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Original Article

Effect of Second-Hand Smoke Exposure on Lung Function among Non-Smoking Korean Women

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Abstract

Background: Previous literature has implicated that there might be an individual susceptibility difference in terms of race/ethnicity and gender in response to second hand smoke (SHS) exposure. This study was done to examine the effect of SHS exposure on lung function in non-smoking Korean women.

Methods: This cross-sectional study was conducted using the Korea National Health and Nutrition Examination Survey (KNHANES) from 2008-2011. A total of 2,513 female participants, age 40 yr and older, with no respiratory symptoms or prior lung diseases, were included in this study. Participants' smoking status was examined using both self-reported history and measurement of urinary cotinine level. Lung function was assessed using spirometry data, including FVC and FEV1. T-test and Chi-square tests were performed to compare diverse variables between groups. Analysis of covariance (ANCOVA) adjusted for age, height, alcohol consumption, and level of exercise was used to see any statistical differences in lung function parameters between non-SHS exposed and SHS-exposed groups.

Results: Among 2,513 non-smoking females, 767 (30.5%) were SHS-exposed. The urinary cotinine levels clearly distinguished SHS exposure, and the mean urinary cotinine levels were 7.1±0.4 and 11±0.7 in non-SHS exposed group vs. SHS-exposed group, respectively ($P < 0.001$). Urinary cotinine levels were correlated with duration of SHS exposure. However, both groups had normal lung function and there was no significant difference between the two groups in lung function.

Conclusions: Urinary cotinine is a valuable marker of SHS exposure. Korean women may have higher tolerance for SHS exposure-induced lung function decline.

Keywords: Lung function, Second-hand smoke, Urinary cotinine, Female, Korea

Introduction

Secondhand tobacco smoke (SHS) is a mixture of two forms of smoke: from the burning end of cigarettes, cigars or pipes as well as smoke exhaled by people who smoke (1). The adverse health outcome of SHS exposure is well accepted since the first study published in 1981 showed an association between lung cancer development and SHS exposure (2). Thus far, SHS exposure has been linked to a broad array of diseases, with the bulk of research focusing on the association between SHS exposure and development of cardiovascular diseases or lung cancer (3-7). People who are exposed to SHS increase their chances of developing heart diseases and lung cancer by 25–30% and 20–30%, respectively (8). Second hand smoke exposure has also been reported to contribute to

asthma flares or COPD pathogenesis (9-13). Therefore, it is not surprising that previous studies have reported that SHS exposure has an adverse effect on lung function (14-20).

However, there are some gaps to be addressed in this regard based on the review of prior literature. First, interestingly, a few studies failed to show an adverse effect of SHS exposure on lung function (21-23). Second, there might be gender, coexisting medical conditions, age, and/or geographical difference related to the effect of SHS exposure on lung function (19, 24, 25). Third, the majority of previous studies assessed the smoking status of study participants only via self-report without validation through the use of biochemical metabolites of nicotine (14-20). Thus, it is possible that some closet smokers could have been grouped as non-smokers in previous studies, possibly leading to the exaggeration of loss of lung function due to SHS exposure. Lastly, there is always the possibility of the presence of confounding factors, or bias, threatening the validity of these studies, such as any effects of indoor air pollution or occupational exposure, given the nature of epidemiologic studies. These findings may suggest that, taking the above questions into account, further studies need to be done to address the effect of SHS exposure on lung function. In other words, a better-designed study using a more homogenous group of people in terms of age, health status, gender, ethnicity and geography, might be needed to address the effect of SHS exposure on lung function more precisely. Further, using biochemical markers of smoking exposure would be needed to verify the status of SHS exposure in order to address this intriguing question. This is the reason why we examined the effect of SHS exposure on lung function among non-smoking Korean women, using nationally representative data: Korea National Health and Nutrition Examination Survey (KNHANES).

