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Smoking During First Pregnancy and Breast Cancer: A Case-Control Study Using Washington State Registry Data

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INTRODUCTION

Breast cell proliferation and differentiation begin in menarche, extending through first pregnancy and lactation (1). First pregnancy may be a period of vulnerability to tobacco mutagens because undifferentiated mammary cells may be more susceptible to carcinogens (2,3) and extensive cell proliferation may lead to promulgation of genetic errors before repair (1).

An increased risk ratio for breast cancer among primiparous women who smoked prenatally [odds ratio (OR) 4.8; 95% confidence interval (CI) 1.6–14.6] was observed using linked 1989–1995 New York State birth-cancer registry data (4). A Massachusetts linked birth-cancer registry study found no increased risk (0.9; 0.7–1.3) (5). We used Washington State data to estimate the association between cigarette smoking during first pregnancy and breast cancer risk.

METHODS

We conducted a population-based case-control study nested within a cohort of women with first deliveries in Washington State 1984–1999, identified in birth and fetal death records of women without previous live births. Linkage to population-based cancer registries identified breast cancer cases, excluding those diagnosed within one year of delivery. Institutional Review Boards of the Washington State Department of Health and Fred Hutchinson Cancer Research Center approved this study.

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Cases

Cases were 1,099 women aged = 65 years diagnosed with invasive or *in situ* breast cancer (International Classification of Diseases for Oncology codes C50.0–50.9) (6) during 1985–2000.

Controls

Up to 10 controls per case (N=10,922) were matched to cases by calendar year of, and age at first delivery (years), race/ethnicity (white, black, Asian, American Indian/Alaska Native, Hispanic), and outcome (live birth, fetal death).

Data sources and linkages

The Cancer Surveillance System of Western Washington identified residents of 13 contiguous counties of western Washington diagnosed with breast cancer 1985–1991 and 2000. Controls were drawn from women residing in the same counties at first delivery. The Washington State Cancer Registry identified cases diagnosed 1992–1999. Corresponding controls were selected from state residents at the time of first delivery.

A sequential deterministic program linked cancer registry to state birth and fetal death records to identify breast cancer cases with first deliveries, using mother's first name, married name, maiden name, birth date, and father's name from vital records, and name, birth date, and spouse's name in the cancer registry.

Vital records provided information on maternal characteristics, prenatal smoking, and conditions of pregnancy and delivery. Exposure was defined as any smoking during the pregnancy.

Although cases resided in Washington at diagnosis, some controls may have out-migrated after delivery and not been identified as cases if breast cancer occurred while residing elsewhere. We linked Department of Licensing data to the birth/fetal death records to ascertain residency status of cases and their matched controls at the time of diagnosis. Known state residents included those with: 1) a state driver's license renewal within 5 years of the matched case's diagnosis, or 2) delivery in Washington State during or after the diagnosis year. We separately analyzed the 76% of cases (N=837) and 64% of controls (N=6,999) who, based on these criteria, were state residents within 5 years of the case's breast cancer diagnosis.

Multiple imputation of missing data

Maternal education was collected in the birth/fetal death records since 1992 and prenatal alcohol consumption since 1989, resulting in 81% and 66% of records missing these variables, respectively. Multiple imputation procedures (software by Schafer for S-Plus) (7–9) were used to impute these values when missing. This method uses an expectation maximization (EM) algorithm to estimate a probability distribution for values in each possible cell of missing data and a Markov-chain Monte Carlo method for simulating draws from cell probabilities. Ten imputation datasets for each imputed variable were used.

Statistical analysis

Conditional logistic regression was used to calculate ORs for breast cancer in relation to prenatal smoking. Marital status, education, prenatal alcohol use, pre-eclampsia, multifetal gestation, infant birth weight, and sex were evaluated as potential confounders. Prenatal alcohol use (yes/no) changed the OR by more than 10%, our criteria for confounder selection (10), so estimates were adjusted for it and the matching variables. Effect

modification was explored by examination of stratum-specific ORs and likelihood ratio tests in logistic regression.

No subjects had previous live births but birth records indicated that some had prior pregnancies resulting in terminations or fetal deaths. To isolate the effect of smoking during first pregnancy, analyses were repeated among the 733 cases and 7,009 controls (and 558 cases and 4,559 controls judged to be state residents) without prior pregnancies.

