Duration of Lactation and Maternal Metabolism at 3 Years Postpartum

Alison M. Stuebe, M.D., M.Sc.,¹ Ken Kleinman, Sc.D.,² Matthew W. Gillman, M.D., S.M.,^{2,3}
Sheryl L. Rifas-Shiman, M.P.H.,² Erica P. Gunderson, Ph.D.,⁴ and Janet Rich-Edwards, Sc.D.⁵

Abstract

Objective: Lactation has been associated with reduced risk of type 2 diabetes and the metabolic syndrome in mothers. We examined the relation between breastfeeding duration and metabolic markers at 3 years postpartum.

Methods: We used linear regression to relate duration of lactation to maternal glucose and lipid metabolism, inflammatory markers, and anthropometry at 3 years postpartum among 570 participants with 3-year blood samples (175 fasting) in Project Viva, a cohort study of mothers and children.

Results: Among the participants, 88% had initiated breastfeeding, and 26% had breastfed ≥ 12 months. In multivariate analyses, we observed no consistent trends relating duration of lactation to maternal metabolism at 3 years postpartum. Women who exclusively breastfed for >6 months had lower postpartum weight retention at 3 years than women with shorter durations of exclusive breastfeeding (multivariate adjusted predicted mean -0.5 , -3.6 – 2.6 kg vs. 4.8 , 2.0 – 7.6 kg for those who never exclusively breastfed, partial F $p = 0.03$).

Conclusions: In this prospective cohort study, we did not observe a dose-response relationship between duration of lactation and metabolic risk at 3 years postpartum.

Introduction

TYPE 2 DIABETES CAUSES substantial morbidity and mortality, affecting more than 9 million women in the United States. Recent epidemiological data suggest that lactation may modify a woman's risk for this disease. In a large cohort study,¹ each year of lactation was associated with a 15% reduction in a woman's risk of type 2 diabetes in the 15 years after her last delivery. Duration of lactation is similarly associated with reduced diabetes risk in other cohorts^{2,3} and with more favorable lipid profiles after weaning,⁴ reduced risk of the metabolic syndrome,⁵ and lower long-term hypertension,³ hyperlipidemia, and myocardial infarction.^{3,6}

These findings suggest that lactation may be a modifiable risk factor for metabolic disease in women.⁷ Alternatively, lactation may be associated with other beneficial health behaviors, such as diet and physical activity, or breastfeeding failure may be a marker for unfavorable maternal metabolism. Few studies have prospectively examined the relation

among maternal metabolic risk factors, health behaviors, breastfeeding duration, and biomarkers after weaning. We, therefore, examined the association between duration of lactation and maternal metabolism at 3 years postpartum in Project Viva, a prospective cohort study of maternal and infant health.

Materials and Methods

Women were recruited for Project Viva at their first prenatal visit at one of eight urban and suburban obstetrical offices of a multispecialty group practice in Eastern Massachusetts. To be eligible for the study, potential participants were required to be fluent in English, be <22 weeks' gestation at study entry, and have a singleton pregnancy; 65% of eligible women were recruited. All participants provided written informed consent. A human studies committee approved all procedures in accordance with ethical standards for human experimentation.

¹Division of Maternal-Fetal Medicine, Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

²Obesity Prevention Program, Department of Ambulatory Care and Prevention, Harvard Medical School/Harvard Pilgrim Health Care, Boston, Massachusetts.

³Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts.

⁴Division of Research, Epidemiology and Prevention Section, Kaiser Permanente, Oakland, California.

⁵Connors Center for Women's Health and Gender Biology, Brigham and Women's Hospital, and ⁶ Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts.

Of the 2128 participating women who gave birth, 1579 were invited to a 3-year follow-up examination because they had completed dietary questionnaires during pregnancy; 761 of these women were eligible for the current analysis because they had not delivered another child since the birth of the index child 3 years previously, they did not have type 1 or type 2 diabetes, and they attended the 3-year visit. Of these women, 611 provided a blood sample. We excluded women with missing data on breastfeeding duration ($n = 33$), gestational weight gain ($n = 4$), or gestational diabetes ($n = 4$), leaving 570 women available for analysis. Fasting blood samples were available for 175 of the 570.

Assessment of lactation

At approximately 28 weeks' gestation, study participants provided information on intention to breastfeed. Shortly after delivery, participants again reported intention to breastfeed and initiation of breastfeeding. At the 6-month follow-up visit, we asked women if they were breastfeeding and if they had introduced formula or solid foods. Women reported timing of weaning and introduction of supplemental foods in months, weeks, or days. We similarly assessed breastfeeding at 12 months postpartum. For our analysis, we coded duration of lactation categorically as 0 months, >0 – <3 , ≥ 3 – <6 , ≥ 6 – <12 , and ≥ 12 months. We calculated exclusive lactation as time to first introduction of solid foods, formula, or juice. We coded duration of exclusive lactation in the categories 0 months, >0 – <1 , 1 – <3 , 3 – <6 , and ≥ 6 months. We excluded from our analysis of exclusive lactation women missing data on timing of introduction of solid or complementary foods ($n = 127$).

Assessment of metabolic parameters at 3 years postpartum

Women returned with their children at 3 years postpartum for a physical examination that included anthropometric measurements and a blood sample. Anthropometric measures included measured weight to the nearest 0.1 kg using a research quality scale, measured height to the nearest 0.1 cm using a stadiometer, waist circumference to the nearest 0.1 cm using a Lefkin woven tape, and subscapular and triceps skinfold measurements to the nearest 0.1 mm using a Holtain caliper. Study staff receive onsite training and twice-yearly retraining for assessment of height, weight, waist circumferences, and skinfolds.

