



Effect of environmental tobacco smoke on atopic dermatitis among children in Korea

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ABSTRACT

The prevalence of atopic dermatitis is increasing in many countries. Several factors are known to be associated with childhood atopic dermatitis. Environmental tobacco smoke (ETS) is one of the most common indoor pollutants, and children are more vulnerable to ETS exposure than adults are. In this study, the possible association of ETS with atopic dermatitis was evaluated in 7030 individuals aged 6–13 years who participated in the Children's Health and Environment Research study. In addition, predictive factors, such as the allergic history of the parents, children's immunoglobulin E levels and children's history of rhinitis and its association with dermatitis, were assessed. After adjustment for possible confounding variables, atopic dermatitis was found to be highly correlated with ETS, especially among children whose mothers had smoked during pregnancy and/or in the first year after birth (OR=2.06, 95% CI: 1.01–4.22). In conclusion, our results show that childhood exposure to ETS is a major risk factor for atopic dermatitis.

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1. Introduction

Environmental tobacco smoke (ETS) is one of the most common indoor air pollutants. There are two types of tobacco smoke: mainstream and sidestream. Sidestream smoke is generated from raw tobacco burnt during smoking, while mainstream smoke permeates the ambient air when a smoker inhales and exhales. Sidestream smoke consists of more harmful compounds than mainstream smoke (Pietinalho et al., 2009), and it constitutes a larger portion (50–90%) of ETS than mainstream smoke (10–50%). Children are more likely to be exposed to ETS than are adults (Kramer et al., 2004). For example, in several recent studies, it was found that 36.1% of non-smokers in Korea aged over 19 years were exposed to ETS at home or at work, while over 40% of

children in Korea were exposed to ETS at home (Warren et al., 2006; Lee and Ha, 2011).

The prevalence of atopic dermatitis (AD) among children is increasing in many countries (Asher et al., 2006). The prevalence of AD among primary school children in Korea shows an upward trend: 16.6% in 1995; 24.9% in 2000; and 28.9% in 2006 (Oh et al., 2004; Jee et al., 2009). Korea has undergone rapid industrialization and urbanization, and the prevalence of AD is higher than that of other countries (Asher et al., 2006). Although there has been no proper study of the causes, numerous factors are thought to be related to the relatively high prevalence of AD in Korea: lifestyle factors, including alcohol consumption and smoking; dietary habits; microbial exposure; indoor and outdoor environments; economic status; awareness of diseases; and management of symptoms.

ETS has been considered to be a risk factor for AD, but the relationship between ETS and AD has not been sufficiently investigated. Several studies have reported that mothers' exposure to smoke during pregnancy may increase the risk of AD among their children (Schäfer et al., 1997; Kramer et al., 2004;

Abbreviations: AD, atopic dermatitis; ETS, environmental tobacco smoke

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Xeppapadaki et al., 2009). However, data from other studies have not supported these findings (Linneberg et al., 2006; Tanaka et al., 2008).

The objective of the present study was to determine whether exposure to ETS during pregnancy and the first year after birth increased the prevalence of AD among 7030 participants in the Children's Health and Environment Research study. In addition, we also determined whether the highly predictive factors for AD, such as the allergic history of the parents, children's immunoglobulin E (IgE) levels and children's history of rhinitis, were related to the prevalence of AD and whether these factors modified the association between exposure to ETS and AD.

2. Materials and methods

2.1. Study design and participants

The study population for this study was drawn from the Children's Health and Environment Research study (Ha et al., 2009), which was a longitudinal study designed to investigate the relationship between environmental factors related to industrialization and health outcomes in school-aged children from 10 representative cities in Korea: Seoul, Busan, Daegu, and Gwanju (urban areas); Incheon, Mokpo, and Yeosu (industrial areas); and Cheonan, Jeongseup, and Jeju (rural areas). The study population for the present analysis included participants in the first wave of the study, who were primarily recruited between 2005 and 2007. Parents of participating children were asked to fill in a questionnaire that included questions concerning their demographics, socioeconomic status, family environment, symptoms of allergic diseases, past medical history, and family history. Each participating child underwent a physical examination and clinical tests.

This study was approved by the institutional review boards of Dankook University College of Medicine and the University of Ulsan College of Medicine. Written consent was obtained from all participants' parents after they had been fully informed of the details of the study.