Materials and Methods

Data source and collection

The KNHANES is a nationwide survey conducted by the Korea Centers for Disease Control and Prevention (KCDC) to illustrate health, dietary habits and lifestyle behaviors of the Korean general population. This nationally representative, cross-sectional survey recruited the target participants using a complex, stratified, multistage, probability-cluster sampling design. According to KCDC, this study design was introduced to minimize the sampling bias. Specifically, data collection was performed as follows. First, 192~200 national administrative districts were chosen as primary sampling units from all the seven metropolitan cities (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) and nine provinces (Gyeonggi, Gangwon, Chungbuk, Chungnam, Jeonbuk, Jeonam, Gyeongbuk, Gyeongnam, and Jeju) throughout South Korea. Then, 20~23 households were sampled from each unit based on gender, age, regional area, and type of residential area using a stratified multistage probability sampling method. The KNHANES survey included a health examination (e.g., chest X-ray, lung function test, basic blood and urine tests, etc.) and a health survey (e.g., past medical history, current medication, physical symptoms, smoking, drinking, diet and exercise habits) (26, 27).

The survey was approved by the institutional review board of the KCDC (Approval numbers: 2008-04EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C, 2011-02CON-06-C), and informed consent was obtained for each individual before the survey. The KNHANES survey data are publicly available nationwide and were downloaded from the KCDC website (http://knhanes.cdc.go.kr/) after researcher's registration process. This study used only de-identified existing data. The KNHANES survey data include all participants' urinary cotinine levels. Urinary cotinine is a valuable biochemical indicator of recent tobacco smoke exposure (28, 29).

In this study, we used data from the 4th (2008~2009) and 5th (2010~2011) survey (26, 27). The 4th survey was conducted from July 1st to December 31st in 2008 and 2009, and 77.8 % and 82.8% of the target participants took part in the survey in 2008 and 2009, respectively. The 5th survey was performed from January 1st to December 31st in 2010 and 2011, with the survey attendance

rates of 81.9 % and 80.4%, respectively. The data collection was done on the same day as this was a cross-sectional survey. (26, 27). All study data were reviewed carefully for missing data, and all the participants with missing data were excluded before analyzing data (Fig. 1).

