REVIEW

Incidence and factors influencing delayed onset of lactation: a systematic review and meta-analysis

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Abstract

Background Breastfeeding has many benefits for mothers and infants. Lactogenesis II is one of the key steps in the implementation of breastfeeding. If lactogenesis II occurs more than 72 h after delivery, it is termed delayed onset of lactation (DOL). DOL is associated with decreased milk production, shortened breastfeeding time, and pathological neonatal weight loss. A comprehensive summary of the incidence and factors influencing DOL is needed to provide a basis for improving breastfeeding practices and health outcomes.

Methods Studies on the incidence and factors influencing DOL were retrieved from 13 Chinese and English databases (PubMed, Embase, Web of Science, Cochrane Library, CINAHL, etc.) from database inception to August 2023. Two researchers independently conducted the study screening, data extraction and quality evaluation. Stata 16.0 SE software was used for data analysis, and sensitivity analysis and publication bias tests were also performed. The qualitative description method was used to analyse studies that could not be combined quantitatively.

Results A total of 35 studies involving 19,176 parturients, including 4,922 who had DOL, were included. The mean Newcastle–Ottawa scale score of the included studies was ≥ 6, indicating that the quality was relatively high. Finally, the incidence of DOL was 30%, and 13 factors influencing DOL with robust results and no publication bias were obtained: prepregnancy body mass index (overweight or obesity), gestational diabetes, gestational hypertension, thyroid disease during pregnancy, serum albumin levels (< 35 g/L), parity, (unscheduled) caesarean section, caesarean section history, daily sleep duration, gestational age, birth weight (< 2.5 kg), breastfeeding guidance and daily breastfeeding frequency. However, there were still six influencing factors with undetermined associations: age, gestational weight gain, birth weight (≥ 4 kg), anxiety, time of first breastfeeding session (maternal separation) and breast massage or treatment.

Conclusions The incidence of DOL is high. Clinicians should pay attention to parturients at high risk of DOL and formulate targeted prevention strategies according to the influencing factors to reduce the occurrence of DOL and promote better maternal and infant outcomes.

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Background

Lactation involves four stages: secretory differentiation, secretory activation, reaching volume, and maintenance of established lactation [1, 2]. Among these stages, secretory activation (lactogenesis II) is triggered by a decrease in progesterone levels after delivery of the placenta and involves changes in prolactin and cortisol (glucocorticoid) secretion and the closure of paracellular pathways [3], indicating that a large amount of milk is being secreted by the mother [4]. Delayed onset of lactation (DOL) is defined as the occurrence of lactogenesis II 72 h after birth [4]. The most commonly used evaluation method for the onset of lactation (OL) is maternal perception of milk coming in [1]. Importantly, studies have shown that the time of OL is negatively correlated with the amount of milk produced on the 14th day postpartum [5]. DOL independently increases the risk of the cessation of any or exclusive breastfeeding at 4 weeks postpartum by 62% [6], thereby shortening the duration of breastfeeding [7, 8] and reducing the rate of exclusive breastfeeding [7, 9]. Moreover, DOL can increase the risk of pathological neonatal weight loss (more than 10% of the birth weight) by 7.1-fold [10, 11]. Consequently, actively taking effective intervention measures to prevent DOL has an important impact on improving maternal and child health outcomes and breastfeeding practices.

Liu et al. [12] and Miao et al. [13] published systematic reviews on the prevalence and factors influencing DOL in Chinese women in 2021 and 2023, respectively. The results revealed that the prevalence of DOL was 24% [12] and 31% [13], respectively, and an increasing trend of DOL, which should attract the attention of clinical workers. In addition, the existing systematic reviews may not be sufficiently comprehensive in literature retrieval and statistical analysis strategies, and their reporting of results may also be inadequate [12–14], potentially affecting the comprehensiveness and consistency of the findings. Therefore, this study focused on the global perspective and prospective research to determine the incidence of DOL and analyse the factors influencing DOL quantitatively through meta-analysis and to summarize the influencing factors that cannot be quantitatively analysed via qualitative description, to provide evidence supporting the development of effective evaluation and intervention measures for preventing DOL.

Methods

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [15] and was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (ID: CRD42023458786).

Inclusion and exclusion criteria

Studies were considered eligible if they met all of the following criteria: (1) included women who chose to breastfeed after delivery; (2) studied the incidence or factors influencing DOL; (3) included the occurrence of DOL as the outcome and used the time of obvious breast tenderness or the sensation of milk coming in more than 72 h after delivery as the diagnostic criteria; and (4) used a prospective observational design.

Studies that met one of the following exclusion criteria were excluded: (1) studies with incomplete or erroneous data on variables; (2) studies for which data could not be directly or indirectly extracted; (3) studies for which the original text could not be obtained or the type of article was a review, conference paper, correspondence, comments, or study protocol; (4) studies published in different articles including the same participants: (a) for multiple studies of the same research object, the study with the most abundant research content or the most detailed description of the data was included; (b) for multiple studies with overlapping samples, the study with the longest study period was included; otherwise, the most recent study was included; 5) studies not published in Chinese or English; 6) studies with a sample size < 60; 7) nonhuman studies; or 8) studies for which the literature quality was low (quality assessment score ≤ 5).

Systematic search and strategy

Three researchers (YJP, KZ, and YH) jointly developed the search strategy and comprehensively searched the following databases for all relevant Chinese and English studies from database inception to August 2023: (1) Chinese databases: China National Knowledge Infrastructure (CNKI), Wanfang Database, China Science and Technology Journal Database (Weipu Database), and Chinese Biomedical Database (CBM); (2) English databases: PubMed, Ovid-Embase, Web of Science (via Web of Science Core Collection), Cochrane Library (the Cochrane central register of controlled trials, CENTRAL), CINAHL Plus (via EBSCOhost), APA Psycinfo (via EBSCOhost), Scopus, OpenGrey, and ProQuest Dissertations and Theses database (see full search strategy in Supplementary Material 1). To prevent the omission of relevant research, we reviewed the references of the included studies and relevant reviews. After the search was completed, duplicates were automatically removed by Endnote X9, followed by manual screening.

Study selection process and data extraction

Two researchers (YJP and KZ) independently screened the studies and extracted the data, and a third senior researcher (YH) independently reviewed and discussed the differences. Preliminary screening was performed by reading the title and abstract, followed by rescreening by reading the full text. If the title and abstract were not sufficient to make a decision, a decision was done by reading the full text. After the screening process was completed using Endnote X9, data were extracted from the final included studies, including the title, first author, year, study design, population characteristics, number of cases of DOL, sample size, study period, country, incidence, follow-up method and endpoint. In addition, all the influencing factors mentioned in the original study were extracted, and the influencing factors mentioned in two or more studies with the same definition were then identified. Finally, the exposure and outcome data of these influencing factors were extracted. For exposure variables, the number of cases for categorical variables and the mean ± standard deviation or median [interquartile range] for continuous variables were extracted.

Quality assessment

Prospective observational studies were included, so the Newcastle−Ottawa Scale (NOS) [16] was used to evaluate the quality of the included studies. The NOS includes three columns and eight items. The three columns specifically include the selection of the research population, comparability between groups, and the measurement of results or exposure factors, and the total score ranges from 0 to 9 points. Because the data extracted were the number of cases, the influence of confounding factors could not be controlled for, which might lead to the deterioration of 'comparability between groups'. The diagnostic criteria for DOL were based on maternal self-reported breast distension, which would lead to an insufficient evaluation; therefore, two points were deducted for all included studies. On this basis, studies with a score ≥ 6 points were considered high-quality studies. Two researchers (YJP and KZ) independently evaluated the quality of the included studies according to the evaluation criteria of the NOS [17]. When the opinions of the two researchers were inconsistent, the study was assigned to a third senior researcher (YH) for independent evaluation and discussion.

