ORIGINAL ARTICLE

Effect of Type 1 Diabetes Mellitus on Bone Status of Children

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ABSTRACT

Background: Children and adolescents with type 1 diabetes mellitus (DM) show severe impairment of bone metabolism and structure, resulting in higher risk of decreased bone mass and its related complications later in life.

Objective: To observe the effects of diabetes mellitus on the bone status of children (aged between 9-15 years) by measuring bone remodeling markers and to find out correlation of these parameters with severity of disease itself.

Methods: This cross sectional study was carried out in Department of Physiology, University of Health Sciences, Lahore. Sixty boys 9-15 years old were selected. The control group consisted of 30 healthy non-diabetic boys. The diabetic group comprised of 30 boys suffering from type 1 diabetes mellitus. Bone remodeling markers parathyroid hormone (PTH), insulin like growth factor-1 (IGF-1), insulin like growth factor binding protein-3 (IGFBP-3) were determined by ELISA.HbA_{1C} values were determined by affinity liquid chromatography. Bone mineral density (Z-score) was measured with bone profiler.

Results: Difference of level of IGF-1, IGFBP-3 and bone mineral density (Z-score) in both groups were found to be statistically non-significant. However serum parathyroid hormone levels were significantly lower ($p<0.05$) in diabetic boys as compared to non-diabetic controls. Correlations of parameters with levels of HbA_{1C} and bone mineral density were found to be non-significant.

Conclusion: Type 1 diabetes mellitus does not significantly affect bone mineral density and serum levels of IGF-1 and IGFBP-3. However diabetes mellitus results significantly lower levels of parathyroid hormone showing that diabetic children have less bone turn over.

Keywords: Type 1 diabetes mellitus, parathyroid hormone (PTH), IGF, IGFBP-3.

INTRODUCTION

The foundation of bone health is established during the pre and postnatal developmental stages especially childhood and adolescence. During this period the bone development and skeletal growth may be altered by genetic and acquired disorders leading to changes in bone mineral density and abnormal skeletal maturation[1].

Insulin deficiency as occurs in type 1 diabetes mellitus or due to tissue resistance to insulin as occurs in type II diabetes both associated with several skeletal growth abnormalities[2].

Type 1 diabetes along with poor glycemic control disturbs the GH-IGF axis (growth hormone-insulin like growth factor) resulting in alteration of levels of bone resorption factors like the parathyroid hormone(PTH), type 1 collagen cross-linked carboxy terminal telopeptide and bone formation markers such as bone alkaline phosphatase and osteocalcin resulting in decreased bone mineral density[3,4].

A number of skeletal defects in associated with type 1 diabetes have been reported like diminished linear bone growth during the pubertal growth spurt, decreased adult bone density, an increased risk for adult osteoporosis, poor bone healing and regeneration characteristics[2].

The current study aimed to observe the effects of type 1 diabetes on skeletal maturation in prepubertal and pubertal boys along with determination of peripheral concentration of bone formation and bone resorption markers.

MATERIAL AND METHODS

This cross sectional study was carried out in department of physiology, university of Health Sciences Lahore. Sixty boys, 9-15 years old were selected. The control group consisted of 30 healthy non-diabetic boys. The diabetic group comprised of 30 boys suffering from type 1 diabetes.

From each subject blood sample (5ml) was drown after overnight fasting of 12 hours. Fasting blood sugar was determined by glucose oxidase method. HbA_{1c} was determined by affinity liquid chromatograph. Bone mineral density was measured by bone profiler. Z-score was determined according to WHO criteria[5]. Serum IGF-1, IGFBP-3 and PTH

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were assayed by ELISA. All calculations were carried out with the SPSS version 15.

Arithmetic mean and standard deviation of each parameter were determined. The significance of differences among the two groups was analyzed by student's t test. Pearson's correlation coefficient was used to determine correlation between variable of interest. P value <0.05 was considered statistically significant.

RESULTS

Table 1: Bone mineral density (Z score) and HbA_{1C} of subject (n=60).

Parameters	Non-diabetic controls (n=30)	Type 1 diabetic (n=30)	P value
HbA_{1C}	5.25±0.2	11.1±3.26	<0.001**
Bone mineral density (Z-score)	-2.68±1.84	-2.66±2.59	>0.05*

*Values are given as mean±SD **Significant *Non-significant*

Table 1 shows the bone mineral density Z-score in diabetic boys was -2.66±2.56 and of non-diabetic control group was -2.68±11.84 respectively .While HbA_{1C} levels were significantly higher in diabetic group.

