Higher dehydroepiandrosterone levels in prepubertal children born very preterm and adequate for gestational age

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Objetive

To evaluate the impact of gestational age and birthweight on dehydroepiandrosterone and dehydroepiandrosterone-sulfate (DHEA and DHEAS) in children born very preterm (VPT) appropriate for gestational age (GA) compared to children born at term (T).

Subjects and methods

We recorded anthropometric parameters in 72 VPT (< 32 GA) and 41 T (≥ 38 GA) aged 5.0 to 8.5 years. Birthweight standard deviation scores (BW-SDS) were calculated using INTERGROWTH-21st standards and Body Mass Index (BMI) percentile according to WHO references. Fasting insulin and Insulin-like Growth Factor 1 (IGF-1) were measured by automated immunoassay, and DHEA, DHEA-S and cortisol by mass spectrometry (LC-MS/MS).

Results

Table 1: General characteristics of the study population

	PRETERM (n=72)		TERM (n=41)		p value
	mean	SD	mean	DS	
Age (years)	6,60	0,90	6,70	1,00	0,535
Bone age (years)	7,20	1,40	7,20	1,30	0,903
Height (SDS)	-0,19	0,86	0,10	1,03	0,109
Abd. circumference (cm)	58,50	7,40	58,50	7,10	0,982
BMI (percentile)	59,00	32,00	64,00	29,00	0,476
Gestational age (weeks)	29,00	2,00	39,00	1,00	<0,001
Birth weigth (SDS)	0,40	1,03	0,52	0,72	0,512
Birth lengh (SDS)	-0,23	1,23	0,56	1,10	<0,001
Systolic BP index	1,04	0,10	1,03	0,08	0,578
Diastolic PB index	1,04	0,12	1,03	0,09	0,803

Table 2: Distribution of adrenal steroids by gestational age

	PRETERM (n=72)		TERM (n=41)		p value
	mean	SD	mean	SD	
ACTH (pmol/L)	4,71	3,41	4,19	2,92	0,428
Cortisol (nmol/L)	207,70	75,90	217,40	75,80	0,517
17 OH Progest. (nmol/L)	0,85	0,46	0,96	0,48	0,263
DHEA (nmol/L)	6,70	3,97	4,44	2,14	0,001
DHEA-S (nmol/L)	862,64	833,49	633,53	450,97	0,107
DHEA-S/DHEA ratio	132,08	99,57	142,62	67,18	0,548
DHEA / Cortisol	0,034	0,020	0,023	0,013	0,003

**Table 3:** Distribution of DHEA and DHEA/cortisol ratio by sex and gestational age

FEMALES	PRETERM (n=26)		TERM (n=23)		p value
	mean	SD	mean	SD	
DHEA (nmol/L)	6,4	3,2	4,2	1,7	0,005
DHEA / Cortisol	0,033	0,014	0,023	0,014	0,019
MALES	**PRETERM (n=46)**		**TERM (n=18)**		**p value**
	mean	DS	mean	DS	
DHEA (nmol/L)	6,88	4,39	4,74	2,63	0,058
DHEA / Cortisol	0,035	0,023	0,023	0,012	0,051

When separated by sex, the diferences observed in DHEA and DHEA/cortisol ratio in children born very preterm, were stronger in females.

Conversion factor multiply by
 DHEA nmol/L x 28.84= ng/dl,   DHEAS nmol/L x 0.0368 = µgr/dl,
Cortisol nmol/L x 0.0363=µgr/dl , 17 OH prog nmol/Lx 0.3304= ng/ml