We tested all blood samples for hemoglobin A1c (HbA_{1c}), sex hormone-binding globulin (SHBG), and C-reactive protein (CRP). We identified as fasting those participants who did not eat or drink anything other than water for 8 hours before blood samples were obtained. We tested fasting blood samples for insulin, glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and interleukin-6 (IL-6). Blood samples were collected by trained phlebotomists and transferred within 24 hours for storage in liquid nitrogen freezers. Sample testing was performed at the Boston Children's Hospital Clinical Chemistry Laboratory, which is certified by the Centers for Disease Control and Prevention/National Heart, Lung, and Blood Institute Lipid Standardization Program.

Glycosylated hemoglobin was assessed using the Hitachi 917 analyzer, which employs turbidimetric immunoinhibition of hemolyzed whole blood or packed red blood cells (Roche

Diagnostics) to calculate the $\% \text{HbA}_{1c}$. We calculated insulin resistance in fasting blood samples using the homeostasis model: $\text{HOMA-IR} = (\text{fasting insulin } [\mu\text{U/mL}] \times \text{fasting glucose } [\text{mmol/L}]/22.5)$. Fasting glucose was measured enzymatically using the Hitachi 911 analyzer with Roche Diagnostic reagents. Fasting insulin was measured using a microparticle enzyme immunoassay on the IMZ analyzer (Abbott Laboratories). Lipoproteins were measured in fasting samples using assays approved by the U.S. Food and Drug Administration (FDA) for clinical use: total cholesterol was measured enzymatically, and LDL-C was assessed by a homogeneous direct method from Genzyme Corp. HDL-C was assessed using a direct enzymatic colorimetric assay, and triglycerides were calculated enzymatically with correction for endogenous glycerol. SHBG was measured using a competitive electrochemiluminescence immunoassay on the 2010 Elecsys autoanalyzer (Roche Diagnostics). CRP was measured using an immunoturbidimetric high-sensitivity assay on a Hitachi 911 analyzer (Roche Diagnostics) and reagents and calibrators from Denka Seiken. Plasma IL-6 was measured by ultrasensitive ELISA.

Study covariates

Participants reported sociodemographic variables, including parity, prepregnancy weight and height, and family history of type 2 diabetes, at the initial prenatal visit. We calculated gestational weight gain as the difference between the last weight before delivery and the self-reported prepregnancy weight. Self-reported prepregnancy weight in Project Viva participants is highly correlated ($r = 0.99$) with clinically recorded prepregnant weight.⁸ Maternal gestational glucose tolerance was assessed clinically with the nonfasting 50-g oral glucose loading test (GLT) administered at 26–28 weeks' gestation. Women with a result of ≥ 140 mg/dL underwent a 100-g oral glucose tolerance test (GTT), administered the morning after an overnight fast. Normal results were defined by Carpenter-Coustan criteria: fasting, <95 mg/dL; 1 hour, <180 mg/dL; 2 hours, <155 mg/dL; 3 hours, <140 mg/dL. Gestational glucose tolerance was categorized as normal (GLT < 140), transient hyperglycemia (GLT ≥ 140 , GTT with no abnormal results), impaired glucose tolerance (IGT) (GTT with one abnormal result), or gestational diabetes (GLT ≥ 140 , GTT with two or more abnormal results).

We assessed several covariates that were potential intermediates in the association between lactation and 3-year metabolic outcomes. On the 6-month questionnaire, we assessed participants' smoking status, intention to lose weight, dietary intake, and physical activity. We assessed dietary intake using the PrimeScreen, a brief food frequency questionnaire that has been validated.⁹ We used these results to calculate energy-adjusted intake of total fat, trans-fat, saturated fat, fiber, and glycemic index. We assessed maternal physical activity by assessing hours per week of walking, moderate, vigorous activity, and television viewing. Participants self-reported weight at 12 months postpartum. Hormonal contraceptive use since the index birth was assessed at the 6-year follow-up visit (missing for $n = 210$).

Data analysis

Prior to regression analysis, we log-transformed measurements of HOMA-IR, insulin, SHBG, triglycerides, CRP,

TABLE 1. BASELINE CHARACTERISTICS OF STUDY POPULATION, BY TOTAL DURATION OF LACTATION. DATA FROM 570 PARTICIPANTS IN PROJECT VIVA AT 3-YEAR POSTPARTUM FOLLOW-UP WITHOUT AN INTERVENING BIRTH

	Months of lactation										p*
	None n = 70		>0-<3 n = 92		3-<6 n = 117		6-<12 n = 141		12+ n = 150		
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	
Prepregnancy BMI (kg/m ²) ^a	26.8	(6.0)	26.9	(7.3)	24.9	(5.0)	24.8	(5.2)	23.7	(3.8)	<0.001
Gestational weight gain (kg)	15.1	(6.7)	14.6	(6.2)	15.7	(5.5)	14.5	(5.2)	14.9	(5.0)	0.54
Age at 3-year visit	36.0	(4.8)	36.8	(6.0)	37.2	(5.3)	38.2	(4.6)	38.8	(5.0)	0.0005
n		%	n	%	n	%	n	%	n	%	
Race											0.10
Asian	0	(0)	5	(5)	7	(6)	5	(4)	5	(3)	
Black	12	(17)	16	(17)	21	(18)	13	(9)	19	(13)	
Hispanic	2	(3)	9	(10)	11	(9)	8	(6)	7	(5)	
Other	3	(4)	4	(4)	8	(7)	3	(2)	6	(4)	
White	53	(76)	58	(63)	70	(60)	112	(79)	113	(75)	
Parity											0.006
1	12	(17)	39	(42)	37	(32)	33	(23)	41	(27)	
2	36	(51)	40	(44)	57	(49)	73	(52)	64	(43)	
3+	22	(31)	13	(14)	23	(20)	35	(25)	45	(30)	0.74
Gestational glucose tolerance											
GDM	3	(4)	6	(7)	4	(3)	4	(3)	5	(3)	
IGT	3	(4)	2	(2)	8	(7)	5	(4)	6	(4)	
Transient hyperglycemia	5	(7)	12	(13)	13	(11)	14	(10)	11	(7)	
Normal	59	(84)	72	(78)	92	(79)	118	(84)	128	(85)	0.85
Parental history of DM											
Yes	11	(16)	17	(19)	19	(16)	20	(14)	20	(13)	
No	59	(84)	75	(82)	98	(84)	121	(86)	130	(87)	0.04
Hormonal contraception ^a											
Yes	4	(10)	16	(28)	7	(10)	17	(21)	16	(15)	
No	37	(90)	42	(72)	64	(90)	65	(79)	92	(85)	
Fasting sample											0.34
Yes	16	(23)	30	(33)	40	(34)	38	(27)	51	(34)	
No	54	(77)	62	(67)	77	(66)	103	(73)	99	(66)	

