JDI Journal of Diabetes Investigation Open access
Official Journal of the Asian Association for the Study of Diabetes
ORIGINAL ARTICLE

Passive smoking and type 2 diabetes among never-smoking women: The Japan Public Health Center-based Prospective Study

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Keywords
Diabetes mellitus, Tobacco smoke pollution, Women

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J Diabetes Investig 2020; 11: 1352–1358

doi: 10.1111/jdi.13259

ABSTRACT

Aims/Introduction: The aim of the current study was to prospectively evaluate the association between passive smoking from a spouse and the risk of diabetes among never-smoking Japanese women. Passive smoking at a workplace (or public facilities) was assessed as a secondary measure.

Materials and Methods: In the Japan Public Health Center-based Prospective Study (baseline 1990 or 1993), we followed 25,391 never-smoking women aged 40–69 years and without diabetes. Passive smoking was defined as having a husband who was a self-reported smoker, and the exposure at a workplace (or public facilities) was self-reported by women. The development of diabetes was identified in questionnaires administered at the 5-year and 10-year surveys. A pooled logistic regression model was used to assess the association between passive smoking and the development of diabetes with adjustment for age and possible confounders.

Results: Compared with women whose husbands had never smoked, women whose husband smoked ≥40 cigarettes/day had significantly higher odds of developing diabetes in an age-adjusted model, but the association was attenuated in a multivariable model (odds ratio 1.34, 95% confidence interval 0.96–1.87). There was a dose–response trend between the number of cigarettes smoked by a husband and the odds of developing diabetes (P = 0.02). Women reporting daily passive smoking at a workplace (or public facilities) had higher odds of developing diabetes than women reporting no such exposure (odds ratio 1.23, 95% confidence interval 0.995–1.53).

Conclusions: Our results indicated a higher risk of diabetes among never-smoking Japanese women with higher exposure to passive smoking from a spouse.

INTRODUCTION

There is a growing interest in the association between passive smoking and the risk of diabetes. Houston *et al.*[1] first reported that passive smoke exposure increased the risk of developing glucose intolerance in a cohort study in 2006, and since then, as many as four systematic reviews have assessed cohort studies on passive smoking and the development of diabetes[2-5]. Nevertheless, just six original cohort studies that assessed the association between passive smoking and the risk of diabetes were cited in the systematic reviews[1,6-10], and the number of studies carried out in Asia is as small as two[6,8]. In contrast, the association between active cigarette smoking and the incidence of diabetes persists in a renowned meta-analysis[11], and 25 original studies were referred to the study, including our previous study[12]. Mechanisms for the association are proposed: active smoking (i) induces insulin resistance[13,14]; or (ii) impaired glucose tolerance[15]. However, passive smoking is the inhalation of environmental tobacco smoke, and its effect on the risk of diabetes might not be the same as that of active smoking. More studies are required to prospectively evaluate the association between passive smoking and the risk of diabetes according to measures of exposure intensity.

Received 29 January 2019; revised 2 February 2020; accepted 22 March 2020

We aimed to examine the relationship between passive smoking and risk of incidental diabetes among never-smoking women in a large prospective cohort study in Japan. In this study, passive smoke exposure was estimated from a spousal-reported smoking status. Spousal smoking has been strongly implicated as a source of secondhand smoke exposure among Japanese women[16]. We assessed the self-reported exposure at the workplace (or public facilities) as a secondary measure.

METHODS

The Japan Public Health Center-based Prospective Study

The Japan Public Health Center-based Prospective Study (JPHC Study) was launched in 1990 for cohort I, and in 1993 for cohort II. The study design has been described in detail elsewhere[17]. Briefly, the study participants were from 11 public health centers across Japan, were residents of Japanese nationality and were aged 40–69 years at the time of the baseline survey. A questionnaire was administered at the baseline, and participants were informed of the objectives of the study at that time. Individuals who responded to the questionnaire were regarded as having consented to participate in the study. Follow-up surveys were carried out 5 and 10 years after the baseline survey. The study was approved by the institutional review board of the National Cancer Center, Tokyo, Japan, and the Gunma University Ethical Review Board for Medical Research Involving Human Subjects.

