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Decline in the Age of Menarche in Istanbul Schoolgirls Over the Last 12 Years

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What is already known on this topic?

In the Western world, the mean age at menarche (AAM) decreased from the 1800s until the 1950s which was explained by improved living conditions and nutritional status. Some studies suggest that the AAM has continued to decrease after the 1950s while others suggest that the downward trend has halted.

What this study adds?

The median menarcheal age was 12.04 years and has declined by 0.7 years during the past 12 years in İstanbul. Sequential studies in Turkey indicate a decline in the AAM of 0.91 years in the last half-century -a speed of -0.56 years per generation of 30 years. Besides the strong influence of the maternal menarcheal age, the secular trend towards a younger AAM during the last decade can be mainly explained by increased rates of obesity in Turkey.

Abstract

Objective: Menarche is the endpoint of a sequence of maturational events of female puberty. The timing of menarche is a strongly heritable trait. However, secular trends suggest that lifestyle and environmental factors are important. To assess the trend in age at menarche (AAM), and its associated factors in İstanbul over the last 12 years.

Methods: A cross-sectional study was carried out between March and April 2022 on schoolgirls aged 9-18 years. A predesigned and self-administered questionnaire was filled out anonymously by the students. The data of AAM was included in the statistical analysis if the time of AAM is remembered in both months and years. A probit model was used to calculate the median AAM. The findings were compared with those from a study performed 12 years ago in the same region of İstanbul.

Results: Among 9000 girls to whom the questionnaire was distributed, 1749 (19.5%) responded. The median AAM of 1374 girls whose AAM information was considered valid was 12.04 years (95% confidence interval: 12.01-12.13), 0.7 years lower than was reported 12 years ago ($p < 0.0001$). AAM was correlated positively with maternal AAM, and negatively with body mass index (BMI) standard deviation score and maternal educational status ($p < 0.0001$, $p < 0.0001$ and $p = 0.002$), respectively. There was no correlation between the AAM and birth weight. Girls with BMI percentile ≥85% (n = 251) had earlier menarche than the ones with BMI percentile <85% (n = 1072) (11.5 vs. 12.1 years, $p < 0.0001$). Among the mother-daughter pairs (n = 1162), AAM of girls was 0.91 years (median 0.94 years) earlier than their mothers.

Conclusion: The present study demonstrates a significant downward trend in the menarcheal age in İstanbul over the last twelve years. These findings support a strong contribution from genetic factors and BMI on AAM.

Keywords: Puberty, age at menarche, secular trend, pubertal timing, Turkey

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Introduction

The age at menarche (AAM) displays considerable variation among girls and has undergone changes over time (1,2). Secular trend in the timing and tempo of puberty and AAM is determined by several intrinsic and environmental variables, such as genetics, lifestyle, nutrition, ethnicity, geographical and socioeconomic background, and endocrine-disrupting chemicals (3,4). In Europe, mean AAM has declined over the past two centuries - from 15-16 years in the early 19th century to 12-13 years in the late 20th century (1,3). Furthermore, early menarche has increased globally by 25-33% in recent generations (5,6,7). Longitudinal studies demonstrated a remarkable increase of early pubertal development and an increased rate of sexual precocity in children (4,8). Our observations suggested similar increase in the number of premature thelarche and precocious puberty cases over the last decade in our clinic. Since the age of menarche is highly correlated with the age of pubertal onset (9), the aim was to revisit the AAM data that we reported 12 years ago in İstanbul (10).

Methods

In the first part of the study, hospital records and clinical files were investigated to compare the number of patients presenting with premature thelarche, premature menarche, precocious puberty, and other conditions in our pediatric endocrinology clinic between January 1, 2008 - December 31, 2009, and January 1, 2020 - December 31, 2021 (Table 1).

