

ORIGINAL ARTICLE

Puberty in modernizing Kazakhstan: A comparison of rural and urban children

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Abstract

Background: Data on puberty development are available for several countries but not for Central Asia. Aim: Using data collected during the Kazakhstan Health and Nutrition Survey (KHA-ES), we evaluated the relationship between the living environment (rural vs. urban), ethnicity (Russians vs. Kazakhs) and pubertal status in children living in Kazakhstan.

Subjects and methods: Genital (G1–G5), breast (B1–B5) and pubic hair (PH1–PH5) development were evaluated in a sample of 2389 boys and 2416 girls using Tanner's criteria. Age at menarche was evaluated using the 'status quo' and 'recall' methods.

Results: Rural children were older than urban children at stages $\geq G2$ for males and $\geq B2$ for females, and this difference was more evident for Russian males. Differences levelled out at later stages of development in Kazakh males and in the pooled girls. The living environment was slightly but significantly associated with median age at menarche (12.89 years for urban Kazakhs to 13.43 years for rural Kazakhs). Male and female Kazakhs were older than Russians at stages 4 and 5, especially in the urban area.

Conclusion: A relationship between pubertal status and the living environment was present in a rapidly modernizing country such as Kazakhstan.

Keywords: Puberty, menarche, urban, rural, Kazakhstan

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Introduction

Puberty, the period of life that marks the transition from childhood to adulthood, is characterized by profound somatic changes (Tanner 1962; Terasawa and Fernandez 2001). Pubertal status is most commonly evaluated using Tanner's criteria, which are based on breast development in females (B1–B5), genital development in males (G1–G5), and pubic hair development (PH1–PH5) in both genders (Marshall and Tanner 1969; Marshall and Tanner 1970; Coleman and Coleman 2002). Age at menarche is another important and commonly employed indicator of puberty (Coleman and Coleman 2002).

Besides genetic factors, the onset of puberty is related to environmental factors such as socio-economic status and nutrition (Delemarre-van der Waal 1993; Parent et al. 2003). Much data about puberty onset and secular trends of puberty are available for developed countries such as European countries and USA (De Muinck Keizer-Schrama and Mul 2001; Parent et al. 2003; Herman-Giddens 2006; Himes 2006; McDowell et al. 2007). Much less data are available for developing countries such as Africa and Asia, even if delayed puberty is generally reported in these countries (Thomas et al. 2001; Parent et al. 2003). There is increasing evidence that the modernization of developing countries may influence the timing of puberty (Thomas et al. 2001; Parent et al. 2003).

Kazakhstan, the former major Soviet Republic of Central Asia, is undergoing a rapid modernization process, fuelled by urbanization (USAID 2005). The coexistence of people of different ethnic groups devoted to sheep breeding and agriculture in rural villages and following a westernized lifestyle in urban centres (Facchini and Fiori 2001) offers a great opportunity to study the relationship between the living environment and pubertal status.

The Kazakhstan Health and Nutrition Examination Survey (KHAN-ES) was aimed at studying the effects of the living environment on the nutrition and health of urban and rural Kazakh children (Facchini et al. 2007). In the present study, we report on the relationship between the living environment, ethnicity and pubertal status in KHAN-ES children.

Methods

Study design

The study protocol of KHAN-ES has been described in detail elsewhere (Facchini et al. 2007). Kazakh and Russian children aged 7-18 years and resident in Almaty (urban environment) or Chilik (rural environment) were studied at local schools between 2002 and 2004. Kazakhs and Russians make up 80% of ethnic groups in Kazakhstan. Almaty is the biggest city of Kazakhstan, numbering 1 200 000 inhabitants. Chilik is a village of about 20000 inhabitants (including neighbourhoods), located at 150km north east from Almaty. Whereas Almaty has experienced an increasingly westernized lifestyle in recent years (Facchini and Fiori 2001), Chilik is only marginally modernized and is not industrialized at all. In fact, most Chilik inhabitants are devoted to sheep breeding and agriculture and follow a traditional lifestyle. Because of this and of the fact that Chilik did not meet the criteria of 'urban area' defined by the United States Department of Agriculture (2005), we classified its environment as 'rural'. Almaty is made of six urban districts and at the time of the study had nearly 180 000 students aged 7–18 years, attending a total of 230 schools. Only 20 schools of three different districts agreed to participate in KHAN-ES, so our Almaty sample should be considered a convenience sample. In Chilik, there were about 5000 students aged 7-18 years attending 15 different schools, 11 of which agreed to participate in KHAN-ES. We recruited about 50 children for every combination of gender (male vs. female), environment (Almaty vs. Chilik), ethnic group (Kazakh vs. Russian) and age group (7–18 years), for a total of 4808 children. We selected a random sample of school classes for each year of age from 7 to 18 years and an equal number of Russian and Kazakh children of both sexes for each class. Exclusion criteria were chronic or acute disease, mental impairment, having a sibling already enrolled into the study, unknown ethnic origin, and different ethnic origin of parents. The participation rate was about 1.5% in Almaty and 50% in Chilik. The study was carried out in conformity with the declaration of Helsinki and the study protocol was approved by the Scientific Committee of the Kazakh National Academy of Sciences. The written consent of the child and of at least one parent was requested for subjects aged <18 years and that of the child alone for subjects aged ≥18 years. Because of missing data for three subjects, the number of subjects available for the present analysis was 4805 (2389 males and 2416 females).

