Establishing age, sex, and method related reference range for anogenital distance – a marker of *in utero* androgen action

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Background

Anogenital distance (AGD) is an indicator of androgen action *in utero*. Reduced AGD has been found in males with hypospadias, cryptorchidism, low semen quality and infertility. Its usefulness as a clinical marker in patients with Disorders of Sex Development (DSD) is currently being investigated. However, detailed age, sex and method related reference ranges do not exist. Whether individual (body-size-adjusted) AGD is stable postnatally also remains to be elucidated.

Aims and Method

Aims

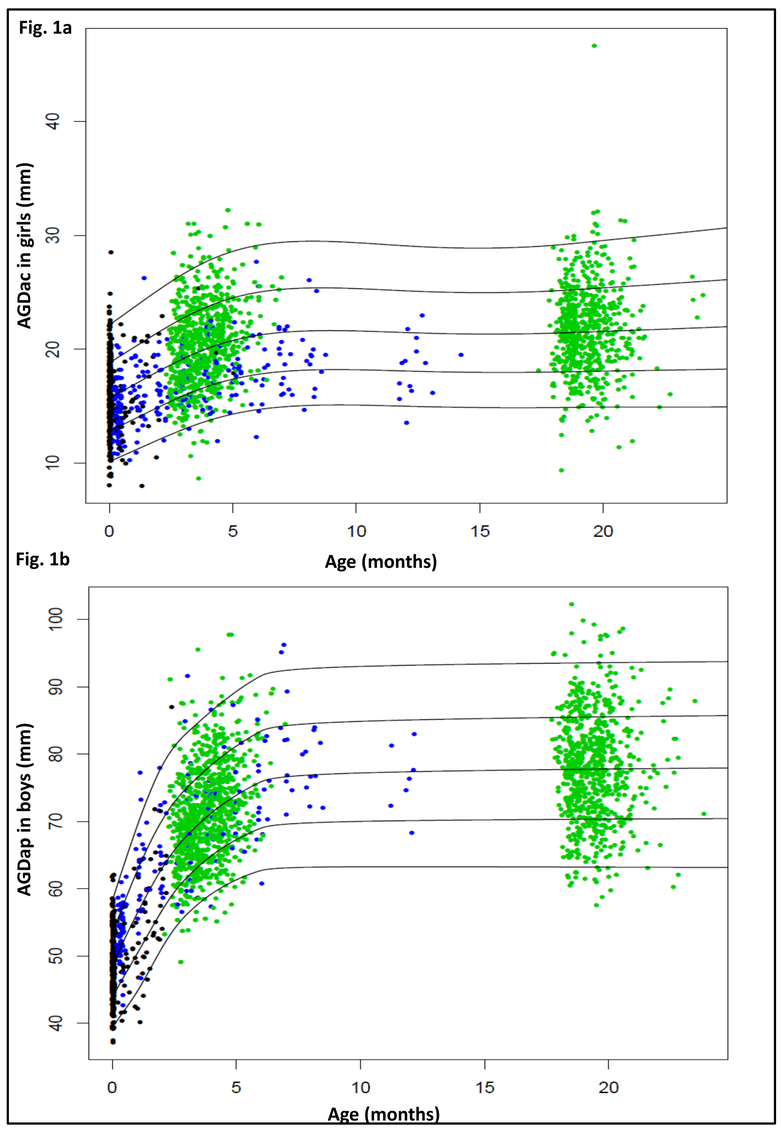
1) To create age, sex and method-related reference ranges for both 'short' (anus-scrotum/fourchette (AGDas/af) and 'long' (anus-penis/clitoris (AGDap/ac) measurement techniques for AGD. 2) To evaluate individual longitudinal changes of AGD in young children.

Method

The International AGD Database contains a total of 7703 AGD examinations performed on 3623 healthy children aged 0-26 months using two different methods (Cambridge and TIDES). Four centers contributed with data 1) The Infant Development and Environment Study (TIDES) 2) Odense Child Cohort 3) Cambridge Baby Cohort 4) COPENHAGEN Minipuberty Study. Reference ranges for AGDas/af and AGDap/ac for both methods were generated using the Lambda-Mu-Sigma (LMS) method. Longitudinal intra-individual variations of AGD were examined using longitudinal observations (146 individuals, 488 observations) of AGD and adjusting for body size (length, weight, body mass index (BMI) and body surface area (BSA)). Coefficients of variation (CVs) were calculated for each individual and then averaged.

Results

We present age-, sex- and method related reference ranges for AGD. E.g. the long AGD in boys (AGDap, TIDES method) increased from birth (49.4 ± 4.8 mm (mean ±2 SD)) to 4 months of age (72.7 ± 6.8 mm) after which it was relatively stable until 20 months, whereas AGDac in girls increased from birth (36.5 ± 3.6) to 4 months of age (39.5 ± 4.8) (Fig. 1). In boys, individual short AGD (AGDas, TIDES method) was relatively stable when adjusting AGD (mm) per body length (cm) or BMI (kg/m^2) from birth to 14 months of age (mean CV of 7.9% and 8.2%, respectively). Similarly, in girls, short AGD (AGDas, TIDES method) was stable from birth to 14 months when adjusting AGD (mm) per body length (cm) and BMI (kg/m^2) (mean CVs of 8.3% for both).