In the second part, a cross-sectional study was conducted between March 2022 and April 2022 on schoolgirls aged 9-18 years living in the Asian part of İstanbul. A questionnaire and consent forms were distributed three days before the study. The predesigned, pretested, structured and self-administered questionnaire was filled out anonymously by the girls and their parents. A total of 9,000 female students from 22 schools located in the same area in İstanbul studied 12 years ago (10) were invited to participate in the study. Consented girls with no chronic medical condition were included.

The questionnaire was designed to obtain the information about menarcheal age of the participants and their mothers, birth weight, actual weight and height measurements of schoolgirls, the education status of the parents and the financial income of the family. The data about AAM was included only if the time of AAM could be recalled in both months and years. Body mass index (BMI) percentiles and BMI- standard deviation (SD) score (SDS) values of the girls were calculated according to national data (11). Educational status of the parents were classified as high (high school and beyond) or low (below high school). Household income was classified as low (costs > income), middle (costs≈income) or high (costs < income).

The study was performed with the approval of the Ethics Committee of Marmara University Faculty of Medicine (date: 05.11.2021, protocol no: 09.2021.1251), and the Turkish Ministry of Education. Participants and parents provided written informed consent.

In addition, the AAM trends were compared with the previous cohort studies performed in Turkey.

Statistical Analysis

The statistical analysis was performed using the GraphPad Prism® V5.0 software (GraphPad Software Inc., San Diego, California, USA). Results were reported as frequencies and percentages, mean, and median with minimum-maximum, interquartile ranges or 95% confidence intervals (CI) as appropriate. To calculate the median AAM, a probit model was used. Parametric t-test was used for comparison of variables. Pearson's correlation coefficients were used to investigate the relationship between various data, as required. The distribution of categorical variables was compared using chi-square test. Statistical significance was set at $p < 0.05$.

Results

According to our clinical records, the number of patients presenting with precocious puberty relative to the patients with other endocrine disorders was higher in the years 2020-2021 than in 2008-2009 ($p < 0.0001$) (Table 1).

Table 1. The prevalence of early puberty in girls among the total number of patients presenting to our pediatric endocrinology clinic

Time interval	Total number of patients (n)	Premature menarche, n (%)	Premature telarche n (%)	Precocious puberty n (%)	Total early pubertal patients n (%)
1 January 2008-31 December 2009	33328	5 (0.015)	88 (0.26)	44 (0.13)	137 (0.41)
1 January 2020-31 December 2021	35818	13 (0.036)	95 (0.26)	135 (0.37)	243 (0.67)
Chi-square test p value		0.08	0.97	**< 0.0001**	**< 0.0001**

The questionnaire was distributed to 9000 girls who were attending schools located in the area where we performed the study to determine AAM 12 years ago (10). Among those, 1749 (19.5%) consented and filled out the questionnaire. Of them, 1374 recalled the year and month of the AAM which was a median of 12.04 years (95% CI: 12.01-12.13) and a mean ± SD of 12.07 ± 1.11 years. The AAM was approximately 0.7 years lower than reported using the same method 12 years ago in the same region of İstanbul ($p < 0.0001$) (Table 2, Figure 1a). Maternal AAM was reported by 1528 mothers and was a median of 12.96 years (95% CI: 12.92-13.08). There were 1162 mother-daughter pairs providing AAM data which showed that the daughters had a mean of 0.91 years (median 0.94) earlier menarche than their mothers ($p < 0.0001$). However, the AAM of the girls was positively and significantly correlated with their mothers' ($R^2 = 0.048$, $p < 0.0001$).

The prevalence of overweight (BMI ≥85% and <95%) and obesity (BMI ≥95%) was 9.1% (n = 121) and 9.8% (n = 130), respectively. The overweight/obese girls (n = 251) had earlier menarche than the rest of the cohort (n = 1072) [median (95% CI); 11.54 (11.39-11.77) vs. 12.12 (12.04-12.23) years, $p < 0.0001$] (Figure 1b). There was a significant negative correlation between BMI-SDS and AAM ($R^2 = 0.066$, $p < 0.0001$).

