Timing of Menarche in Girls Adopted from China: a Cohort Study

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Abstract

Background: Girls adopted internationally from some states have been found to have high rates of early puberty, including early menarche. Explanations for the link between international adoption and early puberty include post-adoption catch-up growth triggering puberty, and under-recorded age.

Methods: We compared menarcheal age in a cohort of 814 girls adopted from China into North America against menarcheal ages in girls in China. Adoptive parents provided survey data on their daughters' weight in 2005 and on menarcheal status and age at menarche in 2011.

Results: Estimated median age at menarche for adopted Chinese girls is 12.37y (95% CI: 11.84-13.00y). Estimated prevalence of menarcheal age ≤10.00y for adopted girls is 3%. These findings are similar to published findings on non-adopted Chinese girls. The distribution of menarche of adopted girls and non-adopted girls at the estimated incidence rates P3-P97 are also similar. Among the 609 girls whose parents reported on their weight shortly after adoption, 148 (24.3%) were –2SD or more below the median weight in the WHO weight-for-age tables. The proportion of these girls who had attained menarche was not statistically different from other girls.

Conclusions: For girls adopted from China, the age of menarche, the percentage of girls attaining menarche <10y and the distribution of menarcheal age are all similar to Chinese girls growing up in China.

Introduction

The possibility of a link between early puberty, including early menarche, and international adoption was first suggested in a case series report on six girls from India and one from Bangladesh adopted into Sweden (Adolfsson & Westphal 1981). The authors hypothesised that puberty may be triggered by the increased metabolic activity of catch-up growth following early deprivation, but also cautioned that the ages of adopted children can be uncertain (Adolfsson & Westphal 1981). Age uncertainty may be a significant issue for children adopted from some states but not others (Hayes 2013). The link between international adoption and early puberty was corroborated by a cohort study of 107 Indian girls adopted into Sweden, which found an increased risk of precocious pubertal onset <8y and menarche <10y (Proos *et al*. 1991). National studies in recipient states of adopted children have also corroborated the link (Krstevska-Konstantinova *et al*. 2001; Teilmann *et al*. 2006; Soriano-Guillen *et al.* 2010).

Menarcheal age provides a notable marker of pubertal timing and is significantly correlated with onset of breast development (Parent *et al*. 2003). The possible existence of a link between international adoption and early puberty, including early menarche, can therefore be tested by comparing the age at menarche of girls adopted from China with girls growing up in China. Here we report on the menarcheal age of 814 girls adopted into the USA and Canada from China.

Methods

Sample

Data from the current study on 814 girls adopted from China into the USA and Canada are compared against reported menarcheal age in 15,388 girls in China (Sun *et al*. 2012), 6,467 girls in southern China (Huen *et al*. 1997) and 20,654 girls in urban China (Ma *et al*. 2009). The adopted girls came from throughout China, although 76% of them were from 9 southern and coastal provinces between Jiangsu and Guangxi, the main area in which the Chinese government

has permitted international adoption. All girls were < 10y at the time of adoption. The study was approved by the University of South Florida Institutional Review Board (IRB#103393).

Procedure

Longitudinal data were collected in 2005 (Survey 1) and 2011 (Survey 2) from the same adoptive parents. In 2005, surveys were sent to 1092 families of both girls and boys adopted from China and returned from 853 (78.1%) families. In 2011, follow-up data (Survey 2) were obtained from 581 (68.1%) of the 853 families. This gave information on age, age at adoption and menarcheal status for 817 girls with an average age of 10.61y (range: 2.02-22.02y), including 730 girls from Survey 1 and 87 girls who were adopted since Survey 1. The results for 814 of these girls are used in statistical analysis. The remaining three girls are considered separately as they had been prescribed leuprolide acetate, a gonadotropin-releasing hormone agonist (GnRHa) that prevents pubertal development.

In Survey 2, the girls' menarcheal status and age at menarche were obtained from the adoptive parents using both *status quo* and recall methods. The parent was first asked to indicate whether or not their daughter had had her first period (yes or no). Where the answer was yes, the parent was then asked to recall the daughter's menarche date as accurately as possible.

Data analysis strategy

To be consistent with the data analysis methods used in all three published studies of Chinese girls, southern Chinese girls and urban Chinese girls, probit analysis of the *status quo* figures using Stata 12 statistics software (StataCorp, College Station, TX, 2011) was used to estimate the distribution of adopted Chinese girls' menarche age, the median and 95% confidence interval (CI). Probit analysis measures the relation between the strength of a stimulus, in this case increasing age, and a certain response to this stimulus, in this case the onset of menses. Results are compared at the percentiles P3, P10, P25, P50, P75, P90 and P97.

Recalled menarcheal age is used to identify the minimum mean age of menarche and to provide an alternative estimate of the proportion of girls attaining menarche < 10y.

According to catch-up theory, girls with early puberty will be of low weight when adopted (Krstevska-Konstantinova *et al*. 2001; Soirano-Guillen *et al*. 2010). To test this theory, adopted Chinese girls' weight distribution at her first post-adoption medical exam was classified in accordance with World Health Organisation (WHO) standard deviation (SD) weight-for-age tables (WHO 2006). There are no significant differences between WHO SD weight curves for girls <10y and weight-for-age reference data for urban Chinese girls (Zong & Li 2013). Chi-square tests, of girls categorised by age at Survey 2, are used to determine if there is a significant difference ($P < .05$) between the menarcheal status of girls below the WHO median weight by at least 2SD at the time of their medical exam and other girls.

