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Original article

Timing of thelarche and menarche and temporal growth trends in internationally adopted girls in Spain: a prospective cohort study

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ARTICLE INFO

Article history:
Received 24 February 2026
Received in revised form 08 May 2026
Accepted 19 May 2026

Keywords:
Thelarche
Menarche
Growth
International adoption
Spain

ABSTRACT

Introduction: This prospective observational study evaluated the age at thelarche and menarche in internationally adopted girls in Spain and analyzed height and body mass index trends at these pubertal milestones.

Material and methods: The study included 102 healthy girls adopted in Spain between 1998 and 2008 from Russia/Ukraine (38), China (34), India/Nepal (17), and Latin America (13). Growth and pubertal development were assessed using standardized procedures. Families were trained to recognize thelarche and menarche, allowing clinical confirmation and anthropometric evaluation. Measurements obtained at adoption, thelarche and menarche were compared with WHO Child Growth Standards, and z-scores were calculated. Pearson correlation coefficients were used to assess associations.

Results: Mean age at adoption was 3.5 years. Girls from India/Nepal and Latin America were adopted later, whereas those from China were adopted younger. At adoption, the cohort showed height delay with greater deficits in height than weight. Mean age at thelarche was 9.7 years, occurring earlier in girls from Latin America and India/Nepal and later in girls from China. A significant negative correlation was found between age at adoption and age at thelarche ($r = -0.43$, $p < 0.001$), indicating that later adoption was associated with earlier pubertal onset. Height normalized at thelarche, reflecting marked catch-up growth, and no association was observed between anthropometric measures at adoption and at thelarche. Mean age at menarche was 11.7 years, with earlier onset in girls from Latin America and India/Nepal and later onset in girls from China. Age at adoption was also negatively correlated with age at menarche ($r = -0.48$, $p < 0.001$). Although menarche occurred earlier in girls adopted later, growth patterns at this pubertal milestone were unrelated to age at adoption.

Conclusions: Internationally adopted girls in Spain experienced early thelarche and menarche, particularly when adopted at older ages, independent of later growth patterns.

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https://doi.org/10.53986/ibjm.2026.0015

Momento de aparición de la telarquia y la menarquia y tendencias temporales del crecimiento en niñas adoptadas internacionalmente en España: un estudio de cohorte prospectivo

INFO. ARTÍCULO

Historia del artículo:
Recibido 24 Febrero 2026
Recibido en forma revisada 08 Mayo 2026
Aceptado 19 Mayo 2026

Palabras clave:
Telarquia
Menarquia
Crecimiento
Adopción internacional
España

RESUMEN

Introducción: Este estudio observacional prospectivo evaluó la edad de la telarquia y la menarquia en niñas adoptadas internacionalmente en España y analizó las tendencias de la talla y el índice de masa corporal en estos hitos puberales.

Material y métodos: El estudio incluyó a 102 niñas sanas adoptadas en España entre 1998 y 2008 procedentes de Rusia/Ucrania (38), China (34), India/Nepal (17) y Latinoamérica (13). El crecimiento y el desarrollo puberal se evaluaron mediante procedimientos estandarizados. Las familias recibieron formación para reconocer la telarquia y la menarquia, lo que permitió la confirmación clínica y la evaluación antropométrica. Las mediciones obtenidas en el momento de la adopción, la telarquia y la menarquia se compararon con los Estándares de Crecimiento Infantil de la OMS, y se calcularon las puntuaciones z. Se utilizaron coeficientes de correlación de Pearson para evaluar las asociaciones.

