

Early adrenal activation in boys with Cystic Fibrosis may explain impaired final height

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Background

Rapid BMI increase in early childhood was found to be a contributing factor for impaired final height in boys with Cystic Fibrosis (CF). This may be explained by early adrenarche triggering an accelerated bone maturation resulting in a compromised growth spurt during puberty, comparable to children with SGA. In healthy Dutch boys, adrenarche starts from the age of 9 years with DHEAS > 1 µmol/L. In Dutch girls, the onset of adrenarche is from age 8 onwards.

Aim

We aimed to analyse the timing of adrenarche in boys with CF and associate early rapid BMI increase to timing of adrenarche. Also, we aimed to analyse differences in DHEAS-levels between boys and girls with CF.

Methods

Boys and girls with CF, aged 8-9 years, visiting the CF expertise center UMCU were included. Since 2018, anthropomorphic, pubertal and endocrine data were collected. Early adrenal activation in boys was defined as a DHEAS ≥ 1 µmol/L before the age of 9 years.

Table 1 Characteristics of the study population at time of DHEAS-measurement

	Boys (n=13)	Girls (n=13)
Age (y)*	8.55 ± 0.27	8.52 ± 0.31
Homozygous ΔF508 (n, (%))	6 (46.2)	3 (23.1)
CFRD (n, (%))	2 (15.4)	2 (15.4)
CFRLD (n, (%))	1 (7.7)	1 (7.7)
Height-SDS	-0.15 ± 1.02	-0.59 ± 0.82
Weight-SDS	0.09 ± 1.16	0.02 ± 0.93
BMI-SDS	0.08 ± 0.96	0.35 ± 0.85
ΔBMI-SDS between 1-6 y	0.36 ± 0.91 (n=11)	0.39 ± 1.08 (n=12)
ΔBMI-SDS between 1-6 y > 0.67	4 (30.8) (n=11)	5 (38.5) (n=12)
SDS (n, (%))		
FEV1pred%	92.3 ± 21.2 (n=11)	93.9 ± 21.2
Bone-age (yrs) (median, interquartile range)	8.30 [7.00 – 11.50] (n=11)	8.75 [7.50 – 10.50] (n=8)
Corticosteroid use (n, %)*A	0 (%)	5 (38.5%)

ys = years; n = number; CFRD = cystic fibrosis related diabetes; CFRLD = cystic fibrosis related liver disease; FEV1pred = the percentage of the predicted FEV1 value

Values are means and standard deviations unless otherwise indicated.

*A statistically significant difference was seen between boys and girl at P < 0.05 using the Chi-square test

A Corticosteroid use six months before DHEAS-measurement

Table 2 Androgen measurements

	Boys (n = 13)	Girls (n=13)	P-value
DHEAS-levels (µmol/L) (median, range)	1.30 [0.30 – 6.30]	0.96 [0.25 – 1.80]	0.20
DHEAS-levels ≥ 1 µmol/L (n, %)	8 (61.5%)	6 (46.2%)	0.431
Androstenedione-levels (nmol/L) (median, range)	0.64 [0.20 – 1.45] (n=11)	0.41 [0.20 – 1.00] (n=12)	0.26

Table 3 Bone maturation (bm) and DHEAS concentration

	Boys (n=11)			Girls (n=8)		
	BM + (n=5)	BM - (n=6)	P-value	BM + (n=4)	BM - (n=4)	P-value
Δbone vs chronological age (yrs)	1.55 ± 0.97	-0.88 ± 0.38	0.003	0.75 ± 0.72	-0.25 ± 0.21	0.063
DHEAS-level (µmol/L)	3.56 ± 2.38	1.03 ± 0.56	0.032	1.60 ± 0.16	0.60 ± 0.24	0.001
Height-SDS	0.41 ± 0.97	-0.32 ± 0.99	0.25	-0.55 ± 1.19	-0.56-0.54	0.99

BM+ = with accelerated bone maturation; BM- = without accelerated bone maturation; yrs = years. Values are means and standard deviations unless otherwise indicated.