Study population

Of the 140,420 men and women, 26,757 individuals did not respond to the questionnaire at the time of the baseline survey, and excluding the 260 individuals who were foreign residents, moved out study area before the beginning of survey, were outside the target age range, or identified as having dual registration resulted in a response rate of 81%. Among the remaining participants, 60,052 were women. We excluded 10,131 women who were from Tokyo-Katsushika public health center or the Osaka-Suita area, because participants surveyed in these places were aged only 40 or 50 years, or were selected from participants of a health checkup program. Furthermore, 3,920 women who were current or former smokers, and 4,361 women who reported a history of diabetes or other severe disease, including cancer, cerebrovascular disease, myocardial infarction, chronic liver disease and renal disease, at the baseline survey were excluded from the analysis. Out of the remaining 41,640 women, we identified 26,716 married women whose husbands were in the JPHC study by surname, address, sex and an age difference of <16 years. After excluding 72 women whose husbands' smoking status was unknown and 277 women whose passive smoking status in the workplace was unknown, 26,367 women remained. Among them, 976 women did not respond to both the 5-year and 10-year follow-up surveys. Thus, 25,391 women were analyzed for the first 5 years (Figure S1). After excluding women who did not respond to the 10-year follow-up survey (n = 2046) and who reported current or past smoking status or number of cigarettes smoked per day in the 5-year survey (n = 241), 23,104 women were analyzed for the second 5 years (Figure S1). The accuracy of the identification of married couples was evaluated in 644 pairs from residence registries. It was shown that 604 pairs (93.8%) were married couples and six (0.9%) were relatives other than a spouse, whereas the relationship of 34 pairs (5.3%) could not be established[18].

Measures of passive smoking

The questionnaire completed by participants' husbands included questions regarding cigarette use. We defined a woman whose husband reported current cigarette smoking as being currently exposed to spousal smoke, a woman whose husband reported formerly smoking cigarettes as being formerly exposed to spousal smoke, and a woman whose husband reported never smoking cigarette as being never exposed to spousal smoke. The average number of cigarettes smoked per day was reported by a currently smoking husband in the same questionnaire, and it was used to quantify the exposure to spousal smoke. The spousal passive smoking exposure was updated with information measured at the 5-year survey, unless data were missing. We further assessed women's passive smoke exposure in the workplace (or public facilities) reported in the questionnaire[18].

Diabetes ascertainment

Newly diagnosed diabetes during the follow-up period was identified based on the questionnaires. Individuals who reported physician-diagnosed diabetes and/or taking diabetes medications were defined as having diabetes. Participants whose diabetes was ascertained at the 5-year survey were defined as having developed diabetes during the first 5-year observation period. After excluding these individuals from further follow up, participants whose diabetes was ascertained at the 10-year survey were defined as having developed diabetes during the second 5-year observation period. To assess the validity of self-reported diabetes, a series of medical records of some study participants in three districts of the study areas was examined, and finding that 94% of self-reported diabetes cases of diabetes were confirmed by medical records; 76 patients out of 81 individuals with self-reported diabetes were confirmed[12,19].

Covariates

Age, height, weight, history of hypertension and parental history of diabetes were reported in the questionnaire. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, and categorized into quartile groups and a group with missing values. The leisure-time physical activity level was reported and classified into three categories: (i) none; (ii) once a week to daily; and (iii) missing. The levels of coffee intake (none, 1–2 cups/week, 3–4 cups/week, ≥5 cups/week, and missing) and alcohol intake (none, occasional,

regular and missing) were also reported in the questionnaire and categorized into groups. Information on BMI, hypertension, leisure-time physical activity, intakes of coffee and alcohol was updated with information measured at the 5-year survey, unless data was missing.

Statistical analysis

To assess the baseline characteristics of participants, arithmetic means with standard deviations of age, BMI and number of cigarettes smoked per day by a husband were calculated according to the passive smoking from husband status. The prevalence of hypertension, parental history of diabetes, alcohol intake, coffee intake, leisure-time physical activity and working status at the baseline survey was obtained. Pooled logistic regression was used to assess the association between passive smoking and the development of diabetes. Data for observed participants who were free of diabetes at the beginning of two 5-year follow-up cycles were stacked to generate a pooled dataset. The spousal passive smoke exposure was analyzed with categorical classification of husband's smoking status (never, former, current smokers), and a composite variable that combined smoking status and the daily number of cigarettes smoked (never smoker, former smoker, current smoker of 1–19, 20–29, 30–39 and ≥40 cigarettes per day). A test for linear trend across categories of the number of cigarette smoked by a husband was carried out by treating a median value of the number of cigarettes smoked per day (for a currently smoking husband) and 0 (for a former-smoker or never-smoker husband) as a continuous value. The age-adjusted odds ratio and the odds ratio after additional adjustment for other potential confounders, which were the nine regions, term of the survey (first 5-year period or second 5-year period), BMI, hypertension, parental history of diabetes, leisure-time physical activity, and intakes of coffee and alcohol[12,19,20], were calculated. A workplace exposure (or public facilities) to passive smoke was additionally adjusted for to assess the passive smoke from a spouse. It was categorized by the level of exposure: (i) no exposure; (ii) exposure less than every day; and (iii) everyday exposure. Women who did not work were categorized into "no exposure." An analysis for all the women and the analysis restricted for working women were both carried out. All statistical analyses were carried out with SAS software (SAS Institute Inc., Cary, NC, USA).

