

# Relationship between Active and Passive Smoking and Total Serum IgE Levels in Japanese Women: Baseline Data from the Osaka Maternal and Child Health Study

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## Key Words

Cross-sectional survey · Japanese women · Passive smoking · Smoking · Total IgE

## Abstract

**Background:** Many studies have shown that cigarette smoking is associated with elevated concentrations of total serum IgE. Few studies, however, have examined total IgE in relation to passive smoking exposure, especially in adults. This cross-sectional study investigated the association of active and passive smoking exposure with levels of total serum IgE in Japan. **Methods:** Study subjects were 981 pregnant women in Osaka. Total IgE levels were measured using UniCAP 1000 and were defined as elevated if they exceeded 170 ml/Ui. Age, gestation, parity, family history of asthma, atopic eczema

and allergic rhinitis, indoor domestic pets, family income, education and the mite allergen level in house dust were selected as potential confounding factors. **Results:** Current smoking of at least 15 cigarettes a day and 8.0 or more pack-years of smoking were independently related to an increased prevalence of elevated total serum IgE (adjusted odds ratios 3.40 and 2.51, 95% confidence intervals 2.12–5.47 and 1.55–4.06, respectively), and both cigarette smoking status and pack-years of smoking were significantly positively associated with total serum IgE levels, especially in subjects with a positive familial allergic history. There was no measurable association of exposure to environmental tobacco smoke (ETS) at home or at work with total serum IgE concentrations among those who had never smoked. **Conclusions:** Our results corroborate a positive relationship between active smoking and total serum IgE levels; however, this study failed to substantiate a positive association of ETS exposure with total IgE. Investigations with more precise and detailed exposure measurements are warranted.

<sup>1</sup> Other members of the Study Group are listed in the Appendix.

## Introduction

While total IgE is known to have a strong genetic component [1], the European Community Respiratory Health Survey suggested that total IgE might also be influenced by the environment because of substantial variations in the level of total serum IgE, including a wide variation within the former West and East Germany [2]. A number of epidemiological studies have showed that cigarette smoking is associated with elevated concentrations of total serum IgE [3–10], even after adjustment for age and sex [11–15]. Also, there have been some studies that investigated the relationship between exposure to environmental tobacco smoke (ETS) and total serum IgE in adults. Passive smoking was significantly related to increased total IgE values in two cross-sectional studies in France and Italy [5, 12]. Another French epidemiological study demonstrated that passive smoking significantly increased IgE levels in a group of nonsmoking female relatives of asthmatics [7]. No significant association was found between passive smoking and total serum IgE in the European Community Respiratory Health Survey [16].

To assess the impact of exposure to smoking on total serum IgE, the present study examined the association of active and passive smoking exposure with levels of total serum IgE in pregnant Japanese females using baseline data from the Osaka Maternal and Child Health Study (OMCHS).

## Subjects and Methods

### Study Population

The OMCHS is an ongoing prospective cohort study of risk factors for maternal and child health problems such as allergic disorders and postpartum depression. The OMCHS required that pregnant females complete a baseline survey, which was followed by several postnatal surveys. In Japan, when females become pregnant, they notify the municipality of the domicile of conception, and the municipality provides them with a maternal and child health handbook. Eligible subjects were those women who became pregnant in Neyagawa City, which is one of the 44 municipalities in Osaka Prefecture, a metropolis in Japan with a total population of approximately 8.8 million. During the period from November 2001 to March 2003, the Neyagawa City Government provided all pregnant females with a set of leaflets explaining our study, an application form and a self-addressed and stamped return envelope together with the maternal and child health handbook. Research technicians asked all of the eligible females to participate in this study by telephone, excluding pregnant females who had already returned the application form to the data management center. Of the 3,639 eligible subjects, 627 pregnant females (17.2%) in Neyagawa City took part in this study. Eight pregnant females who did not live in Neyagawa City but who had become aware of the present study at an obstetric clinic before

August 2002 decided by themselves to participate in this study. Also, there were 77 participants who received explanations of the OMCHS from public health nurses in six other municipalities from August 2002 to March 2003. From October 2002 to March 2003, 290 participants were recruited from a university hospital and three obstetric hospitals in three other municipalities; these women were recommended for participation in the OMCHS by an obstetrician. Finally, a total of 1,002 pregnant women gave their fully informed consent in writing and completed the baseline survey. The OMCHS was approved by the ethics committees of the Osaka City University School of Medicine and the Osaka Prefectural Institute of Public Health.

