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ERICA: age at menarche and its association with nutritional status ☆

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Abstract

Objective: To estimate the mean age at menarche and its association with nutritional status in Brazilian adolescents.

Methods: The study sample included female adolescents aged 12–17 who participated in a multicenter, school-based, country-wide, cross-sectional study entitled *The Study of Cardiovascular Risk in Adolescents* (*Estudo de Riscos Cardiovasculares em Adolescentes [ERICA]*). Mean and median ages at menarche in Brazil were estimated. The association of age at menarche with sociodemographic data and nutritional status were described as means and their respective 95% confidence intervals. Survival analysis was used to assess the age at menarche according to nutritional status categories and the log-rank test was used to compare the medians. Bivariate and multivariate analyses were performed using Cox regression to verify the association between menarche and other variables.

Results: A total of 73,624 students were evaluated, comprising 40,803 girls, of whom 37,390 reported menarche at a mean age of 11.71 years and a median of 12.41 years. Median age at menarche was lower in overweight and obese girls ($p < 0.001$). The multivariate analysis showed that excess weight (HR = 1.28; 95% CI 1.21−1.36; $p < 0.001$) and studying in a private school (HR = 1.06; 95% CI 1.02−1.10; $p = 0.003$) were associated with menarche.

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Conclusions: This is a pioneering study in Brazil with national and regional representativeness to estimate the mean and the median age of occurrence of menarche. Adolescents with excess weight had an earlier menarche than their peers, even after adjustment for confounding factors.
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ERICA: idade da menarca e sua associação com o estado nutricional

Resumo

Objetivo: Estimar a média de idade de ocorrência da menarca e sua associação com o estado nutricional em adolescentes brasileiras.

Métodos: Foram avaliados dados de meninas com 12 a 17 anos a partir de um estudo seccional de base escolar, com representatividade nacional e macrorregional, o ERICA (Estudo de Riscos Cardiovasculares em Adolescentes). Foram estimadas média e mediana de idade de ocorrência da menarca no Brasil, pelo método recordatório. A associação da idade da menarca com dados sociodemográficos e estado nutricional foi descrita como médias e seus respectivos IC95%. Análise de sobrevida foi utilizada para explorar a idade da menarca segundo categorias de estado nutricional e teste logrank foi utilizado para comparação das medianas. Análises bivariada e multivariada foram realizadas por meio da regressão de Cox para verificar a associação entre menarca e demais variáveis.

Resultados: Foram avaliados 73.624 estudantes, 40.803 meninas, das quais 37.390 referiram ter apresentado menarca, sendo a média da idade de ocorrência de 11,71 anos e a mediana de 12,41 anos. As medianas da idade de ocorrência da menarca foram menores naquelas com sobrepeso e obesidade (p < 0,001). A análise multivariada evidenciou que excesso de peso HR = 1,28, IC95% 1,21 -1,36, p < 0,001 e estudar em escola privada HR = 1,06, IC95% 1,02 -1,10, p = 0,003 estão associados à menarca.

Conclusões: Este foi o primeiro estudo brasileiro com representatividade nacional a estimar a média de idade de ocorrência da menarca. As adolescentes com excesso de peso apresentaram menarca em idade inferior às demais, mesmo após ajuste.

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Introduction

The first menstrual cycle in the adolescent's life is called menarche. It is a late event of puberty and an important indicator of sexual maturation. This milestone typically occurs within two to three years after puberty onset, and is characterized by thelarche, which is represented by the development of the mammary bud.[1]

Regarding the age group, menarche usually occurs between the ages of 12 and 13 years.[2] Approximately 50–80% of the variation in puberty onset age and milestones is determined by genetic factors; however, the substantial decline at the age at menarche between the early 19th century and the mid-20th century was associated with a significant improvement in nutrition and living conditions during the process of modern civilization.[3,4]

The declining trend in the age at menarche has undergone an apparent stabilization since the 1960s.[5,6] However, in the last two decades, a trend toward menarche anticipation has been reported, especially in developing countries.[7,8]

Studies have shown that greater weight gain and body mass index (BMI) during childhood is related to an earlier puberty onset. Therefore, these are determining factors of the age at menarche.[9,10] In Brazil, data from the Family Budget Survey (POF), carried out between 2008 and 2009, showed that approximately 20% of the adolescents were overweight and approximately 5% were obese. When compared with the values obtained in 1974 and 1975, it was observed that the prevalence of excess weight increased almost three-fold in females.[11]

Menarche in younger age groups has been correlated with adverse health events, including breast cancer, cardiovascular incidents, and increased overall mortality.[10] Thus, the present study aimed to estimate the mean age at menarche onset and its association with nutritional status in Brazilian adolescents.

