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Review Article

The effect of early nipple stimulation on third stage of labour duration and estimated blood loss: A systematic review and meta-analysis

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ABSTRACT

Background: Post-partum haemorrhage due to uterine atony remains a leading cause of maternal mortality worldwide with a high portion occurring in under resourced settings. The risk of post-partum haemorrhage increases with prolonged duration of the third stage of labour. Early nipple stimulation promotes the early release of oxytocin, which has beneficial effects on uterine tone. Therefore, this meta-analysis evaluates the impact of early nipple stimulation on the duration of the third stage of labour and estimated blood loss.
Aim: To assess whether early nipple stimulation following uncomplicated deliveries effects the duration of the third stage of labour and estimated blood loss.
Methods: A comprehensive search was conducted in PubMed, EMBASE, Cochrane, CiNAHL, Scopus and Web of Science, covering studies published up to February 5th 2024. Eligible studies included randomised control trials and observational studies involving women with singleton pregnancies and live foetuses who engaged in nipple stimulation in the third stage. Studies that reported the duration of the third stage of labour and/or estimated blood loss were included. Exclusion criteria comprised stillbirths, multiple pregnancies and the use of general anaesthesia. Data was analysed using a random-effects model. This review was registered with PROSPERO (CRD42023494605).
Results: Nine studies involving 789 mothers were included. Early nipple stimulation reduced blood loss and improved uterine tone. When synthetic oxytocin was not used, early nipple stimulation reduced the duration of the third stage of labour.
Conclusion: Early nipple stimulation may be a viable alternative to uterotonics in uncomplicated deliveries, especially in low-resource settings. Further high-quality primary research is indicated to build upon the preliminary findings of this current meta-analysis.

Introduction

Statement of significance

Problem or issue	Post-partum haemorrhage (PPH) is one of the largest contributors to maternal mortality globally with rates appearing to be increasing globally. Rates of PPH in under-resourced countries is still very high. Many women are choosing to opt for a non-medicalised labour and may prefer not to receive uterotonic agents.
What is already known?	A Cochrane review was published titled "Breastfeeding or nipple stimulation for reducing PPH in the third stage of

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(*continued*)

	labour" which found that there were not enough studies that reported on PPH. The quality of the research was low and more high-quality research is required.
What does this paper add?	This paper provides a systematic review on the available literature regarding the impact of early nipple stimulation in the third stage of labour on maternal morbidity – through measuring for significance in estimated blood loss (EBL) and duration of third stage. Although early nipple stimulation did influence the EBL and in the sub analysis of duration of third stage, this paper supports the findings published in Cochrane; that the quality of the included papers is sub optimal. This paper provides a foundation and direction for future primary research, in the form of high-quality randomised control trials.

The third stage of labour; the period between the birth of the baby and delivery of the placenta, is a pivotal period that significantly influences both maternal and neonatal outcomes. Traditionally, 'active management' of the third stage of labour—entailing the use of uterotonics, controlled cord traction, and fundal massage—has been the standard approach (Begley et al., 2019). However, there is growing interest in alternative or adjunctive methods, such as early nipple stimulation that could complement or substitute traditional interventions. This may be particularly relevant in resource-poor settings, where the availability of synthetic uterotonics is limited.

Early nipple stimulation, which encompasses early breastfeeding (EBF) and manual stimulation of the nipple, is a useful component in physiological management of the third stage of labour. Early release of endogenous oxytocin promotes uterine contraction and compression of the spiral arteries of the myometrium, which may be enhanced by early nipple stimulation (Drew and Balki, 2019). It is proposed that early nipple stimulation may prevent a prolonged third stage of labour, preventing uterine atony and reducing estimated blood loss (EBL) (Almutairi et al., 2021; Davis and Nelson, 2022). Since 1991, a prolonged third stage of labour has been defined as lasting greater than 30 minutes, however the risk of postpartum haemorrhage (PPH) increases after only 20 minutes (Combs et al., 1991; Frolova et al., 2016; Magann et al., 2005).

As a strong link exists between prolonged third stage of labour and increased risk of PPH, it is imperative that the relationship between early nipple stimulation, EBL and length of the third stage is explored. Several studies have already demonstrated the effectiveness of skin-to-skin contact and EBF combined in reducing third stage length, EBL and PPH (Almutairi et al., 2021; Saxton et al., 2015). Skin-to-skin contact is already a well-established method implemented in the third stage of labour, as it is known to stimulate oxytocin release and offer other benefits such as facilitating EBF, regulating the baby's vital signs and promoting bonding between mother and child (Gupta et al., 2021; Karimi et al., 2020; Safari et al., 2018). Early nipple stimulation is not so well described, and so its exploration is valuable and worthwhile, with the view that it may stand in its own right as a method to improve maternal outcomes (Almutairi et al., 2021; Ruiz et al., 2023).The most significant cause of maternal mortality globally is PPH due to uterine atony, therefore more research is required as to whether early nipple stimulation can decrease the rate of this.

This paper defines early nipple stimulation as any form of manual nipple stimulation or breast feeding occurring during the third stage of labour. This meta-analysis seeks to assess the safety and efficacy of early nipple stimulation as a method to improve third-stage labour management and provide an alternative approach to reducing the risk of PPH. This would be especially significant in the context of under-resourced settings and non-medicalised births.

Methods

Search strategy and data sources

Following the requirements outlined in Preferred Reporting Items for Systemic Reviews and Meta-analyses (PRISMA) guidelines, an extensive search was carried out across multiple electronic databases, ranging from their creation to 5th February 2024. The databases included PubMed, EMBASE, Cochrane, CiNAHL, Scopus, and Web of Science. Additional references were searched for in google scholar and the references of systematic reviews found in the original search (search terms: 'nipple stimulation/suckling' and 'early breastfeeding' and 'third stage of labour' and 'bleeding' and 'postpartum/postpartum haemorrhage'). The actual strategy listing all search terms used and how they are combined is available in Supplementary Item 1. This review was registered prospectively with PROSPERO (CRD42023494605).