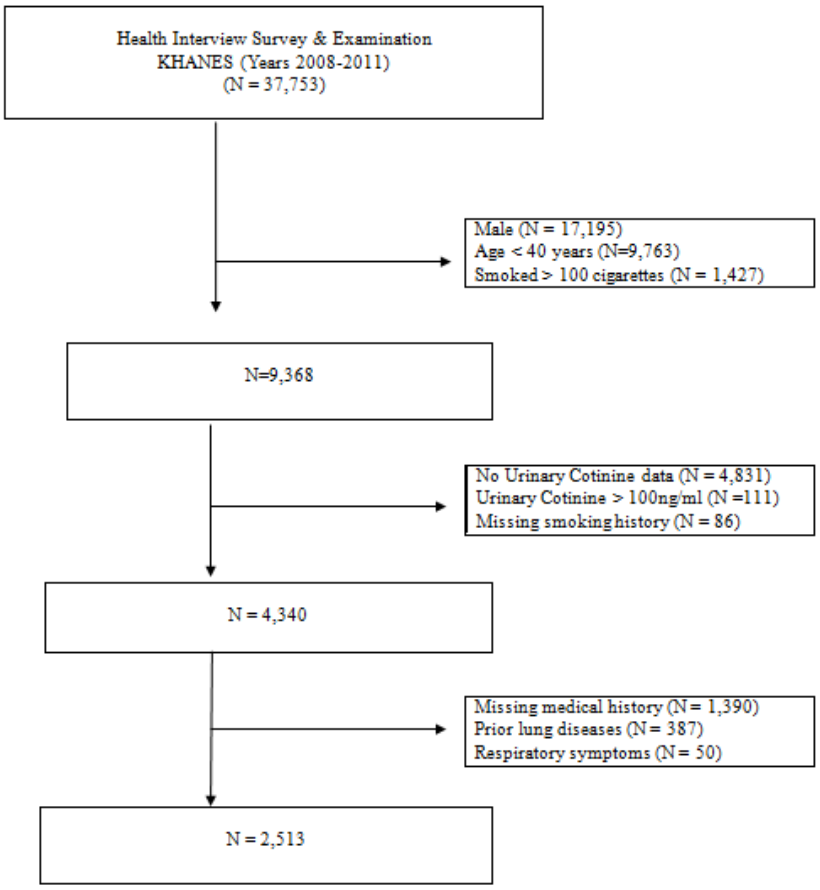

Fig. 1: Flow diagram showing inclusion and exclusion of study participants

Smoking questionnaire

Based on the self-report surveys, the participants were grouped into three categories: smoker, ex-smoker and nonsmoker. Current and ex-smokers were defined as persons with smoking history of more than 100 cigarettes in their lifetime and who current smokers (current) are or not (ex). Non-smokers were defined as persons with a smoking history of less than 100 cigarettes in their lifetimes who are not smokers at the time of the survey (30). Exposure to SHS was also obtained. The participants were asked about the duration of SHS exposure per day, either at home or in the work-place (0, >0 to <1 h, and ≥1 h).

Urinary cotinine measurement and spirometry

Urinary cotinine, a biomarker of previous nicotine exposure (28), was measured by gas chromatography using a Perkin Elmer Clarus 600 T (PerkinElmer, Finland). A urinary cotinine level of 100 ng/mL was adopted as a cutoff value to distinguish active smokers from nonsmokers in this study as suggested by one study using KNHANES data (31). To assess lung function, spirometry was performed and only pre-bronchodilator data were available and used in this study. Data on forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1) and the ratio of FEV1/FVC were analyzed for this study. Although other parameters

were available to us, such as FEF (forced expi-ratory flow) 25-75%, the current guideline for interpreting spiromery data relies on FEV1 and FVC; therefore, we decided to focus on only these two parameters and the ratio of FEV1/FVC (32). Since lung function is influenced by age, sex, race, height, etc. (33), interpretation of lung function parameters other than FEV1/FVC ratio depends on % of what is measured to what is predicted using the prediction formula based on the individual's age, sex, race, height, etc (34). Spirometry data are interpreted as normal if the % predicted value is higher than 80% (32). In general, smoking is known to induce obstructive lung diseases such as COPD, which is defined by < 0.7 (70%) of FEV1/FEV ratio (32).

The validity and reliability of lung function parameters were improved by reinforcement of lung function test guideline and quality control measures according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines (32). The validity and reli-ability of urinary cotinine measurement were imp-roved through the review by a central quality cont-rol center as recommended by the manufacturer's instruction. We tried to minimize potential sources of measurement bias by doing this.

Study population

A total of 37,753 individuals completed the survey during the study period. Among these, 20,558 of the participants were female. The inclusion criteria for participants in this study consisted of being at least 40 years old, non-smoker and with no prior history of lung disease or respiratory symptoms such as cough or dyspnea. Among the people who met the criteria, we excluded: 1) those with urine cotinine level higher than 100 ng/ml; 2) those who did not answer the smoking history questions; 3) those without urinary cotinine data. Figure 1 summarizes the inclusion and exclusion case numbers in our study. In addition, the chest X-ray readings of the study participants were also reviewed and were read as normal. A total of 2,513 females meeting the criteria were included in this study.

Statistical analysis

The independent variables in this study were SHS exposure status (Yes or No) and the duration of SHS exposure per day, either at home or in the workplace (0 h, >0 to <1 h, or ≥ 1 h). The outcome variables in this study were lung function parameters, such as FEV1, FVC, and FEV1/FVC ratio. In general, lung function is influenced by such factors as age, sex, race, height and environment (33), thus these potential confounders were further adjusted using analysis of covariance (ANCOVA).