Statistical analysis

The extracted data and quality evaluation results were collated into Microsoft Excel 2021, and the data that could be used for quantitative analysis were entered into Stata 16.0 SE software for statistical analysis. In this study, a combined analysis or qualitative description of the influencing factors was performed only for variables included in at least two or more original studies. Because these were prospective observational studies, the risk ratio (RR) was used to combine the effect values for categorical variables, and the weighted mean difference (WMD) was used to combine the effect values for continuous variables. Cochran's Q test and the I^2 statistic were used to quantitatively analyse the heterogeneity between studies: (1) if $I^2 < 50\%$ and $p > 0.05$, the heterogeneity between studies was considered low, then a fixed effect model was used; (2) if $I^2 \geq 50\%$ or $p \leq 0.05$, the heterogeneity between studies was considered high, then a random effect model was used for more conservative statistical analysis. Subgroup analysis was performed to explore the source of heterogeneity.

When a certain influencing factor was included in three or more original studies, sensitivity analysis was carried out by eliminating the studies one by one and merging the remaining studies to test whether the results of the meta-analysis were robust, and we explored the reasons for nonrobust results. If not, the meta-analysis was abandoned, and a qualitative description was carried out instead. When the number of original studies including a certain influencing factor was ≥ 10, a funnel plot was drawn, and Egger's test was performed to explore whether publication bias existed. If so, the clipping method was used to correct the asymmetry of the funnel plot and the combined effect caused by publication bias. $p < 0.05$ was considered statistically significant.

Results

Search results and selection

We retrieved 13,112 studies from Chinese and English databases conducted before August 2023, and 9,489 studies were obtained by removing duplicate studies through Endnote and manual methods. After title and abstract screening, 189 studies were included. After rescreening by reading the full text, 32 studies that reported both the incidence and factors influencing DOL and 3 studies that reported only the incidence were ultimately included. No new studies were found after reviewing the references of the included studies and related reviews. The study screening process is shown in Fig. 1.

Characteristics and quality evaluation of the included studies

A total of 35 included studies were conducted from 1999 to 2023 in 8 countries, including China ($n=23$), the United States of America (USA, $n=6$), Canada ($n=1$), Peru ($n=1$), India ($n=1$), Australia ($n=1$), Brazil ($n=1$), and Ghana ($n=1$). A total of 19,176 women were included in these studies, 4,922 of whom had DOL. The methods of follow-up involved medical records, questionnaires, or interviews. The mean NOS score of all the studies was ≥ 6 points, indicating that these studies had
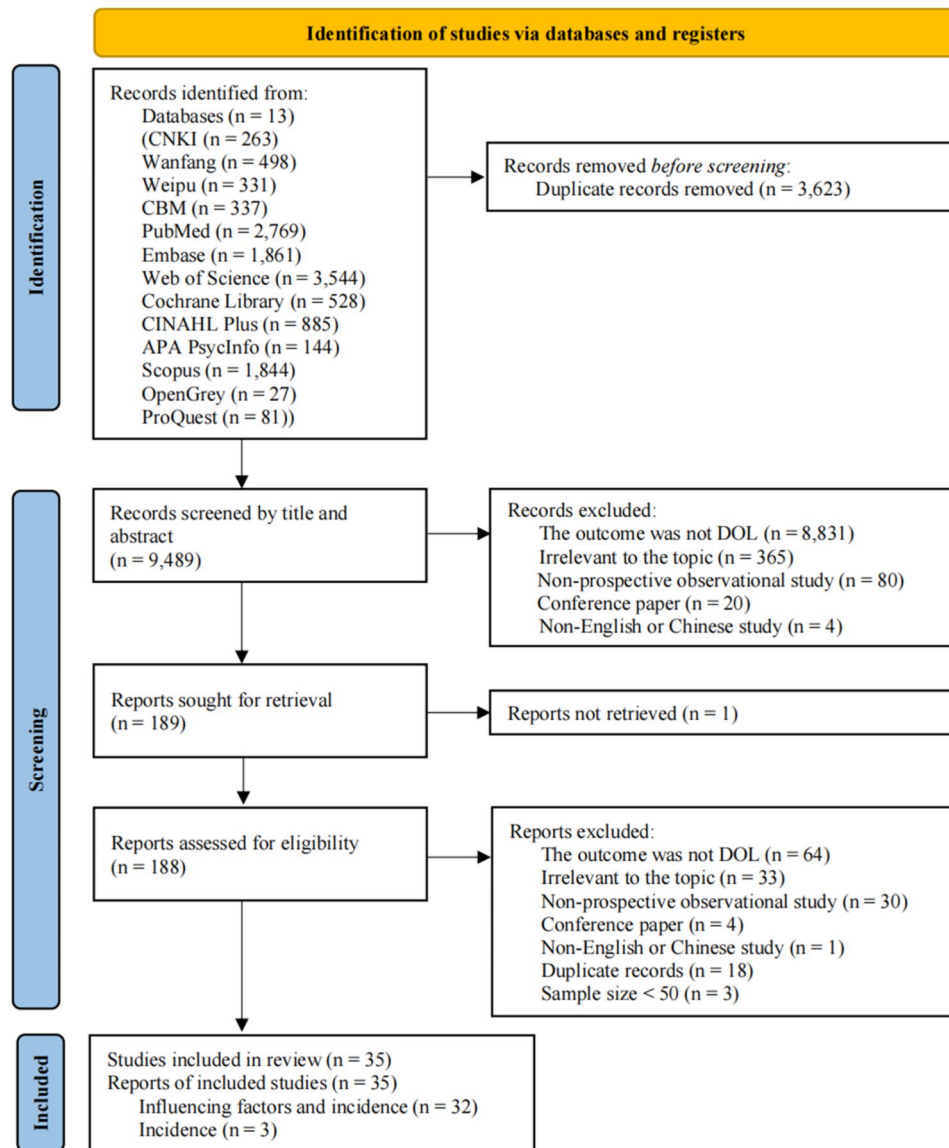
Fig. 1 PRISMA flowchart for the identification of studies

good methodological quality. The general characteristics and NOS scores of the included studies, sorted alphabetically by author name, are summarized in Table 1.

Meta-analysis and systematic review results

The combined incidence of DOL was obtained via meta-analysis. The meta-analysis results of factors influencing DOL are summarized in Table 2 according to the order of reporting. Combined with the qualitative description of the influencing factors, all the influencing factors involved could be divided into three categories: maternal-related factors, infant-related factors, and breastfeeding-related factors.

DOL incidence

A random-effects model was used to assess the incidence of DOL in 35 studies, and the result was 30% (95% CI 26, 34) (Fig. 2). Subgroup analysis by country category, combined with at least two or more studies, revealed an incidence of DOL of 30% in China (95% CI 26, 35) and 34% in the USA (95% CI 24, 43). The incidence of DOL in the USA was slightly higher than that in China (Fig. 3).