Eligibility criteria and quality assessment

Studies were included if they: 1) were written in the English language; 2) included women who participated in early nipple stimulation, initiated during the third stage of labour; 3) reported duration of third stage of labour and/or EBL; 4) included singleton pregnancies of live foetuses; 5) included randomised control trials or observational studies. Women who had still births, multiple pregnancies and general anaesthetic were excluded from the analysis. Case reports, conference abstracts and case series were excluded to maintain the reliability of the analysis. Article screening and data extraction were conducted independently by three authors (D.Z, R.Z, M.W). Any disagreements were adjudicated by Z.Z and discussed with co-authors as necessary. The methodological quality of each study was assessed independently by two authors (N.B, F.A), and adjudicated by a third (C.T), using the RoB-2 Tool and the ROBINS-I Tool (Sterne et al., 2016, 2019).

Data extraction

The following data were extracted from each included study: maternal age, primigravida or multigravida status, range of gestational age and education level (illiterate, primary, secondary, university). The following maternal outcomes were extracted: EBL (mL), length of third stage of labour (min), uterine tone and the success of the first breastfeed.

Statistical analysis

Pooled means and proportions of the data were analysed using an inverse variance method for continuous data and the Mantel-Haenszel method for dichotomous data, which assigns the weight of each study based on its variance. A direct comparison between the inverse variance method and the Mantel-Haenszel method was conducted by assessing studies that reported outcomes of both treatments (two-arm analysis). Subgroup analyses were also conducted to address potential sources of heterogeneity (the use of oxytocin and the study type). The heterogeneity of effect size estimated across the studies was quantified using the Q statistic and I^2 with $P<0.10$ considered significant for heterogeneity. A value of I^2 of 0-25% indicates insignificant statistical heterogeneity, 26-50% low heterogeneity, and 51-100% high heterogeneity (Higgins et al., 2003). The Random-effects model was used. If mean was unavailable, the median was converted to the mean using formulas from the Cochrane Handbook for Systematic Reviews of Interventions (Cumpston et al., 2019). Analysis was performed using RevMan© v5.4 (Review Manager (RevMan©) [Computer program]. The Cochrane Collaboration, 2020, Copenhagen, Denmark).

Results

Study selection

A comprehensive search of electronic databases initially yielded 407 studies. After removing duplicates, titles and abstracts were screened according to predefined inclusion and exclusion criteria, resulting in 32 articles considered suitable for further assessment. Ultimately, 9 studies, including 789 women, met inclusion criteria (Al Sabati and Mousa, 2019; Anto and Dash, 2018; Dashtinejad et al., 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016; Kim et al., 1986; Lumbanraja et al., 2021; Manisha et al., 2023; Safari et al., 2018). Details of the study selection process can be found in the PRISMA flowchart (Fig. 1). Three out of the nine studies were randomised control trials (Dashtinejad et al., 2018; Kim et al., 1986; Lumbanraja et al., 2021). Whilst six out of the nine studies were a prospective cohort study design (Al Sabati and Mousa, 2019; Anto and Dash, 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016; Manisha et al., 2023; Safari et al., 2018).

Risk of bias

The quality of included studies is presented in Figs. 2 and 3. Three randomised controlled trials were assessed with the RoB-2 tool (Dashtinejad et al., 2018; Kim et al., 1986; Lumbanraja et al., 2021). Dashtinejad et al. (2018) and Kim et al. (1986) were rated as a low risk of bias whereas Lumbanraja et al. (2021) was judged to have 'some concerns'. The six non-randomised control trials were assessed by the ROBINS-I and were all found to have a serious risk of bias except Al Sabati & Mousa and Safari et al. These serious biases were attributed to insufficient randomisation procedures, participant selection processes and bias in measurement of outcomes (Anto and Dash, 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016; Manisha et al., 2023). The other studies presented moderate risks of bias (Al Sabati and Mousa,

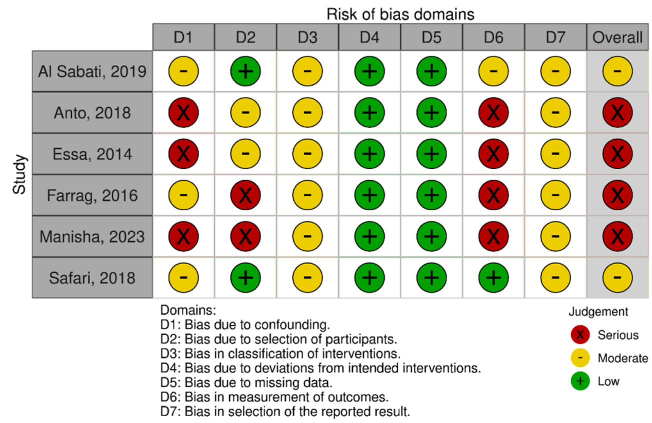

Fig. 2. ROBINS I traffic light plot for non-randomised control trials. This graphic demonstrates the risk of bias present in each of the six included studies that were non-randomised control trials.

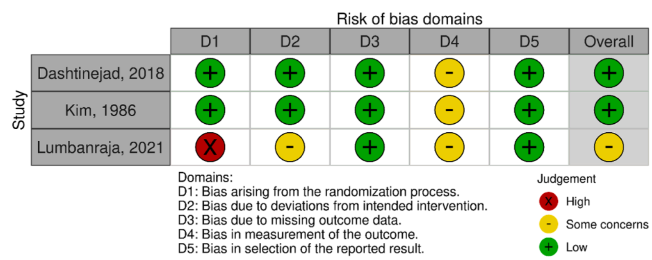

Fig. 3. ROB2 traffic light plot for randomised control trials. This graphic demonstrates the risk of bias present in each of the three included studies that were randomised control trials.

