



## Research Article

## Association between Delayed Lactogenesis II and Early Milk Volume among Mothers of Preterm Infants

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## ABSTRACT

**Purpose:** This study aimed to evaluate the effect of delayed lactogenesis II on early milk volume in mothers expressing milk for their preterm infants.**Methods:** 142 mothers with preterm infants participated in a longitudinal cohort study, the milk volumes over 14 days postpartum between mothers with delayed lactogenesis II ( $\geq 72$  hours) and mothers with non-delayed lactogenesis II ( $< 72$  hours) were compared using Wilcoxon's rank sum tests.**Results:** The prevalence of delayed lactogenesis II among mothers of preterm infants was 36.0% (36/100). There existed negative correlations between the onset of lactogenesis II and the daily milk volumes ( $r_s = -0.525 \sim -0.354$ ,  $p = .002 \sim p < .001$ ). The milk volumes in every 24-hour of the 14 days postpartum in delayed group were significantly less than that in non-delayed group ( $p = .002 \sim p < .001$ ). After controlling for the covariates, pregnancy-induced hypertension syndrome, delayed expression initiation, shorter daily sleeping time were found to be the risk factors for delayed lactogenesis II.**Conclusion:** Delayed lactogenesis II was associated with lower milk volume in early postpartum period. Women who were at risk for delayed lactogenesis II need targeted interventions and additional support during pregnancy and postpartum.© 2019 Korean Society of Nursing Science, Published by Elsevier Korea LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Lactogenesis II is defined as the onset of copious milk production after birth [1,2]. This stage usually starts 30 to 48 hours (hrs) postpartum in term delivery, and breast fullness or engorgement is reported by most women at that time [3,4].

The timing of lactogenesis II is an important variable for milk secretion as it reflects the initiation of lactation [5–7]. Delayed lactogenesis II, which usually occurs after 72 hrs postpartum [2,7], has been correlated with a decline in the breastfeeding rate in full-term mothers. According to Chapman et al. [5], a delay in lactogenesis II can result in shorter breastfeeding duration than do their counterparts with an earlier onset of lactation. Delayed lactogenesis II is not a rare phenomenon among all mothers, with the prevalence of 22–31% after 72-hr postpartum [3,4]. The risk factors

associated with delayed lactogenesis II in full-term delivery [2,8] include maternal obesity, increasing maternal age, prolonged stage II labor, unscheduled cesarean section, gestational diabetes, and formula-feeding before onset of lactation. Dewey et al [9] reported that a delay in breastfeeding and the premature delivery had also been correlated with later lactogenesis II.

Breast milk is the optimum food for newborns, especially for preterm infants [10]. Mothers who deliver prematurely are strongly encouraged to breastfeed their own milk to the infants [11]. However, owing to the poor development of sucking and swallowing reflexes in preterm infants, mothers may need to pump or express breast milk for considerable periods when the infants stay in neonatal intensive care unit (NICU) and are physically separated from their mothers. In fact, the preterm mothers have more difficulties establishing and sustaining lactation compared with full-term mothers, and premature delivery is associated with less milk volume [1,7,10]. Hill et al. [11] reported that only 50% of mothers who delivered prematurely were able to express sufficient milk to meet their infant's needs at 6 weeks after birth. Thus, the objective of exclusive breastfeeding for all infants poses a great challenge, and research is needed to identify barriers to reach this objective.

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Therefore, the purpose of this longitudinal cohort study was (a) to objectively measure the early milk volume and the timing of lactogenesis II in mothers expressing breast milk for their preterm infants and to analyze the correlation between the delayed lactogenesis II and the insufficient early milk volume and (b) to identify risk factors predicting the delayed lactogenesis II in preterm mothers.

## Methods

### Study design

This longitudinal cohort study followed up a convenience sample of mothers who delivered prematurely in the department of obstetrics in a level III tertiary hospital in Shandong province, China. The recruitment of mothers was conducted through individual interview on Day 1 postpartum.

The mothers were surveyed every day in person by the research nurses during their stay in hospital; and then, they were followed up daily through a telephone call or WeChat (Tencent Holdings Limited, Shenzhen, China) after being discharged home, with regard to the data of milk expression and the timing of lactogenesis II over the course of their infants staying in NICU.