Maternal-related influencing factors

There was a statistically significant difference in age [5, 26, 28, 33] between the DOL and non-DOL groups (WMD =-0.30; 95% CI -0.573, -0.40), but the sensitivity analysis result was not robust. The combined results of 9 studies [24, 31, 36, 41–43, 45, 46, 48] and 5 studies [4, 20, 30, 40, 49], respectively, could not determine the

Table 1 Characteristics and quality of the included studies

Study	Maternal characteristic	DOL/total	Period	Country	Incidence (%)	Follow-up Method	Endpoint	NOS score
Bai [18]	General	112/553	NR	China	20.3	ITV	OL	7
Chapman [19]	Full-term	68/192	Dec. 1996-May 1997	USA	35.4	MR, ITV	OL	7
Dewey [11]	General	62/271	Feb.-Dec. 1999	USA	22.9	ITV	3 d pp	7
Ding [20]	Full-term	107/340	Jan. 2018-Jan. 2019	China	31.5	QTN, ITV	72 h-7 d pp	7
Ding J [21]	Caesarean delivery	104/330	Sept. 2021-Jan. 2022	China	31.5	MR, ITV	7 d pp	7
Ding QY [22]	Age ≥ 35 years	106/277	Mar. 2021-Oct. 2021	China	38.3	MR, QTN, ITV	72 h pp	7
Dong [23]	Vaginal delivery	241/622	6 Nov. 2020-16 Jan. 2021	China	38.8	MR, QTN, ITV	OL	7
Haile [24]	General	487/2,053	2005–2007	USA	23.7	QTN	21 d pp*	7
Hilson [25]	General	28/114	Aug.-Nov. 1998	USA	24.6	MR, QTN, ITV	8–12 m pp*	7
Huang [26]	General	604/3,282	started in Jan. 2013	China	18.4	MR, QTN, ITV	OL	6
Kong, 2008 [27]	General	29/75	Oct.-Nov. 2005	Australia	38.7	MR, ITV	NR	6
Li [28]	MS, Premature	107/300	Feb. 2020-May 2021	China	35.7	QTN, ITV	OL	7
Lian [29]	Caesarean delivery	156/468	9 Oct. 2021-17 May 2022	China	33.3	MR, ITV	7 d pp	7
Lu [30]	MS	56/154	Jan.-Jun. 2021	China	36.4	QTN, ITV	7 d pp	7
Luan [5]	Premature	36/100	Feb. 2016-Dec. 2016	China	36.0	QTN	14 d pp	7
Luo [31]	GDM	99/388	Jan. 2015-Dec. 2018	China	25.2	MR, QTN, ITV	3 d pp or OL	7
Matias [32]	Primipara	30/171	Nov. 2005-Jun. 2006	Peru	17.5	MR, QTN, ITV	72–96 h pp	7
Mullen [33]	Non-GDM	98/177	Apr. 2009-Jul. 2010	Canada	55.4	MR, QTN, ITV	7 d pp	7
Nommsen-Rivers [4]	Primipara	190/431	Jan. 2006-Dec. 2007	USA	44.0	MR, ITV	7 d pp	7
Otoo [34]	General	19/425	Jan. 2004-Jun. 2007	Ghana	4.5	QTN	OL	7
Preusting [35]	General	114/219	27 Aug. 2014-15 Oct. 2015	USA	52.1	MR, QTN, ITV	14 d pp*	7
Quan [36]	General	268/1,185	1 Mar. 2021-27 Feb. 2022	China	22.6	QTN	NR	7
Rocha [37]	Primipara	42/224	19 Jan. 2017-23 May 2017	Brazil	18.8	MR, ITV	7 d pp	7
Salahudeen [38]	General	50/200	Jun. 2011-Dec. 2011	India	25.0	MR, ITV	7 d pp	6
Si [39]	GDM	96/284	Mar.-Oct. 2016	China	33.8	MR, QTN, ITV	72 h pp	7
Wang [40]	General	68/240	Jan.-Apr. 2018	China	28.3	MR, ITV	7 d pp	6
Wei [41]	General	722/2,109	Mar. 2019-Feb. 2021	China	34.2	QTN	NR	7
Xie [42]	Admitted to MICU	97/229	May-Oct. 2019	China	42.4	MR, QTN	OL	7
Xu [43]	General	91/269	Dec. 2019-Nov. 2020	China	33.8	QTN, ITV	NR	7
Xue [44]	General	58/204	Sept. 2013-May 2014	China	28.4	MR, QTN, ITV	72 h pp	7
Zhang [45]	Primipara	86/300	Jan.-Jun. 2022	China	28.7	MR, QTN, ITV	NR	6
Zhang YY [46]	General	64/334	Mar.-Jun. 2020	China	19.2	MR, QTN, ITV	72 h pp	7
Zhang ZY [47]	General	110/281	Jan.-Dec. 2019	China	39.1	MR, ITV	OL	6
Zhao [48]	General	119/358	Oct. 2020-Nov. 2021	China	33.2	QTN, ITV	3 d pp	7
Zhu [49]	General	198/2,017	Mar.-Nov. 2008	China	9.8	MR, QTN, ITV	2 m pp*	7

MS, maternal separation; *GDM*, gestational diabetes mellitus; *MICU*, maternal intensive care unit; *MR*, medical record; *QTN*, questionnaire; *ITV*, interview; *NR*, not reported; *pp*, postpartum; *m*, months; *d*, days; *h*, hours

*For the studies with longer follow-up times, the dropout rates were 19.65% (Haile 2017 [24]), 16.79% (Hilson 2004 [25]), 4.00% (Preusting 2017 [35]), and 20.58% (Zhu 2013 [49]), respectively

association between a maternal age≥35 years (RR=1.40; 95% CI 0.96, 2.04) and ≥30 years (RR=1.33; 95% CI 0.98, 1.80) and DOL.

The pooled results of 8 studies [20, 21, 23, 24, 37, 40, 45, 48] and 3 studies [27, 29, 46], respectively, revealed that a prepregnancy BMI≥25.0 kg/m^2 (RR=1.47; 95% CI 1.17, 1.84) and a prepregnancy BMI≥24.0 kg/m^2 (RR=1.41; 95% CI: 1.14, 1.74) were risk factors for DOL. However, the correlation between prepregnancy BMI [26, 30, 33] (WMD=1.26; 95% CI -1.22, 3.75) and DOL was uncertain. Excessive gestational weight gain (GWG) [24, 37,

40, 41, 45, 46, 48] (RR=1.38; 95% CI 1.07, 1.77) was a risk factor for DOL, but the sensitivity analysis result was not robust.

The combined results of 14 [20, 21, 24, 26, 28–30, 33, 36–38, 41, 45, 48], 13 [5, 20, 21, 27–30, 36–38, 41, 42, 45], 6 [21, 29, 35, 38, 41, 47] and 2 [5, 29] studies, respectively, revealed that gestational diabetes mellitus (GDM) (RR=1.32; 95% CI 1.18, 1.49), hypertensive disorders of pregnancy (HDP) (RR=1.66; 95% CI 1.30, 2.12), thyroid disease during pregnancy (RR=1.18; 95% CI 1.05, 1.32), and a serum albumin level<35 g/L (RR=1.57; 95%