2.2. Definition of health outcomes

We used the Korean version of the International Study of Asthma and Allergies in Childhood (ISAAC), validated by Choi et al. (1998), to define the health outcome (AD). Four indicators of AD were considered: lifetime dermatitis, 12-month dermatitis, diagnosed dermatitis, and treated dermatitis. Each of the four indicators was dichotomized; a 1 indicates that the parents provided a positive response

to the relevant question in the questionnaire and a 0 indicates that they did not. For example, the answer to the question "Has your child ever had an itchy rash that was better and then worse for at least 6 months?" was used to define lifetime dermatitis. The other three questions used to define the indicators in this study were as follows: "has your child had this itchy rash at any time in the past 12 months?"; "has your child ever had a diagnosis of eczema from a physician during his/her lifetime?"; and "has your child ever had clinical treatment for eczema at any time in the past 12 months?"

Physician-diagnosed rhinitis was defined based on the parents' answer to a question regarding the child's lifetime history: "has your child ever had a diagnosis of rhinitis by a physician in his/her lifetime?"

2.3. Environmental tobacco smoke and other exposures

Childhood exposure to ETS was classified as one of the following (Fig. 1): the child's mother smoked during pregnancy and/or in the first year after the child's birth (*Mother smoking group*); the child's mother did not smoke, but other household member(s) smoked during pregnancy and/or in the first year after the child's birth (*Other household smoking group*); the child was not exposed to ETS during pregnancy or in the first year after birth, but at least one household member smoked at the time of the interview (*Current ETS group*); the child was not exposed to ETS (*No exposure group*). Children in all exposure group categories, with the exception of those from the *No exposure group*, were currently exposed to ETS.

2.4. Other factors

Information on covariates was based on questionnaire responses and analyses of blood samples. The covariates in the present analysis included children's demographic variables, parental socioeconomic status variables, and predictive factor variables. Children's ages were used as a continuous variable, and gender was considered a dichotomous variable.

The parental socioeconomic status variables were residential area, household income, and parental education. The residential area of the children was categorized as urban, rural, or industrial. Household income (per month in USD) was categorized as <\$1800; \$1800–2700; and ≥\$2700 per month. In 2005, the average monthly household income in Korea, excluding singles, was \$2600 (1 USD ≈ 1100 KRW). Parental educational attainment was dichotomized as ≤12 or >12 years. The predictor factors were a parental history of atopic allergy, the child's co-morbidity, and the child's total IgE level. The medical history of the parents related to allergy was a dichotomous variable with a value of 1 if the biological parents had a diagnosis of asthma, rhinitis, or AD and 0 if they did not. Child co-morbidity was a dichotomous variable with a value of 1 for children who had been diagnosed with rhinitis or asthma by a physician and 0 for those who

