

The Effect of Hidden Female Smoking on the Association between Smoking and Asthma

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Keywords

Asthma · Smoking · Environmental factors

Abstract

Background: The association between smoking and asthma remains controversial. In our previous study, we were not able to show an association between asthma and smoking in Korean adults. One Korean study demonstrated underreporting of smoking history by female adults. The aim of the present study was to investigate the effects of hidden female smoking on the association between asthma and smoking in Korean adults. **Methods:** Data were acquired from 23,483 men and women aged ≥ 19 years who participated in the Korean National Health and Nutrition Examination Surveys (KNHANES). **Results:** The prevalence of asthma was 1.5%, the self-reported smoking prevalence was 32.4%, and the cotinine-verified smoking prevalence was 30.3%. Of the male cotinine-verified smokers, 6.4% were self-reported non-smokers (2.7% never smokers and 3.7% ex-smokers), whereas 48.8% of the female cotinine-verified smokers were self-reported nonsmokers (43.2% never smokers and 5.6% ex-smokers). In males, the adjusted odds ratio of the association between smoking and asthma was 0.738 (confidence interval, CI: 0.393–1.173) in self-reported and 0.767 (CI: 0.515–1.143) in cotinine-verified smoking; in females, the adjusted

odds ratio was 1.945 (CI: 1.348–2.805) in self-reported and 1.531 (CI: 1.076–2.179) in cotinine-verified smoking. **Conclusions:** Our study showed smoking was associated with asthma in females but not in males.

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Introduction

Asthma is one of the most common chronic respiratory diseases and a serious public health problem. The prevalence of asthma in adults has increased in recent decades [1–3], with a concomitant increase in the prevalence of physician-diagnosed asthma in Korea [4, 5].

While the reason for the increasing prevalence of asthma is unclear, it is widely believed that the Western lifestyle that has resulted from industrialization, which includes increased levels of air pollution [6], changes in indoor environments [7], increased hygiene [8], and a reduced incidence of infections early in life [9], has contributed to the risk of developing asthma.

Smoking is a well-known indoor air pollutant and is known to be a risk factor for asthma [10–12]. However, our previous study did not show a positive association between asthma and smoking history in Korean adults [13].

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Table 1. Definition of survey cotinine-verified smoking status (SCS), (*n* = 23,483)

Self-reported smoking status	Cotinine-verified smoking status	
	nonsmoker	smoker
Never smoker	Nonsmoker (SCS) (<i>n</i> = 13,434)	Smoker (SCS) (<i>n</i> = 718)
Ex-smoker	Nonsmoker (SCS) (<i>n</i> = 2,291)	Smoker (SCS) (<i>n</i> = 211)
Smoker	Smoker (SCS) (<i>n</i> = 1,681)	Smoker (SCS) (<i>n</i> = 5,148)

We assumed this result might be due to misclassification bias, especially regarding the smoking history of women. This assumption was based on a previous Korean study that reported ratios of cotinine-verified to self-reported smoking rates of 2.36 for women and 1.12 for men [14]. Studies from other developed countries showed negligible gender differences in the underreporting of smoking history [15, 16]. In a study from the United States, there were no gender differences in the underreporting rates of smoking history [15]. A study from Finland documented that 2.5% of male and 2.7% of female self-reported nonsmokers had a positive serum cotinine level [16].

The first aim of the present study was to investigate the effect of hidden smoking in females on the association between asthma and smoking in Korean adults using Korean National Health and Nutrition Examination Survey (KNHANES) data. The second aim was to investigate the association between asthma and smoking, including all kinds of smoking types, such as passive, light, intermittent, heavy, and hidden smoking, in order to better understand the link between asthma and smoking.

Materials and Methods

Study Subjects

This study was based on KNHANES data from 2008– to 2016 (excluding 2012–2013, as urinary cotinine level was not investigated during that survey). KNHANES is a cross-sectional survey designed to examine the health and nutritional status of the noninstitutionalized Korean population that was conducted by the Division of Chronic Disease Surveillance at the Korean Centers for Disease Control and Prevention (KCDC). Data were collected through household interviews, physical examinations, laboratory tests, and nutritional status assessments. All survey protocols were approved by the KCDC Institutional Review Board. Written informed consent was obtained from all participants before the survey.

We included 40,298 people ≥ 19 years of age from the total of 52,683 who participated in KNHANES. We excluded 16,815 participants as they had no smoking history (6,260 subjects, 15.5%), no urine cotinine test results (24,949 subjects, 61.9%), a history of renal failure (138, 0.3%), or a serum creatinine ≥ 1.5 mg/dL (243 subjects, 0.6%). The remaining 23,483 participants were included in the final analysis.