Maternal educational status was negatively correlated with AAM. The AAM was lower in girls with mothers of higher educational status (HES) than the ones with mothers of lower educational status (LES) [median (95% CI); 11.96 (11.87-12.04) vs. 12.17 (12.03-12.28) years, $p = 0.002$] (Figure 1c).

The correlation between the AAM and birth weight, paternal educational status or household income were not significant ($p = 0.18$, 0.17, and 0.07, respectively).

Table 2. The number of schoolgirls and the percentage of those having menarche at the respective ages in two studies with 12 years intervals in İstanbul

Age (years)	Atay et al. (10) (2010)	Guran et al. (2022) (current study)
	Menarche, n (%)	Menarche, n (%)
10	520 (1.5)	31 (12.9)
11	501 (12.6)	213 (19.2)
12	463 (42.5)	232 (49.5)
13	535 (78.3)	230 (84.3)
14	355 (92.7)	283 (94.6)
15	311 (98.1)	377 (98.9)
16	203 (100)	311 (99)
17	124 (100)	51 (100)
18	71 (100)	21 (100)

The total prevalence of preterm and small for gestational age (SGA) births was 14.5% in the cohort (n = 200). There was no correlation between AAM and birthweight ($r = 0.03$, $p = 0.18$). There was no significant difference for AAM between preterm +/- SGA and term +/- appropriate for gestational age (AGA) births (mean 12.01 vs. 12.07 years, $p = 0.50$).

Previous studies reporting AAM in the various regions of Turkey also showed an ongoing decline in the menarcheal age since 1970s (Figure 2) (10,12,13,14,15,16,17).

Discussion

This study on a large cohort of schoolgirls demonstrated that the median AAM was 12.04 years and has declined by 0.7 years during the past 12 years in İstanbul. Current data presents evidence of a significant shift in menarche to earlier ages in recent years in Turkey.

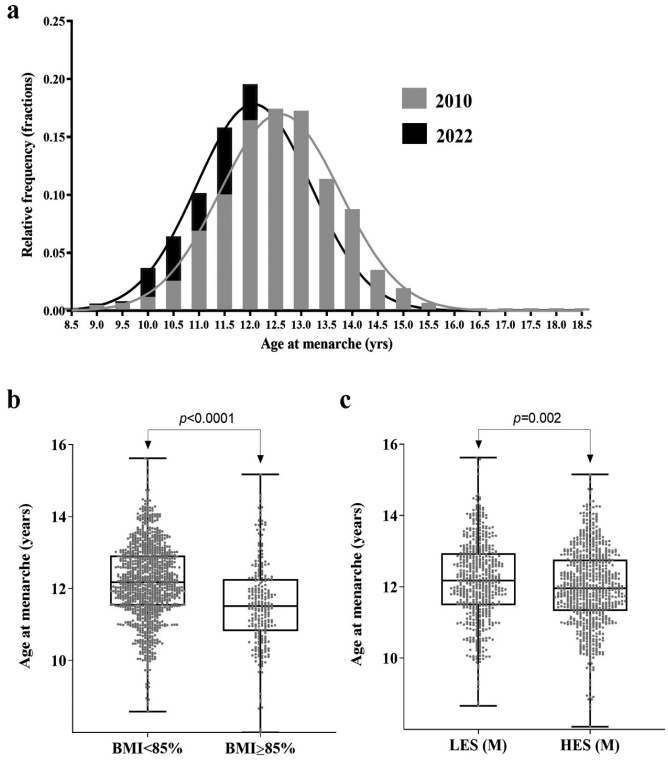

Figure 1. Characteristics of age at menarche (AAM) in İstanbul. a) Change in the AAM in İstanbul in the last 12 years. The results of the study by Atay et al. (10) in 2010 are compared with the current study. Bars indicate the fractions (percentage) of the girls having menarche at the respective ages. b) Comparison of AAM between girls with BMI <85% and ≥85%, c) Comparison of AAM among the girls whose mothers have HES or LES

LES: lower educational status, HES: higher educational status, BMI: body mass index, yrs: years