Pubertal status and age at menarche

Genital development (G1–G5), breast development (B1–B5) and pubic hair growth (PH1–PH5) were assessed by the same Kazakh paediatrician assisted by two trained health professionals. The medical staff visited about 25 children per day between 8:00 am and 1:00 pm, making a total of 200 working days for all the study. No fatigue or routine effect was reported by the medical staff. The paediatrician and her staff agreed in 95% of cases for the assessment of stages 1–3 and in 80% of cases for the assessment of stages 4–5. When the attribution of pubertal stage was discordant, final attribution was achieved on the basis of two concordant results from the medical staff. A question of the KHAN-ES general health and nutrition questionnaire asked whether girls had already had their menarche ('status quo' method). A total of 2403 of 2416 (99%) girls gave a valid response to this question and 1047 of them (44%) declared to have had menarche. These girls were then asked to specify the month and year of menarche ('recall' method) and the age at menarche was calculated as the difference between the date they declared (rounded to the 15th day of the month) and the date of birth. A total of 1037 of 1047 (99%) girls gave a valid response to this question and were used for analysis.

Statistical analysis

The relationship between pubertal status and age was evaluated using probit regression. The predictor variable was age class from 7 to 18 years, for a total of 12 classes. Each age class was defined by pooling all subjects with continuous age between the second half of the previous year and the first half of the same year in a decimal scale (e.g. class 13 was formed by children aged between 12.51 and 13.49 years). The outcome variables (genital development, pubic hair development, and breast development) were dichotomized at stages ≥ 2 , ≥ 3 , ≥ 4 and 5 and regressed against age. The 'status quo' age at menarche was dichotomized as 0 (not had menarche) and 1 (had menarche). IC50 of the probit curves, i.e. the median value of age at stages 2, 3, 4 and 5 and age at 'status quo' menarche, were reported with 10th and 90th percentiles and 95% confidence intervals (95% CI). Probit regression was performed separately for each combination of environment and ethnic group and group estimates were compared using the relative median potency test. Goodness of fit of the models was evaluated using the chi-square test. When lack of fit was detected, the dependent variable was log-transformed or a heterogeneity factor was used to calculate

confidence intervals. Residual plots were inspected to check model fit. Mean age at stages G2 and B2 was calculated using age as continuous variable only for subjects in these two stages. Mean (continous) 'recall' age at menarche was calculated only for girls who reported the date of the first menstruation. Between-group differences in age at stages G2 and B2 and 'recall' age at menarche were evaluated using ANOVA followed by Tukey's HSD *post hoc* test after verification of normality (Shapiro–Wilk test). Statistical significance was set to a two-tailed *P*-value <0.05 for all tests. Statistical analysis was performed using SPSS 14.0 (SPSS, Chicago, IL, USA).

Results

Table I gives the 10th, 50th and 90th percentiles of age for stage of pubertal development obtained by probit regression in KHAN-ES boys stratified by ethnic group and living environment. In terms of genital development, urban Kazakhs were significantly older than urban Russians at stages $\geq G4$ [median absolute deviation (MAD), 95% CI = 0.55, 0.24 - 0.88 years and G5 (MAD = 1.06, 0.67-1.47). Rural Russians were older than rural Kazakhs at stages \geq G2 (MAD = 0.99, 0.81–1.39 years) and \geq G4 (MAD = 0.51, 0.19-0.85 years). While rural Kazakhs were older than urban Kazakhs at stages >G2 (MAD = 0.84, 0.46-1.24 years), rural Russians were older than urban Russians at all stages (MAD = 1.93, 1.49-2.40 for >G2; MAD = 1.09, 0.53-1.71 for >G3; MAD = 0.82, 0.5-1.17 years for $\geq G4$; MAD = 0.93, 0.55-1.33 for stage G5). Median age was generally lower than mean age at stage G2 but the results of probit regression were confirmed. Rural Russians reached puberty later than rural Kazakhs (p < 0.01), and urban Kazakhs and Russians reached puberty sooner than their rural peers (p < 0.05 and p < 0.001, respectively). In terms of pubic hair growth, urban Kazakhs were older than urban Russians at stages >PH2 (MAD = 0.61, 0.27–0.98 years), >PH4 (MAD = 1.06, 0.70–1.45 years) and at PH5 (MAD = 1.41, 0.90-1.98) but there were no differences between Kazakhs and Russians in the rural environment. Similar to genital development, rural Kazakhs were older than urban Kazakhs at stages \geq PH2 (MAD=0.78, 0.43–1.16 years) and rural Russians were older than urban Russians at all stages (MAD = 1.60, 1.20-2.04 years for >PH2; MAD = 0.80, 0.12-1.60 years for \geq PH3; MAD = 1.04, 0.6-1.43 years for \geq PH4; MAD = 1.00, 0.54-1.50years for PH5).

Table II gives the 10th, 50th and 90th percentiles of age for stage of pubertal development obtained by probit regression in KHAN-ES girls stratified by ethnic group and living environment. In terms of breast development, Kazakh girls were older than Russian girls at stages \geq B4 in both urban (MAD = 0.87, 0.27–1.51 years) and rural areas (MAD = 1.29, 0.67–1.94 years). Rural Kazakhs and Russians were older than their urban counterparts at stages \geq B2 (MAD = 0.95, 0.63–1.30 years and MAD = 1.05, 0.72–1.41 years, respectively). In this case, the median age at B5 > 18 years for all groups. Figure 1(a) reports the frequency of stage B5 for age from 12 to 18 years. Russian girls tended to have a higher frequency of B5 stages at all ages, especially in the rural area. Median age was lower than mean age at B2 but the results of probit regression were confirmed. Urban Kazakhs and Russians reached puberty sooner than their rural counterparts (p<0.01 and p<0.05, respectively). In terms of pubic hair growth, no ethnic difference was observed in the urban environment. However, in the rural environment, Kazakh girls were older than Russian girls at stages \geq PH2 (MAD = 0.51, 0.21–0.83 years), \geq PH3 (MAD = 0.51, 0.20–0.84 years) and \geq PH4 (MAD = 0.79, 0.20–1.42 years). Rural girls were older than their urban peers at stages

Table I. (A) Median age (10th and 90th percentiles) at $\geq G2$, $\geq G3$ and $\geq G4$ and G5 for the four groups of boys. Total number of subjects for each group is also reported. (B) Median age (10th and 90th percentiles) at $\geq PH2$, $\geq PH3$ and $\geq PH4$ and PH5 for the four groups of boys. 95% CI is also reported in parenthesis. Total number of subjects for each group is also reported. (C) Mean, SD and median age of the only G2 stage for each of the four groups. Total number of subjects for each group is also reported.

