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Association between Changes in Menarcheal Age and Adolescent Idiopathic Scoliosis: An Analysis of 38,879 Patients over 20 Years

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Background: Menarche has a significant impact on the progression of adolescent idiopathic scoliosis (AIS); however, studies in this area are insufficient. This study used large-scale school screening data to investigate the relationship between menarcheal age and AIS, especially the severity of scoliosis.

Methods: Of 2,326,577 students who participated in school screening for scoliosis (SSS) in South Korea from 2001 to 2021, 38,879 girls with AIS, who experienced menarche, were included. Data including the patient's demographics, such as menarcheal age, Cobb angle, Risser stage, and the interval between menarche and the time of screening were retrieved from the SSS database. Pearson correlation coefficient was used to identify the changes in menarcheal age according to the birth year and to investigate the relationship between menarcheal age and each variable of interest.

Results: Based on the birth year, the mean menarcheal ages in girls with AIS from 1988 to 2008 demonstrated a steadily decreasing trend over time (r = –0.857, p < 0.001). Girls with AIS and late menarche demonstrated a higher Cobb angle at the time of screening (r = 0.095, p < 0.001). Other variables did not significantly correlate with menarcheal age.

Conclusions: Based on the SSS, a large-scale school screening dataset, menarcheal age in girls with AIS demonstrated an ongoing downward trend in the recent 20 years in South Korea. Notably, girls with AIS and late menarche had a higher Cobb angle at screening. Our findings indicate the need for earlier screening of AIS in girls who have not undergone menarche.

Keywords: *Spinal curvatures, Menarche, Puberty, Mass screening, Trends*

Menarche is associated with a deceleration of growth velocity. It is an identifiable indicator of maturity and a predictor of growth potential.[1] Menarcheal age has been continuously investigated worldwide for centuries due to its significance on pubertal maturation, fertility, and female health.[2,3] Menarcheal age has demonstrated continuous downward trends in most countries for decades, although the rate of decline has slowed.[4-7]

In girls, adolescent idiopathic scoliosis (AIS) has a positive relationship with growth. A rapid increase in spinal height during pubertal growth spurt can aggravate the spinal curvature.[8-10] Therefore, menarcheal age is a critical consideration in AIS because the risk of curve acceleration is appreciably higher before than after menarche.[11] Late menarche has exhibited a parallel with a higher prevalence of AIS.[12]

Despite the importance of menarche in AIS, few studies have investigated menarcheal age in patients with AIS. The available results have also been inconsistent.[12-16] Therefore, this study aimed to identify the menarcheal age of girls with AIS using a large-scale school screening dataset. Furthermore, we analyzed the relationship between the severity of scoliosis and menarcheal age to determine

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whether the menarcheal age contributes to curve progression in AIS.

METHODS

This study was approved by the Ethics Committee of Korea University Guro Hospital (IRB No. 2022GR0115). As the study was retrospective in design, informed consent was waived by the Ethics Committee. The study was conducted in accordance with the approved protocol and investigator compliance, and all applicable regulations, including the Declaration of Helsinki and International Conference on Harmonization-Good Clinical Practice standards, were followed at all times.

Study Population

This study utilized the primary data from school screening for scoliosis (SSS), which was conducted by local community health centers and our institution.[17] SSS has been implemented since 2001 as a youth health promotion project for understanding the current status of AIS in South Korea. The first step of the screening was performed through clinical assessments for scoliosis (e.g., shoulder or iliac crest imbalance, asymmetry in the spine contour, humpback, etc.) and measurements were obtained by experienced nurses of the SSS team using a scoliometer. If a student met the screening parameter (either a clinical suspicion or a scoliometer reading of ≥ 5°), standing anterior-posterior and lateral radiographs were obtained as the next step.[18] Concurrently, the menarcheal age of the female students was surveyed. The diagnosis of AIS, defined as the lateral Cobb angle > 10°, was determined by orthopedic surgeons.[19] From 2001 to 2021, 2,326,577 students, ranging from 10 to 14 years of age, participated in SSS. Of those, 38,879 girls with AIS and records of menarcheal age were included in this study (Fig. 1). There were no duplicate screenings of students or schools.