General Characteristics, Anthropometrics, and Definition of Asthma

The health interview and health behavior surveys included well-established questions to determine the demographic and socioeconomic characteristics of the participants. These surveys included questions regarding sex, age, marital status, employment status, education level, monthly family income, number of household members, residence area, smoking habits, body mass index (BMI), atopic dermatitis, and asthma. The respondents' residential areas were categorized as urban (an administrative division of a city) or rural (not classified as an administrative division of a city). The definition of a city in Korea is a place where $>50,000$ people live that is larger than a town. Monthly family income indicates monthly equalized family income and was calculated by dividing total family income by the square root of the number of household members. In KNHANES, monthly family income was classified into quartiles to determine the monthly household income level (1: low; 2: middle low; 3: middle high; and 4: high). Education level was defined as less than middle school, middle school, high school, or college or more. BMI was categorized into 3 groups: normal weight (<23); overweight (23–25); and obese (≥ 25) [17]. Asthma and atopic dermatitis were defined by self-report of a physician's diagnosis. The following survey question was used in this study: "Have you ever been diagnosed with asthma by a physician?" Cigarette use was divided into 3 categories: smoker, ex-smoker, and never smoker. Respondents who reported having consumed ≥ 100 cigarettes in their lifetime were regarded as smokers, based on a "yes" response to the question, "Do you smoke cigarettes now?" Ex-smokers were classified based on a "no" response to the same question. Respondents who consumed <100 cigarettes in their lifetime were regarded as never smokers.

Urinary cotinine was measured by tandem mass spectrometry with a tandem mass API 4000 (Applied Biosystems, Carlsbad, CA, USA) and by gas chromatography and mass spectrometry with a PerkinElmer Clarus 600T (PerkinElmer, Turku, Finland). Respondents with urinary cotinine concentrations ≥ 50 ng/ml were considered cotinine-verified smokers and those with cotinine levels <50 ng/mL were cotinine-verified nonsmokers [18].

To better understand the link between asthma and smoking, we created new variables to define smoking status (SCS, survey cotinine-verified smoking status) (Table 1). We assumed smoking in this variable meant all smoking types, including light smoking, intermittent smoking, passive smoking, hidden smoking, and active heavy smoking.

Statistical Analysis

We conducted all statistical analyses using Statistical Package for the Social Sciences (SPSS) complex sample procedures because

KNHANES data were collected through a representative, stratified, and clustered sampling method. We carried out logistic regression analysis to identify the relationships between risk factors and the prevalence of asthma. Statistical analysis was conducted using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). For all analyses, p values were two tailed, and $p < 0.05$ was considered statistically significant.

Ethics Approvals

The study protocol was approved by the Institutional Review Board (IRB) of the Samsung Changwon Hospital (IRB No. 2016-10-001). Informed consent was exempted by the board.

Results

Clinical Characteristics

A total of 23,483 subjects from KNHANES were included in this study. Slightly over half (52.6%) were female. The majority was married (68.2%) and employed (64.5%), and most had an education level of high school or higher (73.5%). Most subjects lived in urban areas (82.3%). The prevalence of asthma was 1.5 and that of atopic dermatitis was 3.0% (Table 2).

Smoking Status

The self-reported smoking prevalence was 32.4% and the cotinine-verified smoking prevalence was 30.3% (Table 2).

Table 3 presents prevalence rates of cigarette smoking, both by self-report and by urine cotinine verification. Self-reported smoking prevalence was 54.9% for men and it was 7.3% for women. Cotinine-verified smoking prevalence rates for men and women were 44.6 and 10.3%, respectively. Of the total of 6,077 cotinine-verified male and female smokers, 929 (19.4%) were self-reported non-smokers (never smokers plus ex-smokers). This under-reporting, however, differed markedly by gender. Of male cotinine-verified smokers, 6.4% were self-reported non-smokers (2.7% never smokers and 3.7% ex-smokers), whereas 48.8% of female cotinine-verified smokers were self-reported nonsmokers (43.2% never smokers and 5.6% ex-smokers).

