Breastfeeding Status and Maternal Cardiovascular Variables Across the Postpartum

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Abstract

Background: There have been recent reports that lactational history is associated with long-term women's health benefits. Most of these studies are epidemiological. If particular cardiometabolic changes that occur during lactation ultimately influence women's health later is unknown.

Methods: Seventy-one healthy women participated in a prospective postpartum study that provided an opportunity to study anthropometric, endocrine, immune, and behavioral variables across time. Variables studied were heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), C-reactive protein, body mass index (BMI), perceived stress, and hormones. A cohort of women without a change in breastfeeding ($N=22$) or formula feeding ($N=23$) group membership for 5 months was used for analysis of effects of feeding status. The data were analyzed using factorial repeated measures analysis of variance and analysis of covariance.

Results: SBP and HR declined across the postpartum and were significantly lower in breastfeeding compared to formula feeding mothers ($p<0.05$). These differences remained statistically significant when BMI was added to the model. Other covariates of income, stress, marital status, and ethnicity were not significantly associated with these variables over time. DBP was also lower, but the significance was reduced by the addition of BMI as a covariate. Stress also was lower in breastfeeders, but this effect was reduced by the addition of income as a covariate.

Conclusions: These data suggest that there are important physiological differences in women during months of breastfeeding. These may have roles in influencing or programming later risks for a number of midlife diseases.

Introduction

THE BENEFITS OF BREASTFEEDING for infant health are well known, but recently there have been reports describing associations of lactation with longer term women's health.¹ Short-term relationships include reductions in stress responsivity, decreased blood pressure, reduced infectious symptoms, more positive moods, pregnancy-associated weight loss, and fertility control.²⁻⁷ These effects may be related to parasympathetic activation,⁶ endocrine factors,⁸ and oxytocinergic mechanisms⁹ during lactation. The long-term relationships of breastfeeding to later women's health now appear to include substantial reductions in the risks of certain cancers, cardiovascular disease, hypercholesterolemia, type 2 diabetes, and metabolic syndrome.¹⁰⁻¹² The magnitude of the

association generally depends on the length of time a woman lactated during her reproductive years. Metabolic, endocrine, neurological, immune, epigenetic, and proteomic programming during lactation may contribute to health later in life. It also is important to ascertain whether the association of lactation with later cardiovascular health derives from healthier lifestyles in women who choose to breastfeed.

Our lab had the opportunity to examine healthy postpartum women by lactational status in a prospective study over the first five postpartum months. The aims of this analysis were to determine if breastfeeding women demonstrated differences in body mass index (BMI), blood pressure, heart rate, moods, stress, and inflammatory biomarkers over the postpartum compared to women who were not breastfeeding. We also sought to determine if these variables were

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related to each other over time as well as to reproductive endocrine status.

Methods

Participants

Institutional review board approval was achieved, and informed consent was gathered during pregnancy, with permission for later postpartum follow-up. Study participants were the comparison group in a study of women at risk for the development of postpartum thyroiditis, as determined by the presence of the antibody to thyroid peroxidase (TPO) during pregnancy. Pregnancy BMIs were extracted from the charts. No other biomarkers were routinely collected during pregnancy. All subjects in the present study (the comparison group) were TPO antibody negative. Exclusion criteria were BMI < 20, age < 18 or > 45 years, known autoimmune disease, previous thyroid disease, HIV positivity, use of medications that affect immunity, chronic diseases such as diabetes, and fetal abnormalities. The initial sample was recruited from a cohort of 631 women tested for the TPO antibody after the 16th week of pregnancy. The comparison group in this study ($n=71$) was selected from the majority who tested TPO negative ($n=568$) using a random number generator. Women recruited into this study received a home visit by a research nurse 1 week after birth and then at months 1 through 6. The visits always took place between 8:00 am and 12:00 noon. Participants received a graduated honorarium totaling \$200 for completion of all 6 months of data collection. Sixty-five of the 71 women completed the entire study. Most of those who did not complete the study dropped out because they had moved to a different location. There were no statistically significant differences in demographics in these six women compared to the group as a whole. They dropped out of the study at the third month ($n=3$), the fourth month ($n=2$), or the fifth month ($n=1$). One was exclusively breastfeeding, and of the remainder, three had stopped breastfeeding and two were formula feeders.