Data Collection

The school screening for female students included a questionnaire on menstrual experience and menarcheal age. All personally identifiable information was codified and stored on a computer with limited access. The menarcheal age and chronological age were surveyed every month. The Cobb angle was measured as the angle made by a line drawn along the upper and lower endplates of the upper-end and lower-end vertebrae, respectively.[20-22] In the case of a double curve, the greater angle was selected for analysis. Mild scoliosis was defined as a Cobb angle between 10° to 20°. Moderate scoliosis was determined by a Cobb angle between 20° to 40°. Severe scoliosis was defined as a Cobb angle > 40°.[23] The Risser stage was evaluated via the following 6 grades: Risser 0, no ossification; Risser 1, ossification within the first quarter of the crest; Risser 2, ossification extending into the second quarter of the crest; Risser 3, ossification into the third quarter of the crest; Risser 4, ossification into the fourth quarter of the crest to completion of the apophyseal line excursion; and Risser 5, a fusion of the apophyseal ring to the ilium, from the start of the process posterior-medially to its completion.[24] Orthopedic surgeons measured the lateral Cobb angle and Risser stage at the time of screening. These data were systematically recorded in the SSS database and retrieved by 1 author (YHP) for analysis in this study.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics for Windows version 23.0 (IBM Corp.). An independent *t*-test was used to determine the difference in menarcheal age between different birth year groups. Pearson correlation coefficient was used to identify the changes in menarcheal age according to birth year and to investigate the relationship among menarcheal age, Cobb angle, Risser stage, age at the time of screening, and the interval between menarche and screening. To identify the relationship between

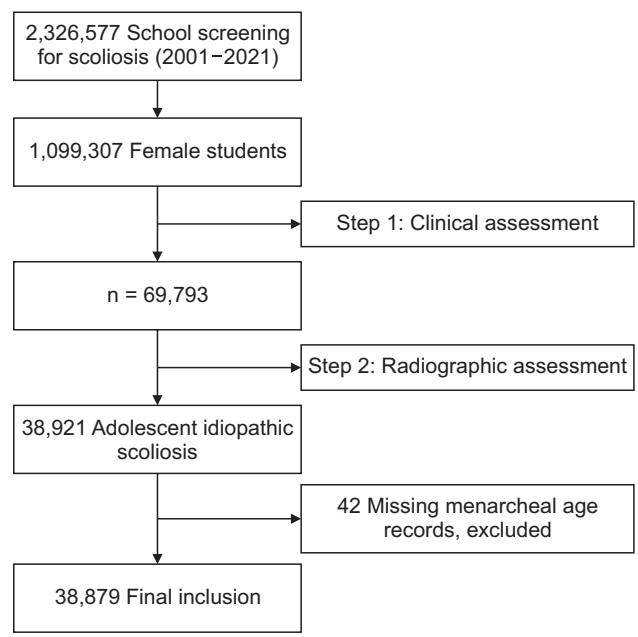

Fig. 1. Patient selection flowchart. The clinical assessment included examining the shoulder or iliac crest for features such as imbalance, asymmetry in the spine contour, or humpback and measuring via a scoliometer. The radiographic assessment involved measuring the lateral Cobb angle.

menarcheal age and severe scoliosis, the receiver operating characteristic (ROC) curve and the associated area under the curve (AUC) were constructed to determine the optimal cut-off age. The 95% confidence interval (CI) for the area under the ROC curve was calculated with MedCalc Statistical Software (16.8.4). Youden's J statistic was used to select a set of optimal cut-off age, with the final decision based on clinical relevance. All analyses were considered statistically significant when the p-value was < 0.05.

RESULTS

Distribution of Menarcheal Age in Girls with AIS

Table 1 presents the distribution of menarcheal age in girls with AIS. The mean menarcheal age for students born between 1998 and 2008 was 11.9 years (95% CI, 11.88–11.91 years), and the median menarcheal age was 11.8 years.