*ANOVA *p* value for continuous variables; chi-square *p* value for categorical variables.

^aUsing hormonal contraception at 2-3 years postpartum, as reported at the 6-year follow-up visit. Missing for 210 participants. BMI, body mass index; DM, diabetes mellitus; GDM, gestational diabetes mellitus; IGT, impaired glucose tolerance.

and IL-6 because these variables were not normally distributed.

To facilitate interpretation of both the magnitude and clinical significance of differences among lactation duration groups, we present results from our linear regression models as predicted values and 95% confidence intervals (95% CI) for participants of average body mass index (BMI) who were white, aged 35–40, had two children, had no parental history of type 2 diabetes, had normal glucose tolerance, and gained 15 kg during the index pregnancy. For outcomes that were log-transformed to improve normality before linear regression modeling, we present predicted means and 95% CI after exponentiation to facilitate interpretation.

We used linear regression to model the relation between lactation duration category and metabolic markers at 3 years, and we used the partial F test to assess the significance of differences among lactation duration categories in predicting metabolic outcome. We included in our multivariate models those covariates that were associated with duration of breastfeeding or that were *a priori* risk factors for an adverse metabolic profile at 3 years postpartum. Because prepregnancy BMI had a nonlinear association with breastfeeding duration, we used a 3-knot quadratic spline model¹⁰ to adjust for prepregnancy BMI. Quadratic splines allow for more complete adjustment for potential confounders than does a linear or categorical approach. In our multivariate models, we further adjusted for maternal age, race, parity, gestational weight gain, gestational glucose tolerance (normal, transient hyperglycemia, IGT, or gestational diabetes), and family history of type 2 diabetes.

We performed similar analyses relating duration of exclusive lactation to metabolic markers at 3 years postpartum. In

our exclusive breastfeeding analyses, we also adjusted for duration of mixed breastfeeding. For women who are exclusively breastfeeding, the metabolic load of lactation may offset increased caloric intake, whereas for women who are partially breastfeeding, increased appetite may not be offset by caloric needs of breastfeeding. Thus, the net effect of breastfeeding on metabolism may be different for a woman who breastfeeds exclusively for 6 months and then weans completely compared with a woman who breastfeeds exclusively for 6 months and then continues to breastfeed partially for an additional period of time.

To evaluate the association of breastfeeding with postpartum health behaviors independent of prepregnancy BMI, we calculated predicted values of health behaviors for a participant with a prepregnancy BMI of 25.1, the mean for the study population, adjusting for BMI using a 3-knot spline model. To address whether postpartum health behaviors mediated any association between lactation and outcome, we added to our multivariate model measures of physical activity (hours per day of walking, moderate, vigorous, and TV watching) and dietary intake (energy-adjusted saturated fat, trans-fat, total fat, fiber, and glycemic index) at 6 months postpartum.

To test whether hormonal contraception use confounded the observed associations, we further adjusted for 3-year postpartum use or nonuse among women for whom this datum was available ($n = 360$ for full cohort and $n = 118$ for fasting outcomes). Hormonal contraception use did not alter the observed associations, and it was excluded from our analyses.

In addition, we hypothesized *a priori* that the association between lactation and metabolic risk profile might differ for women at high risk for diabetes. We defined as at low risk

TABLE 2. PHYSICAL ACTIVITY, DIET, AND HEALTH BEHAVIORS AT 6 MONTHS POSTPARTUM, BY TOTAL DURATION OF LACTATION, ADJUSTED FOR PREPREGNANCY BMI. DATA FROM 570 PARTICIPANTS IN PROJECT VIVA AT 3-YEAR POSTPARTUM FOLLOW-UP WITHOUT AN INTERVENING BIRTH

	Months of lactation					p
	None	>0–<3	3–<6	6–<12	12+	
Physical activity (mean hours/week)						
Walking	6.0	4.7	5.2	4.2	4.1	0.07
Moderate	1.6	1.5	1.7	1.2	1.4	0.59
Vigorous	1.5	1.0	1.1	1.1	0.8	0.50
TV watching	12.3	12.7	12.9	12.3	10.2	0.14
Nutrient intake ^a (mean)						
Total fat, g/day	37.0	35.0	35.9	34.2	30.9	<0.001
Saturated fat, g/day	14.5	13.3	14.0	13.6	12.2	<0.001
Trans-fat, g/day	1.5	1.4	1.4	1.2	1.1	<0.001
Glycemic index	262.0	264.6	260.1	281.6	313.3	<0.001
Fiber, g/day	8.1	8.2	7.7	8.3	9.7	<0.001
Health behaviors (%)						
Trying to lose weight	76.4	71.2	72.6	72.0	59.5	0.10
Smoking	4.1	10.0	3.0	2.2	1.0	0.006

Predicted values for a participant with a prepregnancy BMI of 25.1, the mean for the study population. Adjusted using a 3-knot quadratic spline model.