Data were analyzed using SAS version 9.2 (SAS Institute, Inc., Cary, NC, USA). T-test and Chi-square tests were performed to compare between groups, SHS vs. non-SHS group, for continuous variables and categorical variables, respectively. A univariate–multivariate modeling strategy was adopted to see any statistical differences in lung function parameters depending on SHS exposure status. First, analysis of variance (ANOVA) was used to evaluate statistical differences in this regard. Then, ANCOVA was used to compare differences in lung function parameters according to the duration and place of SHS exposure, after adjusting for age, height, alcohol consumption, and level of exercise. Given the nature of the target population, gender and race did not need to be adjusted. $P < 0.05$ was considered statically significant.

Results

Characteristics of the study participants

Among a total 37,753 survey participants, 9,368 participants met the inclusion criteria, which consisted of being at least 40 years old, non-smoker and with no prior history of lung disease or respiratory symptoms such as cough or dyspnea. After excluding some participants with any missing data, only 2,513 participants were included in this study (Fig. 1). Table 1 demonstrates the characteristics of our study participants. Among 2,513 non-smoking females, 767 (30.5%) were SHS-exposed. A majority of the participants in the SHS group (75.4%) were employed, compared to 39.3% in the non-SHS group. The SHS group was slightly younger than the non-SHS group, and

mean ages of both groups were 53±0.4 and 56.5±0.4, respectively. Basic physical characteristics were not significantly different between the two groups.

Table 1: Characteristics of study participants

	SHS exposure (n=2,513)		
Variables	**No** n=1,746 (N=2,944,684)	**Yes** n=767 (N=1,396,445)	***P* value**
Age, years	56.5±0.4	53±0.4	<0.001
Weight, Kg	58.2±0.2	59±0.4	0.063
Height, Cm	155±0.2	155.5±0.2	0.122
BMI, Kg/m2	24.2±0.1	24.4±0.1	0.266
WC	81.1±0.3	81.4±0.4	0.482
Age, groups, years, % (SE)			<0.001
40-49	34.5 (4.1)	45.9 (4.8)	
50-59	33.8 (3.9)	38.3 (4.7)	
60-69	18.6 (2.8)	14.9 (2.8)	
>=70	13.2 (2.4)	0.9 (0.5)	
Occupation, % (SE)			<0.001
No	60.7 (1.5)	24.6 (2.0)	
Yes	39.3 (1.5)	75.4 (2.0)	
Living Place % (SE)			0.071
Rural	21.5 (1.8)	25.5 (2.6)	
Urban	78.5 (1.8)	74.5 (2.6)	
Income % (SE)			0.020
1 lowest income quartile	25 (1.5)	20.5 (1.8)	
2	24 (1.3)	29.5 (2.2)	
3	22.9 (1.3)	25.9 (2.0)	
4 highest income quartile	28.1 (1.7)	24.1 (2.1)	
Drinker % (SE)			<0.001
Non-drinker	46.4 (1.6)	31.6 (2.1)	
Light-to-moderate drinker	53.2 (1.6)	67.3 (2.1)	
Heavy drinker	0.4 (0.2)	1.0 (0.4)	
Regular exercise % (SE)			0.007
No	77.0 (1.4)	70.8 (2.1)	
Yes	23 (1.4)	29.2 (2.1)	

Data presented as mean±standard error (SE) or % (SE); T-test and Chi-square test were adopted for continuous and categorical variables, respectively; N= weighted sample size; BMI, body mass index; WC, waist circumference; Income quartiles are age and gender adjusted. Light-to-moderate drinker, < 30 g per drinking occasion; Heavy drinker, ≥ 30 g per drinking occasion.