Trends of Menarcheal Age in Girls with AIS over Time

The mean menarcheal ages stratified by birth year are presented in Fig. 2. The mean menarcheal age was significantly lower among adolescent girls with AIS born in 2008 (11.0 years; 95% CI, 10.95–11.04 years) than those born in 1988 (12.6 years; 95% CI, 12.44–12.69 years) ($p < 0.001$). During the study period, the mean menarcheal age of girls with AIS demonstrated a steadily decreasing trend over time ($r = -0.857$, $p < 0.001$).

The Relationships between Menarcheal Age, the Cobb Angle, and the Risser Stage

At the time of screening, the mean Cobb angle was 14.8° (95% CI, 14.79°–14.89°), and there was no difference according to the birth year or the screening year. The Pearson correlation coefficient showed a significant correlation between menarcheal age and the Cobb angle. Girls with AIS and late menarche had a higher Cobb angle at the time of screening ($r = 0.095$, $p < 0.001$). The most frequent Risser stage was 4 (41%), followed by 0, 3, 2, 1, and 5 (19%, 14%, 10%, 9%, and 7%, respectively). The Risser stage did not correlate with menarcheal age.

Table 1. Menarcheal Age Distribution in Patients with Adolescent Idiopathic Scoliosis

Percentile	Menarcheal age (yr)
3rd	10.2
5th	10.3
25th	11.2
50th	11.8
75th	12.5
95th	13.9
97th	14.3

Timing of the Screening and the Cobb Angle

The mean age at screening was 12.9 years (95% CI, 12.89–12.92 years). The mean interval between menarche and screening was 1.25 years (95% CI, 1.24–1.26 years). Pearson correlation coefficients did not show a significant correlation among the Cobb angle, the age at the time of screening, or the interval between menarche and screening.

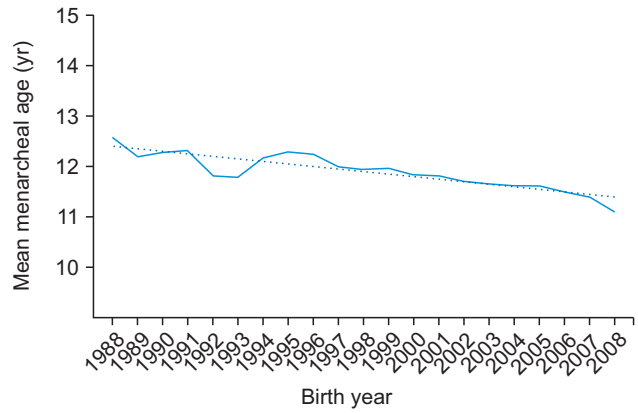

Fig. 2. Trends in the age of menarche stratified by birth year in girls with adolescent idiopathic scoliosis. The solid line illustrates the mean menarcheal age by birth year, and the dotted line is a linear, exponential trend line for the menarcheal age.

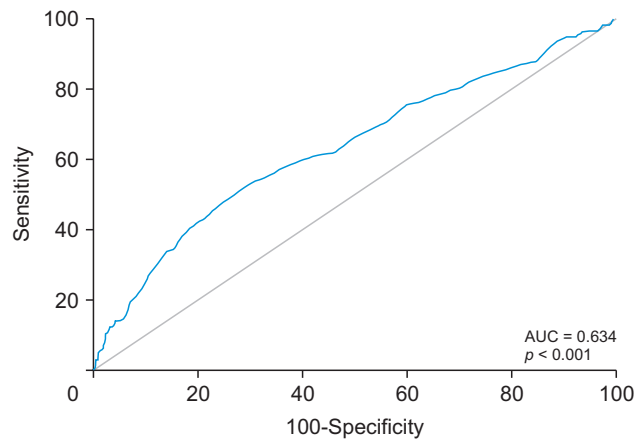

Fig. 3. A receiver operating characteristic curve for the relationship between menarcheal age and severe scoliosis. A cut-off value of menarcheal age of 13.5 years demonstrated 90% sensitivity and 34% specificity, while a cut-off value of 12.4 years demonstrated 72% sensitivity and 51% specificity. AUC: area under the curve.