RESULTS

During the first 5-year follow up, 334 individuals developed diabetes out of 25,391 individuals. During the second 5-year follow-up, 374 individuals developed diabetes out of 23,104 individuals. Table 1 summarizes the characteristics of participants according to status of passive smoke exposure from a spouse. Women who had a former-smoker husband were more likely to be older and to have no occupation. Women who had a currently smoking husband were less likely to have leisure-time physical activity.

Table 2 summarizes the association between passive smoke exposure from a spouse and the odds of developing diabetes. Women with a husband who currently smoked ≥40 cigarettes per day had significantly higher odds of developing diabetes in an age-adjusted model (odds ratio [OR] 1.40, 95% confidence interval [CI] 1.01–1.95), which was somewhat attenuated in a multivariable model (OR 1.34, 95% CI 0.96–1.87). A significant trend of increasing likelihood of developing diabetes with increasing number of cigarettes smoked by a husband was implied ($P = 0.02$). The spousal smoking status of never, former or current cigarette smoking, regardless of the number of cigarettes smoked per day, was not associated with the likelihood of developing diabetes.

Table 3 summarizes the association between passive smoking in the workplace (or public facilities) and the odds of developing diabetes. No significant association was observed between daily workplace (or public facilities) exposure to passive smoke and a subsequent likelihood of developing diabetes (OR 1.16, 95% CI 0.96–1.40). In the analysis restricted to working women, individuals who were exposed to passive smoke everyday had higher odds of developing diabetes as compared with those without exposure in borderline significance (OR 1.23, 95% CI 0.995–1.53).

DISCUSSION

The current study among Japanese women observed a higher likelihood of developing diabetes with higher exposure to spousal cigarette smoke. Self-reported exposure to secondhand smoke at the workplace (or public facilities) showed a borderline significantly higher likelihood of developing diabetes among working women. To the best of our knowledge, this study was the only study that used spousal self-reported smoking status to identify women's exposure to passive smoking.

Previous meta-analyses reported a weak correlation between passive smoking exposure and the development of diabetes; in those meta-analyses, the overall odds ratios ranged from 1.11 to 1.28[2-5]. The present study did not observe a significant difference in the likelihood of developing diabetes between women with a currently smoking spouse and those with a never-smoking spouse. Nevertheless, the significant trend of increasing likelihood was observed with increasing number of cigarettes smoked by a husband after multivariable adjustment. It is unknown why the passive smoking exposure estimated from a simple classification of husband smoking status (never, former or current smoker) did not show a significant difference in the likelihood of developing diabetes. The frequency and intensity of exposure might need to be considered to evaluate its risk.

Using the husband's self-reported smoking information on number of cigarettes might have an acceptable accuracy to estimate the passive smoking exposure at home for Japanese women. A previous study showed that Japanese individuals who reported themselves as current smokers in a questionnaire had high salivary cotinine levels [21]. In the same study, the sensitivity and specificity of the salivary cotinine levels were higher

Table 1 | Baseline characteristics of non-smoking women according to status of passive smoking from a spouse

