



Published in final edited form as:

*Am J Med.* 2010 September ; 123(9): 863.e1–863.e6. doi:10.1016/j.amjmed.2010.03.016.

## Lactation and Maternal Risk of Type-2 diabetes: a Population-based Study

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### Abstract

**BACKGROUND**—Lactation has been associated with improvements in maternal glucose metabolism.

**METHODS**—We explored the relationships between lactation and risk of type-2 diabetes in a well-characterized, population-representative cohort of women, aged 40–78, who were members of a large integrated health delivery organization in California and enrolled in the Reproductive Risk factors for Incontinence Study at Kaiser (RRISK), between 2003 and 2008. Multivariable logistic regression was used to control for age, parity, race, education, hysterectomy, physical activity, tobacco and alcohol use, family history of diabetes, and body mass index (BMI), while examining the impact of duration, exclusivity and consistency of lactation on risk of having developed type-2 diabetes.

**RESULTS**—Of 2233 women studied, 1828 were mothers; 56% had breastfed an infant for  $\geq 1$  month. In fully-adjusted models, the risk of type-2 diabetes among women who consistently breastfed all of their children for  $\geq 1$  month remained similar to that of women who had never given birth (OR=1.01, 95% CI=0.56–1.81). In contrast, mothers who had never breastfed an infant were more likely to have developed type-2 diabetes than nulliparous women (OR=1.92, 95% CI=1.14–3.27). Mothers who

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All authors had access to the data and an active role in writing this manuscript.

None have any conflicts of interest.

never exclusively breastfed were more likely to have developed type-2 diabetes than mothers who exclusively breastfed for 1–3 months (OR=1.52, 95% CI=1.11–2.10).

**CONCLUSIONS**—Risk of type-2 diabetes increases when term pregnancy is followed by <1 month of lactation, independent of physical activity and BMI in later life. Mothers should be encouraged to exclusively breastfeed all of their infants for at least 1 month.

### Keywords

women; type-2 diabetes; pregnancy; lactation; breastfeeding

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Over the last century there have been dramatic increases in the prevalence of diabetes in many countries.<sup>1</sup> In the United States, it is estimated that 10% of all women aged 20 years or older have diabetes.<sup>2</sup> As such, it is important to identify behaviors that modify women's risk of diabetes. Diet and exercise are widely known to impact risk of type-2 diabetes,<sup>3</sup> but less is known about the impact a woman's decision to breastfeed her children may have on her future risk of diabetes. Animal studies have suggested that lactation may increase sensitivity to insulin.<sup>4–6</sup> In women with recent gestational diabetes, lactation has been found to improve glucose and lipid metabolism.<sup>7–8</sup> Data from large cohorts in the USA<sup>9–10</sup> and China<sup>11</sup> have indicated that longer duration of breast-feeding may reduce women's risk of developing type-2 diabetes mellitus. However, many of these studies have lacked detailed information about the duration and exclusivity with which women breastfed each of their children. As such, the minimum duration, exclusivity, and consistency of lactation required to reduce a woman's risk of developing diabetes is unknown. In this study, we examined the associations between duration, exclusivity, and consistency of lactation with the prevalence of type-2 diabetes mellitus among a multiethnic cohort of middle-aged women who were members of a large integrated health delivery organization in California.

## MATERIALS AND METHODS

The Reproductive Risk Factors for Incontinence Study at Kaiser (RRISK) enrolled 2270 women, aged 40–78 years, between 2003 and 2008. Women were recruited from within the Kaiser Permanente Medical Care Program (KPMC) of Northern California, an integrated health maintenance organization with over 3 million members that serves approximately 25–30% of the population in the geographic area served. The design and sampling methods have been previously described.<sup>12</sup> Briefly, random samples within age and race strata were drawn such that a roughly equal number of women would be in each 5-year age group, and the race distribution would be approximately 40% white, 20% African American, 20% Hispanic, and 20% Asian. In addition, women with diabetes were oversampled within each age and race sampling strata to reach the goal of at least 400 diabetic women.

Data for the study were collected by self-reported questionnaires and in-person interviews. Physical measurements of height and weight, which were used to calculate body mass index (BMI), were obtained by a trained research assistant. Most interviews took place either in the home of the participant (57%) or at a Kaiser Permanente Medical Care Program clinic (28%). Informed consent was obtained by phone and in writing at the time of the interview. The Institutional Review Boards at University of California, San Francisco, Kaiser Permanente, and the University of Pittsburgh approved this study.

