The Relationship between Pre-Pregnancy BMI, Pregnancy-Related Breast Changes, and Postpartum Onset of Lactogenesis II

by

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Background: Lactogenesis-II (LII) marks the onset of copious milk secretion postpartum. High pre-pregnancy body mass index (BMI) is linked with delayed lactogenesis II (DLII) and subsequent breastfeeding challenges. Prenatal breast changes may be early phenotypic markers for delayed lactogenesis. **Purpose:** To examine the relationship between pre-pregnancy BMI, prenatal breast changes, and postpartum onset of lactogenesis II. **Methods:** This is a secondary analysis of a prospective randomized trial of a breastfeeding support intervention for 250 first-time birthing parents. Participants were surveyed on observed breast changes at 13-25 and 34-36 gestational weeks and onset of LII in postpartum days at one week postpartum. Delayed lactogenesis was operationalized as ≥ 4 days postpartum. Pre-pregnancy BMI was abstracted from the health record. Relationships between BMI, prenatal breast changes, and DLII were examined with contingency tables and chi-square statistics. Bonferroni corrections were made for comparisons evaluating relationships between breast changes and BMI and between breast changes and DLII (α=.004). **Results:** Overall, there were few differences in self-reported breast changes during pregnancy between BMI groups. One exception was that more participants in the normal/underweight group, compared to overweight and obese participants, experienced breast growth by the second trimester ($p<0.001$). However breast growth in pregnancy was not associated with onset of LII. Although prevalence of leaking milk in pregnancy did not vary between BMI groups, it was positively associated with normal onset of LII, without the Bonferroni adjustment (unadjusted $p=0.02$). The majority of participants experienced LII on days 3 or 4 postpartum. About 30% of obese participants experienced LII >4 days postpartum, with a dose-response effect observed between

increasing pre-pregnancy BMI and higher prevalence of LII beyond 4 days postpartum. **Conclusions**: Delayed lactogenesis-II has been defined as ≥4 days postpartum, but these data suggest that 4 days may be typical for first-time birthing parents regardless of BMI. Obese first-time birthing parents may be less likely to experience early pregnancy breast growth and more likely to experience onset of LII past 4 days postpartum or not at all. Regardless of observable breast changes, first-time birthing parents with high BMI may need increased lactation support.

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Preface

I would like to thank everyone who has helped me and supported me on this endeavor. This research is a secondary analysis of data from a parent study on "The Development and Evaluation of a Text Message Program to Prevent Perceived Insufficient Milk Among First-Time Mothers," for which Jill R. Demirci PhD, RN, IBCLC was the principal investigator. I have always had a personal interest in breastfeeding and the pediatric population, and I am very grateful to Jill Demirci for granting me permission to conduct this research using her study database and sharing her knowledge with me. I also want to thank Jill Demirci for being my Thesis Advisor and for all her guidance, mentorship, and patience over the past three years in the Undergraduate Research Mentorship Program.

Thank you also to my external thesis committee member, Dr. Laura Kair M.D., M.A.S, the Medical Director of Well Newborn Care at UC Davis Children's Hospital. Dr. Kair works clinically on the mother-baby postpartum unit and as a pediatric hospitalist, as well as conducting clinical research focused on overcoming breastfeeding barriers and disparities. Her expertise in this area and clinical experience were valuable to this project. I also want to thank Susan Sereika, PhD for taking the time to guide me through the statistical process and create the data set for my project. The statistical analyses would not have been possible without her guidance. Also, thank you to Cynthia Chew DNP, CPNP-PC, IBCLC for teaching me about maternal changes throughout pregnancy and newborn nutrition in her obstetrics course. Dr. Chew's knowledge and experience as both an assistant professor and Pediatric Nurse Practioner served as an asset to this project.

1.0 Introduction

Breastfeeding offers both infant and lactating parent many short-term and long-term health benefits. Breastfed infants have fewer ear infections, fewer colds and viruses, and lower rates of childhood obesity, diabetes, infant mortality, and sudden infant death syndrome. Birthing parents who breastfeed have a lower risk of developing type 2 diabetes, subclinical and clinical cardiovascular disease (Gunderson et al., 2015; McClure et al., 2012; Perrine et al., 2016), breast and ovarian cancer, and accelerated uterine involution that reduces postpartum blood loss and risk of hemorrhage (Sayres & Visentin, 2018; Victora et al., 2016). Despite all the benefits that breastfeeding offers, many lactating parents cannot or choose not to breastfeed.

Several barriers exist that affect a lactating parent's ability to successfully breastfeed, including a lack of knowledge from parents and healthcare providers, lack of family and social support, and societal norms. Many parents are simply uninformed or misinformed on how to initiate breastfeeding and how to resolve lactation complications (U.S. Department of Health and Human Services, 2011). Support from healthcare providers, family, and partners is vital to the success of breastfeeding. Lactating parents are influenced by past success or failure of breastfeeding by their parents and their friends (Bernie 2013; Reid et al., 2010; Woods Barr et al., 2021). Bottle feeding has become more prevalent in society, which has contributed to parental discomfort breastfeeding outside of the home or in the presence of others (Hauck et al., 2021; U.S. Department of Health and Human Services, 2011). One risk factor for suboptimal breastfeeding that intersects each of the barriers mentioned above is a high pre-pregnancy body mass index.

Breastfeeding rates are lower among overweight and obese lactating parents due to a multitude of factors including physiological, mechanical, psychological and support barriers.

Overweight/obese lactating parents have higher rates of metabolic conditions that can negatively impact hormonal balance necessary for lactation and affect the development of glandular breast tissue (Babendure et al., 2015; Jevitt et al., 2010; Rasmussen 2007). Overweight/obese lactating parents also have a higher risk of experiencing birth complications, infant morbidity and pregnancy morbidity, all of which can result in prolonged mother-infant separation after birth and formula supplementation (Jevitt et al., 2010; Poston et al., 2016). Also, some obese/overweight parents may struggle with body image and thus may be hesitant to seek lactation help, which often requires body/breast exposure (Dieterich et al., 2021). Healthcare providers may provide less breastfeeding support to overweight and obese parents due to weight stigma and lack of knowledge of how to assist overweight/obese parents with, for example, breastfeeding positioning with larger breasts (Dieterich et al., 2021; Jarlenski et al., 2014; U.S. Department of Health and Human Services, 2011).

This analysis begins to parse the physiological versus psychosocial basis for breastfeeding challenges for overweight/obese birthing parents by examining early physiological markers of potential insufficient milk production in this population. Specifically, we examine pregnancy-related breast changes and timing of onset of lactogenesis-II by pre-pregnancy BMI. Both pregnancy-related breast changes and lactogenesis onset before 4 days postpartum are considered soft markers of a hormonal milieu and breast tissue architecture favorable to a robust milk supply (Pandya, 2011; Preusting et al., 2017; Żelaźniewicz & Pawłowski, 2019).

1.1 Background

1.1.1 Physiological Origins of Successful Lactation

1.1.1.1 Mammogenesis

The process of breast development occurs across the female lifespan in three critical periods, collectively known as mammogenesis. Breast development begins in utero when the fetal nipple, areola, mammary glands and lactiferous ducts start to form. At 40 weeks' gestation, approximately 15 to 20 lobes of glandular tissue, each containing a lactiferous duct, have formed (Javed and Lteif, 2013). The second stage of development occurs at the onset of puberty. A surge of estrogen at this period is responsible for stimulating mammary development. Branching and elongation of the mammary ducts also occur due to both estrogen and progesterone release. Although these structures are reaching maturity, they are not fully activated until pregnancy. During pregnancy, estrogen continues to stimulate ductal growth and progesterone continues to stimulate glandular bud growth as the breast milk-producing structures mature. Also at this time, progesterone elicits many other breast changes including breast growth, darkening of the areola, sensitivity of the breast and increased vascularity (Javed and Lteif, 2013).