Table 2 Meta-analysis results of factors influencing DOL

Influencing factors	No. of studies	Heterogeneity test		Test model	Meta-analysis			Sensitivity analysis (Robust)	Egger's test (t/p-value)
		p-value	I² (%)		Effect size	Value (95% CI)	*p*-value		
Age									
Age (y)	4	0.788	0.0	F	WMD	-0.30 (-0.57, -0.04)	0.022	No	-
≥ 35 y	9	0.000	94.9	R	RR	1.40 (0.96, 2.04)	0.081	Yes	-
≥ 30 y	5	0.007	71.9	R	RR	1.33 (0.98, 1.80)	0.064	Yes	-
Prepregnancy BMI									
≥ 25.0 kg/m²	8	0.001	71.9	R	RR	1.47 (1.17, 1.84)	0.001	Yes	-
≥ 24.0 kg/m²	3	0.228	32.4	F	RR	1.41 (1.14, 1.74)	0.001	Yes	-
BMI (kg/m²)	3	0.000	96.6	R	WMD	1.26 (-1.22, 3.75)	0.319	Yes	-
GWG (excessive)*	7	0.000	81.5	R	RR	1.38 (1.07, 1.77)	0.013	No	-
GDM	14	0.010	53.0	R	RR	1.32 (1.18, 1.49)	0.000	Yes	1.63/0.129
HDP	13	0.000	82.1	R	RR	1.66 (1.30, 2.12)	0.000	Yes	-1.61/0.136
Thyroid disorders during pregnancy	6	0.262	22.9	F	RR	1.18 (1.05, 1.32)	0.005	Yes	-
Serum albumin level (g/L) < 35	2	0.294	9.3	F	RR	1.57 (1.12, 2.20)	0.008	-	-
Primipara	23	0.000	60.2	R	RR	1.40 (1.25, 1.56)	0.000	Yes	1.60/0.125
Caesarean delivery	20	0.000	77.0	R	RR	1.33 (1.17, 1.52)	0.000	Yes	0.43/0.675
Unscheduled caesarean delivery	2	0.749	0.0	F	RR	1.24(1.02, 1.51)	0.033	-	-
Caesarean delivery history	2	0.673	0.0	F	RR	0.75 (0.60, 0.93)	0.009	-	-
Duration of labour (h)	2	0.000	96.4	R	WMD	1.97 (-2.21, 6.16)	0.356	-	-
Vaginal delivery, stage 2 labour duration > 1 h	2	0.023	80.8	R	RR	1.41(0.73, 2.72)	0.308	-	-
Sleep duration (h/d)	2	0.585	0.0	F	WMD	-0.24 (-0.45, -0.02)	0.029	-	-
EPDS score ≥ 9	2	0.046	75.0	R	RR	1.24 (0.80, 1.93)	0.340	-	-
Education level									
≥ high school	2	0.511	0.0	F	RR	1.04 (0.70, 1.55)	0.848	-	-
≥ junior college	3	0.098	56.9	R	RR	1.22 (0.84, 1.77)	0.291	Yes	-
≥ undergraduate	7	0.030	57.0	R	RR	1.07 (0.90, 1.27)	0.472	Yes	-
> 9 years	2	0.069	69.8	R	RR	1.00 (0.62, 1.62)	0.998	-	-
Occupational status (Yes)	5	0.192	34.4	F	RR	0.99 (0.87, 1.14)	0.927	Yes	-
Mean monthly household income									
≤ 5,000 RMB/per person	3	0.952	0.0	F	RR	1.13 (0.92, 1.37)	0.238	Yes	-
≥ 10,000 RMB/per person	3	0.365	0.9	F	RR	1.00 (0.91, 1.10)	0.940	Yes	-
Nationality									
Hispanic	3	0.268	24.1	F	RR	1.10 (0.94, 1.29)	0.236	Yes	-
White	2	0.150	51.8	R	RR	0.97 (0.72, 1.30)	0.841	-	-
Han Chinese	5	0.957	0.0	F	RR	0.90 (0.72, 1.13)	0.352	Yes	-
Prenatal smoking status	4	0.622	0.0	F	RR	1.02 (0.83, 1.24)	0.872	Yes	-
Prenatal alcohol consumption status	5	0.038	60.7	R	RR	1.41 (0.88, 2.26)	0.157	Yes	
ART	2	0.225	32.1	F	RR	1.10 (0.81, 1.49)	0.547	-	-
Planned pregnancy	2	0.000	97.8	R	RR	0.51 (0.11, 2.39)	0.392	-	-
Insulin treatment	2	0.483	0.0	F	RR	1.15 (0.71, 1.86)	0.571	-	-
Fluid infusion (ml/d)	2	0.211	36.0	F	WMD	-21.31 (-72.93, 30.30)	0.418	-	-
Gestational weeks									
< 37 w	7	0.019	60.4	R	RR	1.29 (1.06, 1.57)	0.012	Yes	-
Weeks (premature, w)	2	0.726	0.0	F	WMD	-0.47 (-0.89, -0.06)	0.027	-	-
≥ 39 w	2	0.656	0.0	F	RR	1.11 (0.86, 1.43)	0.432	-	-
Weeks (term, w)	3	0.080	60.4	R	WMD	-0.04(-0.26, 0.19)	0.744	Yes	-
Birth weight									

Table 2 (continued)

Influencing factors	No. of studies	Heterogeneity test		Test model	Meta-analysis				Sensitivity analysis (Robust)	Egger's test (t/*p*-value)
		p-value	I² (%)		Effect size	Value (95% CI)	*p*-value			
<2.5 kg	2	0.590	0.0	F	RR	1.34 (1.07, 1.67)	0.011		-	-
≥4 kg	3	0.271	23.5	F	RR	1.29 (1.07, 1.56)	0.009		No	-
Weight (kg)	3	0.000	94.5	R	WMD	-0.36 (-0.86, 0.14)	0.160		Yes	-
Premature infants (g)	2	0.862	0.0	F	WMD	-17.09 (-102.28, 68.09)	0.694		-	-
Neonatal sex (male)	9	0.897	0.0	F	RR	0.97 (0.89, 1.05)	0.462		Yes	-
Apgar score										
<7 (1 min)	3	0.721	0.0	F	RR	1.29 (0.92, 1.81)	0.141		Yes	-
<8 (1 min)	3	0.018	75.1	R	RR	1.51 (0.78, 2.93)	0.218		Yes	-
Breastfeeding guidance (Yes)	7	0.116	41.3	F	RR	0.72 (0.64, 0.81)	0.000		Yes	-
Breastfeeding information sources ≥ 3	2	0.000	95.0	R	RR	0.50 (0.15, 1.65)	0.256		-	-
Breastfeeding frequency										
Frequency (t)	5	0.000	84.7	R	WMD	-0.63 (-1.10, -0.16)	0.008		Yes	-
Postoperative day 1 ≤ 2 t	2	0.581	0.0	F	RR	1.92 (1.36, 2.72)	0.000		-	-
Postoperative day 2 ≤ 2 t	2	0.583	0.0	F	RR	1.71 (1.34, 2.20)	0.000		-	-
Day 1 < 8 t	2	0.904	0.0	F	RR	1.00 (0.78,1.28)	0.970		-	-
History of breastfeeding	3	0.007	79.6	R	RR	0.73 (0.46, 1.17)	0.191		Yes	-
Previous insufficient lactation	2	0.916	0.0	F	RR	0.89 (0.64, 1.24)	0.491		-	-
Prenatal breast enlargement (No or a little)	2	0.041	75.9	R	RR	1.35 (0.86, 2.11)	0.192		-	-
Nipples (flat or sunken)	4	0.009	74.2	R	RR	0.99 (0.62, 1.58)	0.956		Yes	-
Bra cup size ≥ D	2	0.080	67.3	R	RR	1.32 (0.74, 2.34)	0.347		-	-