Methods

This study is part of the Cardiovascular Risk Study in Adolescents (Estudo de Risco Cardiovascular em Adolescentes [ERICA]), a national, cross-sectional, school-based study, aiming to estimate the prevalence of metabolic syndrome and other cardiovascular risk factors in adolescents aged 12–17 years.[12]

The study population was stratified into 32 geographic strata, consisting of 27 capitals, and five sets of other

municipalities with more than 100,000 inhabitants from each of the five macro-regions of the country. The stratification was made according to three categories: school, class, and students. Thus, the sample is representative at national and regional level, as well as in the level of state capitals. The details of the sampling plan have been previously published.[13]

For the present study, the sample consisted of adolescents between 12 and 17 years of age who attended schools located in all five Brazilian regions. The exclusion criteria comprised pregnant adolescents, those with physical or mental disabilities or with prosthetic devices of any kind, and those whose anthropometric measurements were not obtained.

The school record informed the type of administration (public or private) and its location (urban or rural). Data on age, age at menarche, and ethnicity were obtained through a self-applicable questionnaire, using an electronic data collector (Personal Digital Assistant [PDA] model LG GM750Q, LG Electronics, CA, USA). The ethnicity was self-reported as white, mixed-race, black, Asian, and native Brazilian, according to the classification of the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística [IBGE]).[14]

Weight was measured using an electronic scale (Líder® P150m, with a capacity of 200 kg and precision of 50 g – SP, Brazil). The scale was placed on a level horizontal floor, with both feet touching the floor simultaneously. For the weight measurement, the adolescents were barefoot and wearing light clothing. Height was measured using a portable and collapsible Alturexata® stadiometer (Alturexata®, MG, Brazil), with a 1-mm precision and extension of up to 213 cm. Two measurements were taken, and a maximum variation of 0.5 cm between the two of them was allowed. If the variation exceeded this value, these measurements were discarded and performed again. The protocol of Lohman et al. was utilized.[15]

The World Health Organization guidelines were utilized to classify the adolescents' nutritional status, using the BMI-for-age index according to gender.[16] The following cut-off points were used: very low weight: Z score < -3; low weight: Z score ≥ -3 and < -2; normal weight: Z score ≥ -2 and ≤ 1; overweight: Z score > 1 and ≤ 2; and obesity: Z score > 2.

The ERICA study was approved by the Research Ethics Committee of each of the 27 participating institutions, one in each unit of the Brazilian federation. All students from the selected groups who signed the term of agreement were interviewed and examined.

Data analyses were performed using Stata software (Stata Statistical Software: Release 14. College Station, TX, USA). The mean age at menarche occurrence and the respective 95% confidence intervals were estimated for the entire Brazil and per geographical macro-region. Using national data, the mean age of menarche onset and the respective 95% confidence intervals were estimated according to sociodemographic data and nutritional status. The Stata survey module was used to analyze complex sample data.

A subsample of adolescents in whom nutritional status was verified at the year of menarche was studied. It consisted of 2274 adolescents who reported age at menarche coinciding with the chronological age at the time of the study. The mean age at menarche and the respective

Table 1 Distribution of the mean age at menarche, Brazil and macro-regions. ERICA, Brazil, 2013–2014.

Brazil/macro-region	Mean age (years)	95% CI
Brazil	11.71	11.69–11.74
North	11.78	11.74–11.82
Northeast	11.73	11.70–11.77
Midwest	11.79	11.74–11.84
Southeast	11.69	11.64–11.74
South	11.68	11.60–11.76

ERICA, Study of Cardiovascular Risk in Adolescents (Estudo de Riscos Cardiovasculares em Adolescentes); 95% CI, 95% confidence interval.

confidence intervals according to the nutritional status (very low weight, low weight, normal weight, overweight, and obesity) were verified.