Relationship between Adult Asthma and Smoking

Univariate analysis did not reveal any statistically significant differences in the area of residence between subjects with and without asthma. Compared with nonasthmatics, asthmatics were more prone to be female ($p < 0.01$), older ($p < 0.01$), single (separated or divorced) ($p < 0.01$), unemployed ($p < 0.01$), and less educated ($p < 0.01$), and had a lower monthly family income ($p < 0.05$) and a

Table 2. Demographic characteristics of the subjects

Characteristics	Sample size	Estimate, % (95% CI)
Sex ($n = 23,483$)		
Male	10,657	47.4 (46.8–48.0)
Female	12,826	52.6 (52.0–53.3)
Age ($n = 23,483$)		
19–30 years	3,447	22.2 (21.3–23.0)
31–40 years	4,390	20.7 (19.8–21.6)
41–50 years	4,395	21.4 (20.7–22.1)
51–60 years	4,619	18.4 (17.8–19.1)
61–70 years	3,980	10.5 (10.0–11.0)
>70 years	2,652	6.8 (6.4–7.3)
Marital status ($n=23,432$)		
Married	16,978	68.2 (67.2–69.1)
Single, separated or divorced	2,876	9.1 (8.6–9.6)
Never married	3,578	22.8 (21.9–23.7)
Employment status ($n = 22,916$)		
Employed	13,950	64.5 (63.7–65.4)
Unemployed	8,966	35.5 (34.6–36.3)
Education level ($n = 22,920$)		
<High School	8,168	26.5 (25.5–27.5)
High School	7,929	39.3 (38.4–40.3)
>High School	6,823	34.2 (33.1–35.3)
Monthly family income (quartile), ($n = 23,180$)		
1	4,346	14.6 (13.8–15.4)
2	5,884	25.3 (24.3–26.4)
3	6,417	29.7 (28.6–30.7)
4	6,533	30.5 (29.1–31.9)
Number of household members ($n = 23,471$)		
1	1,947	6.8 (6.2–7.4)
2	6,282	21.6 (20.8–22.4)
3	5,670	26.5 (25.6–27.5)
4	6,376	31.0 (30.0–32.1)
>5	3,196	14.1 (13.2–15.0)
Residence area ($n = 23,483$)		
Urban	18,319	82.3 (80.0–84.4)
Rural	5,164	17.7 (15.6–20.0)
Self-reported smoking status ($n = 23,483$)		
Smoker	6,829	32.4 (31.6–33.2)
Ex-smoker	2,502	11.6 (11.1–12.2)
Never smoker	14,152	56.0 (55.3–56.8)
Urine cotinine-verified smoking status ($n = 23,612$)		
Smoker	6,077	30.3 (29.5–31.1)
Nonsmoker	17,406	69.7 (68.9–70.5)
Body mass index ($n = 23,483$)		
<23	10,157	43.8 (43.0–44.6)
23–25	5,623	23.7 (23.1–24.4)
≥25	7,703	32.5 (31.8–33.3)
Atopic dermatitis ($n = 23,483$)		
Yes	592	3.0 (2.7–3.3)
No	22,891	97.1 (96.7–97.3)
Asthma ($n = 23,483$)		
Yes	440	1.5 (1.3–1.7)
No	23,043	98.5 (98.4–98.7)

Table 3. Self-reported and cotinine-verified smoking status in men and women ($n = 23,483$)

	Total <i>n</i> (%)	Cotinine-verified smoking status	
		nonsmoker, <i>n</i> (%)	smoker, <i>n</i> (%)
<i>Self-reported smoking status</i>			
Men			
Total	10,657	5,902	4,755
Never smoker	2,499 (25.6)	2,379 (46.3)	120 (2.7)
Ex-smoker	2,208 (19.5)	2,051 (33.7)	157 (3.7)
Smoker	5,950 (54.9)	1,472 (20.0)	4,478 (93.6)
Women			
Total	12,826	11,504	1,322
Never smoker	11,653 (89.8)	11,055 (95.3)	598 (43.2)
Ex-smoker	294 (2.9)	240 (2.5)	54 (5.6)
Smoker	879 (7.3)	209 (1.7)	670 (51.2)

lower number of household members ($p < 0.01$). The prevalence rates of obesity and atopic dermatitis were higher in asthmatics ($p < 0.01$). In all 3 smoking status types, the prevalence of smoking was lower in asthmatics ($p < 0.05$), and this relationship differed by gender. Male asthmatics were prone to be nonsmokers, while female asthmatics were prone to be smokers ($p < 0.01$) (Table 4).

After adjusting for confounders, logistic regression analysis revealed significant associations with adult asthma and female sex (adjusted odds ratio [aOR]: 1.640, 95% confidence interval [CI]: 1.209–2.224), older age ($p < 0.01$), obesity (aOR: 1.329, 95% CI: 1.048–1.685), and atopic dermatitis (aOR: 3.344, 95% CI: 1.82–6.15) (Table 5).