For a repeated measures analysis participants' data were used only if their feeding group did not change across time. However, we analyzed only from month 1 through month 5 because the numbers in the breastfeeding group diminished greatly at the sixth month. Women were classified as breastfeeders if they were breastfeeding exclusively or were high partial breastfeeders according to the well-established Labbok definitions.¹³ High partial breastfeeders provide the majority of calories from human milk, so we excluded mothers who reported giving more than 300 mL of formula per day at each monthly visit over the first five postpartum months. We implemented a conservative form of this classification in that women were considered breastfeeders only if they continued breastfeeding over the entire 5-month observation window; 22 of 48 women who initiated breastfeeding were still doing so at month 5. There were 23 women who were formula feeding from the first postpartum month through 5 months. Most of these women had not breastfed at all, although 9 of the 23 women had attempted to breastfeed and stopped between the 1-week and 1-month visits. The data were analyzed with the inclusion of women who presented at week 1 and remained throughout the postpartum with hypertension ($n=2$, systolic blood pressure [SBP] > 140, diastolic blood pressure [DBP] > 90). It was observed that the

BMI of both of these women was in the severe (BMI of 39) or morbidly obese (BMI of 42) range. One woman was categorized as a breastfeeder and one as a formula feeder. The results of the analyses did not differ whether these women were included or excluded.

Instruments

At the first visit participants completed a demographic questionnaire and then at each subsequent visit they completed the Perceived Stress Scale (PSS).¹⁴ PSS assesses levels of self-reported stress. The 14-item version of the scale evaluates perceptions of stress with a Likert scale ranging from 0 (never) to 4 (very often). The internal consistency reliability was reported to be 0.84 to 0.86 in young adults. Congruent and criterion validity for the scale are considered excellent, although predictive validity declines over time.¹⁴

Data on birth history, breastfeeding status, medications, health behaviors and health status, birth histories, hours worked outside the home, and alcohol and tobacco use were collected with an investigator-developed instrument. Most of the health-related behaviors were related to thyroid function and collected with a Thyroid Symptom Checklist. However additional data were collected on weekly hours and types of regular exercise each month as well as on smoking behaviors and working status. We did not collect data about when the mothers had last fed their infants.

Procedures

At each home visit, participants received a targeted physical examination, and body weight, heart rate, and blood pressure were measured. They also completed the instruments in the study. A calibrated aneroid sphygmomanometer was used to measure blood pressure and women were seated for 5 minutes before measurement. Hematocrit was assayed, and if the participant's hematocrit exceeded 34%, a venipuncture was done and 15 mL of blood was drawn into heparinized vacutainers. The blood was collected aseptically and transported in a cooler to the laboratory within the following 2 hours. Immediately upon receipt, blood was centrifuged at 2000 g for 25 minutes at 4°C, the plasma aliquotted into multiple Eppendorf tubes, and frozen at -80°C until later batch analysis.

High sensitivity C-reactive protein (HS-CRP) was measured by enzyme-linked immunosorbent assay (ELISA; DRG, Mountainside, NJ) according to kit directions. Hormones were measured by ELISA, according to kit directions at months 1, 3, and 6, and included cortisol (ALPCO, St. Louis, MO), estradiol, progesterone (DRG), and prolactin (Calbiotech, Spring Valley, CA). Coefficients of variation for these assays were under 10%.

Statistical analysis

Descriptive statistics, including summary statistics and Pearson product-moment correlation coefficients, were first computed to help us understand the data to build statistical models. Logarithmic transformation was applied to those measures that did not meet the normality assumption.