^aEnergy adjusted using the nutrient residual method.

BMI, body mass index.

women with a prepregnancy BMI <25, normal gestational glucose tolerance, and no family history of type 2 diabetes. Women with one of more of these risk factors were categorized as high risk. We, therefore, repeated our main analysis among high-risk women.

We hypothesized that we would find a dose-response association between duration of lactation and metabolic outcomes at 3 years postpartum. For our sample size of 570 women, we estimated that we had 80% power to detect a 1/6 standard deviation (SD) difference per 6 months of breastfeeding. In our smaller group of women who provided fasting samples, we estimated that we had 80% power to detect a 1/3 SD difference per 6 months of breastfeeding.

Results

Breastfeeding was common in our cohort, with 88% reporting ever breastfeeding and 26% breastfeeding for ≥ 12 months. Women who breastfed for ≥ 12 months were older and were more likely to have three or more children than those who breastfed for shorter periods of time (Table 1). Prepregnancy BMI was lower among women who would

later initiate and sustain breastfeeding: women who did not breastfeed had a mean pregravid BMI of 26.8 kg/m² (SD 6.0), and those who would breastfeed for ≥ 12 months had a mean BMI of 23.7 kg/m² (SD 3.8). Gestational weight gain, gestational glucose tolerance, and parental history of diabetes were not significantly related to breastfeeding duration. When we compared women who provided fasting samples with those who did not, we found no differences in metabolic markers, breastfeeding duration, prepregnancy BMI, gestational weight gain, age, race, parity, gestational glucose tolerance, or family history of diabetes.

In Table 2, we present health behaviors at 6 months postpartum by breastfeeding duration for women with a typical prepregnancy BMI. Compared with women with shorter breastfeeding durations, those who breastfed ≥ 12 months walked for fewer hours per week, consumed less fat and more fiber, had a higher glycemic index diet, and were less likely to be trying to lose weight at 6 months postpartum.

Although unadjusted analyses suggested dose-response associations of total breastfeeding duration with HOMA-IR, fasting insulin, SHBG (Table 3), CRP (Table 4), 3-year

TABLE 3. MARKERS OF GLUCOSE METABOLISM AT 3 YEARS POSTPARTUM, BY BREASTFEEDING DURATION, PREDICTED VALUES FROM LINEAR REGRESSION MODELS. DATA FROM 570 PARTICIPANTS IN PROJECT VIVA AT 3-YEAR POSTPARTUM FOLLOW-UP WITHOUT AN INTERVENING BIRTH

	n	Months of lactation					p*
		None Mean (95% CI)	>0-<3 Mean (95% CI)	3-<6 Mean (95% CI)	6-<12 Mean (95% CI)	12+ Mean (95% CI)	
%HbA _{1c} , n		70	90	115	141	150	
Unadjusted	566	5.11 (5.04-5.17)	5.15 (5.09-5.21)	5.08 (5.03-5.13)	5.13 (5.09-5.18)	5.12 (5.08-5.17)	0.43
MV adjusted	566	5.03 (4.96-5.11)	5.05 (4.98-5.12)	4.98 (4.91-5.04)	5.06 (5.00-5.12)	5.05 (4.99-5.11)	0.10
HOMA-IR, ^a n		16	30	40	38	51	
Unadjusted	175	2.0 (1.4-2.8)	1.6 (1.3-2.1)	1.2 (1.0-1.5)	1.6 (1.2-1.9)	1.3 (1.1-1.6)	0.07
MV adjusted	175	1.4 (1.0-2.0)	1.3 (0.9-1.8)	1.0 (0.8-1.3)	1.3 (1.1-1.7)	1.3 (1.0-1.7)	0.13
Fasting insulin, μ /mL ^a							
Unadjusted	175	11.9 (8.6-16.4)	9.4 (7.5-11.9)	7.0 (5.8-8.6)	8.2 (6.7-10.1)	7.1 (5.9-8.4)	0.03
MV adjusted	175	8.1 (5.8-11.1)	7.1 (5.3-9.4)	5.6 (4.4-7.0)	7.0 (5.7-8.7)	6.9 (5.4-8.8)	0.14
Fasting glucose, mg/dL							
Unadjusted	175	70.6 (63.4-77.7)	72.9 (67.6-78.1)	70.6 (66.1-75.2)	78.5 (73.8-83.1)	75.4 (71.4-79.4)	0.13
MV adjusted	175	72.1 (63.4-80.8)	75.4 (67.7-83.0)	73.4 (67.1-79.7)	78.5 (72.8-84.3)	77.3 (70.8-83.8)	0.40
SHBG, ^a n		70	92	116	139	150	
Unadjusted	567	40.4 (34.4-47.4)	43.8 (38.0-50.4)	50.7 (44.8-57.5)	46.8 (41.8-52.5)	52.1 (46.6-58.1)	0.06
MV adjusted	567	45.1 (37.5-54.3)	49.5 (41.3-59.3)	53.0 (44.8-62.6)	47.6 (41.1-55.2)	50.4 (43.3-58.7)	0.53

For multivariate adjusted model, data presented are mean predicted values for a participant with a prepregnancy BMI of 25.1, the mean for the study population, modeled using a 3-knot quadratic spline model for BMI, who is a white woman aged 35–40, has two children, has no parental history of diabetes, had normal glucose tolerance, and gained 15 kg during the index pregnancy.

*Partial F test *p* values for differences among categories.

^aResults presented for these biomarkers are geometric means. Because these outcomes were not normally distributed, they were modeled on the log scale. Predicted values are exponentiated for presentation to improve interpretability.

