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REVIEW

Factors Influencing Delayed Onset of Lactogenesis: A Scoping Review

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Purpose: Delayed onset of lactogenesis is a significant barrier to achieving the WHO-recommended 50% exclusive breastfeeding rate in the first six months. This study maps the main factors influencing this condition, addressing gaps in the current research landscape.

Methods: Following Arksey and O'Malley's scoping review framework, databases such as PubMed, Web of Science (WOS), Embase, Cochrane Library, CINAHL plus with full text, China National Knowledge Infrastructure (CNIK), Weipu Chinese Journal Service Platform (VIP), Wanfang Data Knowledge Service Platform, and China Biomedical Literature Database (CBM) were searched on February 1, 2023. Studies in Chinese and English involving pregnant and postpartum women, focusing on delayed onset of lactogenesis, were included without restrictions on publication date or geography.

Results: Forty-six studies published between 2002 and 2022 met the inclusion criteria, revealing variable incidences of delayed lactogenesis among different groups. Thirty-four influencing factors were identified and organized into five themes: maternal-infant characteristics, perinatal mental state, physical activity participation during pregnancy, breastfeeding behaviors, and medical staff interventions. Within eighteen major factors highlighted, factors such as age, pre-pregnancy BMI, gestational weight gain, average LATCH score within 24 hours postpartum, labor analgesia, sleep, frequency of postpartum breastfeeding, and timing of initial breast suckling/pumping showed inconsistent or conflicting conclusions.

Conclusion: High and variable incidences of delayed lactogenesis underline its multifactorial nature. Effective interventions require strong advocacy from healthcare professionals and adherence by pregnant women. Further research using standardized methods is essential to clarify inconsistent or conflicting findings on the influencing factors.

Keywords: lactation, influencing factors, nursing, scoping review

Introduction

Breastfeeding is widely recognized for its unique benefits in enhancing the health of both mothers and infants. It can help mothers prevent breast cancer, ovarian cancer, and type 2 diabetes.[1] Additionally, breastfeeding plays a vital role in infants' immune regulation and tissue development. It provides a rich source of essential nutrients necessary for growth and development, along with active cells, probiotics, immune-active components, triglycerides, oligosaccharides, etc.[2] Beyond these direct benefits, research has suggested that various nutrients in breast milk may regulate genetic inheritance characteristics through DNA damage repair, stable methylation modification, and real-time gene transcription regulation.[3,4]

Given these numerous benefits, the World Health Organization recommends an exclusive breastfeeding rate of over 50% for the first six months.[5] However, global rates of exclusive breastfeeding within this period are suboptimal.[1,6] Delayed onset of lactogenesis (DOL), a critical factor affecting exclusive breastfeeding, has a significant global occurrence rate. Studies indicate that DOL rates vary from 10.1% to 58.0% in different countries,[7] with a global average rate of 26%,[8] meriting serious attention.

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Lactogenesis typically occurs in two stages: Stage I during pregnancy and Stage II, characterized by the onset of copious milk production, usually between 24 and 72 hours post-childbirth.[9] Delayed onset of lactogenesis or delayed Stage II involves delayed breast fullness and engorgement experienced by mothers after 72 hours postpartum.[10] This delay can affect breastfeeding duration,[10,11] leading to early termination and resulting in complications such as jaundice, hypoglycemia, dehydration, hypernatremia, and pathological weight loss in newborns.[12] Therefore, reducing the incidence of DOL is crucial for long-term health benefits.

Several factors influence DOL, including parity,[13–15]delivery mode,[15–17] maternal age,[18–20] pre-pregnancy BMI,[19,21,22] gestational weight gain,[13,19,23] gestational diabetes,[24–26] gestational hypertension disorders,[24,26,27] average LATCH score within 24 hours postpartum,[18,28,29] preterm birth,[30,31] depression,[14,20,32] anxiety,[24,31,33] labor analgesia,[17,19,34] sleep,[35–37] prenatal physical activity and sedentary time,[38] postpartum breastfeeding frequency,[23,39,40] initial breast suckling/pumping time,[15,24,41] breastfeeding education and knowledge,[33,42] among others.

However, due to variations in research methods, such as inconsistent age categorization and different tools for measuring sleep quality, research findings have been diverse. Additionally, existing reviews tend to focus primarily on specific core factors and lack a comprehensive examination.[8,9,43] Therefore, there is a need for a thorough and universally applicable summary, encompassing the main influencing factors, diverse conclusions, and key reasons for discrepancies, to facilitate early identification and support for women at potential risk and to enhance the quality of relevant research.

Methods

A scoping review, a method designed to rapidly map research progress in a specific area and identify its limitations,[44] is suitable for systematically reviewing the main influencing factors of delayed onset of lactogenesis, summarizing various conclusions, and explaining the reasons for their variations.

Adopting the methodological framework for scoping reviews proposed by Arksey and O Malley,[45] we addressed the following research question: What are the current status and main influencing factors of delayed onset of lactogenesis?

Inclusion/Exclusion Criteria

Based on the "PCC: Participants, Concept, Context" principle,[46] the inclusion criteria were as follows: ① Participants: Pregnant and postpartum women, aged ≥18 years. ② Concept: Delayed onset of lactogenesis. ③ Context: Current situation and influencing factors. ④Types of evidence sources: Primary research published in English or Chinese.

The exclusion criteria included: ①Studies not defining delayed onset of lactogenesis as delayed maternal perception. ②Studies directly using the mean and standard deviation of lactogenesis time from the sample for regression analysis. ③Editorials, reviews, study protocols, studies without full texts, incomplete data, and duplicates.