Urinary cotinine levels between SHS exposed and non-exposed female nonsmokers

Table 2 shows the mean urinary cotinine levels from two groups. Urinary cotinine levels clearly distinguished SHS-exposed female nonsmokers from non-exposed female nonsmokers (11±0.7 vs. 7.1±0.4, respectively). Thus, the participants' self-reported status of SHS exposure was verified using a reliable biochemical marker of recent smoke exposure, namely, urinary cotinine level. Next, we examined whether urinary cotinine levels were increased in response to longer duration of SHS exposure. As shown in Table 3, urinary cotinine levels increased when participants were exposed to SHS for a longer duration. Cotinine levels were higher in the setting of home exposure, which means that the subjects are exposed to SHS at home for a longer duration compared to workplace exposure.

Table 2: Urinary cotinine levels of SHS group vs. non-SHS group

Variable	SHS exposure (n=2,513)		
	No (n=1,746)	Yes (n=767)	*p* value
Urinary cotinine, ng/mL	7.1±0.4	11±0.7	<0.001

Data are presented as mean±SE

Table 3: Urinary cotinine levels according to duration and place of SHS exposure

Variables	n	n	Cotinine level	*P* value
Duration of SHS at work per day				0.0037
0 h	2009	3,440,844	7.8±0.4	
>0 to <1 h	361	635,693	10.6±1.0	
≥ 1hr	143	264,592	10.9±1.4	
Duration of SHS at home per day				<0.0001
0 h	2106	3,549,489	7.5±0.4	
>0 to <1 h	312	608,811	11.2±1.0	
≥ 1hr	95	182,829	16.5±2.0	
Total duration of SHS per day				<0.0001
0 h	1746	2,944,684	7.1±0.4	
>0 to <1 h	553	990,806	10.4±0.8	
≥ 1hr	214	405,639	12.5±1.2	

Data are presented as mean±SE; N, weighted sample size

Effects of SHS on lung function

To examine the effect of SHS on lung function, first, FVC and FEV1 and their % predicted values (% of what is measured to what is predicted) were compared between the two groups. As demonstrated in Table 4, the mean absolute values of FVC and FEV1 were significantly higher in the SHS group than the non-SHS group.

Table 4: Spirometry results in non-SHS exposed and SHS exposed groups

Variables	SHS exposure (n=2,513)			
	No	Yes	Mean Difference	*P*
	(n=1,746, N=2,944,684)	(n=767, N=1,396,445)	(95% CI)	value
FVC	2.9±0.0	3.0±0.0	-0.059 (-0.111, -0.007)	0.026
FVCp*	81.7±1.2	80.9±1.6	0.346 (-0.833, 1.526)	0.687
FEV1	2.3±0.0	2.4±0.0	-0.072 (-0.118, -0.026)	0.002
FEV1p*	82.7±1.2	81.3±1.7	0.963 (-0.315, 2.242)	0.457
FEV1p* FVC	0.80±0.0	0.81±0.00	-0.009 (-0.014, -0.003)	0.004

Data are presented as mean±SE; N, weighted sample size; p*, percent (%) predicted values; CI, confidence interval

However, the mean % predicted values of FVCs were 81.7±1.2 and 80.9±1.6, and those of FEV1s were 82.7±1.2 and 81.3±1.7, in the non-SHS and the SHS groups, respectively, without having any significant differences. Given that the mean % predicted values of lung function parameters were

higher than 80% in both groups, both groups have normal lung function. In addition, the mean FEV1/FVC ratios were higher than 70% in both groups, thus, there was no PFT evidence to support COPD diagnosis in our study participants. In sum, both groups had normal lung function without any significant difference regardless of SHS exposure status. Table 5 shows the mean absolute values of FEV1 and FVC, not the % predicted values, after adjusting for age, height, alcohol consumption and level of exercise. Once again, there was no significant difference in lung function parameters between the groups. To further address the effect of SHS on lung function, FVC and FEV1 were also compared between the two groups according to the duration and place of SHS exposure (Table 5), however, there was no significant difference between the groups.