The data were analyzed using a 2×5 (group by time point) factorial repeated measures analysis of variance (ANOVA). Separate analyses were conducted on each of the dependent

variables (SBP, DBP, heart rate, BMI, and HS-CRP). This approach permitted us to assess group differences (main effect, collapsed over time) as well as differences in the patterns of change over time (interaction effect). Between-subjects differences were tested using main effect of group, while within-subjects differences were tested using the main effect of time and group by time interaction. This approach does not permit missing data. The correlation structure assumed was compound symmetry, and where sphericity was violated Greenhouse-Geiser corrections were applied. To address confounding due to baseline differences between formula feeders and breastfeeders, significant group differences were reassessed in the presence of covariates. When bivariate associations were observed (using a threshold correlation coefficient ≥ 0.20 in absolute magnitude), they were treated as covariates and added to multivariate models. We treated income and education as continuous variables. If a covariate was determined to be a potential confounder (as already stated), it was added to the ANOVA model to assess whether it was significant ($p < 0.05$) in the context of the independent factors, and to assess whether its inclusion resulted in a substantial change in the test of our main effect and interaction terms. We report both the significance test for the covariate and the test of significance for the hypothesized presence of the covariate. Data analyses were performed using SPSS 20.

Cronbach's alpha was computed for the PSS.

Results

Participants

The 45 participants in the two groups differed in ethnicity. There were fewer whites in the formula group (43% compared to 57% in the breastfeeding group) and more African Americans in the formula feeding group (24% compared to 10% in the breastfeeding group) and the same percentage of Hispanics (29%). The breastfeeders were older (28.5 years compared with 26.4 years; $t = 3.6$, $p < 0.001$). They also had higher incomes ($t = 2.4$, $p = 0.03$) and were more likely to be married ($t = 2.7$, $p = 0.009$). Demographic data are presented in Table 1.

TABLE 1. WOMEN WHO BREASTFED FOR 5 MONTHS COMPARED WITH WOMEN WHO STOPPED BREASTFEEDING BEFORE 1 MONTH

	Formula feeding (n=23)	Breastfeeding (n=22)	Stopped breastfeeding (n=9)
Age, years	26	28.5	25.9
Income > \$40,000	—	17	3
Vaginal delivery	—	14	7
Pregnancy BMI	30.6	28.1	31.6
Marital status			
Divorced	9	2	3
Married	14	18	6
No. of children	1.84	1.83	1.22
College graduate	11	18	4
Smoker	1	0	1
Working full time	8	1	2
Exercise > 1 h/week	1	2	0

BMI, body mass index.

We did a separate analysis of the data from the nine women who had begun to breastfeed in the first weeks but abandoned breastfeeding entirely by month 1, and were therefore classified as formula feeders in our analyses, to determine if they were a very different cohort (Table 1). They were younger (25.9 years) and heavier (BMI=31.6) but none of the demographics were significantly different from the group as a whole.

SBP, DBP, HR, BMI, CRP, and stress were compared by *t*-tests at week 1 postpartum between the individuals who would ultimately comprise the two feeding groups. This was done because we did not form the feeding groups for analysis until 1 month postpartum. None of these variables were significantly different at week 1.

Blood pressure

There were no significant within-subjects or interaction effects with SBP. There was a significant between-subjects effect on SBP ($F_{1,43} = 6.15$, $p = 0.017$). Breastfeeders had lower SBP across the postpartum compared to formula feeders. Analyses were done with covariates of income and BMI entered separately. BMI and income were entered as continuous variables. Only BMI added to the model had a significant relationship with SBP ($F_{1,42} = 7.4$, $p = 0.009$), which reduced the relationship of breastfeeding to the following: ($F_{1,42} = 4.05$, $p = 0.049$; Fig. 1). DBP was also lower for the breastfeeding

FIG. 1. Systolic blood pressure (SBP) by feeding group across the postpartum. Error bars are standard errors of the means. The graph represents the differences between groups after controlling for BMI.

FIG. 2. Diastolic blood pressure (DBP) by feeding group across the postpartum. Error bars are standard errors of the means. The graph represents the differences between groups after controlling for BMI.

group ($F_{1,43}=5.18, p=0.03$). However, when BMI was added to the model ($F_{1,42}=4.6, p=0.04$) it reduced the effect of breastfeeding on DBP ($F_{1,42}=3.44, p=0.07$; Fig. 2).

Heart rate

There were no within-subjects effects or interactions. Heart rate was lower across time for the breastfeeding group ($F_{1,43}=4.97, p=0.03$; Fig. 3). Covariates of income and stress scores were added to the analysis and were not significant. BMI did have a significant relationship with heart rate ($F_{1,42}=4.18, p=0.047$), but breastfeeding status remained significant when BMI was added to the model ($F_{1,42}=3.95, p=0.049$).