In males, aOR of the association between smoking and asthma was 0.738 (CI: 0.393–1.173) in self-reported and 0.767 (CI: 0.515–1.143) in cotinine-verified smoking. aOR of the association of female smokers with asthma was 1.945 (CI: 1.348–2.805) in self-reported and 1.531 (CI: 1.076–2.179) in cotinine-verified smoking. Regardless of the smoking status, male adult asthma was significantly associated with never-married status ($p < 0.01$) and female adult asthma was significantly associated with older age ($p < 0.01$), smoking ($p < 0.05$), obesity ($p < 0.01$), and atopic dermatitis ($p < 0.01$) (Tables 6, 7).

Discussion

In our study, smoking was significantly associated with female adult asthma but not with male adult asthma. The association between adult asthma and smoking is controversial. Many previous studies showed an elevated risk of asthma in smokers [10, 11], whereas other studies

did not [19–21]. Some studies found an increased risk of asthma only in female smokers, consistent with our study [22–24]. We thought these differences may be due to cross-sectional and case-control designs and their reliance on self-reported smoking status.

The prevalence rates of asthma and atopic dermatitis were 1.5 and 3.0%, respectively, in our study, and these percentages were lower than those of other countries [25–28]. These previous studies reported that the prevalence of physician-diagnosed asthma was 3.9% in Japan and 20.09% in Sweden, and the prevalence of physician-diagnosed atopic dermatitis was 6.9% in Japan and 10.6% in the United States. The prevalence rates of asthma and atopic dermatitis in previous Korean studies using the National Nutrition Survey were in agreement with our study [4, 29], but a previous Korean study using both questionnaire and bronchial challenge reported that the prevalence of asthma was 3.4%. We infer that the prevalence of allergic diseases in our patients, which differs from other countries, may be affected by race, culture, and some underreporting [30].

One previous study reported a higher number of secret female smokers in Korea than in other countries [14], and we found similar results in our study. We assumed that the self-reported underestimated prevalence of smoking in Korean women might be affected by Confucianism. Confucianism can cause a patriarchal culture in which female smoking is stigmatized [31]. In addition, we found that the education level and employment status of women was significantly lower than that of men, and these results might be related to Confucianism in the Korean society (online suppl. Table S1, S2; for all online suppl. material, see www.karger.com/doi/10.1159/000488677) [32].

Table 4. Crude odds ratio and their 95% confidence intervals (CI) for the prevalence of adult asthma ($n=23,483$)

Characteristics	Odds ratio (95% CI)		
	total ($n = 23,483$)	male ($n = 10,657$)	female, ($n = 12,826$)
Sex			
Male	Reference		
Female	1,862 (1.498–2.315)		
Age			
19–30 years	Reference		
31–40 years	2.307 (1.354–3.929)	2.380 (1.029–5.502)	2.211 (1.111–4.401)
41–50 years	2.254 (1.334–3.808)	2.290 (0.950–5.521)	2.159 (1.111–4.196)
51–60 years	3.579 (2.174–5.892)	3.550 (1.570–8.028)	3.412 (1.811–6.431)
61–70 years	5.860 (3.593–9.557)	5.153 (2.287–11.610)	5.812 (3.099–10.901)
>70 years	8.551 (5.276–13.859)	8.652 (3.913–19.130)	7.516 (4.005–14.106)
Marital status			
Married	Reference		
Single, separated or divorced	2.193 (1.743–2.758)	1.178 (0.621–2.235)	2.173 (1.683–2.805)
Never married	0.371 (0.244–0.564)	0.277 (0.140–0.547)	0.522 (0.306–0.891)
Employment status			
Employed	Reference		
Unemployed	1.608 (1.317–1.962)	1.394 (0.965–2.015)	1.370 (1.074–1.748)
Education level			
<High School	2.895 (2.253–3.719)	2.163 (1.436–3.258)	3.177 (2.282–4.424)
High School	0.895 (0.649–1.233)	0.718 (0.442–1.165)	1.076 (0.703–1.649)
>High School	Reference		
Monthly family income (quartile)			
1	2.900 (2.188–3.845)	2.332 (1.409–3.862)	3.034 (2.159–4.264)
2	1.376 (1.023–1.850)	1.393 (0.846–2.294)	1.333 (0.923–1.926)
3	1.413 (1.034–1.929)	1.195 (0.706–2.022)	1.586 (1.088–2.310)
4	Reference		
Number of household members			
1	1.877 (1.286–2.740)	1.962 (0.839–4.589)	1.817 (1.174–2.814)
2	1.973 (1.431–2.720)	2.839 (1.561–5.163)	1.670 (1.170–2.385)
3	0.987 (0.703–1.387)	1.441 (0.758–2.379)	0.858 (0.575–1.282)
4	0.949 (0.658–1.367)	1.691 (0.883–3.240)	0.710 (0.461–1.093)
>5	Reference		
Residence area			
Urban	Reference		
Rural	1.201 (0.949–1.520)	1.085 (0.727–1.620)	1.295 (0.963–1.743)
Smoking status			
Self-reported			
Smoker	0.737 (0.579–0.936)	0.907 (0.600–1.370)	1.806 (1.259–2.591)
Ex-smoker	0.708 (0.495–1.013)	1.080 (0.648–1.802)	0.679 (0.296–1.557)
Never smoker	Reference		
Cotinine verified			
Smoker	0.672 (0.521–0.868)	0.666 (0.457–0.970)	1.261 (0.886–1.797)
Nonsmoker	Reference		
Survey cotinine verified			
Smoker	0.758 (0.607–0.947)	0.810 (0.571–1.149)	1.415 (1.038–1.928)
Nonsmoker	Reference		
Body mass index			
<23	Reference		
23–25	1.278 (0.971–1.681)	1.116 (0.694–1.796)	1.556 (1.125–2.152)
≥25	1.503 (1.201–1.881)	1.070 (0.713–1.605)	2.158 (1.664–2.798)
Atopic dermatitis present	2.172 (1.283–3.679)	2.424 (0.967–6.078)	2.054 (1.097–3.844)