The survival analysis was performed to assess the age at menarche according to nutritional status categories, also using data from adolescents who had not yet reported having menarche. The life table allowed the estimation of the percentage of adolescents who reported menarche at each age, and to graphically analyze the survival function of the total population, according to nutritional status. The log-rank test was used to compare median age at menarche according to the nutritional status. The Cox model was used to estimate the hazard ratio (HR) of each nutritional status category, having as reference the category defined as normal weight. The analysis was considered statistically significant when $p < 0.05$.

Subsequently, bivariate analyses were performed using Cox regression to verify the association between menarche and the nutritional status variables (reference: adolescents without excess weight [very low weight, low weight, and normal weight]); type of school administration; school region; and ethnicity (reference: black). The multivariate analysis was performed only with variables that showed $p < 0.1$ in the bivariate analysis.

Results

According to the schools' records, 102,327 students were eligible in the age group of 12–17 years. Complete anthropometric data and questionnaire responses were obtained from 73,624 students, of whom 40,803 (55.4%) were females. Of these, 37,390 had already had menarche.

When assessing the adolescents who had already undergone it, it was observed that the mean age at menarche was 11.71 years (Table 1). When analyzing all assessed girls, considering not having menstruated or not knowing the age at menarche, the median age at menarche was 12.41 years.

The mean age at menarche in the geographic macro-regions of the country was similar, and the lowest mean age at menarche was recorded in the South region, while the highest mean age was observed in the Midwest region, with no statistically significant difference (Table 1).

The distribution of adolescents in Brazil, according to the age at menarche, showed that approximately 15% of the girls menstruate for the first time before the age of 11; 60% of the adolescents had the menarche between 11 and 12 years

Table 2 Distribution of the mean age at menarche according to sociodemographic data and nutritional status. ERICA, Brazil, 2013–2014.

Characteristics	Mean	95% CI
Ethnicity		
White	11.70	11.64–11.76
Black	11.63	11.53–11.73
Mixed-race	11.74	11.69–11.79
Asian	11.65	11.49–11.82
Native Brazilian	11.89	11.63–12.14
Others	11.73	11.57–11.90
Type of school		
Public	11.74	11.71–11.78
Private	11.57	11.49–11.65
School location		
Urban	11.71	11.68–11.74
Rural	11.84	11.74–11.95
Nutritional status		
Very low weight	12.83	11.70–13.95
Low weight	12.37	12.17–12.56
Normal weight	11.82	11.79–11.85
Overweight	11.37	11.31–11.44
Obesity	11.34	11.25–11.43

ERICA, Study of Cardiovascular Risk in Adolescents (Estudo de Riscos Cardiovasculares em Adolescentes); 95% CI, 95% confidence interval.

Table 3 Mean age at menarche by nutritional status in the subsample that showed age at menarche coinciding with the chronological age in the study year. ERICA, Brazil, 2013–2014.

Nutritional status	Mean age (years)	95% CI
Low weight + very low weight	14.02	13.71–14.34
Normal weight	13.33	13.23–13.44
Overweight + obesity	12.94	12.78–13.10

ERICA, Study of Cardiovascular Risk in Adolescents (Estudo de Riscos Cardiovasculares em Adolescentes); 95% CI, 95% confidence interval.
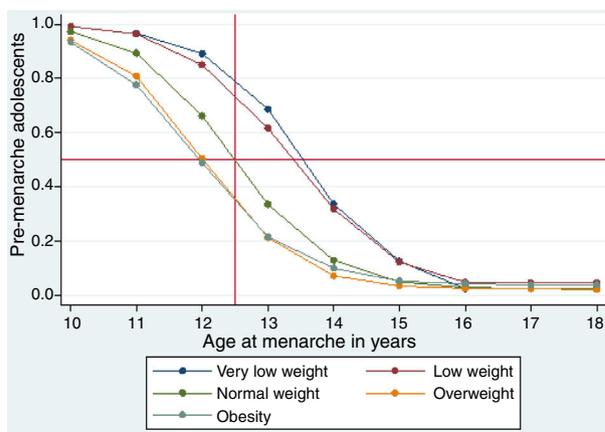
Figure 1 Survival function of the age distribution of menarche in the entire studied population.

and 11 months, and approximately 99% of the adolescents had already menstruated at 14 years and 11 months.