	Urt	Urban Kazakh (UK)	(2)	Ru	Rural Kazakh (RK)		Urt	Urban Russian (UR)	হ	Ru	Rural Russian (RR)	
	10th	50th	90th 1	10th 5	50th 9	90th 1	10th 5	50th 9	90th 1	10th	50th	90th
A												
>G2	7.57	29.6	11.77	8.41	10.51	12.61	7.42	9.52	11.62	9.34	11.44	13.55
	(7.23-7.88)	(9.40-9.94)	(11.48-12.09)	(8.08 - 8.70)	(10.25-10.76)	(12.32-12.92)	(7.08-7.73)	(9.25-9.78)	(11.33-11.93)	(9.03-9.64)	(11.19-11.70)	(13.25–13.87)
>G3	11.33	13.01	14.70	11.59	13.27	14.96	10.96	12.64	14.33	12.04	13.73	15.41
	(10.87 - 11.73)	(10.87-11.73) (12.64-13.39) (14.30-15.16)	(14.30 - 15.16)	(11.15-11.97)	(12.91-13.63)	(14.56-15.41)	(10.51 - 11.35)	(12.28-13.00)	(13.94-14.77)	(11.59-12.45)	(13.35-14.10)	(15.00-15.87)
>G4	13.16	14.72	16.28	12.91	14.48	16.04	12.60	14.17	15.73	13.43	14.99	16.55
((12.89-13.40)	12.89-13.40) ($14.50-14.94$) ($16.03-16.54$)	(16.03-16.54)	(12.65-13.16)	(14.25-14.70)	(15.78-16.31)	(12.34-12.84)	(13.95-14.38)	(15.49 - 15.99)	(13.13-13.67)	(14.77-15.21)	(16.30-16.82)
S	(14.52–15.11)	14.83 16.61 14.52–15.11) (16.34–16.88)	Over 18	14.58 (14.28–14.86)	16.36	Over 18	(13 47–14 04)	15.55	(17.04–17.66)	14.70	16.48	Over 18
	(11:01 20:11)	(00:01 10:01)		(00:11 07:11)	(50:01 01:01)		(10:11 11:01)	(61:61 16:61)		(17:17)	(1.01 17:01)	
Total n 588	588			602			604			595		
В												
\geq PH2	10.51	10.51 12.48 14.46	14.46	11.29	13.27	15.24	68.6	11.87	13.84	11.49	13.47	15.44
	(10.21 - 10.78)	(12.24-12.73)	(14.18 - 14.76)	(11.00-11.56)	(13.02-13.51)	(14.97 - 15.54)	(9.69-10.16)	(11.63-12.11)	(13.57 - 14.14)	(11.19-11.77)	(13.22-13.72)	(15.16 - 15.75)
$\geq PH3$	12.53	14.11	15.70	12.86	14.45	16.03	12.03	13.61	15.20	12.83	14.42	16.00
	$\overline{}$	(11.91–13.05) (13.62–14.60) (15.18–16.31)	(15.18-16.31)	(12.26 - 13.37)	(13.96 - 14.94)	(15.51 - 16.66)	(11.42-12.53)	(13.14 - 14.08)	(14.69 - 15.80)	(12.21 - 13.35)	(13.93-14.90)	(15.49-16.61)
$\geq \mathrm{PH4}$	13.84	15.64	17.44	13.68	15.48	17.28	12.78	14.58	16.38	13.82	15.62	17.42
	(13.55-14.11)	(15.40-15.88) $(17.17-17.75)$	(17.17-17.75)	(13.39-13.95)	(15.23-15.73)	(16.99 - 17.60)	(12.49 - 13.04)	(14.34-14.81)	(16.11 - 16.68)	(13.52-14.08)	(15.37 - 15.86)	(17.13-17.73)
PH5	15.72	17.87	Over 18	15.84	18.00	Over 18	14.31	16.47	Over 18	15.31	17.47	Over 18
	(15.33-16.08)	(17.50 - 18.29)		(15.45-16.21)	(17.60-18.45)		(13.94-14.64)	(16.18-16.78)		(14.93-15.64)	(17.14-17.82)	
Total n 588	588			602			604			595		
C	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
G2	11.26	1.71	11.34	11.72	1.59	11.89	11.01	1.72	10.92	12.41	1.46	12.56
Total	173			159			171			123		

Table II. (A) Median age (10th and 90th percentiles) at >B2, >B3 and >B4 for the four groups of girls. Total number of subjects for each group is also reported. (B) Median age, 10th and 90th percentiles at >PH2 >PH3 and >PH4 for the four groups of girls of Single and some of girls of single and some of girls also reported.

	Ur	Urban Kazakh (UK)	(2:	Rı	Rural Kazakh (RK)	(2)	Ur	Urban Russian (UR)	R)	Rı	Rural Russian (RR)	(
	10th	50th	90th	10th	50th	90th	10th	50th	90th	1 0th	50th	90th
A >B2	9.06	9.06 10.54 12.02 (8.81-9.30) (10.33-10.75) (11.79-12.28)	12.02	10.02	11.50	12.98		10.48	11.96	10.05	11.53	13.01
≥B3	11.11	(11.11 12.84 14.56 11.11 12.84 14.56 11.56–11.59) (12.39–13.28) (14.09–15.10)	14.56	11.24			11.32	13.03	13.03 14.76 (12.59–13.48) (14.28–15.30)	_		14.68
>B4	(12.96–13.93)	16.50 (16.05–16.90)	Over 18	13.49 (12.99–13.95)				(15.22–16.06)	Over 18			Over 18
Total n 601	601			209			909			603		
В												
>PH2	10.09 (9.83–10.32)	10.09 11.60 13.11 (9.83–10.32) (11.39–11.81) (12.87–13.37)	13.11 (12.87–13.37)	10.90 (10.64–11.13)	12.41 (12.20–12.62)	13.92 (13.69–14.18)	9.93 (9.68–10.17)	11.45 (11.24–11.65)		12.96 10.39 (12.72–13.21) (10.13–10.62)	11.90 (11.68–12.11)	13.41 (13.17–13.67)
>PH3	11.27	11.27 12.89 14.51 11.00–11.52) (12.67–13.11) (14.27–14.77)	14.51	11.84						11.33		14.57
>PH4	(11.93–12.90)	(14.51–15.36)	(16.92–17.99)	12.41 (11.90–12.97)								(16.13–17.13)
Total n 601	601			209			605			603		
C B2	Mean 11.75	SD 1.60	Median 11.54	Mean 12.50	SD 1.38	Median 12.25	Mean 11.69	SD 1.53	Median 11.64	Mean 12.28	SD 1.23	Median 12.18
Total	123			81			139			78		