BMI, body mass index; *GWG*, gestational weight gain; *GDM*, gestational diabetes mellitus; *HDP*, hypertensive disorders of pregnancy; *EPDS*, Edinburgh Postnatal Depression Scale; *RMB*, renminbi; *ART*, assisted reproductive technology; *y*, years; *w*, weeks; *h*, hours; *t*, times; 'R', random; 'F', fixed; '-', not applicable

* Classification according to the recommendations of *Weight Gain During Pregnancy: Reexamining the Guidelines* [50]
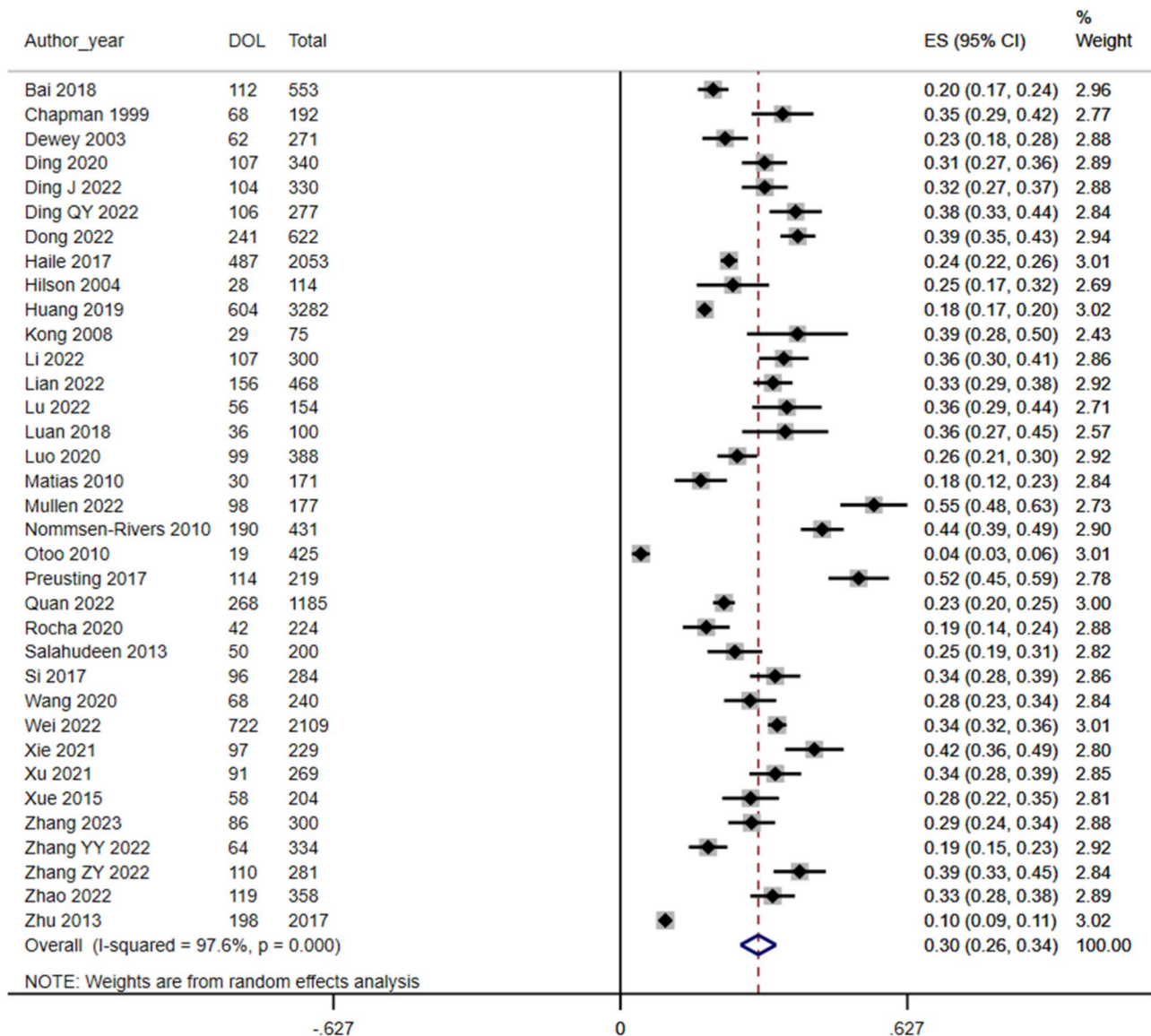
CI 1.12, 2.20) were risk factors for DOL. The descriptive analysis could not determine whether anaemia [21, 29, 38] was associated with DOL, and there might be no association between ovarian cysts during pregnancy [21, 29] and DOL.

The pooled results of 23 studies [5, 19–23, 25–29, 31, 33, 35, 36, 38–41, 43, 44, 46, 48] revealed that primiparity (RR=1.40; 95% CI 1.25, 1.56) was a risk factor for DOL. The combined results of 20 [4, 5, 24, 26, 28, 30–33, 35–38, 40, 41, 44–46, 48, 49] and 2 [21, 29] studies, respectively, revealed that caesarean delivery (RR=1.33; 95% CI 1.17, 1.52) and unscheduled caesarean delivery (RR=1.24; 95% CI 1.02, 1.51) were risk factors for DOL. A history of caesarean delivery [21, 29] (RR=0.75; 95% CI 0.60, 0.93) was a protective factor against DOL. The correlations between the duration of labour [23, 45] (WMD=1.97; 95% CI -2.21, 6.16), vaginal delivery, and the duration of the second stage of labour > 1 h [4, 19] (RR=1.41; 95% CI 0.73, 2.72) and DOL were undefined.

Daily sleep duration [5, 28] (WMD =-0.24; 95% CI -0.45, -0.02) was a protective factor against DOL. The correlation between an Edinburgh Postnatal Depression Scale (EPDS) score ≥ 9 points [35, 48] (RR=1.24; 95% CI 0.80, 1.93) and DOL was unknown. Moreover, descriptive analysis revealed that the relationship between depression [4, 31, 45] and DOL remained unknown, but there might be a correlation between anxiety [22, 31, 45] and DOL.

The results of the meta-analysis revealed that the relationships between the following variables and DOL could not be determined: education level (≥ high school [22, 32], ≥ junior college [20, 41, 44], ≥ junior undergraduate [4, 21, 23, 24, 37, 46, 48], and > 9 years [29, 49]), occupational status [21, 23, 29, 44, 48], mean monthly household income per person (≤ 5000 RMB [29, 31, 44], and ≥ 10000 RMB [21, 26, 41]), nationality (Hispanic [4, 24, 35], White [33, 35], and Han Chinese [20, 22, 26, 44, 45]), prenatal smoking status [4, 24, 26, 35], prenatal alcohol consumption status [21, 26, 27, 35, 37], assisted reproductive technology (ART) use [21, 41], planned pregnancy [22, 43], insulin treatment [21, 31], and fluid infusion [5, 28]. The descriptive results revealed that height [4, 26], intraoperative or delivery blood loss [4, 21, 29], and drug-induced labour [4, 35, 37] might not be related to DOL, whereas the relationships between stressful life events [22, 45, 49] during pregnancy, exercise during pregnancy [20, 48], and anaesthesia or painkiller use [4, 21, 24, 27, 29, 35, 37] and DOL remained unclear.