Table 2: IGF-1 , IGFBP-3 levels and parathyroid hormone of subjects (n=60)

Parameters	Non-diabetic controls (n=30)	Type 1 diabetic (n=30)	P value
IGF-1 (ng/ml)	92.31±34.69	73.91±61.37	>0.05*
IGFBP-3 (ng/ml)	2071±936	2286±610	>0.05*
Serum Parathyroid hormone (pg/ml)	75.69±77.69	29.74±20.84	<0.003**

**Non-significant* ***Statistically significant*

Mean IGF-1 levels were found to non-significant in type 1 diabetic boys in table 2. There was no statistically significant difference P>0.05 observed in mean IGF BP-3 value between diabetic boys and control group. Mean serum parathyroid hormone levels were significantly (P<0.05) lower in type 1 diabetic boys as shown in table 2.

Table 3 and Table 4 showing correlation between HbA_{1c} and various parameters in type 1 diabetics and correlation between bone mineral density and bone markers in type 1 diabetics. We did not found any statistically significant value in this regard.

Table 3: Correlation between HbA_{1c} and various parameters in type 1 diabetics

Correlation between HbA_{1c}	Pearson's correlation coefficient (r)	P value
PTH	-0.289	0.-121*
Z-score	-0.154	0.417*
IGF-1	-0.341	0.065*
IGFBP-3	-0.105	0.581*

*Non-significant

Table 4: Correlation between BMD (Z-score) and bone markers in type 1 diabetics

Correlation between BMD (Z-score) and	Pearson's correlation coefficient (r)	P value
PTH	0.096	0.614*
IGF-1	-0.059	0.757*
IGFBP-3	0.129	0.498*

* Statistically non significant

DISCUSSION

Type 1 diabetes has been related to reduce bone mineral density in children[6]. In children with type 1 diabetes, osteopenia is found to be an early complication[7,8] and a relatively frequent complication in type 1 diabetic adult male patients[9].

Quantitative ultrasound measurement technique was used in diabetic children in Italy and found reduced Z-score in comparison with control group[10].

Bone status was evaluated at radius and phalanx in children and adolescent with type 1 diabetes by using quantitative ultrasound measurement, and it was found that male and female patients with type 1 diabetes did not have significantly different bone mineral density. (Z-score) at radius and tibia[11]. It supports the finding of our study. Similarly a study conducted in Germany showed that bone mineral density of children with type 1 diabetes were within the reference range[12].

Our study showed that bone mineral density of diabetic boys and of non-diabetic control group did not show significant difference showing that type 1 diabetics has no significant effect in acquisition of bone mineral density. Bone mineral density showed no significant correlation with HbA_{1c} and bone markers in diabetic boys.

Parathyroid hormone increases bone formation as well as bone resorption. Parathyroid hormone enhances the function of osteoblasts, so most obvious effects of parathyroid harmones are to increase bone formation probably by indirect actions such as stimulation of synthesis of insulin like growth factors (IGF-1) and other growth factors by osteoblast lineage cells. Parathyroid hormones also augments the bone resorption by osteoclast cells but under the

effect of parathyroid hormone, rate of bone formation is more than bone resorption[13].

Type 1 diabetes also effect parathyroid hormone secretion and its actions on bone. It has been shown that children with type 1 diabetes has lower serum levels of calcium and parathyroid hormone and bone mineral density was not related to any marker of bone resorption or formation[14]. While other studies showed that type 1 diabetes had no significant effect on parathyroid hormone level and there was no correlation between type 1 diabetes and parathyroid hormone levels[15,16].

The present study showed significantly lower parathyroid level in diabetic children, however it showed no correlation with bone mineral density.

Insulin like growth factors is a family of peptides that are in part growth hormone dependent and mediated many of anabolic and mitogenic actions of growth hormone. Insulin like growth factors and insulin like growth factors binding proteins are important regulators of bone growth and metabolism[17]. A number of studies have demonstrated that low bone mineral density in type 1 diabetes was associated with lower serum levels of IGF-1 and IGFBP[3,4,18], while our study did not show any significant change in IGF-1 and IGFBP-3 in diabetic boys as compared to control group. IGF-1 and IGFBP-3 also showed no significant correlation with bone mineral density and HbA_{1C}.

CONCLUSION

This study elucidates the effects of type 1 diabetes on bone mineral density and markers of bone growth in boys aged 9-15 years. The results of present study demonstrate that type 1 diabetes does not significantly affect bone mineral density, IGF-1 and IGFBP-3. However type 1 diabetes results in significantly low levels of parathyroid hormone which can affect the bone status of growing children.

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