Resultados: La edad media en el momento de la adopción fue de 3,5 años. Las niñas de India/Nepal y Latinoamérica fueron adoptadas a edades más avanzadas, mientras que las de China lo fueron a edades más tempranas. En el momento de la adopción, la cohorte mostró retraso en la talla, con mayores déficits en talla que en peso. La edad media de la telarquia fue de 9,7 años, apareciendo antes en las niñas de Latinoamérica e India/Nepal y más tarde en las de China. Se encontró una correlación negativa significativa entre la edad de adopción y la edad de la telarquia ($r = -0,43$, $p < 0,001$), lo que indica que una adopción tardía se asoció con un inicio puberal más temprano. La talla se normalizó en la telarquia, reflejando un marcado crecimiento recuperador, y no se observó asociación entre las medidas antropométricas en el momento de la adopción y en la telarquia. La edad media de la menarquia fue de 11,7 años, con aparición más temprana en las niñas de Latinoamérica e India/Nepal y más tardía en las de China. La edad de adopción también se correlacionó negativamente con la edad de la menarquia ($r = -0,48$, $p < 0,001$). Aunque la menarquia ocurrió antes en las niñas adoptadas a edades más avanzadas, los patrones de crecimiento en este hito puberal no se relacionaron con la edad de adopción.

Conclusiones: Las niñas adoptadas internacionalmente en España experimentaron telarquia y menarquia tempranas, especialmente cuando fueron adoptadas a edades más avanzadas, independientemente de los patrones de crecimiento posteriores.

HOW TO CITE THIS ARTICLE: Oliván-Gonzalvo G. Timing of thelarche and menarche and temporal growth trends in internationally adopted girls in Spain: a prospective cohort study. Iberoam J Med. 2026. doi: 10.53986/ibjm.2026.0015. [Ahead of Print].

1. INTRODUCTION

Puberty is a critical stage of life that results from the reactivation of the hypothalamic–pituitary–gonadal axis after a quiescent period during childhood. The precise mechanisms underlying pubertal onset are not yet fully understood [1]. Several studies have reported earlier pubertal development and an increased incidence of precocious puberty in children—primarily girls—who migrate for international adoption to various Western European countries [2-6]. However, few studies have clinically verified the age at onset of thelarche and the timing of menarche in cohorts of internationally adopted girls.

Delayed growth is a commonly observed phenomenon among internationally adopted girls. Studies suggest that this may be attributable to factors such as malnutrition, stress, and psychosocial deprivation prior to adoption [7, 8]. Following adoption, catch-up growth in height and weight, together with improved nutritional and psychological conditions, may trigger the onset of puberty. The underlying pathophysiological mechanisms remain unclear, and current hypotheses include the influence of racial, nutritional, emotional, and environmental factors [1, 7, 9].

This study aimed to determine clinically the age at onset of thelarche (defined as Tanner breast stage 2) and the age at menarche (first menstruation) in a cohort of healthy internationally adopted girls. Additionally, the study sought to describe temporal trends in height and body mass index (BMI) at these key stages of pubertal development.

2. MATERIAL AND METHODS

A prospective observational epidemiological study was conducted in a cohort of 102 healthy internationally adopted girls in Spain between 1998 and 2008, all of whom were followed at a specialized referral center. Within a few days of arrival, their families voluntarily brought the girls to the center for evaluation. Growth and pubertal development were assessed twice yearly from the time of adoption until the occurrence of menarche. The girls' regions of origin were Russia/Ukraine (n = 38; Russia, 26; Ukraine, 12), China (n = 34), India/Nepal (n = 17; India, 15; Nepal, 2), and Latin America (n = 13; Colombia, 7; Bolivia, 4; Brazil, 2).

At the beginning of the study, the cohort of internationally adopted girls consisted of 193 individuals. During follow-up, ten girls were excluded due to diagnoses of conditions that could affect growth (four with hypothyroidism, two with celiac disease, two with fetal alcohol syndrome, one with growth hormone deficiency, and one with cerebral palsy). In addition, four girls were excluded because they presented with early breast development before the age of 7 (two from India, one from China, and one from Ukraine). These girls were referred to pediatric endocrinology and were diagnosed with idiopathic central precocious puberty. Furthermore, seventy-seven girls were lost to follow-up for various reasons—including changes of address, changes in healthcare center, loss of private health insurance, financial constraints, and lack of interest—fifty-seven before thelarche and twenty before menarche.

During the initial evaluation at the time of adoption and at subsequent follow-up visits, weight and height were measured and recorded using a standardized protocol. The same clinician performed all measurements. The equipment used included a Seca 708 electronic platform scale (maximum capacity 200 kg; precision 0.1 kg) with an integrated stadiometer for height measurement, a GC-1104 electronic pediatric scale (maximum capacity 20 kg; precision 10 g), and a Seca length board (maximum 100 cm) for children under 3 years of age.