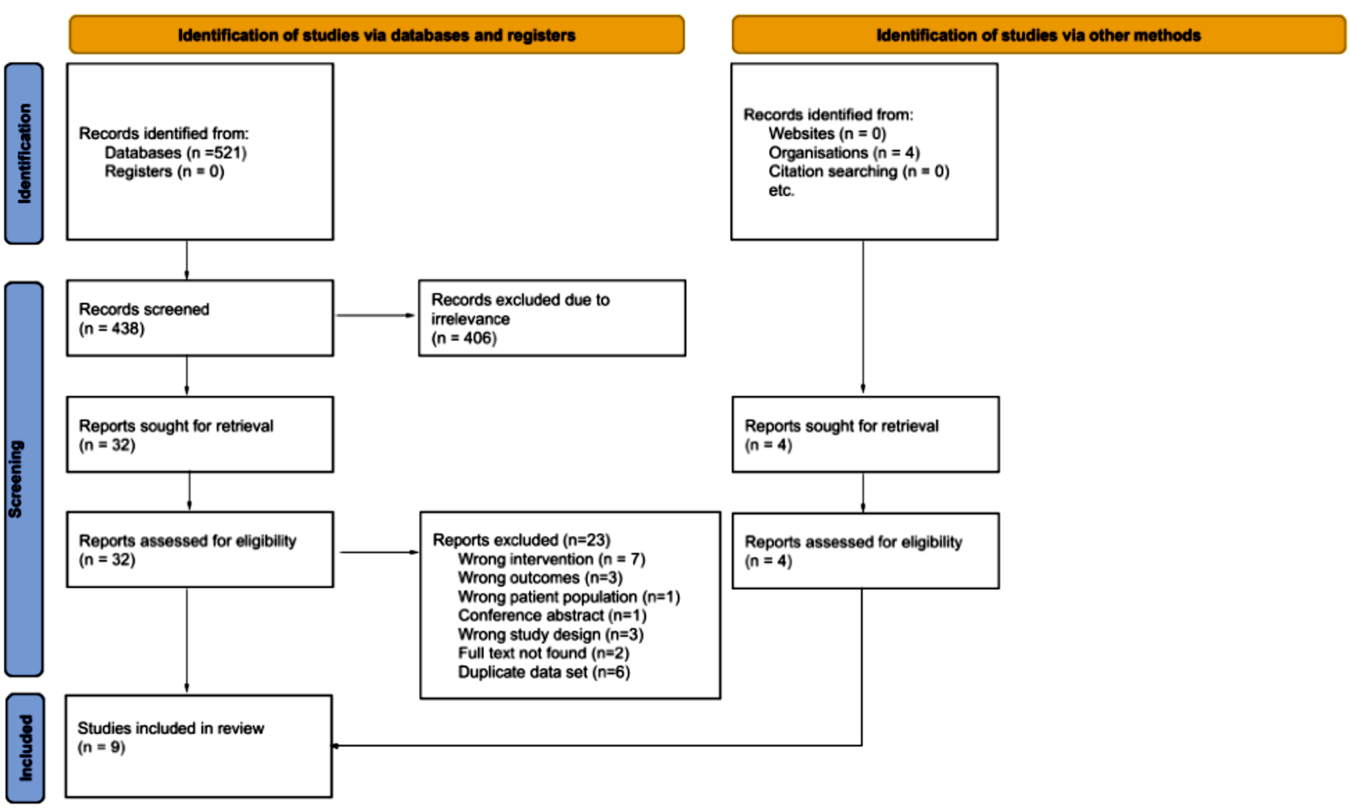

Fig. 1. The PRISMA 2020 flow diagram that was referred to in the study selection process.

2019; Safari et al., 2018). All studies clearly reported the intended interventions, outcome measures, and had low rates of missing data. Certainty of evidence for the primary outcomes of EBL and duration of third stage of labour was also assessed using GRADE in Table 2.

Demographics and patient characteristics

Data from nine studies involving 789 singleton mothers were extracted. Six studies (Al Sabati and Mousa, 2019; Dashtinejad et al., 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016; Kim et al., 1986; Safari et al., 2018) reported 589 women with a mean age range of 22.95 to 33 years. Three studies (Dashtinejad et al., 2018; Essa and Abdel Aziz Ismail, 2015; Kim et al., 1986) included 291 women and reported an average gestational age of 38.96±2.44 weeks. Seven studies (Al Sabati and Mousa, 2019; Anto and Dash, 2018; Dashtinejad et al., 2018; Essa and Abdel Aziz Ismail, 2015; Lumbanraja et al., 2021; Manisha et al., 2023; Safari et al., 2018) identified 362 women as primigravida (59.0%) and 251 as multigravida (40.9%) and the remaining 1 woman (0.2%) was classified as nulliparous. Six studies investigated the education levels of the women, finding that 54 (14.7%) were illiterate, 149 (31.4%) had primary education, 154 (32.5%) had secondary education, and 109 (19.3%) had a university education, while 40.9% were not reported (Al Sabati and Mousa, 2019; Anto and Dash, 2018; Dashtinejad et al., 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016; Safari et al., 2018). The demographics and mother's characteristics are reported in Table 1.

