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"STUDY OF THE EFFECT OF DIABETIC CONTROL AND COMPLICATIONS ON BONE MINERAL DENSITY IN TYPE 2 DIABETIC PATIENTS"

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ABSTRACT

Background: Type 2 DM is still remains one of the leading causes of morbidity and mortality. Diabetic patients are more prone to osteoporosis. The development of osteoporosis in diabetes is also promoted by the coexistence of chronic microvascular complications, which also affect the bone marrow blood vessel. In uncontrolled diabetic patients, there is high prevalence of vitamin D deficiency and hyperparathyroidism leading to osteoporosis. **Aims:** To study the effect of diabetic control and complications on Bone mineral density in type 2 diabetes patients. **Methods:** A total 100 type-2 diabetic patients were enrolled from Nehru Hospital, B.R.D. Medical College, Gorakhpur during the study period from Jan-2017 to Dec -2017. All the patients were subjected to detailed clinical history, examination and investigations. Patient's clinical profile, HbA1C, urine microscopy, fundus examination, NCV, BMD, vitamin D, PTH and various other relevant factors were measured in all patients. **Result:** The prevalence of osteopenia and osteoporosis were more in uncontrolled diabetic patients as compared to those in whom blood sugar was controlled. In uncontrolled diabetic group, the prevalence of abnormal BMD was more in patients with microvascular complications as compare to those who had no chronic complications of diabetes. The microvascular complications further lead to worsening of BMD due to increased PTH and low level of vitamin D by vicious cycle. **Conclusions:** Diabetic patients who had poor control of blood sugar level are more prone to develop microvascular complications along with osteoporosis. In poorly controlled diabetic patients there is increased prevalence of raised PTH and low vitamin D levels, which further worsen blood sugar control and osteoporosis.

KEYWORDS: T2DM, Microvascular complications, BMD, PTH, vitamin D.

INTRODUCTION

T2DM is still remain one of the leading cause of morbidity and mortality. The complications of diabetes are related to long term elevation of blood glucose concentration (hyperglycemia). Hyperglycemia results in the formation of advanced glycation end products (AGEs). These AGEs act to prime endothelial cells and monocytes, making them more susceptible to stimuli that induce the cells to produce the inflammatory mediators. Accumulation of AGEs in plasma and tissues of diabetic patients has been linked to diabetic complications.

Diabetes itself is associated with increased risk of fracture. Diabetic osteopathy is a significant co morbidity of both forms of diabetes and is characterized by micro architectural changes that decrease bone quality leading to an increased risk of bone fracture in diabetes. In T1DM, the deficiency of insulin and IGF-1, which is present since the diagnosis, leads to impaired bone formation, abnormal mineralisation, abnormal bone microarchitecture, increased fragility of the bone, and reduced peak bone mass.[9-10] In T2DM initial hyperinsulinimia (the stimulatory effects of insulin on bone formation) coupled with insulin resistance increases bone mass through effects on bone formation via IRS-1 and IRS-2 surface receptors on osteoblasts while in long standing type 2 diabetes when insulin deficiency occurs due to excessive β- cells loss then bone changes start to occurs similarly as in Type 1 diabetics which leads to reduced bone mass or osteoporosis.

Regardless of the source, however, low level of serum vitamin D can reduce circulating calcium and induce secondary hyperparathyroidism. The increase in PTH may induce weight gain, obesity and T2DM. The cause

of osteoporoses is multifactorial and vitamin D deficiency is one possible risk factor.

MATERIAL AND METHODS

INCLUSION CRITERIA A total of 100 type-2 diabetic patients of age group 45- 65 years who were admitted in Department of Medicine, Nehru Hospital, B.R.D Medical College, Gorakhpur from Jan- 2017 to Dec-2017 were included in this study.