To standardize the hand expression and data collection, three graduate nurse students were chosen as the research nurses, who were trained in hand expression and data collecting techniques by the first author, and they were available to assist with milk expression and measurement on mothers' requests. For mother's initial expression, the research nurse would demonstrate and teach the mothers enrolled the detailed procedure of hand expression in accordance with the hand expression technique protocol and assessed them timely to make sure they expressed the breast properly.

### Setting and participants

At the hospital, it is a routine postpartum care for obstetric nurses to assist and/or instruct mothers to perform manual expression and pumping of breast milk during the period of mother–infant separation (the preterm infants are usually transferred to NICU as soon as being delivered). The mothers are encouraged to initiate breast expression as early after delivery as possible, in accord with their condition, usually starting within 6 h postpartum.

The discharge date at the obstetric department depends on the delivery mode. Mothers who deliver vaginally are normally discharged on Day 3 postpartum. Mothers who deliver by cesarean are normally discharged on Day 4 postpartum.

From January 2018 to September 2018, a convenience sample of 142 eligible mothers was recruited. The inclusion criteria were the following: (a)  $\geq 20$  years, married, and delivered in the hospital; (b)  $< 37$  weeks of gestation, singleton; (c) with the intention to breastfeed and no related contraindications; (d) the preterm infants had been transferred to NICU; (e) the mothers were in clear consciousness, could understand, and answer questions independently; and (f) available for telephone call or WeChat follow-up. The exclusion criteria were the following: (a) severe maternal illness; (b) presence of major infant anomalies; and (c) the infant not expected to live over 2 weeks after birth or known plans to transfer the infant to another facility. The mothers were approached for enrollment after delivery in their postpartum room. Among the mothers recruited, 42 were withdrawn for the following reasons: the worsening condition of the preterm infants (10), incomplete log books of milk expression and pumping (16), infants discharged home before 14 days postpartum (12), additional 4 mothers were lost to follow-up without any reason. Thus,

the statistical design of this study dictated that the data could only be analyzed from these final sample of 100 preterm mothers with complete data.

### Ethical considerations

The research started after receiving approval from Binzhou Medical University Hospital review board (Approval no. 2018-016-01). During the individual interview with each mother, the research nurse explained the procedures and purpose of the research, including voluntary participation and withdrawal, as well as anonymous data collection for research purposes only. The study proceeded after obtaining mothers' written consent forms.

### Data Collection

The baseline data, which included details of maternal demographic, perinatal complications, and infant characteristics, were collected by maternal interview and medical chart. The mothers were required to record their milk expression each day, including the date, time, duration, and volume removed from each breast and the onset timing of lactogenesis II on a logbook which was given by the research nurse. The daily sleeping time and the daily liquid input were also recorded during the preterm infants' hospitalization in NICU.

Before the onset of lactogenesis II, the mothers were instructed to hand express the colostrum as early and frequently as possible, and the duration of the expression was 5–10 minutes for each breast. The milk was collected into a sterile collection bag provided to them by the research nurse and measured in a syringe to the nearest 0.2 ml. After the onset of lactogenesis II, an electronic breast pump with a graduated scale on the bottle (the Small White Bear, Shenzhen, China) was used for pumping breast milk. The mother was encouraged to pump breasts at least eight times per day for 10 minutes on each breast. If milk was still flowing, the mother was instructed to continue pumping for 2 more minutes after flow of milk ceased. All mothers used the same electronic breast pump during hospitalization and an equivalent breast pump for use at home. The Milk volume was measured by mothers after each completed pumping session by reading the graduated scale on the bottle to the nearest 1 ml. Mothers had access to lactation services that were provided on request from the nurses. The use of hand expression and breast pump was assessed routinely by the research nurse, which was a standard postpartum care at the department. After the mother was discharged home, two follow-up visits were made to ensure compliance with the pumping frequency, accurate measurement, and documentation of pumping sessions, and these visits were made on Day 5 and 10 of the study by the research nurses.

