Variations in Morning Serum Cortisol Levels Based on Sex and Pubertal Status

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Introduction

- Morning cortisol levels <5 µg/dL (<138 nmol/L) indicate likely adrenal insufficiency, while levels >13 µg/dL (>365 nmol/L) may suggest adrenal sufficiency, with levels between 5-13 µg/dL remaining indeterminate[1]; however, these cut-off values remain highly debated in the literature.
- In the pediatric population, the effect of sex and pubertal status on morning cortisol levels remains unclear. This study aims to quantify these relationships.

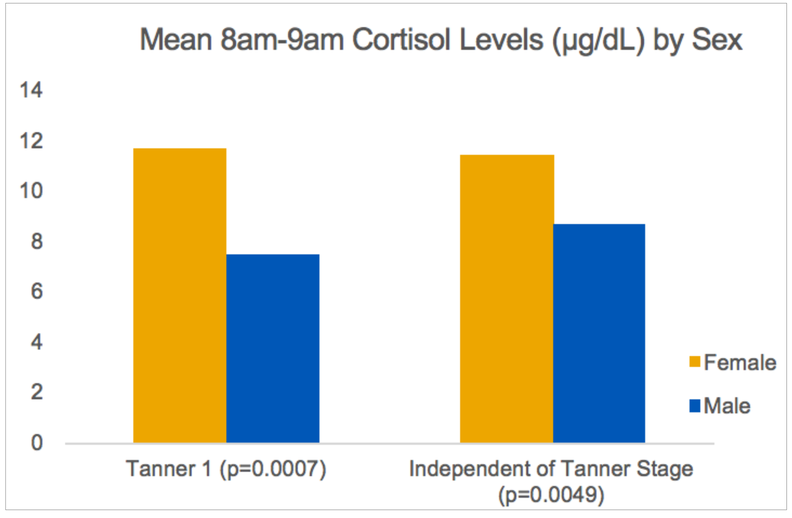
Methodology

- Data was gathered via electronic medical records of 107 patients seen at Children's Mercy Hospital from 11/01/2007 to 11/01/2017.
- Inclusion criteria included: 1) Tanner staging performed by an endocrinologist, 2) serum morning cortisol levels drawn between 8am-9am, 3) high dose ACTH stimulation testing using 250 mcg Cosyntropyn IV and 4) confirmed adrenal sufficiency (cortisol level >18 µg/dL (>500 nmol/L) at 30 or 60 minutes during high dose ACTH stimulation testing).
- Two-tailed t-tests were used to compare 1) mean morning cortisol levels between females and males by Tanner stage, and 2) mean morning cortisol levels between females and males.
- Multivariable linear regression analyses was used to assess 1) sex and tanner stage to morning cortisol level, and 2) morning cortisol level, sex, and Tanner stage to peak cortisol value on ACTH stimulation. Age was excluded due to collinearity with Tanner stage.

Results

Table 1: Characteristics of Study Population

Sex	Female (n=53)	Male (n=54)
Pubertal status	Tanner Stage 1 (Pre-pubertal) (n=58)	Tanner Stage 2-5 (Pubertal) (n=49)



- Mean morning cortisol levels differed between Tanner 1 females and males at 11.69±5.24 µg/dL (322.53±144.57 nmol/L) and 7.47±3.77 µg/dL (206.1±104.01 nmol/L), respectively (p= 0.0007). No difference was seen between Tanner 2-5 females and males (p=0.6096).
- Mean morning cortisol levels differed in females and males independent of Tanner stage at 11.46 ± 5.99 µg/dL (316.18±165.26 nmol/L) and 8.65 ± 3.83 µg/dL (238.65±105.67 nmol/L), respectively (p= 0.0049).

Results (cont.)

- Multivariable linear regression analysis showed sex as a significant predictor of morning cortisol levels, with males having 2.74 µg/dL lower morning cortisol levels than females (p=0.006). Tanner stage was not a significant predictor.
- Multivariable linear regression analysis showed morning cortisol as a significant predictor of peak cortisol value on ACTH stimulation, with each µg/dL increase in morning cortisol level corresponding to a 0.41 unit increase in peak cortisol value on ACTH stimulation (p<0.001). Tanner stage and sex were not significant predictors.

Discussion

- Serum morning cortisol >7 µg/dL (>193 nmol/L) in males and >11 µg/dL (>302 nmol/L) in females could reflect normal cortisol secretion in the pediatric population.
- Morning cortisol levels remain a valuable screening tool for adrenal insufficiency.
- Further investigation is required to determine whether morning cortisol levels require stratification by pubertal status and sex.

References

1: Kazlauskaite R, Evans AT, Villabona CV, Abdu TAM, Ambrosi B, Atkinson AB, et al. Corticotropin Tests for Hypothalamic-Pituitary- Adrenal Insufficiency: A Metaanalysis. J Clin Endocrinol Metab. 2008 Nov 1;93(11):4245–53.