Author_year	DOL	Total		ES (95% CI)	% Weight
Bai 2018	112	553		0.20 (0.17, 0.24)	2.96
Chapman 1999	68	192		0.35 (0.29, 0.42)	2.77
Dewey 2003	62	271		0.23 (0.18, 0.28)	2.88
Ding 2020	107	340		0.31 (0.27, 0.36)	2.89
Ding J 2022	104	330		0.32 (0.27, 0.37)	2.88
Ding QY 2022	106	277		0.38 (0.33, 0.44)	2.84
Dong 2022	241	622		0.39 (0.35, 0.43)	2.94
Haile 2017	487	2053		0.24 (0.22, 0.26)	3.01
Hilson 2004	28	114		0.25 (0.17, 0.32)	2.69
Huang 2019	604	3282		0.18 (0.17, 0.20)	3.02
Kong 2008	29	75		0.39 (0.28, 0.50)	2.43
Li 2022	107	300		0.36 (0.30, 0.41)	2.86
Lian 2022	156	468		0.33 (0.29, 0.38)	2.92
Lu 2022	56	154		0.36 (0.29, 0.44)	2.71
Luan 2018	36	100		0.36 (0.27, 0.45)	2.57
Luo 2020	99	388		0.26 (0.21, 0.30)	2.92
Matias 2010	30	171		0.18 (0.12, 0.23)	2.84
Mullen 2022	98	177		0.55 (0.48, 0.63)	2.73
Nommsen-Rivers 2010	190	431		0.44 (0.39, 0.49)	2.90
Otoo 2010	19	425		0.04 (0.03, 0.06)	3.01
Preusting 2017	114	219		0.52 (0.45, 0.59)	2.78
Quan 2022	268	1185		0.23 (0.20, 0.25)	3.00
Rocha 2020	42	224		0.19 (0.14, 0.24)	2.88
Salahudeen 2013	50	200		0.25 (0.19, 0.31)	2.82
Si 2017	96	284		0.34 (0.28, 0.39)	2.86
Wang 2020	68	240		0.28 (0.23, 0.34)	2.84
Wei 2022	722	2109		0.34 (0.32, 0.36)	3.01
Xie 2021	97	229		0.42 (0.36, 0.49)	2.80
Xu 2021	91	269		0.34 (0.28, 0.39)	2.85
Xue 2015	58	204		0.28 (0.22, 0.35)	2.81
Zhang 2023	86	300		0.29 (0.24, 0.34)	2.88
Zhang YY 2022	64	334		0.19 (0.15, 0.23)	2.92
Zhang ZY 2022	110	281		0.39 (0.33, 0.45)	2.84
Zhao 2022	119	358		0.33 (0.28, 0.38)	2.89
Zhu 2013	198	2017		0.10 (0.09, 0.11)	3.02
Overall (I-squared = 97.6%, p = 0.000)				0.30 (0.26, 0.34)	100.00

NOTE: Weights are from random effects analysis

-.627   0   .627

Fig. 2 Forest plot of DOL incidence

Infant-related influencing factors

The pooled results of 7 [29–31, 40–42, 49] and 2 [5, 28] studies, respectively, revealed that a gestational age < 37 weeks (RR=1.29; 95% CI 1.06, 1.57) and a young gestational age at birth (WMD =-0.47; 95% CI -0.89, -0.06) were risk factors for DOL. Nevertheless, whether gestational age ≥ 39 weeks [4, 32] (RR=1.11; 95% CI 0.86, 1.43) and gestational age (full-term) [26, 45, 46] (WMD =-0.04; 95% CI -0.26, 0.19) were associated with DOL could not be determined.

A birth weight < 2.5 kg [29, 31] (RR=1.34; 95% CI 1.07, 1.67) was a risk factor for DOL. A birth weight ≥ 4 kg [22, 26, 48] (RR=1.29; 95% CI 1.07, 1.56) was also a risk factor, but the sensitivity analysis result was not robust. However, the correlations between neonatal birth weight [30, 33, 45] (WMD =-0.36; 95% CI -0.86, 0.14) and preterm birth weight [5, 28] (WMD =-17.09; 95% CI -102.28, 68.09) and DOL were unclear.

The meta-analysis results could not determine whether neonatal sex [4, 21, 22, 26, 29, 32, 46, 48, 49] and the 1-min Apgar score (<7 points [21, 28, 38] and <8 points [4, 32, 35]) were associated with DOL. The descriptive results revealed that the relationships between maternal separation [21, 36, 43] and skin-to-skin contact [4, 35–37] and DOL were unknown.

Breastfeeding-related influencing factors

The combined results of 7 studies [21, 22, 29, 36, 37, 46, 48] revealed that receiving breastfeeding guidance (RR=0.72; 95% CI 0.64, 0.81) was a protective factor against DOL. The correlation between ≥3 breastfeeding information sources [22, 43] (RR=0.50; 95% CI
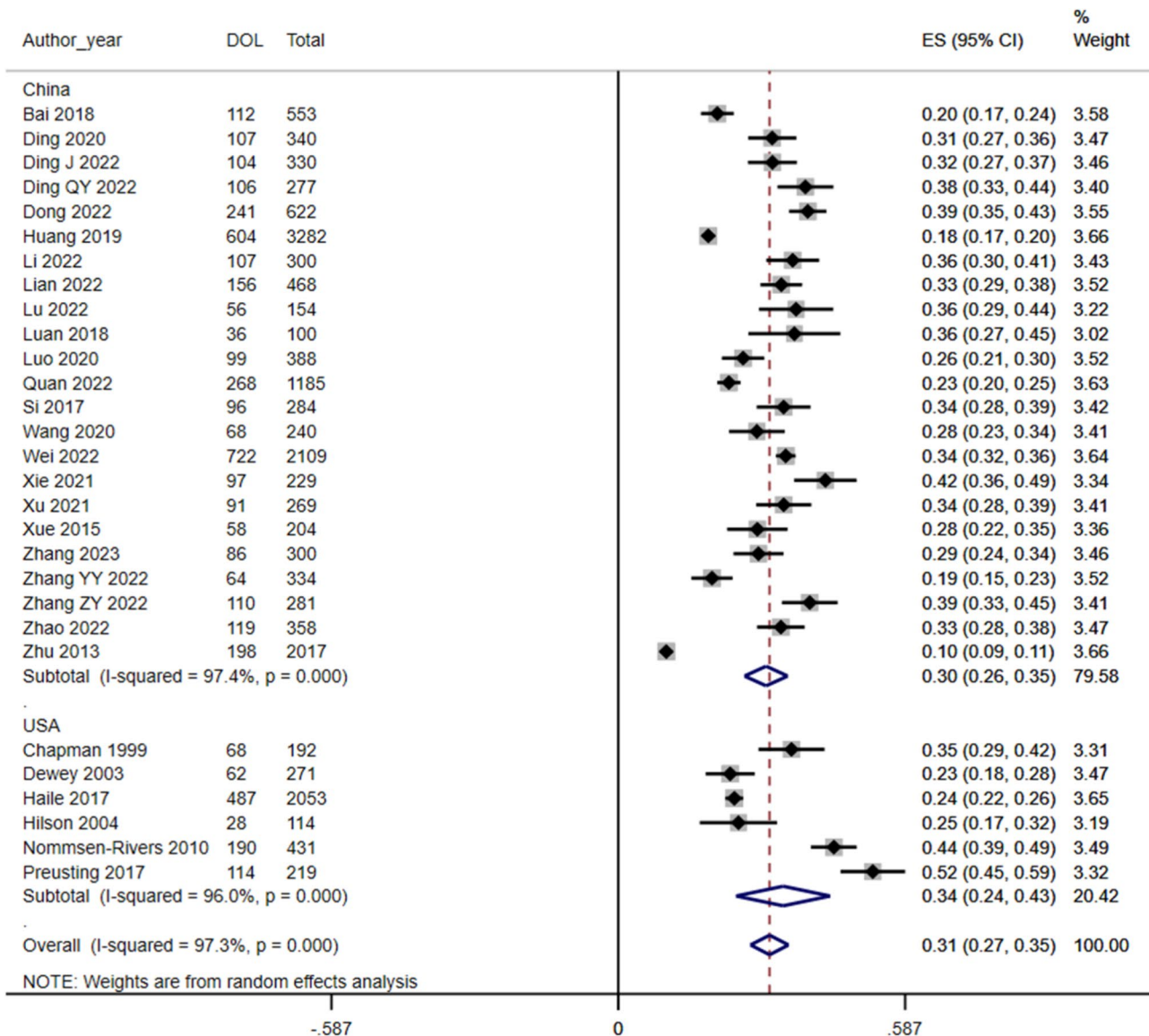
Fig. 3 Forest plot of the subgroup analysis of DOL incidence

0.15, 1.65) and DOL was unknown. Descriptive analysis revealed that breast massage or treatment [22, 36] might be associated with DOL.