The timing of lactogenesis II was recorded by the mother based on her perception of breast symptoms of sudden hardness, fullness, swelling, and leakage of milk from the breast, which had been proved to be a valid method [7,15]. The timing was recorded to the nearest hour of the postpartum day.

The follow-up data collection was conducted through a daily telephone call or WeChat by the research nurse after the mother was discharged home. In addition, each mother received a pamphlet with specific instruction on breast expression, milk pumping, collection, and storage as per the preterm infant care protocol.

The measurement of 24-hr milk volumes during the infants' stay in NICU was conducted by weighing each collection bag, which were labeled with the specific date and time and were brought to NICU by the mothers. The weight of breast milk in gram is equivalent to the volume in milliliter, and that has been validated as a precise measurement of the milk volume yielded [5,7].

## Data analysis

Data entry and analysis were conducted using SPSS18.0 (IBM-Corp., Armonk, NY, USA). The bivariate differences between groups (mothers who experienced delayed lactogenesis II vs mothers who did not experience delayed lactogenesis II) were compared using t test for continuous data and  $\chi^2$  test for categorical data. The milk volumes in 24-hr periods for each group were compared using the Wilcoxon rank-sum test. Multiple logistic regression was used to identify the variables associated with the outcome of delayed lactogenesis II. All variables appeared in bivariate analysis were included in the model to avoid eliminating the significant ones. The odds ratio in a forward stepwise approach is used to indicate the risk for delayed lactogenesis II on the model.  $p < .05$  was considered statistically significant.

## Results

The mothers were followed up for 14 days for the measurement of milk volume and the timing of lactogenesis II.

### Sample characteristics

The mean age of the 100 mothers was 29.71 years. The mean gestational age of the preterm infants whose mothers enrolled in

this study was 33.92 weeks, with the mean birth weight of 2093.43 grams. The mothers were predominantly primiparas (58.0%), vaginally delivered (54.0%), combined with pregnancy-induced hypertension syndromes (PIHS, 64.0%), and without any previous breastfeeding experience (57.0%). Approximately 85% of the mothers' serum albumin was less than 35 g/L. Table 1 demonstrated the sample characteristics by the lactogenesis II status.

### The timing of lactogenesis II

For the 100 mothers enrolled, the mean timing of onset of lactogenesis II was 68.23 hrs [standard deviation (SD) 26.42]. Among them, 36 mothers (36.0%) experienced a delay in lactogenesis II ( $\geq 72$  hrs, delayed group), and the mean timing was 97.56 hrs (SD 26.68); 64 mothers (64.0%) reported the onset less than 72 hrs (nondelayed group), and the mean timing was 51.73 hrs (SD 6.32).

In this study, mothers in the delayed group were similar to those in the nondelayed group in the years of age, parity, weeks of gestational age, birth weights, delivery methods, serum albumin, previous breastfeeding experience, daily frequency of milk expression, daily sleeping time, and daily liquid input. However, the mothers of the delayed group initiated breast expression later, more combined with PIHS. The results are shown in Table 1.

**Table 1** Characteristics and Timing of Lactogenesis II of the Sample (N = 100).

Variables	Total (N = 100)	Timing of lactogenesis II		p
		$\geq 72$ hrs (n = 36)	< 72 hrs (n = 64)	
		n (%) or Mean (SD)		
Age (yrs)	29.71 (5.21)	30.08 (5.08)	29.45 (5.25)	.562
Parity				
Primiparas	58 (58.0)	21	37	.961
Multiparas	42 (42.0)	15	27	
Gestational age (weeks)	33.92 (1.91)	33.71 (2.16)	34.06 (1.67)	.414
Birth weight (g)	2093.43 (437.93)	2073.33 (450.97)	2104.69 (433.62)	.732
Pregnancy-induced hypertension syndrome				
Yes	64 (64.0)	18	46	.034
No	36 (36.0)	18	18	
Delivery method				
Vaginal	54 (54.0)	19	35	.851
Cesarean section	46 (46.0)	17	29	
Serum albumin (g/L)	30.62 (4.01)			
< 35	85 (85.0)	34	51	.052
$\geq 35$	15 (15.0)	2	13	
Previous breast feeding experience				
Yes	43 (43.0)	16	27	.834
No	57 (57.0)	20	37	
Expression initiation (hrs)	9.21 (6.41)			
$\leq 6$	30 (30.0)	6	24	.029
$> 6$	70 (70.0)	30	40	
Daily expression frequency (times)	6.39 (0.83)	6.39 (0.79)	6.39 (0.85)	.982
Daily sleeping time (hrs)	8.46 (1.30)	8.22 (1.28)	8.59 (1.30)	.181
Daily liquid input (ml)	3863.91 (667.62)	3741.94 (658.80)	3932.52 (667.84)	.172