The Cut-off Value for Late Menarche in Students with AIS

Using the ROC curve (AUC 63.4%), we identified 2 potential cut-off values of menarcheal age for the risk of severe scoliosis. At a threshold cut-off of 13.5 years (90th percentile), the risk of severe scoliosis demonstrated a sensitivity of 34%, a specificity of 90%, a positive predictive value (PPV) of 22%, and a negative predictive value (NPV) of 91%. In contrast, when the threshold was set at a menarcheal age of 12.4 years (70th percentile), the sensitivity, specificity, PPV, and NPV were 51%, 72%, 49%, and 72%, respectively (Fig. 3).

DISCUSSION

Using the SSS database for South Korean female students, we analyzed the distribution of menarcheal age in girls with AIS and evaluated the trend over 20 years. We found that the menarcheal age in girls with AIS had declined. This finding makes a similar statement to that in previous studies as early menarche is known to be in a continuous downtrend in relation to modern diet, higher body mass index, and lower insulin sensitivity.[4-7] Moreover, those with AIS and late menarche had a higher Cobb angle at the time of screening. Based on our results, we recommend that SSS be performed at a younger age than the present. Furthermore, since AIS tends to progress more in girls with late menarche, particular attention should be paid to those with AIS who have not undergone menarche at the time of screening.

Late menarche causes delayed skeletal maturity, resulting in prolonged rapid pubertal growth and an accompanying period of spine vulnerability.[25,26] As AIS progresses with pubertal growth, late menarche implies a potential aggravation of the scoliotic curve. Our result demonstrated a positive correlation between late menarche and the degree of Cobb angle, consistent with what is known about AIS. Our findings are also supported by previous studies that demonstrated an association between late menarche and a higher prevalence and severity of AIS.[12,13]

This study revealed that AIS tends to be more progressive in girls with late menarche and emphasized the need for greater caution among those with AIS and potentially late menarche. Paradoxically, a general trend of earlier onset of menarche in girls with AIS has simultaneously been described. If menarche in girls with AIS is indeed experienced earlier, a lower prevalence of late menarche and an improvement in the overall severity of AIS should be observed. However, the Cobb angle did not differ according to this study's birth year or screening year. This paradox was also observed in a previous study of Irish girls with AIS.[16] To explain this paradox, we hypothesized that the onset of AIS may also be earlier. Thus, menarche and the onset of scoliosis may accelerate; hence, the overall severity has not changed. However, studies on the age of the onset of AIS are currently limited to expert opinions, and there are no numerical data to verify the hypothesized change in the onset of AIS. To address this hypothesis, we plan to investigate this further in a follow-up study.

Early menarche is well studied due to several later-life physical and psychosocial problems. Conversely, there is no clear definition of late menarche.[27] Generally, late menarche is regarded as menarche later than 15 years.[28] Recent studies have also reported late menarche based on the 97th percentile of menarcheal age among adolescent girls (later than 15.4 years) or 1 standard deviation from the mean menarcheal age (later than 13.9 years).[7,29] Since girls with AIS and late menarche tend to have a higher Cobb angle at the time of screening, it is essential to define the age of late menarche in AIS and attempt to specify the cut-off value of menarcheal age using the ROC curve. Our results demonstrated that a menarcheal age of > 13.5 years best predicts progression to severe scoliosis. However, this cut-off age demonstrated low sensitivity, and the AUC value was insufficient to calculate the predictive value. Therefore, we concluded that our finding needs to be further verified before clinical application.

To date, several studies have compared menarcheal age between girls with AIS and the normal population; however, the results have been inconsistent. Menarche occurred earlier in girls with AIS than in normal controls in an Irish study. Similarly, no difference was found between the AIS and control groups in the Mediterranean.[14,16] In contrast, studies conducted in Hong Kong and China have indicated that menarche appeared later in girls with AIS.[13,15] According to a cross-sectional study of 351,006 Korean girls based on the Korea Youth Risk Behavior Survey, the mean menarcheal age of girls born between 1988 and 2003 was 12.9 years. During the same period, the mean menarcheal age of girls with AIS in this study was 12.1 years. These results suggest that the menarcheal age in girls with AIS was younger than that of those without AIS. This finding aligns with results from the Irish study; however, it is not supported by the other 2 studies.[13,15,16] A definitive explanation for this discrepancy is difficult. However, considering that our study was conducted in a large sample of tens of thousands of female students, as opposed to previous studies with study samples of hundreds to thousands, our results are more persuasive.