Families were instructed and trained to identify the onset of thelarche and the occurrence of menarche, enabling clinical verification and additional anthropometric assessments at those stages.

Data on age and anthropometric measurements at the time of adoption, onset of thelarche, and occurrence of menarche were entered into an Excel spreadsheet. Means and standard deviations (SDs) were calculated, as well as body mass index (BMI = kg/m^2).

WHO Anthro v3.2.2 (0–5 years) and WHO AnthroPlus v1.0.4 (5–19 years), developed by the World Health Organization (WHO) Multicentre Growth Reference Study Group, were used to compare height and BMI measurements at adoption, onset of thelarche, and occurrence of menarche with the WHO Child Growth Standards. Corresponding z-scores were calculated to determine how many SDs each value lay above or below the mean, as well as age- and sex-specific percentiles.

According to the WHO Child Growth Standards, z-scores below -2 SD indicate severe growth delay, values between -1 and -2 SD indicate moderate delay, and values above -1 SD are considered normal [10]. A clinically relevant increase in height between the onset of thelarche and the occurrence of menarche was defined as an increase in height z-score ≥ 0.25 SD [11].

The Kolmogorov–Smirnov test was used to assess normality. Linear associations between two continuous quantitative variables were evaluated using the Pearson correlation coefficient, with statistical significance set at $p < 0.05$.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The procedures involving participants were performed after obtaining informed consent from their legal guardians. Data were handled in compliance with Organic Law 3/2018 on the Protection of Personal Data and Guarantee of Digital Rights, in force in Spain.

3. RESULTS

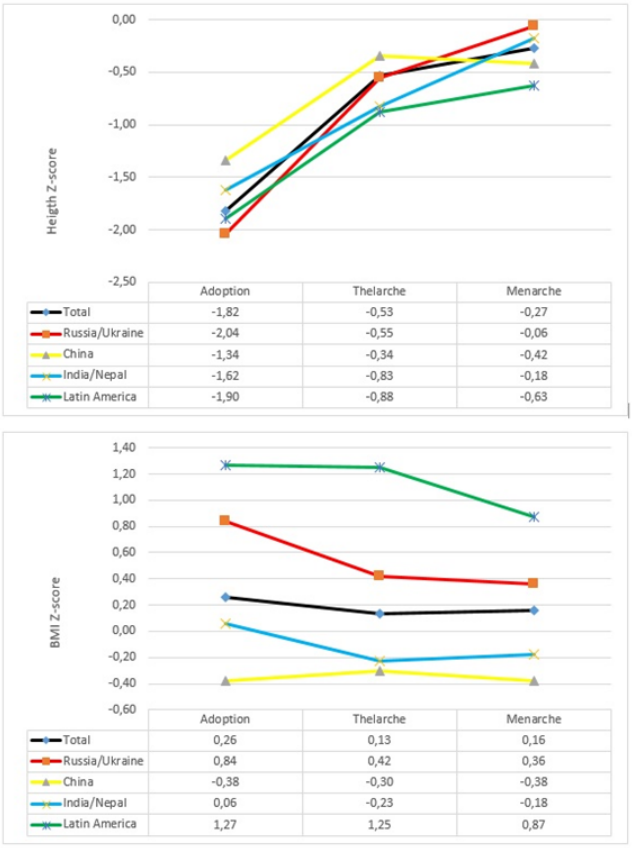
Table 1 presents height and BMI measurements at the time of adoption, onset of thelarche, and occurrence of menarche in internationally adopted girls. Data are shown for the total cohort as well as for subgroups according to their geographical region of origin. All measurements are compared with the WHO Child Growth Standards. Figure 1 illustrates temporal trends in height and BMI z-scores at adoption, onset of thelarche, and occurrence of menarche, using the WHO Child Growth Standards as the reference. The main findings are summarized below.