As these structural changes occur in pregnancy, milk production is also initiated. This process is called lactogenesis and it comes in two stages. The first stage, lactogenesis I occurs during pregnancy, beginning in the second trimester, and is defined by the process of secretory differentiation (Nommsen-Rivers et al., 2010). The mammary alveolar epithelial cells differentiate into secretory cells called lactocytes, at which point the breast begins to produce small volumes of milk, called colostrum, rich in antibodies and other immune factors. Colostrum can sometimes be expressed, collected, and banked during pregnancy, and is typically available to the infant during

breastfeeding sessions in the first days postpartum prior to onset of LII (Demirci et al., 2019; Forster et al., 2017). LII occurs after birth, normally occurring before the fourth day postpartum, with the precipitous drop of progesterone after delivery of the placenta (Preusting et al., 2017). LII is marked by the onset of copious milk secretion, known as milk "coming in," and its timing correlates with the infant's increased caloric needs after the first days postpartum.

1.1.1.2 Perturbations in Mammogenesis and Delayed Lactogenesis-II

DLII is defined as lactogenesis after 72 hours postpartum (Brownell et al., 2012; Chapman & Perez-Escamilla, 2000; Preusting et al., 2017). Previous studies have shown that 23-46% of birthing parents experience DLII (Nommsen-Rivers et al., 2010; Preusting et al., 2017). This delay is mostly seen in primiparous, obese and diabetic birthing parents, as well as those who experience a stressful labor or delivery, a cesarean section delivery, a prolonged second stage of labor, high birthweight infant, postpartum edema, and a negative perception of effective breastfeeding immediately postpartum (Brownell et al., 2012). The factor that this study focuses on is obesity. A study completed in 2017 with 216 participants found that 57.9% of women with a BMI $\geq$30kg/m2 experienced DLII, compared to 46% of women with a BMI <30kg/m2 (Preusting et al., 2017), when DLII is defined as greater than 72 hours postpartum.

Multiple factors may cause this association between higher BMI and DLII. One factor is hormonal variations due to obesity throughout the stages of mammogenesis. Adipose tissue can create and store hormones, such as estrogen, and during the stages of mammogenesis, excess estrogen may disrupt mammary gland development (Neville & Morton, 2001; Parker et al., 2012). Another factor affecting LII is delayed initial breastfeeding. Early and often milk removal around the time of birth with accompanying oxytocin and prolactin release occurring with direct breastfeeding may be responsible for setting the number of prolactin receptors in breast tissue, as

outlined by the prolactin receptor theory. Upregulation of these receptors may only be amenable in a critical window around birth and may set the theoretical maximum volume of milk production possible in any given lactating individual (Wambach & Genna, 2016). Overweight/obese lactating parents have a higher risk of experiencing birth complications, such as preterm birth and preeclampsia, and interventions such as Cesarean sections (Chen et al., 1988; Dewey, 2001; Dewey et al., 2003; Laughon et al., 2014) which can delay immediate breastfeeding, and thus disrupt ideal prolactin receptor creation and maximum milk production. It can also lead to early formula supplementation, which is a risk factor for continued formula use and reduced breastfeeding (Chantry et al., 2014).

1.1.2 Phenotypic Predictors of Physiological Capacity for Sufficient Postpartum Milk Volume

Breast changes during pregnancy including breast growth, darkening of the areola, breast and nipple sensitivity/soreness, increased vascularity, and leaking of milk may serve as prognosticators for mammary gland responsiveness to the hormones of pregnancy. In particular, breast growth during pregnancy is thought to be indicative of normal secretory differentiation: transition of mammary epithelial cells to lactocytes and proliferation of mammary lactation architecture, including ducts and alveoli (Pandya, 2011). However, no studies have examined whether different types of pregnancy-related breast changes are predictive of normal transition to normal lactogenesis-II—the latter an event which is reassuring of physiologic capacity to produce an adequate volume of milk to meet an infant's nutritional needs. Understanding these relationships is particularly important for individuals with high pre-pregnancy BMI, who are at heightened risk for inadequate physiologic milk production. If self-reported breast changes can be leveraged to

predict who is at risk for later milk volume concerns, education and support can be tailored for these individuals proactively so that they can better meet their breastfeeding goals.

1.2 Purpose

The purpose of this study was to explore the relationship between pre-pregnancy BMI, self-reported breast changes during pregnancy, and postpartum onset of lactogenesis II in first-time birthing parents.

1.3 Research Questions

Is pre-pregnancy BMI associated with type and timing of breast changes during pregnancy among first-time birthing parents?

Is the onset of lactogenesis II in first-time birthing parents associated with pre-pregnancy BMI?

Are the types and timing of breast changes in first-time birthing parents associated with the time of onset of lactogenesis II?

2.0 Methods

2.1 Design

This study was a secondary analysis of existing data from the MILK Study (a mobile, semi-automated text message-based intervention to prevent perceived low or insufficient milk supply (PIM)). The MILK Study was a randomized controlled trial that examined the effectiveness of an SMS (short message service, i.e., text message) program to prevent perceived insufficient milk (PIM) versus an attention control group receiving general prenatal breastfeeding support. The trial included nulliparous-to-primiparous birthing parents in southwestern Pennsylvania, United States (Funding: NIH NINR R00NR015106, PI: Demirci; ClinicalTrials.gov registration: ClinicalTrials.gov/NCT02724969). The University of Pittsburgh Human Research Protection Office (HRPO) approved the study (STUDY19050021). The MILK Study enrolled, randomized, and collected baseline data on 250 eligible participants at 13-25 weeks of pregnancy and delivered the assigned intervention from 25 weeks of pregnancy to 8 weeks postpartum. Interim data on pregnancy and perceptions of the interventions were collected via survey at 34-36 weeks of pregnancy. Breastfeeding outcomes (e.g., breastfeeding self-efficacy, perception of insufficient milk, any and exclusive breastfeeding) were assessed via review of the birth hospital electronic health record and self-report survey administered at 1, 2, 5, and 8 weeks postpartum, and 6 months postpartum.

For this secondary analysis, we used data inclusive of the entire MILK Study sample, regardless of group assignment. This was because there is no theoretical relationship between additional breastfeeding/lactation education and support provided by the tested intervention and the physiological lactation changes we assessed in the analysis, including pregnancy-related breast changes and onset of lactogenesis-II.

2.2 Sample

The parent study (MILK Study) recruited participants at their prenatal visits during the second trimester of pregnancy at University of Pittsburgh Medical Center Magee-Women's Hospital prenatal clinics and through local advertising, social media, and a university research registry. Inclusion criteria included the following: nulliparity, age 18 years or older, English-speaking, 13 to 25 gestational weeks, pregnant with one infant, access to a cell phone with internet access and an unlimited SMS text message plan, and intent to breastfeed exclusively or nearly exclusively (<2 ounces of formula per day) for at least two months. Exclusion criteria consisted of any contraindications to breastfeeding and maternal or fetal conditions with a high risk of compromising breastfeeding or milk supply (e.g., breast reduction surgery, major congenital fetal anomalies). All participants provided written informed consent for participation.