Note. hrs = hours; yrs = years.

### The comparison of daily milk volumes between two groups on Day 1 through Day 14 postpartum

As shown in Table 2 and Figure 1, the milk volumes in the nondelayed group increased obviously during 2-3 days postpartum, while the milk volumes in the delayed group did not rise significantly until 3-4 days postpartum. The maximum daily growth of milk volume in the nondelayed group was 143.00 ml on Day 4 postpartum. However, the largest daily increase of milk volume in the delayed group did not happen until the 5th day postpartum, with the milk yield of 92.50 ml increased. At the end of the first week postpartum, the discrepancy of milk volume between two groups was 155.00 ml. While the difference at the second weekend increased to 207.50 ml.

**Table 2** Comparison of Milk Volumes between Two Groups on Day 1-14 Postpartum (N = 100).

PP (d)	Nondelayed group (ml, n = 64)		Delayed group (ml, n = 36)		Z <sup>a</sup>	p
	M <sup>b</sup>	P <sub>25</sub> -P <sub>75</sub> <sup>c</sup>	M <sup>b</sup>	P <sub>25</sub> -P <sub>75</sub> <sup>c</sup>		
1	0.30	0.00-1.20	0.00	0.00-0.18	-4.34	<.001
2	5.50	1.45-19.10	1.70	0.73-2.95	-3.42	.001
3	31.00	12.50-87.75	13.50	5.25-29.75	-3.42	.001
4	174.00	78.00-276.00	42.00	23.40-124.00	-4.89	<.001
5	232.50	123.25-485.00	134.50	81.75-196.25	-3.40	.001
6	272.50	192.50-475.00	166.50	127.00-227.50	-3.65	<.001
7	357.50	200.00-545.25	202.50	164.75-280.00	-3.71	<.001
8	436.50	230.00-545.00	290.00	188.75-343.75	-3.39	.001
9	497.50	282.50-595.00	300.00	217.50-370.00	-3.67	<.001
10	535.00	321.25-635.00	310.00	262.50-392.50	-3.52	<.001
11	550.00	333.75-645.00	352.50	302.50-420.00	-3.33	.001
12	587.50	350.00-695.00	357.50	322.50-420.00	-3.23	.001
13	587.50	353.75-683.75	385.00	341.25-423.75	-3.10	.002
14	600.00	391.25-707.50	392.50	322.50-447.50	-3.53	<.001

Note. d = day; PP = postpartum.

<sup>a</sup> Z is the test value in the Wilcoxon rank-sum test.

<sup>b</sup> M is the median value of milk volumes of the group.

<sup>c</sup> P<sub>25</sub>-P<sub>75</sub> is the interquartile range (25<sup>th</sup>-75<sup>th</sup> percentile).