Defining early nipple stimulation

The studies employed two main approaches to nipple stimulation: natural stimulation by the infant and artificial methods. In studies like Anto and Dash (2018) and Safari et al. (2018), the focus was on natural stimulation. Anto and Dash (2018) highlighted the importance of initiating breastfeeding immediately after birth, allowing the newborn to naturally stimulate the nipples. Similarly, Safari et al. (2018) placed undressed infants on their mother's bare chests in a prone position (skin-to-skin contact) and encouraged natural stimulation before any medical interventions were employed (Anto & Dash, 2018; Safari et al., 2018).

In contrast, Dashtinejad et al. (2018) and Kim et al. (1986) utilised artificial methods. Dashtinejad et al. (2018) involved using a breast shield on one nipple immediately after the birth, followed by pumping at a negative pressure of 250 mmHg for five minutes per nipple, alternating between them for a total of 20 minutes after the placenta was delivered. Kim et al. (1986) also employed breast shields but used intermittent stimulation for 10 minutes per breast, totalling 20 minutes immediately after birth of the baby (Dashtinejad et al., 2018; Kim et al. (1986)).

Primary outcomes

In a collective analysis of nine studies, 379 women underwent early nipple stimulation during the third stage of labour, while 403 women were in the control groups (Al Sabati and Mousa, 2019; Anto and Dash, 2018; Dashtinejad et al., 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016; Kim et al., 1986; Lumbanraja et al., 2021; Manisha et al., 2023; Safari et al., 2018). Note that 7 women were excluded from analysis of outcomes due to failure to initiate breastfeeding (Farrag and Atea, 2016). The duration of the third stage of labour was reported in eight studies with no difference between groups (MD: -0.98 min; 95% CI: -7.36, 5.40; Tau ^{2}= 84.10; I^2: 100%) (Fig. 4(a)) (Anto and Dash, 2018; Dashtinejad et al., 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016; Kim et al., 1986; Lumbanraja et al., 2021; Manisha et al., 2023; Safari et al., 2018).

The EBL was recorded in six studies (Al Sabati and Mousa, 2019; Anto and Dash, 2018; Farrag and Atea, 2016; Kim et al., 1986; Lumbanraja et al., 2021; Manisha et al., 2023). Early nipple stimulation, comprising 220 women, had lower EBL than the control groups, consisting of 248 women (MD: -53.86 mL; 95% CI: -101.78, -5.93; Tau ^{2}= 3399.89 I^2: 97%) (Fig. 4(b)).

Subgroup analysis

In three out of eight studies that reported on the duration of the third stage of labour, oxytocin was used in the control groups (Dashtinejad et al., 2018; Kim et al., 1986; Lumbanraja et al., 2021) (MD: 4.48 mins; 95% CI: -4.37, 13.34; Tau ^{2} = 60.73; I^2: 100%). Conversely, in the remaining five studies, oxytocin was not used in the control group and a shorter third-stage duration was demonstrated in the early nipple stimulation group (Anto and Dash, 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016; Manisha et al., 2023; Safari et al., 2018) (MD: -4.31 mins; Cl 95%: -7.22, -1.41; Tau ^{2} = 10.40; I^2: 97%) (Fig. 4(c)).

The EBL with oxytocin in the controls was recorded in two studies (Kim et al., 1986; Lumbanraja et al., 2021). In total, 52 women were in the early nipple stimulation group and 73 women in the no early nipple stimulation group (MD: -1.41 mL; 95% CI: -8.78, 5.96; Tau ^{2} = 0.00; I^2: 0%). Whereas, four studies reported EBL without using oxytocin (Al Sabati and Mousa, 2019; Anto and Dash, 2018; Farrag and Atea, 2016; Manisha et al., 2023), with intervention groups showing lower EBL than controls (MD: -85.13 mL; 95% CI: -108.97, -61.28; Tau^2 = 427.07; I^2: 75%) (Fig. 4(d)).

In a subsequent subgroup analysis comparing study type, three randomised controlled trials measured the duration of the third stage of labour (Dashtinejad et al., 2018; Kim et al., 1986; Lumbanraja et al., 2021) (MD: 4.48 mins; 95% CI: -4.37, 13.34; Tau ^{2} = 60.73; I^2: 100%).

There was no difference between nipple stimulation and the control. The remaining five studies were observational studies and a shorter third-stage duration was demonstrated in the early nipple stimulation group (Anto and Dash, 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016; Manisha et al., 2023; Safari et al., 2018) (MD: -4.31 mins; Cl 95%: -7.22, -1.41; Tau ^{2} = 10.40; I^2: 97%) (Fig. 4(e)).

In the study type subgroup analysis for EBL two of the six studies that estimated blood loss were randomised controlled trials (Kim et al., 1986; Lumbanraja et al., 2021) (MD: -1.41 mins; Cl 95%: -8.78, -5.96; Tau ^{2} = 0.00; I^2: 0%). These showed no difference between the intervention and control. The remaining four studies were observational studies and showed reduced EBL (Al Sabati and Mousa, 2019; Anto and Dash, 2018; Farrag and Atea, 2016; Manisha et al., 2023) (MD: -85.13 mins; Cl 95%: -108.97, -61.28; Tau ^{2} = 427.07; I^2: 75%) (Fig. 4(f)).

Additional characteristics

Uterine tone

Uterine tonicity was recorded in three studies (Al Sabati and Mousa, 2019; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016), with a total of 283 women, 138 (48.8%) in the intervention group and 145 (51.2%) in the control group. Firmer uterine tone was found in the early nipple stimulation group. (OR: 5.55; 95% CI: 1.22, 25.19; Tau^2 = 0.97; I^2: 56%) (Fig. 4(g)).