EXCLUSION CRITERIA

Type 1 diabetic patients
Critically ill patients
Non- diabetic cases of chronic kidney disease
Patients on Anticonvulsant therapy
Patients with extensive Skin disorders
Post total-thyroidectomy patients
Patients with chronic infective diseases like HIV, active tuberculosis etc.

INVESTIGATIONS

1. HbA1C level (controlled <7%, uncontrolled>7%)
2. Fundus examination, Urine albumin:creatinine ratio, NCV etc.
3. Serum PTH (normal 7-68 pg/ml, increased >68 pg/ml)
4. Serum vitamin D (normal >20 ng/ml, low level <20 ng/ml)
5. BMD: Dual energy x ray absorptiometry (DXA) Scan at lumbar spine (L_2-L_4) and dual femur (trochanter and femoral neck) was done and patients were categorized by using WHO criteria as.

- Normal BMD T-score : at or above -1 SD
- Osteopenia T-score: between -1 and -2.5 SD
- Osteoporosis T-score: at or below -2.5 SD.

Statistical analysis

Data entry was done in IBM SPSS Statistics Version 22 and was analyzed using appropriate statistical tests i.e. Pearson Chi-square test.

RESULT

Total 100 patients were included in study in which total 62 % patients had abnormal BMD (30% osteoporosis and 32% osteopenia)**.** Prevalence of osteoporosis was more (86.67%) in uncontrolled diabetic patients as compare to controlled patients (13.33%). Patients who had microvascular complications were more significantly prone to develop osteoporosis or osteopenia (p value=0.028). Patients who had both, low level of vitamin D and increased PTH had significantly high prevalence of osteopenia or osteoporosis (p valve=0.002).

TABLES

Table 1: Table showing relation between Diabetes control (HbA1C) and BMD.

BMD	NO. OF PATIENTS	HbA1C	
		CONTROLLED (N=22)	UNCONTROLLED (N=78)
NORMAL	38	8 (21.05%)	30 (78.94%)
OSTEOPENIA	32	10 (31.25%)	22 (68.75%)
OSTEOPOROSIS	30	4 (13.33%)	26 (86.67%)

Table 2: Table showing relation between microvascular complications of diabetes and BMD.

DIABETIC COMPLICATIONS	NO OF PATIENTS WITH COMPLICATIONS	BMD			PEARSON CHI-SQUARE TEST
		NORMAL	OSTEOPENIA	OSTEOPOROSIS	
DIABATIC RETINOPATHY	14 (14%)	2 (14.28%)	5 (35.72%)	7 (50%)	p=0.028
DIABETIC NEPHROPATHY	20 (20%)	4 (20%)	7 (35%)	9 (45%)	
BIABETIC NEUROPATHY	21 (21%)	4(19.04%)	8 (38.09%)	9 (42.85%)	

Table 3: Correlation between vitamin D, PTH with BMD in type-2 diabetic patients (N=100).

BMD	VITAMIN D (N=100)		PTH (N=100)			PEARSON CHI-SQUARE TEST
	NORMAL	LOW LEVEL	NORMAL	DECREASED	INCREASED	
NORMAL (N=38)	26(68.42%)	12(31.25%)	36(94.73%)	0	2(5.26%)	p=0.002
OSTEOPENIA (N=32)	10(31.25%)	22(68.75%)	18(56.25%)	2(6.25%)	12(37.5%)	
OSTEOPOROSIS(N=30)	4(13.33%)	26(86.66%)	10(33.33%)	0	20(66.67%)	

DISCUSSION

As shown in table 1, 30(30%) patients had osteoporosis in which 26(86.67%) had uncontrolled diabetes and 4(13.33%) controlled diabetes. Among 32(32%) patients with osteopenia, 22(68.75%) had uncontrolled diabetes and 10(31.25%) had controlled diabetes. This signifies that the uncontrolled diabetes carries a major risk of abnormal BMD (osteoporosis and osteopenia).Similar studies done by Schwartz et al.[3] in a large prospective study of older women obtained from the Study of Osteoporotic Fractures, confirmed that women with type 2 diabetes experience higher fracture rates than non-diabetic women. Study by Gregorio et al[4] also conform that bone loss has been observed to be greater in patients with poorly controlled diabetes than in those whose diabetes is in good control.