Table 5: Lung function parameters after adjusting for potential confounders in non-SHS vs. SHS exposed groups

	FEV1	FVC	FEV1/FVC
SHS: No	2.364±0.03	2.955±0.03	0.800±0.00
SHS: Yes	2.348±0.03	2.929±0.03	0.801±0.00
p value	0.326	0.174	0.580
Duration of SHS at work			
0 h	2.356±0.03	2.942±0.03	0.8±0.00
>0 to <1 h	2.364±0.03	2.942±0.04	0.803±0.00
≥ 1hr	2.366±0.03	2.958±0.04	0.799±0.01
p value	0.890	0.886	0.659
Duration of SHS at home			
0 h	2.364±0.03	2.951±0.03	0.8±0.00
>0 to <1 h	2.332±0.03	2.914±0.04	0.8±0.01
≥ 1hr	2.368±0.04	2.956±0.05	0.799±0.01
p value	0.388	0.375	0.959
Total duration of SHS per day			
0 h	2.362±0.03	2.952±0.03	0.800±0.00
>0 to <1 h	2.339±0.03	2.915±0.03	0.802±0.00
≥ 1hr	2.365±0.03	2.954±0.04	0.799±0.00
p value	0.431	0.198	0.723

Data are presented as least square mean±SE; ANCOVA adjusted for age, height, drink, and exercise was used

Discussion

Secondhand smoke, also called environmental tobacco smoke (ETS) or passive smoke, has been reported to be more toxic and carcinogenic (35), and the health hazard of SHS-exposure has been well-established (3, 9). Previous studies have reported that SHS exposure influences lung function adversely, possibly leading to the development of COPD (14-19). The odds ratios of developing COPD from SHS exposure have been reported between 1.31 and 2.24 (9, 10, 14, 15, 17-19). However, intriguingly, a few studies failed to show a negative effect of SHS exposure on lung function (21-23). Considering the well-accepted health hazard of SHS to the respiratory system, it is interesting to speculate on the reasons for the somewhat controversial reports by previous researchers. Due to the nature of this question, previous studies that addressed the effect of SHS exposure on lung function were mostly epidemiologic studies (14-19). Thus, it is always possible that unexpected confounders, such as any effects of indoor air pollution or occupational exposure, might have contributed to the contradictory study

findings. Also, most of the studies used a self-report survey to examine smoking status of study participants. Thus, some participants who did not answer the questionnaire honestly may have introduced some variability in the study results. Furthermore, as suggested by a few studies, there may be gender, coexisting medical conditions, age or geographical differences in response to SHS exposure, although the reported results were varied (19, 24, 25). Given this background, this cross-sectional study was conducted to address whether SHS-exposure influences lung function adversely in non-smoking Korean women ≥ 40 years of age. To investigate this, we analyzed KNHANES data from 2008-2011. In order to minimize any confounder effect, we excluded all the study participants with current respiratory symptoms or prior respiratory disease history such as pulmonary tuberculosis or pneumonia. In addition, all of the chest X-ray readings of our study participants were confirmed normal. Further, we used both a self-reported survey and a biochemical marker of nicotine exposure, urinary cotinine, to examine smoking status. Initially we included both males and females, but we decided to exclude males because of missing information.

