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Bone mass and vitamin D status in children and adolescents with generalized epidermolysis bullosa

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Background

Inherited epidermolysis bullosa (EB) comprises a cluster of genetic disorders characterized by blistering of skin and mucosae following minimal mechanical traumas. Severely affected individuals have high risk of extracutaneous complications, including low bone mass.[1,2]

EB-related risk factors that may compromise bone metabolism include undernourishment, increased metabolic rate due to the constant wound healing, low muscle strength, reduced mobility, low vitamin D status due to skin lesions and the chronic inflammatory state which leads to increased levels of proinflammatory cytokines with pro-osteoclastic activity.[3,4]

Objectives

The aims of this study were:
-to assess the areal bone mineral density (aBMD) and vitamin D status of children and adolescents with generalized forms of EB
-to search for clinical parameters correlated to the aBMD

Methods

Transversal study comprising 14 patients with EB, aged 5 to 20 years old, attending the Pediatric Endocrinology Outpatient Clinic at the Brasilia University Hospital. The determination of the EB type was based upon clinical findings and electron microscopy of skin biopsy.

Individuals with EB had their anthropometry, bone mass and 25-hydroxy-vitamin D (25OHD) levels compared with a control group comprised of 42 healthy children and adolescents (matched for age and sex). Bone mass was analyzed in terms of areal bone mineral density (aBMD) through DXA scans of total body less head (TBLH) and lumbar spine (L1L4).

aBMD was adjusted for height-age (aBMD-Ht) and it was defined as normal if > 2.0 SD and low bone mass if aBMD-Ht ≤ 2.0 SD.[5]

EB patients were scored according to their physical mobility level: severe limitation; low mobility; moderate mobility and fully active.

Statistical significance was determined for P values < 0.05.

Results and Discussion

Fourteen individuals (aged 5.6 to 16.8 years) were recruited, all presenting generalized forms of EB:
-6 epidermolysis bullosa simplex (EBS) and
-8 dystrophic recessive epidermolysis bullosa (DREB).
Clinical and DXA data from the studied individuals are shown in tables 1 and 2.

	EB group (n = 14)	Controls (n = 42)	P
Age (years)	10.5 ± 3.7	9.9 ± 3.1	0.401
Sex (F:M)	8 : 6	23 : 19	-
Z-Height	-1.4 ± 1.6	0.3 ± 0.9	< 0.001
Z-BMI	-1.7 ± 1.7	0.3 ± 1.3	< 0.001
Z-aBMD-Ht L1L4	-1.3 ± 1.1	-0.1 ± 0.9	0.002
Z-aBMD-Ht TBLH	-0.1 ± 0.8	0.3 ± 1.0	0.424
25OHD (ng/mL)	30.1 ± 11.6	25.2 ± 10.7	0.261

Table 1- Clinical and DXA data from patients with EB and controls. Values shown as mean ± SDS. Legend- Z-Height: Height Z-score; Z-Weight: Weight Z-score; Z-BMI: BMI Z-score; Z-aBMD-Ht: Z-score for areal BMD adjusted for height at lumbar spine (Z-aBMD-Ht L1L4) and total body less head (Z-aBMD-Ht TBLH)

	EBS subgroup (n = 6)	DREB subgroup (n = 8)	P
Age (years)	9.9 ± 3.8	10.9 ± 3.8	0.619
Sex (F:M)	3 : 3	5 : 3	-
Z-Height	0.1 ± 1.0	-2.3 ± 1.3	0.004
Z-BMI	-0.2 ± 0.8	-2.9 ± 1.1	0.0005
Z-aBMD-Ht L1L4	-0.4 ± 0.6	-1.9 ± 0.9	0.005
Z-aBMD-Ht TBLH	-0.2 ± 0.8	-0.4 ± 1.3	0.238
25OHD (ng/mL)	25.6 ± 10.9	33.3 ±11.8	0.277

Table 2- Clinical and bone DXA data from patients with EB simplex (EBS) and dystrophic recessive EB (DREB). Values are shown as mean ± SDS.
Same legend used for Table 1

Two female patients with DREB presented lumbar spine fractures:
-1: 11.7 years, Z-Height -4.6 SDS; Z-BMI -4.7 SDS, Z-aBMD-L1L4 -2.3
-2: 16.1 years, Z-Height -2.4 SDS; Z-BMI -2.7 SDS; Z-aBMD-L1L4 -2.0

Low mobility was significantly associated with lower height, BMI and L1L4 aBMD Z-scores, as presented in table 3.

	Moderate mobility subgroup (n = 4)	Low mobility subgroup (n = 10)	P
Z-Height	0.0 ± 0.9	-1.9 ± 1.5	0.04
Z-aBMD-Ht L1L4	-0.3 ± 0.6	-1.7 ± 1.0	0.021

Table 3- Clinical and bone DXA data from patients with EB grouped according the physical mobility pattern. Values are shown as mean ± SDS. Same legend used for Table 1

Table 4 shows the clinical variables which presented significant statistical correlation with aBMD-Ht-L1L4

Clinical Variable	r	P
Z-Weight	0.718	0.004
Z-Height	0.637	0.014
Z-BMI	0.607	0.021

Table 4- Clinical variables correlated with low bone mass in L1L4 site.

No correlation was found between aBMD-Ht-L1L4 and 25OHD.
Z-aBMD-Ht-TBLH presented no statistical correlation with anthropometrical or biochemical parameters.
When comparing clinical and DXA data, no statistical difference was found between females and males.

Conclusion

This group of children and adolescents with EB presented lower L1L4 bone mass when compared with healthy controls.

Growing patients with DREB tend to be smaller, thinner, less-active and to have lower aBMD-Ht-L1L4 than the EBS ones.

Disease severity and low physical mobility were clinical parameters significantly associated with compromised nutritional status and reduced L1L4 bone mass.

Clinical osteoporosis is not only a potential but an actual occurring event among paediatric patients with DREB.

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All authors declare no conflict of interest

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