2.3 Procedures

In the parent study (MILK Study), participants who met eligibility were randomized with equal allocation to the intervention or control group. Control group participants were instructed to enroll in the freely available national Text4Baby program, which delivered automated texts on general aspects of pregnancy and postpartum topics, including breastfeeding, immediately following enrollment. Participants assigned to the MILK intervention group received messages starting at week 25 of gestation that focused specifically on cultivating breastfeeding confidence and behaviors to prevent PIM. All participants received prenatal and postpartum text messages 3 to 7 times per week.

In the parent MILK Study, data on participant demographics and medical history was collected via electronic medical record abstraction and participant self-report survey during prenatal visits or remotely-delivered survey. Participants completed surveys at two points during pregnancy: 13-25 weeks (second trimester) and 34-36 weeks (third trimester) of gestation. These surveys included questions regarding breast changes at these two points in time, with a check-all-that-apply style item. For the question, "Have you noticed any breast changes so far this pregnancy?," the following options were given: "None; Growth (breasts bigger); Soreness, sensitivity or pain in breasts; Darkening in skin around nipple (areola); Increased vascularity (more visible veins in breasts); Leaking milk or able to see drops of milk when I squeeze my nipples; Other." Postpartum data regarding pregnancy and birth complications and breastfeeding and/or formula use were collected from the birth hospitalization electronic health record and via remote emailed or telephone survey at 1, 2, 5, and 8 weeks postpartum and 6 months postpartum. Onset of LII was assessed at the one-week postpartum survey via a single item, adapted from a validated

assessment of onset of LII: “How long did it take for your milk to come in after your baby was born (i.e., when did you notice a big increase in the amount of milk)?” (Chapman & Perez-Escamilla, 2000). Answer options included: “1 day or less; 2 days; 3 days; 4 days; More than 4 days; My milk never came in; I don’t remember when my milk came in.” Delayed lactogenesis was operationalized as ≥ 4 days postpartum. Pre-pregnancy BMI was calculated from participant reported pre-pregnancy weight and height collected at the enrollment visit (13-25 weeks of pregnancy).

2.4 Analysis

For this secondary analysis, data were analyzed using IBM® SPSS® Statistics version 26 (IBM Corp., Armonk, NY). First, descriptive statistics were used to find central tendencies and dispersion within the data. The mean and standard deviation of the continuous variables of age and pre-pregnancy BMI were calculated. BMI was also categorized into normal/underweight: <25, overweight: 25-29.9, and obese: ≥30. Frequencies were calculated for each categorical variable, including demographic and birth data, proportion of sample experiencing breast changes at each study assessment point, and proportion of sample experiencing lactogenesis-II at pre-defined points in the postpartum period (e.g., 1, 2, 3, 4, >4 days, never). We used crosstabulations with Pearson chi-square tests to assess the relationship between two categorical variables. Specifically these tests examined associations between pre-pregnancy BMI category and breast changes at two different time points throughout pregnancy (13-25 weeks and 34-36 weeks); between pre-pregnancy BMI category and the timing of onset of lactogenesis-II; and between timing of onset of lactogenesis-II and breast changes in pregnancy at 13-25 weeks and 34-36 weeks. Bonferroni

corrections were made for multiple comparisons in the evaluating relationships between breast changes and BMI and relationships between breast changes and delayed onset of LII. We considered 12 comparisons for each of the two relationships studied, and therefore set a significance level of α=.004 (α=.05/12=.004). We also examined trends in data graphically. After examining graphical distribution of lactogenesis onset by postpartum day, we conducted a post-hoc analysis of lactogenesis timing and BMI category using a different cut-off day for lactogenesis (i.e., “4 days or less” to “more than 4 days or never.”).

3.0 Results

3.1 Sample Characteristics

Characteristics of the study cohort are shown in Table 1. The main study sample consisted of 250 first time birthing parents, though 247 had baseline data available and were included in the current analysis. The majority of participants were white, non-Hispanic, married, and had earned either a bachelor's or post-graduate degree. The average BMI was 26.4, which falls into the overweight category. Half of the participants were normal/underweight (BMI <24.9), while the other half fell into the overweight (BMI 25-29.9) or obese (BMI ≥ 30) categories. Over half of participants' newborns received formula in the hospital. The data revealed a higher proportion of obese participants supplementing with infant formula, with 66% (n=31) of obese participants supplementing compared to 51% (n=37) and 47% (n=56) of the overweight and normal/underweight groups, respectively. Also, participants with obesity supplemented greater volumes of infant formula, with 57.4% (n=27) of obese participants supplementing >60mL, compared to 27.5% (n=19) and 36.1% (n=43) of overweight and normal/underweight participants supplementing with this volume, respectively. The data also revealed that nearly one quarter of the obese participants endorsed a non-diabetes endocrine or metabolic condition (polycystic ovarian syndrome, Cushing's syndrome, or hypothyroidism), compared to only 11% of both the overweight and normal/underweight groups.

Table 1. Sample Characteristics

Sample Characteristics	**Total Sample (n=247)**	**Normal/ Under Weight (BMI <24.9) n=125**	**Overweight (BMI 25-29.9) n=74**	**Obese (BMI ≥30) n=48**
Age [M. (SD)] n=247	28.8 (5.3)	29.3 (5.2)	28.5 (5.8)	28.3 (5.0)
Pre-pregnancy BMI [M, (SD)] n=247	26.4 (6.3)	22.0 (1.9)	27.3 (1.4)	36.4 (6.7)
Weight classification [n (%)] n=247		n/a	n/a	n/a
- Normal/ Under Weight (BMI <24.9)	125 (50.6)			
- Overweight (BMI 25-29.9)	74 (30)			
- Obese (BMI ≥ 30)	48 (19.4)			
Race [n (%)] n=238				
- White	169 (70.0)	100 (80.0)	48 (64.9)	33 (68.8)
- Black	46 (19.3)	14 (11.2)	22 (29.7)	11 (22.9)
- Other[1]	23 (9.7)	11 (8.8)	4 (5.5)	4 (8.3)
Ethnicity [n (%)] n=246				
- Non-Hispanic	236 (95.9)	118 (95.2)	70 (94.6)	48 (100)
- Hispanic	10 (4.1)	6 (4.8)	4 (5.4)	0 (0.0)

[1] Asian/Indian, Native American, Mixed/Bi-Racial

Table 1. Sample Characteristics (continued)

Sample Characteristics	**Total Sample (n=247)**	**Normal/ Under Weight (BMI <24.9) n=125**	**Overweight (BMI 25-29.9) n=74**	**Obese (BMI ≥30) n=48**
Marital Status [n (%)] n=247				
- Married	158 (64.0)	92 (73.6)	37 (50.0)	29 (60.4)
- Living with a Partner	37 (15.0)	16 (12.8)	14 (18.9)	7 (14.6)
- Single	52 (21.1)	17 (13.6)	23 (31.1)	12 (25.0)
Level of Education [n (%)] n=247				
- High School Diploma or Less	28 (11.3)	12 (9.6)	10 (13.5)	6 (12.5)
- Some College, Associates Degree, or Vocational Program	56 (22.7)	16 (12.8)	21 (28.4)	19 (39.6)
- Bachelor's Degree	69 (27.9)	32 (25.6)	26 (35.1)	11 (22.9)
- Post-graduate Degree	94 (38.1)	65 (52.0)	17 (23.0)	12 (25.0)
WIC Recipient [n (%)] n=246	60 (24.4)	24 (19.4)	22 (29.7)	14 (29.2)
Diabetes [n (%)] n=239				
- Type 1	1 (0.4)	1 (0.8)	0 (0.0)	0 (0.0)
- Type 2	2 (0.8)	0 (0.0)	1 (1.4)	0 (0.0)
- Gestational	4 (1.6)	0 (0.0)	1 (1.3)	3 (6.3)
Non-Diabetes Endocrine/Metabolic Conditions[2] [n (%)] n=239	32 (13.4)	13 (10.8)	8 (11.1)	11 (23.4)