CI, confidence interval; HbA_{1c}, hemoglobin A_{1c}; MV, multivariate; SHBG, sex hormone = binding globulin.

postpartum BMI, and waist circumference (Table 5), we found no association between lactation duration and these outcomes in the multivariate model. Adjustment for BMI before pregnancy accounted almost entirely for the elimination of these associations. We observed no associations between breastfeeding duration and lipid metabolism (Table 6). We noted that women who breastfed for 3–<6 months had a consistently better metabolic profile than other groups, with the most favorable HbA_{1c}, HOMA-IR, fasting insulin, SHBG (Table 3), and HDL-C levels (Table 6), although only differences in HDL-C reached statistical significance. We hypothesized that differences in health behaviors might explain this finding, but adjustment for diet and physical activity at 6 months postpartum did not change the observed associations.

We found no dose-response association between duration of exclusive breastfeeding and glucose metabolism, lipid profile, or inflammatory markers; however, women who exclusively breastfed for longer periods had more favorable anthropometric measures, even after adjusting for prepregnancy BMI. Women who exclusively breastfed for >6 months had the lowest BMI at 3 years postpartum (multivariate adjusted predicted mean 25.2, 95% CI 24.0–26.4 kg/m² vs. 27.0, 26.0–28.1 kg/m² for those who either never breastfed or never exclusively breastfed, partial $F p = 0.05$) as well as the lowest postpartum weight retention at 3 years (multivariate adjusted predicted mean –0.5, –3.6–2.6 kg vs. 4.8, 2.0–7.6 kg for those who never exclusively breastfed, partial $F p = 0.03$). We found the smallest waist circumference among women who exclusively breastfed for 1–<3 months (83.9, 95% CI 81.6–86.2 cm vs. 89.4, 95% CI 86.2–92.5 cm for those who never breastfed or never exclusively breastfed, partial $F p = 0.01$).

Finally, we examined whether the relation between breastfeeding duration and metabolic markers differed for women at high risk of diabetes ($n = 312$) (Table 7). In this high-

risk group, we found an unexpected association between 3–<6 months of breastfeeding and several markers of glucose metabolism at 3 years postpartum. Women who breastfed for 3–<6 months had lower multivariate adjusted levels of HbA_{1c}, HOMA-IR, and fasting insulin than women with longer or shorter durations of breastfeeding. We also found higher levels of HDL-C in the 3–<6 months group. Among women at high risk for diabetes, we did not find an association between breastfeeding category and total cholesterol, LDL-C, triglycerides, inflammatory markers, or anthropometric measures.

Discussion

In a prospective cohort study, we did not find a dose-response association between duration of breastfeeding and markers of glucose and lipid metabolism at 3 years postpartum. Our finding of more favorable metabolic profiles among women who breastfed for 3–<6 months was unexpected and is likely the result of chance.

Strengths of our study include its prospective assessment of maternal BMI, weight change, health behaviors, and breastfeeding duration; standardized assessment of 3-year outcomes; and our very high rate of breastfeeding initiation and continuation. We also faced several limitations, including the relatively small number ($n = 175$) of participants with fasting blood samples, which may have limited our power to detect subtle differences among duration groups. However, our study is the largest, to our knowledge, to measure metabolic markers after weaning. The two other published studies included 109 and 27 women, respectively.^{4,11} We also had limited information on hormonal contraception use at the time of the 3-year visit. Adjustment for contraception use among those for whom data were available did not alter associations between lactation and outcomes, however, making

TABLE 4. MARKERS OF INFLAMMATION AT 3 YEARS POSTPARTUM, BY BREASTFEEDING DURATION, MEAN PREDICTED VALUES FROM LINEAR REGRESSION MODELS. DATA FROM 570 PARTICIPANTS IN PROJECT VIVA AT 3-YEAR POSTPARTUM FOLLOW-UP WITHOUT AN INTERVENING BIRTH

	n	Months of lactation					P*
		None Mean (95% CI)	>0– <3 Mean (95% CI)	3–<6 Mean (95% CI)	6– <12 Mean (95% CI)	12+ Mean (95% CI)	
CRP, mg/dL, ^a n		70	92	116	141	150	
Unadjusted	569	1.2 (0.9–1.7)	0.9 (0.7–1.2)	0.8 (0.6–1.0)	0.9 (0.7–1.1)	0.6 (0.5–0.8)	0.02
MV adjusted	569	1.1 (0.8–1.5)	0.8 (0.6–1.2)	0.8 (0.6–1.1)	1.0 (0.7–1.3)	0.8 (0.6–1.1)	0.34
Fasting IL-6 pg/mL, ^a N		16	30	40	38	51	
Unadjusted	175	1.2 (0.8–2.0)	1.2 (0.8–1.6)	1.0 (0.8–1.3)	1.1 (0.8–1.4)	1.1 (0.9–1.5)	0.93
MV adjusted	175	0.9 (0.5–1.5)	0.8 (0.5–1.3)	0.7 (0.5–1.1)	0.9 (0.7–1.3)	0.9 (0.6–1.3)	0.84

For multivariate adjusted model, data presented are mean predicted values for a participant with a prepregnancy BMI of 25.1, the mean for the study population, modeled using a 3-knot quadratic spline model for BMI, who is a white woman aged 35–40, has two children, has no parental history of diabetes, had normal glucose tolerance, and gained 15 kg during the index pregnancy.

*Partial F test p values for differences among categories.

^aResults presented for these biomarkers are geometric means. Because these outcomes were not normally distributed, they were modeled on the log scale. Predicted values are exponentiated for presentation to improve interpretability.

BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; IL-6, interleukin-6; MV, multivariate.