Table 1: Height and body mass index measurements at adoption, thelarche, and menarche in internationally adopted girls in Spain. Comparison with the World Health Organization Child Growth Standards

Variable	Total adopted girls (n=102)			Russia/Ukraine (n=38)			China (n=34)			India/Nepal (n=17)			Latin America (n=13)		
	Mean±SD	Z	PCTL	Mean±SD	Z	PCTL	Mean±SD	Z	PCTL	Mean±SD	Z	PCTL	Mean±SD	Z	PCTL
Adoption															
Age (years)	3.5±2.8			3.7±2.3			1.3±0.5			6.5±2.8			6.1±3.6		
Height (cm)	92.5±19.1	-1.82	3.4	92.0±17.7	-2.04	2.0	73.7±5.4	-1.34	9.0	109.8±18.1	-1.62	5.3	105.9±27.3	-1.90	2.9
BMI	15.5±1.5	0.26	60.2	15.7±1.6	0.84	80.1	15.1±0.9	-0.38	35.2	14.7±1.9	0.06	52.6	16.6±0.4	1.27	89.8
Thelarche															
Age (years)	9.7±1.1			9.7±1.1			10.1±1.2			9.2±0.9			9.0±0.6		
Height (cm)	133.4±7.5	-0.53	29.8	133.3±7.9	-0.55	29.3	137.0±5.9	-0.34	36.5	129.0±5.9	-0.83	20.1	127.1±6.0	-0.88	18.8
BMI	16.7±2.0	0.13	55.2	17.3±1.9	0.42	66.4	16.0±1.6	-0.30	38.3	15.7±1.6	-0.23	40.8	19.0±2.1	1.25	89.5
Menarche															
Age (years)	11.7±1.1			11.8±1.1			12.2±1.0			11.0±1.0			10.9±0.7		
Height (cm)	147.6±8.3	-0.27	39.5	149.6±7.3	-0.06	47.5	149.5±5.9	-0.42	33.7	143.8±12.1	-0.18	42.9	140.2±7.2	-0.63	26.6
BMI	18.0±1.8	0.16	56.2	18.7±1.7	0.36	64.1	17.3±1.2	-0.38	35.1	16.9±1.5	-0.18	42.8	20.0±2.3	0.87	80.7

BMI: body mass index; SD: standard deviation; Z: z-score; PCTL: percentile.

At the time of adoption, the mean age (SD) of the total cohort was 3.5 (2.8) years, and delayed linear growth was observed. Girls from India/Nepal and Latin America were adopted at older ages, whereas those from China were adopted at younger ages. Girls from Russia/Ukraine showed severe height delay, while those from Latin America, India/Nepal, and China exhibited moderate delay. BMI z-scores indicated that, across all groups, height delay was greater than weight delay.



	Adoption	Thelarche	Menarche
Total	-1,82	-0,53	-0,27
Russia/Ukraine	-2,04	-0,55	-0,06
China	-1,34	-0,34	-0,42
India/Nepal	-1,62	-0,83	-0,18
Latin America	-1,90	-0,88	-0,63

	Adoption	Thelarche	Menarche
Total	0,26	0,13	0,16
Russia/Ukraine	0,84	0,42	0,36
China	-0,38	-0,30	-0,38
India/Nepal	0,06	-0,23	-0,18
Latin America	1,27	1,25	0,87

Figure 1: *Temporal trends in height and body mass index (BMI) z-scores at adoption, thelarche, and menarche in internationally adopted girls in Spain, compared with the World Health Organization Child Growth Standards.*

At the onset of thelarche, the mean age (SD) of the total cohort was 9.7 (1.1) years. Girls from Latin America and India/Nepal experienced thelarche earlier, whereas girls from China experienced it later. A moderate, statistically significant negative correlation was observed between age at adoption and age at onset of thelarche ($r = -0.43$, $p < 0.001$), indicating that later adoption was associated with earlier thelarche, and vice versa. The scatter plot is shown in Figure 2a. Within the total cohort, thelarche occurred between 7 and 8 years of age in 3 girls (2.9%): 2 from Russia/Ukraine and 1 from China. At the time of thelarche, height had normalized for both the total cohort and all subgroups, reflecting significant catch-up growth since adoption. Girls from Latin America had the highest BMI, whereas those from China had the lowest. No correlation was found between height or BMI at the onset of thelarche and height, BMI, or age at adoption.