### Measurements

In the baseline survey, each participant filled out a set of two self-administered questionnaires, put a passive diffusion sampling tube on her clothes for 24 h on a usual day to measure concentrations of nitrogen dioxide and formaldehyde, and collected two dust samples from a 1-m<sup>2</sup> area of the bedclothes and flooring for 1 min using a vacuum cleaner fitted with a collection apparatus. Participants then mailed these materials to the data management center. Research technicians completed missing or illogical data by telephone interview.

Venous blood samples were taken from each subject to measure total IgE during the period of pregnancy or during the hospital stay for delivery. Almost all of the samples were drawn during pregnancy at the obstetric clinic that served each participant. The serum samples were collected by Japan Clinical Laboratories, Inc. (Kumiyama, Kyoto, Japan) and sent to a central laboratory at that company. Total IgE levels were measured using UniCAP 1000 (Pharmacia Diagnostics AB, Uppsala, Sweden). Total serum IgE levels were defined as elevated if they exceeded 170 ml/UI.

One of the self-administered questionnaires was used to ascertain age, gestation, parity, indoor domestic pets, family income, education, family history of asthma, atopic eczema and allergic rhinitis, smoking habits and passive smoking exposure. A family history of asthma, atopic eczema and allergic rhinitis (including cedar pollinosis) was considered to be present if one or more parents or siblings of the study subject had manifested any of these allergic disorders.

Antigen levels from extracts of fine dust fractions were measured by a double-antibody sandwich enzyme-linked immunosorbent assay using a soluble antigen prepared from whole *Dermatophagoides farinae* mite bodies as a reference standard and were expressed as antigen equivalent in µg/m<sup>2</sup> of surface area (Mitey checker®, Shinto Fine Co., Ltd., Osaka, Japan) [17, 18]. Antigen levels were semiquantitatively classified with scores of – (<2 µg/m<sup>2</sup>), ± (5 µg/m<sup>2</sup>), + (10–15 µg/m<sup>2</sup>) and ++ (>35 µg/m<sup>2</sup>). The *D. farinae* antigen detected by this assay is cross-reactive to the equivalent antigen contained in *Dermatophagoides pteronyssinus*, and the antigen level of 10 µg obtained with the reference antigen corresponds to approximately 100 mites of either *D. farinae* or *D. pteronyssinus* [19]. In the present study, we used only antigen levels in the sample collected from the bedclothes because the correlation between antigen levels from the bedclothes and flooring was almost collinear (Spearman correlation coefficient = 0.54,  $p < 0.0001$ ).

The other instrument was a validated self-administered diet history questionnaire. Data regarding diet and concentrations of formaldehyde and nitrogen dioxide were not used in this study.

### Statistical Analysis

Age, gestation, parity, family history of asthma, atopic eczema and allergic rhinitis, indoor domestic pets, family income, education and the mite allergen level in house dust were selected as potential confounding factors. Cigarette smoking was classified into four categories (never, former and current smoking consuming <15 or ≥15 cigarettes per day); pack-years of smoking into four (none, 0.1–2.9, 3.0–7.9 and ≥8.0 pack-years); passive smoking at home into four (never, former and current passive smoking exposed to <10 or ≥10 cigarettes per day); pack-years of passive smoking at home into four (none, 0.1–2.9, 3.0–9.9 and ≥10.0 pack-years); passive smoking at work into four (never, former and current passive smoking exposure intermittently or constantly); years of passive smoking at work into four (none, 1–3, 4–6 and ≥7 pack-years); age into three (<29, 29–31 and ≥32 years); gestation into three (<15, 15–20 and ≥21 weeks); parity into two (0 and ≥1); family income into three (JPY <4,000,000, 4,000,000–5,999,999 and ≥6,000,000 a year); education into three (<13, 13–14 and ≥15 years); and dust mite allergen levels into four (–, ±, + and ++).