[2] Hypothyroidism (obtained from medical record) or Polycystic Ovarian Syndrome (self-report) or Cushing's Syndrome (self-report)

Table 1. Sample Characteristics (continued)

Sample Characteristics	Total Sample (n=247)	Normal/ Under Weight (BMI <24.9) n=125	Overweight (BMI 25-29.9) n=74	Obese (BMI ≥30) n=48
History of Breast Augmentation or Surgery [n (%)] n=239	3 (1.3)	0 (0.0)	1 (1.4)	2 (4.2)
Diagnosed Mood Disorders[3] [n (%)] n=240	86 (35.8)	42 (34.7)	24 (33.3)	20 (42.6)
Pregnancy and Birth Complications [n (%)] n=241				
- Pre-Eclampsia	23 (9.5)	11 (9.2)	4 (5.6)	8 (17.0)
- Chorioamnionitis	9 (3.7)	5 (4.2)	3 (4.2)	1 (2.1)
- Postpartum Hemorrhage	5 (2.1)	0 (0.0)	3 (4.2)	2 (4.3)
Total Weight Gain in Pregnancy in lbs [M, (SD)] n=237	31.7 (14.1)	33.7 (12.3)	33.5 (13.6)	23.6 (16.2)
Mode of Delivery [n (%)] n=240				
- Vaginal, non-operative	160 (66.7)	79 (65.8)	49 (69.0)	63.8)
- Vaginal, operative	11 (4.6)	6 (5.0)	3 (4.2)	2 (4.3)
- Cesarean Section	69 (28.7)	35 (29.2)	19 (26.8)	15 (31.9)

[3] Anxiety, depression, and/or Bipolar Disorder; counted as mood disorder if self-reported at baseline survey during pregnancy or noted in electronic health record during postpartum hospitalization

Table 1. Sample Characteristics (continued)

Sample Characteristics	Total Sample (n=247)	Normal/ Under Weight (BMI <24.9) n=125	Overweight (BMI 25-29.9) n=74	Obese (BMI ≥30) n=48
Anesthesia during Birth [n (%)] n=241	217 (90)	108 (90.0)	61 (84.7)	46 (97.9)
NICU Admission [n (%)] n=241	45 (18.7)	23 (19.2)	10 (13.9)	11 (23.4)
Direct Chest/Breastfeeding following Birth [n (%)] n=237				
- Not initiated	11 (4.6)	4 (3.3)	5 (7.0)	2 (4.3)
- ≤1 hour	71 (31.2)	37 (31.1)	19 (26.8)	15 (31.9)
- >1 hour	155 (65.4)	78 (65.5)	47 (66.2)	30 (63.8)
Use of Formula in Hospital [n (%)] n=238	124 (52.1)	56 (47.1)	37 (51.4)	31 (66)
Total Volume of Formula in Hospital [n (%)] n=235				
- 0mL	115 (48.5)	63 (52.9)	35 (50.7)	16 (34)
- 1-60mL	32 (13.5)	13 (10.9)	15 (21.7)	4 (8.5)
- >60mL	90 (38.0)	43 (36.1)	19 (27.5)	27 (57.4)

3.2 Breast Changes by Pre-Pregnancy BMI

During the second trimester (13-25 weeks), more participants in the normal/underweight group, compared to the overweight and obese groups experienced breast growth $\chi^2(2, n=247)=19.3$, $p<.001$. In fact, 96% of birthing parents in the normal/underweight group experienced second trimester breast growth, compared to 82.4% of overweight birthing participants and 72.9% of obese birthing participants.

During the third trimester (34-36 weeks), breast soreness, sensitivity and pain were reported more frequently among obese birthing participants (75%), compared to normal/underweight (53%) or overweight participants (54%), though the difference was not significant with the Bonferroni correction ($p= 0.034$).

We found no other relationships between breast changes and BMI group, either during the second or third trimesters. For the sample as a whole, the most common breast change was breast growth (86% and 90% endorsement in second and third trimester, respectively). The least common breast change overall was leaking milk—with fewer than 10% of participants reporting it in the second trimester and fewer than 25% reporting experiencing it by the third trimester.

There was higher endorsement of areolar darkening, vascularity, and leaking milk at 34-36 weeks compared to 13-25 weeks for the sample as a whole. There was lower endorsement of growth, and soreness, sensitivity, pain at 34-36 weeks compared to 13-25 weeks for the sample as a whole.

Table 2. Participant-endorsed breast changes during pregnancy by pre-pregnancy BMI

Breast Change	**Total Sample n=247 (13-25 weeks) n=222 (34-36 weeks)**	**Normal/ Under Weight (BMI <24.9) n=125**	**Overweight (BMI 25-29.9) n=75**	**Obese (BMI≥ 30) n=48**	**p-value**
Growth [n (%)]					
13-25 weeks	216 (86.4)	120 (96)	61 (82.4)	35(72.9)	**<.001**
34-36 weeks	199 (89.6)	104 (92.0)	58 (89.2)	37 (84.1)	0.34
Soreness, sensitivity, pain [n (%)]					
13-25 weeks	198 (80.2)	100 (80)	55 (74.3)	43 (89.6)	0.12
34-36 weeks	128 (51.8)	60 (53.1)	35 (53.8)	33 (75.0)	0.03
Areolar darkening [n (%)]					
13-25 weeks	115 (46.6)	61 (48.8)	30 (40.5)	24 (50)	0.46
34-36 weeks	180 (72.9)	88 (77.9)	55 (84.6)	37 (84.1)	0.46
Increased vascularity [n (%)]					
13-25 weeks	73 (29.4)	37 (29.6)	23 (30.7)	13 (27.1)	0.89
34-36 weeks	129 (52.2)	67 (59.3)	39 (60.0)	23 (52.3)	0.68
Leaking milk [n (%)]					
13-25 weeks	18 (7.3)	10 (8)	5 (6.8)	3 (6.3)	0.94
34-36 weeks	61 (24.7)	27 (23.9)	20 (30.8)	14 (31.8)	0.47

Table 2. Participant-endorsed breast changes during pregnancy by pre-pregnancy BMI (continued)

Breast Change	**Total Sample n=247 (13-25 weeks) n=222 (34-36 weeks)**	**Normal/ Under Weight (BMI <24.9) n=125**	**Overweight (BMI 25-29.9) n=75**	**Obese (BMI≥ 30) n=48**	**p-value**
Other [n (%)]					
13-25 weeks[4]	2 (0.8)	2 (1.6)	0 (0)	0 (0)	
34-36 weeks[5]	4 (1.6)	2 (1.8)	1 (1.5)	1 (2.3)	