Uterotonic drugs

Three studies (Dashtinejad et al., 2018; Essa and Abdel Aziz Ismail, 2015; Farrag and Atea, 2016) assessed the need for additional uterotonic drugs, finding that 289 women in total required them. There was no difference between 141 (48.8%) of intervention women and 148 (51.2%) of control women requiring them (OR: 0.13; 95% CI: 0.01, 1.58; Tau^2 = 4.26; I^2: 86%) (Fig. 4(h)).

Quality of breastfeeding

Three studies (Dashtinejad et al., 2018; Essa and Abdel Aziz Ismail,

Table 1
Comparison of baseline characteristics of the studies evaluated in this review. Abbreviations: BF = breastfeeding, SD = standard deviations, IU = international units, NR = not recorded.

Citation	Study type	Intervention & comparator	Country	Sample size (n)	Age means (SD)a	Gestational age means (SD)a	Primigravida (%)	Multigravida (%)	Education level
Dashtinejad et al. (2018)	Randomised control trial	**Intervention:** Immediately after the delivery of the baby, a shield was placed on each breast and the breasts were stimulated intermittently for 10 minutes (20 minutes for both breasts). **Comparator:** Mothers received 30IU of oxytocin in 1000 ml of Ringer's serum with a maximum rate of 10 ml infusion per minute.	Iran	106	22.95 (3.95)	39.06 (1.18)	71 (66.98)	35 (33.02)	Illiterate: NR Primary: 25 (23.58) Secondary: 32 (30.19) University: 8 (7.55)
Farrag and Atea (2016)	Prospective cohort study	**Intervention:** Pronurturance plus i.e. skin-to-skin contact and BF within 30 minutes of birth **Comparator:** Routine hospital care	Egypt	90	33 (3.66)	NR	NR	NR	Illiterate: NR Primary: NR Secondary: NR University: 33 (36.67)
Kim et al. (1986)	Randomised control trial	**Intervention:** Immediately after delivery, a breast shield was placed on one of the nipples, and a pump was turned on to a negative pressure of 250 mmHg for five minutes. Alternating nipples were stimulated for 5-minute periods, for a total of 20 minutes after delivery of the placenta. **Comparator:** 20IU of oxytocin was added to the infusion bottle after delivery of the placenta.	United States	85	23.60 (5.23)	38.32 (4.19)	NR	NR	NR
Lumbanraja et al. (2021)	Randomised control trial	**Intervention:** Early initiation of breastfeeding. **Comparator:** Oxytocin (dose not specified)	Indonesia	40	NR	NR	3 (7.50)	36 (90)	NR
Manisha et al. (2023)	Prospective cohort study	**Intervention:** Initiation of breastfeeding as soon as possible in the newborn. **Comparator:** Routine care	India	100	NR	NR	40 (40)	60 (60)	NR
Safari et al. (2018)	Prospective cohort study	**Intervention:** Newborns placed on mother's chest immediately after birth. **Comparator:** Routine care, newborn wrapped in blankets, placed under a warmer and then dried. Returned to mother after being weighed, dressed and measured.	Iraq	108	26.16 (6.01)	NR	25 (23.15)	83 (76.85)	Illiterate: 42 (38.89) Primary: 39 (36.11) Secondary: 15 (13.89) University: 12 (11.11)
Essa and Abdel Aziz Ismail (2015)	Prospective cohort study	**Intervention:** Their babies were placed undressed in a prone position against the mother's bare chest between breasts immediately after birth, before placental delivery, and suturing of tears or episiotomy.	Egypt	100	23.91 (3.21)	39.39 (0.70)	100 (100)	0 (0)	Illiterate: 10 (10.00)

(continued on next page)

Table 1 (*continued*)

Citation	Study type	Intervention & comparator	Country	Sample size (n)	Age means (SD)a	Gestational age means (SD)a	Primigravida (%)	Multigravida (%)	Education level
		Comparator: Routine hospital care. The baby was delivered from the mother, quickly dried, put under a heating device to complete nursing care. When complete and after placental delivery and episiotomy repair, the baby was wrapped in a blanket and handed to mother who was encouraged to start breastfeeding.							Primary: 23 (23.00) Secondary: 49 (49.00) University: 18 (18.00)
Al Sabati and Mousa (2019)	Prospective cohort study	**Intervention:** Early skin-to-skin contact and initiation of breastfeeding. **Comparator**: Routine hospital care.	Egypt	100	24.35 (3.96)	NR	100 (100)	0 (0)	Illiterate: 2 (2.00) Primary: 15 (15.00) Secondary: 47 (47.00) University: 36 (36.00)
Anto and Dash (2018)	Prospective cohort study	**Intervention:** Once the baby was born, the cord was clamped immediately and cut. After clamping the umbilical cord, suctioning was done and the baby was wiped with a clean towel and checked that it was active and breathing normally. Immediately the baby was put on the mother's breast and initiated breastfeeding before separation of placenta. **Comparator:** Routine hospital care was provided to the control group.	India	60	NR	NR	23 (38.33)	37 (61.67)	Illiterate: 0 Primary: 47 (78.33) Secondary: 11 (18.33) University: 2 (3.33)

2015; Safari et al., 2018) reported on the successful initiation of breastfeeding, with 314 women. Among these, 159 (50.6%) were in the early nipple stimulation group and 155 (49.4%) were in the control group (OR: 3.72; 95% CI: 0.68, 20.49; $Tau^2 = 1.91$; I^2: 86%) (Fig. 4(i)).

Discussion

Main findings

The third stage of labour, its duration, and associated blood loss can place a woman at high risk of complications in the postpartum period. PPH due to uterine atony is the leading cause of maternal mortality worldwide. This meta-analysis has shown that early nipple stimulation may reduce third stage duration in the absence of exogenous oxytocin and improve uterine tone. It also reduces the EBL seen within this stage, with an even more pronounced effect against the control whom received no adjunct oxytocin. Early nipple stimulation may have a role in third-stage management and reduction of EBL in the absence of conventional active management. However, due to the poor quality of the included research studies it is not possible to draw out finite conclusions in this study.