Between the onset of thelarche and the occurrence of menarche, the total cohort experienced a clinically relevant increase in height (+0.26 SD), with a mean gain of 14.2 cm. The largest increases were observed in girls from India/Nepal and Russia/Ukraine (+0.65 SD and +0.49 SD, respectively), corresponding to mean gains of 14.8 cm and 16.3 cm. In contrast, girls from China did not experience a relevant increase in height.

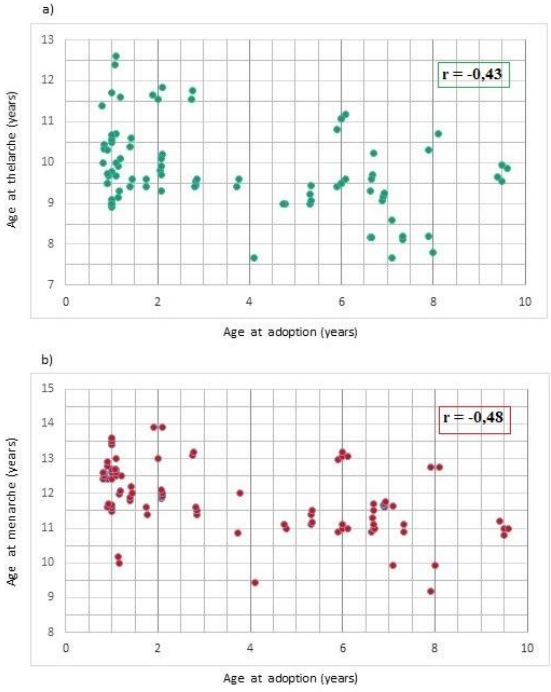


Figure 2: *Scatter plots: a) Age at thelarche versus age at adoption; b) Age at menarche versus age at adoption.*

At the time of menarche, the mean age (SD) of the total cohort was 11.7 (1.1) years. Girls from Latin America and India/Nepal experienced menarche earlier, whereas girls from China experienced it later. A moderate, statistically significant negative correlation was observed between age at adoption and age at menarche ($r = -0.48$, $p < 0.001$), indicating that later adoption was associated with earlier menarche, and vice versa. The scatter plot is shown in Figure 2b. Within the total cohort, menarche occurred between 9 and 10 years of age in 5 girls (4.9%): 2 from China, 1 from Russia/Ukraine, 1 from India/Nepal, and 1 from Latin America. At menarche, height in girls adopted from Russia/Ukraine and India/Nepal was comparable to WHO standards, whereas it was slightly lower in girls adopted from China and Latin America. Girls from Latin America had the highest BMI, and those from China had the lowest.

No correlation was found between height or BMI at menarche and height, BMI, or age at adoption.

4. DISCUSSION

Several studies have reported an advance in the onset of puberty, determining that the average age of thelarche has shown a downward trend worldwide since the 1970s [3, 12, 13]. The study by Eckert-Lind et al. [13] stands out, who conducted a systematic review and meta-analysis to evaluate the worldwide secular changes in age at pubertal onset in healthy girls measured by age at thelarche assessed by clinical examination from 1977 to 2019. They found a secular trend in ages at thelarche according to race/ethnicity and geography. Median ages at thelarche ranged from 8.8 to 10.3 years in the United States, from 9.8 to 10.8 years in Europe, from 9.7 to 10.3 years in the Middle East, from 8.9 to 11.5 years in Asia, and from 10.1 to 13.2 years in Africa. The results of meta-analyses showed a significant overall decrease in age at the onset of thelarche by 0.24 years per decade, equivalent to almost 3 months per decade from 1977 to 2013. Based on these findings, the authors suggested that an earlier age at thelarche in girls in the general population would change current diagnostic decision-making in girls with suspected precocious puberty. It is important to note that studies reporting on puberty in girls with malnutrition or obesity, as well as those adopted internationally, were excluded from this systematic review.