As shown in table 2, among 14(14%) patients with diabetic retinopathy, 5(50%) were osteoporosed and 5(35.72%) osteopenic. In 20(20%) patients with diabetic nephropathy, 9(45%) were osteoporosis and 7(35%) osteopenia. Out of 21(21%) patients with diabetic nephropathy, 9(42.85%) had osteoporosis and 8(38.09%) osteopenia. This signifies that diabetic patients who had microvascular complications were more prone to develop abnormal BMD and as the duration of diabetes increases, the risk of microvascular complications also increases which further leads to increase risk of osteoporosis or osteopenia.

According to ADA[1] guideline all patients should be assessed for diabetic peripheral neuropathy starting at diagnosis of type 2 diabetes and 5 year after the diagnosis of type 1 diabetes and at least annually thereafter . In most prospective follow up Landmark trials studies done in patients of diabetes mellitus (UKPDS[2]) have found retinopathy to be the earliest complication in type 2 diabetes and also to be invariably associated with nephropathy.

As shown in table 3, among 30 patients with osteoporosis, 26(86.67%) had low vitamin D and 4(13.33%) had normal vitamin D, in this group of patients, 20(66.67%) had increased PTH, 10(33.33%) had normal PTH. Similarly in 32 patients with osteopenia, 22(68.75%) had low vitamin D and 10(31.2%) normal vitamin D, in this group of patients only 12(37.5%) had increased PTH and 18(56.25%) had normal PTH which signifies that patients with low vitamin D and increased PTH were osteoporosed or osteopenic. It means that PTH and vitamin D together are highly specific to diagnosed osteoporosis or osteopenia.

Similar results were shown by many other studies. The study done by **Sahota et al**[13] found that prevalence of hypovitaminosis D was 39% and not all patients with hypovitaminosis D develop secondary hyperparathyroidism. **Patel et al.**[14] suggested that glomerular filtration rate is the single most important factor in maintaining PTH levels. Gunnarsson et al.[15] while supporting the kidney function hypothesis, felt that body mass index may play a role in women by blunting the level of PTH and added that in men, insulin-like growth factor 1, smoking, and testosterone levels may do the same. A study done by Chang et al[17] shows that high level of PTH is associated with abnormal glucose metabolism due to interference of PTH with either with ability of the pancreas to release insulin, the action of insulin or both. High PTH level causes suppression of insulin signal transduction in adipocytes that resulted in insulin resistance and high prevalence of diabetes mellitus (2-4 times) in hyperparathyroidism.

CONCLUSION

1. Patients with uncontrolled Diabetes mellitus had more prevalence of abnormal BMD (osteopenia/ osteoporosis).
2. Patients with uncontrolled diabetes had significantly more microvascular complications.
3. The prevalence of abnormal BMD was more in patients with microvascular complications as compared to those who had no chronic complications of diabetes.
4. There is raised PTH and low vitamin D level in the patients with abnormal BMD of uncontrolled diabetic group. This may be one of the causes of increased resorption and defective mineralisatin of bone which leads to further high prevalence of osteoporosis or osteopenia.
5. Increased PTH and low level of vitamin D in osteoporosed patients is one of the major cause of poorly controlled diabetes with increased risk of microvascullar complications. The microvascular complications further leads to increased risk of abnormal BMD via vicious cycle. By this we can say vitamin D supplementation is necessary for better control of diabetes and prevention of osteoporosis.
6. Insulin is necessary for prevention and treatment of osteoporosis due to it's anabolic action on bone and glucose metabolism which also leads to better control of diabetes, decrease risk of microvascular complications and decrease prevalence of osteoporosis.

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