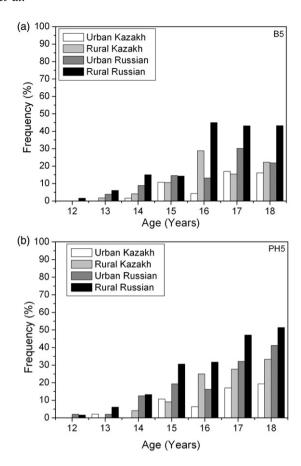


Figure 1. Frequency of B5 (A) and PH5 (B) stages in girls considered in this study, distinguished on the basis of living environment and ethnicity.

 \geq PH2 (MAD=0.81, 0.49–1.15 years) and \geq PH3 (MAD=0.57, 0.25–0.89 years). This difference was evident for Russian girls only at stages \geq PH2 (MAD=0.45, 0.15–0.77 years) while at stages \geq PH4 an inversion of tendency was observed, with urban girls older than rural girls (MAD=0.68, 0.10–1.29 years). In this case, the median age at stage PH5 was over 18 years for all groups except for rural Russians. Figure 1(b) shows the frequency of stage PH5 for age from 12 to 18 years. These data confirm those obtained with B5 stage analysis.

Table III gives the frequency of menstruated girls as a function of age and Table IV reports the mean and the median age at menarche as determined by status quo method, and mean age at menarche by recall method with stratification for ethnic group and environment. Between-groups comparisons, performed on log-transformed values, identified only the rural Kazakh vs. urban Kazakh relationship as statistically significant ($\log \text{MAD} = 0.013$, 0.002-0.025). Age at menarche determined by the recall method was in good agreement with that determined by the status quo method in rural children. Estimates were however different for urban Kazakhs (12.89 vs. 13.12 years) and Russians (13.16 vs. 12.79 years). Besides the difference between urban and rural Russians (p < 0.001), Russians had puberty sooner than Kazakhs in the urban environment (p = 0.027).

Table III. Distribution of menstruated girls and relative frequency as a function of the class of age. Urban Kazakhs, rural Kazakhs, urban Russians and rural Russians are reported separately.

	Urt	Jrban Kazakh (UK)	kh (UK)	Rı	Rural Kazakh (RK)	th (RK)	Urt	Urban Russian (UR)	an (UR)	Ru	Rural Russian (RR)	ın (RR)
Age class	Menarche	Total	Frequency (%)	Menarche	Total	Frequency (%)	Menarche	Total	Frequency (%)	Menarche	Total	Frequency (%)
7	0	26	0.0	0	26	0.0	0	28	0.0	0	10	0.0
∞	0	62	0.0	0	28	0.0	0	38	0.0	0	55	0.0
6	0	22	0.0	0	48	0.0	0	9	0.0	0	55	0.0
10	0	45	0.0	0	09	0.0	0	28	0.0	0	49	0.0
11	0	29	0.0	П	20	2.0	1	22	1.8	1	22	1.8
12	13	52	25.0	6	99	13.6	3	51	5.9	10	64	15.6
13	26	48	54.2	24	25	43.6	24	51	47.1	21	49	42.9
14	99	63	88.9	36	46	73.5	43	99	2.97	39	59	66.1
15	54	99	96.4	59	99	89.4	59	62	95.2	43	49	87.8
16	46	47	6.76	52	52	100	89	89	100	54	09	0.06
17	46	47	6.76	63	9	6.96	53	53	100	51	51	100
18	31	31	100	∞	œ	100	17	17	100	37	37	100
Total	271	601	45.1	252	603	41.8	268	604	44.4	256	562	43.0

Table IV. (A) Median age, 10th and 90th percentiles at menarche (status quo method) for the four groups of girls. Total number of subjects for each group is also reported. (B) Mean, SD, and median age at menarche using the retrospective recall method. Total number of subjects for each group and 95% CI in parenthesis are also reported.

	Ū	Urban Kazakh (UK)	2	R	Rural Kazakh (RK)	c	Ür	Urban Russian (UR)	િ	Rural Ru	Rural Russian (RR)	
	10th	50th	90th	10th	50th	90th	10th	50th	90th	10th	50th	90th
A Menarche,	11.44	12.89	14.51	11.80	13.28	14.96	11.68	13.16	14.82	11.93	13.43	15.12
status quo	(11.17–11.69)	status quo (11.17–11.69) (12.64–13.14) (14.21–14.84) (11.53–12.04) (13.04–13.53) (14.66–15.29) (11.41–11.94) (12.90–13.41) (14.51–15.15) (11.66–12.17) (13.18– (14.83–13.64) (13.18– (14.83– (14.83–13.64) (13.18– (14.83– (1	(14.21–14.84)	(11.53–12.04)	(13.04–13.53)	(14.66–15.29)	(11.41–11.94)	(12.90–13.41)	(14.51–15.15)	(11.66–12.17)	(13.18– 13.68)	(14.83– 15.46)
Total n	601			603			604			595		
B Menarche, recall	Mean 13.12	SD 1.39	Median 13.06	Mean 13.27	SD 1.32	Median 13.31	Mean 12.79	SD 1.25	Median 12.82	Mean 13.40	SD 1.43	Median 13.34
Total n	267			252			262			256		