Table 2 shows the distribution of the mean age at menarche according to sociodemographic characteristics and nutritional status. Girls attending private schools showed a difference of approximately two months less in the mean age at menarche when compared with those attending public schools. This difference was close to that found among adolescents who studied in urban areas, when compared with those in rural areas, who had a higher mean age at menarche occurrence. In relation to ethnicity, it was observed that black adolescents had the lowest mean age at menarche while native Brazilians had the highest, but this difference was not statistically significant.

Regarding the nutritional status, adolescents with excess weight (overweight and obese) showed a lower mean age at menarche than the national mean, and significantly lower than those without excess weight.

The analysis of the subsample consisting of 2274 adolescents, who reported age at menarche coinciding with chronological age at the time of the study, indicated that the mean age at menarche for those with excess weight was one year less than the mean of those with low weight and very low weight, with a statistically significant difference (Table 3).

The median age of the adolescents with very low weight was 13.53 years; in those with low weight it was 13.39 years; those with normal weight, 12.5 years; those with overweight, 12.01 years; and those with obesity, 11.96 years (log rank test, $p < 0.001$). Considering that the described nutritional status preceded menarche, the occurrence of

menarche in overweight and obese adolescents precedes that of adolescents with normal weight, and menarche in the latter precedes that of adolescents with low and very low weight (Fig. 1).

Cox model estimates for associations between the occurrence of menarche and each nutritional status had adolescents with normal weight as reference (HR = 1) and showed HR = 0.62 (95% CI: 0.42–0.92; $p = 0.017$) for adolescents with very low weight; HR = 0.56 (95% CI: 0.47–0.67; $p < 0.001$) for adolescents with low weight; HR = 1.31 (95% CI: 1.24–1.38; $p < 0.001$) for overweight adolescents; and HR = 1.17 (95% CI: 1.06 – 1.30; $p = 0.001$) for adolescents with obesity.

The bivariate analyses evidenced the associations between menarche and excess weight (HR = 1.29; 95% CI: 1.22–1.36; $p < 0.001$); studying in a private school (HR = 1.07; 95% CI: 1.03–1.11, $p < 0.001$); in urban area (HR = 1.06; 95% CI: 0.98 –1.14, $p = 0.14$); and being black (HR = 1.05; 95% CI: 0.97–1.12; $p = 0, 22$). In the multivariate analysis, using the variables excess weight and studying in a private school, the associations observed for excess weight and studying in a private school were: HR = 1.28 (95% CI: 1.21–1.36; $p < 0.001$) and HR = 1.06 (95% CI: 1.02–1.09; $p = 0.002$), respectively.

Discussion

The mean age at menarche occurrence in Brazilian girls was 11.71 years. There were no differences in age at menarche in the different macro-regions of Brazil. An association was

observed between menarche and excess weight in the bi- and multivariate analysis, with statistical significance. As for the mean age found (11.71 years), the result was similar to that of other Brazilian studies, such as that carried out in the city of Rio de Janeiro, which evaluated 502 adolescents between 11 and 15.9 years from a public and a private school and observed mean ages at menarche of 11.7 and 11.5 years, respectively.[17]

The mean age at menarche found in the present study was also similar to that observed in a Mexican study, which showed that in Mexico City, the mean age at menarche occurrence in students aged 8–17 years was 11.4 years.[7] Similarly, the median age at which menarche occurred in the present study (12.41 years) was close to that found in a Colombian study (12.6 years), a national survey with 15,441 adolescents aged 10–18 years.[18]

However, the mean age in the present study was approximately one year lower than that reported in a Korean study, which analyzed 3409 girls aged 10–18 years (12.7 years)[8] and in a cohort study of 610 girls between 3 and 17 years of age in the United States, in which a mean age at menarche of 12.8 years was observed in white girls and of 12.2 years in black girls, using the prospective method.[19]

Brazilian studies also showed discordant results in relation to the present study. Roman et al., using the *status quo* method in 2009, observed a mean age at menarche of 12.2 years in a cross-sectional study with 2761 schoolchildren from a city in Southern Brazil.[20] Castillo et al. assessed the secular trend of menarche from two cross-sectional studies, in 2001 and 2010, conducted in private schools in a city in Southeastern Brazil, and observed that, in 2010, the median age at menarche was 12.08 years.[21]

However, it is not possible to establish comparisons between the previous results and the present study. Apart from the socioeconomic and cultural differences between countries and within Brazil, the difference between the results can be explained by the different methods of determining age at menarche and the selection of sample units of the studies.