Fig.1: DHEA, DHEA-S and Cortisol in children born very preterm and adequate for gestational age, compared to children born at term
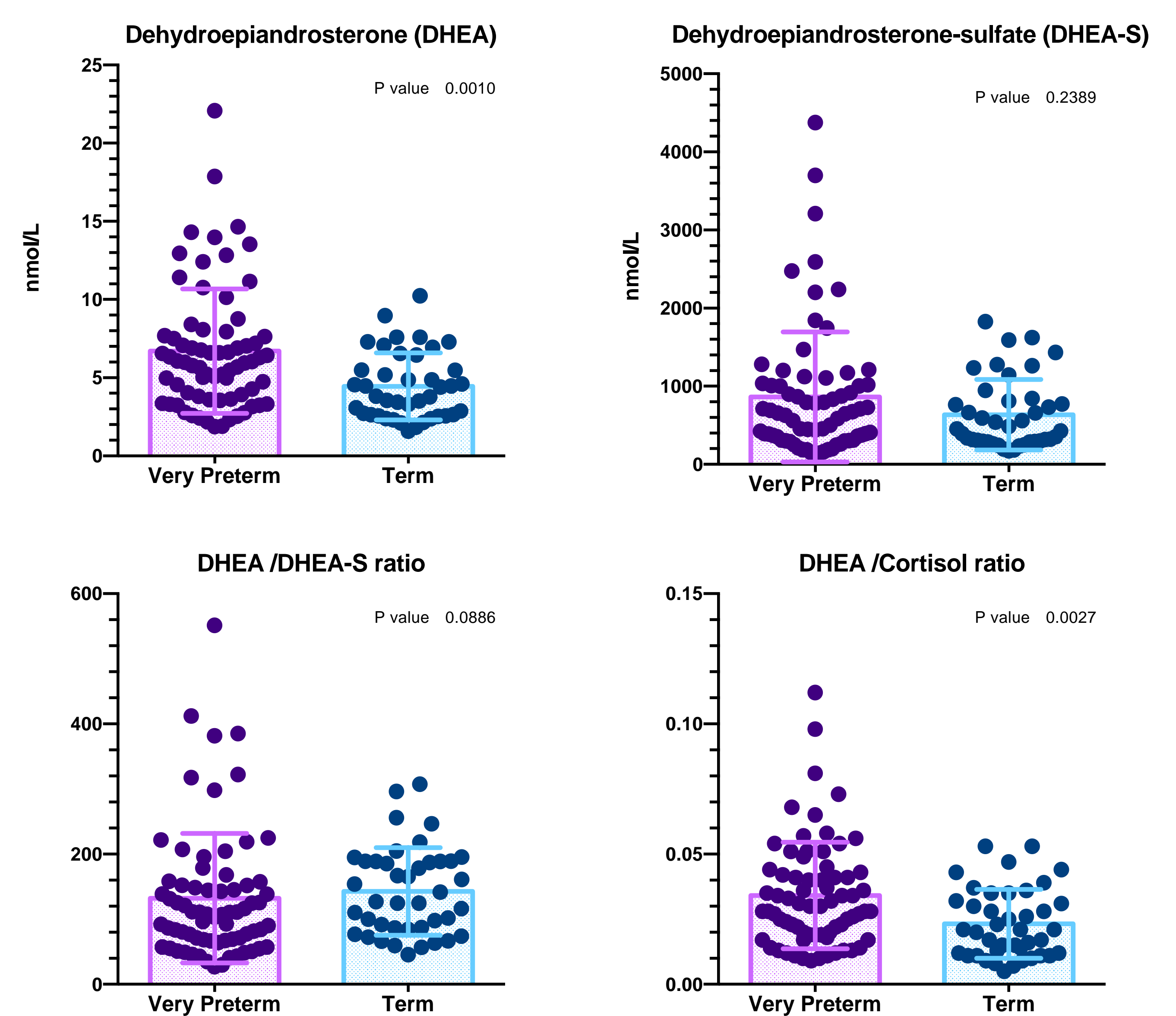
In VPT higher DHEA concentrations and higher DHEA/cortisol ratios were observed compared to T, but not for cortisol and DHEA-S

Table 4: Pearson correlation beetween DHEA and DHEA-S with clinical and biochemical variables by sex

	FEMALES (n=49)		MALES (n=64)	
	Log DHEA	Log DHEA-S	Log DHEA	Log DHEA-S
Gestational age	-0.375**	-0.129	-0.260*	-0.122
Birth weigth -SDS	-0.051	-0.241	0.017	0.105
Age	0.141	0.317*	0.385**	0.400**
BMI-percentile	-0.109	-0.131	-0.057	0.038
Abd. circumference	0.134	0.260	0.124	0.169
Log Insulin	0.060	0.146	-0.087	0.098
Log HOMA-IR	0.050	0.135	0.075	0.100
Log IGF-1	0.005	0.120	-0.139	0.187

* $p < 0.05$; ** $p < 0.001$

Gestational age was inversely associated to DHEA in both sexes. This association persisted after controlling by cronological age. On the other hand, no association were observed between DHEA with birth weight-SDS, BMI percentile, abdominal circumference, insulin and IGF1.

Conclusion

- **Higher DHEA concentrations were observed in children who were born very preterm, especially in females, independently of birthweight, chronological age, BMI and abdominal circumference.**
- **Lower gestational age could determine a higher activity of the reticulata which could contribute to an earlier pubertal maturation.**