Search Strategy

A comprehensive search strategy was employed across multiple databases, including PubMed, Web of Science (WOS), Embase, Cochrane Library, CINAHL plus with full text, China National Knowledge Infrastructure (CNKI), VIP, Wanfang Data Knowledge Service Platform, and China Biomedical Literature Database (CBM). The research utilized subject headings and relevant keywords to identify pertinent peer-reviewed literature. Keywords included: ①Pregnant Women or expectant mother(s); ②Lactation; ③Risk factors, protective factors, causality, root cause analysis, or social determinants of health (Appendix Table 1 for the complete PubMed search strategy). The references of the included studies were manually tracked for additional relevant studies.

Study Selection

All retrieved records were imported into EndNote X9 for deduplication. To enhance the reliability of the screening process, two reviewers, including the first author and co-first author, independently performed an initial screening based on the inclusion and exclusion criteria by reviewing titles and abstracts, followed by a secondary screening of full texts. Any disagreements were resolved through consultation with the corresponding author. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)[47] chart documented document decisions related to inclusion/exclusion, ensuring transparency and rigor.

Review and Extraction

Upon finalizing the set of studies for inclusion, the following information was extracted using a custom template in Microsoft Office Word 2019:

- Author(s), publication year
- Study location, study design
- Description of sample (eg, first-time mothers, maternal separation mothers), participant numbers
- Occurrence rate of delayed onset of lactogenesis
- Assessment tools, influencing factors, data analysis results

The initial extraction was conducted by Sen Li and Tajiguli Wupuer. Rui Hou then reviewed the extraction to ensure completeness and accuracy. The initial analysis was prepared by Tajiguli Wupuer, and all authors reviewed and agreed upon the descriptive and narrative summary of findings.

Results

A total of 20,806 records were identified from nine electronic databases. After removing 5289 duplicates, 15,517 records were screened by titles and abstracts. Since the literature search did not restrict the field of study, studies involving animal experiments were excluded, resulting in 15,432 records being labeled as "exclude". The full texts of the remaining 85 records were retrieved for eligibility assessment. Following full-text screening, 41 studies were excluded. Two additional records were identified through hand-searching reference lists, culminating in 46 unique studies (Figure 1 for the PRISMA diagram).

As indicated in Table 1, the review encompasses 28 Chinese and 18 English studies, comprising 43 journal articles, 2 conference papers, and 1 dissertation. It includes 2 cross-sectional studies and 44 prospective cohort studies, published between 2002 and 2022. A majority (73.91%) were published from 2017 to 2022. Of these studies, 95.65% were prospective cohort studies. Among the English studies, the most publications originated from the United States (44.44%),

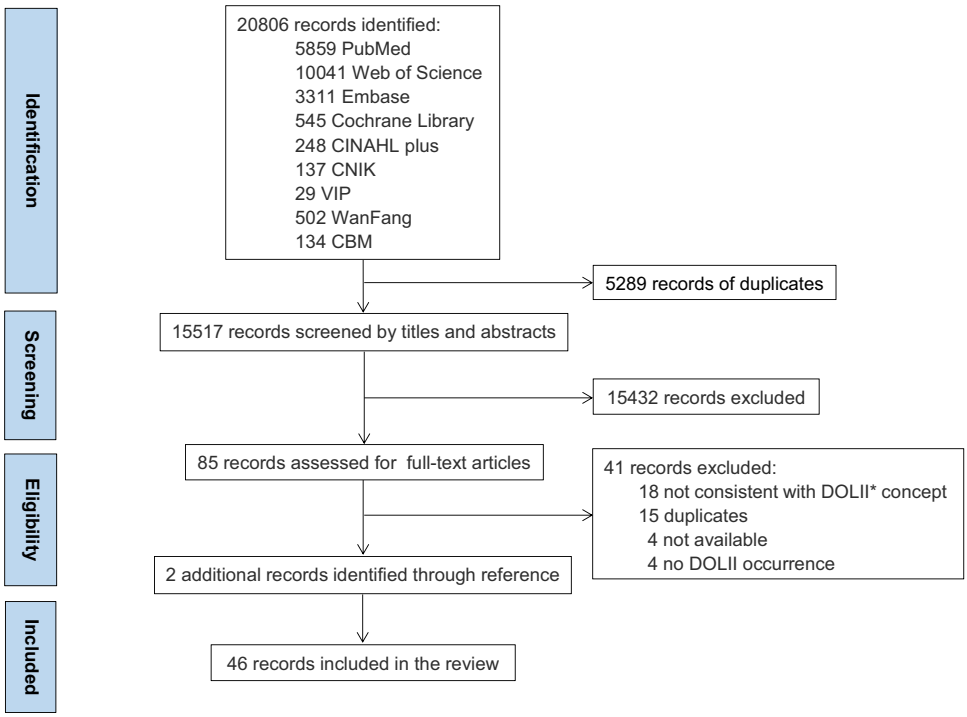

Figure 1 PRISMA diagram.
Note: *Delayed onset of Lactogenesis II.

