

STROBE: The relationship between asthma and early menarche in Korean adolescents

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Abstract

We explored the relationship between asthma and early menarche in a representative sample of Korean adolescents.

Web-based self-reported data collected from 2006 to 2015 by the Korean Youth Risk Behavior Web-based Survey were used. Menarche status was divided into “early” (<12 years of age, n=69,520) and “not early” (≥12 years of age, n=234,065).

Adolescent girls with early menarche exhibited a higher incidence of asthma (8.1% vs 7.4%, $P < .001$), more frequent school absences because of asthma (10.8% vs 8.7%), and more frequent ≤4-day stretches of school absence (4.6% vs 2.4%) compared with girls with “not early” menarche (all $P < .001$). Multivariate analysis performed after adjusting for multiple confounders revealed a 1.04-fold (95% confidence interval [CI] 1.00–1.07) greater likelihood of asthma in the early menarche than not early menarche group. In addition, the odds ratios for missing school due to asthma for 1 to 3 and ≥4 days per year in the early menarche group were 1.00 (95% CI 1.00–1.02) and 1.21 (95% CI 1.01–1.46), respectively.

Adolescents with early menarche exhibited increased incidences of asthma and severe asthma.

Abbreviations: CI = confidence interval, KCDC = the Centers for Disease Control and Prevention of Korea, KYRBWS = Korea based on the data from the Korea Youth Risk Behavior Web-Based Survey, OR = odd ratios.

Keywords: adolescent, asthma, early menarche

1. Introduction

Asthma is a common chronic respiratory disease, and its prevalence has been increasing in Korea (from 0.7% in 1998 to 2.0% in 2008).^[1] A previous study reported that early menarche was significantly associated with bronchial hyper-responsiveness (a key feature of asthma).^[2,3] However, an increased risk of wheezing during adolescence was not associated with menarche onset before 11 years of age.^[4] Varraso et al,^[5] Chang et al,^[6] and Shehata and Sheikh^[7] reported that early menarche was associated with a higher risk of asthma. However, very few nationwide population-based studies have comprehensively adjusted for potentially confounding factors when evaluating this association. The cited studies differed epidemiologically, and therefore ethnicity-specific evaluations are necessary. Here, we used data from the Korean Youth Risk Behavior Web-based Survey (KYRBWS) and demonstrated, for the first time, a possible cross-sectional association between asthma and early menarche in Korean adolescents.

2. Methods

2.1. Study participants

This nationwide survey used 2006 to 2015 KYRBWS data to explore the health-related behaviors of 12 to 18-year-old girls. The Institutional Review Board of the Centers for Disease Control and Prevention of Korea (KCDC) approved this study (2014-06EXP-02-P-A). This consent procedure was approved by the KCDC IRB. All KYRBWS data analyses were conducted in accordance with the guidelines and regulations provided by the KCDC. The survey was anonymous and voluntary; informed consent was provided by the parents or legal guardians. Girls who did not provide menarche details or who had not entered menarche were excluded. A total of 303,585 girls with early menarche (n=69,520) or “not early” menarche (n=234,065) were included.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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2.2. Socioeconomic and demographic factors

The KYRBWS self-report questionnaire was used to collect socioeconomic data and information on health behaviors, psychological factors, and sexual behaviors. The residence area was categorized as urban or rural. Asthma is associated with smoking,^[8] alcohol use,^[9] and exercise status.^[10] Smoking was defined as the use of cigarettes for >1 day during the past month.^[11] Alcohol consumption was defined as at least 1 drink on >1 day during the past month.^[11] Regular exercise was defined as exercise ≥3 times/wk or <3 times/wk if the heart or respiration rate was increased for at least 1 h/d during the past 7 days.^[12] Sexual intercourse experience was categorized as “never” or “ever.” Participants reported their self-rated stress levels, health status, and happiness. The use of substances such as illicit drugs (glue, stimulants, marijuana, butane gas, high-dose cold medicine, amphetamine, or heroin) or anxiolytics to induce hallucinations or elevate mood, or abnormal dieting, was reported as “yes” or “no.”^[13]

2.3. Menarche measures

Based on the cut-off values of previous studies,^[14,15] we divided the patients into “early” (<12 years of age) and “not early” (≥12 years of age) menarche groups. Girls who had not entered menarche were excluded.

2.4. Asthma

Asthma and asthma severity were explored by asking “Have you ever been diagnosed with asthma by your doctor?” To assess severity, asthmatics were asked about the number of days absent from school due to asthma during the past 12 months; the response options were “0,” “1–3,” and “4 or more” days.