TABLE 5. ANTHROPOMETRIC MEASURES AT 3 YEARS POSTPARTUM, BY BREASTFEEDING DURATION, MEAN PREDICTED VALUES FROM LINEAR REGRESSION MODELS. DATA FROM 570 PARTICIPANTS IN PROJECT VIVA AT 3-YEAR POSTPARTUM FOLLOW-UP WITHOUT AN INTERVENING BIRTH

	n	Months of lactation					p*
		None Mean (95% CI)	>0–<3 Mean (95% CI)	3–<6 Mean (95% CI)	6–<12 Mean (95% CI)	12+ Mean (95% CI)	
BMI, kg/m ² , <i>n</i>							
Unadjusted	555	66 28.5 (27.1–29.9)	90 27.6 (26.4–28.8)	114 26.3 (25.3–27.4)	140 26.1 (25.1–27.0)	145 24.8 (23.8–25.7)	<0.0001
MV adjusted	555	26.1 (25.4–26.9)	25.3 (24.6–26.0)	25.5 (24.9–26.2)	25.8 (25.2–26.3)	25.4 (24.8–26.0)	0.17
Postpartum weight retention at 3 years, kg, <i>n</i>							
Unadjusted	557	67 3.7 (2.1–5.3)	90 1.8 (0.4–3.2)	113 2.9 (1.7–4.2)	140 2.4 (1.3–3.6)	147 1.8 (0.7–2.9)	0.28
MV adjusted	557	2.5 (0.6–4.3)	0.2 (–1.6–2.0)	0.9 (–0.8–2.6)	1.3 (–0.1–2.8)	0.4 (–1.2–1.9)	0.16
Subscapular:Triceps skinfold ratio, <i>n</i>							
Unadjusted	560	68 0.8 (0.8–0.9)	90 0.8 (0.8–0.8)	114 0.8 (0.8–0.8)	141 0.8 (0.7–0.8)	147 0.7 (0.7–0.8)	0.13
MV adjusted	560	0.8 (0.7–0.8)	0.7 (0.7–0.8)	0.7 (0.7–0.8)	0.7 (0.7–0.8)	0.7 (0.7–0.8)	0.49
Waist circumference, cm, <i>n</i>							
Unadjusted	562	68 92.4 (89.5–95.4)	91 89.2 (86.6–91.7)	114 86.9 (84.6–89.1)	141 86.1 (84.1–88.2)	148 84.0 (82.0–86.0)	<0.0001
MV adjusted	562	87.1 (85.0–89.2)	84.3 (82.3–86.4)	84.8 (82.9–86.7)	85.0 (83.4–86.7)	84.7 (83.0–86.4)	0.18

For multivariate adjusted model, data presented are mean predicted values for a participant with a prepregnancy BMI of 25.1, the mean for the study population, modeled using a 3-knot quadratic spline model for BMI, who is a white woman aged 35–40, has two children, has no parental history of diabetes, had normal glucose tolerance, and gained 15 kg during the index pregnancy.

*Partial F test *p* values for differences among categories.

BMI, body mass index; CI, confidence interval; MV, multivariate.

it unlikely that more complete information would change our results.

Our results contrast with epidemiological studies that have found a protective association between breastfeeding duration and metabolic disease risk. Authors have reported inverse associations between duration of lifetime breastfeeding and incidence of type 2 diabetes^{1,2} and myocardial infarction,⁶ as well as prevalence of the metabolic syndrome,⁵ hypertension,¹² hyperlipidemia, and cardiovascular disease.¹³ Several factors may explain our disparate results. In the cohort studies showing inverse associations between breastfeeding and metabolic disease, most participants gave birth between 1950 and 1980, an era when breastfeeding rates were at historic lows in the United States. In this time period, the decision to breastfeed may have been more strongly associated with other healthy behaviors, leading to greater confounding. In addition, our participants were recruited from a multi-specialty group practice that prides itself on outstanding breastfeeding support. In this setting, a mother's decision to initiate and continue breastfeeding may be less related to other health behaviors, reducing unmeasured confounding and, thus, attenuating associations between breastfeeding and health outcomes.

In addition, we assessed intermediate end points, and it is possible that other biomarkers not measured in our study underlie associations between breastfeeding and diabetes or

cardiovascular risk. It is unlikely, however, that such factors would be completely uncorrelated with the numerous markers of glucose and lipid metabolism, inflammation, and anthropometry assessed in our study. It is also possible that greater breastfeeding intensity would be associated with greater changes in metabolic markers. However, rates of breastfeeding in our cohort exceeded those in the general U.S. population,¹⁴ and we did not find evidence of a stronger association between exclusive breastfeeding and outcome. Finally, it is possible that women in our study are too healthy to allow us to detect differences in the assessed markers. Among the 91 women aged 30–39 for whom we had data on waist circumference, blood pressure, serum lipids, and glucose, only 5 (5.5%, 95% CI 1.8–12.4%) met criteria for the metabolic syndrome, compared with 15% of women in this age range in the general U.S. population.¹⁵ Among relatively healthy women, metabolic differences related to breastfeeding duration may be too small to be detected. The nature of our study population may, therefore, limit generalizability of our findings.

Only two other studies, to our knowledge, have directly examined the relation between breastfeeding and metabolic markers after weaning. Kallio et al.¹¹ examined longitudinal changes in total cholesterol among exclusively breastfeeding women (*n* = 27). Levels declined from delivery until 6 months postpartum and remained stable through 9 months of

lactation. Two months after weaning, cholesterol levels rose to delivery levels and were similar 5 years later. Gunderson et al.⁴ examined 3-year changes in lipid and glucose metabolism between prepregnancy and postweaning among 109 women in the CARDIA cohort. Among breastfeeders, prepregnancy to postweaning LDL-C decreased slightly, compared with an increase among women who had given birth but never breastfed (-0.8 mg/dL vs. 6.7 mg/dL, $p = 0.045$). Women who breastfed for >3 months had more favorable changes in HDL-C levels than women who breastfed <3 months (<3 months, HDL-C, -7.3 mg/dL; ≥ 3 months, HDL-C, -1.3 mg/dL, $p < 0.01$). Also, there were trends toward more favorable changes in waist girth and total cholesterol, LDL-C, triglyceride, and fasting glucose levels in the longer lactation group. Differences in prepregnancy to postlactation weight change did not explain these associations, which were adjusted for age, BMI, race, education, parity, smoking, oral contraceptive use, and time since weaning to the examination.