Multiple logistic regression analysis was used to estimate adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) for elevated IgE levels (>170 ml/UI) according to active and passive smoking exposure as well as other covariates. Analysis of covariance was employed to calculate adjusted means of total serum IgE according to active and passive smoking exposure with allowance for confounding factors. Trend of an association was assessed by a logistic regression model or multiple linear regression analysis assigning scores to the levels of the independent variable. *p* values (two-sided) less than 0.05 were regarded as statistically significant. Since the distribution of total serum IgE concentrations was skewed to the right side, natural logarithms of the values were used in statistical analysis. Presented means of total serum IgE and their 95% CIs are geometric. All computations were performed using the SAS software package version 8.2 (SAS Institute, Inc., Cary, N.C., USA).

Of the 1,002 participants in the baseline survey, 21 were excluded because of missing data on total serum IgE, leaving 981 subjects for analysis. The analysis of the effects of ETS exposure at home and at work on total serum IgE was based only on the 682 participants who had never smoked.

### Results

Total serum IgE concentrations were distributed over a wide range (1–10,190 ml/UI). The median and the 95th percentile values were 76 and 734 ml/UI, respectively. The geometric mean of total IgE for the population was 67.7 ml/UI. Of the 981 study subjects, 284 (29.0%) had total serum IgE levels in excess of 170 ml/UI.

Table 1 shows adjusted ORs and 95% CIs for elevated total IgE (>170 ml/UI) according to selected characteristics of the 981 pregnant females. Adjustment was made for cigarette smoking status and the covariates listed in the table. Family history of atopic eczema, but not asthma or allergic rhinitis, was independently associated with an increased prevalence of elevated total serum IgE levels.

**Table 1.** Adjusted ORs and 95% CIs for elevated total serum IgE levels (>170 ml/UI) according to selected characteristics in 981 pregnant females (OMCHS, Japan)

| Factor                                               | Prevalence (%) | Adjusted OR (95% CI) <sup>1</sup> |
|------------------------------------------------------|----------------|-----------------------------------|
| Age, years                                           |                |                                   |
| <29                                                  | 110/373 (29.5) | 1.00                              |
| 29–31                                                | 89/292 (30.5)  | 1.26 (0.88–1.81)                  |
| ≥32                                                  | 85/316 (26.9)  | 1.01 (0.69–1.47)                  |
| Gestation, weeks                                     |                |                                   |
| <15                                                  | 104/351 (29.6) | 1.00                              |
| 15–20                                                | 97/323 (30.0)  | 0.93 (0.66–1.31)                  |
| ≥21                                                  | 83/307 (27.0)  | 0.87 (0.61–1.24)                  |
| Parity                                               |                |                                   |
| 0                                                    | 141/478 (29.5) | 1.00                              |
| ≥1                                                   | 143/503 (28.4) | 0.93 (0.69–1.25)                  |
| Family history of asthma                             |                |                                   |
| No                                                   | 248/881 (28.2) | 1.00                              |
| Yes                                                  | 36/100 (36.0)  | 1.39 (0.87–2.18)                  |
| Family history of atopic eczema                      |                |                                   |
| No                                                   | 230/845 (27.2) | 1.00                              |
| Yes                                                  | 54/136 (39.7)  | 1.61 (1.08–2.38)                  |
| Family history of allergic rhinitis                  |                |                                   |
| No                                                   | 151/561 (26.9) | 1.00                              |
| Yes                                                  | 133/420 (31.7) | 1.21 (0.90–1.63)                  |
| Indoor domestic pets (cats, dogs, birds or hamsters) |                |                                   |
| No                                                   | 252/870 (29.0) | 1.00                              |
| Yes                                                  | 32/111 (28.8)  | 0.81 (0.50–1.28)                  |
| Family income, JPY/year                              |                |                                   |
| <4,000,000                                           | 92/295 (31.2)  | 1.00                              |
| 4,000,000–5,999,999                                  | 107/393 (27.2) | 0.85 (0.59–1.21)                  |
| ≥6,000,000                                           | 85/293 (29.0)  | 0.97 (0.65–1.43)                  |
| Education, years                                     |                |                                   |
| <13                                                  | 90/317 (28.4)  | 1.00                              |
| 13–14                                                | 116/404 (28.7) | 1.22 (0.86–1.75)                  |
| ≥15                                                  | 78/260 (30.0)  | 1.30 (0.87–1.96)                  |
| Mite allergen level in house dust                    |                |                                   |
| –                                                    | 108/426 (25.4) | 1.00                              |
| ±                                                    | 83/290 (28.6)  | 1.20 (0.85–1.69)                  |
| +                                                    | 65/193 (33.7)  | 1.59 (1.08–2.34)                  |
| ++                                                   | 28/72 (38.9)   | 1.89 (1.09–3.23)                  |

<sup>1</sup> Adjusted for cigarette smoking (never, former and current smokers consuming <15 or ≥15 cigarettes per day) and covariates listed in the table.

