GROWTH AND PUBERTY IN PATIENTS WITH OSTEOGENESIS IMPERFECTA

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INTRODUCTION

- Osteogenesis imperfecta (OI) is a heritable systemic connective tissue disorder characterized by low bone mass, bone fragility, impaired linear growth, short stature, and bone deformities.
- Patients with OI are classified by the Sillence classification that designates patients based on clinical features and severity of the disease.

AIM

The study aims to evaluate growth and pubertal characteristics of 83 patients with OI.

RESULTS

- 83 (31 female/52 male) patients were enrolled.
- The median follow-up duration was 4.7 (0.6-17.7) years.
- 51 out of 83 patients (61.4%) received bisphosphonate therapy.
- The median Z-score of the bone mineral density improved in patients with OI-I and OI-III with the treatment.
- During follow-up, height-SDS significantly increased in both OI-I and OI-III on treatment; however, final adult height SDS of patients did not improve.
- The frequency of overweight and obesity was found to be increased at the last evaluation compared to the admission.
- The rate of precocious puberty (PP) and early puberty (EP) were 20% and 10% in girls, and they were 15.7% and 47.3% in boys, respectively.

Table-1. Anthropometric, clinical and laboratory characteristics at admission

	Type-I (n=43)	Type-III (n=36)	Type-IV (n=3)	Type-V (n=1)	p-value
Birth characteristics					
Gender (F/M)	14/29	16/20	½	0/1	0.5
Consanguineous marriage, n(%)	8 (18.6%)	19 (52.7%)	1 (33.3%)	1	0.01
Gestational age (week)	40 (30-40) (n=26)	40 (33-40) (n=24)	40 (n=1)	40	0.7
Birth status , n(%)					
SVD	24 (55.8%)	19 (52.7%)	2 (66.6%)		-
C/S	19 (44.2%)	17 (47.3%)	1 (33.3%)		
Birth-weight SDS	-0.9 (-4.4 and 1.6) (n=23)	-0.8 (-6 and 2.2) (n=23)	-0.3 (n=1)	-2.9	0.9
SGA n,(%)		3 (13.1 %)	-	1	
AGA n (%)	5 (21.7%)	19 (82.6%)	1 (100%)		
LGA n(%)	18 (78.2%)	1 (4.3%)	-		
At admission	-				
Age (years)	3.9 (0.1-13.1)	0.6 (0.0-7.5)	15 (2.7-15.5)	0.4	0.01
HC-SDS	-0.03 (-2.5 and 2.1)	-1.5 (-4.1 and 1.3)	0.3 (-0.2 and 0.8)	0.5	0.012
Height-SDS	-0.6 (-3 and 1.6)	-2.8 (-10 and 0.8)	-1.5 (-1.6 and 0.3)	-1.2	<0.001
BMI-SDS	-0.2 (-3.3 and 3.9)	0.03 (-8.6 and 2.5)	0.8 (0.5 and 1.5)	0.3	0.09
Low	5 (11.6%)	1 (2.8%)	-	-	
Normal	33 (76.7%)	25 (69.4%)	2 (66.6%)	1	
Overweight	3 (6.9%)	7 (19.5%)	1 (33.3%)	-	
Obese	2 (4.6%)	3 (8.3%)	-	-	
Pubertal stage (Tanner) (n=)					
I	39	32	1	1	
II-III-IV	4	2	1		
V	0	2	1		
Blue sclera, n (%)	37 (86%)	24 (66.6%)	2 (66.7%)	1	0.5
Bone Deformity n (%)	19 (44.1%)	29 (80.5%)	1 (33%)	-	0.01
Time of the first fracture (years)	2 (0.5-10)	0.1 (0.0-1.5)	11.5 (9-13)	2	<0.001
Number of fractures, n (%)	32 (74.5%)	22 (61.1%)	1 (33.3%)	1	0.09
1-5	7 (16.2%)	3 (8.4%)	1 (33.3%)		
5-10	4 (9.3%)	11 (30.5%)	1 (33.3%)		
>10					
BMD Z-score	-3.2 (-10.5 and 0.3)	-4.9 (-11 and -1.8)	-1.1 (-2.9 and -0.3)	0.2	0.006

Table-2 Anthropometric, clinical, and laboratory characteristics at last evaluation