Table 2 Key

Normal/Under Weight: 13-25 weeks, n=125; 34-36 weeks, n=113

Overweight: 13-25 weeks, n= 74; 34-36 weeks, n= 65

Obese: 13-25 weeks, n=48; 34-36 weeks, n=44

[4] Other= thickening of areola skin, itching

[5] Other= hyperpigmentation, slight stretch marks

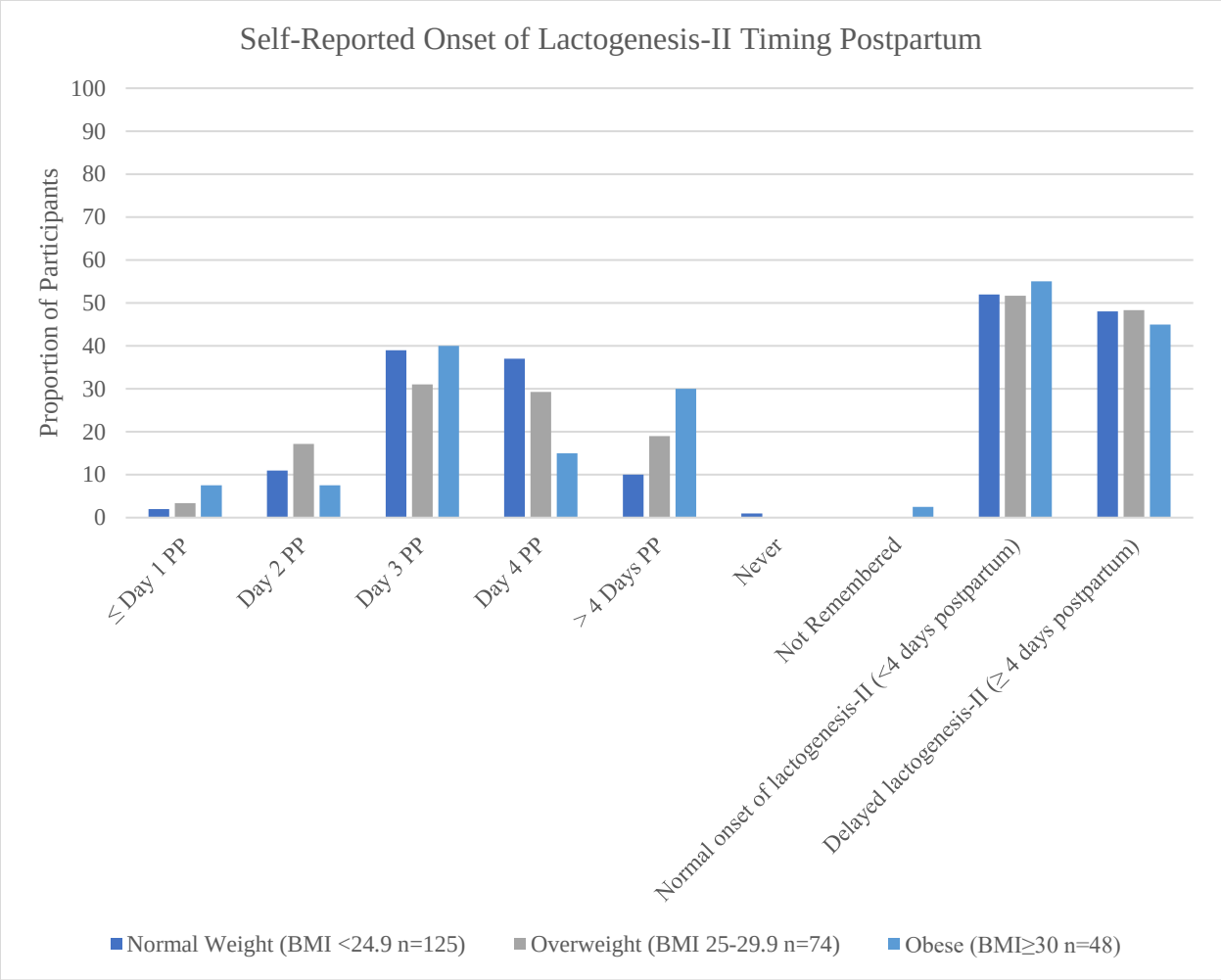
3.3 Timing of Lactogenesis-II

Regardless of BMI group, most participants experienced LII on day 3 (n=73, 36.9%) or day 4 (n=60, 30.3%). There was near equal distribution within the sample for those experiencing normal onset of LII defined as <4 days postpartum (n=104; 53%) and those experiencing DLII, defined as ≥4 days postpartum (n=94; 48%). Likewise, there was no difference between BMI groups in delayed versus normal onset of LII, using the cut-off of four days postpartum $\chi^2(2, n=198)=0.124$, $p=0.94$. See Table 3 and Figure 1.

After examining graphical distribution of lactogenesis onset by postpartum day, we conducted a post-hoc analysis utilizing the cut-off day for lactogenesis as more than 4 days or never, instead of 4 days or less. Approximately 17% of the sample (n=34) experienced LII beyond four days postpartum or never. We observed a dose-response type effect between increasing pre-pregnancy BMI category and higher prevalence of lactogenesis beyond 4 days postpartum. About 30% of obese participants experienced LII more than 4 days postpartum, compared to only 19% of overweight birthing parents and 10% of normal/underweight birthing parents $\chi^2(2, n=198)=7.44$, $p=0.02$.

Table 3. Timing of lactogenesis-II reported by participants at 1 week postpartum, by pre-pregnancy BMI

Lactogenesis-II Timing [n (%)]	**Total Sample (n=198)**	**Normal/ Under Weight (BMI <24.9) n=100**	**Overweight (BMI 25-29.9) n=58**	**Obese (BMI≥30) n=40**
Day 1 or less postpartum	7 (3.5)	2 (2.0)	2 (3.4)	3 (7.5)
Day 2 postpartum	24 (12.1)	11 (11.0)	10 (17.2)	3 (7.5)
Day 3 postpartum	73 (36.9)	39 (39.0)	18 (31.0)	16 (40.0)
Day 4 postpartum	60 (30.3)	37 (37.0)	17 (29.3)	6 (15.0)
More than 4 days postpartum	33 (16.7)	10 (10.0)	11 (19.0)	12 (30.0)
Milk never came in	1 (0.5)	1 (1.0)	0 (0.0)	0 (0.0)
Do not remember	1 (0.5)	0 (0.0)	0 (0.0)	1 (2.5)
Normal onset of lactogenesis-II (<4 days postpartum)	104 (52.5)	52 (52.0)	30 (51.7)	22 (55.0)
Delayed lactogenesis -II (≥ 4 days postpartum or never)	94 (47.5)	48 (48.0)	28 (48.3)	18 (45.0)



[6]Figure 1. Graph of Onset of Lactogenesis-II

[6] PP= postpartum

3.4 Breast Changes and Lactogenesis-II

The only breast change approaching significance in its relationship with LII was leaking milk by 13-25 weeks of gestation; leaking milk by the second trimester occurred more frequently among participants reporting normal onset of LII (< 4 days postpartum), compared to those with DLII (10.6% vs. 2.1%, respectively; $\chi^2(1, n=198)=5.75, p=0.02$).

No other individual breast changes experienced by the second or third trimesters were statistically associated with normal or delayed onset of lactogenesis-II. However, other than breast growth, there was a collective trend toward endorsement of breast changes by second or third trimester and normal onset of LII. In other words, a higher absolute proportion of participants who experienced normal onset of LII reported the pregnancy-related breast changes we assessed, and fewer participants who experienced DLII reported those breast changes.