Results

Median and Mean Age at Menarche

The median age at menarche of 814 adopted girls is estimated as 12.37y (95% CI 11.84-13.00). This is slightly higher than the estimate of 12.27y for urban Chinese girls and slightly lower than the estimate of 12.43 for Chinese girls. It is almost identical to the estimate of 12.38y for southern Chinese girls (Table 1).

The minimum mean recalled menarcheal age is calculated for 167 girls aged ≥ 13.5y at Survey 2. 160 (96%) of these girls were postmenarcheal and menarcheal age was reported for 155 girls with a mean of 12.2y. When the 7 (4%) premenarcheal girls are included, the mean age of recalled menarche rises to at least 12.3y.

Early Menarche

It is estimated that 3% of adopted girls will attain menarche ≤ 10.00y (Table 1). This estimate is virtually identical to the estimate for southern Chinese girls and is midway between the 3% estimates of 9.74y for Chinese girls and 10.26y for urban Chinese girls (Table 1). Ten

adopted girls had a recalled age of menarche <10y. This represents 2.5% of responses on recalled menarche for 399 girls aged >10y at the time of Survey 2. The recalled age of menarche for 8 of these 10 girls was ≥ 9.5y.

Two of the 3 girls prescribed GnRHa may have increased the incidence of early menarche, as they were treated after being diagnosed with early pubertal onset. (The third girl had been prescribed GNRHa for reasons unconnected with early puberty.) If it is assumed that both girls treated for early puberty would have attained menarche <10y without treatment, then the percentage of adopted girls with a recalled menarcheal age <10y rises from 2.5% to 3.0%, a figure that replicates the *status quo* estimate (Table 1).

Distribution of Menarche

The distribution of menarche of adopted girls at the estimated incidence rates P3-P97 are similar to estimates for Chinese girls and urban Chinese girls and are virtually identical to southern Chinese girls. In no case do adopted girls provide the outlying figure (Table 1).

Weight shortly after Adoption

There were 609 girls with weight data from first medical exam. The mean period between arrival date in the USA or Canada and exam date was 1.5 weeks. Comparing to the WHO weight-for-age categories, 503 (82.5%) girls were below the WHO median weight, including 148 (24.3%) girls of very low weight, with weights –2SD or more below the median. Controlling for age, a smaller proportion of girls who had been of very low weight shortly after adoption had attained menarche than other girls but the differences are not significant (Table 2).

Discussion

The findings that girls adopted from China have no increased risk of early menarche add to evidence that correlations between international adoption and early puberty vary by state of

origin. Girls adopted from South Asian states appear to have high rates of early puberty (Parent *et al*. 2003). By contrast, girls from South Korea, do not appear to have increased rates of precocious puberty (Teilmann *et al*. 2006), and girls adopted from China into the Netherlands are less likely to be prescribed medication for precocious puberty than non-adopted girls (Van Ginkel *et al*. 2016).

Probit analysis of the menarcheal *status quo* of 814 girls adopted into the USA and Canada from China indicates that the median age of menarche, the percentage of girls attaining menarche <10y and the distribution of menarcheal age are all similar to Chinese girls growing up in China. There is no evidence of an increased risk of early menarche amongst girls of very low weight shortly after adoption. The link between international adoption and early menarche for girls adopted from China has not been confirmed.

Key Messages

The median menarcheal age and distribution of menarcheal age of girls adopted from China is very similar to published data on girls growing up in China.

Girls adopted from China are not at risk of early menarche.

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Table 1

Attainment of Menarche: Comparison of Adopted and Non-Adopted Girls

Study	Age, y						
	P_3	P_{10}	P_{25}	P_{50} (95% CI)	P_{75}	P_{90}	P_{97}
Girls adopted from China	10.00	10.75	11.52	12.37 (11.84-13.00)	13.22	13.98	14.74
Chinese girls (Sun *et al.* 2012)	9.74	10.60	11.47	12.43 (11.97-12.88)	13.40	14.27	15.13
Urban Chinese girls (Ma *et al.* 2009)	10.26	10.86	11.51	12.27 (12.16-12.39)	13.09	13.87	14.68
Southern Chinese girls (Huen *et al.* 1997)	10.01	10.77	11.53	12.38 (11.98-12.78)	13.24	14.00	14.76

Note. P_3 ~ P_{97} represent the 3rd to the 97th percentile respectively.

Table 2

Weight-For-Age at First Medical Exam and Menarcheal Status

Age at Survey 2	Weight-for-age	N	Mean age at Survey 2	Post-menarche, n (%)	P
≥ 11.5y	> –2SD	152	14.1y	121 (79.6 %)	NS
	≤ –2SD	74	14.2y	53 (71.6%)	
< 11.5y	> –2SD	309	9.1y	9 (3.0 %)	NS
	≤ –2SD	74	9.4y	2 (2.7%)	