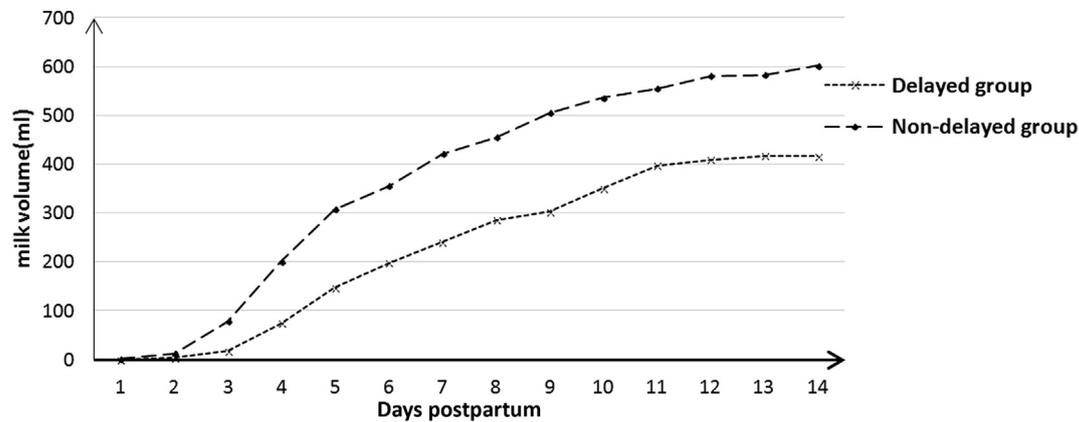


Figure 1. The comparison of milk volumes between two groups on Day 1–14 postpartum. This figure demonstrates the median daily volumes of expressed milk over the course of 14-day study of the two groups as defined by the timing of onset of lactogenesis II, the delayed group (the timing of onset of lactogenesis II  $\geq$  72 hrs,  $n = 36$ ) and nondelayed group (the timing of onset of lactogenesis stage II  $<$  72 hrs,  $n = 64$ ).

Table 3 Logistic Regression of Factors Predicting Delayed Lactogenesis II ( $N = 100$ ).

Risk factors	B <sup>a</sup>	Wald X <sup>2</sup>	Standard error	p	OR (95% CI)
PIHS	1.52	8.35	.53	.004	4.59 (1.63, 12.91)
Expression initiation ( hrs )	0.11	9.44	.04	.002	1.12 (1.04, 1.21)
Daily sleeping time ( hrs )	-0.43	4.86	.20	.027	0.65 (0.44, 0.95)

Note. CI = confident interval; hrs = hours; OR = odds ratio; PIHS = pregnancy-induced hypertension syndromes.

Model X<sup>2</sup> = 110.61,  $p < .001$ .

<sup>a</sup> B is the constant coefficient of logistic regression.

#### Risk factors influencing the delayed onset of lactogenesis II

When all factors in the bivariate analysis were combined in a stepwise regression model, significant predictors for delayed lactogenesis II were PIHS, later expression initiation time, and shorter daily sleeping time. The odds ratios indicate the risk for delayed lactogenesis II when other variables in the model are controlled. Mothers combined with PIHS had 4.59-fold [95% confidence interval (CI) 1.63 – 12.91,  $p = .004$ ] greater odds of delayed lactogenesis II compared with those without PIHS. In addition, the mother's extra risk for a delay in lactogenesis II increased by 1.12-fold (95% CI 1.04 – 1.21,  $p = .002$ ) for every hour of initiation postponed. While the daily sleeping time was a protective factor, the probability of occurrence of delayed lactogenesis decreased to 0.65-fold (95% CI 0.44 – 0.95,  $p = .027$ ) for every added hour of sleeping time. The results are shown in Table 3.

#### Discussion

The purpose of the study was to investigate the correlation between the delayed lactogenesis II and the insufficient early milk volume in mothers of preterm infants. Although this was a longitudinal observational research in a short period of 14 days, there were at least three notable findings resulting from the analysis. First, the prevalence of delayed lactogenesis II in premature mothers was higher compared with that reported in full-term mothers. Second, the delayed onset of lactogenesis II critically associated with the insufficient milk volumes during the 14-day

postpartum. Third, we identified that PIHS, delayed expression initiation time, and shorter daily sleeping time were the significant factors predicting delayed lactogenesis II.

The timing of lactogenesis II in full-term mothers usually starts 30 to 48 hrs postpartum [3,4], while women in this study initiated lactogenesis II on an average of 68.23 hrs after delivery, and 36 mothers (36.0%) experienced a delay in lactogenesis II ( $\geq$  72 hrs), which indicated that mothers of preterm infants were the highly risk population for delayed lactogenesis II. Such a delay is consistent with the findings of Henderson et al. [17], who found that, compared with full-term puerperants, the timing of lactation in preterm mothers was delayed at least 1 day. Similarly, Parker et al [1] reported that the average onset timing of lactogenesis II in mothers delivering very low birth weight infants was 97.15-hr postpartum. In fact, preterm mothers had been noted to have a decrease in prolactin response to suckling [10], and the prolactin and other hormones that normally occur during full-term pregnancy had a weak effect on breasts, causing a decreased development of mammary gland [13,14]. In addition, different from the suckling effect of direct breastfeeding on initiation of lactation, the effect of manual expression was significantly weaker [11,12], which may therefore interfere with the pathway to lactogenesis II.