Table 4. Breast changes in pregnancy and delayed lactogenesis-II

Breast Changes	**Normal onset LII: <4 days postpartum (n=104)**	**Delayed onset LII: ≥4 days postpartum (n=95)**	**p-value**
Growth [n (%)]			
13-25 weeks	88 (84.6)	85 (90.4)	0.22
34-36 weeks	87 (83.7)	81 (86.2)	0.44
Soreness, sensitivity, pain [n (%)]			
13-25 weeks	88 (84.6)	74 (78.7)	0.28
34-36 weeks	60 (57.7)	47 (50)	0.1
Areolar darkening [n (%)]			
13-25 weeks	51 (49)	40 (42.6)	0.36
34-36 weeks	81 (77.9)	72 (76.6)	0.22
Increased vascularity [n (%)]			
13-25 weeks	35 (33.7)	25 (26.3)	0.26
34-36 weeks	61 (58.7)	47 (50)	0.07
Leaking milk [n (%)]			
13-25 weeks	11 (10.6)	2 (2.1)	0.02
34-36 weeks	29 (27.9)	22 (23.4)	0.31
Other [n (%)]			
13-25 weeks[7]	2 (1.9)	0 (0)	
34-36 weeks[8]	1 (1.0)	1 (1.1)	

[7] Other= thickening of areola skin, itching

[8] Other= hyperpigmentation, slight stretch marks

4.0 Discussion

In a sample of mostly white, non-Hispanic, married, and college-educated birthing parents, about half of whom had a pre-pregnancy BMI considered overweight or obese, we found associations between higher pre-pregnancy BMI and non-endorsement of breast growth in the second trimester of pregnancy. We also found a relationship between higher pre-pregnancy BMI and DLII beyond four days postpartum. However, we found no evidence of a link between all three variables: pre-pregnancy BMI, pregnancy-related breast changes, and timing of lactogenesis-II.

This was the first study to document the frequency and timing of specific pregnancy-related breast changes in first-time parents. In terms of pregnancy-related breast changes for the sample as a whole, the increased endorsement of areolar darkening, increased vascularity, and milk leaking at the 34-36 week assessment compared to the 13-25 week assessment was not unexpected. As pregnancy progresses through the third trimester, the mammary glands continue the process of secretory differentiation, thus the closer to parturition, the more cumulative breast changes would be expected (Javed and Lteif, 2013). However, there was an unexpected decrease in growth, and soreness, sensitivity, and pain reported between 13-25 weeks and 34-36 weeks. Since the survey for breast changes was asked cumulatively (e.g., if participant had experienced changes at all during pregnancy), there should not have been higher rates in 13-25 weeks than 34-36 weeks. This discrepancy may be due to recall bias, or participants becoming accustomed to the symptom or experiencing symptom resolution, such as in the case of soreness or pain. A second explanation is misinterpretation of the question and only reporting current symptoms. Another possible explanation is fewer parents completing the survey at 34-36 weeks due to participants not completing the entirety of the study.

The frequency of the breast changes of growth and of soreness, sensitivity, and pain were not uniform throughout the three BMI groups. In fact there was significantly more reported breast growth during 13-25 weeks in the normal/underweight population compared to the obese and overweight populations, and more reported breast soreness, sensitivity, and pain in the obese weight population at 34-36 weeks compared to the normal/under and overweight populations (though not statistically significant with the Bonferroni adjustment). Differences in early pregnancy breast growth may point to a physiologic or metabolic difference in normal/underweight individuals that leads to earlier or faster glandular development of milk making structures, causing this increased growth and possibly later increased capacity for milk production. A study conducted in 2019 of 93 birthing parents found a positive correlation between breast volume in pregnancy and postpartum milk production (Żelaźniewicz & Pawłowski, 2019), however, our data showed no association between breast growth in pregnancy and onset of LII. Increased breast pain and sensitivity among obese participants by their third trimester may be due to a trend toward larger and heavier breasts in this weight classification prior to pregnancy. Pain and soreness may become accentuated as pregnancy progresses with larger breasts. In support of this theory, a study conducted with over 750 pre-pregnancy parents in 2017 found that BMI >30 was a significant risk factor for breast pain in birthing parents pre-pregnancy (Koçoğlu et al., 2017).

The commonly accepted definition of DLII is onset at greater than 72 hours postpartum (Brownell et al., 2012). However, our findings grouped nearly half of the sample into the "delayed lactogenesis" category using this definition. Thus, our findings challenge the conventional cut-off of greater than three days postpartum for DLII. Previous studies with solely first-time birthing parents, or primiparas, have found similar results. A longitudinal cohort study conducted in 2010

found that 44% of 431 primiparous participants experienced DLII, when defined as greater than three days postpartum (Nommsen-Rivers et al., 2010). However, it is important to note the discrepancy in rates of DLII between primiparous and multiparous birthing parents. For example, in a prospective cohort study conducted in central China including multiparas, DLII (defined as greater than 3 days postpartum) occurred at a rate of only 17.9% in a 2877-person study (Huang et al., 2020). When we re-classified DLII as >4 days postpartum, about 17% of the sample met the threshold for delayed lactogenesis, which is similar to the frequency of studies including multiparous birthing parents (Huang et al., 2020). In addition, there was a dose-response effect between increasing pre-pregnancy BMI and higher prevalence of DLII with onset greater than four days postpartum. This finding supports existing data stating that obese birthing parents experience lactogenesis-II later than their lower BMI counterparts (Jevitt et al., 2007; Preusting et al., 2017; Rasmussen et al., 2001).

The only pregnancy-related breast change approaching an association with the categorical definition of normal versus delayed onset of LII using the 3-day cut-off was leaking milk (positive relationship), though other breast changes showed trends toward a positive association with LII. This may indicate that our sample size was not large enough to detect additional associations, that self-reported pregnancy-related breast changes other than leaking milk are not sensitive markers for normal mammary gland secretory differentiation, and/or that pregnancy-related breast changes have greater predictive value when a cut-off of DLII is set later (e.g., > 4 days vs. >3 days for first-time birthing parents). Few studies have been completed tracking the association of breast changes, LII, and later breastfeeding outcomes, indicating a need for further research.

While in general parents with increasing pre-pregnant BMI (particularly obese pregnant parents) may be at higher risk for DLII, our data did not support that breast changes in pregnancy

would be sensitive markers to detect a heightened risk for DLII. Future research should explore the three-way relationship between pregnancy-related breast changes, pre-pregnancy BMI, and onset of LII in larger, more diverse samples with more sophisticated multivariate statistical modeling. Future research should also address breastfeeding outcomes past LII, such as perception of sufficient milk, breastfeeding satisfaction, rates of formula supplementation, and rates of continued breastfeeding.

In this group of first-time parents highly committed to breastfeeding, there was a high rate of in-hospital infant formula supplementation (52%). When observing disparities in in-hospital formula supplementation by BMI group, it was found that participants with obesity had higher rates of supplementation. Previous studies conducted by Nommsen-Rivers and Chantry support this attribution of formula supplementation with DLII or breastfeeding difficulties. In a 2010 longitudinal cohort study of 431 first-time parents of full-term infants, there was a significant relationship between formula supplementation (1-60 or >60mL) and delayed onset of lactogenesis, revealing that the factors of greater maternal age, higher BMI, and increased infant birth weight had the greatest effect on timing of lactogenesis (Nommsen-Rivers et al., 2010). Chantry's study of 393 parents of full-term infants intending to exclusively breastfeed for greater than one week, found that use of in-hospital formula supplementation was significantly more common among parents who had risk factors for breastfeeding difficulties, including obesity and lack of pre-natal breast enlargement (Chantry et al., 2014). Either of these causes, DLII or breastfeeding difficulties, could explain our study population's high rate of formula supplementation.