**Table 2.** Adjusted ORs for elevated total serum IgE levels (>170 ml/UI) and geometric means of total serum IgE levels according to active smoking status in 981 pregnant females (OMCHS, Japan)<sup>1</sup>

| Smoking status           | Prevalence (%) | Adjusted OR (95% CI) | Adjusted means of total serum IgE, ml/UI (95% CI) |
|--------------------------|----------------|----------------------|---------------------------------------------------|
| Cigarette smoking        |                |                      |                                                   |
| Never                    | 181/682 (26.5) | 1.00                 | 63.8 (56.8–71.8)                                  |
| Former                   | 31/117 (26.5)  | 1.05 (0.66–1.65)     | 60.3 (45.5–79.9)                                  |
| Current <15/day          | 21/81 (25.9)   | 0.96 (0.55–1.63)     | 56.9 (40.6–79.8)                                  |
| Current ≥15/day          | 51/101 (50.5)  | 3.40 (2.12–5.47)     | 132.3 (96.5–181.4)                                |
| p value for linear trend |                | <0.0001              | 0.003                                             |
| Pack-years of smoking    |                |                      |                                                   |
| None                     | 181/682 (26.5) | 1.00                 | 64.2 (57.1–72.2)                                  |
| 0.1–2.9                  | 22/89 (24.7)   | 0.94 (0.54–1.56)     | 53.5 (38.7–74.1)                                  |
| 3.0–7.9                  | 40/118 (33.9)  | 1.43 (0.92–2.22)     | 75.5 (56.8–100.3)                                 |
| ≥8.0                     | 41/92 (44.6)   | 2.51 (1.55–4.06)     | 109.6 (78.9–152.2)                                |
| p value for linear trend |                | 0.0003               | 0.009                                             |

<sup>1</sup> Adjusted for age (<29, 29–31 and ≥32 years), gestation (<15, 15–20 and ≥21 weeks), parity (0 and ≥1), family history of asthma, atopic eczema and allergic rhinitis, indoor domestic pets, family income (JPY <4,000,000, 4,000,000–5,999,999 and ≥6,000,000/year), education (<13, 13–14 and ≥15 years) and mite allergen level in house dust (–, ±, + and ++).

There was a stepwise increase in the OR of having high total IgE values with increasing levels of mite allergen (p for linear trend = 0.004). Age, gestation, parity, indoor domestic pets, family income and education were not statistically significantly related to elevated total IgE.

Table 2 presents adjusted ORs for elevated total IgE and geometric means of total serum IgE levels according to active smoking status in 981 pregnant women. Current heavy smoking (≥15 cigarettes per day) was associated with a 3.4-fold increased prevalence of raised total IgE, whereas the prevalence was not substantially increased for former or light smoking, although a highly significant linear trend across the four categories of cigarette smoking exposure was observed (p for linear trend <0.0001). The adjusted geometric means of total serum IgE were 63.8 and 132.3 ml/UI among those who had never smoked and those consuming at least 15 cigarettes a day, respectively (p for linear trend = 0.003). Pregnant women with 8.0 or more pack-years of smoking had a 2.5-fold increase in the OR of having total IgE greater than 170 ml/UI compared with those who had never smoked (p for linear trend = 0.0003). The number of pack-years of smoking was significantly positively related to total serum IgE levels. The adjusted geometric mean of total serum IgE was 109.6 ml/UI among those with 8.0 or more pack-years of smoking (p for linear trend = 0.009).

