CHILDHOOD GROWTH ADVANCEMENT IN GIRLS WITH PREMATURE ADRENARCHE HERALDS ANABOLIC EFFECTS BY ADULTHOOD

Jani Liimatta[1] // Pauliina Utriainen[1] // Tomi Laitinen[2] // Raimo Voutilainen[1] // Jarmo Jääskeläinen[1]

[1]Department of Pediatrics, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland
[2]Department of Clinical Physiology and Nuclear Medicine, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland

BACKGROUND AND AIM

Prepubertal children with premature adrenarche (PA) have often tall stature, advanced bone maturation, and a tendency to be overweight (1), and PA girls tend to have higher fat mass and BMI also at pubertal age (2,3). It has been speculated that PA may lead to unfavourable outcome, including obesity-related metabolic disturbances (4), but the data on long-term outcome of PA are insufficient. The main aim of this work was to describe body composition in young adult females with a history of PA.

METHODS

This prospective case-control study included 30 PA and 42 control females, who were born mostly full-term and appropriate for gestational age. They were evaluated first at the median age of 7.6 years (5) and now at 18.1 years. Main outcome measures were body mass index (BMI), body fat mass and percentage, lean and muscle mass, and bone mineral density (BMD; areal at prepuberty, total body excluding the head in adulthood). BMDs and body fat, lean, and muscle masses were measured using dual-energy X-ray absorptiometry. Additionally, determinants for adult body composition parameters were analysed using linear regression models.

RESULTS

Compared to the controls at prepubertal age, the PA females had higher BMI standard deviation score (SDS) and fat mass and percentage, but similar BMI SDS -adjusted areal BMDs, lean and muscle mass (Table 1). In adulthood, BMI, waist measures, and fat mass and percentage were comparable between the study groups. Furthermore, adult lean and muscle mass, and BMD were higher in the PA than control females, also after adjustment for BMI (Table 1). Among all females, higher prepubertal height SDS and serum insulin concentration were determinants for higher adult lean mass and BMD (Table 2).

TABLE 1. Body composition at pre- and postpuberty.

	PA (N=30)	CONTROLS (N=42)	P[a]
AT PREPUBERTY			
Age, years	7.6 (4.8 to 9.1)	7.4 (5.8 to 8.8)	NS[b]
Height, cm	130.5 (8.7)	124.7 (6.8)	0.002
Weight, kg	31.5 (16.7 to 50.5)	24.8 (16.5 to 48.4)	0.001
BMI, kg/m^2	17.1 (14.2 to 25.1)	16.0 (13.2 to 22.5)	0.023
BMI SDS	0.79 (1.30)	0.10 (1.10)	0.020
Fat mass, kg	7.2 (1.6 to 17.6)	4.2 (2.0 to 16.4)	0.008
Fat percentage	21.8 (9.7 to 38.2)	17.3 (9.2 to 33.4)	0.023
Lean mass, kg	24.3 (4.2)	21.7 (3.0)	0.006/NS[b]
Muscle mass, kg	22.6 (4.1)	20.2 (2.8)	0.006/NS[b]
BMD, lumbar spine, g/cm^2	0.72 (0.08)	0.67 (0.07)	0.015/NS[b]
BMD, femoral neck, g/cm^2	0.73 (0.09)	0.68 (0.10)	0.045/NS[b]
BMD, femur, g/cm^2	0.75 (0.10)	0.71 (0.07)	NS/NS[b]
AT POSTPUBERTY			
Age, years	18.1 (16.5 to 23.5)	18.1 (16.9 to 19.8)	NS
Height, cm	167.2 (6.8)	164.5 (5.1)	NS
Weight, kg	63.3 (47.4 to 115.0)	59.8 (47.5 to 88.4)	0.014
BMI, kg/m^2	22.8 (18.4 to 42.2)	21.6 (18.5 to 32.5)	NS
Waist circumference, cm	75.5 (64.5 to 108.7)	72.1 (53.0 to 92.0)	NS
Waist-to-height ratio	0.46 (0.38 to 0.66)	0.44 (0.33 to 0.56)	NS
Waist-to-hip ratio	0.81 (0.71 to 0.90)	0.79 (0.62 to 0.94)	NS
Fat mass, kg	23.3 (11.7 to 55.5)	19.2 (5.8 to 42.7)	NS
Fat percentage	36.5 (24.4 to 53.6)	32.4 (11.4 to 49.3)	NS
Lean mass, kg	43.8 (6.1)	40.3 (3.2)	0.001/0.025[b]
Muscle mass, kg	41.1 (5.8)	37.8 (3.0)	0.005/0.032[b]
BMD, g/cm^2	1.18 (0.06)	1.13 (0.07)	<0.001/0.004[b]
BMD SDS	0.74 (0.77)	0.01 (0.98)	0.001/0.008[b]