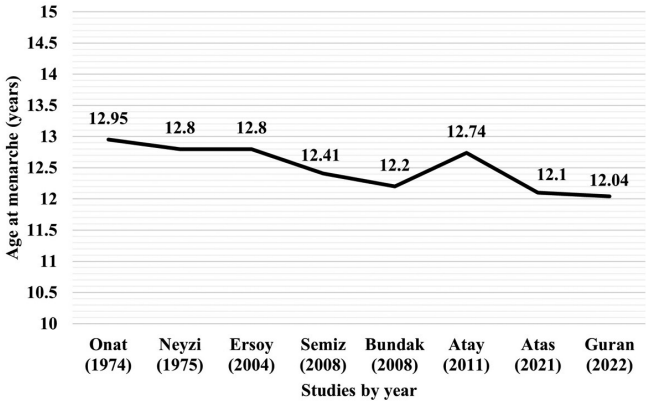

Figure 2. Schematic representation of previous studies determining AAM in Turkey by years (10,11,12,13,14,15,16,17)

AAM: age at menarche

The starting point of our attempt to update our data on AAM was an observation of increased clinical presentation of early puberty in recent years in our department. Although menarche is a relatively late marker of puberty, it is significantly correlated with age at the onset of thelarche and is therefore considered to be an indicator of the onset of puberty (1). Indeed, a higher number of admissions to our outpatient clinic for premature thelarche, premature menarche and precocious puberty by 50% in last 12 years is in line with the finding of a decline in AAM in İstanbul schoolgirls. The AAM was found to be 12.74 years in 2011 by Atay et al. (10) in 1732 girls attending schools at the same region of İstanbul. Not only in İstanbul, in which resides almost 18% of Turkey's population (18), but sequential studies in Turkey indicate a decline in AAM of 0.91 years in the last half-century -a speed of -0.56 years per generation of 30 years (12,13,14,15,16,17).

Data published during 1990-2000 on the AAM in different European countries showed a north-to-south gradient that ranged from 13.4 years in the north to 12 years in the south of Europe. There was also an east-to-west gradient that was reported at 12.6 years in France to lower ages in the Eastern European/Mediterranean countries such as 12.3 years in Greece and 12 years in Italy (1). Geographical, genetic/ethnic, and environmental similarities between Turkey and other Mediterranean countries may partly explain earlier menarche in Turkey compared to Northern/Eastern Europe. Nevertheless, the rate of decline in AAM is sharper in Turkey relative to other European and Mediterranean countries. A study from The Netherlands in 2009 showed a greater decrease in median AAM in Turkish girls between 1997 and 2009 compared to Dutch girls (from 13.15 to 13.05 in Dutch vs. from 12.80 to 12.50 years in Turkish girls). These authors reported that 33% of Turkish girls younger than 12 years start menstruating in primary school (6). Compared to Dutch girls they found a faster decrease in AAM in girls of Turkish descent, even after adjustment for BMI-SDS.

An increased rate of obesity may account for the downward trend of AAM in Turkey, as childhood obesity figures are also on the rise in the comaprative period. Between, 2000 and 2010 different regions of Turkey have demonstrated varying prevalence rates of 10.3-17.6% and 1.9-7.8% for overweight and obesity, respectively, in children aged 6-16 years (19). In the last decade, the prevalence of overweight (including obesity) and obesity among children and adolescents aged 10-19 years raised significantly to 27-28% and 9-10%, respectively (20). Lower AAM in obese/overweight girls and remarkable negative correlation of BMI and AAM in our study supports the major influence of obesity on the tempo of puberty, as shown by several others (21,22,23,24).