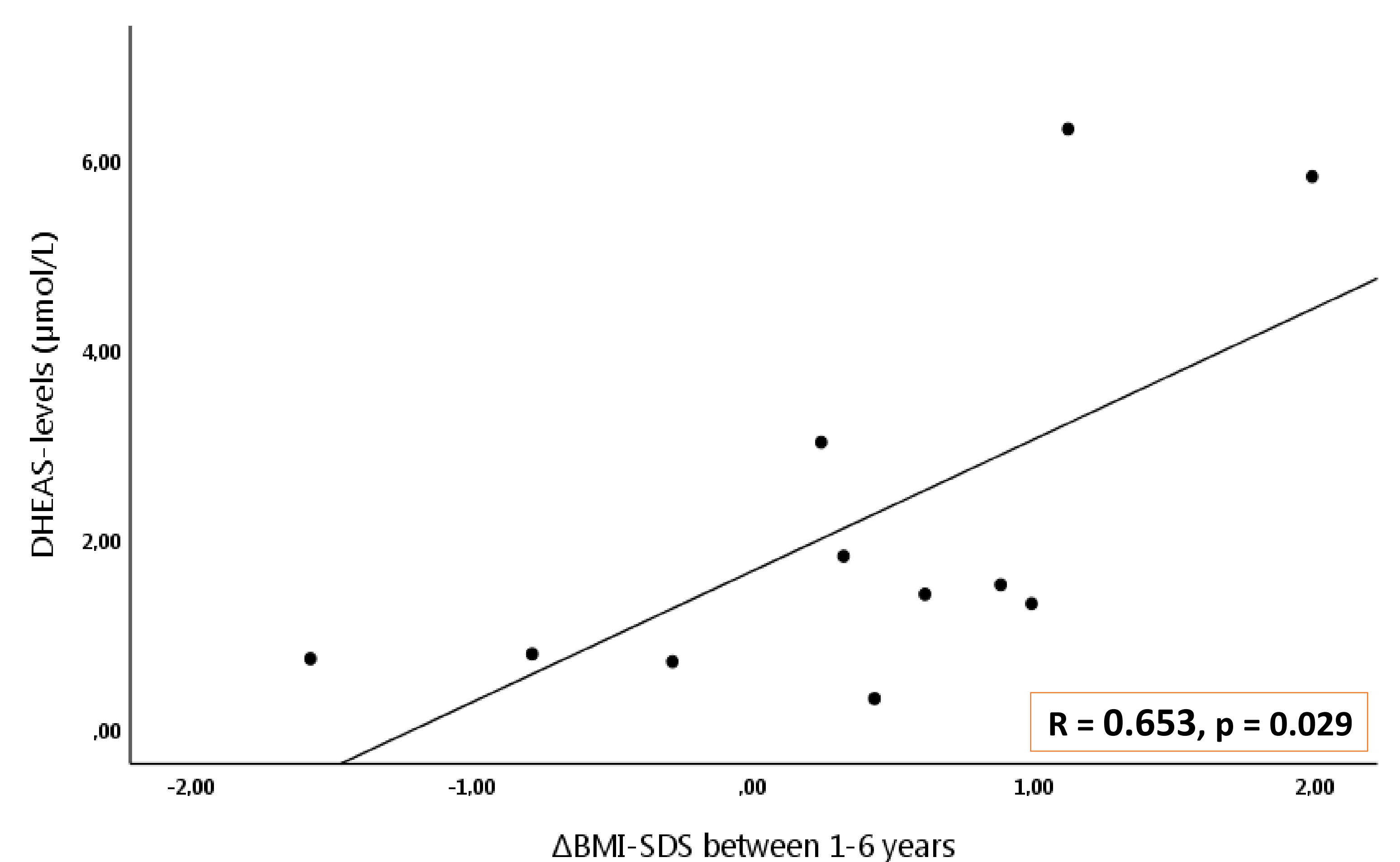


Figure 1. DHEAS-levels (µmol/L) plotted against ΔBMI-SDS between 1-6 yrs in boys

Conclusion

In this small cohort, **61.5 % of boys with CF between 8-9 years had an early rise of DHEAS, which could be correlated to ΔBMI-SDS between 1-6 years.** In comparison to girls, boys had higher DHEAS-levels. Early adrenal activation may be one of the factors contributing to early and suboptimal growth during puberty and impaired final height in boys with CF.