The present study comprised the largest number of girls ever assessed in a single study in Brazil, and it was the first to presented data, with national and regional representation, of adolescents between 12 and 17 years old who attend schools and live in municipalities with over 100,000 inhabitants. Thus, it was possible to demonstrate the mean age at menarche occurrence in each Brazilian macro-region.

The mean age at menarche occurrence in the geographic macro-regions were similar. The Southeast and South regions showed mean values below the national mean, whereas the highest means were found in the North and Midwest regions. Although these differences did not present statistical significance, it is important to observe that the Southeast and South regions comprise the five richest states of the federation.[22] This negative trend in age at menarche in groups more likely to benefit from socioeconomic development has been previously described in the literature.[18]

As for ethnicity differences regarding the age at menarche, it is known that racial and ethnic differences should be understood as reflecting a combination of genetic, social and environmental factors. Euling et al. observed that black girls had an earlier onset of puberty and menarche, followed by Latin-American or Mexican girls, while white girls started puberty and had menarche at a later age.[5]

Similarly, Ossa et al. showed that the mean age at menarche in native Chilean women was five months higher when compared with the mean of non-native Chilean women.[23] In the present study, although a tendency to menarche occurrence at an earlier age was observed in black girls and at an older age in native Brazilian girls, this result did not show a statistically significant difference.

In the present study, when comparing the mean values of age at menarche between the adolescents from public and private schools, a higher and statistically significant value was observed among those attending private schools. This association persisted even after adjustment. When the mean values between urban and rural areas were compared, those from urban areas had a lower mean age at menarche occurrence, but without statistical difference. Similar associations were reported in other studies.[18,20]

Although the results of the present study suggest that menarche tends to occur earlier in girls who belong to a higher socioeconomic level, i.e., those living in the South and Southeast regions, in urban areas, and those attending private schools, it was observed that the difference was relatively small, of approximately two months (Table 2), with little impact on clinical practice.

Regarding the associations between nutritional status and puberty, review studies have been carried out to better understand their complexity.[9,10] In the present study, when the mean age at menarche was estimated according to the nutritional status classification, it was observed that girls with a higher BMI (overweight and obesity) menstruated earlier than those without excess weight, as shown in Table 2. This association has been reported in previous epidemiological studies.[8,18,24]

Aiming to minimize a possible disagreement between the current BMI and that at menarche, a subsample was analyzed with 2274 adolescents whose menarche occurred at the chronological age when the study was performed. Thus, the association between the age at menarche and nutritional status at the outcome was evaluated. The result found in this group was in agreement with that of the total sample, as the mean age at menarche was lower among those with excess weight and higher among those with low and very low weight.

Survival analysis was used to quantify the effect of nutritional status on the age at menarche, corroborating the association observed in the sample that reported having already had menarche and remembered the age at occurrence. Moreover, excess weight remained significant even after adjustment.

The occurrence of menarche in younger age groups has been associated with an increased risk of type 2 diabetes mellitus, cardiovascular disease, and cancer (such as breast cancer) in adulthood.[25–27] Thus, individuals with earlier sexual maturity can be identified as being at risk for the future development of these diseases.

One limitation of the present study was the use of the recall method to assess age at menarche. However, as the adolescents were evaluated at ages close to the event, the probability of memory bias was reduced. A Brazilian study observed that age at menarche obtained by the recall method was similar for girls who had menstruated three

years before or less, but for more than three years, the memory bias was significant.[28] However, another study indicated that the correlation between the age obtained during the longitudinal follow-up and the reported age is high, even 30 years after the event.[29]

In conclusion, the knowledge of the mean age at menarche is relevant, since the early age of occurrence of this event may be a sign of increased risk of type 2 diabetes mellitus, cardiovascular diseases, and cancer in adult life. Considering that the age of menarche depends on the interaction between genetic and environmental factors, and that excess weight is a modifiable risk factor, measures should be taken concerning the increasing rates of overweight and obesity among the population, including the pediatric population, in Brazil.

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Conflicts of interest

The authors declare no conflicts of interest.

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