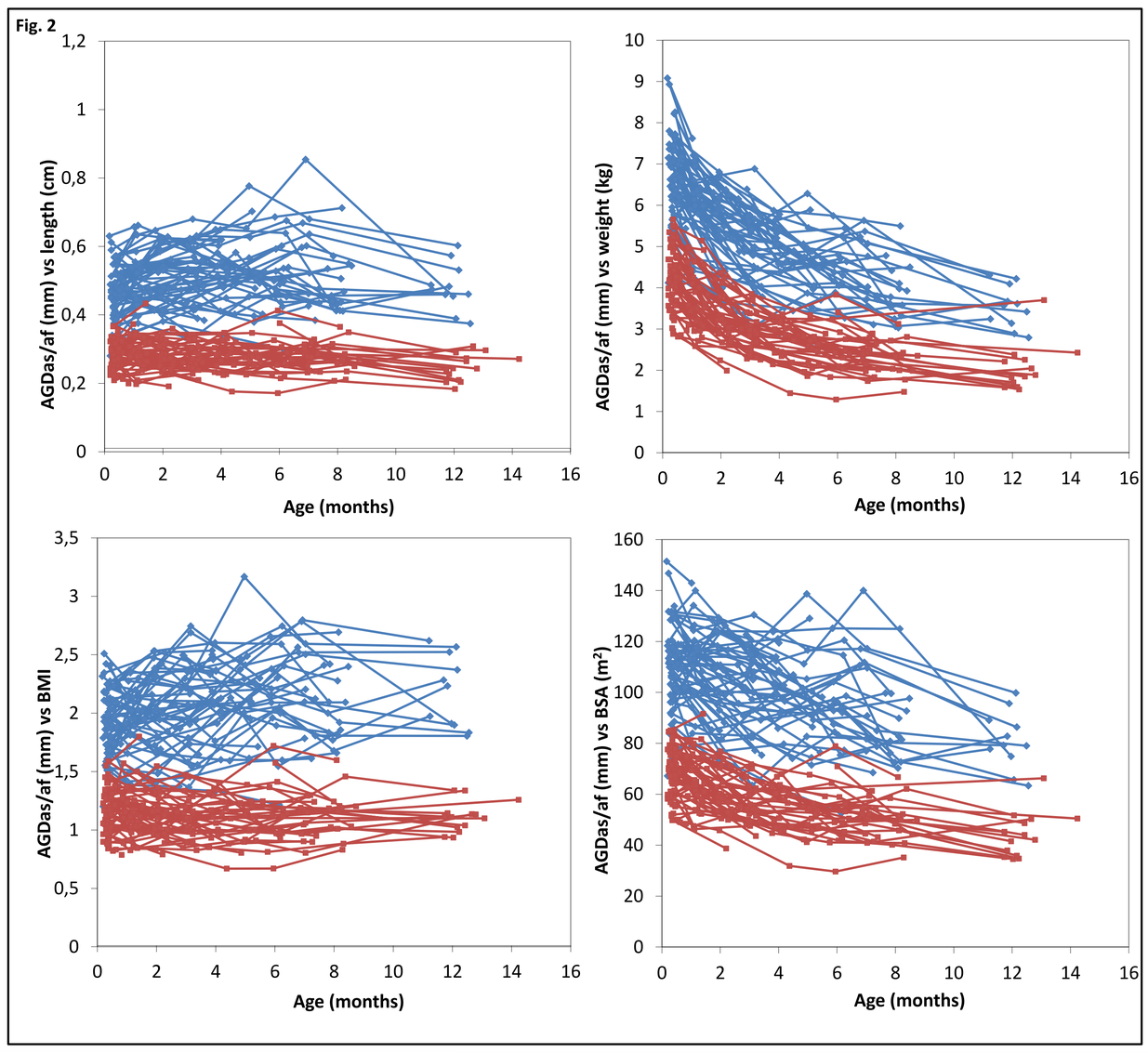


Fig. 1.
An example of age-, sex and method related reference ranges for long AGD (AGDap/ac) in girls (1a) and boys (1b). Black dots represent data from Center 1, green dots represent data from Center 2, and blue dots represent data from Center 4.

Fig. 2.
Longitudinal short AGD measurements (AGDas/af) from Center 4 adjusted for body size in terms of length, weight, BMI, and BSA. Blue lines represent individual boys and red lines represent individual girls.

Conclusion

Intra-individual AGD adjusted for body size remained relatively stable during infancy which supports AGD as a prenatally determined marker. Reference ranges could be used for epidemiological research and may have a clinical application when evaluating prenatal androgen action in DSD patients.

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