When study subjects were divided according to a positive or negative familial allergic history in at least one parent or sibling, a positive association of cigarette smoking status and pack-years of smoking with total serum IgE concentrations was more evident in those with a positive than with a negative familial allergic history; the association was statistically significant only among women with a positive familial allergic history (table 3). The multivariate OR of having total IgE above 170 ml/UI for comparison of a positive with a negative familial allergic history was 1.56 (95% CI 1.17–2.08). No marked differences were found in the prevalence of elevated total IgE between pregnant females with a positive and negative familial allergic history (p = 0.22, 0.07 and 0.87 for homo-geneity of OR for former, light and heavy cigarette smoking, respectively).

Results for ETS exposure in the sample of 682 subjects who had never smoked are summarized in table 4. Passive smoking exposure both at home and at work was virtually unrelated to total serum IgE levels. There was no dose-response relationship with cumulative exposure to ETS expressed as pack-years of passive smoking at home or years of passive smoking in the workplace.

**Table 3.** Adjusted geometric means of total serum IgE levels according to active smoking status in 981 pregnant females with a positive or negative familial allergic history (OMCHS, Japan)<sup>1</sup>

| Smoking status           | Adjusted means of total serum IgE, ml/UI (95% CI) |                                              |
|--------------------------|---------------------------------------------------|----------------------------------------------|
|                          | positive familial allergic history (n = 502)      | negative familial allergic history (n = 479) |
| Cigarette smoking        |                                                   |                                              |
| Never                    | 77.4 (65.9–90.9)                                  | 52.2 (43.9–62.0)                             |
| Former                   | 73.8 (50.5–107.8)                                 | 49.2 (32.2–75.4)                             |
| Current < 15/day         | 73.6 (46.6–116.4)                                 | 43.8 (26.5–72.5)                             |
| Current ≥ 15/day         | 186.2 (118.3–293.2)                               | 93.5 (59.9–145.9)                            |
| p value for linear trend | 0.009                                             | 0.11                                         |
| Pack-years of smoking    |                                                   |                                              |
| None                     | 77.8 (66.2–91.5)                                  | 52.4 (44.1–62.3)                             |
| 0.1–2.9                  | 70.4 (44.6–111.0)                                 | 38.6 (24.3–61.5)                             |
| 3.0–7.9                  | 89.0 (60.8–130.3)                                 | 68.5 (44.6–105.2)                            |
| ≥ 8.0                    | 145.6 (92.1–230.2)                                | 79.2 (49.1–127.9)                            |
| p value for linear trend | 0.03                                              | 0.11                                         |

<sup>1</sup> Adjusted for age (<29, 29–31 and ≥ 32 years), gestation (<15, 15–20 and ≥ 21 weeks), parity (0 and ≥ 1), indoor domestic pets, family income (JPY <4,000,000, 4,000,000–5,999,999 and ≥ 6,000,000/year), education (<13, 13–14 and ≥ 15 years) and mite allergen level in house dust (–, ±, + and ++).

## Discussion

The present study demonstrated that current heavy cigarette smoking and 8.0 or more pack-years of smoking were independently related to an increased prevalence of elevated total serum IgE (>170 ml/UI), and that both cigarette smoking status and pack-years of smoking were significantly positively associated with total serum IgE levels, especially in the pregnant females with a positive familial allergic history. There was no measurable association of ETS exposure at home or at work with total serum IgE concentrations among those who had never smoked.

Our results corroborate previous observations that showed a positive relationship between active smoking and total serum IgE levels [3–15]. It is possible that persons with any allergic disorder are more likely not to start smoking or to quit smoking if they do smoke and that those without such symptoms are likely to go on smoking (healthy smoker effect). When 186 subjects who had been treated with medications for asthma, atopic eczema or allergic rhinitis in the previous 12 months were excluded from the analysis, the positive association of active cigarette smoking and pack-years of smoking with elevated total serum IgE remained similar, although overall the adjusted means of total IgE were lower than those in the total population. We are not able to estimate the magnitude of the healthy smoker bias, however. In a French epi-

demiological study, current smokers had significantly higher IgE than subjects who had never smoked; the relationship was significant even when excluding nonasthmatics from the analysis [7].

