

Sex steroids, IGF-I, and vascular morphology from birth to adulthood in individuals born small for gestational age

Akademisk avhandling

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av Kerstin Allvin

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Avhandlingen baseras på följande delarbeten:

- I. **Allvin K**, Ankarberg-Lindgren C, Fors H, Dahlgren J. Elevated serum levels of estradiol, dihydrotestosterone, and inhibin B in adult males born small for gestational age. *J Clin Endocrinol Metab.* 2008 Apr; 93(4):1464-1469.
- II. **Allvin K**, Hellström A, Dahlgren J, Andersson Grönlund M. Birth weight is the most important predictor of abnormal retinal vascularisation in moderately preterm infants. *Acta Paediatr.* 2014 Jun; 103(6):594-600.
- III. **Allvin**, Ankarberg-Lindgren C, Niklasson A, Jacobsson B, Dahlgren J. Altered umbilical sex steroids in preterm infants born small for gestational age. *J Matern Fetal Neonatal Med.* 2019 Apr 18:1-7.
- IV. **Allvin K**, Ankarberg-Lindgren C, Dahlgren J. Minipuberty in moderately to late preterm boys: longitudinal sex steroid and IGF-I data. *Manuscript.*

**SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER**



Sex steroids, IGF-I, and vascular morphology from birth to adulthood in individuals born small for gestational age

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Abstract

Aim: To study whether there is an association between size at birth, sex steroids, IGF-I, and retinal vascular morphology.

Patients and methods: Two different cohorts were studied. In paper I, 25 young adult men born small for gestational age (SGA) were compared to 44 young adult men born appropriate for gestational age (AGA). In papers II–IV, participants were recruited from a cohort of 247 moderately to late preterm infants (137 boys and 110 girls). In paper II, 78 infants underwent an examination of retinal vascular morphology in the neonatal period and IGF-I was determined in umbilical cord blood. In paper III, the steroid hormone pattern in umbilical cord blood from 168 infants (99 boys and 69 girls) was determined by gas chromatography tandem mass spectrometry (GC-MS/MS) and liquid chromatography tandem mass spectrometry. In paper IV, sex steroids were analyzed by GC-MS/MS and IGF-I determined from birth to 10 months corrected age in 98 boys.

Results: In paper I, young men born SGA were found to have elevated serum levels of estradiol and dihydrotestosterone (DHT), possibly due to increased activity of the enzymes aromatase and 5 α -reductase, respectively. Birth weight standard deviation scores correlated inversely with estradiol-to-testosterone ratio and with DHT-to-testosterone ratio at adult age. Catch-up growth from birth to adult age also correlated with estradiol-to-testosterone ratio and with DHT-to-testosterone ratio.

In paper II, birth weight and IGF-I in umbilical cord blood were found to be the most important predictors of abnormal retinal vascularization.

In paper III, boys born SGA had lower estrone levels and girls born SGA had higher androstenedione levels than those born AGA, possibly due to decreased placental aromatase. Infants born SGA of both genders had lower cortisone levels.

In paper IV, boys born SGA had elevated testosterone levels at around the estimated date of birth. A DHT surge during minipuberty was seen, but this was less pronounced in boys born SGA. At 10 months corrected age, testosterone and androstenedione levels correlated to catch-up growth.

Conclusions: Individuals born SGA have an altered sex steroid pattern at different time-points in life. Further longitudinal studies are needed to investigate whether these changes are permanent and have a clinical impact.

Keywords: small for gestational age, preterm, sex steroid, estradiol, testosterone, dihydrotestosterone, glucocorticoid, IGF-I, retina