There are few studies examining the age at onset of thelarche and the occurrence of menarche in cohorts of internationally adopted girls, as well as on temporal trends in growth at these key stages of pubertal development.

Teilmann et al. [14], in a longitudinal study on a cohort of 276 internationally adopted girls in Denmark, used probit analysis to estimate a mean age at thelarche of 9.5 years and at menarche of 12.1 years, both significantly lower than those observed in Danish reference girls. They also estimated that 16% of the girls experienced thelarche before the age of 8 years. In the total cohort of internationally adopted girls in Spain, the mean age at thelarche was slightly higher and the mean age at menarche slightly lower than those reported by these authors, and the percentage of girls with thelarche before 8 years of age was significantly lower.

Hayes et al. [15], in a survey study of parents of 814 Chinese girls adopted in North America, reported a mean age at menarche of 12.37 years, like Chinese reference values. They also found that 3% of the girls experienced menarche before the age of 10 years. Tan et al. [16] studied 298 Chinese girls with a mean (SD) age of 8.8 (0.9) years who had been adopted in North America at a mean (SD) age of 1.1 (0.3) years. They observed that 3.5% developed thelarche before the age of 8 years and that 2.3% experienced menarche before the age of 11 years. In the group of Chinese girls adopted in Spain, the mean age at menarche was slightly lower than that reported by Hayes et al. The percentage of girls who developed thelarche before the age of 8 years was 2.9% and 5.8% experienced menarche before the age of 10 years.

Proos [17] retrospectively studied growth and pubertal development in 107 adopted Indian girls in Sweden. He reported a median age at menarche of 11.6 years, significantly earlier than the mean age in Swedish girls and Indian girls from higher socioeconomic backgrounds. He also found that 4.7% experienced menarche before the age of 9 years and that girls adopted at an older age had and an earlier menarche. When analyzing growth patterns and final height in relation to nutritional status at arrival and age at menarche, he observed that most girls showed catch-up growth in height and about half in weight, although catch-up growth was incomplete in those with greater growth delay and poorer nutritional status at arrival. Poorer nutritional status at arrival and more rapid catch-up growth were associated with earlier menarche. He suggested that pre-adoption growth delay and nutritional status, together with the extent of subsequent catch-up growth and the timing of puberty, influenced linear growth and final height. In the group of girls from India/Nepal adopted in Spain, the mean age at menarche was lower than reported by Proos, and 5.8% experienced menarche before the age of 10 years. These girls, along with those from Latin America, were adopted at an older age and experienced an earlier menarche.

Studies on secular trends in puberty among Spanish girls [18-20] have reported a mean age at thelarche ranging from 10.1 to 10.7 years and at menarche from 12.0 to 12.9 years. The total cohort of internationally adopted girls in Spain experienced both thelarche and menarche at significantly younger ages than Spanish reference girls, particularly those from Latin America and India/Nepal who had been adopted at an older age.

Regarding temporal height trends among internationally adopted girls in Spain, significant height deficits were observed at the time of adoption across the overall cohort, particularly among girls adopted from Russia/Ukraine. By the onset of thelarche, height had normalized both in the total cohort and across geographic groups, suggesting substantial catch-up growth following adoption. From thelarche to menarche, a marked increase in height was documented, especially among girls adopted from Russia/Ukraine and India/Nepal. At menarche, the height of girls adopted from Russia/Ukraine and India/Nepal was

comparable to WHO reference standards, whereas girls adopted from China and Latin America remained slightly below these standards.

The temporal BMI trends among internationally adopted girls in Spain revealed that, across all geographic groups, deficits in height were more pronounced than deficits in weight both at the time of adoption and at the onset of thelarche and menarche. Specifically, girls from Latin America exhibited earlier thelarche and menarche and presented higher BMI values during these stages of pubertal development. In contrast, girls from China experienced a later onset of thelarche and menarche and had lower BMI values. Interestingly, girls from India and Nepal also showed early thelarche and menarche despite having comparatively lower BMI values at these developmental stages.