	Spouse's smoking status			Total
	Never	Former	Current	
No. participants	6,569	6,390	12,432	25,391
	Mean (SD)			
Age	50.3 (6.7)	51.9 (7.3)	50.0 (6.9)	50.6 (7.0)
BMI (n = 25,155)	23.6 (3.1)	23.6 (3.0)	23.5 (3.1)	23.6 (3.1)
Spouse's no. cigarettes/day[†]	0	24.3 (14.5)	22.4 (11.2)	
	Prevalence (%)			
Hypertension	16.8	17.4	16.5	16.8
Parental history of diabetes	8.3	8.4	9.0	8.7
Alcohol intake				
None	80.9	80.1	79.2	79.9
Occasional	9.6	9.3	10.0	9.7
Regular	8.1	9.2	9.2	8.9
Missing	1.5	1.4	1.5	1.5
Coffee intake				
Almost never	30.1	31.7	29.2	30.0
1–2 cups/week	19.2	20.9	19.5	19.8
3–4 cups/week	11.7	11.6	11.5	11.6
≥1 cup/day	38.0	35.1	39.2	37.8
Missing	1.1	0.8	0.7	0.8
Leisure-time physical activity				
None	81.6	80.7	83.9	82.5
Once a week to daily	17.2	18.2	15.0	16.4
Missing	1.1	1.1	1.2	1.1
Work				
No occupation	28.1	31.3	26.8	28.3
Full time or part time	71.0	67.9	72.2	70.8
Missing	0.9	0.9	1.1	1.0

[†]n = 6,233 for former smokers and 12,287 for current smokers. SD, standard deviation.

to detect self-reported active smoking status than to detect self-reported passive smoking status[21]. Although no studies among the Japanese population that we know of have directly validated the use of spousal smoking status to measure the level of passive smoking exposure, one study reported that Japanese non-smokers who lived with a smoker(s), as ascertained through a questionnaire, had a higher urinary cotinine excretion than those not living with a smoker[22].

Women whose husbands were heavy smokers were at risk for diabetes, even if they themselves did not smoke. There is a male–female difference in smoking prevalence in Japan; 30.2% of men and 8.2% of women in Japan were smokers in 2016[23]. The discrepancy was even wider in the baseline survey of the JPHC study[24]. No laws limit exposure to cigarette smoke in homes, and never-smoking women who are married to a smoking man are passively exposed to smoking[25]. However, the use of spousal smoking status as a measure of environmental tobacco smoke exposure has come under criticism, especially in countries where the woman is no longer in the traditional role of homemaker[26].

Plausible biological mechanisms for the association between cigarette smoke exposure and diabetes risk have been reported, implying that cigarette smoke might induce insulin resistance, impair glucose tolerance and decrease insulin secretion[13-15,27]. Yet, there is a different preponderance of toxic compounds in mainstream cigarette smoke and side-stream cigarette smoke[28,29], and the effect of passive smoking on the risk of diabetes would be different from that of active smoking. Still a low level of β-cell function was observed among never-smoking women with smoking husbands[30], and passive smoke exposure might deteriorate pancreatic β-cell function[31].

The current study had several limitations. The development of diabetes was self-reported, although the validity of self-reported diabetes has been previously examined[19]. Passive smoking status was not measured with biological specimens. Previously, underestimation was reported for the self-reported smoking status[32]. If there was an underestimation of spousal cigarette smoking status, its influence on the risk of diabetes might have been attenuated in the present analysis. Still, the number of cigarettes smoked by a spouse might be valid for ranking individuals by the level of exposure, even if it was underreported. Furthermore, environmental tobacco smoke is ubiquitous, and health-conscious individuals might be more likely to report their exposure. The use of spousal-reported smoking status and the number of cigarettes smoked per day

Table 2 | Association between the incidence of diabetes during 10-year follow up and passive smoking from a spouse among non-smoking women

Type of exposure	Age adjusted OR[†]	95% CI	Multivariable OR[†,‡]	95% CI
Spouse's smoking status				
Never smoker	1		1	
Former smoker	0.90	(0.73–1.11)	0.93	(0.75–1.14)
Current smoker	1.03	(0.85–1.23)	1.03	(0.86–1.25)
Spouse's smoking status with number of cigarettes per day[§]				
Never smoker	1		1	
Former smoker	0.90	(0.73–1.01)	0.92	(0.75–1.13)
Current smokers, <20/day	0.76	(0.58–0.99)	0.75	(0.57–0.98)
Current smoker, 20 to <30/day	1.12	(0.90–1.38)	1.11	(0.89-1.38)
Current smoker, 30 to <40/day	1.11	(0.81–1.54)	1.10	(0.79–1.53)
Current smoker, ≥40/day	1.40	(1.01–1.95)	1.34	(0.96–1.87)
P for trend[¶]		0.01		0.02