2.5. Data analysis

All variables were analyzed using SPSS ver. 22 (SPSS Inc., Chicago, IL). Descriptive statistics (numbers with percentages) were used to describe basic characteristics. Multiple logistic regression analysis was performed (after complex sampling) with adjustments for age, school type, residence area, family structure, family affluence, body mass index, smoking and alcohol consumption statuses, exercise status, perceived stress, health status, episodes of depression, and allergic disease (allergic rhinitis and atopic dermatitis) status. A *P*-value <.05 was considered statistically significant.

3. Results

The characteristics of the study population (N = 303,585), which was divided into the early (69,520) and not early (234,065) menarche groups, are shown in Table 1. Girls with early menarche more frequently lived in urban areas, less frequently lived with both parents, drank more alcohol, smoked more cigarettes, and had higher household incomes, compared with girls in the not early menarche group. The early menarche group reported more substance abuse, higher levels of moderate-to-severe stress, poorer perceived health status, more unhappiness, and more frequent depression compared with the not early group. The differences in allergic disease status according to menarche status are shown in Table 2. The rates of asthma (8.1% vs 7.4%, *P* < .001), school absences, allergic rhinitis, and

Table 1

Clinical, socioeconomic, and demographic characteristics of study populations.

	Not early menarche (n = 234,065)	Early menarche (n = 69,520)	<i>P</i> -value
Age	15.1 ± 1.7	15.1 ± 1.7	.883
School			<.001
Middle school	110,354 (47.1)	34,790 (50.0)	
Academic high school	93,936 (40.1)	26,702 (38.4)	
Vocational high school	29,775 (12.7)	8028 (11.5)	
School type			<.001
Girl school	87,562 (37.4)	25,198 (36.2)	
Coeducation	146,503 (62.6)	44,322 (63.8)	
Residence			<.001
Rural	27,451 (11.7)	7306 (10.5)	
Urban	206,614 (88.3)	62,214 (89.5)	
Living with both parents			<.001
No	10,052 (4.3)	3683 (5.3)	
Yes	224,103 (95.7)	65,837 (94.7)	
Subjective academic achievement			<.001
Poor	88,061 (37.6)	25,081 (36.1)	
Average	66,122 (28.2)	18,548 (26.7)	
Well	79,882 (34.1)	25,891 (37.2)	
Alcohol	42,278 (18.1)	13,288 (19.1)	<.001
Smoking	14,585 (6.2)	4990 (7.2)	<.001
Exercise	52,125 (22.3)	17,001 (24.5)	<.001
BMI	20.1 ± 2.6	21.2 ± 2.6	<.001
Underweight (<18.5 kg/m ²)	63,711 (27.2)	9644 (13.9)	
Normal weight (18.5–24.9 kg/m ²)	159,379 (68.1)	53,908 (77.5)	
Overweight (>25 kg/m ²)	10,975 (4.7)	5968 (8.6)	
Father education level			<.001
Less than high school	136,002 (58.1)	40,803 (58.2)	
More than university	98,063 (41.9)	28,717 (41.3)	
Mother education level			<.001
Less than high school	159,805 (68.3)	74,260 (31.7)	
More than university	74,296 (31.7)	22,224 (32.0)	
Household income			<.001
Low	53,941 (23.0)	17,572 (25.3)	
Moderate	118,538 (50.6)	33,343 (48.0)	
High	61,586 (26.3)	18,605 (26.8)	
Substance Use	1675 (0.7)	1010 (1.5)	<.001
Sexual experience	5486 (2.3)	2683 (3.9)	<.001
Stress			<.001
Severe to very severe	113,481 (48.5)	36,070 (51.9)	
Moderate	92,241 (39.4)	25,855 (37.2)	
None to mild	28,343 (12.1)	7595 (11.8)	
Perceived health status			<.001
Good	145,899 (62.3)	40,863 (58.8)	
Moderate	68,708 (29.4)	21,410 (30.8)	
Bad	19,458 (8.3)	7247 (10.4)	
Perceived happiness			<.001
Happy	122,593 (53.7)	36,115 (51.9)	
Moderate	77,595 (33.2)	23,106 (33.2)	
Unhappy	30,877 (13.2)	10,299 (14.8)	
Experiences of depressive mood for 2 or more continuous weeks	90,538 (38.7)	28,455 (40.9)	<.001

atopic dermatitis were higher in the early menarche than the not early group. The adjusted regression models for associations of asthma and asthma severity with menarche status are shown in Table 3. After adjusting for all factors listed above in “Data analysis,” the models revealed a 1.04-fold (95% confidence

Table 2
Differences in allergic diseases status according to the menarche status.