This study has 2 limitations. First, as a control

group, there was no comparative analysis of girls with AIS who had not undergone menarche. If the Cobb angle of girls with AIS without menarche at the time of screening was higher than that of girls with AIS and menarche, it would further support our finding that late menarche affected the progression of AIS. However, this comparison could not be performed because in the SSS database, only 114 female students (0.3%) diagnosed with AIS had not had menarche at the time of screening. Although the comparison could not be performed in this study, it is possible if the age of scoliosis screening is lowered. Hence, based on our findings, we recommend lowering the age of scoliosis screening. Second, due to the inherent limitation of studies based only on screening data, the possibility that the cause of scoliosis was an endocrine disorder rather than idiopathic cannot be excluded, especially in cases of severe scoliosis with late menarche. However, scoliosis caused by an endocrine disorder is generally syndrome-related and diagnosed early due to other accompanying symptoms.[30] Therefore, it is very unlikely that this would impact our results significantly.

Our results highlighted the distribution of mean menarche age in girls with AIS and its downward trend over the last 20 years. Late menarche is related to a higher Cobb angle, thus suggesting that late menarche contributes to AIS progression. However, further studies in other nations or ethnicities are warranted to generalize our findings.

Based on the SSS, a large-scale school screening dataset, menarcheal age in girls with AIS had an ongoing downward trend in the recent 20 years in South Korea. Notably, girls with AIS and late menarche had a higher Cobb angle at screening. Our findings indicate the need for earlier screening of AIS in girls who have not undergone menarche.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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REFERENCES

1. Sanders JO, Qiu X, Lu X, et al. The uniform pattern of growth and skeletal maturation during the human adolescent growth spurt. Sci Rep. 2017;7(1):16705.
2. Tanner JM. Trend towards earlier menarche in London, Olso, Copenhagen, the Netherlands and Hungary. Nature. 1973;243(5402):95-6.
3. de Muinich Keizer SM, Mul D. Trends in pubertal development in Europe. Hum Reprod Update. 2001;7(3):287-91.
4. Talma H, Schonbeck Y, van Dommelen P, Bakker B, van Buuren S, Hirasing RA. Trends in menarcheal age between 1955 and 2009 in the Netherlands. PLoS One. 2013;8(4):e60056.
5. Jansen EC, Herran OF, Villamor E. Trends and correlates of age at menarche in Colombia: results from a nationally representative survey. Econ Hum Biol. 2015;19:138-44.
6. Song Y, Ma J, Wang HJ, et al. Trends of age at menarche and association with body mass index in Chinese school-aged girls, 1985-2010. J Pediatr. 2014;165(6):1172-7.
7. Seo MY, Kim SH, Juul A, Park MJ. Trend of menarcheal age among Korean girls. J Korean Med Sci. 2020;35(49):e406.
8. Charles YP, Daures JP, de Rosa V, Dimeglio A. Progression risk of idiopathic juvenile scoliosis during pubertal growth. Spine (Phila Pa 1976). 2006;31(17):1933-42.
9. Cheung J, Veldhuizen AG, Halbertsma JP, et al. The relation between electromyography and growth velocity of the spine in the evaluation of curve progression in idiopathic scoliosis. Spine (Phila Pa 1976). 2004;29(9):1011-6.
10. Loncar-Dusek M, Pecina M, Prebeg Z. A longitudinal study of growth velocity and development of secondary gender characteristics versus onset of idiopathic scoliosis. Clin Orthop Relat Res. 1991;(270):278-82.
11. Busscher I, Wapstra FH, Veldhuizen AG. Predicting growth and curve progression in the individual patient with adolescent idiopathic scoliosis: design of a prospective longitudinal cohort study. BMC Musculoskelet Disord. 2010;11:93.
12. Grivas TB, Vasiliadis E, Mouzakis V, Mihas C, Koufopoulos G. Association between adolescent idiopathic scoliosis prevalence and age at menarche in different geographic latitudes. Scoliosis. 2006;1:9.
13. Mao SH, Jiang J, Sun X, et al. Timing of menarche in Chinese girls with and without adolescent idiopathic scoliosis: current results and review of the literature. Eur Spine J. 2011;20(2):260-5.