Body mass index

The BMI of the breastfeeding group dropped nearly one BMI point over time (from 27.7 at month 1 to 26.8 at month 5) compared with no change in the formula feeding group. However, these were not statistically significant differences ($F_{1,42}=2.0, p=0.16$; Fig. 4).

Perceived stress

The Cronbach's alpha reliability for the PSS in this population was 0.89. The perceived stress scores of breastfeeders compared to formula feeders differed significantly across time

FIG. 3. Heart rate by feeding group across the postpartum. Error bars are standard errors of the means. The graph represents the differences between groups after controlling for BMI.

FIG. 4. BMI by feeding group across the postpartum. Error bars are standard errors of the means.

($F_{1,42}=4.3$, $p=0.04$). However, this relationship disappeared when income was added to the model, with income having a significant effect ($F_{1,42}=4.9$, $p=0.03$).

C-reactive protein

CRP levels were lower in breastfeeders compared with formula feeders across the postpartum, but this was not statistically significant. BMI was highly correlated with CRP across all time points ($r=0.39$ to 0.5 , $p=0.001$ to 0.002).

Hormones

Prolactin was significantly higher in breastfeeders compared to formula feeders at every time point. Estradiol was lower at every time point for breastfeeders, and this reached statistical significance only at month 1. Progesterone and cortisol levels did not differ by group. Total plasma cortisol was measured, which reflected both free and bound hormone and therefore may not have given an accurate estimate of available cortisol. However, there were no direct relationships with the hormones measured and the cardiovascular or anthropometric variables.

Effect sizes

Partial eta-squared (η^2) effect sizes for all F tests reported are the following: SBP, $F_{1,43}=6.15$, $\eta^2=0.125$; $F_{1,42}=7.40$, $\eta^2=0.150$; $F_{1,42}=4.05$, $\eta^2=0.088$; $F_{1,43}=5.18$, $\eta^2=0.108$; $F_{1,42}=4.60$, $\eta^2=0.099$; $F_{1,42}=3.44$, $\eta^2=0.076$; heart rate: $F_{1,43}=4.97$, $\eta^2=0.104$; $F_{1,42}=4.18$, $\eta^2=0.091$; $F_{1,42}=3.95$, $\eta^2=0.086$; BMI: $F_{1,42}=2.00$, $\eta^2=0.045$; perceived stress: $F_{1,42}=4.30$, $\eta^2=0.093$; $F_{1,42}=4.90$, $\eta^2=0.104$.

Discussion

Accumulating evidence suggests that a history of lactation in women is associated with decreased risk for later midlife diseases such as diabetes, cardiovascular disease, and metabolic syndrome.^{10,15–20} A relationship between lower blood pressure and breastfeeding has been previously described. A recent chart review of data from 407 mothers at 1 month postpartum found very similar results to the data reported here for SBP, with breastfeeders having lower SBP than mixed feeders and formula feeders. Importantly, these mothers did not vary in blood pressure during the last trimester.²¹ While we do not have data from pregnancy, we did have measures at week 1 postpartum, and SBP and DBP did not differ between the groups at that point in time. In another study of mothers in the laboratory, SBP was lower after baby contact.² Breastfeeding mothers had lower blood pressure during speech stress sessions and after nursing their infants at home. Oxytocin was measured in this study and results suggest that oxytocin had antistress and blood pressure-lowering effects. In a more recent study, early postpartum mothers provided multiple blood samples for oxytocin, prolactin, and norepinephrine while they were being monitored for cardiovascular responsivity to laboratory stressors. In this study, oxytocin appeared to modulate cardiovascular responses to stressors.⁹

Oxytocin is a hormone associated with affiliative behaviors and cardiovascular tone, along with its well-known role in milk let-down and sexual response. Oxytocin synthesis and receptors are found in both the heart and vascular tissue.