Table 5. Adjusted odds ratio (aOR) and their 95% confidence intervals (CI) for the present adult asthmatics (self-reported smoking status) ($n = 22,575$)

Characteristics	aOR	95% CI
Sex		
Male	Reference	
Female	1.643	1.128–2.393
Age		
>19–30 years	Reference	
>31–40 years	2.049	1.146–3.661
>41–50 years	1.922	1.048–3.525
>51–60 years	2.506	1.328–4.728
>61–70 years	3.127	1.619–6.039
>70 years	3.982	2.016–7.864
Marital status		
Married	Reference	
Single, separated or divorced	1.156	0.865–1.546
Never married	0.847	0.504–1.424
Employment status		
Employed	Reference	
Unemployed	1.126	0.901–1.406
Education level		
<High School	1.296	0.902–1.861
High School	0.825	0.592–1.151
>High School	Reference	
Monthly family income (quartile)		
1	1.445	0.999–2.090
2	1.071	0.777–1.477
3	1.339	0.972–1.843
4	Reference	
Number of household members		
1	1.100	0.703–1.722
2	1.387	0.973–1.976
3	1.024	0.724–1.449
4	1.105	0.760–1.607
>5	Reference	
Self-reported smoking status		
Smoker	1.162	0.809–1.669
Ex-smoker	0.933	0.591–1.471
Never smoker	Reference	
Body mass index		
<23	Reference	
23–25	1.190	0.896–1.579
≥25	1.330	1.049–1.687
Atopic dermatitis present	3.338	1.817–6.132

aOR, adjusted for sex, age, marital status, employment status, education level, monthly family income, number of household members, smoking status, body mass index, and atopic dermatitis.

A previous Korean study reported that the ratios of cotinine-verified to self-reported smoking rates were 2.36 for women and 1.12 for men [14]. These results indicate a higher number of hidden female than male smokers. In

a study from the United States, there was no gender difference in the underreporting rate of smoking history [15]. A study from Finland documented that 2.5% of male and 2.7% of female self-reported nonsmokers had positive serum cotinine levels [16]. In our study, ratios of cotinine-verified to self-reported smoking rates were 1.50 for women and 0.80 for men, which were similar to a previous Korean study [14]. We found gender differences in the underreporting of smoking history, indicating more hidden female than male smokers. We also found an effect of hidden smoking on the association between asthma and smoking in female subjects, but this effect did not change the association. In males, aOR of the association between smoking and asthma was 0.738 (CI: 0.393–1.173) in self-reported and 0.767 (CI: 0.515–1.143) in cotinine-verified smoking. aOR of the association of female smokers with asthma was 1.945 (CI: 1.348–2.805) in self-reported and 1.531 (CI: 1.076–2.179) in cotinine-verified smoking.

Accurate assessments of passive smoking and light smoking are difficult. The number of cigarettes smoked, the length of time in the smoking area, the ventilation properties of the building, and the absorptive qualities of elements contained in the building, all contribute to passive smoking [33]. In the assessment of passive smoking, the nicotine metabolite cotinine is the most widely used biomarker because it has a much longer half-life than nicotine [34].