In contrast to the CARDIA cohort, we did not measure metabolic markers before pregnancy. Our cross-sectional design does not allow us to detect intraindividual changes in metabolic markers with pregnancy and lactation. However, metabolic markers are highly correlated with BMI, and we found that adjustment for prepregnancy BMI effectively eliminated any suggestion of a protective association between breastfeeding and postpartum metabolic risk. This attenu-

tion of effect suggests that differences in metabolic markers are more likely to be related to prepregnancy maternal adiposity rather than lactation. Breastfeeding rates also differed in the two study populations. In Project Viva, 86% of women initiated breastfeeding, and 70% continued for ≥ 3 months, compared with 56% initiation and 39% continuation in CARDIA.

We found that prepregnancy BMI was inversely related to duration of breastfeeding in our cohort, consistent with multiple studies relating obesity to lower initiation and shorter duration of breastfeeding.^{16–20} After adjustment for pregravid BMI, total breastfeeding duration was not associated with maternal anthropometry at 3 years postpartum; however, exclusive breastfeeding duration was associated with maternal weight at follow-up. In multivariate adjusted models, we found that women who exclusively breastfed for ≥ 6 months had the lowest postpartum weight retention and BMI at 3 years postpartum. These results are consistent with recent findings from the Danish National Birth Cohort,²¹ where the authors found that >6 months of exclusive breastfeeding was associated with a reduced risk of postpartum weight retention.

In an unexpected finding, we saw the most favorable metabolic profile among women who breastfed for 3– <6 months. This pattern was more pronounced among women who were at increased risk of developing type 2 diabetes.

TABLE 6. MARKERS OF LIPID METABOLISM AT 3 YEARS POSTPARTUM, BY BREASTFEEDING DURATION; MEAN PREDICTED VALUES FROM LINEAR REGRESSION MODELS. DATA FROM 570 PARTICIPANTS IN PROJECT VIVA AT 3-YEAR POSTPARTUM FOLLOW-UP WITHOUT AN INTERVENING BIRTH

		Months of lactation					p*
	n	None Mean (95% CI)	>0 – <3 Mean (95% CI)	3 – <6 Mean (95% CI)	6 – <12 Mean (95% CI)	12 + Mean (95% CI)	
Total cholesterol, mg/dL							
Unadjusted	175	167.1 (152.2–182.0)	181.6 (170.7–192.4)	176.5 (167.1–185.9)	177.5 (167.9–187.2)	179.2 (170.9–187.5)	0.63
MV adjusted	175	161.6 (143.4–179.8)	174.9 (158.9–191.0)	172.6 (159.4–185.8)	175.3 (163.3–187.3)	173.3 (159.6–187.0)	0.63
LDL-C, mg/dL							
Unadjusted	175	101.6 (88.0–115.2)	111.4 (101.4–121.3)	102.8 (94.2–111.4)	106.9 (98.0–115.7)	109.6 (102.0–117.3)	0.61
MV adjusted	175	92.1 (75.7–108.4)	102.6 (88.1–117.0)	95.8 (83.9–107.7)	104.3 (93.5–115.0)	103.1 (90.8–115.3)	0.39
HDL-C, mg/dL							
Unadjusted	175	51.6 (45.8–57.4)	51.7 (47.5–56.0)	57.9 (54.2–61.6)	53.4 (49.6–57.1)	52.4 (49.1–55.6)	0.14
MV adjusted	175	56.8 (50.5–63.2)	55.6 (50.0–61.2)	61.0 (56.4–65.7)	54.2 (50.0–58.4)	52.2 (47.4–56.9)	0.003
Triglycerides, mg/dL ^a							
Unadjusted	175	67.8 (54.3–84.5)	80.6 (68.5–94.7)	69.2 (60.1–79.5)	82.6 (71.5–95.3)	79.0 (69.8–89.4)	0.31
MV adjusted	175	64.6 (49.8–83.7)	78.5 (62.5–98.7)	71.0 (58.8–85.8)	81.9 (69.0–97.2)	83.4 (68.6–101.3)	0.16

For multivariate adjusted model, data presented are mean predicted values for a participant with a prepregnancy BMI of 25.1, the mean for the study population, modeled using a 3-knot quadratic spline model for BMI, who is a white woman aged 35–40, has two children, has no parental history of diabetes, had normal glucose tolerance, and gained 15 kg during the index pregnancy.

*Partial F test p values for differences among categories.

^aResults presented for these biomarkers are geometric means. Because these outcomes were not normally distributed, they were modeled on the log scale. Predicted values are exponentiated for presentation to improve interpretability.

BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MV, multivariate.