Table 1 Characteristics of Studies

No.	First Author (Year)	Study Site	Study Design	Participants	Sample Size	DOLII Occurrence
1	Jiang et al (2022)[41]	Henan Province	Cross-sectional study	Hospitalized parturients	2064	22.09%
2	Ding et al (2022)[39]	Henan Province	Prospective cohort study	Singleton cesarean section parturients	330	31.5%
3	Ding et al (2022)[10]	Guangxi Zhuang Autonomous Region	Prospective cohort study	Direct rooming-in singleton elective cesarean section parturients with advanced maternal age	277	38.3%
4	Dong et al (2022)[30]	Shandong Province	Prospective cohort study	Vaginal delivery parturients	622	38.75%
5	Lu et al (2022)[25]	Shanghai	Prospective cohort study	Parturients with mother-to-child separation	154	36.36%
6	Li et al (2022)[27]	Shandong Province	Prospective cohort study	Parturients with mother-to-child separation (preterm baby)	300	35.67%
7	Zhao et al (2022)[38]	Anhui Province	Prospective cohort study	Singleton parturients	247	27.9%
8	Wei et al (2022)[26]	Beijing	Prospective cohort study	Singleton parturients	2109	34.2%
9	Quan et al (2022)[33]	Henan Province	Prospective cohort study	Hospitalized parturients	1185	22.62%
10	Zhang et al (2022)[42]	Jiangsu Province	Prospective cohort study	Direct rooming-in singleton full-term parturients	334	19.2%
11	Zhang et al (2022)[48]	Jiangsu Province	Prospective cohort study	Direct rooming-in parturients with hypothyroidism	150	45.3%
12	Lian et al (2022)[14]	Henan Province	Prospective cohort study	Singleton cesarean section parturients	468	33.3%
13	Mullen et al (2022)[15]	Canada	Prospective cohort study	Direct rooming-in parturients without pre-existing diabetes	177	55.4%
14	Ren et al (2022)[21]	Jiangsu Province	Prospective cohort study	Direct rooming-in full-term overweight/obese primiparous parturients (20–35 years old)	30	26.7%
15	Huang et al (2021)[24]	Shanghai	Prospective cohort study	Direct rooming-in singleton full-term parturients	1188	26.26%
16	Wang et al (2021)[32]	Jiangsu Province	Prospective cohort study	Singleton cesarean section parturients	150	33.3%
17	Xie et al (2021)[49]	Zhejiang Province	Prospective cohort study	High-risk pregnant women separated from baby in Maternal Intensive Care Unit (MICU)	229	42.35%
18	Zhang et al (2021)[50]	Shanghai	Prospective cohort study	Direct rooming-in singleton full-term parturients	10,751	21.31%
19	Ding et al (2020)[51]	Anhui Province	Prospective cohort study	Direct rooming-in full-term parturients	340	31.5%

(*Continued*)

Table 1 (Continued).

No.	First Author (Year)	Study Site	Study Design	Participants	Sample Size	DOLII Occurrence
20	Luo et al (2020)[31]	Guangdong Province	Prospective cohort study	Direct rooming-in singleton parturients with gestational diabetes	388	25.2%
21	Wang et al (2020)[52]	Shanghai	Prospective cohort study	Singleton parturients	240	28.33%
22	Rocha et al (2020)[20]	Brazil	Prospective cohort study	Direct rooming-in singleton full-term primiparous parturients	224	18.8%
23	Lin et al (2019)[53]	Guangdong Province	Cross-sectional study	Direct rooming-in singleton full-term parturients with advanced maternal age	120	42.5%
24	Casey et al (2019)[35]	America	Prospective cohort study	Singleton primiparous parturients	44	31%
25	Huang et al (2019)[13]	Hubei Province	Prospective cohort study	Direct rooming-in singleton full-term parturients	3282	18.4%
26	Yu et al (2019)[37]	Shandong Province	Prospective cohort study	Parturients with mother-to-child separation (preterm baby	100	36%
27	Teng et al (2018)[54]	Zhejiang Province	Prospective cohort study	Direct rooming-in parturients with advanced maternal age	286	39.16%
28	Liao et al (2018)[55]	Sichuan Province	Prospective cohort study	Parturients with gestational diabetes (gestational age ≥ 35 weeks)	394	34.3%
29	Luan et al (2018)[36]	Shandong Province	Prospective cohort study	Parturients with mother-to-child separation (preterm baby)	100	36%
30	Huang et al (2017)[28]	Hubei Province	Prospective cohort study	Direct rooming-in parturients who received prenatal care and delivery services at a maternity and child health care hospital	3636	18.7%
31	Si et al (2017)[56]	Jiangsu Province	Prospective cohort study	Singleton gestational diabetes parturients	284	33.8%
32	Haile et al (2017)[17]	America	Prospective cohort study	Singleton parturients with late preterm birth admitted to the Neonatal Intensive Care Unit (NICU) for up to 3 days without influencing breastfeeding	2053	23.7%
33	Preusting et al (2017)[19]	America	Prospective cohort study	Direct rooming-in singleton full-term parturients	216	57.9%
34	Tao et al (2017)[22]	Anhui Province	Prospective cohort study	Direct rooming-in singleton full-term parturients	3196	8.7%
35	Su et al (2016)[57]	Guangdong Province	Prospective cohort study	Singleton parturients	100	28%
36	Huang et al (2015)[29]	Hubei Province	Prospective cohort study	Direct rooming-in parturients who received prenatal care and delivery services at a maternity and child health care hospital	794	30.7%
37	Xue et al (2015)[58]	Guangdong Province	Prospective cohort study	Singleton parturients	204	28.4%

(*Continued*)

Table 1 (Continued).

No.	First Author (Year)	Study Site	Study Design	Participants	Sample Size	DOLII Occurrence
38	LIND et al (2014)[34]	America	Prospective cohort study	Singleton parturients with late preterm birth admitted to the Neonatal Intensive Care Unit (NICU) for up to 3 days without influencing breastfeeding	2366	23.4%
39	Matias et al (2014)[18]	America	Prospective cohort study	Direct rooming-in singleton parturients with gestational diabetes	883	33.3%
40	Zhu et al (2013)[23]	Anhui Province	Prospective cohort study	Singleton primiparous parturients (without pregnancy complications)	2017	9.8%
41	Nommsen-Rivers et al (2010)[40]	America	Prospective cohort study	Direct rooming-in singleton full-term primiparous parturients	431	44%
42	Zhu et al (2010)[59]	Anhui Province	Prospective cohort study	Primiparous parturients (20–35 years old)	2017	9.5%
43	Scott et al (2007)[60]	Australia	Prospective cohort study	Hospitalized parturients	453	11.7%
44	Hilson et al (2004)[61]	America	Prospective cohort study	Direct rooming-in singleton full-term parturients	114	24.56%
45	Dewey et al (2003)[16]	America	Prospective cohort study	Direct rooming-in singleton full-term parturients	280	22.14%
46	Grajeda et al (2002)[62]	Guatemala	Prospective cohort study	Direct rooming-in full-term parturients	136	27%

followed by China (33.33%), with lesser representation from other countries. Within China, the 34 articles (English: n = 6; Chinese: n = 28) spanned 11 provincial-level administrative regions, with Anhui and Jiangsu provinces being the most represented (14.29% each).