Animal studies suggest that oxytocin activates an “antistress” response that reduces cardiovascular and neuroendocrine stress reactivity. Reduced autonomic activity to stress has been found in women during the time they are actually suckling an infant.^{2,22} More persistent or long-term effects on stress reactivity in lactating human mothers, compared to animal models, have not been well characterized. The persistently lower SBP and heart rates of lactating women found in this study suggests that breastfeeding may be associated with increased vagal tone or may be mediated by oxytocinergic mechanisms.

A number of epidemiologic studies have been done that demonstrate long-term relationships between lactation and blood pressure. One large cohort study of Korean women found that breastfeeding decreased the risk of hypertension in a 6-year follow-up, and the longer the lactational period, the greater this effect.²³ Both SBP and DBP were lower in women with a history of consistent lactation compared with inconsistent lactation or no lactation as measured in the Study of Women’s Health Across the Nation (SWAN) study, which enrolled 3302 women who were 42 to 52 years of age. This study provided an opportunity to examine the relationship between lactational history and preclinical indicators of cardiovascular disease in women.¹⁰ Women who breastfed for at least 3 months had significantly reduced aortic and coronary artery calcification compared to nonbreastfeeding women. This effect remained highly significant after adjusting for lifestyle, BMI, and other traditional risk factors for cardiovascular disease.

The Nurses’ Health Study also examined relationships between breastfeeding and cardiovascular disease.²⁴ A total of 89,326 parous women were eligible, and history of breastfeeding was available for 63% of them. An inverse association between long duration of lactation and myocardial infarction was found. The strongest protective relationship with myocardial infarction was found for women who had breastfed for over 23 months, suggesting a threshold of protection.

The effects of lactation on both concurrent and long-term blood pressure levels may represent independent pathways affecting cardiovascular physiology. There may be resetting of pathways through lactational hormones, metabolic and adipokine changes, autonomic effects, or neurological alterations. On the other hand, women who choose to breastfeed may be inherently different than nonbreastfeeding mothers. Breastfeeding women are more likely to be younger, married, and white and of higher socioeconomic status. This was true in our study as well. They also may be more likely to be thinner, exercise more, and have healthier lifestyles. All studies investigating an independent effect of lactation must adjust for these factors. It is not always possible to adjust for all these factors in a large data set, but most studies, including the one reported here, have attempted to control for some of these influences.

CRP was also highly and significantly correlated with BMI in the sample. BMI was lower and decreased over time in breastfeeders compared with the formula feeders. These effects did not reach statistical significance, perhaps due to sample size, but a one point drop in BMI is clinically significant. CRP is an inflammatory biomarker that is high in pregnancy and remains high during the early postpartum. CRP has a role in the clearance of bacteria and of dying and altered cells. A major role is in activation of complement. CRP

serum levels rise in response to bacterial infection, trauma, tissue necrosis, obesity, and inflammation.²⁵ The findings suggest that heavier women may have an increased inflammatory state during the postpartum.

Limitations

The study has several limitations that may potentially affect its generalizability. The two-group design of women who were consistently either breastfeeding or formula feeding for the 5 months of measurement was a requirement for the repeated measures approach. This study was exploratory in order to determine if there were effects observed in a fairly small group. This approach necessarily eliminated the partial breastfeeding group and women who dropped breastfeeding along the postpartum trajectory, about 26% of the women enrolled in this comparison group. Our analyses do not address any health or anthropometric variables in these partial breastfeeders or women breastfeeding for shorter periods than 5 months. Larger sample sizes will permit more extensive exploration of these multiple groups across time. The effects sizes we observed were small, suggesting that multiple variables are involved and larger sample sizes are needed to confirm the findings.

New methods for measuring oxytocin are becoming available, and these data would be informative because our data suggest a possible oxytocinergic or parasympathetic effect. Standardization of the time of feeding would also improve the study. Our mothers fed their infants before the measurements, but the interval between feeding and measurement was not standardized. The measurements were only done over five postpartum months, and it would be of interest to observe how long these differences exist. Our lab intends a longer follow-up of our participants in order to determine the duration of these changes.

Better health behavior instruments should be employed in future studies to more accurately determine the effects of lifestyle on effects associated with feeding status.

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Author Disclosure Statement

None of the authors have any competing financial interests that might create a conflict of interest.

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