Passive smoke consists of side and main stream smoke [33]. Main stream smoke is the portion exhaled by smokers and accounts for 15% of total passive smoking. Side stream smoke is released from the burning tip of a cigarette and accounts for 85% of total passive smoking. Side stream smoke is especially hazardous to health, as this smoke reaches the most distal alveoli in the lung due to the smaller particle size [35] and contains more harmful compounds than main stream smoke [36]. Two Finnish studies showed that passive smoking increased the risk of asthma [37, 38]. They reported that continuous lifelong and recent exposure to environmental tobacco smoke increased the risk of asthma [38].

There is no consensus on the definitions of light smoking and intermittent smoking [39–41]. Light smoking is defined as smoking <1 pack/day, <15 cigarettes/day, <10 cigarettes/day, and smoking 1–39 cigarettes/week [39]. Intermittent smoking is generally defined as smoking on a nondaily basis [39, 40]. Light and intermittent smokers are often not detected because many of them do not think of themselves as smokers and deny their habit when asked by family, friends, and health care providers [42]. The as-

Table 6. Adjusted odds ratio (aOR) and their 95% confidence intervals (CI) for the male adult asthmatics ($n = 10,253$)

Characteristics	aOR (95% CI)		
	self-reported	cotinine-verified	survey cotinine-verified
Age			
19–30 years	Reference		
31–40 years	1.377 (0.636–2.981)	1.333 (0.617–2.878)	1.344 (0.622–2.902)
41–50 years	1.220 (0.497–2.993)	1.138 (0.465–2.786)	1.160 (0.476–2.825)
51–60 years	1.639 (0.681–3.942)	1.483 (0.624–3.524)	1.521 (0.646–3.589)
61–70 years	1.987 (0.790–4.994)	1.743 (0.702–4.327)	1.817 (0.740–4.462)
>70 years	2.698 (1.069–6.812)	2.288 (0.915–5.719)	2.426 (0.977–6.024)
Marital status			
Married	Reference		
Single, separated or divorced	0.801 (0.331–1.941)	0.813 (0.335–1.972)	0.802 (0.331–1.946)
Never married	0.393 (0.205–0.753)	0.402 (0.210–0.770)	0.403 (0.210–0.771)
Education level			
<High School	1.167 (0.666–2.045)	1.175 (0.670–2.059)	1.170 (0.667–2.054)
High School	0.742 (0.440–1.250)	0.740 (0.438–1.250)	0.735 (0.435–1.241)
>High School	Reference		
Monthly family income (quartile)			
1	1.574 (0.831–2.980)	1.620 (0.852–3.081)	1.602 (0.842–3.047)
2	1.293 (0.746–2.239)	1.304 (0.755–2.253)	1.295 (0.749–2.241)
3	1.238 (0.721–2.125)	1.240 (0.723–2.125)	1.233 (0.718–2.115)
4	Reference		
Number of household members			
1	2.446 (0.847–7.059)	2.412 (0.830–7.004)	2.369 (0.812–6.910)
2	1.989 (0.999–3.962)	1.979 (0.994–3.942)	1.954 (0.977–3.907)
3	1.473 (0.757–2.868)	1.468 (0.752–2.863)	1.458 (0.749–2.841)
4	1.819 (0.937–3.531)	1.810 (0.931–3.518)	1.799 (0.926–3.495)
>5	Reference		
Smoking status			
Self-reported			
Smoker	0.738 (0.393–1.173)		
Ex-smoker	0.679 (0.484–1.126)		
Never smoker	Reference		
Cotinine verified			
Smoker		0.767 (0.515–1.143)	
Nonsmoker	Reference		
Survey cotinine verified			
Smoker			0.832 (0.571–1.213)
Nonsmoker	Reference		

aOR, adjusted for age, marital status, education level, monthly family income, number of household members, and smoking status.

sociation between light smoking and asthma has not been revealed yet. Considering the relationship between cardiovascular disease and light smoking, light smoking and intermittent smoking are inferred to have effects similar to severe cigarette smoking on asthma [43, 44].

In order to better understand the link between asthma and smoking, we created a new variable, the survey cotinine-verified smoking status, to consider the effect of hid-

den and other types of smoking. This new variable showed results similar to self-reported and cotinine-verified smoking. Thus, we hypothesized that passive and light smoking might have a similar effect on asthma as active smoking.