Socioeconomic status (SES) may account for variations in the timing of puberty. However, the results of studies into the effects of SES on AAM are inconsistent and differentiate not only between countries but within countries as well (23,25,26,27). According to a general conception, a low socioeconomic living environment may involve nutritional problems, high energy expenditure, insufficient access to health services, large family size, and social and emotional injuries and ultimately delayed puberty and menarche. On the other hand, declining trends in AAM have been reported from high SES populations (23,25,28,29). Previous studies indicated that girls of Turkish descent with high SES had an earlier AAM than girls with low SES (10,14). In the present study we did not observe a correlation between SES and AAM. However, income per capita in Turkey declined by 1156 $/year-nearly 11% in 2021 compared to that in 2010 (10,743 $/year in 2010 while it is 9,587 $/year in 2021) (https://www.macrotrends.net/countries/TUR/turkey/gdp-per-capita), which may have an effect in the decline in AAM.

Similar to SES, parental education has been found to be associated with AAM in some studies (30,31), but this has not been replicated in others (29,32). A similar discrepancy in the effect of parental education on AAM was also observed in studies from Turkey. Ataş Aslan and Ünüvar et al. (17) found that LES was associated with earlier menarcheal age but this was not supported by Ersoy et al. (14). We have found that higher maternal education was associated with earlier onset of menarche, as shown in some previous studies (23,26). Overall, our results and previous studies suggest that obesity is the major and consistent non-genetic variable responsible for declining menarcheal age. Besides the non-genetic factors, we also demonstrated that AAM

of the mothers was significantly positively correlated with the AAM of their daughters, which is the most consistent finding of the majority of the studies reporting AAM (1,3).

SGA children are more prone to have precocious pubarche and an earlier onset of pubertal development and menarche, and faster progression of puberty than children born AGA (33). However, we could not demonstrate a relationship between birth weight and AAM in our cohort and AAM was similar between girls born SGA or AGA.

This study also provides the first AAM data after the Coronavirus disease-2019 (COVID-19) pandemic. There is some evidence of increased frequency of idiopathic central precocious puberty in girls during the COVID-19 pandemic in Turkey and in other countries (34,35,36,37,38,39,40). Some studies found an association between earlier pubertal onset and increased body mass, disturbed sleep patterns or increased screen exposure during COVID-19 lockdown. The possible increased rate of earlier pubertal onset during the pandemic may have contributed to the observed decline in menarcheal age in the present study, and this should be investigated in the future.

Study Limitations

The main limitation of the study, as in the most of the studies reporting AAM, is the collection of AAM based on recall by girls and their mothers, which is susceptible to various forms of error (1). However, the same method was used 12 years ago and the AAM data was included only if both month and year of menarcheal age was remembered precisely. Utilization of the same method for the collection of the data, the same statistical analysis for AAM, and doing the survey in the same area are the strengths of the study.

Conclusion

In conclusion, our data suggests that a downward trend in the AAM continues and a plateau for AAM has not yet been reached in Turkey. Besides the strong influence of the maternal menarcheal age, the secular trend towards a younger AAM during the last decade can be explained mainly by increased rates of obesity among children in Turkey.

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Ethics

Ethics Committee Approval: The study was performed with the approval of the Ethics Committee of Marmara University Faculty of Medicine (date: 05.11.2021, protocol no: 09.2021.1251), and the Turkish Ministry of Education.

Informed Consent: Participants and parents provided written informed consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Didem Helvacıoğlu, Büşra Gürpınar Tosun, Zehra Yavaş Abalı, Zeynep Atay, Belma Haliloğlu, Serap Turan, Tülay Güran, Abdullah Bereket, Analysis or Interpretation: Tülay Güran, Korcan Demir, Abdullah Bereket, Concept: Tülay Güran, Seyhan Hıdıroğlu, Design: Tülay Güran, Seyhan Hıdıroğlu, Abdullah Bereket, Data Collection or Processing: Didem Helvacıoğlu, Büşra Gürpınar Tosun, Zehra Yavaş Abalı, Fahriye Alır, Yusuf Taha Arslan, Giasim Molla, Berk Şahin, Mehmet Emir Sayar, Zeynep Atay, Belma Haliloğlu, Literature Search: Tülay Güran, Abdullah Bereket, Writing: Tülay Güran, Abdullah Bereket.

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