Discussion

KHAN-ES is the first study to investigate the relationship between the living environment, ethnicity and pubertal status in a Central Asia population. Brooks-Gunn and Warren (1985) and Coleman and Coleman (2002) have split the maturational events of puberty into secondary sexual characteristics and anthropometric measurements. Traditionally, the first sign of pubertal development in boys is an increase of testicular volume > 3 mL, which is consistent with Tanner's G2 stage. Also the growth of pubic hair (PH2) is considered a first sign of puberty (Parent et al. 2003). Thelarche and age at menarche are traditionally used as markers of puberty onset in girls. Thelarche corresponds to Tanner's B2 stage and age at menarche occurs generally after thelarche (Parent et al. 2003). The second stage of pubic hair development (PH2) in girls is less informative about pituitary—ovarian maturation and therefore puberty (Parent et al. 2003). It should be noted that some authors have questioned the validity of Tanner's criteria for puberty onset and proposed other criteria (Mueller et al. 2001; Coleman and Coleman 2002; Bond et al. 2006; Himes 2006). To better assess the effects of ethnicity and of the living environment on puberty, we reported all Tanner stages.

In KHAN-ES, the living environment had a strong influence on the timing of puberty in Russian children. In the rural environment, Kazakhs were older than Russians at stages $\geq G2$ but not at later stages. On the other hand, rural Russians had higher values of age at all genital stages as compared to urban Russians. Moreover, while Kazakhs were older than Russians only at stages $\geq G4$ and G5 in the urban environment, Russians were older than Kazakhs at stages $\geq G2$ and $\geq G4$ in the rural environment, indicating an association between ethnicity and the living environment. The development of pubic hair growth confirmed the differences observed for genital development. The median age at G2 for urban Kazakhs, urban Russians and rural Kazakhs was similar to that reported for US white children (Figure 2). Rural Russians had a median age at G2 between 11 and 12 years, which

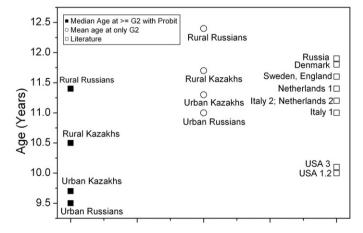


Figure 2. The comparison of median age at \geq G2 stage and mean age at only G2 stage for Kazakh children with some of the American and European reference values reported in literature. USA 1 from Himes (2006); USA 2 from Sun et al. (2002); USA 3 from Herman-Giddens et al. (2001); Italy 1 from Castellino et al. (2005); Italy 2 from De Simone et al. (2004); Netherlands 1 from Fredriks et al. (2000); Netherlands 2 from Mul et al. (2001); Denmark from Juul et al. (2006); Sweden from Lindgren (1996); England from De Muinck Keizer-Schrama and Mul (2001); Russia from Lee et al. (2003).

is consistent with European data. This discrepancy may be partly explained by the different methods of analysis. In fact, the mean age at G2 ranged between 11.01 years (urban Russians) and 12.41 years (rural Russians), very near to European reference values. Probit analysis of stages ≥G2 does not take into account the partial overlapping features of G2, G3 and G4 stages at low ages. The results were however consistent with the two methods of analysis and led to the same conclusions. The median age of male children at PH2 was slightly higher than that of US children (Herman-Giddens et al. 2001; Sun et al. 2002; Himes 2006) and similar to that of European children (Lindgren 1996; Fredriks et al. 2000; Mul et al. 2001; Lee et al. 2003; De Simone et al. 2004; Castellino et al. 2005; Godina et al. 2005; Juul et al. 2006).

Although there are few studies on the relationship between pubertal status and the living environment, it is known that a delay of puberty may be due to nutritional and socio-economic factors. Cameron et al. (1993) observed a delayed puberty in black rural boys compared to urban boys of high socio-economic status in South Africa and this finding was confirmed in Zambia boys (Campbell et al. 2004). Even if the effect of ethnicity of pubertal status is widely known (Himes 2006), KHAN-ES is the first study comparing Caucasian and Mongolian children in the same country.

In females, the living environment was associated with age at stages $\geq B2$ to a lesser degree than in males. Rural Kazakh and Russian females had delayed puberty compared to urban peers only at stage ≥B4. Moreover, female Kazakhs had delayed puberty compared to female Russians at stages > B4 in both urban and rural environments. Finally, rural Russians had the highest frequency of B5 stages at all ages from 12 to 18 years. Mean age at stage B2 was consistent with results obtained from probit analysis. As for breast development, rural Kazakh and Russian females had delayed puberty compared to urban peers at stages \geq PH2. However, rural Kazakhs had delayed puberty also at stages ≥PH3. For Russians, there was an inversion of tendency at stages \geq PH4. Finally, rural Russians had the highest frequency of PH5 stage at all ages from 12 to 18 years. Lastly, while in Almaty the differences between Kazakh and Russian females were never significant, in Chilik, Kazakhs had always delayed puberty as compared to Russians. The median age at menarche determined using the 'status quo' method was similar to the median age of >B3 stage. The rural environment was associated with a slight but significantly higher median age at menarche for Kazakhs but not for Russians, confirming that the living environment was associated with the passage from Tanner stage 1 to 2 more then further stages.