Values are expressed as mean (SD) or median (range). As part of a larger original cohort, prepubertal data have been reported previously in Utriainen et al. 2009 (5). From other aspects than in the present study; heights, weights, BMIs, and waist measures at adult age have been reported previously in Liimatta et al. 2018 (6) [a] Independent samples t-test or Mann-Whitney U test; [b] BMI (BMI SDS at prepubertal age) -adjusted using the one-way ANCOVA. NS, non-significant.

TABLE 2. Determinants for higher adult lean mass and BMD in all females of the study.

		LEAN BODY MASS SDS				BMD SDS			
		Standardized B	P (variable)	R^2	P (model)	Standardized B	P (variable)	R^2	P (model)
MODEL 1	Birth length SDS	0.082	NS	0.557	<0.001	-0.243	NS	0.417	<0.001
	Birth weight SDS	-0.30	NS			0.030	NS		
	Prepubertal height SDS[a]	0.627	<0.001			0.567	<0.001		
	Prepubertal BMI SDS[a]	0.174	NS			0.097	NS		
MODEL 2	Serum DHEAS SDS[a]	-0.083	NS	0.246	0.005	0.247	NS	0.330	<0.001
	Serum Androstenedione SDS[a]	0.015	NS			-0.146	NS		
	Serum Insulin SDS[a]	0.459	0.001			0.536	<0.001		
	Serum IGF-1 SDS[a]	0.124	NS			0.037	NS		

All models are adjusted for age at examination in childhood. [a] Anthropometric and biochemical parameters at prepuberty (median age 7.6 years). NS, non-significant.

CONCLUSIONS

In our cohort, PA is associated with long-term anabolic development as the relative adiposity, compared to peers, decreases and muscularity and BMD increase, in PA females from childhood by early adulthood. This modulation is mostly determined by advanced childhood growth and higher prepubertal serum insulin concentration, rather than adrenal androgen levels. Limitations of the present study, due to small sample size, may hide some differences between the study groups, and further studies are needed to clarify these issues.

CONTACT INFORMATION
jani.liimatta@kuh.fi
+358 45 639 0483

UNIVERSITY OF EASTERN FINLAND

1. Utriainen P, et al. Premature adrenarche – a common condition with variable presentation. Horm Res Paediatr. 2015;83:221-31.
2. Ibáñez L, et al. Fat distribution in non-obese girls with and without precocious pubarche: central adiposity related to insulinaemia and androgenaemia from prepuberty to postmenarche. Clin Endocrinol (Oxf). 2003;58:372-9.
3. Potau N, et al. Fasting insulin sensitivity and post-oral glucose hyperinsulinaemia related to cardiovascular risk factors in adolescents with precocious pubarche. Clin Endocrinol (Oxf). 2003;59:756-62.
4. Ibáñez L, et al. Clinical spectrum of premature pubarche: links to metabolic syndrome and ovarian hyperandrogenism. Rev Endocr Metab Disord. 2009;10:63-76.
5. Utriainen P, et al. Body composition and bone mineral density in children with premature adrenarche and the association of LRP5 gene polymorphisms with bone mineral density. J Clin Endocrinol Metab. 2009;94:4144-51.
6. Liimatta J, et al. Trajectories of growth and serum DHEAS and IGF-1 concentrations in girls with a history of premature adrenarche: attenuation of the phenotype by adulthood. Front Endocrinol. 2018;9:375.