

Pubertal development in internationally adopted girls:

epidemiological, clinical and biochemical indications of increased risk of precocious puberty due to early central activation of the pituitary-gonadal axis

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This PhD dissertation was accepted by the Faculty of Health Sciences of the University of Copenhagen, and defended on June 14, 2007.

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Dan Med Bull 2007;54:239

ABSTRACT

The study was carried out in Department of Growth and Reproduction, Rigshospitalet, Denmark.

In internationally adopted girls a high frequency of idiopathic precocious puberty as well as a low age at menarche has been reported in retrospective studies. However, epidemiological data as well as prospective clinical studies are lacking. The aims of this study were to estimate the risk of precocious puberty and to estimate ages of entry into all stages of puberty in internationally adopted girls. In addition we aimed to study early clinical and biochemical markers of activation of the hypothalamo-pituitary-gonadal-axis in adopted girls.

The risk of precocious puberty (PP) was estimated in a nationwide register-based study including all cases of PP in the period 1993-2001 identified through The National Patient Registry (N=655). The background population was identified through the Danish Civil Registration System. The risk of developing PP was significantly higher in internationally adopted children (Incidence Rate Ratio (IRR) 10.6 (95% CI 8.0-14.2)) compared to children with Danish background. Adopted children born in South Korea had a low risk of PP (IRR 0.57 (0.08-4.09)) as compared to adoptees originating from all other regions. Children adopted after the age of two years had a significantly higher risk of PP compared to children adopted before two years of age (IRR 35.19 (24.71-50.11) vs. 4.65 (2.91-7.45)).

A clinical, longitudinal study was carried out in a randomly selected cohort of internationally adopted girls (N=276), aged 4-13 years. Participants were examined biannually throughout two years including anthropometrical measurements, evaluation of pubertal stage and blood sampling. The internal genitals were examined through transabdominal ultrasonography. Mean age at onset of puberty was 9.5 years (7.1-12.0) and mean age at menarche was 12.1 (10.2-14.0) years in adopted girls. 16% of adopted girls had breast development before eight years of age. Pubertal development and menarche commenced on average 1.3 years earlier in adopted girls as compared to a reference group of Danish-born girls. The puberty-related rise in LH, FSH and estradiol was detected at earlier ages in adoptees as compared to the reference group. Prepubertal adopted girls aged 5-8.5 (N=99) had significantly higher serum levels of FSH and estradiol as compared to a control group of girls of Danish origin (N=93). Uterine size as well as the number of follicles increased with age in adopted girls, but not in controls of Danish origin.

These studies indicate a highly increased risk of PP in internationally adopted girls, and that early puberty is a general trait in this group, probably mediated by central activation of the pituitary-gonadal axis. The underlying mechanisms are still unknown, but future genetic and chemical analyses can possibly enhance our understanding of this. The high frequency of early maturing adopted girls is a challenge in the medical management of the condition.