A cause-effect relationship between active smoking and total IgE levels may be supported by the present observation that the amount of lifetime smoking assessed by pack-years was an independent predictor for total serum IgE concentrations, especially in those with a positive familial allergic history. We do recognize, though, that cross-sectional surveys are not an appropriate study design to investigate causal relationships. However, no association with former smoking and light smoking (less than 15 cigarettes a day) was found in this study. On average, ex-smoking subjects were women who had smoked for 6.9 years and stopped smoking 3.6 years prior to the present survey, and light-smoking subjects were those who had been consuming 8.3 cigarettes a day for 9.4 years. These facts may explain the null association with former and light smoking.

We have no immediate explanation for differences in total IgE levels between smokers and nonsmokers. Change in some IgE regulator mechanisms may cause a general increase in IgE levels among smokers [20]. Alternatively, the differences may be related to increased levels of specific IgE to tobacco antigens or bacterial antigens infecting the airways of smokers [21]. The European

**Table 4.** Adjusted ORs for elevated total serum IgE levels (>170 ml/UI) and geometric means of total serum IgE levels associated with passive smoking status in 682 pregnant females who had never smoked (OMCHS, Japan)<sup>1</sup>

| Passive smoking status                | Prevalence (%) | Adjusted OR (95% CI) | Adjusted means of total serum IgE, ml/UI (95% CI) |
|---------------------------------------|----------------|----------------------|---------------------------------------------------|
| Passive smoking at home               |                |                      |                                                   |
| Never                                 | 66/240 (27.5)  | 1.00                 | 64.4 (52.9–78.5)                                  |
| Former                                | 41/169 (24.3)  | 0.78 (0.49–1.24)     | 61.2 (48.3–77.5)                                  |
| Current <10/day                       | 36/149 (24.2)  | 0.88 (0.53–1.42)     | 60.1 (46.6–77.4)                                  |
| Current ≥10/day                       | 38/124 (30.7)  | 1.22 (0.74–2.00)     | 72.2 (54.8–95.1)                                  |
| p value for linear trend              |                | 0.57                 | 0.68                                              |
| Pack-years of passive smoking at home |                |                      |                                                   |
| None                                  | 66/240 (27.5)  | 1.00                 | 64.5 (52.9–78.6)                                  |
| 0.1–2.9                               | 42/151 (27.8)  | 1.04 (0.65–1.66)     | 65.9 (51.4–84.6)                                  |
| 3.0–9.9                               | 32/144 (22.2)  | 0.72 (0.43–1.17)     | 58.4 (45.2–75.3)                                  |
| ≥10.0                                 | 41/147 (27.9)  | 1.03 (0.64–1.65)     | 66.9 (52.0–86.1)                                  |
| p value for linear trend              |                | 0.70                 | 0.97                                              |
| Passive smoking at work               |                |                      |                                                   |
| Never                                 | 79/267 (29.6)  | 1.00                 | 71.9 (59.6–86.7)                                  |
| Former                                | 83/340 (24.4)  | 0.75 (0.51–1.09)     | 58.2 (49.3–68.6)                                  |
| Current, intermittently               | 16/52 (30.8)   | 1.02 (0.50–1.98)     | 80.3 (52.3–123.3)                                 |
| Current, constantly                   | 3/23 (13.0)    | 0.33 (0.08–1.01)     | 39.7 (21.1–74.6)                                  |
| p value for linear trend              |                | 0.11                 | 0.17                                              |
| Years of passive smoking at work      |                |                      |                                                   |
| None                                  | 79/267 (29.6)  | 1.00                 | 71.4 (59.2–86.1)                                  |
| 1–3                                   | 35/144 (24.3)  | 0.71 (0.44–1.15)     | 45.5 (35.2–58.8)                                  |
| 4–6                                   | 31/126 (24.6)  | 0.75 (0.45–1.23)     | 65.2 (49.7–85.6)                                  |
| ≥7                                    | 36/145 (24.8)  | 0.79 (0.47–1.29)     | 72.0 (55.1–94.0)                                  |
| p value for linear trend              |                | 0.25                 | 0.99                                              |

<sup>1</sup> Adjusted for age (<29, 29–31 and ≥32 years), gestation (<15, 15–20 and ≥21 weeks), parity (0 and ≥1), family history of asthma, atopic eczema and allergic rhinitis, indoor domestic pets, family income (JPY <4,000,000, 4,000,000–5,999,999 and ≥6,000,000/year), education (<13, 13–14 and ≥15 years) and mite allergen level in house dust (–, ±, + and ++).