The descriptive analysis results revealed that there might be a relationship between a first breastfeeding session after maternal separation [5, 28, 42] and DOL, but it was not clear whether the first breastfeeding session of general mothers [22, 29, 32, 33, 35, 37, 45] was related to DOL. The combined results of 5 studies [5, 28, 42, 45, 46] revealed that breastfeeding frequency (WMD =-0.63; 95% CI -1.10, -0.16) was a protective factor against DOL. Similarly, a breastfeeding frequency≤2 times on the first day [22, 44] (RR=1.92; 95% CI 1.36, 2.72) and the second day after surgery [22, 44] (RR=1.71; 95% CI 1.34, 2.20) was a risk factor for DOL. The correlation between a breastfeeding frequency<8 times [4, 32] from 0 to 24 h

after birth (RR=1.00; 95% CI 0.78, 1.28) and DOL was unknown.

The meta-analysis results revealed that the relationships between a history of breastfeeding [5, 22, 28], previous insufficient lactation [21, 29], prenatal breast enlargement [4, 19], flat or sunken nipples [4, 21, 32, 35], and a bra cup size≥D [4, 46] and DOL could not be confirmed. The descriptive results revealed that the relationships between formula milk use (within 24 h [4, 32, 46] or 48 h [4, 32, 35, 48]), LATCH score [26, 35, 46] and nipple pain during lactation [4, 22, 35] and DOL remained unknown.

Sensitivity and publishing bias analysis

The sensitivity analysis results for age (continuous variable), GWG and neonatal birth weight≥4 kg were not

robust, whereas the results for the remaining variables were robust. An analysis of the full texts of the studies including these three variables and the sensitivity analysis results revealed that when studies with relatively small samples (<400 participants) were excluded one by one, the sensitivity analysis results were robust; however, when studies with relatively large samples (>1,000 participants) were excluded, the sensitivity analysis results became not robust (see Supplementary Material 2).

The results of Egger's test indicated that there was no publication bias for GDM ($p=0.129$), HDP ($p=0.136$), primipara ($p=0.125$), and caesarean delivery ($p=0.675$) (see Table 2). The funnel plots for these four variables also exhibited a basically symmetrical distribution, further suggesting the absence of significant publication bias (see Supplementary Material 3, 4, 5, and 6).

Discussion

The total incidence of DOL was 30% among the 35 included studies. Subgroup analysis revealed that the incidence of DOL was 30% in China and 34% in the USA. Both China and the USA have made many efforts to support breastfeeding and have introduced policies related to breastfeeding, which focus on the positive role of baby-friendly hospitals and policy support, as well as the 'Ten Steps to Successful Breastfeeding' framework, breastfeeding clinics and human milk donation programs [51, 52]. Additionally, the American Academy of Pediatrics policy mentions relevant content regarding OL [52]; however, attention to the important impact of OL on breastfeeding is lacking, and China's policy does not consider OL [51], which may be the reason for the high DOL incidence. Moreover, Patel et al.'s systematic review [53] revealed the effectiveness of dedicated certified lactation consultants or counsellors in promoting breastfeeding, which suggests that they may also have a positive effect on OL support, but this remains to be verified.

The analysis of potential factors influencing DOL revealed statistically significant correlations between DOL and 15 factors: maternal age, prepregnancy BMI (overweight or obesity), GWG, GDM, HDP, thyroid disease during pregnancy, serum albumin levels (<35 g/L), parity, (unscheduled) caesarean section, caesarean section history, daily sleep duration, gestational age, birth weight (<2.5 kg or ≥4 kg), breastfeeding guidance and daily breastfeeding frequency. However, the sensitivity analysis results for age, GWG and birth weight≥4 kg were not robust. Through descriptive analysis, three factors were found to be likely related to DOL: anxiety, time of first breastfeeding session (maternal separation), and breast massage or treatment.

Maternal-related influencing factors

Combined with the meta-analysis and sensitivity analysis results, although there was a correlation between age and DOL, the result was not robust. A relationship between a maternal age≥35 years or ≥30 years and DOL was not found. This suggests that the relationship between maternal age and DOL is still controversial, and more research is needed.

Although the WHO [54] and China [55] have slightly different BMI classification criteria, when the prepregnancy BMI reaches the overweight or obese range, the risk for DOL increases. Studies have shown that women who are overweight or obese before pregnancy have a lower response to prolactin stimulated by sucking [56]. Animal experiments have shown that obesity may impair lactation performance by inducing prolactin resistance [57]. Obesity is an important risk factor for insulin resistance and impaired insulin secretion; insulin is now thought to play a direct role in lactation, including secretory differentiation, secretory activation and mature milk production [58]. The results of this study also revealed that a high prepregnancy BMI was a risk factor for DOL after the standard of overweight or obesity was reached. High GWG may increase the risk of DOL. Although the sensitivity analysis results were not robust, considering the adverse effects of overweight or obesity on DOL, these findings still suggest that GWG has a potentially dangerous effect on DOL, which still requires exploration and verification in further research.

Our analysis revealed that GDM, HDP and thyroid disease during pregnancy were risk factors for DOL. De Bortoli et al.'s systematic review [59] also supports that GDM is a risk factor for DOL. The possible mechanism is that insulin resistance and/or insulin secretion disorders in β cells lead to GDM, of which insulin resistance is the main cause [60], and insulin resistance affects lactation [61]. The ratio of insulin to glucose and adiponectin may also be related to the start time of lactation [62]. Combined with the relationship between obesity and insulin resistance, GDM, obesity and insulin resistance may be associated with DOL in some way [63]. HDP can affect the initiation and duration of breastfeeding [64], and the treatment of HDP may also affect lactation; for example, diuretics may reduce milk production [65]. HDP may also lead to placental dysfunction and decreased prolactin secretion, thereby affecting lactation [66]. Endothelial dysfunction caused by preeclampsia may lead to hypoalbuminaemia in women [67], and lower serum albumin levels indicate poor nutritional status, which may be the cause of DOL [29]. Consistently, this study also revealed that low serum albumin levels were a risk factor for DOL. Animal experiments have shown that hypothyroidism may hinder the ability of the breast to achieve normal milk synthesis and excretion, leading to lactation

disorders in pregnant women with thyroid dysfunction [68]. Similarly, hyperthyroidism can also induce impaired release of oxytocin, resulting in milk deposition, apoptosis of glandular cells that secrete milk, and lactation effects [69].