The incidence rate of delayed onset of lactogenesis in postpartum women ranged from 8.70% to 57.90%. Among the 46 included studies, only five[25,27,36,37,49] focused on maternal-infant separation in postpartum women. Out of eight categories of research subjects, only one study each investigated high-risk pregnant women in maternal intensive care unit (MICU)[49] and pregnant women with hypothyroidism[48] (Table 2 and Appendix Table 2 for details).

Based on an analysis of narrative findings from this review, 34 influencing factors extracted from 46 records were categorized into five themes: ①maternal-infant characteristics. ②perinatal mental state. ③physical activity participation during pregnancy. ④breastfeeding behaviors. ⑤medical staff interventions. These are discussed below.

Maternal-Infant Characteristics

This including parity (41.30%, 19/46), maternal age (34.78%, 16/46), perinatal complications (34.78%, 16/46), pre-pregnancy BMI (30.43%, 14/46), delivery mode (30.43%, 14/46), gestational weight gain (26.09%, 12/46), average LATCH score within 24 hours postpartum (6.52%, 3/46), gestational age (4.35%, 2/46), labor duration (4.35%, 2/46), baby birth weight (4.35%, 2/46), social support for breastfeeding (4.35%, 2/46), alcohol consumption during pregnancy (2.17%, 1/46), nipple morphology (2.17%, 1/46), and family economic status (2.17%, 1/46).

There was unanimous agreement that primiparity is an independent risk factor for delayed onset of lactogenesis (100%, 19/19).[13–15,24,26,28,30,39,51–58,60–62]

Table 2 DOLII* Study Status

		Total Sample Size	Number of Published Papers	Publication Year	DOLII Occurrence
Three major aspects					
	Direct rooming-in only	27,233	22	2002–2022	8.70%–57.90%
	Mother-to-child separation only	883	5	2018–2022	35.67%–42.40%
	Direct rooming-in + mother-to-child separation	16,725	19	2007–2022	9.50%–38.75%
Eight categories of research participants					
	Uncomplicated parturients	36,119	27	2002–2022	8.70%–57.90%
	Primiparous parturients	4763	6	2010–2022	9.50%–44.00%
	Gestational diabetes parturients	1949	4	2014–2020	25.20%–34.30%
	Advanced maternal age parturients	683	3	2018–2022	38.30%-–42.50%
	Cesarean section parturients	1225	4	2021–2022	31.50%–38.30%
	High-risk pregnancy women in the intensive care unit (ICU)	229	1	2021	42.40%
	Vaginal delivery parturients	622	1	2022	38.75%
	Gestational hypothyroidism parturients	150	1	2022	45.30%

Note: A literature (Ding et al 2022)[10] reported the delay in lactogenesis initiation in elderly cesarean section parturients. Therefore, the total number of published papers for the eight categories of research subjects is 47. *Delayed onset of Lactogenesis II.

Regarding maternal age, one study[40] identified age ≥30 years as a risk factor (6.25%, 1/16), while nine studies[24–26,30–32,49,54,56] proposed age ≥35 years (56.25%, 9/16). Additionally, six studies[18–20,53,55,62] did not specify a specific age threshold (3.75%, 6/16).

Research on perinatal complications primarily focused on gestational hypertension (37.50%, 6/16),[24,26,27,36,37,49] gestational diabetes mellitus (31.25%, 5/16),[24–26,28,51] insulin therapy for gestational diabetes (12.50%, 2/16),[18,55] and irregular blood glucose monitoring (6.25%, 1/16).[56] Other complications investigated included perineal lacerations or episiotomy during delivery (6.25%, 1/16),[30] hypothyroidism in pregnancy (6.25%, 1/16),[48] serum albumin concentration <35g/L (6.25%, 1/16),[14] and postpartum hemorrhage ≥300mL (6.25%, 1/16).[29]

Concerning pre-pregnancy BMI, studies since 2003 have not reached consensus. Five studies[18,19,31,40,55] found that pre-pregnancy BMI ≥30kg/m^2 could be a risk factor (37.71%, 5/14), while two studies[21,42] reported that pre-pregnancy BMI ≥24kg/m^2 could also predict delayed onset of lactogenesis (14.29%, 2/14). Other viewpoints include BMI ≥29kg/m^2 (7.14%, 1/14),[61] BMI ≥28kg/m^2 (7.14%, 1/14),[22] BMI >27kg/m^2 (7.14%, 1/14),[16] BMI ≥25kg/m^2 (14.29%, 2/14),[17,39] besides the studies[25,52] that did not suggest a specific BMI threshold (14.29%, 2/14).

Similarly, for gestational weight gain, the same situation arises. Two studies[23,59] identified a gestational BMI gain of ≥7.6kg/m^2 as a risk factor for delayed onset of lactogenesis (16.67%, 2/12), while another study[27] suggested that a gain of ≥7.2kg/m^2 could also be a predictor (8.33%, 1/12). Furthermore, nine studies[10,13,17,19,26,28–30,52] proposed excessive gestational weight gain as an indicator (75.00%, 9/12). Additionally, one study[42] posited that a pre-pregnancy BMI of ≥24kg/m^2, combined with appropriate gestational weight gain, may contribute to the occurrence of delayed onset of lactogenesis.