At stage B2, the median age of urban Kazakhs and Russians was similar to that reported for Italy, Lithuania, USA, Greece, UK, Sweden, Germany, Sweden, Holland and Denmark (Dacou-Voutetakis et al. 1983; De Muinck Keizer-Schrama and Mul 2001; Mul et al. 2001; Coleman and Coleman 2002; Sun et al. 2002; Danubio et al. 2004; Castellino et al. 2005; Zukauskaite et al. 2005; Himes 2006; Juul et al. 2006). Median age at stage B2 was however slightly higher in rural children and lower than that observed for some African countries (Garnier et al. 2005; Leenstra et al. 2005). Moreover, median age at PH2, especially in the urban environment, was consistent with that of children from UK, Denmark and Russia (Coleman and Coleman 2002; Godina et al. 2005; Juul et al. 2006) but higher from 4 to 12 months than that reported for other western countries such as USA, Italy, Holland and Lithuania (Mul et al. 2001; Sun et al. 2002; Danubio et al. 2004; Castellino et al. 2005; Zukauskaite et al. 2005; Himes 2006). The gap in median age at B2 and PH2 stages was thus slightly higher in our children than in the available literature. While ethnic differences in puberty are well reported in the literature (Chumlea et al. 2003), KHAN-ES is the first study comparing Caucasian and Mongolian groups in the same country.

Surprisingly, the median age at stages B5 and PH5 was above 18 years, while in the literature it is reported to vary between 14.0 and 16.5 years (Belmaker 1982; Mul et al. 2001; Sun et al. 2002; Danubio et al. 2004; Juul et al. 2006). This may be due to a difficulty in distinguishing stages 3-5 and therefore should be considered a limitation of or study. Not unexpectedly, age at menarche determined by the recall method was slightly different from that determined using the status quo method. The two estimates were nearly the same for rural children but there was a difference of 0.37 years for urban Russians and one of 0.23 years for urban Kazakhs. However, only the difference between urban and rural Russians was significant. Status quo age is however universally recognized as better than its recall counterpart (Parent et al. 2003). The median age at menarche of KHAN-ES children was similar to that of European and Chinese children (Figure 3). Environmental differences are few in Italy (Martuzzi-Veronesi and Gueresi 1994), Spain (Marrodan et al. 2000) and Poland (Wronka and Pawlinska-Chmara 2005), and slightly more in France (Marrodan et al. 2000). On the contrary, in developing countries, the living environment has a great influence on age at menarche (Pasquet et al. 1999; Pawloski 2002; Padez 2003a). Our data are also consistent with data from China, which is undergoing a rapid modernization process (Wang and Adair 2001; Hesketh et al. 2002). A comparison of our data with those from Russia and the former Soviet Union is of particular interest. In some Russian studies performed in the 1970s, the median age at menarche was 13.0 years in Moscow, 12.5 years in Tbilisi and 13.0 in Sukumi (reviewed in Eleveth and Tanner 1990). In the 1980s, the

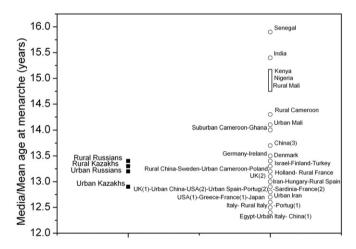


Figure 3. The comparison of median age at menarche for Kazakh children with some of the reference values around the world reported in literature. UK(1) from Coleman and Coleman (2002); UK(2), Japan, India, Finland Sweden, Germany, France(1), China(3) from Parent et al. (2003); China(1), Turkey, Ghana and Nigeria from Thomas et al. (2001); Urban/Rural Spain, Portug(2), France(2) and Rural France from Marrodan et al. (2000); USA(1) from Chumlea et al. (2003); USA(2) from Himes (2006); Kenya from Leenstra et al. (2005); Iran from Ayatollahi et al. (2002); urban Iran from Razzaghy-Azar et al. (2006); Israel from Belmaker (1982); Italy from Danubio et al. (2004); Urban and Rural China from Hesketh et al. (2002); Hungary from Dober and Kiralyfalvi (1993); Greece from Dacou-Voutetakis et al. (1983); Egypt from Hosny et al. (2005); Portug(1) from Padez (2003b); Denmark from Juul et al. (2006); Holland from Mul et al. (2001); Urban/Rural Italy from Martuzzi-Veronesi and Gueresi (1994); Sardinia from Floris et al. (1990); Urban, Suburban and Rural Cameroon from Pasquet et al. (1999); Senegal from Garnier et al. (2005); Poland from Wronka and Pawlinska-Chmara (2005); Ireland from Hoey et al. (1986); Mali from Pawloski (2002).

median age at menarche was 13.4 years in Russian rural areas and 13.0 in urban areas (Godina et al. 1995) and in Moscow median age at menarche was constantly between 12.6 and 13 years from 1964 to 1984 (Godina 1998). These data were confirmed by two later studies performed in the Moscow area, with a median age at menarche of 12.8–13.0 years (Godina et al. 2003; Godina et al. 2007). Dubrova et al. (1995) reported a median age at menarche of 13.2 years in urban areas and no difference was found between urban and rural areas during the Russian Longitudinal Monitoring Survey (13.2 years in both areas, Wang and Adair 2001). Lastly, Godina et al. (2005) have found slight differences in median age at menarche in different regions of Russia with different degrees of modernization (13.4 years in Khvalynsk area vs. 13.2 years in Balakovo and Saratov area). These data are consistent with the results of our study. Socio-economic and lifestyle factors could explain the differences observed in our study. Further work is needed to better understand the effects of modernization on puberty.

In conclusion, KHAN-ES rural children had a delayed puberty as compared with urban peers and this was especially evident at B2 and G2 stages. The delay was more relevant for Russian males, while it tended to disappear for Kazakh males and for pooled females at later Tanner stages. The living environment had also a slight but statistically significant influence on age at menarche. The KHAN-ES data may represent a starting point to study secular trends in central Asia during the coming years of economic development, as is currently being done for Russia (Dubrova et al. 1995; Godina 1998; Kalichman et al. 2006).

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References

Ayatollahi SM, Dowlatabadi E, Ayatollahi SA. 2002. Age at menarche in Iran. Ann Hum Biol 29:355-362.