TABLE 7. MARKERS OF GLUCOSE AND LIPID METABOLISM AT 3 YEARS POSTPARTUM, BY BREASTFEEDING DURATION, MEAN PREDICTED VALUES FROM LINEAR REGRESSION MODELS. DATA FROM 312 PARTICIPANTS IN PROJECT VIVA AT 3-YEAR POSTPARTUM FOLLOW-UP WITHOUT AN INTERVENING BIRTH AND AT HIGH RISK OF DIABETES, DEFINED AS BMI ≥ 25 , ABNORMAL GLUCOSE TOLERANCE DURING PREGNANCY, OR FAMILY HISTORY OF DIABETES

		Months of lactation					
	n	None Mean (95% CI)	>0-<3 Mean (95% CI)	3-<6 Mean (95% CI)	6-<12 Mean (95% CI)	12+ Mean (95% CI)	p*
Glucose metabolism, n							
HbA _{1c} , %		49	52	63	74	71	
Unadjusted	309	5.12 (5.04-5.20)	5.23 (5.16-5.31)	5.09 (5.02-5.16)	5.18 (5.12-5.25)	5.14 (5.08-5.21)	0.07
MV adjusted	309	5.03 (4.94-5.12)	5.10 (5.00-5.19)	4.95 (4.86-5.04)	5.08 (5.00-5.16)	5.03 (4.95-5.11)	0.01
HOMA-IR, ^a n		12	16	21	24	24	
Unadjusted	97	2.1 (1.5-3.1)	2.4 (1.8-3.3)	1.2 (0.9-1.6)	1.9 (1.4-2.4)	1.8 (1.4-2.4)	0.03
MV adjusted	97	1.5 (0.9-2.3)	1.7 (1.1-2.7)	0.9 (0.6-1.2)	1.4 (1.1-2.0)	1.6 (1.1-2.2)	0.003
Fasting insulin, μ /mL ^a							
Unadjusted	97	11.9 (8.4-16.9)	13.0 (9.7-17.6)	7.3 (5.6-9.6)	9.8 (7.6-12.5)	9.6 (7.5-12.3)	0.06
MV adjusted	97	8.0 (5.4-12.0)	9.0 (6.2-13.2)	5.0 (3.7-6.7)	7.6 (5.8-10.0)	8.1 (5.9-11.1)	0.008
Fasting glucose, mg/dL							
Unadjusted	97	73.8 (65.7-82.0)	78.2 (71.2-85.2)	69.2 (63.1-75.4)	79.4 (73.6-85.1)	78.5 (72.8-84.3)	0.13
MV adjusted	97	74.6 (63.0-86.2)	79.1 (68.0-90.2)	70.2 (61.6-78.8)	77.5 (69.5-85.4)	78.9 (69.8-88.1)	0.28
Lipid metabolism, n							
Total cholesterol mg/dL		12	16	21	24	24	
Unadjusted	97	173.0 (156.4-189.6)	182.6 (168.2-197.0)	169.8 (157.2-182.4)	183.1 (171.3-194.8)	178.1 (166.4-189.9)	0.55
MV adjusted	97	171.8 (148.2-195.4)	173.0 (150.4-195.5)	164.7 (147.2-182.2)	181.6 (165.5-197.8)	177.9 (159.2-196.6)	0.4
LDL-C, mg/dL							
Unadjusted	97	108.2 (93.0-123.4)	112.2 (99.0-125.4)	97.8 (86.3-109.3)	112.6 (101.8-123.4)	110.7 (99.9-121.5)	0.37
MV adjusted	97	103.5 (82.7-124.3)	103.0 (83.1-122.9)	91.3 (75.9-106.8)	110.2 (96.0-124.4)	110.1 (93.7-126.6)	0.13
HDL-C, mg/dL							
Unadjusted	97	49.9 (43.5-56.3)	48.5 (42.9-54.0)	55.4 (50.6-60.3)	52.1 (47.5-56.6)	49.9 (45.3-54.4)	0.37
MV adjusted	97	50.8 (42.7-58.9)	49.0 (41.3-56.8)	56.2 (50.1-62.2)	51.4 (45.8-56.9)	46.0 (39.6-52.4)	0.04
Triglycerides, mg/dL ^a							
Unadjusted	97	74.5 (56.5-98.1)	86.4 (68.0-109.7)	69.2 (56.2-85.2)	88.5 (72.8-107.6)	84.5 (69.5-102.7)	0.44
MV adjusted	97	80.4 (56.0-115.4)	83.3 (59.0-117.7)	72.5 (55.4-94.8)	91.6 (71.6-117.2)	96.8 (72.7-128.8)	0.27

For multivariate adjusted model, data presented are mean predicted values for a participant with a prepregnancy BMI of 28.0, the mean for women in the high-risk group, modeled using a 3-knot quadratic spline model for BMI, who is a white woman aged 35-40, has two children, has no parental history of diabetes, had normal glucose tolerance, and gained 14.4 kg during the index pregnancy.

^aPartial F test *p* values for differences among categories.

^aResults presented for these biomarkers are geometric means. Because these outcomes were not normally distributed, they were modeled on the log scale. Predicted values are exponentiated for presentation to improve interpretability.

BMI, body mass index; CI, confidence interval; HbA_{1c}, hemoglobin A1C; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Although women who continued to breastfeed beyond 6 months walked less, were less likely to be trying to lose weight, and consumed a higher glycemic index diet, adjustment for these behaviors did not attenuate our findings. The unexpectedly beneficial metabolic profile in this group was

probably a chance finding. Further studies are needed to explore the relation between lactation beyond 6 months and maternal metabolism.

In conclusion, in a prospective study of maternal and infant health, we did not observe a protective association between

duration of breastfeeding and markers of maternal metabolism, inflammation, or anthropometry at 3 years postpartum. We did not find evidence that beneficial lactation-related changes in glucose and lipid metabolism persist beyond weaning. Further studies will be needed to assess whether lactation duration impacts other metabolic biomarkers.

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Disclosure Statement

The authors have no conflicts of interest to report.

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Address correspondence to:
Alison M. Stuebe, M.D., M.Sc.

Assistant Professor

Division of Maternal-Fetal Medicine

Department of Obstetrics and Gynecology

School of Medicine

University of North Carolina at Chapel Hill

3010 Old Clinic Building, CB#7516

Chapel Hill, NC 27599-7516

E-mail: astuebe@med.unc.edu