Detailed information on lactation was collected by asking women who reported one or more live births, “Did you breastfeed any of your children for more than a month?” Women who answered, “yes,” were then asked to specify for each infant “the number that best describes your baby's age in months at the time when you stopped nursing, breastfeeding, expressing or pumping breast milk for your baby at least once a day” (duration of lactation) and “the number

that best describes your baby's age in months at the time when he/she first received a bottle of formula, cow's milk, water, juice, tea, or cereal at least once a day" (duration of exclusive lactation). This information was used to calculate the average number of months a woman lactated following the birth of each of her children. In addition, we examined consistency of lactation by considering 3 groups of women: those who consistently breastfed all of their children for >1 month, those who breastfed some (but not all) of their children for >1 month, and those who had never lactated.

Women were identified as having diabetes if they self-reported a history of diabetes and were currently taking insulin or oral medications at the time of the interview, had fasting glucose and/or HbA1C laboratory values taken within one year of the interview date suggestive of diabetes, or had previously been identified for inclusion in the Kaiser Permanente Diabetes Registry, which uses an algorithm based on age at diagnosis, length of time between initial diagnosis and start of insulin treatment, intervals of 3 months or longer off insulin after initiation, and obesity at diagnosis. To avoid the chance of undiagnosed type-2 diabetes, all RRISK participants who reported no diagnosis of diabetes had a fasting glucose measured, and the population of non-diabetic RRISK participants was limited to those who self-reported no diabetes history, were not taking a diabetes medication, and had a fasting glucose < 100 mg/dl.

Variables initially considered as covariates included age, parity, race, education, income, physical activity, tobacco and alcohol use, history of hysterectomy, family history of diabetes, and body mass index. However, due to the large amount of missing income data, this variable was dropped from the final multi-variable models.

Descriptive statistics were used to characterize the study population. We excluded 37 subjects who were missing data on parity and on lactation from further analyses. The remaining 2233 women, who reported one or more live births and had complete lactation data (n=1828) or had never been pregnant (n=405), were included in the following analyses. We examined the significance of differences in demographic variables by lactation history using Chi-square tests for categorical variables, Student t-test for continuous variables, and the Wilcoxon test when appropriate. We also used descriptive statistics to assess whether duration or exclusivity of lactation varied by parity.

We used multivariable models to analyze the effect on risk of developing diabetes of average duration per child of total lactation and exclusive lactation among parous women. As there was not a linear relationship between risk of diabetes and duration of either exclusive or total lactation, we categorized exclusive lactation as  $\geq 3$  months, 1 to <3 months, or never, and total duration of lactation as  $\geq 6$  months, 1 to <6 months, or never. We then examined risk of type-2 diabetes among nulliparous women and parous women who had or had not consistently breastfed their children using bivariate analyses. We used separate multivariable logistic regression models to examine these relationships while controlling for age, parity, race, education, physical activity, tobacco and alcohol use, history of hysterectomy, family history of diabetes, and body mass index. In addition, we examined whether the relationship between lactation and diabetes differed by race, or there was a differential effect by race, by entering an interaction term in all models.  $P \leq 0.05$  was considered statistically significant in all models. All analyses were performed using SAS 9.2 (SAS Institute, Cary, NC).

## RESULTS

Participants' average age upon enrollment in the study was  $55 \pm 9$  years. Twenty percent were African-American, 18% were Asian and 18% were Latina or another race. Obesity was

common, with 68% of participants having a BMI  $\geq 25$ . Most (70%) women had given birth more than once.

Most parous women (62%) reported a history of breastfeeding an infant for one or more months. Most (97%) of mothers who reported any period of exclusive lactation breastfed for at least one month. Table 1 compares the demographic characteristics of women who breastfed to those who did not. Women who breastfed their infants were younger, more likely to be white, in a committed relationship, working full-time, have multiple children, and less likely to have undergone hysterectomy. Duration of exclusive lactation was highly correlated with duration of total lactation,  $p < 0.001$ . On average, women who ever lactated had breastfed each of their children for a total of  $6.0 \pm 5.7$  months and breastfed exclusively for  $3.0 \pm 2.2$  months. Average duration of total or exclusive lactation varied little by parity.

In bivariate analyses, women who had never breastfed an infant were more likely to be obese and have type-2 diabetes than women who had ever breastfed an infant (Table 2). When we used multivariable models to examine the effect of duration of lactation on maternal risk of type-2 diabetes (Table 3), we found that mothers who had never breastfed were more likely to have developed diabetes than those who on average breastfed their children for 6 or more months. Similarly, women who never exclusively breastfed were more likely to have developed diabetes than mothers who had exclusively breastfed each of their children for an average of one or more months (OR=1.38, 95% CI 1.06–1.81).