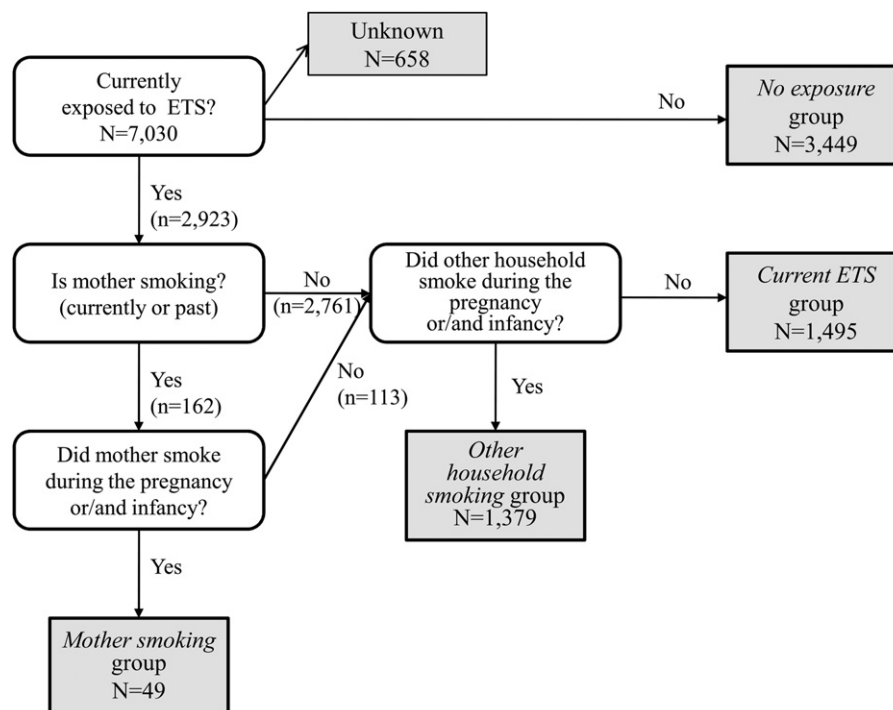


Fig. 1. Classification of study participants by exposure to environmental tobacco smoke.

had not. Total serum IgE concentrations $> 180 \text{ IU ml}^{-1}$ were considered to be outside the normal range.

2.5. Statistical analysis

First, bivariate associations between ETS and AD were examined using a simple logistic regression. Second, multiple logistic regression analyses were conducted to assess the effects of exposure to ETS. To select covariates for inclusion in the multivariate models, we identified risk factors associated with AD from the literature (Linneberg et al., 2006; Schäfer et al., 1997; Wen et al., 2009). These factors included the age and sex of the child, residential area, household income, the parents' level of education and history of atopic allergy, and the child's total serum IgE and lifetime diagnosis of rhinitis by a physician. There were many factors reported to be highly predictive of AD in the literature. Among four predictive factors that were available in our data set – history of allergy (parents); high IgE level (child); history of rhinitis (child); and history of asthma (child) – sensitivity analysis of selecting suspected risk factors regarding children's allergy co-morbidity and literature review led to exclusion of history of asthma (child) in our model (Gustafsson et al., 2000; Spergel, 2010). Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for estimated coefficients. Third, we explored whether associations between exposure to ETS and AD were modified by highly predictive variables possibly associated with AD: a history of allergy (parents); high IgE level (child); and a history of rhinitis (child). All results are presented as ORs comparing the *Mother smoking* group with the *No exposure* group. After exclusion of missing information, all analyses were conducted using SAS version 9.2 (SAS Institute, Inc., Cary, NC, USA).

3. Results

The parents of 7030 children, of the 8319 eligible children in the CHEER study, submitted the consent form. A total of 658 were excluded from the analysis because no information about exposure to ETS was available. Finally, 6372, which was 76.6% of all eligible children, were available for analysis of the association between exposure to ETS and AD.

The descriptive statistics of the study sample, according to exposure to ETS and covariates, are given in Table 1. Children were classified into four mutually exclusive groups according to their exposure to ETS (Fig. 1): no exposure to ETS (*No exposure* group) (49.1%); the child's mother smoked during pregnancy and/or in the first year after birth (*Mother smoking* group) (0.7%); the child's mother did not smoke but others in the household smoked during pregnancy and/or in the first year of life (*Other household smoking* group) (19.6%); and other members of the household smoked at the time of the survey but not during pregnancy or the first year after birth (*Current ETS* group) (21.3%). All exposure groups, except the *No exposure* group, were exposed to ETS at the time when the survey was conducted. The mean age of the children was 7.6 years, and 29.2% of the children had abnormally high IgE levels ($> 180 \text{ UI ml}^{-1}$) at the time of interview. In addition, 22.0% had at least one parent who had been diagnosed by a physician with dermatitis, asthma, and/or rhinitis during their lifetime, and 23.4% had been diagnosed with rhinitis by a physician. The prevalences of lifetime dermatitis and 12-month dermatitis among children were 34.7% and 21.5%, respectively. Thirty percent of children had been diagnosed by a physician with dermatitis in the past (diagnosed dermatitis), and 12.4% reported being treated for dermatitis in the past 12 months (treated dermatitis).