Regarding delivery mode, thirteen studies[15–17,23,24,26,41,48,57–60,62] unanimously identified cesarean section as a risk factor for delayed onset of lactogenesis (100%, 13/13). Additionally, one study[30] focused on women who underwent vaginal delivery, suggesting that the use of single or combined induction methods during delivery can contribute to delayed onset of lactogenesis.

Moreover, three studies[18,28,29] found that a low average LATCH score within 24 hours postpartum could be a contributor for delayed onset of lactogenesis. Among them, one study[18] considered average LATCH score of ≤7.5 points within 24 hours postpartum as an indicator (33.33%, 1/3), while another study[29] proposed a LATCH score of ≤8 points (33.33%, 1/3). Furthermore, one study[28] directly described specific items from the LATCH scoring system, stating that weak newborn suckling, unclear swallowing movements, and the need for assistance during breastfeeding on the first day postpartum are risk factors for delayed onset of lactogenesis (33.33%, 1/3).

Additionally, two studies each reported that preterm birth,[30,31] longer labor duration[16,30] and higher baby birth weight[29,40] are associated with a higher incidence of delayed onset of lactogenesis. Two studies[10,22] found that social support for breastfeeding is a protective factor. Also, one study each reported alcohol consumption during pregnancy,[20] a poverty income ratio of ≥3.5,[17] and flat or inverted nipples[16] as predictors of delayed onset of lactogenesis.

Perinatal Mental State

This includes depression (17.39%, 8/46), anxiety (15.22%, 7/46), pain (10.87%, 5/46), sleep (6.52%, 3/46), childbirth stress (4.35%, 2/46), stressful life events (4.35%, 2/46), childbirth experience (2.17%, 1/46), and coping strategies for the mother–infant relationship (2.17%, 1/46).

The conclusions regarding the correlation between antenatal depression, anxiety, and delayed onset of lactogenesis were relatively consistent, with studies indicating that antenatal depression[14,20,24,31–33,53,54] (100%, 8/8) and anxiety[10,24,31–33,53,54] (100%, 7/7) are risk factors for delayed onset of lactogenesis.

Studies on pain were categorized mainly into two main types: breastfeeding-related nipple pain and labor analgesia. One study[40] found that experiencing no nipple discomfort during the first 3 days postpartum could predict the occurrence of delayed onset of lactogenesis. Regarding labor analgesia, one study[30] considered it a protective factor, while three others[17,19,34] suggested the opposite.

Regarding the impact of sleep on delayed onset of lactogenesis, two studies[36,37] identified shorter sleep duration as a risk factor in mothers experiencing mother-infant separation, while another study[35] found higher sleep efficiency and more consistent nocturnal sleep duration as protective factors in primiparous mothers.

Additionally, two studies each reported that higher labor stress[25,62] and greater exposure to stressful life events during early pregnancy[23,59] are linked to a higher incidence of delayed onset of lactogenesis. Furthermore, one study each found a correlation between mothers who had negative experiences with vaginal delivery,[30] employed negative coping strategies for mother–infant relationship[25] and experienced delayed onset of lactogenesis.

Physical Activity Participation During Pregnancy

This includes physical activity in late pregnancy (2.17%, 1/46) and sedentary time (2.17%, 1/46). One study[38] indicated that an adequate level of physical activity (moderate or higher) acts as a protective factor, while sedentary time of ≥6.5 hours/day is a risk factor.

Breastfeeding Behaviors

These include postpartum breastfeeding frequency (15.22%, 7/46), initial breast suckling/pumping time (6.52%, 4/46), breastfeeding knowledge consultation during pregnancy (6.52%, 3/46), early mother-infant contact (6.52%, 2/46), maternal breast massage/lactation stimulation (4.35%, 2/46), and the use of pacifiers or formula supplements (4.35%, 2/46).

Seven studies[10,23,39–42,58] noted a correlation between a lower frequency of postpartum breastfeeding and a higher incidence of delayed onset of lactogenesis. Among them, two studies[23,40] specifically reported breastfeeding less than 2 times within 24 hours[40] or less than 3 times[23] (28.57%, 2/7) as contributing factors. Two other studies[10,58] suggested

breastfeeding ≤2 times within 24–48 hours as a risk factor (28.57%, 2/7). Three studies[39,41,42] did not specify a threshold for postpartum breastfeeding frequency (42.86%, 3/7).

Moreover, four studies[15,24,41,49] reported an association between delayed initial breast suckling/pumping time and delayed onset of lactogenesis. Among them, one study[49] did not provide a specific time threshold (25.00%, 1/4), two studies[24,41] concluded that ≥30 minutes is a risk factor (50.00%, 2/4), while another study[15] identified ≥2 hours as a risk factor (25.00%, 1/4).

Besides, three studies[39,41,42] indicated that breastfeeding knowledge consultation during pregnancy can effectively reduce the occurrence of delayed onset of lactogenesis. Two studies each identified maternal breast massage/nipple stimulation during pregnancy[10,41] and early mother-infant contact[33,41] as protective factors. Finally, two studies[10,21] reported predominant formula feeding as a contributing factor to delayed onset of lactogenesis.

Medical Staff Interventions

This includes antenatal breastfeeding education (4.35%, 2/46), direct rooming-in (2.17%, 1/46), breast stimulation using a low-frequency pulse rehabilitation therapy instrument (2.17%, 1/46), and psychological intervention (2.17%, 1/46).

Regarding medical staff interventions, two studies[33,41] indicated that incorporating antenatal breastfeeding education into routine care effectively reduces the incidence of delayed onset of lactogenesis. Additionally, one study each reported that direct rooming-in post-childbirth,[41] breast stimulation with a low-frequency pulse rehabilitation therapy instrument, and psychological intervention[33] act as protective factors against delayed onset of lactogenesis.