Belmaker E. 1982. Sexual maturation of Jerusalem schoolgirls and its association with socio-economic factors and ethnic group. Ann Hum Biol 9:321–328.

Bond L, Clements J, Bertalli N, Evans-Whipp T, McMorris BJ, Patton GC, Toumbourou JW, Catalano RF. 2006. A comparison of self-reported puberty using the pubertal development scale and the sexual maturation scale in a school-based epidemiologic survey. J Adolesc 29:709–720.

Brooks-Gunn J, Warren MP. 1985. Measuring physical status and timing in early adolescence: A developmental perspective. J Youth Adolesc 14:163–189.

Cameron N, Grieve CA, Kruger A, Leschner KF. 1993. Secondary sexual development in rural and urban south African black children. Ann Hum Biol 20:583–593.

Campbell BC, Gillett-Netting R, Meloy M. 2004. Timing of reproductive maturation in rural versus urban Tonga boys, Zambia. Ann Hum Biol 31:213–227.

Castellino N, Bellone S, Rapa A, Vercellotti A, Binotti M, Petri A, Bona G. 2005. Pubertà in northern Italy: A random sample of 3597 Italian children. J Endocrin Invest 28:589–594.

Chumlea WC, Schubert CM, Roche AF, Kulin HE, Lee PA, Himes JH, Sun SS. 2003. Age at menarche and racial comparisons in US girls. Pediatrics 111:110–113.

Coleman L, Coleman J. 2002. The measurement of puberty: A review. J Adolesc 25:535-550.

Dacou-Voutetakis C, Klontza D, Lagos P, Tzonou A, Katsarou E, Antoniadis S, Papazisis G, Papadopoulos G, Matsaniotis N. 1983. Age of pubertal stages including menarche in Greek girls. Ann Hum Biol 10:557–563.

- Danubio ME, De Simone M, Vecchi F, Amicone E, Altobelli E, Gruppioni G. 2004. Age at menarche and age of onset of pubertal characteristics in 6–14-year-old girls from the province of L'Aquila (Abruzzo, Italy). Am J Hum Biol 16:470–478.
- De Muinck Keizer-Schrama SMPF, Mul D. 2001. Trends in pubertal development in Europe. Hum Reprod Upd 7:287–291.
- De Simone M, Danubio ME, Amicone E, Verrotti A, Gruppioni G, Vecchi F. 2004. Age of onset of pubertal characteristics in boys aged 6–14 years of the province of L'Aquila (Abruzzo, Italy). Ann Hum Biol 31:488–493.
- Delemarre-van der Waal HA. 1993. Environmental factors influencing growth and pubertal development. Environ Health Perspect 101:(Suppl. 2)39–44.
- Dober I, Kiralyfalvi L. 1993. Pubertal development in south-Hungarian boys and girls. Ann Hum Biol 20:71–74. Dubrova YE, Kurbatova OL, Kholod ON, Prokhorovskaya VD. 1995. Secular growth trend in two generations of the Russian population. Hum Biol 67:755–767.
- Eleveth PB, Tanner JM. 1990. Worldwide variation in human growth. 2nd ed. Cambridge, UK: Cambridge University Press.
- Facchini F, Fiori G. 2001. The modernizing Kazakhstan: A review of biomedical data. J Physiol Anthropol Appl Hum Sci 20:95–103.
- Facchini F, Fiori G, Bedogni G, Galletti L, Belcastro MG, Ismagulov O, Ismagulova A, Sharmanov T, Tsoy I, Rizzoli S, Goldoni M. 2007. Prevalence of overweight and cardiovascular risk factors in rural and urban children from central Asia: The Kazakhstan Health And Nutrition Examination Survey. Am J Hum Biol 19:809–820.
- Floris G, Murgia E, Sanciu GM, Sanna E. 1990. Il menarca in Sardegna: Nuovi dati. Antrop Cont 13:383–390.
 Fredriks AM, Van Buuren S, Burgmejer RJ, Meulmeester JF, Beuker RJ, Brugman E, Roede MJ, Verloove Vanhorick SP, Wit JM. 2000. Continuing positive secular growth change in the Netherlands 1955–1997.
 Pediatr Res 47:316–323.
- Garnier D, Simondon KB, Benefice E. 2005. Longitudinal estimates of puberty timing in Senegalese adolescent girls. Am J Hum Biol 17:718–730.
- Godina EZ, Iampol'skaia I, Giliarova OA, Zubareva VV. 1995. The age of appearance of first menses in women of different regions of Russia. Gigiena I Sanitariia 3:30–32 [In Russian].
- Godina EZ. 1998. Secular changes in Russia, the former Soviet Union. In: Bodzsar EB, Susanne C, editors. Secular growth changes in Europe. Budapest: Eotvos University Press. pp. 351–367.
- Godina EZ, Khomyakova IA, Zadorozhnaya LV, Purundzhan AL, Guilyarova OA, Zubareva VV, Stepanova AV, Fomina EI. 2003. Moscow children: Main trends of development on the verge of the centuries. Voprosy Antropologii 91:42–60 [in Russian].
- Godina EZ, Khomyakova IA, Purundjan AL, Zadorozhnaya LV, Stepanova AV. 2005. Some trends in the somatic development of children and adolescents under iodine-deficiency: Materials from the Saratov region. J Physiol Anthropol Appl Hum Sci 24:313–319.
- Godina E, Khomyakova I, Purundzhan A, Zadorozhnaya L. 2007. Some differences in body composition in Moscow adolescent children according to the level of their physical activity: Comparison of anthropometric and bioelectrical impedance methods of assessment. J Hum Ecol, special issue 15:63–74.
- Herman-Giddens ME, Wang L, Koch G. 2001. Secondary sexual characteristics in boys: Estimates from the national health and nutrition examination survey III, 1988–1994. Arch Pediatr Adolesc Med 155:1022–1028.
- Herman-Giddens ME. 2006. Recent data on pubertal milestones in United States children: The secular trend toward earlier development. Int J Androl 29:241–246.
- Hesketh T, Ding QJ, Tomkins A. 2002. Growth status and menarche in urban and rural China. Ann Hum Biol 29:348–352.
- Himes JH. 2006. Examining the evidence for recent secular changes in the timing of puberty in US children in light of increases in the prevalence of obesity. Mol Cell Endocrinol 254–255:13–21.
- Hoey H, Cox L, Tanner J. 1986. The age of menarche in Irish girls. Ir Med J 79:283-285.
- Hosny LA, El-Ruby MO, Zaki ME, Aglan MS, Zaki MS, El Gammal MA, Mazen IM. 2005. Assessment of pubertal development in Egyptian girls. J Pediatr Endocrinol Metab 18:577–584.
- Juul A, Teilmann G, Scheike T, Hertel NT, Holm K, Laursen EM, Main KM, Skakkebaek NE. 2006. Pubertal development in Danish children: Comparison of recent European and US data. Int J Androl 29:247–255.
- Kalichman L, Malkin I, Livshits G, Kobyliansky E. 2006. Age at menarche in a Chuvashian population. Ann Hum Biol 33:390–397.
- Lee MM, Sergeyev O, Williams P, Korrick S, Zeilert V, Revich B, Hauser R. 2003. Physical growth and sexual maturation of boys in Chaevsk, Russia. J Pediatr Endocrinol Metab 16:169–178.