The relationship between increased BMI during childhood and earlier pubertal onset is currently understood as the result of a complex interaction among biological, endocrine, and psychosocial factors, rather than a simple linear relationship. Epidemiological evidence consistently demonstrates that higher childhood BMI is associated with an increased likelihood of precocious or early puberty, particularly in girls. In the context of international adoption, increased BMI may accelerate pubertal development through three principal mechanisms: 1. Catch-up growth and metabolic adaptation. Girls adopted from disadvantaged environments frequently undergo rapid nutritional recovery, resulting in accelerated body fat accumulation and activation of the somatotropic and insulin-like growth factor axes. This process generates a metabolic signal of "energy abundance," which may promote earlier pubertal onset. 2. Leptin as a permissive signal for puberty. Leptin acts as a key indicator of energy reserves to the central nervous system, and higher BMI is associated with increased leptin secretion. Elevated leptin levels may facilitate activation of the neuroendocrine pathways involved in pubertal initiation. 3. Psychosocial stress and neuroendocrine reorganization. The adoption process involves substantial environmental and emotional transitions that may expose children to early-life stress. Chronic stress may sustain elevated cortisol levels, altering hypothalamic-pituitary-adrenal axis regulation and its interaction with the reproductive axis, thereby influencing pubertal timing. Overall, although adoption itself is not considered a direct cause of early puberty, it may potentiate the effects of increased BMI on sexual maturation. In conclusion, the increase in BMI associated with adoption may contribute to earlier pubertal onset through its effects on metabolic signaling pathways (including leptin and insulin), neuroendocrine regulation, and adaptation to environmental change. Nevertheless, these effects are not exclusively biological and are substantially modulated by psychosocial, epigenetic, and early developmental factors [21-26].

Based on the results of this study, we can conclude that the cohort of internationally adopted girls in Spain experienced thelarche and menarche at early ages. These earlier pubertal milestones were associated with adoption at older ages. However, temporal growth patterns at these stages of pubertal development were not influenced by age at adoption.

Although the adoptions took place between 1998 and 2008, and data on thelarche and menarche were collected between 2006-2018 and 2008-2021, respectively, we believe that the data obtained remain relevant to current clinical practice. To the best of our knowledge, this study represents the first prospective investigation providing clinically detailed follow-up of pubertal development in a cohort of internationally adopted girls. Moreover, the main biological and psychosocial conditions associated with international adoption—such as rapid nutritional recovery after adoption, environmental changes, early-life stress, and the catch-up growth phenomenon—continue to be observed in current clinical settings [8]. These findings also remain relevant because most girls adopted from abroad today come from socioeconomic and health environments like those of the period studied [8]. Furthermore, the physiological mechanisms underlying early pubertal onset have not changed. In addition, our findings were interpreted and compared with data from studies on internationally adopted girls published between 2009 and 2016 [14-17], studies on secular trends in pubertal development among Spanish girls published between 2005 and 2018 [18-20], and the WHO Child Growth Standards published between 2006 and 2007 [10].

Potential limitations of this study. Although the substantial loss to follow-up—an inherent limitation of the long-term prospective design—occurred completely at random, and the girls lost to follow-up did not differ systematically from those who completed the study, the possibility of attrition bias cannot be entirely excluded. Although we consider this risk to be limited, it may nonetheless have affected the representativeness of the sample. Other potential limitations include the lack of information regarding the pubertal history of biological families, as pubertal timing may be influenced by genetic background. Additionally, the relatively small proportion of girls adopted from India/Nepal and Latin America may have influenced the results.

The major strengths of the study include its prospective follow-up design, the final sample size being adequate for

the observed correlations, and the fact that the same professional clinically verified the onset of thelarche and menarche following family detection. This approach minimized recall bias and allowed anthropometric measurements to be obtained promptly after the onset of these pubertal milestones.

Several studies have shown that early puberty can cause social adjustment difficulties and long-term adverse physiological and psychological effects. Therefore, further research is needed on the onset of puberty as a potentially sensitive and early marker of the interactions between ethnic and geographic background, environmental conditions, and genetic susceptibility, which can influence both physiological and pathological processes [1, 7, 9, 13].

5. ACKNOWLEDGEMENTS

We thank the girls and their families for participating in this study.

6. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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