CI, confidence interval; OR odds ratio. [†]Total n = 25,391. Pooled logistic regression model. The number of observations changed at the second follow-up period. [‡]Adjusted for nine regions, age, the term of survey (baseline to 5-year survey or 5-year survey to 10-year survey), body mass index (quartile groups, missing), hypertension, parental history of diabetes, leisure-time physical activity (none, once a week to daily, missing), intakes of coffee (none, 1–2 cups/week, 3–4 cups/week, ≥5 cups/week, and missing) and alcohol (none, occasional, regular, missing), and workplace (or public facilities) passive smoke exposure (no exposure, less than every day, every day). [§]Excluding individuals whose smoking husbands did not provide the number of cigarettes per day. [¶]Never and former smokers assigned 0, and current smokers were assigned a median value for each category.

Table 3 | Association between incidence of diabetes during 10-year follow up and passive smoking at workplace (or public facilities)

Type of exposure	Age adjusted OR[†]	95% CI	Multivariable OR[†,‡]	95% CI
Workplace (or public facilities) exposure				
No exposure	1		1	
Less than everyday	0.74	(0.50–1.09)	0.77	(0.52–1.14)
Everyday	1.15	(0.96–1.39)	1.16	(0.96–1.40)
Workplace (or public facilities) exposure among women who worked full-time or part-time				
No exposure	1		1	
Less than everyday	0.84	(0.54–1.29)	0.86	(0.55–1.33)
Everyday	1.23	(0.996–1.52)	1.23	(0.995–1.53)

CI, confidence interval; OR odds ratio. [†]Total n = 25,391. Pooled logistic regression model. The number of observations changed at the second follow-up period. [‡]Adjusted for nine regions, age, the term of survey (baseline to 5-year survey or 5-year survey to 10-year survey), body mass index (quartile groups, missing), hypertension, parental history of diabetes, leisure-time physical activity (none, once a week to daily, missing), intakes of coffee (none, 1–2 cups/week, 3–4 cups/week, ≥5 cups/week, and missing).

might have lessened such bias. As we identified married couples based on surname, address, sex and age range, misclassification might have occurred. For example, a man identified as a husband could be in reality a male relative living with a study-participating woman, but even so, she was still passively exposed to his smoking in the same household. Unmarried couples, with different surnames, living together could not be identified, but the prevalence of such cases was estimated to be low[18]. Although spousal smoking status was used as a measure of passive smoking exposure at home, household smoking rules were not recorded in this study, and it is unknown whether the spouse in fact smoked cigarettes at home. Likewise, there is no information on how long the couple lived together, but it is likely that a majority of women who participated in the present study were in a stable marriage; the divorce rate was <4 out of 1,000 marriages among married men and women who were born between 1946 and 1950, according to statistics from the Japanese Ministry of Health, Labor and Welfare[33]. We observed a low likelihood of developing diabetes among women whose husbands were current smokers and smoked <20 cigarettes per day. The present data have no explanation for the result, but it could have been observed by chance. Passive smoking status in the workplace (or public facilities) was not updated after the 5-year observation period, as that information was not collected at the 5-year survey. The participants of Tokyo-Katsushika public health center or the Osaka-Suita area were not assessed, but it was because of a lack of consistency of data collection. Finally, possible residual confounding, and non-random measurement errors on socioeconomic status and lifestyle factors might have influenced the results.

In summary, the current study implied that high exposure to passive smoking at home, which was estimated from the spouse-reported number of cigarettes smoked per day, led to a higher likelihood of developing diabetes among Japanese never-smoking married women. This implies that women who have a high intensity of passive exposure to spousal smoking had a higher risk of diabetes than women without exposure to spousal smoking. It is desirable for heavy smokers to quit smoking or reduce the number of cigarettes smoked per day in order to reduce passive smoking exposure and its associated risk of diabetes for a never-smoking spouse and, presumably, for any other never-smoking household members. Carrying out further research in various populations with their suitable measures of passive smoking is recommended.

ACKNOWLEDGMENTS

This study was supported by the National Cancer Center Research and Development Fund (since 2011), and a Grant-in-Aid for Cancer Research from the Ministry of Health, Labour and Welfare of Japan (from 1989 to 2010).

DISCLOSURE

The authors declare no conflict of interest.

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APPENDIX

Members of the JPHC Study Group listed at the following site (as of April 2018): https://epi.ncc.go.jp/en/jphc/781/8233.html

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Flow of study population.