RESULTS

Cases had a mean age of 39.2 years (SD 5.6) at diagnosis and a mean interval of 8.1 years between first delivery and diagnosis (range 1–16, SD 3.7). Most cases and controls were white, aged ≥ 30 years, and had > 12 years of education. Cases were more likely than controls to be married and drink alcohol during pregnancy, but were similar regarding other characteristics examined.

The OR for the breast cancer-prenatal smoking association was 0.9 (95% CI 0.7–1.1); after adjustment for prenatal alcohol consumption it was 0.8 (0.7–0.9) (Table). When the analysis was restricted to women categorized as residents at the time of diagnosis, the adjusted OR was 1.0 (0.8–1.1). Restriction of analyses to women without prior pregnancies did not change these results. There was no evidence that the association differed by age at first pregnancy or at matched case's diagnosis.

DISCUSSION

In this third data linkage study of this topic to date, we did not observe an increased risk of breast cancer in relation to prenatal smoking during the first pregnancy. This is consistent with results from Massachusetts (5), but not New York (4). We used more controls per case than the previous studies (4,5), and may have controlled more completely for any effect of age than the New York study (4) by matching as closely as possible on year of, and age at first delivery. All studies relied on prenatal smoking from birth records, which is likely underreported (11), although probably without variation by case status. Our results do not suggest that smoking during first pregnancy is associated with breast cancer risk.

Acknowledgments

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Abbreviations used

OR	Odds ratio
CI	confidence interval

References

1. Colditz GA. Fat, estrogens, and the time frame for prevention of breast cancer. Epidemiology 1995;6(3):209–211. [PubMed: 7619924]
2. Russo J, Russo IH. Development pattern of human breast and susceptibility to carcinogenesis. Eur J Cancer Prev 1993;2 (Suppl 3):85–100. [PubMed: 7905315]
3. Russo J, Hu YF, Silva ID, Russo IH. Cancer risk related to mammary gland structure and development. Microsc Res Tech 2001;52(2):204–223. [PubMed: 11169868]

4. Innes KE, Byers TE. Smoking during pregnancy and breast cancer risk in very young women (United States). Cancer Causes Control 2001;12(2):179–185. [PubMed: 11246847]
5. Fink AK, Lash TL. A null association between smoking during pregnancy and breast cancer using Massachusetts registry data (United States). Cancer Causes Control 2003;14(5):497–503. [PubMed: 12946045]
6. Fritz, AG.; Percy, C.; Jack, A.; Shanmugarathan, S.; Sobin, L.; Parkin, DM., et al., editors. International classification of diseases for oncology: ICD-O. Vol. vii. Geneva: World Health Organization; 2000. p. 240
7. Schafer, JL. Software for multiple imputation. Department of Statistics, Pennsylvania State University; 1997 [Accessed December 2001]. (http://www.stat.psu.edu/~jls/misoftwa.html)
8. Schafer, JL. Analysis of Incomplete Multivariate Data. New York: Chapman & Hall; 1997. p. 143-144.
9. S-Plus 4.5 Professional Release. Mathsoft, Inc; 1998.
10. Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. Am J Epidemiol 1989;129(1):125–137. [PubMed: 2910056]
11. Allen AM, Dietz PM, Tong VT, England L, Prince CB. Prenatal smoking prevalence ascertained from two population-based data sources: birth certificates and PRAMS questionnaires, 2004. Public Health Rep 2008;123(5):586–592. [PubMed: 18828413]

Table

Association between smoking during pregnancy and breast cancer among women with first deliveries in Washington State from 1984–1999

	Cases n (%)		Controls n (%)		Odds Ratio* (95% CI)	
	All subjects (N=1,099)	**Restricted sample† (N=837)**	**All subjects (N=10,922)**	**Restricted sample† (N=6,999)**	**All subjects**	**Restricted sample†**
Smoked during pregnancy						
Yes	128 (12.5)	**95 (12.2)**	1,421 (13.9)	**772 (11.8)**	0.8 (0.7, 0.9)	**1.0 (0.8, 1.1)**
No	899 (87.5)	**682 (87.8)**	8,802 (86.0)	**5,748 (88.2)**	1.0 (reference)	**1.0 (reference)**
Missing	72	**60**	699	**479**		

*Accounting for matching variables through conditional logistic regression (age at first birth, year of delivery, race/ethnicity and birth outcome) and adjusting for imputed and known maternal prenatal alcohol use

†Subjects judged to be Washington State residents within five years of the date of the case's diagnosis (and similar period for her matched controls)