ORIGINAL ARTICLE

RISK OF OSTEOPOROSIS IN FIRST DEGREE RELATIVES OF PATIENTS WITH DIABETES MELLITUS: A STUDY OF BONE MINERAL IONS

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Background: Diabetes may influence the bone in multiple pathways, some with contradictory effects. These mechanisms include changes in insulin and hypercalciuria, phophatemia, hypomagnesaemia associated with glycosuria. We tried to find out level of minerals in first degree relatives of patients with diabetes mellitus as there is relationship between bone minerals and glycemic controls. **Methods:** Fifty local subjects age range 40−50 years with family history of diabetes (first degree relatives) were included in the study. Duration of study was 6 months. Levels of blood sugar, serum calcium, phosphorus and magnesium were estimated by standard Randox kits. 10 males and 10 female subjects with no history of diabetes were considered as normal controls. **Results:** The level of blood glucose in both sexes was increased as compared to their controls but this showed no significant difference. Level of serum calcium and magnesium were significantly decreased (p<0.05, 0.001) in both males and females when compared with the values of their controls. Level of phosphorous was significantly increased (p<0.05) in both first degree relatives of male and females as compared to level of phosphorous of their controls. **Conclusion:** Pre-diabetes and undiagnosed T2DM are conditions for which screening can be helpful to find out that first degree relatives not only at risk to develop diabetes but they also likely to develop osteoporosis in a sizable portion of the population. However there is a need for further research including the incidence and risk factors for osteoporotic fractures in first degree relatives of diabetics.

Keywords: first degree relatives, bone minerals, diabetes mellitus, osteoporosis

INTRODUCTION

Diabetes mellitus represents a group of diseases of heterogeneous etiology, characterized by chronic hyperglycemia and other metabolic abnormalities, which are due to deficiency of insulin effect. Adults who have 1 or more first- or second-degree relatives affected with diabetes are at high risk of developing diabetes. The evidence is strong; however, that youth with a positive family history already show signs of increased risk for diabetes.[1,2]

The old concept of bone as inert metabolic tissue, with minor contributions to metabolic adaptations has been reconsidered in light of findings that bone is involved in the development of insulin sensitivity.[3] Bone metabolism is regulated by complicated mechanisms that involve mineral metabolism and endocrine systems.[4]

Diabetes may influence the bone in multiple pathways, some with contradictory effects. These mechanisms include changes in insulin and insulin-like growth factors levels, hypercalciuria associated with glycosuria, obesity, higher concentrations of advanced glycation end-products in collagen etc. Along these lines, many cohort studies undeniably indicated that diabetes itself is associated with increased risk of osteoporosis.[5,6] Recent studies have indicated that bone cells contribute to metabolic activity by the production of peptides such as osteocalcin that impacts insulin sensitivity and energy metabolism.[3]

It was shown that insulin and insulin like growth factors (IGF-1, IGF-2) have an influence on bone metabolism itself and other growth factors, cytokines and hormones may determine changes in diabetic bone metabolism.[7]

There was a very strong dose-dependent relationship between duration of diabetes and risk of hip fracture in Asian population like their Western counterparts.[8] Early human diabetes mellitus can result in hypercalciuria and reduced bone mass (osteopenia). Experimentally it is proved that altered mineral balance is due to the disturbances in pancreatic function. It is observed that bone of diabetic rats in the early stage of diabetes (32 days) loses magnesium, while the calcium and phosphorus content does not change significantly. During longer persistence of severe diabetes (70 days) a significant drop of all three minerals in bone was observed. The bones of diabetic animals on the 70th experimental day were macroscopically smaller and were very fragile.[9,10]

Diabetes mellitus is the also associated with secondary magnesium deficit. Plasma magnesium concentrations may correlate inversely with the degree of hyperglycaemia. Clinical studies have speculated on a potential link between the magnesium deficit of diabetes and several diabetic complications, including cardiovascular problems and retinopathy.[11] Early recognition and treatment of severe hypophosphatemia are important to reduce the risk of neurological complications.[12]

A family history of diabetes is a major risk factor for the disease. As such, it is often included in a variety of tools designed to detect either people at risk of diabetes or people with undiagnosed diabetes. One of the reasons to screen for diabetes is that it has a prolonged asymptomatic phase, which includes impaired fasting glucose, impaired glucose tolerance, and the early stages of diabetes.

Present study tried to find out the level of minerals in first degree relatives of patients with diabetes mellitus which may confirm the risk of osteoporosis in first degree relatives of patients with diabetes.

MATERIAL AND METHODS

50 local subjects age range 40−50 years with family history of diabetes (1st degree relatives) were included in the study. Duration of study was 6 months. Levels of blood sugar, serum calcium, phosphorus and magnesium were estimated by standard Randox kits. Ten males and 10 female subjects with no history of diabetes were considered as normal controls.

Student's *t*-test was applied for comparing the biochemical parameters between patients and controls. Data was analyzed by using soft ware program SPSS-15.