This study revealed that primiparity and (unscheduled) caesarean section were risk factors for DOL, whereas a history of caesarean section was a protective factor against DOL. Compared with multiparas, primiparas may experience longer delivery times, resulting in higher cortisol levels [70, 71], and multiparas may have more prolactin receptors than primiparas [72]. Multiparas may also have better breastfeeding skills than primiparas [73]; hence, primiparas are more likely to experience DOL than multiparas. Similarly, women with a history of caesarean section could have certain breastfeeding experiences; their fear of childbirth in late pregnancy is relatively low [74], and the pressure of childbirth seems to be related to DOL [71]. These factors may be why a history of caesarean section is a protective factor against DOL. Compared with vaginal delivery, (unscheduled) caesarean section may lead to lower levels of oxytocin and prolactin secretion [75, 76], thus increasing the risk of DOL.

Sleep and emotional state may affect the occurrence of DOL. Prolactin secretion has circadian rhythm changes, and sleep deprivation may lead to decreased levels of prolactin secretion [77]. Anxiety and depression are associated with lower oxytocin during feeding [78], and mothers with depression may have insufficient confidence in their ability to breastfeed [79]. In addition, studies have shown that poor sleep quality is associated with depression and anxiety [80, 81]. However, combined with the results of the meta-analysis and descriptive analysis of this study, the relationship between depression and DOL needs further exploration.

Infant-related influencing factors

This study revealed that young gestational age and low birth weight were risk factors for DOL. The shortening of pregnancy may lead to insufficient prenatal breast preparation, and the immature sucking skills of premature infants can lead to insufficient milk discharge [82]. A low birth weight may mean that an infant's motor development is deficient, which may also affect the infant's sucking skills, subsequently increasing the risk of DOL [73, 83]. Colostrum is produced before OL (paracellular pathway closure) [84]. Unlike mature milk formed after OL, colostrum is rich in immune factors and cytokines, and the concentration of these substances is inversely proportional to the duration of gestation [84]. Newborns have immature immune systems, especially premature infants whose immune substance transport through the placenta is interrupted prematurely, and colostrum can address this lack of development by providing many

bioactive substances [85]. In addition, preterm birth may trigger delayed closure of the paracellular pathway to prolong the supply of protective substances in colostrum [84], although this can lead to DOL. These findings also suggest that medical staff should pay attention to the special therapeutic effect of colostrum on premature infants. For example, oropharyngeal colostrum administration, as proposed by Rodriguez et al. [84] in 2009, has been shown to have a positive effect on the outcomes of preterm infants [86]. Therefore, in clinical practice, it is necessary to help mothers start breastfeeding early and express colostrum, especially for mothers with premature or low-birth-weight infants, to facilitate the use of colostrum for neonatal immune protection.

Breastfeeding-related influencing factors

The WHO recommends that breastfeeding counselling be provided to all pregnant women and women with babies to help enhance their skills, abilities and confidence in breastfeeding [87]. McFadden et al.'s systematic review [88] also revealed that breastfeeding counselling has a positive effect on breastfeeding. Consistent with the results of our study, breastfeeding counselling had a positive protective effect on OL. This study revealed that the frequency of breastfeeding was a protective factor against DOL and should not be less than 2 times/day. Sucking stimulation can trigger the pituitary to release oxytocin, which may be beneficial for uterine involution [89], and frequent breastfeeding and effective milk emptying have positive effects on milk secretion [90, 91]. These findings suggest that in the case of maternal separation, due to the lack of infant sucking, it is necessary to start hand expressing or using a breast pump as soon as possible to mechanically stimulate the areola to promote the release of oxytocin [91], thereby reducing the risk of DOL; moreover, informing mothers of the potential benefits of frequent sucking on uterine involution is recommended to improve their compliance. However, whether the time of the first breastfeeding session of general parturients is related to DOL still needs further exploration. This study revealed that breast massage or treatment might be a protective factor against DOL, and the protective effect may be achieved by simulating sucking and dredging the mammary duct [36].

Strengths and limitations

In the original studies included, different researchers might use different criteria for the same influencing factor. Therefore, this study combined quantitative and qualitative analyses to comprehensively summarize the available studies on the incidence and factors influencing DOL. However, this study inevitably has several limitations: (1) Since most of the original studies reported only statistically significant multivariate analysis results and

the multivariate analysis methods used were inconsistent, we chose to extract the exposure and outcome data corresponding to the influencing factors after weighing the effects of bias and confounding on the results; regrettably, few studies reported only statistically significant univariate analysis results, but no publication bias was found by funnel plots or Egger's tests. (2) There were three factors for which the sensitivity analysis results were not robust. A review of the original studies included revealed that some studies had relatively small sample sizes, which might have resulted in insufficient statistical power. When large-sample studies are eliminated, the results might be affected by the combination of small-sample studies; moreover, sensitivity analysis is not applicable to factors that sourced from only two original studies, so robustness cannot be evaluated. Accordingly, larger samples and higher-quality studies are needed to improve the accuracy and robustness of the results. (3) At present, there are no objective and unified diagnostic criteria for DOL, and the most commonly used method is still the subjective perception of maternal breast distension; however, this method may have a large bias. Therefore, it is still necessary to research milk biomarkers to develop an objective and standard evaluation method for use in clinical practice. (4) The selection of the qualitative description method for some influencing factors was due to the high degree of heterogeneity among the studies, so the results of the qualitative description only have implications, and exact conclusions cannot be drawn. (5) As Chinese researchers, considering the accessibility of the Chinese language, we searched Chinese databases, which may have resulted in the inclusion of many Chinese studies. The studies included were mainly from China and the USA, owing to differences in culture and policy, the results concerning the incidence and factors influencing DOL may vary greatly across countries and even within individual countries. Nevertheless, the results may play a role in the implementation of DOL incidence and influencing factor research by researchers from other countries.

Conclusions

This study revealed that the incidence of DOL was 30%, and the factors influencing DOL may include prepregnancy BMI (overweight or obesity), GDM, HDP, thyroid disease during pregnancy, serum albumin levels (<35 g/L), parity, (unscheduled) caesarean section, caesarean section history, daily sleep duration, gestational age, birth weight (<2.5 kg), breastfeeding guidance and daily breastfeeding frequency; however, the relationships between age, GWG, birth weight (≥4 kg), anxiety, time of first breastfeeding session (maternal separation) and breast massage or treatment and DOL remain unknown. Considering the adverse effects of DOL, policymakers

should pay more attention to OL, a critical period of breastfeeding, and formulate corresponding supportive policies. Researchers are advised to explore and verify objective diagnostic criteria for DOL and the influencing factors for which the associations with DOL remain unknown. In addition, establishing breastfeeding support teams in hospitals is recommended, and clinicians should conduct targeted assessments, risk stratification management, health education and interventions for mothers according to the influencing factors to reduce the occurrence of DOL in the case of rational medical resource use.

Abbreviations

ART	Assisted reproductive technology
BMI	Body mass index
DOL	Delayed onset of lactation
EPDS	Edinburgh Postnatal Depression Scale
GDM	Gestational diabetes mellitus
GWG	Gestational weight gain
HDP	Hypertensive disorders of pregnancy
MICU	Maternal intensive care unit
MS	Maternal separation
NOS	Newcastle–Ottawa Scale
OL	Onset of lactation
RMB	Renminbi
RR	Risk ratio
USA	United States of America
WHO	World Health Organization
WMD	Weighted mean difference

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

Supplementary Material 6

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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