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Research Article

THE RELATIONSHIP BETWEEN DIABETIC NEUROPATHY AND BONE MINERAL DENSITY

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ABSTRACT
It is known that there is an increase in musculoskeletal system diseases in patients with diabetes mellitus. The aim of the present study was to evaluate the relation between chronic complications of type 2 DM and osteoporosis in postmenopausal patients. 69 postmenopausal women with diabetes mellitus and as control group 52 healthy postmenopaıusal women were included in the present study. Lumbar vertebrae (L2-L4) and femur neck mineral density age, body mass index and some biochemical values were recorded. The findings of patients with type II diabetes mellitus and those of chronic compliacations of DM were compared statistically. While there was no significant difference between patient and control groups in terms of bone density (at L2-L4, p value 0.05), bone density was found to be decreased in patients with neuropathy. In diabetic patients who are not insulin dependent, bone mineral densities were found to be similar to those of control group. However, in patients with neuropathy; aignificant decrease was found in bone mineral density; whether this result is related to diabetes itself or other factors and the claim that good control of diabetes will slow down the dcrease in bone mineral density is controversial.

Keywords: *Diabetic Neuropathy, Bone Mineral Density*

INTRODUCTION
Diabates mellitus is a metabolic disease chracterized by chronic hyperglicemia, leading to impairment in carbohydrade, protein or fat metabolism as a consequence of absolute or relative decrease in insulin secretion and/or tissue response to insulin and requiring constant medical care. As a consequence of the rise in the number of patients with diabetes and prolongation of the life of patients, musculoskeletal diseases are encountered more commonly in diabetes. Diabetes is probabaly associated with osteporosis as well. The decrease in bone mineral density in patients with type I DM is beyond dispute, but the relation between bone mineral density and type II DM is still controversial. In various studies, discrepant results have been found regarding bone mineral density in patients with type II DM. However, in patients with severe loss of bone tissue, diabetic control was found to be poor. In recent years, with the advent of methods determining bone mineral density quite accurately, the relation between diabetes and osteoporosis was elucidated better. In comparative studies, in bone densitomety measurments made in forearm, 8% decrease was found in diabetes group while the decrease was 14% in trabecular bone densitometry. The decrease in bone tissue is similar in adult diabetics as well. It is at the highest level at theinitial period of the disease or immediately after. The decrease in bone tissue correlates with endogenous insulin levels. Namely, as insulin level decreases, the incidenc e of osteopenia increases. No relation could be demonstrated between metabolic complications of diabetes and osteoporosis. Insulin is an anabolic hormone, which stimulates the synthesis of nucleotides in osteoblasts and increases the uptake of aminoacids in membranous bone. In insulin deficiency, proteoglican composition of bone and cartilage changes and osteoblast activity decreases. IGF-1 stimulates bone collagen synthesis by increasing osteoblast activity. When insulin and IGF-1 levels decrease, bone matrix synthesis is not carried out properly and bone can not be calcified, all of which willl be influential in the development of osteopenia. In type 2 DM, insulin resistance and hyperinsulinemia are present, which increases bone formation. In various studies, it has been established that in type II DM, bone mineral density is the same

with or higher than that in non diabetic population.

MATERIALS AND METHODS

Methods

Postmenopausal 69 female patients with type II diabetes mellitus who referred to diabetes outpatient clinic of Haseki Training and Research Hospital and as control group 52 healthy postmenopausal women were included in the present study. The age of diabetes, retinopathy, nephropathy and neuropathy development were recorded. In both groups, daily physical activities, daily intake of calcium with diet, body mass index (BMI), the use of drugs that can influence bone metabolism, the age of menopause, serum creatinin, BUN, serum calcium and serum phosphate levels were noted. Besides in both groups, the presence of other pathologies which can lead to osteoporosis was questioned. Lumbar vertebra (L2-L4) and femur neck bone mineral density was measured with dual energy X-ray absorptiometry (LUNAR, DEXA) and results were expressed as t scores. Data of the study were expressed as mean and Standard deviation. Also, Mann-Whitney U test was employed.