Interpretation

The combination of skin-to-skin contact and EBF provides an immediate oxytocin release which has been found to decrease maternal complications by ensuring uterine contraction and placental separation (Chua et al., 1994). Additionally, EBF and skin-to-skin contact are considered essential in routine care by the Baby Friendly Health Initiative, a joint project by UNICEF and the WHO which has initiated the 'Ten Steps to Successful Breastfeeding' (WHO technical staff, 2013). Although these recommendations are in place, the rate of EBF within one hour remains astonishingly low. A report by UNICEF and the WHO found that globally, only two out of five neonates were breastfed within an hour of birth (Friedrich, 2018). The findings of this meta-analysis support the recommendations by highlighting the potential to improve labour outcomes for women, especially in under resourced settings.

Early nipple stimulation can optimise the third stage of labour to reduce maternal adverse outcomes. A strong correlation exists between the length of the third stage and the risk of PPH. Studies show an increased duration in third stage in women increases their risk of PPH (Almutairi et al., 2021; Begley et al., 2019; Davis and Nelson, 2022; Frolova et al., 2016; Magann et al., 2005; Prendiville et al., 1988). Length of third stage may be reduced by breastfeeding and suckling, as they trigger the release of oxytocin and prolactin in a pulsatile manner in

Table 2
Grade summary of findings: Nipple Stimulation vs Control.

Summary of findings:						
Nipple Stimulation compared to Control for reducing blood loss and duration of third stage of labour						
Patient or population: reducing blood loss and duration of third stage of labour						
Setting:						
Intervention: Nipple Stimulation						
Comparison: Control						
Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Control	**Risk with Nipple Stimulation**				
Estimated Blood Loss (EBL)	The mean estimated Blood Loss ranged from **139.8-398** mL	MD **53.86 mL lower** (101.78 lower to 5.93 lower)	-	468 (6 studies)	-[a,b]	Nipple stimulation resulted in a reduction in EBL.
Duration of Third Stage of Labour	The mean duration of Third Stage of Labour ranged from **2.8-11.22** minutes	MD **0.98 minutes lower** (7.36 lower to 5.4 higher)	-	682 (8 studies)	-[a,b,c]	There was no difference in the duration of third stage between the intervention and control.

[*] **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.
Explanations
[a] ROB-2 analysis resulted in 'some concerns' for one study and ROBINS resulted in 'serious' concern in a number of studies
[b] High heterogeneity may compromise the consistency of the results
[c] Results ranged widely between studies

the mother (McNeilly et al., 1983; Uvnas-Moberg et al., 2020). Elevated concentrations of oxytocin promote uterine contraction and involution by ensuring adequate myometrial tone. This process is believed to shorten the length of the third stage of labour and minimises the risk of uterine atony, the most common cause of PPH (Parvin et al., 2016). The results of this report did support this theory by demonstrating that early nipple stimulation and exogenous oxytocin showed similar results in the reduction of blood loss and of the length of the third stage of labour. In the latter, the subgroup analysis demonstrated heterogeneity in the results by establishing a significant length of third stage reduction in early nipple stimulation in the absence of exogenous oxytocin. These results signify that early nipple stimulation may serve as an effective alternative to exogenous oxytocin in shortening the third stage and thus potentially reduce the risk of PPH in settings where no uterotonic may be available. Unfortunately, there was a lack of research that explored a direct relationship between early nipple stimulation and PPH. The length of third stage and EBL have a strong correlation with PPH and therefore the relationship between early nipple stimulation and PPH in the data has been extrapolated. Further research is required which directly explores this relationship, requiring larger population sizes and more robust study designs than that which are included in this study. Additionally, the studies that employed the use of exogenous oxytocin were also the randomised controlled trials. This does not allow for a clear distinction to be drawn as to whether the absence of exogenous oxytocin is the cause of significance in the data or whether the study type is contributing to this effect.

This meta-analysis demonstrated that adequate uterine tone after birth was achieved more frequently in the nipple stimulation group. Firm uterine tone demonstrates adequate uterine contraction and therefore a decreased chance of PPH. These findings confirm those of Chua et al. (1994) that demonstrated more than a 7-fold increase in uterine activity with manual nipple stimulation and breast feeding in comparison to their pre- and post-stimulation levels. They found the largest increase in uterine contractions was from actual breast feeding rather than manual nipple stimulation alone (Chua et al., 1994). Unfortunately, only three studies in this analysis assessed uterine tone and therefore it was not possible to compare nipple stimulation to the use of exogenous oxytocin in a subgroup analysis. Future research through meta-regression may explore the direct correlation between firm uterine tone and the rate of PPH.

There are several benefits to an exogenous oxytocin alternative in certain contexts. Firstly, a systematic review by Begley et al. (2019) assessed active management of labour in mixed and low-level risk of women in labour. They found that the effect of active management – which includes the use of a uterotonic – was unclear in its role to reduce the risk of severe primary PPH (Begley et al., 2019). This though may be due to certain causes of severe PPH being shown to not respond to active management (Calvert et al., 2012). Although active management was found to reduce blood loss it also reduces birth weight of the baby whilst increasing the need for postpartum analgesia. Additionally, the risk the woman will return to hospital due to bleeding after discharge also increases, as does maternal diastolic blood pressure and the chance she will experience headaches, nausea and vomiting. The side effects are thought to be predominantly due to the uterotonic agent used in active management (Begley et al., 2019; Fry, 2007; Maaløe et al., 2023).