- Leenstra T, Petersen LT, Kariuki SK, Oloo AJ, Kager PA, Ter Kuile FO. 2005. Prevalence and severity of malnutrition and age at menarche; cross-sectional studies in adolescent schoolgirls in western Kenya. Eur J Clin Nut 59:41–48.
- Lindgren G. 1996. Pubertal stages 1980 of Stockholm school children. Acta Paediatr 85:1365-1367.
- Marrodan MD, Mesa MS, Arechiga J, Perez-Magdaleno A. 2000. Trend in menarcheal age in Spain: Rural and urban comparison during a recent period. Ann Hum Biol 27:313–319.
- Marshall WA, Tanner JM. 1969. Variations in pattern of pubertal changes in girls. Arch Dis Child 44:291–303.
- Marshall WA, Tanner JM. 1970. Variations in the pattern of pubertal changes in boys. Arch Dis Child 45:13-23.
- Martuzzi-Veronesi F, Gueresi P. 1994. Trend in menarcheal age and socioeconomic influence in Bologna (Northern Italy). Ann Hum Biol 21:187–196.
- McDowell MA, Brody DJ, Hughes JP. 2007. Has age at menarche changed? Results from the national health and nutrition examination survey (NHANES) 1999–2004. J Adolesc Health 40:227–231.
- Mueller WH, Cho SD, Meininger JC, Liehr P, Chan W. 2001. Strategies for combining and scaling sexual maturity indicators: The Heartfelt Study. Ann Hum Biol 28:422–430.
- Mul D, Fredriks M, Van Buuren S, OOstdijk W, Verloove-Vanhorick SP, Wit JM. 2001. Pubertal development in the Netherlands 1965–1997. Pediatr Res 50:479–486.
- Padez C. 2003a. Age at menarche of schoolgirls in Maputo, Mozambique. Ann Hum Biol 30:487-495.
- Padez C. 2003b. Social background and age at menarche in Portuguese university students: A note on the secular changes in Portugal. Am J Hum Biol 15:415–427.
- Parent AS, Teilmann G, Juul A, Skakkebaek NE, Toppari J, Bourguignon JP. 2003. The timing of normal puberty and the age limits of sexual precocity: Variations around the world, secular trends, and changes after migration. Endocr Rev 24:668–693.
- Pasquet P, Biyong AM, Rikong-Adie H, Befidi-Mengue R, Garba MT, Froment A. 1999. Age at menarche and urbanisation in Cameroon: Current status and secular trends. Ann Hum Biol 26:89–97.
- Pawloski LR. 2002. Growth and development of adolescent girls from the Segou region of Mali (West Africa). Am J Phys Anthropol 117:364–372.
- Razzaghy-Azar M, Moghimi A, Sadigh N, Montazer M, Golnari P, Zahedi-Shoolami L, Van Buuren S, Mohammad-Sadeghi H, Zangeneh-Kazemi A, Fereshtehnejad SM. 2006. Age of puberty in Iranian girls living in Tehran. Ann Hum Biol 33:628–633.
- Sun SS, Schubert CM, Chumlea WC, Roche AF, Kulin HE, Lee PA, Himes JH, Ryan AS. 2002. National estimates of the timing of sexual maturation and racial differences among US children. Pediatrics 110:911–919.
- Tanner JM. 1962. Growth at adolescence. 2nd ed. Oxford, UK: Blackwell.
- Terasawa E, Fernandez DL. 2001. Neurobiological mechanisms of the onset of puberty in primates. Endocr Rev 22:111–151.
- Thomas F, Renaud F, Benefice E, De Meeus T, Guegan JF. 2001. International variability of ages at menarche and menopause: Patterns and main determinants. Hum Biol 73:271–290.
- USAID (United States Agency International Development). 2005. Kazakhstan Economic Performance Assessment. Arlington, VA, USA: Nathan Associates Inc. Available at http://pdf.usaid.gov/pdf_docs/PNADE692.pdf
- Wang Y, Adair L. 2001. How does maturity adjustment influence the estimates of overweigh prevalence in adolescents from different countries using an international reference? Int J Obesity 25:550–558.
- Wronka I, Pawlinska-Chmara R. 2005. Menarcheal age and socio-economic factors in Poland. Ann Hum Biol 32:630–638.
- Zukauskaite S, Lasiene D, Lasasa L, Urbonaite B, Hindmarsh P. 2005. Onset of breast and pubic hair development in 1231 preadolescent Lithuanian schoolgirls. Arch Dis Child 90:932–936.