RESULTS AND DISCUSSION

Results

There were no statistically significant difference between patient and control groups in terms of body mass index, serum calcium and inorganic phosphorus levels. Patients with diabetic retinopathy and diabetic nephropathy were compared with control group. No significant difference was found between two groups with respect to age, age of menopause, body mass index, femur neck scores. Only L2-L4 t scores showed a significant difference between diabetic retinopathy and nephropathy groups and control groups in terms of duration of diabetes. In addition, significant difference was found between diabetic neuropathy group and control group with regard to duration of diabetes, (p:0.004).

Discussion and Conclusion

Many studies have been carried out in order to investigate the relation between diabetes mellitus and osteoporosis and discordant results have been found. However, there are quite few studies carried out with dual energy ray absorbtiometry (DEXA), which makes it possible to evaluate cortical and trabecular bone in the spine and femur most accurately. In the study of Wakasugi *et al.*, (1985) performed with 78 diabetes patients (38 male, 40 female), bone mineral density was measured with DEXA in lumbar vertebra and femur and no decrease was found in comparison to non diabetic patients.

Table 1: The Comparison of Parameters of the Patient and Control Groups

	Diabetic Patients	Control Group	P
Age	57,86 + 4,75	56,57+ 4,2	P >0,05
Age of menopause	12,13+5,57	11,42+6,78	P>0,05
BMI	30,20 +3,41	29,75 +3,53	P>0,05
Creatinin Clearance	99.98+42.41	96.78+21.78	P>0,05
Serum Calcium	9,4 ±0,79	9,1 ± 0,76 '	P>0,05
Serum Phosphate	3,5 ±0,48	3,9 ± 0,5 '	P>0.05

Table 2: Comparison of Denisitometric Measurements between Patienst and Control Groups

	Patient	Control	P
L2-L4 T Score	(-1İ29) ± 1.26	(-0,91) ± 1,22	P=0,05
Femur Neck T Score	(-1.07) ± 1,17	(-0,84) ± 0,89	P>0,05

In an epidemiological study carried out by Barrett-Connor *et al.*, in bone densitometry of male and fmele patients measured with SPA in ultradistal wrist and midradius, and with DEXA in femur neck and lumbar vertebra, better results were obtained in non insulin dependent female DM patients than normal controls. Likewise, in the present study, carried out using DEXA in lumbar vertebra and femur, no significant difference was found between postmenopausal type II diabetes patients and normal control group with respect to bone densitometry. In diabetes patients, the effect of the duration of disease on the decrease in bone mass is uncertain.

Table 3: The Comparison between Patients with Diabetic Retinopathy and those without Retinopathy

	With Retinopathy	**Without Retinopathy**	**P**
Numb rof patients	24	45 ..	
Age of patients	58,33 ± 4,6	57,62 ±4,8	P>0,05
Menopause	13,16 ± 5	11,57 ±5,8	P>0,05
V1İI			
Diabetes	14,16 ± 6,08	9,04 ±4,15	P<0,05
Vılı			(P=0,00)
BMI	29,41+2,6	30,62 ± 3,72	P>0,05
L2-L4 T Score	H, 63)± I, 04	(-1,26) ± 1,35	P>0,05
Femur neck T Score	(-1,14) ± 0,96	(-1,03) ± 1,28	P>0,05

In insulin dependent DM, many investigators have observed that bone loss occurring before the onset of DM or within a few days of its development, did not take place afterwards. In addition, in most of studies conducted with patienst who have non insulin dependent DM, the degree of the loss in cortical and trabecular bone was not found to be corrleated with the duration of diabetes. In a study performed by Dr. Zuhal Gündü, pateints were divided into two groups according to the duration of diabetes in order that the effect of diabetes on bone mineral density can be investigated. In the grousp whose duration of disease was over 5 years, significant decrease was found in bone mineral density compared to both the group whose durationof disease was less than 5 years and control group. This finding was evaluated with the results of studies suggesting that in type II DM, delayed bone loss is mainly due to decreased bone turnover (demonstrated in histological studies as well), and finding low serum osteocalcin levels in diabetes and was attributed to complications of the disease (DM) rather than abnormality of bone formation. In the present study, patients were compared first as postmenopausal diabetic and postmenopausal non diabetic groups. While no significant difference was found between two groups with regard to bone mineral density in femur neck, significant difference was found in L2-L4 scores with a p value o p=0.05. Secondarily, diabetic patients were evaluated regarding the complications of diabetes. It was thought the evaluation of the effects of duration rather than its duration would yield more valuable information. In patients with nephropathy, retinopathy and neuropathy, the overall duration of diabetes was over 12 years.

