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STUDY TO KNOW EFFECTS ON BONE METABOLISM IN TYPE 1 DIABETIC CHILDREN

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Abstract:

Children and adolescents with diabetes mellitus (DM) type 1 demonstrate a significant deterioration of metabolism and bone structure, resulting in a reduction in bone mass and associated risk of complications in the future.

Objective: *To observe the effects of diabetes mellitus on bone status of children (9 to 15 years of age) by measuring bone remodeling markers and correlating these parameters with the severity of the disease.*

Study Design: *Across-sectional study.*

Place and Duration:*In the Paediatric Department of Services Hospital Lahore in collaboration with physiology department for Six months duration from November 2018 to April 2019.*

Method: *Sixty children aged 9-15 years were selected. The control group comprised of 30 healthy non-diabetic children. The diabetic group consisted of 30 children suffering from diabetes mellitus type 1. Insulin-like growth factor 1 (IGF-1), growth factor binding protein and Parathyroid hormone (PTH) and bone remodeling were determined by insulin type 3 (IGFBP-3) ELISA. HbA1C values were determined by liquid affinity chromatography. Bone mineral density (Z score) was measured with a bone profile.*

Results: *The difference between IGF-1, IGFBP-3 and bone mineral density (Z score) levels was not statistically significant in both groups. However, parathyroid hormone levels were expressively lower in diabetic children paralleled to non-diabetic controls ($p < 0.05$). Correlation of parameters with HbA1C levels and bone mineral density was not significant.*

Conclusion: *Type 1 diabetes mellitus did not significantly affect bone mineral density and serum IGF-1 and IGFBP-3 levels. However, diabetes mellitus produces significantly lower levels of parathyroid hormones, indicating that diabetic children have less bone turnover.*

Key words: *diabetes mellitus type 1, parathyroid hormone (PTH), IGF, IGFBP-3.*

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INTRODUCTION:

The basis of bone health is determined in the stages of development before and after development, especially in childhood and adolescence. In this period, bone development and skeletal growth can be altered by genetic and acquired disorders that lead to changes in bone mineral density and abnormal skeletal maturation. Both are associated with several skeletal growth abnormalities, either due to deficiency of insulin in diabetes mellitus Type I or tissue resistance by insulin that occurs in type II diabetes. Diabetes mellitus Type I along with deprived control over glycemia, changes the GH-IGF (growth hormone - insulin-like growth factor) axis, which causes changes in levels of bone resorption factors such as hormone Parathyroid (PTH), the cross-linked carboxy terminal of collagen type 1 telopeptide and bone formation markers such as bone alkaline phosphatase and osteocalcin cause a decrease in bone mineral density. Some skeletal disorders associated with diabetes mellitus Type I have been described, such as linear bone growth during the outbreak of puberty growth, decreased bone density in adults, risk of osteoporosis in adults, poor bone healing and regenerative properties. The purpose of this analysis was to observe the effects of diabetes mellitus Type I on skeletal maturation in prepubertal and pubertal children, together with the determination of peripheral concentration of bone formation and markers of bone resorption.

MATERIALS AND METHODS:

This cross-sectional study was performed in the Paediatric Department of Services Hospital Lahore in collaboration with physiology department for Six months duration from November 2018 to April 2019. Sixty children aged 9-15 years were selected. The control group comprised of 30 healthy non-diabetic children. The diabetic group comprised of thirty children with diabetes mellitus Type I, for each subject the blood sample (5 ml) taken overnight for 12 hours. Blood sugar fasting was determined by glucose oxidase method. HbA1c was determined by liquid affinity chromatography. Bone mineral density was measured with a bone profiler. Z score was determined according to WHO criteria. Serum IGF-1, IGFBP-3 and PTH were analyzed by ELISA. All controls were performed with SPSS version 17. Each parameter Standard deviation and Arithmetic mean were determined. Using Student's t-test; the importance of variations between the two groups was analyzed. To evaluate the association between the variables of interest Pearson correlation coefficient was used. P <0.05 was taken significantstatistically.

RESULTS:

Table 1 shows that the Z mineral bone density score in diabetic children is -2.66 ± 2.56 and the non-diabetic control group is -2.68 ± 11.84, respectively. HbA1C levels were higherexpressively in diabetic group.

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*

The mean IGF-1 levels in children who are type 1 diabetic given in Table 2 were not significant. There was no significantstatisticallyalteration between mean IGF BP-3 values between diabetic children and control groupP> 0.05.

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 parathyroid hormone levels in serum were lowersignificantly in Type 1 diabetic children as shown in Table 2 (P <0.05).

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 3 and Table 4 show the relationship between various parameters in HbA1c and type diabetic.

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

The correlation between bone markers and bone mineral density in diabetic patients of type 1 was not found to be statistically significant.

DISCUSSION:

Type 1 diabetes has been linked with a reduction in bone mineral density in children. In children with type 1 diabetes, osteopenia is an early complication and a relatively common complication in adult male patients with type 1 diabetes. Quantitative ultrasound measurements were performed to evaluate bone status in radio and phalanx in children and adolescents with type 1 diabetes, and it was found that there was no significant difference in bone mineral density in women and men with type 1 diabetes. (Z-score) radius and tibia11. Support our work. Similarly, a study in Germany showed that the bone mineral density of children with type 1 diabetes was within the reference range.

Quantitative ultrasound measurement technique was used in diabetic children in Italy and Z score decreased compared to control group.

Type 1 diabetes also affects the secretion of the parathyroid hormone and its effects on the bones. It has been shown that children with type 1 diabetes have low calcium and parathyroid hormonelevels in serum and that bone mineral density is not related with any markers of resorption or bone formation.

Other studies have shown that type 1 diabetes has no significant effect on parathyroid hormone levels and that there is no relationship between type 1 diabetes and parathyroid hormone levels.IGFs are a family of peptides that are partly dependent on growth hormone and mediated by many of the mitogenic and anabolic effects of growth hormone. Growth factors similar to insulin and insulin-like growth factors are important regulators of bone growth and metabolism. Some studies have shown that low bone mineral density in type 1 diabetes is associated with low serum IGF-1 and IGFBP-3 levels, but our study did not show a significant change in IGFBP-3 and IGF-1 in children compared with control groups. IGFBP-3 and IGF-1 also exhibited no significant relation with bone mineral density and HbA1C.

This study showed a significantly low parathyroid level in diabetic children, but did not correlate with bone mineral density.

CONCLUSION:

This study clarifies the effects of diabetes mellitus Type I on bone mineral density and bone growth markers in children aged 9 to 15 years. The results of this study show that type 1 diabetes does not significantly affect bone mineral density, IGF-1 and IGFBP-3. However, type 1 diabetes produces low levels of parathyroid hormones that can affect the bone status of growing children.

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