Discussion

The incidence of delayed onset of lactogenesis varied significantly across different populations with higher incidence among particular groups.

The incidence rate of delayed onset of lactogenesis in postpartum women from 2002 to 2022 ranged between 8.70% and 57.90%. Women who experienced mother-infant separation(35.67%-42.40%),[25,27,36,37,49] had advanced maternal age (38.30%-42.50%),[10,53,54] and underwent cesarean section(31.50%-38.30%),[10,14,32,39] were in high-risk pregnancies in intensive care unit(42.40%)[49] or had comorbid hypothyroidism(45.30%)[48] showed higher incidence rates than the global average(26%).[8] These results highlight substantial variations in the occurrence of delayed onset of lactogenesis among different populations, with particular groups experiencing higher rates, underscoring the need for heightened focus. Recent studies suggest future research trends and propose more targeted clinical interventions for delayed onset lactogenesis.

There are numerous influencing factors of delayed onset of lactogenesis, but some of them are still waiting to be verified.

Maternal-Infant Characteristics

Factors such as parity, delivery mode, maternal age, pre-pregnancy BMI, gestational weight gain, perinatal complications, average LATCH score within 24 hours postpartum, and preterm birth have been identified as primary influencers in maternal-infant characteristics.

From 2002 to 2022, numerous studies have confirmed that primiparity,[13–15,24,26,28,30,39,51–58,60–62] cesarean delivery,[15–17,23,24,26,41,48,57–60,62] advanced maternal age,[18–20,24–26,30–32,40,49,53–56,62] high pre-pregnancy BMI,[16–19,21,22,25,31,39,40,42,52,55] excessive gestational weight gain,[10,13,17,19,23,26–30,52,59] gestational diabetes,[24–26,28,51] pregnancy-induced hypertension,[24,26,27,36,37,49] and low LATCH scores[18,28,29] are risk factors for delayed onset of lactogenesis. The physiological mechanism linking primiparity, cesarean delivery, and advanced maternal age involves stress-induced stimulation of the vagus nerve, affecting lactogenesis initiation by increasing blood catecholamine levels.[14,26,52] Research on cesarean delivery has focused more on timing[63] and urgency,[15,62] suggesting that emergency and nighttime cesarean deliveries are more predictive. Regarding advanced maternal age, three different conclusions have been drawn: age ≥30 years,[40] possibly related to the sample's age distribution and criteria (primiparous women), age ≥35 years,[24–26,30–32,49,56,64] in line with the

domestic definition of advanced maternal age for high-risk pregnancies, and studies that do not specify an age threshold, likely due to inclusion of analyses treating age as a continuous variable.[18–20,53,55,62]

Primiparity, cesarean delivery, and advanced maternal age are uncontrollable risk factors. Therefore, clinical and primary healthcare professionals should inform women with these conditions about the potential for delayed onset of lactogenesis.[19,60] Additionally, they should enhance women's breastfeeding knowledge and skills through videos, live demonstrations, simulations, and experience sharing before delivery.[56] During labor, providing supportive and comforting companionship can help improve positive experiences, reducing childbirth fear and negative emotions.[51,52] Post-delivery, continuous breastfeeding support and encouragement are crucial to ensure successful initiation of lactogenesis.[14,15,26,52,60] Researchers should also meticulously select appropriate age classification standards to align with the specific population.

Although there is a consensus that high pre-pregnancy BMI and excessive gestational weight gain are risk factors for delayed onset of lactogenesis, details surrounding these factors remain controversial and require further exploration.

Research on the pre-pregnancy BMI threshold presents multiple conclusions, attributable to:

①Variations in the BMI classification guidelines referenced by researchers. Three studies[21,22,42] used the Blue Book of Obesity Prevention and Control in China, while nine studies[16–19,31,39,40,52,55] followed the World Health Organization BMI Classification Guidelines. One study[16] adjusted the overweight threshold to BMI > 27 kg/m^2 based on actual circumstances. Additionally, one study[61] utilized the Institute of Medicine BMI Classification Guidelines (pre-2009 version), and another study[25] did not use any specific BMI classification.

②Differences in statistical analysis methods. Twelve studies[16–19,21,22,31,39,40,42,55,61] conducted categorical regression analysis on pre-pregnancy BMI, while one study[52] only presented the trend of BMI changes in logistic regression, and another study[25] performed regression analysis on the continuous variable. Consequently, the latter two studies[25,52] did not include BMI classification thresholds.

Furthermore, while theories such as insulin resistance[55] decreased sensitivity of breast peripheral nerves,[65] and hormonal imbalance[42] have been proposed to explain why overweight or obese mothers experience a higher incidence of delayed onset of lactogenesis, the exact risk factor—whether obesity or overweight—and the underlying reasons remain uncertain.

The physiological mechanism underlying excessive gestational weight gain is similar to that of high pre-pregnancy BMI; specifically, progesterone in adipose tissue competes with and inhibits the effects of prolactin, consequently delaying lactogenesis.[13,17,26,27] Three different perspectives on gestational weight gain merit discussion. The first perspective suggests that a greater increase in gestational BMI correlates with a higher incidence of delayed onset of lactogenesis.[23,27,59] The second indicates that an increased body weight during pregnancy raises the incidence of delayed onset of lactogenesis.[10,13,17,19,26,28–30,52] The third suggests that it may be necessary to perform a combined analysis of pre-pregnancy BMI and gestational weight gain.[42] Concerning the first viewpoint, although Zhu et al argued that gestational BMI increase has a stronger correlation with delayed onset of lactogenesis compared to relative gestational weight gain,[23] setting a gestational BMI increase threshold based on quartiles alone cannot eliminate the impact of sample gestational BMI increase on statistical analysis results. Regarding the second viewpoint, six studies[13,17,19,26,30,52] referenced the gestational weight gain recommendations by the Institute of Medicine, while four studies[10,13,28,29] utilized quartiles to categorize gestational weight gain. Huang et al, in their 2019 study, observed significant data when categorizing gestational weight gain by quartiles, but not when using the Institute of Medicine's standards.[13] This discrepancy might be attributed to the study's Chinese population, highlighting the importance of selecting suitable reference indicators.