The data revealed that nearly one quarter of the obese participants endorsed a non-diabetic endocrine or metabolic condition, such as polycystic ovarian syndrome (PCOS), Cushing's syndrome, or hypothyroidism. These comorbid conditions may act as confounding factors, causing

lactation complications in addition to the difficulties already caused by obesity. Those with PCOS experience insulin resistance, and previous studies have shown that insulin may play a key role in normal mammary gland differentiation, thus a lack of insulin secretion can lead to poor differentiation and insufficient milk secretion (Lemay et al., 2013; Rassie et al., 2021). Cortisol is a naturally occurring stress hormone that in excess amounts can have negative effects on the body and cause Cushing's syndrome. In fact, increased cortisol levels during the peripartum and postpartum stages are associated with delayed lactogenesis, thus birthing parents with Cushing's syndrome are at greater risk for unsuccessful breastfeeding (Chen et al., 1988; Wambach & Genna, 2016). Through a feedback system, the thyroid, anterior pituitary gland and hypothalamus interact to determine the release of hormones. The release of the main hormone of lactation, prolactin, is controlled by the anterior pituitary in this pathway. Thus, when the breastfeeding parent has hypothyroidism, this pathway can become interrupted, affecting the levels of lactation hormones and leading to a reduced milk supply (Morrison & Wambach, 2016).

Our small sample size limited our ability to conduct more advanced modeling and controlling for relevant covariates. Another limitation is that onset of lactogenesis-II was self-reported, allowing for subjectivity and possible error. Strengths of this study included the prospective data collection which assessed breast changes during pregnancy and lactogenesis-II during the first week of postpartum, which limited recall bias.

5.0 Conclusion

First time birthing parents with an overweight or obese BMI are at higher risk of DLII. This delay in onset of breastmilk can lead to delay in proper nutrition for the newborn, and thus excess neonatal weight loss and early formula supplementation (Nommsen-Rivers et al., 2010). As found in our study, despite high rates of anticipated breastfeeding, participants with obesity had the highest rates of any in-hospital formula supplementation, and the greatest volumes of formula supplementation. This indicates that those with a higher pre-pregnancy BMI may need increased prenatal and postnatal education and lactation support to ensure they meet their lactation/breastfeeding goals.

Future research should further explore relationships between breast changes and onset of lactogenesis, as this data may be utilized to predict who is at risk for later milk volume concerns. Additional education and support could then be tailored for these individuals prior to birth to better meet their breastfeeding goals.

Although DLII has long been defined as onset 4 days or more postpartum, our data suggests that “4 days or more” may no longer be appropriate as the marker for delayed onset for first-time birthing parents regardless of pre-pregnancy BMI. Changing the definition of DLII to “5 days of more” may discourage fewer birthing parents from halting attempts at breastfeeding due to concerns about impaired milk production. This new finding would also allow providers to better educate their first-time birthing patients on what to expect and how to provide nutrition for the newborn between birth and onset of LII.

Bibliography

Bernie, K. (2014). The factors influencing young mothers' infant feeding decisions: the views of healthcare professionals and voluntary workers on the role of the baby's maternal grandmother. *Breastfeeding Medicine : The Official Journal of the Academy of Breastfeeding Medicine*, *9*(3), 161–165. https://doi.org/10.1089/bfm.2013.0120

Bever Babendure, J., Reifsnider, E., Mendias, E., Moramarco, M. W., & Davila, Y. R. (2015). Reduced breastfeeding rates among obese mothers: a review of contributing factors, clinical considerations and future directions. *International Breastfeeding Journal*, *10*, 21. https://doi.org/10.1186/s13006-015-0046-5

Brownell, E., Howard, C. R., Lawrence, R. A., & Dozier, A. M. (2012). Delayed onset lactogenesis II predicts the cessation of any or exclusive breastfeeding. *The Journal of Pediatrics*, *161*(4), 608–614. https://doi.org/10.1016/j.jpeds.2012.03.035

Chantry, C. J., Dewey, K. G., Peerson, J. M., Wagner, E. A., & Nommsen-Rivers, L. A. (2014). In-hospital formula use increases early breastfeeding cessation among first-time mothers intending to exclusively breastfeed. *The Journal of Pediatrics*, *164*(6), 1339–45.E5. https://doi.org/10.1016/j.jpeds.2013.12.035

Chapman, D. J., & Pérez-Escamilla, R. (2000). Maternal perception of the onset of lactation is a valid, public health indicator of lactogenesis stage II. *The Journal of Nutrition*, *130*(12), 2972–2980. https://doi.org/10.1093/jn/130.12.2972

Chen, D. C., Nommsen-Rivers, L., Dewey, K. G., & Lönnerdal, B. (1998). Stress during labor and delivery and early lactation performance. *The American Journal of Clinical Nutrition*, *68*(2), 335–344. https://doi.org/10.1093/ajcn/68.2.335

Demirci, J. R., Glasser, M., Fichner, J., Caplan, E., & Himes, K. P. (2019). "It gave me so much confidence": First-time U.S. mothers' experiences with antenatal milk expression. *Maternal & Child Nutrition*, *15*(4), e12824. https://doi.org/10.1111/mcn.12824

Demirci, J., Schmella, M., Glasser, M., Bodnar, L., & Himes, K. P. (2018). Delayed lactogenesis II and potential utility of antenatal milk expression in women developing late-onset preeclampsia: a case series. *BMC Pregnancy and Childbirth*, *18*(1), 68. https://doi.org/10.1186/s12884-018-1693-5

Dewey K. G. (2001). Maternal and fetal stress are associated with impaired lactogenesis in humans. *The Journal of Nutrition*, *131*(11), 3012S–3015S. https://doi.org/10.1093/jn/131.11.3012S

Dewey, K. G., Nommsen-Rivers, L. A., Heinig, M. J., & Cohen, R. J. (2003). Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. *Pediatrics*, *112*(3 Pt1), 607–619. https://doi.org/10.1542/peds.112.3.607

Dieterich, R., Chang, J., Danford, C., Scott, P. W., Wend, C., & Demirci, J. (2021). She "didn't see my weight; she saw me, a mom who needed help breastfeeding": Perceptions of perinatal weight stigma and its relationship with breastfeeding experiences. *Journal of Health Psychology*, e1359105320988325. https://doi.org/10.1177/1359105320988325

Forster, D. A., Moorhead, A. M., Jacobs, S. E., Davis, P. G., Walker, S. P., McEgan, K. M., Opie, G. F., Donath, S. M., Gold, L., McNamara, C., Aylward, A., East, C., Ford, R., & Amir, L. H. (2017). Advising women with diabetes in pregnancy to express breastmilk in late pregnancy (Diabetes and Antenatal Milk Expressing [DAME]): A multicentre, unblinded, randomised controlled trial. *Lancet*, *389*(10085), 2204–2213. https://doi.org/10.1016/S0140-6736(17)31373-9

Gunderson, E. P., Quesenberry, C. P., Jr, Ning, X., Jacobs, D. R., Jr, Gross, M., Goff, D. C., Jr, Pletcher, M. J., & Lewis, C. E. (2015). Lactation duration and midlife atherosclerosis. *Obstetrics and Gynecology*, *126*(2), 381–390. https://doi.org/10.1097/AOG.0000000000000919

Hauck, Y. L., Bradfield, Z., & Kuliukas, L. (2021). Women's experiences with breastfeeding in public: An integrative review. *Women and Birth: Journal of the Australian College of Midwives*, *34*(3), e217–e227. https://doi.org/10.1016/j.wombi.2020.04.008

Jarlenski, M., McManus, J., Diener-West, M., Schwarz, E. B., Yeung, E., & Bennett, W. L. (2014). Association between support from a health professional and breastfeeding knowledge and practices among obese women: Evidence from the Infant Practices Study II. *Women's Health Issues*, *24*(6), 641–648. https://doi.org/10.1016/j.whi.2014.08.002