Secondly, uterotonic agents are not widely available in the developing world and alternative approaches must be taught and practiced in this context to improve maternal outcomes. Where uterotonics are available in developing countries, the correct refrigeration and storage and the lack of expertise with administration means that a uterotonic may still not be adequately utilised. Additionally, due to the lack of urbanisation and access to medical facilities in these environments, many births are conducted within homes meaning that not only are the medications not available but also there are a lack of trained

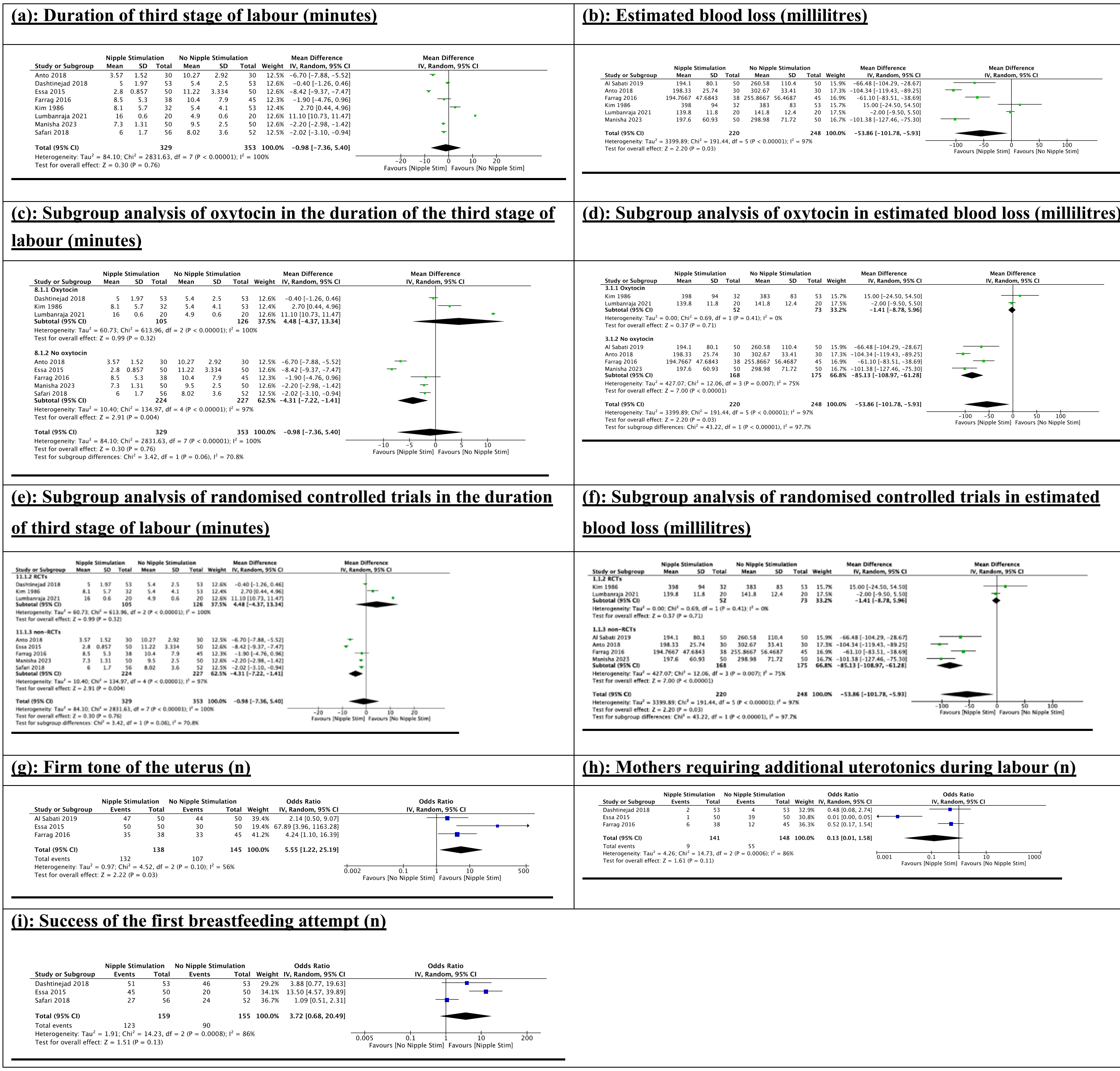

Fig. 4. Graphics detailing the primary outcomes of the analyses of this review. Fig. 4(a) shows the effects of early nipple stimulation on the duration of third stage of labour. Fig. 4(b) shows the effects of early nipple stimulation on estimated blood loss. Fig. 4(c) presents the results of a subgroup analysis showing the effect of oxytocin on the third stage of labour. Fig. 4(d) presents the results of another subgroup analysis showing the effect of oxytocin on estimated blood loss. Fig. 4(e) is a subgroup analysis of randomised controlled trials vs non-randomised controlled trials in the duration of third stage of labour. Fig. 4(f) is the final subgroup analysis of randomised controlled trials vs non-randomised controlled trials in estimated blood loss. Fig. 4(g) shows the effects of nipple stimulation on uterine tone. Fig. 4(h) presents the results of women who had early nipple stimulation and required additional uterotonic drugs compared to those who did not. Fig. 4(i) shows the effects of nipple stimulation on breastfeeding success in the first attempt.

professionals (Geller et al., 2006; Miller et al., 2004; Tsu et al., 2004). This makes it essential that the appropriate demographic population in these countries is trained in simple strategies such as early nipple stimulation to prevent blood loss and reduce risk of PPH by shortening third stage of labour (Geller et al., 2006). Also, many women in developed countries still opt for non-medicalised homebirths, with home birthing rates potentially on the rise in the US (Macdorman et al., 2013). Therefore, it is imperative to explore the potential of nipple stimulation as a safe alternative to uterotonic drugs. Additionally, more significant interventions must also be found that may act to treat PPH – not only prevent it – in settings that lack these resources (Miller et al., 2004; Tsu et al., 2004). A medical intervention for treating rather than preventing PPH is tranexamic acid. This has demonstrated effectiveness in low-income countries as it is low cost and does not require refrigeration (Brenner et al., 2019).