Weak awareness, inadequate knowledge, lack of skills, and insufficient support from healthcare institutions are key influencing factors for high pre-pregnancy BMI and excessive gestational weight gain.[66] Therefore, weight management-related education, motivational interviews,[27] and other methods can effectively enhance pregnant women's awareness of weight management and correct misconceptions about prenatal care, promoting lactogenesis.

Gestational hypertension and diabetes can disrupt lactogenesis through mechanisms such as ischemic necrosis of trophoblast cells[19,24,26,27,36,37,49,67–69] and disturbances in glucose metabolism.[17,24,70,71] Women with these conditions can reduce the risk of delayed onset of lactogenesis through regular prenatal check-ups, daily monitoring, and therapeutic

medications. Furthermore, although only one included study[48] discusses the association between gestational hypothyroidism and delayed onset of lactogenesis, research has confirmed that elevated thyroid-stimulating hormone levels can inhibit protein synthesis.[72] Hence, clinical attention to pregnant women with hypothyroidism remains crucial.

Although studies[18,28,29] have demonstrated that the LATCH score can identify mothers who may need additional breastfeeding guidance, covering five aspects: newborns' latching and swallowing, mothers' breastfeeding experience and comfort, and the need for external assistance, there is still debate over the specific score thresholds. Matias et al considered a LATCH score ≤7.5 as a risk factor for delayed onset of lactogenesis,[18] while Huang et al in their 2015 study suggested a LATCH score ≤8 as the threshold,[29] and later in 2017, they proposed a LATCH score ≤8.5.[28] The main reason for this discrepancy lies in the statistical analysis method used, where researchers set the median LATCH score of the sample as the threshold.

Despite these differences, healthcare professionals, in both clinical and primary care settings, can offer personalized health education on early breastfeeding initiation and exclusive breastfeeding based on the LATCH score. However, caution is needed when interpreting varying LATCH score results.

Research indicates that mothers of preterm infants are more prone to experience delayed onset of lactogenesis than mothers of full-term infants, due to lactation system immaturity and post-delivery mother-infant separation.[30,31] Therefore, clinical practice should encourage such mothers to engage in breast massage and lactation stimulation[10,41] to promote the timely establishment of the prolactin axis.

Perinatal Mental State

Depression, anxiety, labor pain, and sleep are significant factors influencing delayed onset of lactogenesis in the perinatal mental state.

Although depression and anxiety have gained prominence only in the last five years, multiple studies confirm their impact on delayed onset of lactogenesis through effects on sleep quality and nutritional intake of pregnant and postpartum women.[10,24,32,54] Their physiological mechanisms[14,20,31,33,54] are akin to those associated with primiparity, cesarean section, and advanced maternal age. Additionally, depression and anxiety often stem from childbirth stress in women who are primiparous,[20] of advanced maternal age,[10,53,54] have undergone cesarean sections,[10,14,32] or have gestational diabetes.[31] Therefore, targeted psychological counseling before delivery can mitigate the impact of negative emotions on lactogenesis.

Regarding labor analgesia's effect on lactogenesis, scholars hold varying opinions on whether it acts as a protective or risk factor for delayed onset. Dong et al believe that analgesics can lessen the impact of negative emotions such as pain and anxiety on prolactin secretion.[30] Conversely, Lind et al argue that analgesics used during labor can affect early effective breastfeeding by entering the fetal bloodstream and influencing lactation reflex by reducing maternal plasma oxytocin levels.[72] Another study indicates that the short half-life and high clearance rate of labor analgesics are unlikely to delay lactogenesis,[64] but due to the small sample size, further validation is needed.

High-quality sleep is identified as a protective factor against delayed onset of lactogenesis. However, slight differences exist in the discussion and analysis of sleep components due to the use of varied survey tools across studies. Some studies,[36,37] like those by Lu et al and Yu et al, mainly focus on sleep duration, while Casey et al also consider sleep efficiency and stability in addition to duration.[35] The main mechanisms influencing this are high levels of prolactin secretion during sleep[35,37,54] and the interaction between negative emotions and sleep.[10] Thus, healthcare professionals can aid lactogenesis by enhancing the sleep environment for pregnant and postpartum women and providing psychological support.

Physical Activity Participation During Pregnancy

Among the 46 studies included, only one[38] explored the correlation between physical activity during pregnancy and delayed onset of lactogenesis. However, the benefits of physical activity during pregnancy in controlling gestational weight gain and improving muscle tissue insulin sensitivity,[73] as well as reducing late pregnancy and early postpartum anxiety and depression, have already been proved in other studies.[74,75] Therefore, sufficient physical activity during pregnancy is a critical protective factor against delayed onset of lactogenesis. It is essential to develop tailored exercise

prescriptions for pregnant women at different pregnancy stages in obstetrics and gynecology clinics. These prescriptions should aim to mitigate the effects of excessive gestational weight gain, gestational diabetes, and negative emotions on lactogenesis. Additionally, increasing physical activity during pregnancy cannot offset the adverse effects of prolonged sitting on lactogenesis initiation.[38] Thus, reducing sedentary time while increasing physical activity is important.

Breastfeeding Behaviors

Postpartum breastfeeding frequency, initial breast suckling/pumping time, and breastfeeding knowledge consultation during pregnancy have been identified as key influencing factors in breastfeeding behaviors.