These ETS exposure groups were significantly associated with all four indicators of AD (Table 2). After adjusting for confounding variables, the odds of lifetime dermatitis in the *Mother smoking* group were 1.98 times higher than in the *No exposure* group (95% CI: 1.01–3.89). The risk of lifetime dermatitis in the *Other household smoking* group was also higher than in the *No exposure* group (OR=1.43, 95% CI: 1.24–1.65). The OR for treated dermatitis in the *Mother smoking* group was 2.74 (95% CI: 1.22–6.18), a larger value than those for the other two groups (*Other household smoking* group: OR=1.26, 95% CI: 1.04–1.53; and *Current ETS*

group: OR=1.32, 95% CI: 1.06–1.64). However, the odds of diagnosed dermatitis in the *Mother smoking* group (OR=1.92, 95% CI: 0.97–3.82) and *Current ETS* group (OR=1.05, 95% CI: 0.90–1.24) were not statistically significant.

The risk of AD associated with ETS was particularly high in the *Mother smoking* group for each of the three variables: elevated serum IgE levels (child), a history of allergy (parents), or a diagnosis of rhinitis (child) (Fig. 2). In the *Mother smoking* group, the odds ratio of treated dermatitis (OR=7.10 [95% CI: 1.94–26.03], $p < 0.05$) was significantly greater for the children with elevated serum IgE levels and was not significantly different for (OR=4.74 [95% CI: 0.77–29.10], $p=0.51$) the children whose parents had a medical history of allergy. In the same group, the odds ratio of 12-month dermatitis (OR=8.86 [95% CI: 1.74–45.15], $p=0.04$) was significantly greater by a small margin in children with a diagnosis of rhinitis.

4. Discussion

Our cross-sectional study showed a significant association between ETS exposure and AD among school-age children in urban, industrial, and rural areas in Korea. Both current ETS exposure and smoking by household members during the mother's pregnancy and the child's infancy had significant adverse effects on AD. Notably, ETS exposure during pregnancy and infancy due to maternal smoking increased the risk of AD two-fold. One of this study's important contributions to the literature is its exploration of the effects of maternal smoking during pregnancy in Korea, where the smoking rate in women is lower than in Western countries (Fukuda et al., 2005; Yang et al., 1999). According to a report from the Korea Centers for Disease Control and Prevention, in 2006, approximately 52.3% of men and 5.8% women over the age of 20 in Korea were smokers (KCDC, 2006). Asian countries have been characterized by a high smoking prevalence among men and a very low smoking prevalence among women (Fukuda et al., 2005; Yang et al., 1999). Few studies have investigated the association between ETS exposure and allergic dermatitis in Asian populations. Additionally, although the effects were not statistically significant, we found that the risk of AD increased if parents had ever been diagnosed with allergies or had elevated serum IgE levels, and if the children themselves had ever been diagnosed with rhinitis. These results should help to identify populations who are especially susceptible to ETS exposure.

The associations between ETS and AD in the literature are not consistent. For example, no significant association was reported between perinatal exposure to tobacco smoke and the development of asthma and AD among Japanese infants (Tanaka et al., 2008). A study using the Danish national birth cohort reported that smoking during pregnancy was associated with a decreased risk of AD in offspring (Linneberg et al., 2006). However, these studies stated that smoking cessation was still recommended to pregnant women even though they did not show a conclusive relationship between ETS and AD (Kaiser, 2004). In contrast, other studies have reported hazardous effects of exposure to ETS on the development of AD, which support our findings. Schäfer et al. (1997) reported that maternal smoking during pregnancy or lactation, or both, might play a role in the development of AD. Some studies have found that children exposed to ETS have an increased risk of AD, which is marked in children with parents who have allergies (Kramer et al., 2004; Xepapadaki et al., 2009). Kramer et al. (2004) reported that exposure to ETS during pregnancy did not increase the frequency of asthma or rhinitis, but did increase the frequency of AD, which supports the finding in our study that maternal smoking or

Table 1
Descriptive statistics of the study participants by exposure to environmental tobacco smoke^a.