Community Respiratory Health Survey demonstrated that compared with lifetime nonsmokers, current smokers had an increased risk of positivity for a specific IgE to house dust mite allergen [11]. The present results were independent of the mite antigen level in house dust, although data on the specific IgE were not available.

The current findings on ETS exposure are in accord with the European Community Respiratory Health Survey, which found no relationship between exposure to ETS and total serum IgE levels [16]. However, our results were inconsistent with previous observations showing a positive association between passive smoking and total IgE in adults [5, 7, 12]. In particular, spousal smoking of more than one cigarette daily in the presence of a non-smoking mother during at least 3 months of pregnancy was significantly positively associated with maternal total

serum IgE levels in French females with uncomplicated pregnancies and full-term newborns [5]. It is impossible to explain why our results differed from these previous reports. Strachan and Cook [22] reported no significant relationship between maternal smoking and total serum IgE levels in neonates or in older children in a systematic review. This is in partial agreement with our findings with regard to ETS.

The present study had methodological strengths. Study subjects were homogeneous in that all were pregnant, and this study could make allowances with extensive information on potential confounding factors. Several limitations of the current investigation should be borne in mind. Objective measurements of ETS exposure such as salivary, serum or urine cotinine levels were not available. Detailed data on active and passive smoking such as the

duration of tobacco exposure were based on information from a questionnaire. However, previous studies found a modest correlation between self-reported passive smoking and biomarkers of ETS exposure [23, 24]. Of a total of 3,639 eligible pregnant females in Neyagawa City, only 627 (17.2%) participated in this study. We were uncertain whether there was a difference between participants and nonparticipants in Neyagawa City, because data on personal characteristics such as age, socioeconomic status and a history of allergic disorders among the nonparticipants were not available. We were not able to calculate the participation rate among the other 375 subjects, because the exact number of eligible subjects among the sources of these subjects was not available. The present findings may not be generalized because study subjects were not likely to be representative of Japanese females in the general population. In fact, educational levels were higher in the present study population than in the general population. According to the 2000 population census of Japan [25], percentages of females aged 30–34 years in Osaka Prefecture with <13, 13–14,  $\geq 15$  and an unknown number of years of education were 49.2, 32.3, 13.6 and 4.9%, respectively. The corresponding figures for the current survey were 32.3, 41.2, 26.5 and 0.0%, respectively. Active smoking status in our subjects was likely to be the same as that in the general population, however. In a nationwide nutritional survey in 1998 [26], percentages of never, former and current smoking in women aged 20–29 years were 76.0, 4.9 and 19.1%, respectively, while the corresponding figures in the present subjects were 69.5, 11.9 and 18.6%, respectively. Information on occupational exposure other than ETS exposure was not available in this study, although a significant positive association between occupational exposure and total serum IgE was observed in previous studies [4, 12, 27]. A few women were possibly exposed at work to occupational agents other than tobacco smoke in this study, however. Data on the season when venous blood was drawn for total serum IgE determinations were not available in the present study.

This report is the first epidemiological study on the relationship between both active and passive smoking exposure and total serum IgE levels in Japan. The present study failed to substantiate a positive association of ETS exposure with total IgE. Investigations with more precise and detailed exposure measurements are necessary to clarify the relationship between smoking exposure and total serum IgE concentrations. Studies regarding the association of smoking exposure with specific IgE, as well as any allergic symptoms, are also required.

## Acknowledgements

The authors would like to acknowledge the Neyagawa City Government, Hirakata City Government, Katano City Government, Shijonawate City Government, Kaizuka City Government, Takaishi City Government, Hannan City Government, Neyagawa City Medical Association, Hirakata City Medical Association and the Kadoma City Medical Association for their valuable support; Dr. Kozo Uehara, Department of Research and Development, Shinto Fine Co. Ltd., Osaka, Japan, for helpful discussions; Mr. Koichi Okuda, Japan Clinical Laboratories, Inc., Kumiyama, Kyoto, Japan, for serum sample collection, and Ms. Tomoko Shibazaki, Nahoko Nishimura and Naomi Takaoka for their assistance.

This study was supported by a Grant-in-Aid (13770206) for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, and Health and Labor Sciences Research Grants from the Ministry of Health, Labor and Welfare, Japan.

## Appendix

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