INTRODUCTION
Exposure to chronic stress and hypercortisolism is associated with decreased leukocyte telomere length (LTL), a marker for accelerated biological aging and cardiovascular disease. Children with congenital adrenal hyperplasia (CAH) are treated with glucocorticoids. It is currently not known whether glucocorticoid treatment in CAH is associated with LTL. Moreover, it is unknown whether treatment quality (undertreatment, optimal treatment, or overtreatment) is associated with LTL.

AIM
To investigate LTL in children with CAH and its relation with CAH subtype, daily glucocorticoid dose and treatment quality.

METHODS
This prospective observational study included children and adolescents, aged 1-18 years, with genetically confirmed CAH due to 21-hydroxylase deficiency. LTL was determined at two consecutive outpatient clinic visits (mean 4.1 ± 0.7 months apart) by monochrome multiplex quantitative real-time polymerase chain reaction. At each visit, all subjects underwent detailed clinical (height, weight) and endocrinologic evaluation, including determination of 17-hydroxyprogesterone and androstenedione concentrations, and were classified as undertreated, optimally treated or overtreated accordingly. BMI z-score (BMI-z) was calculated according to International Obesity Task Force definitions. The influence of clinical factors on LTL was investigated using linear mixed models.

RESULTS
We studied 78 children and adolescents prospectively. Of those, 33 (42%) were girls, 63 (81%) had classic CAH, 70 (90%) received hydrocortisone and 8 (10%) prednisolone. Median age at first visit was 12.0 years (IQR 6.2-15.1), and median BMI-z 0.51 (IQR -0.16-1.43). Optimal treatment was achieved in 48 (62%) (55%) patients at first and second visit, respectively, versus undertreatment in 22 (29%)/32 (42%), and overtreatment in 7 (9%)/2 (3%). Median LTL at first visit was 1.18 (IQR 1.04-1.40); mean ΔLTL was 0.02 ± 0.09. After adjustment for age, sex, and BMI-z, children with classic CAH had shorter LTL than children with non-classic CAH (coefficient -0.29, 95% CI -0.52; -0.06, p=0.012). In addition, treatment success influenced LTL (global p=0.007): overtreated children had shorter LTL (coefficient -0.07, 95% CI -0.12; -0.03), while undertreated children had similar LTL (coefficient 0.01, 95% CI -0.05; 0.03) compared with children on optimal treatment. Children using prednisolone had shorter LTL than children using hydrocortisone (coefficient -0.34, 95% CI -0.51; -0.16, p<0.001). LTL was not associated with hydrocortisone-equivalent dose.

CONCLUSIONS
In children and adolescents with CAH due to 21-hydroxylase deficiency, LTL is shorter in the classic than in the non-classic form of the disease, as well as in overtreated patients or patients treated with long-acting glucocorticoids. These findings may be attributed to chronic exposure to supraphysiologic glucocorticoid concentrations, and indicate that LTL may be used as a biomarker for monitoring optimal treatment with glucocorticoids.

REFERENCES

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