	Not early menarche (n = 234,065)	Early menarche (n = 69,520)	P-value
Asthma	17,366 (7.4)	5652 (8.1)	<.001
Absence school for asthma			<.001
Never	15,584 (91.3)	5041 (89.2)	
1–3 d/yr	1087 (6.3)	351 (6.2)	
≥4 d/yr	425 (2.4)	260 (4.6)	
Allergic rhinitis	68,663 (29.3)	22,214 (32.0)	<.001
Atopic dermatitis	57,446 (24.5)	17,646 (25.4)	<.001

interval [CI] 1.00–1.07) greater likelihood of asthma in the early menarche than not early menarche group. In addition, the odds ratios (ORs) for missing school due to asthma for 1 to 3 days and ≥4 days per year in the early menarche group were 1.00 (95% CI, 1.00–1.02) and 1.21 (95% CI, 1.01–1.46), respectively.

4. Discussion

This is the first nationwide study in Korea to explore the association between early menarche and asthma after adjusting for multiple potential confounders. We found associations between early menarche and both asthma and severe asthma, as reported in earlier studies.^[8,16] Shehata and Sheikh^[7] reported that a lower age at menarche increased the risk of asthma. Guerra et al^[16] found that a higher body mass index and early menarche were related to asthma development. Lieberoth et al^[17] reported a pooled OR of 1.37 (95% CI 1.15–1.64) for new-onset asthma in those who entered menarche before the age of 12 years, and a significant association reportedly persisted in women aged 12 to 41 years^[18] and in those aged 18 to 35 years.^[19] However, Gnatiuc et al^[20] found no significant association between early menarche and asthma at age 33 years, and Jartti et al^[21] found no significant association in women aged 24 to 39 years. In the cited meta-analysis,^[17] girls with early menarche were at an increased risk of asthma relative to those with late menarche (OR, 1.37 [95% CI, 1.15–1.64]).

Although the mechanism by which early menarche may provoke asthma remains unclear, several factors may be in play. Firstly, both menarche timing and asthma risk may be determined genetically and/or by the early living environment.^[22,23] Genes promoting obesity, metabolic syndrome, and poor intrauterine development have been linked to early

Table 3
Adjusted relative odds (95% CI) on multivariate analysis of the association between early menarche and asthma.

	Adjusted ORs (95% CI)
Asthma	
No	Reference
Yes	1.04 (1.00–1.07)
Absence school for asthma	
Never	Reference
1–3 d/yr	1.00 (1.00–1.02)
≥4 d/yr	1.21 (1.01–1.46)

Adjusted for age, school type, residence area, family structure, family affluence scale, BMI, smoking, alcohol, regular exercise, perceived stress and health status, depression episodes, and allergic diseases (allergic rhinitis and atopic dermatitis). CI=confidence interval, OR=odd ratio.

menarche^[24,25] and asthma.^[26] Second, early menarche may directly cause asthma because of changes in airway function. Asthma is associated with poor airway smooth muscle function and pulmonary inflammation, both of which are affected by female sex hormones. Menstruation elevates serum estrogen and progesterone levels. Estrogens binds to alpha- and beta-estrogen receptors in the lung to activate endothelial nitric oxide synthase, and nitric oxide may play roles in asthma pathogenesis at various times during the menstrual cycle.^[27] Early menarche induces hormonal and immunological changes,^[28] and the hormonal effects of early menarche may induce major (enduring) changes in immunogenesis, in turn triggering asthma. Lymphocytes (predominantly of the Th2 phenotype) secrete cytokines such as IL-4 and IL-5, which cause asthma. After early menarche, suppression of Th1 cells and promotion of Th2 cells lead to fetal immunotolerance. However, the precise mechanism underlying the association between early menarche and asthma remains poorly understood.

Our work had certain limitations. First, it was cross-sectional in nature, and thus we could not explore causality. Second, we identified asthma based exclusively on a “yes” answer to the question “Have you ever been diagnosed with asthma by your doctor?” We did not evaluate asthma medication use, current asthma symptoms, spirometry data, or asthma control. Thus, our findings should be interpreted with caution. The strengths of our study include the use of nationwide data and the first report of an association between asthma and early menarche in Korea. Further well-designed prospective studies are needed.

5. Conclusion

Adolescent girls with early menarche were likely to suffer from severe asthma.

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Author contributions

All authors contributed analysis and final approval of the manuscript. Chang Hoon Han and Jae ho Chung take responsibility for the integrity of the datas and the accuracy of the data analysis. Soo Rim Kim served as an author of the thesis, principal investigator, and had full access to all of the data in the study.

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