Lastly, many studies have found that the rate of PPH is increasing around the world, notably in high income countries such as the US, Australia, Canada and Ireland where active management acts as a standard practice for all labours (Begley et al., 2019; Callaghan et al., 2010; Ford et al., 2007; Goffman et al., 2016; Joseph et al., 2007; Lutomski et al., 2012). Studies appear to be at a loss as to the cause of this problem. One thought is that exogenous oxytocin in induction of labour has been found to oversaturate oxytocin receptors, potentially leading to uterine atony in the third stage, especially when administered for longer periods of time (Phaneuf et al., 1998; Parvin et al., 2016). In agreeance with this, a large Norwegian population-based study of 307, 415 women found a significant increase in severe PPH rates in women with induction of labour (Al-Zirqi et al., 2009). Additionally, Knight et al. (2009) found that adjustment for mode of delivery and maternal age still found that syntocin infusion for induction independently increases the odds of PPH. Other factors that were postulated to influence the increasing rates was the lack of a single, consistent definition of PPH and consistent methods of measuring or estimating blood loss (Knight et al., 2009). Additionally, increases in rates of obesity, caesarean section birth and maternal age at childbirth may also contribute (Callaway et al., 2006; Chu et al., 2009; Knight et al., 2009; Martin et al., 2007).

Limitations

While this meta-analysis offers valuable insights into the effects of early nipple stimulation during the third stage of labour, it is essential to recognise several limitations. The first limitation pertains to the heterogeneity of the included studies. The studies varied in design, with many being observational or retrospective, which may introduce biases such as selection and information bias. The observational nature of these studies limits the ability to establish causation and may affect the reliability of the results. This specifically concerns the subgroup analysis of EBL and duration of third stage that compared the randomised controlled trials to observational studies (Fig. 4(e and f)). A difference in EBL and duration of third stage was found in the observational studies and not in the randomised controlled trials. Although the data is limited by the small number of randomised controlled trials. This highlights the need for a larger number of high-quality randomised trials to explore this research question.

Additionally, a notable concern is the risk of bias in the included studies, as many were rated as having a serious risk of bias based on the ROBINS-I assessment. The majority of these studies lacked rigorous randomisation and adequate participant selection, leading to potential confounding factors that may skew the outcomes of this meta-analysis. This limitation emphasises again, the necessity for future research to incorporate well-designed randomised controlled trials to yield more robust findings.

Furthermore, the absence of comprehensive data on secondary outcomes, such as uterine atony requiring uterotonics and the need for surgical interventions, restricts the depth of our analysis. Many studies did not report these crucial variables, highlighting the need for larger cohort studies that capture a broader spectrum of outcomes related to early nipple stimulation.

Moreover, demographic variations among the included populations, such as maternal age and socioeconomic status, could contribute to high heterogeneity in the findings. The lack of stratification by these factors may hinder the generalisability of the results to the wider population. Future studies should aim to incorporate diverse demographic data to better understand how these characteristics influence the effectiveness of early nipple stimulation.

Lastly, the definitions and methods of assessing EBL varied among the studies, leading to potential inconsistencies in the reported outcomes. A lack of standardised criteria for EBL measurement complicates comparisons across studies and may contribute to selection bias. Establishing a consensus on these definitions will enhance the quality of future research and improve clinical practice regarding the management of PPH.

In summary, these limitations underscore the need for more rigorous and comprehensive research in this field to substantiate the findings of this meta-analysis and facilitate the development of evidence-based practices in maternal care.

Conclusion

This meta-analysis provides some evidence that early nipple stimulation may reduce both the duration of the third stage of labour and blood loss when compared to non-early nipple stimulation mothers. This has particular relevance in contexts where exogenous oxytocin is not available. These findings support the incorporation of early nipple stimulation into routine labour management, especially in settings where access to uterotonics is limited. The poor quality of the studies available on this topic, however, prevents the ability to draw firmer conclusions in this study. Certainly, there is additional need to explore the benefits of early nipple stimulation with higher quality research as there is little to lose and much to gain.

Abbreviations and acronyms

EBF	Early breastfeeding
EBL	Estimated blood loss
PPH	Postpartum haemorrhage

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used an artificial intelligence language tool to enhance readability and identify grammatical errors. After utilising this tool, the authors reviewed and refined the content as necessary and take full responsibility for the final version of the publication.

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The data set used for this meta-analysis can be shared upon request.

CRediT authorship contribution statement

Zoe Y. Zervides: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Maria M. Witkowiak:** Writing – review & editing, Writing – original draft, Validation, Project administration, Methodology, Investigation, Data curation. **Dana O. Alzoubi:** Writing – review & editing, Writing – original draft, Resources, Methodology, Data curation. **Reem B. Zalloum:** Writing – original draft, Data curation. **Natalie E. Bourdakos:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Fatma A.M. Abdulsalam:** Writing – review & editing, Supervision, Formal analysis, Data curation, Conceptualization. **Hayato Nakanishi:** Writing – review & editing, Supervision, Formal analysis, Conceptualization. **Christian A. Than:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Shavi Fernando:** Writing – review & editing, Supervision, Data curation. **Sir Sabaratnam Arulkumaran:** Writing – review & editing, Supervision, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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