It was apparent in this study that the delayed lactogenesis II indicated the poor lactation status during the first 2 weeks postpartum. The later the onset, the less the expression of milk volume. The onset timings of lactogenesis II were all negatively related to the milk volumes in early postpartum. Neifert et al. [18] found that the delayed onset of lactogenesis stage II, if measures were not timely and effectively taken, would lead to inadequate milk secretion, and thus resulted in the neonatal weight loss or even dehydration. Because early milk volume is associated with the later adequacy of milk production in preterm mothers [1,7], clinical staff should therefore pay much attention to the onset of lactogenesis II, and strategies to facilitate the initiation of lactogenesis in premature mothers are suggested to be conducted as soon as possible. Early initiation of breastfeeding within the first half hour of life is the fourth step in the Baby-friendly Hospital Initiative criteria, and early initiation of milk expression before 1 hr after delivery is a critical strategy in the effort to promote earlier lactogenesis II in mothers of preterm infants [7]. Recommendations for early initiation of milk expression should be incorporated into breastfeeding

protocols, and mothers should be encouraged and provided with support to initiate milk expression as soon after delivery as possible.

The result of this study adds support to the already known adverse effects of PIHS. Mothers combined with PIHS were 4.59 times prevalence of delayed lactogenesis II than that of mothers without PIHS. This may be associated with the PIHS-induced placental trophoblast-cell ischemic necrosis, which could happen in PIHS cases and decreased placental lactogen secretion [19]. Sievers et al. [16] found that PIHS was an important risk factor for the delayed onset of lactation, which was consistent with our result. For this reason, health-care workers should detect and target women with PIHS diagnostic during periparturient period and provide them with additional/professional lactation support and assistance to improve their likelihood of lactation success.

The identification of later initiation time for manual expression as a risk factor (odd ratio = 1.12) for delayed lactogenesis II suggests that breast expression for premature mothers should be started as early as possible. Parker et al [1] found that the expression initiation within 1-hr postpartum could significantly improve the lactation success than that of 1 to 6 hrs. In this study, the average initiation time was 9.21 hrs postpartum, of which the expression within 1 hr after delivery only accounted for 2%, within 6 hrs accounted for 30%, thereby encouraging and helping mothers to initiate breast expression as soon after delivery as possible is imperative. Mothers should be informed about the critical importance of early initiation of expression or pumping and should be encouraged to view this as a time-limited intervention.

Dewey et al. [9] found that there was correlation between sleeping time and the onset of lactogenesis II, which was consistent with the results of our study. The longer the daily sleeping time, the lower the incidence of delayed lactogenesis II. For this group of mothers, the sleeping time increased every each hour, and the probability of delayed onset of lactogenesis II would decrease to 0.65 odds. This may be explained by the fact that sleeping is closely related to hormone secretion and metabolism, and insufficient sleep could interfere with and/or inhibit the secretion of prolactin, oxytocin, and cortisol [17,20,21], thereby affecting the onset timing of lactogenesis. In clinical postpartum setting, medical staff should keep ward environment quiet and warm and congregate all the nursing procedures as much as possible to reduce the disturbance to maternal sleep.

## Conclusion

Findings from this study demonstrated that the delayed lactogenesis II in premature delivery was associated with lower milk volume in early postpartum period. Mothers who were at risk for delayed lactogenesis II may benefit from professional education, intervention, and nursing care both prenatally and postnatally. Further studies are needed to investigate the milk volume increase in mothers with delayed lactogenesis II after appropriate interventions are specifically targeted to the risk factors.

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## Conflicts of interest

The authors had no conflict of interest to declare.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.anr.2019.02.001>.

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