Variable N (%)	Total number of subjects (N=7030)	Mother smoking (N=49)	Other household smoking (N=1379)	Current ETS (N=1495)	No exposure (N=3449)
Age (year), mean $\pm$ SD ^b	7.6 $\pm$ 1.1	7.4 $\pm$ 1.1	7.3 $\pm$ 0.9	7.8 $\pm$ 1.2	7.5 $\pm$ 1.1
Sex					
Male	3658	28(0.8)	753(20.6)	763(20.9)	1754(48)
Female	3372	21(0.6)	626(18.6)	732(21.7)	1695(50.3)
Residential area					
Urban	1741	9(0.5)	331(19)	266(15.3)	951(54.6)
Industrial complex	2804	17(0.6)	575(20.5)	594(21.2)	1423(50.8)
Rural	2485	23(0.9)	473(19)	635(25.6)	1075(43.3)
Paternal education					
< 12 years	2976	29(1)	712(23.9)	809(27.2)	1291(43.4)
$\geq$ 12 years	2962	15(0.5)	647(21.8)	472(15.9)	1765(59.6)
Unknown	1092	5(0.5)	20(1.8)	214(19.6)	393(36)
Maternal education					
< 12 years	3705	31(0.8)	856(23.1)	944(25.5)	1724(46.5)
$\geq$ 12 years	2158	10(0.5)	489(22.7)	300(13.9)	1319(61.1)
Unknown	1167	8(0.7)	34(2.9)	251(21.5)	406(34.8)
Household income ^c					
< \$1800	2634	35(1.3)	443(16.8)	679(25.8)	1023(38.8)
\$1800–2700	2210	6(0.3)	474(21.5)	471(21.3)	1153(52.2)
$\geq$ \$2700	2186	8(0.4)	462(21.1)	345(15.8)	1273(58.2)
Parental history of allergy					
Yes	1549	6(0.4)	357(23.1)	265(17.1)	850(54.9)
No	4714	37(0.8)	939(19.9)	1073(22.8)	2357(50)
Unknown	767	6(0.8)	83(10.8)	157(20.5)	242(31.6)
Immunoglobulin E (IU/ml)					
< 180	4016	29(0.7)	800(19.9)	843(21)	2024(50.4)
$\geq$ 180	2055	13(0.6)	416(20.2)	458(22.3)	1011(49.2)
Unknown	959	7(0.7)	163(17)	194(20.2)	414(43.2)
Atopic dermatitis					
Lifetime dermatitis	2437	21(0.9)	584(24)	526(21.6)	1208(49.6)
12-month dermatitis	1512	16(1.1)	370(24.5)	339(22.4)	727(48.1)
Diagnosed dermatitis	2112	18(0.9)	523(24.8)	426(20.2)	1078(51)
Treated dermatitis	870	12(1.4)	210(24.1)	194(22.3)	424(48.7)
Rhinitis					
Diagnosed	1646	10(0.6)	397(24.1)	304(18.5)	888(54)

^a The *Mother smoking* group and *Other household smoking* group were defined by the child's mother and other member(s) of the household, respectively, having smoked during the mother's pregnancy, and/or in the first year after the child's birth in addition to children's current exposure to ETS. The *Current ETS* group included children who were not exposed to ETS prenatally and/or in the first year after birth but were currently exposed to ETS.

^b Standard deviation.

^c The average monthly household income in Korea in 2005, excluding singles, was 2600 USD (1 USD $\approx$ 1100 KRW).

Table 2
Effects of environmental tobacco smoke on dermatitis subcategories.

Exposure Groups	Lifetime dermatitis		12-month dermatitis		Diagnosed dermatitis		Treated Dermatitis	
	Crude OR (95% CI)	Adjusted ^a OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Mother smoking (N=49)	1.35 (0.76, 2.39)	1.98 (1.01, 3.89)	1.77 (0.97, 3.24)	2.06 (1.01, 4.22)	1.24 (0.69, 2.23)	1.92 (0.97, 3.82)	2.38 (1.2, 4.73)	2.74 (1.22, 6.18)
Other household smoking (N=1379)	1.36 (1.2, 1.55)	1.43 (1.24, 1.65)	1.37 (1.19, 1.58)	1.35 (1.15, 1.58)	1.34 (1.18, 1.53)	1.40 (1.22, 1.62)	1.29 (1.08, 1.55)	1.26 (1.04, 1.53)
Current ETS (N=1495)	1.01 (0.89, 1.15)	1.18 (1.01, 1.37)	1.10 (0.95, 1.28)	1.27 (1.07, 1.52)	0.88 (0.77, 1.01)	1.05 (0.9, 1.24)	1.14 (0.95, 1.38)	1.32 (1.06, 1.64)
No Exposure (N=3449)	Ref. ^b	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.