No significant difference was found between retinopathy and nephropathy groups and the groups without these complications in terms of bone mineral density (femur neck and L2-L4). However, while no significant differece was found between the group with neuropathy and those without neuropathy in bone mineral density of femur neck, significant difference was found in L2-L4 T scores (p=0.019). The interesting finding here was that there was no significant difference between patients with neuropathy and those with nephropathy with respect to age, age of menopause, duration of diabates and body mass index, and that although patients with neuropathy and retinopathy had no significant difference in age, the age of menopause, and body mass index, the duration of diabetes was 12.17 +-5.6 years in patients with neuropathy and 14.16+-6.08 in those with retinopathy. The conclusion that may be drawn here is that significant difference betwen patients with neuropathy and those without neuropathy in terms of bone

mineral density in L2-L4 is independent of the duration of diabetes and the effects of the disease. One cause of the difference between type I DM patients and those with type II DM may be anthropometric differences between two groups. Whilst patients with type I DM are lean, those with type II DM are obese. It has been reported that obesity is usually protective against osteopororosis. Bone loss tends to be more marked in menopausal women with low weight than those who are obese. Endogenous estrogen produced in subcutanesous fat tissue in association with aromatization of androstenoidon to estron is implicated for this difference. In the present study, all individuals in patients and control grousp were obese. Mean body mass index, used in the grading of obesity, was 30.2+ 3.41 in diabetic groups while it was 29.7+-3.51 in the control group. There fore, absence of a decrease in these subjects suggests the effect of obesity. In DM, especially in patienst whose diabetes is poorly controlled, hypercalcurea occurring owing to osmotic effects of glucoseurea and resulting negative calcium balance and phosphatourea and systemic acidosis may lead to osteopeny by exerting an adverse effect on bone metabolism.

Table 4: The Comparsiıon between Patients with Diabetic Nephropathy (in 24 Hour Urine, Albuminurea over 30mg) with those without Nephropathy

	With Nephropathy	**Without Nephropathy**	**P**
Number of patients	45	24	
Age of patients	5 £13 ±4,4	57,37 + 5,4	P>0,05
Menopause	**12,13+4,9**	12,12 + 6,7	P>0,05
Yılı			
Diabetes	12,11 ± 5,6	8,39 ±4,0	P<0,05
Yılı			(P-0,007)
BMI	29,95 ± 3.24	30,66 ± 3,72	P>0,05
L2-L4 T	(-1,52) ±	(-U4)±	p>0.05
Score	132	ı,n	
Femur	(-U 9) ± .	(-0,83) .±	P>0,05
Neck T Score	1,21	1,09	

Table 5: The Comparison of Patients with Diabetic Neuropathy (whose Neuropathy was Proven with EMG) with those without Neuropathy

	With Neuropathy	**Without Neuropathy**	**P**
Number of patients	45	24 .	
Age of patienst	58,24 ± 4,5	57,16 + 5	P>0,05
Duration of menopause menopause	12,02 + menopause	12,33 +	p>0,05
Menopause	5,1	6,4	
Duration of diabetes	12,17 + 5,3	8,26+4,7	P<0,05 (p=0,004)
BMI	29,75 + 3,19	31,04 +3,71	p>0,05
L2-L4 T Score	(-1,65) ± 1,19	(-0,91) ± 1,29	P<0,05 (P=0,019)
Femur Neck T score	(-U3) ± 1,23	(-0,76) + 1,01	p>0,05

However, in the present study, no abnormality was found in plasma levels of calcium and phsophorus in our patients with type II DM. In conclusion, similar bone mineral density levels between non insulin dependent diabetes patients and control group may be explained by such factors as hyperinsulinemia and

obesity in these patients. No relation was found between the decrease in bone mineral density and the duration of diabetes, and the development of retinopathy and nephropathy. Whether the significant decrease found in bone mineral density in patients with neuropathy is related to diabetes itself or other factors is debatable. In addition, the claim that good regulation of diabetes will slow down the fall in bone mineral density is also disputable. Among other factors,which influence bone tissue in diabetic population, the use of alcohol and smoking, physical activity and types of drugs used are worth mentioning.

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