We assumed that previous inconsistent results regarding the association between adult asthma and smoking might be due to hidden and other types of smoking, such

Table 7. Adjusted odds ratio (aOR) and their 95% confidence intervals (CI) for the female adult asthmatics ($n = 12,330$)

Characteristics	aOR (95% CI)		
	self-reported	cotinine-verified	survey cotinine-verified
Age			
>19–30 years	Reference		
>31–40 years	3.123 (1.295–7.531)	3.141 (1.302–7.579)	3.142 (1.306–7.560)
>41–50 years	2.982 (1.249–7.119)	2.930 (1.221–7.031)	2.982 (1.250–7.113)
>51–60 years	3.714 (1.531–9.010)	3.630 (1.485–8.874)	3.714 (1.526–9.040)
>61–70 years	4.613 (1.835–11.594)	4.498 (1.778–11.379)	4.632 (1.838–11.676)
>70 years	5.532 (2.158–14.182)	5.432 (2.107–14.003)	5.558 (2.160–14.299)
Marital status			
Married	Reference		
Single, separated or divorced	1.232 (0.899–1.689)	1.265 (0.923–1.735)	1.248 (0.909–1.714)
Never married	1.626 (0.758–3.487)	1.654 (0.771–3.550)	1.650 (0.771–3.528)
Employment status			
Employed	Reference		
Unemployed	1.135 (0.878–1.466)	1.144 (0.885–1.477)	1.139 (0.882–1.472)
Education level			
<High School	1.449 (0.938–2.239)	1.487 (0.963–2.295)	1.467 (0.950–2.266)
High School	0.914 (0.607–1.377)	0.927 (0.616–1.396)	0.916 (0.607–1.382)
>High School	Reference		
Monthly family income (quartile)			
1	1.371 (0.883–2.127)	1.386 (0.891–2.158)	1.379 (0.886–2.147)
2	0.937 (0.625–1.406)	0.943 (0.629–1.415)	0.943 (0.629–1.415)
3	1.415 (0.955–2.097)	1.420 (0.959–2.102)	1.421 (0.960–2.105)
4	Reference		
Number of household members			
1	0.875 (0.535–1.433)	0.881 (0.537–1.447)	0.885 (0.540–1.451)
2	1.181 (0.789–1.768)	1.203 (0.804–1.800)	1.202 (0.803–1.798)
3	0.870 (0.575–1.316)	0.881 (0.583–1.331)	0.881 (0.582–1.331)
4	0.842 (0.540–1.312)	0.853 (0.548–1.327)	0.854 (0.549–1.329)
>5	Reference		
Smoking status			
Self-reported			
Smoker	1.945 (1.348–2.805)		
Ex-smoker	0.833 (0.354–1.959)		
Nonsmoker	Reference		
Cotinine verified			
Smoker		1.531 (1.076–2.179)	
Nonsmoker	Reference		
Survey cotinine verified			
Smoker			1.630 (1.188–2.235)
Nonsmoker	Reference		
Body mass index			
<23	Reference		
>23–25	1.241 (0.902–1.708)	1.244 (0.905–1.710)	1.242 (0.904–1.707)
≥25	1.511 (1.155–1.977)	1.508 (1.153–1.972)	1.507 (1.152–1.972)
Atopic dermatitis present	2.807 (1.341–5.876)	2.889 (1.378–6.053)	2.851 (1.360–5.975)

aOR, adjusted for age, marital status, employment status, education level, monthly family income, number of household members, smoking status, body mass index, and atopic dermatitis.

as light, intermittent, and passive smoking [10, 11, 19–24]. Now, we infer carefully that adult asthma in females is associated with smoking, but that adult asthma in males is not. The rates of hidden and other types of smoking may vary between countries, and, thus, more studies are needed to clarify these effects on the association with asthma.

Several mechanisms regarding the association between adult-onset asthma and smoking have been suggested.

First, smoking increases bronchial hyperresponsiveness, eosinophilia, and T-helper type 2 cell-oriented immune responses following allergen exposure [45, 46]. At the individual level, these mechanisms could increase the risk of asthma in susceptible groups.

Second, the effects of smoking on asthma are influenced by genetic factors. A history of parental atopy and female sex increase the risk of asthma in smokers [47], and some gene polymorphisms interacting with active smoking suggest gene-environmental interactions in the development of adult asthma [48, 49].

Third, smoking activates bronchial epithelial cells to release proinflammatory cytokines, chemokines, growth factors, and TGF- β , which are known to modulate smooth muscle cells and fibroblast proliferation with subsequent progression to fibrosis and extracellular matrix deposition [50]. Persistent exposure to smoking drives remodeling responses in asthmatic airways, thus accelerating a decline in lung function and increasing the severity of airflow obstruction [11, 51].

Although there are many hypotheses about the mechanisms, more conclusive data are needed to clarify the underlying mechanisms of the association between asthma and smoking.

This study has several limitations. First, because this study has a cross-sectional design, we could not confirm causality. Second, the diagnosis of asthma was based on

participant self-reports, which may have produced a misclassification bias. Third, even though this study was based on a national survey, our study results might be due to selection or recall bias. Fourth, respondents using nicotine replacement therapy could not be excluded, and we could not investigate dietary nicotine exposure.