^a The models were adjusted for age, sex, residential area, household income, parental education, parental history of atopic allergy, total serum IgE level, and lifetime diagnosis of rhinitis by a physician.

^b Reference category.

exposure to ETS was associated with AD among children. Air pollutants, in general, have irritating effects on the skin and mucous membranes, thereby facilitating the penetration of

potential allergens into the body and leading to AD symptoms and an elevated risk of sensitization. ETS is thought to operate through the same mechanism as other air pollutants; however,

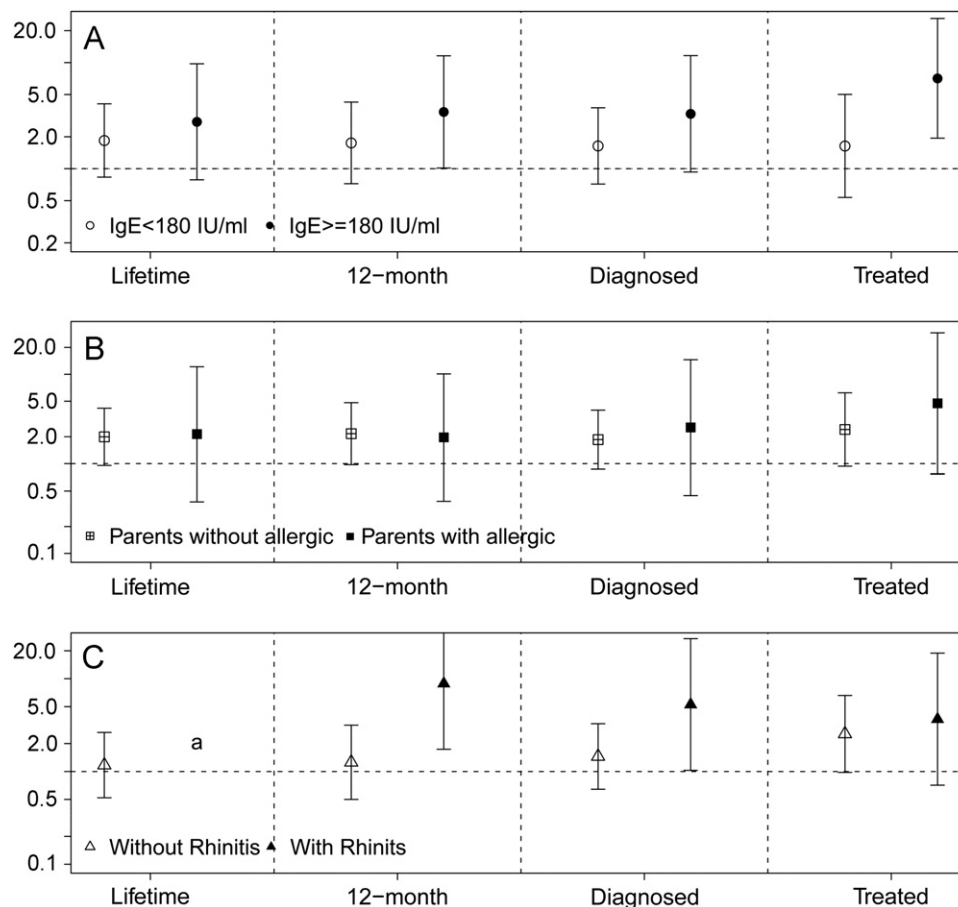


Fig. 2. Mediation of the effects of a child's mother smoking during pregnancy and/or in the first year after birth on dermatitis by other factors: abnormal child total serum immunoglobulin E (IgE) level, parental history of atopic allergy, and child history of rhinitis (OR, 95% CI). (A) Child IgE level, (B) parental history of allergy, and (C) child diagnosis of rhinitis. Lifetime, lifetime prevalence of dermatitis; 12-month, prevalence of dermatitis in the past 12 months; Diagnosed, lifetime diagnosis of dermatitis by a physician; Treated, treatment of dermatitis in the past 12 months. Note: "no observation defined.

this must be examined further (Kramer et al., 2004; Seymour et al., 1997).