RESULTS

Level of blood glucose, serum calcium, Phosphorous and magnesium in first degree male and female relatives of diabetics was tabulated. It was observed that the level of blood glucose in both sexes was increased as compared to their controls but this showed no significant difference. It was observed level of serum calcium was significantly decreased ($p<0.05$, 0.001) in both and males and females when compared these values with the values of their controls. Level of phosphorous was significantly increased ($p<0.05$) in both first degree relatives of male and females as compared to level of phosphorous of their controls. Level of magnesium was decreased in both sexes of first degree relatives, but significant difference ($p<0.05$) was only observed in case of male first degree relatives. (Table-1).

Table-1: Level of blood glucose, serum calcium, Phosphorous and magnesium in first degree male and female relatives of diabetics (Mean±SD)

Subjects	Age (Yr)	Calcium (mg/dl)	Phosphorous (mg/dl)	Magnesium (mg/dl)	Fasting blood glucose (mg/dl)
Females (25)	30.54±6.5	6.56±5.35*	5.98±2.06*	1.44±1.18	88.75±12.81
Males (25)	34.81±6.9	5.89±4.45**	7.04±4.55*	1.07±1.23*	84.41±8.73
Female controls (10)	32.53±5.8	9.0±1.1	4.0±1.55	1.90±1.4	80.75±9.5
Male controls (10)	33.82±4.5	9.5±2.5	4.2±1.25	2.1±1.0	81.41±6.73

*$p<0.05$= Significant difference, **$p<0.001$= Highly significant difference

DISCUSSION

Minerals including calcium, phosphorus and magnesium have been identified as playing a potential role in the prevention of bone diseases, particularly osteoporosis. Prolonged supplementation of Ca and vitamin D in elderly has been shown to prevent bone loss, and in some intervention studies to prevent fragility fractures.[13]

Bone remodelling, the mechanism necessary to maintain bone strength, is sensitive to metabolic disarrangements such as DM and obesity. Recent studies have indicated that bone cells contribute to metabolic activity by the production of peptides such as osteocalcin that impacts insulin sensitivity and energy metabolism.[3]

Very few studies were carried out to find out the relationship between bone minerals ion and poor glycemic controls in first degree relatives of diabetics in order to detect the relatives at risk of osteoporosis.

Present study was observed that the level of blood glucose in both sexes was increased as compared to their controls but this showed no significant difference However lack of relationship between glycemic control and bone mineral density in type 2 diabetes mellitus was reported by a group of workers.[14] It is reported that the siblings of type 2 diabetes are more at risk of developing diabetes as compared to siblings of type 1.[15] Turnover of bone biochemical markers are very much affected in people with diabetes. Reduced bone mass, occurring with increased frequency in diabetes mellitus, has been attributed to poor glycemic control, but the pathogenic mechanisms remain unknown.[16]

Our study was observed level of serum calcium was significantly decreased ($p<0.05$, 0.001) in both and males and females when compared these values with the values of their controls. Level of phosphorous was significantly increased ($p<0.05$) in both first degree relatives of male and females as compared to level of phosphorous of their controls. Level of magnesium was decreased in both sexes of first degree relatives, but significant difference ($p<0.05$) was only observed in case of male first degree relatives.

A number of studies are in accord with our study who observed that poor glycemic control or diabetes markedly influence the calcium phosphate metabolism and bone metabolism, with an early drop of magnesium in bone.[9] Another study also found an association of minerals of calcium, magnesium, phosphorus, glucose metabolism and bone metabolism.[17] A study reported that disturb metabolism

of calcium and phosphate is associated with hypercalciuria, a potential risk factor for osteoporosis, has long been noted in patients with poorly controlled type 2 diabetes.[18] An experimental study on rats proved increased level of ions which in turn significantly increased the urinary losses of calcium, magnesium and phosphorus.[8] However, recently a group of workers reported that there is was no significant relationship between the level of serum calcium and phosphorus in diabetics.[19]

No of studies were carried out on relationship of serum magnesium and glycemic control. A study reported that serum magnesium correlated inversely with both fasting blood glucose. These data indicate that the net tubular reabsorption of magnesium is decreased in diabetic patients in presence of hyperglycaemia, leading to hyper-magnesiuria and hypomagnesaemia.[20] The hypo-magnesaemia of diabetes might be expected to affect intracellular concentrations of the ion. However, although some animal and clinical studies have reported subnormal magnesium concentrations in blood cells, bone, and soft tissues of diabetics, the relationship between plasma magnesium concentration and intracellular level of the ion is inconsistent. It is possible that a common mechanism involving magnesium may be responsible for some of the diverse complications of diabetes. It is found that the development of diabetic hypomagnesaemia may be associated with prolonged hyperglycaemia, insulinopenia and disturbance of phosphate metabolism.[10] A contradictory report was observed by a group of workers who observed no significant correlation between fasting plasma magnesium and fasting plasma glucose concentrations. Furthermore plasma magnesium concentrations were not affected by the degree of blood glucose control.[21]

CONCLUSION

It is therefore concluded that pre-diabetes and undiagnosed T2DM are conditions for which screening can be helpful to find out that first degree relatives not only at risk to develop diabetes but they also likely to develop osteoporosis in a sizable portion of the population. However there is a need for further research including the incidence and risk factors for osteoporotic fractures in 1st degree relatives of diabetics.

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