	Type-I (n=41)	Type-III (n=32)	Type-IV (n=3)	Type-V (n=1)	p-value
Last evaluation					
Age (years)	14 (1.3-21.1)	9.3 (0.1-21.8)	16.3 (9.5-16.6)	4.4	0.01
Height-SDS	-1 (-12 and 1)	-3.3 (-13.9 and 0.7)	-1.8 (-0.3 and -2)	-1.1	0.005
BMI-SDS	-0.5 (-3.9-2.6)	0.3 (-3.7-2.8)	-1.5 (-2.5-1.2)	-0.6	0.2
Low	5 (12.2%)	1 (3.1%)	1 (33.3%)	-	
Normal	26 (63.4%)	22 (68.8%)	1 (33.3%)	1	
Overweight	3 (7.3%)	7 (21.9%)	1 (33.3%)	-	
Obese	7 (17.1%)	2 (6.2%)	-	-	
BMD Z-score	-1.3 (-3.8 and 1.2)	-2.4 (-7.2 and 0.4)	-2.3 (-4.2 and -1.1)	0.6	0.006
Characteristics of patients' FAH					
Patients achieved FAH (n=)	12 (4F/8M)	7 (3F/4M)	2 (1F/1M)	-	-
FAH-SDS	-1.2 (-3.4 and 0.5)	-5.7 (-13.9 and -3.3)	-0.3 and -2	-	0.02
Δ FAH-TH SDS	-0.3 (-3.1 and 1.4)	-4.4 (-12 and -1.5)	N/A	-	0.01

Table-3. Pubertal features of patients

	Type-I	Type-III	p-value
At onset of puberty	(n=20)	(n=9)	
Age (years)	10 (7.6-14.1)	10.5 (5.7-12.7)	
Female	9.9 (8.4-11.5) (n=5)	9.7 (5.7-11.1) (n=5)	0.6
Male	10.1 (7.6-14.1) (n=15)	10.8 (9.8-12.7) (n=4)	0.4
Height-SDS	-1.2 (-5.1 and 2)	-2.1 (-10 and -0.2)	0.19
BMI-SDS	-0.5 (-2.5- 2.6)	-0.6 (-3.4-2.4)	0.3
Low	2 (10%)	1 (11.1%)	
Normal	12 (60%)	4 (44.4%)	
Overweight	2 (10%)	1 (11.1%)	
Obese	3 (15%)	2 (22.2%)	
Pubertal status			-
Delayed	1 (M) (5%)	-	
Normal	8 (3F/5M) (40%)	5 (4F/1M) (55.5%)	
Early	8 (2F/6M) (40%)	3 (3M) (33.3%)	
Precocious	3 (M) (15%)	1 (F) (11.1%)	
At the end of puberty	(n=12)	(n=7)	
Age (years)			*
Female	14.6 (13.3-15.5) (n=4)	15.5 (13.6-16) (n=3)	
Male	15.4 (12.5-17.8) (n=8)	16.3 (16.2-17.2) (n=4)	
Height-SDS	-1.2 (-3.4 and 0.5)	-5.7 (-13.9 and -3.3)	0.02
BMI-SDS	-0.2 (-3.3 and 2.1)	1.4 (-2.4 and 1.9)	0.5
Low	1 (8.3%)	1 (14.4%)	
Normal	6 (50%)	4 (57.1%)	
Overweight	4 (33.3%)	2 (28.5%)	
Obese	1 (8.3%)	-	
Age at menarche	12.6 (10.6-14) (n=4)	12.3 (11.5-13) (n=3)	*
Duration of puberty (years)	4.9 (3.7-5.3)	4.5 (4.1-4.7)	*
Female	4.4 (3.5-4.7)	5.1 (4.7-5.4)	
Male			
Pubertal height gain (cm)	22.3 (12.8-24.5)	16 (12.2-21.5)	*
Female	26.1 (19.2-32)	24.2 (17-26.3)	
Male			

† F; female, M; male, SVD; Spontaneous vaginal delivery, C/S; Caesarean sections, SGA; Small for gestational age, AGA; Appropriate for gestational age, LGA; Large for gestational age, SDS; standard deviation score, BMI; body mass index, HC; head circumference, BMD; Bone mineral density, TH; Target height, FAH; Final adult height, Δ FAH-TH SDS; The height SDS difference between FAH and TH, N/A; Not applicable

‡ Median and minimum-maximum range or % values are given.

**p-value was not computed due to insufficient sample size*

METHOD

- This study was designed as a retrospective study involving children with OI who received care at the Pediatric Endocrinology Department of Istanbul University Faculty of Medicine.
- Medical charts of patients who were followed up every 3-6 months between 1992-2019 were evaluated.
- Demographic findings, data on birth status (gestational age, birth weight, and length), clinical features, growth and pubertal data, and laboratory findings were gathered from medical files.

CONCLUSIONS

- FAH-SDS did not improve despite remarkable amelioration in BMD Z-scores on therapy.
- There is a trend toward earlier puberty in OI patients, and the frequency of overweight and obesity was found to be increased over time.
- Reduced growth, significant weight gain over time due to impaired mobility, and high frequency of PP/EP require effective interventions to improve mobility and functional parameters as early as possible in children with OI

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