With regard to the development of AD in children, exposure to maternal smoking *in utero* and/or exposure to smoke in the first year after birth might be more detrimental than paternal smoking (Hjern et al., 2001). Fetal exposure to tobacco smoke products in the amniotic fluid can have long-term effects on gut immune responses and could be important in allergic sensitization (Gilliland et al., 2002). Therefore, toxins from prenatal exposure to smoke may influence sensitization to common antigens, which may increase the risk of childhood AD (Wang et al., 2010). Maternal cigarette smoking may disturb the balance between oxidants and anti-oxidants in fetal cord blood and lead to increased oxidative stress, which can cause DNA damage (Aycicek et al., 2008). Alterations in physiological processes may affect fetal development and increase the prevalence of allergies (Metsios et al., 2009). Maternal smoking behavior is more important in the first year of life, mainly because children tend to spend more time with their mothers than their father or other members of the household.

Recent studies have shown that cigarette smoking and indoor ETS are associated with endotoxins (Sebastian et al., 2006). In addition, other studies have reported that elevated endotoxin exposure increases the IgE level in families that are exposed to ETS and thus influences the risk of atopy and subsequent asthma (Larsson et al., 2004; Vork et al., 2007). In our study, when the effects of ETS exposure on AD were compared between

children with abnormally high total serum IgE concentrations ($> 180 \text{ UI ml}^{-1}$) and children with normal levels, a significant increase in the frequency of AD among children with abnormally high IgE levels was observed in the *Mother smoking* group.

Parental history of atopy is an important risk factor for atopic disease in children (Wen et al., 2009). In particular, exposure to ETS is a strong risk factor for AD, especially among children who have parents with allergies, and similar strong associations have also been found for allergic sensitization and asthma (Kramer et al., 2004; Keil et al., 2009). Our study revealed that the association with AD in the *Mother smoking* group was stronger among children whose parents had a history of atopic allergy. However, these results were not statistically significant, except with respect to the prevalence of 12-month dermatitis.

There are several points to be further considered in this study. First, due to the cross-sectional nature of our study design, we could not assess the causality of the relationship between duration of maternal smoking and elevation in total serum IgE or the progressive development of allergic diseases. In general, AD is the primary manifestation of allergic diseases and has been used as a predictor of the later development of asthma and rhinitis; (Gustafsson et al., 2000; Spergel, 2010). However, in the *Mother smoking* group, we found a strong association between exposure to ETS and both 12-month and diagnosed dermatitis among children with a diagnosis of rhinitis. That is, our study evaluated how co-morbidity of allergic diseases affected the associations between exposure to ETS and AD. Future studies covering additional waves of the CHEER

study or other panels of data should be able to investigate causality as well as the atopic march. Second, categorization of samples according to ETS exposure was complicated. Because maternal smoking during pregnancy is culturally and socially unacceptable in Korea, under-reporting by mothers is not implausible (Morrow et al., 2002; Waldron et al., 1988; Park et al., 2010). Additionally, the size of the *Mother smoking* group was insufficient. To test the assumption that the relationship of child AD with maternal smoking is different from that of child AD with smoking by other household members, it was necessary to categorize samples according to period of exposure to ETS. Although we could not disentangle the effects of prenatal exposure to ETS from those of postnatal exposure to ETS, our results showed a high risk of developing AD in a group of children whose mothers had smoked during pregnancy and/or in the first year after childbirth. The ability to identify exposure status in this study was further impaired by the structure of the questionnaire, which was not designed to ascertain past ETS exposure status in children who were currently not exposed to ETS. Therefore, some members of the *No exposure* group were likely exposed to ETS prenatally and during pregnancy. As the *No exposure* group was used as the reference category, the effects of exposure to ETS are likely to have been underestimated in our study. Third, we lacked information on a number of potential confounders that could affect atopic dermatitis, such as maternal nutrition, lifestyle factors such as alcohol consumption, and exposure to other potentially toxic substances during pregnancy. The sample used in this study was extracted from a nationally representative cohort study (the CHEER study), and our results represent a useful addition to the literature, notwithstanding the above limitations. One final limitation is that our sample included only school-age children. Caution must therefore be exercised when extrapolating the results to other age groups.

5. Conclusion

Our results show a statistically significant relationship between exposure to ETS and AD among school-age children in Korea. Childhood exposure to ETS is a major risk factor for AD. The provision of a smoke-free environment, especially for children with allergic disorders, is a public health intervention that can improve and prevent allergic disorders.

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