Consistency of lactation was also associated with risk of developing type-2 diabetes (Table 4). Mothers who had never breastfed were more likely to have developed type-2 diabetes than mothers who consistently breastfed (OR 1.41, 95% CI 1.03–1.92). Mothers who had never breastfed also tended to be more likely to have developed diabetes than mothers who inconsistently breastfed, OR 1.42, 95% CI 0.96–2.09,  $P = 0.07$ . Interestingly, in fully-adjusted logistic regression models, the risk of type-2 diabetes among women who had consistently breastfed all of their children for at least one month remained similar to that of women who had never been pregnant (OR=1.01, 95% CI 0.56–1.81). However, mothers who had never breastfed were more likely to develop type-2 diabetes than nulliparous women (OR=1.93, 95% CI=1.14–3.27). None of the relationships between lactation and diabetes identified differed by race (for all interaction terms  $p > 0.60$ ).

## DISCUSSION

Among middle-aged participants of a well-characterized population-based cohort of women, we found that mothers who did not breastfeed their children were at increased risk of developing type-2 diabetes. These findings highlight the importance to maternal health of consistent lactation after each birth, and add to a growing body of literature that indicates that women who give birth but do not breastfeed face an increased risk of developing diabetes mellitus<sup>9–11</sup> and subsequent cardiovascular disease.<sup>9</sup> While one prior study<sup>7–8</sup> suggested that a beneficial association with regards to diabetes begins to accrue after 6 months of lactation, this study's more detailed information on the duration and exclusivity with which women breastfed their children showed significant benefits with only one month of lactation. Future studies will need to explore whether mothers who lactate for shorter periods accrue similar benefits, as the data collected for this study did not allow such analyses.

The reasons why mothers who do not breastfeed are at increased risk of diabetes remain incompletely understood. In women with recent gestational diabetes, lactation has been found to improve glucose and lipid metabolism.<sup>7–8</sup> Animal studies have suggested that lactation may increase sensitivity to insulin.<sup>4–6</sup> Lactation suppresses gonadotropin levels, and has been associated with lower and slower responses to growth hormone.<sup>13</sup> Lactation may decrease

visceral adiposity and may also induce long-term changes in the hypothalamic-pituitary axis. During pregnancy, women experience an increase in visceral fat;<sup>14</sup> nulliparous women never gain this visceral fat. With lactation, women lose the visceral fat gained during pregnancy. However, mothers who breastfeed for shorter durations may not lose all the visceral fat they acquire during pregnancy. As visceral fat is more metabolically active than fat depots in other body areas,<sup>15</sup> mothers who retain visceral fat face an increased risk of diabetes. In addition, in one study, postmenopausal women who had breastfed for more than 1 year were found to have significantly higher fasting cortisol levels.<sup>16</sup> However, further studies are needed to identify the pathways and mechanisms through which lactation reduces subsequent risk of diabetes.

Strengths of this study include the racially diverse group of women who participated. However, our findings must be interpreted with the understanding that all observational studies may be subject to residual confounding. All RRISK participants were members of a large Health Maintenance Organization (HMO) at baseline which facilitated linking of cohort questionnaire data to electronic clinical data, including the KPMCP Diabetes Registry. Moreover, the cohort has essentially equal access to care. Previous studies have found that members of this HMO include slightly fewer people in the very lowest and highest socioeconomic classes<sup>17</sup> and tend to be slightly more educated than the general population, but they are very similar to the general population in terms of other demographic characteristics such as race and ethnicity.

This study may be limited by recall or reporting bias which may have led to some misclassification of women's lactation history. Prior research has found that women with shorter durations of lactation tended to over-report, while women with longer durations tended to underreport.<sup>18</sup> Presuming this misclassification is non-differential with respect to risk of diabetes, it would attenuate estimates of associations between lactation and later risk of diabetes. In addition, studies have linked obesity and insulin resistance to difficulties with breastfeeding,<sup>19–20</sup> suggesting that decreased duration of lactation could be a marker for an existing abnormal metabolic profile. It is also possible that pregnancy complications such as preterm birth or pre-eclampsia may have led to shortened duration of breastfeeding. Such complications are associated with risk for glucose intolerance and cardiovascular mortality in later life.<sup>21</sup> While data on women's level of obesity or insulin resistance at the time of pregnancy was not collected from RRISK participants, we controlled for family history of diabetes which has been correlated with early onset insulin resistance and BMI on enrollment in RRISK which has been associated with BMI in earlier life.

In conclusion, this study adds to a growing body of literature that indicates that women who do not breastfeed their children are at increased risk of developing type-2 diabetes. While breastfeeding is widely acknowledged to benefit infant health,<sup>22</sup> and the American Academy of Pediatrics recommends that mothers exclusively breastfeed their infants for the first six months,<sup>23</sup> in 2006, only 14% of US mothers were able to follow this recommendation.<sup>23–24</sup> Ongoing support of breastfeeding is therefore needed from women's health care providers<sup>25</sup> as well as legislators and workplace policy-makers.<sup>26</sup>

## Acknowledgments

The RRISK study was funded by the National Institute of Diabetes and Digestive and Kidney Diseases/Office of Research on Women's Health Specialized Center of Research Grant # P50 DK064538. Dr. Schwarz was supported by National Institute of Child Health and Development grant K23 HD051585-01.

