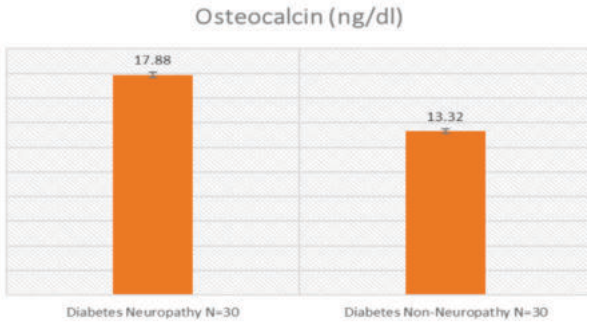

Figure 5: Serum Osteocalcin level in Diabetes Neuropathy & Diabetes Non-Neuropathy groups in study population

DISCUSSION

Diabetic peripheral neuropathy is the most common complication of Diabetes Mellitus having high morbidity and mortality.Diabetic neuropathy causes malfunctioning of peripheral nerves which can progress to foot ulceration, ultimately leading to limb amputation. Early diagnosis and protective measures can reduce this burden to a great extent.

In our study, 43.3.% in neuropathy group and 46.7% in without neuropathy were male and there was no significant difference between the two groups regarding sex.The mean Osteocalcin level of the neuropathy group was 17.88, whereas that of the Diabetes Non-Neuropathy was 13.32 showing significant difference between the two groups (P = 0.000) .

The DEXA Scan results showed no significant difference between the studied groups. The mean T-score of the spine of the neuropathy group was 0.96 and that of the Diabetes Non-Neuropathy was 1.17 (P = 0.421). The Mean T-score of the hip of the neuropathy group was 0.26 and that of the Diabetes Non-Neuropathy was 0.83 (P = 0.072).The Mean T-score of the forearm of the neuropathy group was 0.98 and that of the Diabetes Non-Neuropathy was 0.33 (P = 0.107) .

According to DEXA Scan, in the neuropathy group, 66.67% patients were with osteopenia, and 10% patients with osteoporosis, whereas in the Diabetes Non-Neuropathy 60% patients were with osteopenia, and 6.67% patient were with osteoporosis with no significant difference between the two groups (P =0.659).In this study, there was a highly significant increase in osteocalcin level in DN patients, this result is in agreement with **Maghbooli et al and El-Kafrawya** N. etal studies who found that osteocalcin level was elevated in diabetic patients with micro vascular complications in the form of peripheral neuropathy than patients without complications .This finding may be owing to oxidative stress because of high glucose levels in the blood which interact with several proteins to generate a higher concentration of advanced glycation end products. Accumulated advanced glycation end products in the body may stimulate apoptosis of osteoblasts, thereby contributing to the defective bone formation .**Piaggesi et al.** measured BMD by DEXA and bone turnover markers.There was no difference between BMD of the lumbar spine, proximal femur, distal forearm, or calcaneus between diabetic patients with and without neuropathy.

CONCLUSION

Our study found that Osteocalcin level – as a marker of osteoporosis – is elevated in diabetic patients with micro vascular complications in the form of peripheral neuropathy, whereas DEXA Scan is not greatly helpful in diagnosis of osteoporosis in diabetic patients. We found by our studies osteocalcin level is better marker than DEXA Scan for diagnosis of osteoporosis in Diabetic neuropathy patients.

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