14. Grivas TB, Samelis P, Pappa AS, Stavlas P, Polyzois D. Menarche in scoliotic and nonscoliotic Mediterranean girls: is there any relation between menarche and laterality of scoliotic curves? Stud Health Technol Inform. 2002;88:30-6.

15. Lee WT, Cheung CS, Tse YK, Chau WW, Qin L, Cheng JC. Persistent osteopenia in adolescent idiopathic scoliosis (AIS) – factors predisposing to generalized osteopenia, a cross-sectional and longitudinal investigation. Int Congr Ser. 2007;1297:25-31.

16. Goldberg CJ, Dowling FE, Fogarty EE. Adolescent idiopathic scoliosis: early menarche, normal growth. Spine (Phila Pa 1976). 1993;18(5):529-35.

17. Suh SW, Modi HN, Yang JH, Hong JY. Idiopathic scoliosis in Korean schoolchildren: a prospective screening study of over 1 million children. Eur Spine J. 2011;20(7):1087-94.

18. Huang SC. Cut-off point of the Scoliometer in school scoliosis screening. Spine (Phila Pa 1976). 1997;22(17):1985-9.

19. Fong DY, Lee CF, Cheung KM, et al. A meta-analysis of the clinical effectiveness of school scoliosis screening. Spine (Phila Pa 1976). 2010;35(10):1061-71.

20. Cobb J. Outline for the study of scoliosis. Instr Course Lect. 1948;5(26):1-275.

21. Mehta SS, Modi HN, Srinivasalu S, et al. Interobserver and intraobserver reliability of Cobb angle measurement: endplate versus pedicle as bony landmarks for measurement: a statistical analysis. J Pediatr Orthop. 2009;29(7):749-54.

22. Ketenci IE, Yanik HS, Erdogan O, Adiyeke L, Erdem S. Reliability of 2 smartphone applications for Cobb angle measurement in scoliosis. Clin Orthop Surg. 2021;13(1):67-70.

23. Horng MH, Kuok CP, Fu MJ, Lin CJ, Sun YN. Cobb angle measurement of spine from X-ray images using convolutional neural network. Comput Math Methods Med. 2019;2019:6357171.

24. Risser JC. The classic: the iliac apophysis: an invaluable sign in the management of scoliosis. 1958. Clin Orthop Relat Res. 2010;468(3):643-53.

25. Limony Y, Koziel S, Friger M. Age of onset of a normally timed pubertal growth spurt affects the final height of children. Pediatr Res. 2015;78(3):351-5.

26. Onland-Moret NC, Peeters PH, van Gils CH, et al. Age at menarche in relation to adult height: the EPIC study. Am J Epidemiol. 2005;162(7):623-32.

27. Kim JH, Lim JS. Early menarche and its consequence in Korean female: reducing fructose intake could be one solution. Clin Exp Pediatr. 2021;64(1):12-20.

28. De Sanctis V, Rigon F, Bernasconi S, et al. Age at menarche and menstrual abnormalities in adolescence: does it matter? The evidence from a large survey among Italian secondary schoolgirls. Indian J Pediatr. 2019;86(Suppl 1):34-41.

29. Al-Sahab B, Ardern CI, Hamadeh MJ, Tamim H. Age at menarche in Canada: results from the National Longitudinal Survey of Children & Youth. BMC Public Health. 2010;10:736.

30. Day GA, McPhee IB, Batch J, Tomlinson FH. Growth rates and the prevalence and progression of scoliosis in short-statured children on Australian growth hormone treatment programmes. Scoliosis. 2007;2:3.