Interestingly, we could not find any significant contribution of SHS-exposure to lung function. We are not sure what has made a difference between our study and most previous research that have clearly demonstrated the adverse effect of SHS exposure on lung function, but a few potential interesting explanations are possible. As mentioned earlier, there might be different individual susceptibilities in this regard (19, 24, 25) and Korean women may have a higher tolerance to SHS-induced reductions in lung function. Further, we used very strict eligibility criteria for this study. As such, only 2513 participants among 37,753 participants, who initially met the criteria of the study, ended up being included (Figure 1). Therefore, it is possible that individuals whose lung functions were affected by SHS exposure were excluded from the beginning through this process. It is also possible that the duration of SHS-exposure was not long enough to affect lung function in our study population. However, the decrement of lung function develops even after short-term exposure to SHS. According to recent human studies, even 1 hour of SHS exposure can induce a significant decrease in FEV1 and FEV1/FVC ratio along with cytokine releases, such as interleukins 1 beta, 4, 5, and 6, tumor necrosis factor alpha, and interferon gamma in the lungs, suggesting significant lung inflammation (36). These findings do not necessarily implicate that SHS-provoked acute decrement in lung function will lead to the development of COPD; however, an adverse effect of SHS exposure on lung function develops regardless of exposure duration. Thus, it is less likely that not enough exposure to SHS was the reason we did not see any significant lung function changes in our study population.

All these things considered the most likely explanation of finding no effect of SHS exposure on lung function among Korean women might be from their higher tolerance to SHS, although this needs to be further verified. A few previous studies also support the presence of different individual susceptibilities in this regard. For instance, one study, using the data from the population-based US Third National Health and Nutrition Examination Survey (NHANES III), observed that SHS provoked reductions in lung function were only observed in nonsmoking females, especially females with asthma, but not in nonsmoking males (24). Opposed to this, others have reported that men are more vulnerable than women in this regard (19). Others have observed that French adult women living in France are more susceptible to SHS-induced decrease in lung function than American adult women living in the U.S. (25).

Viewed in combination, the findings of these studies, including ours, strongly implicate that there might be a difference in individual susceptibility in terms of lung function impairment in response to SHS exposure. Our study has a few strengths that are worth mentioning. First, this study included a large number of participants with homogenous ethnic/racial background as well as gender. Second, our study had very strict eligibility criteria compared to others, to minimize any role of confounders in study results. Third, the participants' self-reported smoking history was

verified using a biochemical tool. We found that measurement of urinary cotinine was very useful. We were also able to exclude some participants who did not honestly report their smoking status. Cotinine is the major metabolite of nicotine, which can be measured in blood, saliva and urine. Cotinine has a longer half-life (16 to 20 hours) than nicotine (2 hours) and it reflects smoke exposure at least from the previous 2–3 days (29). Thus, cotinine is thought to be a better marker than nicotine. We also found that the self-reported smoking history, if answered honestly, correlated well with urinary cotinine levels. We can say that our study has provided supporting evidence for the use of a biochemical marker in this kind of research that addresses the role of SHS as a health hazard.

On the other hand, there are also a few limitations or potential bias in our study findings. We could not assess the cumulative effect of SHS exposure on lung function. For example, we did not know how many years the participants were exposed to SHS, because the survey did not address this. Consequently, this study could have underestimated or overestimated SHS exposure. And, as mentioned earlier, the inclusion criteria of our study were designed to avoid any potential confounders. However, these strict inclusion criteria could have introduced selection bias at the beginning of the study. For example, some participants with decreased lung function due to SHS exposure could have been ruled out during the prescreening period because of having respiratory symptoms. In addition, only spirometry data were evaluated in our study in terms of lung function, thus it is also possible we could have missed some important changes in other lung function parameters, such as changes in diffusing capacity or lung volume. However, our study findings are valuable in that we analyzed nationally representative data, and we found further support for the existence of individual susceptibilities in SHS-provoked lung function impairment in terms of race/ethnicity and gender. Regarding the generalizability of our study finding, we need further studies designed in a similar fashion to examine whether our study finding is reproducible in other populations with different race, gender, geography, etc. In addition, longitudinal studies to address the same research question will be needed to further support the generalization of our study finding.

Conclusion

Supporting evidence of decrement in lung function from SHS exposure may not be as strong as those for lung cancer. This study implicates that there might be an individual susceptibility difference in terms of race/ethnicity and/or gender in response to SHS exposure. Future studies addressing the specific role of potential contributors in determining a different response to SHS exposure would elucidate this issue more accurately.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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