Regarding the research on postpartum breastfeeding frequency, although the association between higher breastfeeding frequency and lower incidence of delayed onset of lactogenesis,[10,23,39–42,58] as well as the physiological mechanism of early postpartum breastfeeding in facilitating the timely formation of the lactation hormone axis via sensory signals from the nipple,[24,39,41] have been demonstrated, inconsistency remains in the specific definition of breastfeeding frequency. The reasons for this inconsistency include:

①Different thresholds for defining enough breastfeeding frequency. Two studies[39,41] used mean ± standard deviation or confidence intervals, three studies[10,23,58] utilized binary classification, one study[41] adhered to the on-demand breastfeeding requirement recommended by Breastfeeding Promotion Strategy Guide (2018), while another[40] did not specify a defining basis.

②Variations in time frames for predictive indicators. Two studies each used the first 24 hours,[23,40] 24–48 hours,[10,58] or the average frequency of daily breastfeeding[41,42] as predictors of delayed onset of lactogenesis, while one study[39] employed 48 hours postpartum as the indicator.

③Different statistical analysis methods. Four studies[10,23,40,58] conducted categorical regression analysis for postpartum breastfeeding frequency, whereas three studies[39,41,42] presented trends in logistic regression without specifying categories.

Regarding the threshold of postpartum breastfeeding frequency, it is necessary to clarify whether the data refer to "breast suckling frequency" or "effective breastfeeding frequency". Until specific thresholds are established, it is advisable for mothers to at least adhere to on-demand breastfeeding requirements.

The initial breast suckling/pumping time is believed to have a physiological mechanism similar to that of postpartum breastfeeding frequency, with three distinct conclusions. The first conclusion identifies an initial breast suckling/pumping time of ≥30 minutes as a risk factor;[24,41] the second suggests ≥2 hours as a risk factor;[15] and the third pertains to late initiation of pumping time.[49] Concerning the first viewpoint, while researchers have justified it as "early suckling stimulates the timely formation of the lactation hormone axis"[24,41] and the Breastfeeding Promotion Strategy Guide (2018) also explicitly recommends newborns should suckle within 30 minutes post-delivery, this advice is considered a strong recommendation with very low-quality evidence.[76] Moreover, the emergence of the second viewpoint indicates the need for further research to validate its scientific basis. The third viewpoint, presented by Xie Xiaoxing et al in their 2021 study involving high-risk pregnant women in the intensive care unit,[49] highlights the importance of pumping for separated mother-infant pairs but necessitates additional research to establish a threshold for initiation pumping time, as they directly conducted regression analysis on continuous variables.

Jiang Yanli,[41] Ding Juan,[39] Zhang Yingying,[42] and others, in 2022, proposed that prenatal counseling on breastfeeding knowledge is an effective preventive measure against delayed onset of lactogenesis. They[39,41] explained its rationale as "changing the breastfeeding perception of pregnant women to make them more actively cope with postpartum breastfeeding". This aligns with the intervention behaviors of healthcare professionals, discussed in detail in Medical Staff Interventions section.

Medical Staff Interventions

Breastfeeding knowledge education, as the primary intervention behavior of healthcare professionals, plays a vital role in promoting lactogenesis and is an important measure to prevent delayed onset of lactogenesis. Specifically, scientific, rigorous, and personalized health education not only enables pregnant women to anticipate the possibility of delayed onset of lactogenesis in advance but also intervenes timely to mitigate the impact of controllable factors such as adverse

mental states and exercise habits during the perinatal period on lactogenesis. Furthermore, it encourages pregnant women to adopt scientifically informed breastfeeding behaviors postpartum. Given that existing breastfeeding knowledge education primarily focuses on the benefits of breastfeeding, incorporating knowledge about preventing delayed onset of lactogenesis is necessary in clinical practice.

Additionally, there is an overlap between certain breastfeeding behaviors of pregnant women, such as breastfeeding knowledge consultation during pregnancy,[39,41,42] breast massage/lactation stimulation,[10,41] early mother-infant contact,[33,41] and the intervention behaviors of healthcare professionals, including prenatal breastfeeding education,[33,41] breast stimulation with a low-frequency pulse rehabilitation therapy instrument,[33] direct rooming-in.[41] This underscores the necessity of providing pregnant women with education and nursing interventions like breast stimulation, while also emphasizing the importance of effective communication and enhancing pregnant women's compliance to improve the efficacy of interventions for delayed onset of lactogenesis.

Conclusion

A comprehensive review of the current status of delayed onset of lactogenesis reveals significant variability in its incidence across different populations, with certain groups exhibiting higher rates, necessitating considerable attention. The review of influencing factors identified several key elements, including maternal-infant characteristics, perinatal mental status, physical activity during pregnancy, breastfeeding behaviors, and medical staff interventions. Uncontrollable factors are mainly associated with maternal-infant characteristics. Among the controllable and uncontrollable factors, inconsistencies were found in maternal age, pre-pregnancy BMI, gestational weight gain, average LATCH scores within 24 hours postpartum, sleep, postpartum breastfeeding frequency, and initial breast suckling/pumping time. Labor analgesia presented conflicting conclusions. Furthermore, this study underscored the critical role of breastfeeding knowledge education in preventing delayed onset of lactogenesis. Based on these findings, it is recommended that clinical and primary healthcare professionals focus more on controllable factors when providing knowledge education and related interventions. Researchers should conduct more targeted studies on special populations and further investigate and validate inconsistent or conflicting influencing factors by using standardized data classification criteria and recognized research methods.

Abbreviations

WOS, Web of Science; CNIK, China National Knowledge Infrastructure; VIP, Weipu Chinese Journal Service Platform; CBM, China Biomedical Literature Database; DOLII, Delayed onset of Lactogenesis II.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article and its supplementary information files.

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