The notable strength of our study is the use of large quantities of data sampled widely across the country, including interviews, physical examinations, and laboratory tests, such as urine cotinine levels, to determine the association between asthma and smoking. In addition, our study is the first report to consider the effect of hidden smoking on the association between adult asthma and smoking.

Conclusion

In our study, we found smoking was associated with female asthma but not with male asthma. The effect of hidden smokers in the association between asthma and smoking was found in females but not in males. Since the effect of secret smoking may vary from country to country, it is necessary to consider the influence of hidden smoking when examining the association between asthma and smoking.

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Table S1. Adjusted odds ratio and their 95% confidence intervals for the employment status (n=23,483)

Characteristics	aOR* (95% CI)	p-value
Sex		
Male	Reference	
Female	0.25 (0.23-0.27)	<0.001
Age (years)		
19-30	Reference	
31-40	1.73 (1.50-2.01)	<0.001
41-50	2.64 (2.25-3.10)	<0.001
51-60	1.37 (1.16-1.62)	<0.001
61-70	0.51 (0.42-0.61)	<0.001
>70	0.19 (0.15-0.23)	<0.001
Marital status		
Married	Reference	
Single (separated or divorced)	1.18 (1.04-1.35)	0.014
Never-married	0.77 (0.66-0.89)	<0.001
Education level		
<High school	1.05 (0.92-1.20)	0.453
High school	0.68 (0.62-0.75)	<0.001
>High school	Reference	
Monthly family income (quartile)		
1	0.44 (0.38-0.51)	<0.001
2	0.70 (0.63-0.77)	<0.001
3	0.89 (0.81-0.98)	0.021
4	Reference	
Number of household members		
1	1.16 (0.95-1.43)	0.146
2	1.03 (0.90-1.18)	0.645
3	0.92 (0.82-1.05)	0.207
4	0.84 (0.75-0.94)	0.003
≥5	Reference	
Residence area		
Urban	Reference	
Rural	2.09 (1.82-2.40)	<0.001

* Adjusted for sex, age, marital status, education level, monthly family income, number of household members, residence area.

Table S2. Adjusted odds ratio and their 95% confidence intervals for the education level (n=23,483)

Characteristics	< High school		High school	
	aOR* (95% CI)	P-value	aOR* (95% CI)	p-value
Sex				
Male	Reference		Reference	
Female	2.08 (1.87-2.32)	<0.001	1.02 (0.94-1.11)	0.628
Age (years)				
19-30	Reference		Reference	
31-40	1.00 (0.65-1.55)	0.984	0.57 (0.50-0.67)	<0.001
41-50	7.93 (5.19-12.12)	<0.001	1.22 (1.03-1.44)	0.019
51-60	47.30 (30.59-73.13)	<0.001	1.71 (1.41-2.08)	<0.001
61-70	76.62 (48.32-121.50)	<0.001	1.50 (1.18-1.89)	0.001
>70	84.01 (51.81-136.22)	<0.001	1.08 (0.81-1.45)	0.583
Marital status				
Married	Reference		Reference	
Single (separated or divorced)	2.60 (2.07-3.28)	<0.001	1.99 (1.61-2.47)	<0.001
Never-married	0.75 (0.53-4.07)	0.109	1.27 (1.09-1.49)	0.003
Employment status				
Employed	1.08 (0.95-1.22)	0.262	0.71 (0.65-0.78)	<0.001
Unemployed	Reference		Reference	
Monthly family income (quartile)				
1	18.58 (14.72-23.46)	<0.001	3.37 (2.80-4.05)	<0.001
2	7.75 (6.43-9.33)	<0.001	2.80 (2.47-3.17)	<0.001
3	2.95 (2.51-3.47)	<0.001	1.68 (1.52-1.87)	<0.001
4	Reference		Reference	

Number of household members				
1	0.63 (0.47-0.85)	0.003	0.69 (0.53-0.88)	0.003
2	0.76 (0.62-0.94)	0.010	0.84 (0.72-0.99)	0.033
3	0.67 (0.55-0.82)	<0.001	0.77 (0.67-0.88)	<0.001
4	0.65 (0.53-0.79)	<0.001	0.94 (0.83-1.07)	0.360
≥5	Reference		Reference	
Residence area				
Urban	Reference		Reference	
Rural	2.56 (2.09-3.13)	<0.001	1.50 (1.30-1.74)	<0.001

* Adjusted for sex, age, marital status, employment status, monthly family income, number of household members, residence area.