Javed, A., & Lteif, A. (2013). Development of the human breast. *Seminars in Plastic Surgery*, *27*(1), 5–12. https://doi.org/10.1055/s-0033-1343989

Jevitt, C., Hernandez, I., & Groër, M. (2007). Lactation complicated by overweight and obesity: Supporting the mother and newborn. *Journal of Midwifery & Women's Health*, *52*(6), 606–613. https://doi.org/10.1016/j.jmwh.2007.04.006

Koçoğlu, D., Kurşun, S., Akın, B., & Altuntug, K. (2017). Mastalgia and associated factors: A cross-sectional study. *The Journal of the Turkish Society of Algology*, *29*(3), 100–108. https://doi.org/10.5505/agri.2017.91069

Laughon, S. K., Berghella, V., Reddy, U. M., Sundaram, R., Lu, Z., & Hoffman, M. K. (2014). Neonatal and maternal outcomes with prolonged second stage of labor. *Obstetrics and Gynecology*, *124*(1), 57–67. https://doi.org/10.1097/AOG.0000000000000278

Huang, L., Xu, S., Chen, X., Li, Q., Lin, L., Zhang, Y., Gao, D., Wang, H., Hong, M., Yang, X., Hao, L., & Yang, N. (2020). Delayed lactogenesis is associated with suboptimal

breastfeeding practices: A prospective cohort study. *The Journal of Nutrition*, *150*(4), 894–900. https://doi.org/10.1093/jn/nxz311

Lemay, D. G., Ballard, O. A., Hughes, M. A., Morrow, A. L., Horseman, N. D., & Nommsen-Rivers, L. A. (2013). RNA sequencing of the human milk fat layer transcriptome reveals distinct gene expression profiles at three stages of lactation. *PLOS One*, *8*(7), e67531. https://doi.org/10.1371/journal.pone.0067531

Morrison, B., & Wambach, K. (2016). Women's health and breastfeeding. In K. Wambach and J. Riordan (Eds.), *Breastfeeding and human lactation.* (5th ed., pp. 598-600). Jones & Bartlett.

McClure, C. K., Catov, J. M., Ness, R. B., & Schwarz, E. B. (2012). Lactation and maternal subclinical cardiovascular disease among premenopausal women. *American Journal of Obstetrics and Gynecology*, *207*(1), 46E1–46E8. https://doi.org/10.1016/j.ajog.2012.04.030

Neville, M. C., & Morton, J. (2001). Physiology and endocrine changes underlying human lactogenesis II. *The Journal of Nutrition*, *131*(11), 3005S–3008S. https://doi.org/10.1093/jn/131.11.3005S

Nommsen-Rivers, L. A., Chantry, C. J., Peerson, J. M., Cohen, R. J., & Dewey, K. G. (2010). Delayed onset of lactogenesis among first-time mothers is related to maternal obesity and factors associated with ineffective breastfeeding. *The American Journal of Clinical Nutrition*, *92*(3), 574-584. https://doi.org/10.3945/ajcn.2010.29192

Pandya, S., & Moore, R. G. (2011). Breast development and anatomy. *Clinical Obstetrics and Gynecology*, *54*(1), 91–95. https://doi.org/10.1097/GRF.0b013e318207ffe9

Parker, L. A., Sullivan, S., Krueger, C., Kelechi, T., & Mueller, M. (2012). Effect of early breast milk expression on milk volume and timing of lactogenesis stage II among mothers of very low birth weight infants: A pilot study. *Journal of Perinatology*, *32*(3), 205–209. https://doi.org/10.1038/jp.2011.78

Perrine, C. G., Nelson, J. M., Corbelli, J., & Scanlon, K. S. (2016). Lactation and maternal cardio-metabolic health. *Annual Review of Nutrition*, *36*, 627–645. https://doi.org/10.1146/annurev-nutr-071715-051213

Poston, L., Caleyachetty, R., Cnattingius, S., Corvalán, C., Uauy, R., Herring, S., & Gillman, M. W. (2016). Preconceptional and maternal obesity: Epidemiology and health consequences. *The Lancet: Diabetes & Endocrinology*, *4*(12), 1025–1036. https://doi.org/10.1016/S2213-8587(16)30217-0

Preusting, I., Brumley, J., Odibo, L., Spatz, D. L., & Louis, J. M. (2017). Obesity as a predictor of delayed lactogenesis II. *Journal of Human Lactation*, *33*(4), 684-691. https://doi.org/10.1177/0890334417727716

Rasmussen, K. M. (2007). Association of maternal obesity before conception with poor lactation performance. *Annual Review of Nutrition*, *27*, 103–121. https://doi.org/10.1146/annurev.nutr.27.061406.093738

Rasmussen, K. M., Hilson, J. A., & Kjolhede, C. L. (2001). Obesity may impair lactogenesis II. *The Journal of Nutrition*, *131*(11), 3009S–11S. https://doi.org/10.1093/jn/131.11.3009S

Rasmussen, K. M., & Kjolhede, C. L. (2004). Prepregnant overweight and obesity diminish the prolactin response to suckling in the first week postpartum. *Pediatrics*, *113*(5), e465–e471. https://doi.org/10.1542/peds.113.5.e465

Rassie, Mousa, A., Joham, A., & Teede, H. J. (2021). Metabolic conditions including obesity, diabetes, and polycystic ovary syndrome: Implications for breastfeeding and breastmilk composition. *Seminars in Reproductive Medicine*, *39*(3-04), 111–132. https://doi.org/10.1055/s-0041-1732365

Reid, J., Schmied, V., & Beale, B. (2010). 'I only give advice if I am asked': examining the grandmother's potential to influence infant feeding decisions and parenting practices of new mothers. *Women and Birth : Journal of the Australian College of Midwives*, *23*(2), 74–80. https://doi.org/10.1016/j.wombi.2009.12.001

Sayres, S., & Visentin, L. (2018). Breastfeeding: Uncovering barriers and offering solutions. *Current Opinion in Pediatrics*, *30*(4), 591-596. https://doi.org/10.1097/MOP.0000000000000647

U.S. Department of Health and Human Services. (2011). *The Surgeon General's call to action to support breastfeeding*. Washington, DC: U.S. Department of Health and Human Services, Office of the Surgeon General.

Victora, C. G., Bahl, R., Barros, A. J., França, G. V., Horton, S., Krasevec, J., Murch, S., Sankar, M. J., Walker, N., Rollins, N. C., & Lancet Breastfeeding Series Group (2016). Breastfeeding in the 21st century: Epidemiology, mechanisms, and lifelong effect. *Lancet, 387*(10017), 475–490. https://doi.org/10.1016/S0140-6736(15)01024-7

Wambach, K., & Genna, C.W. (2016). Anatomy and physiology of lactation. In K. Wambach and J. Riordan (Eds.), *Breastfeeding and human lactation.* (5th ed., pp. 79-120). Jones & Bartlett.

Woods Barr, A. L., Miller, E., Smith, J. L., Cummings, S. M., & Schafer, E. J. (2021). #EveryGenerationMatters: Intergenerational perceptions of infant feeding information and communication among African American women. *Breastfeeding Medicine : The Official Journal of the Academy of Breastfeeding Medicine*, *16*(2), 131–139. https://doi.org/10.1089/bfm.2020.0308

Żelaźniewicz, A., & Pawłowski, B. (2019). Maternal breast volume in pregnancy and lactation capacity. *American Journal of Physical Anthropology*, *168*(1), 180–189. https://doi.org/10.1002/ajpa.23734