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**Table 1**

## Demographic Characteristics of Participating Women by Birth and Lactation History

Variable	Nulliparous women		Mothers		p-value*
	(N=405) %	>1 month of lactation (N=1125) %	No lactation (N=703) %		
<b>Age, mean ± SD</b>	51.6±7.7	54.2±9.2	58.3±9.0		<0.001**
<b>Race</b>					
African-American	75 (18.5)	167 (14.8)	196(27.9)		<0.001
Caucasian	206 (50.9)	519 (46.1)	262(37.3)		
Asian	74 (18.3)	222 (19.7)	101 (14.4)		
Latina or other	50 (12.3)	217 (19.3)	143(20.4)		
<b>Parity</b>					0.02
One birth	0	147(13.1)	125(17.8)		
Two births	0	436(38.8)	264(37.6)		
Three births	0	328(29.2)	201(28.6)		
Four or more births	0	214(19.0)	113(16.1)		
<b>Post-menopausal</b>	264 (65.2)	781 (69.2)	584 (83.4)		<0.001
<b>Had hysterectomy</b>	77 (19.0)	241(21.4)	206 (29.3)		<0.001
<b>Married or significant relationship</b>	223 (55.1)	843(75.0)	452 (64.3)		<0.001
<b>Current full-time job</b>	224 (56.9)	522(47.2)	235 (33.9)		<0.001
<b>Income less than \$60,000/year</b>	149 (38.8)	381(36.1)	344 (52.2)		<0.001

\* P-values comparing mothers who did and didn't breastfeed using Chi-square tests for categorical variables and Student t-test for continuous variables unless otherwise marked

\*\* P-values calculated with Wilcoxon test



**Table 2**

## Metabolic Characteristics of Participating Women by Birth and Lactation History

Variable	Nulliparous women (N=406) %		Mothers >1 month of lactation (N=1129) %		p-value*
			No lactation (N=703) %		
<b>Type-2 diabetes</b> **	71 (17.5)		202(18.0)	188 (26.7)	<0.001
<b>Current BMI, mean±SD</b>	29.72±8.66		29.00±6.98	29.72±8.66	0.004***
<b>Body Mass Index</b>					
Less than 25	142(35.1)		374(33.6)	188(26.9)	0.01
25 to less than 30	113(28.0)		322(28.9)	229(32.7)	
30 or more	149(36.9)		418(37.5)	283(40.4)	
<b>Waist, mean±SD inches</b>	37.35±8.00		36.86±6.34	38.13±6.50	<0.001***

\* P-values comparing mothers who did and didn't breastfeed using Chi-square tests for category variables and Student t-test for continuous variables unless otherwise marked.

\*\* Women with type-2 diabetes were identified as those who had a fasting glucose  $\geq 126$  mg/dl, an oral glucose tolerance test 2-hour glucose  $\geq 200$  mg/dl, or random glucose  $\geq 200$  mg/dl with symptoms of diabetes, or were taking a diabetes medication.

\*\*\* P-values calculated with Wilcoxon test.

**Table 3**

## Odds of Type-2 Diabetes by Duration of Lactation

Average months of total lactation per child	Diabetic N (%)	Adjusted OR* (95% CI)
≥ 6 months	75 (16.0)	Reference**
1 to 6 months	126 (19.3)	1.04 (0.72–1.48)
None	188 (26.8)	1.43 (1.01–2.04)

\* Odds Ratio (OR) adjusted for age, parity, race, education, smoking and alcohol use, history of hysterectomy, family history of diabetes, physical activity and body mass index (BMI).

\*\* The American Academy of Pediatrics recommends that mothers exclusively breastfeed their infants for the first six months.<sup>20</sup>

**Table 4**

## Odds of Type-2 Diabetes by Consistency of Lactation

	Among mothers		Among all women
	Diabetes N(%)	Adjusted OR* (95% CI)	Adjusted OR* (95% CI)
<b>Nulliparous (n=405)</b>	71 (17.5)	n/a	Reference
<b>Consistent lactation** (n=800)</b>	136 (17.0)	Reference	1.01 (0.56–1.81)
<b>Inconsistent lactation** (n=325)</b>	66 (20.3)	0.80 (0.53–1.21)	0.73 (0.36–1.48)
<b>No Lactation (n=703)</b>	188 (26.7)	1.41 (1.03–1.92)	1.93 (1.14–3.27)

\* Adjusted for age, parity, race, education, smoking and alcohol use, history of hysterectomy, family history of diabetes, physical activity and body mass index (BMI).

\*\* Women who consistently breastfed all of their children for >1 month, those who inconsistently lactated breastfed some, but not all, of their children for >1 month.