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Review Article

Does the odor of breast milk benefit newborns babies? A Systematic Review

Semiha Dertli [a,*], Meltem Özcan [b]

[a] Firat University, Faculty of Health Science, Department of Pediatric Nursing, Elazig, Turkey
[b] Erzincan Binali Yildirim University, Vocational School of Health Services, Department of Health Care Services, Home Patient Care Programme, Erzincan, Turkey

[*] Corresponding author: *Firat University, Faculty of Health Science, Department of Pediatric Nursing, Elazig, Turkey*
E-mail addresses: semihadertli15@gmail.com (S. Dertli)

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Highlights

- The use of breast milk odor application is neither standard nor common.
- Breast milk odor has been shown to reduce pain, improve feeding, and positively affect the physiological parameters of infants.
- This odor can be utilized in NICUs and obstetric clinics to soothe infants.

Abstract

Many drug and non-drug methods are used for the diagnosis and treatment of newborn babies in a safe environment. Various odor stimulations such as the mother and breast milk odor are stated highly effective on babies. This research aimed to determine the effect of breast milk odor on newborns. This review of published articles in peer-reviewed journals in the past 17 years focused on breast milk odor on newborn. This review includes the results of studies on the effect of breast milk odor. Keywords of "odor", "olfactive", "smell", "scent", "newborn", "infant", "preterm", "breast milk", "breast milk odor", "olfactive stimulation" were searched together or separately from four databases. The breast milk odor was given by means such as cotton, sponge, gauze, olfactometer, and diffuser. In the studies, babies whose breast milk odor was applied pain reduced, physiological parameters positively affected, feeding behavior improved, crying duration shortened, motor activity and grimacing decreased. The breast milk odor was found has a positive effect on pain, feeding, physiological parameters.

Keywords: Breastmilk odor, feeding, newborn, pain, physiological parameters.

Introduction

Every year, approximately 15 million preterm newborns are born worldwide. Of these, around 27% and as many as 83-95% of very preterm newborns require mechanical ventilation. These infants undergo numerous painful procedures, prolonged treatments, and extended hospital stays (Silveira et al., 2013).

Advancements in science and technology have improved survival rates, enabled the early diagnosis of complications, and facilitated timely treatment for preterm infants (Aoyama et al., 2010). However, despite these advancements, the incidence of neurological problems, developmental delays, and cognitive impairments remains high among premature and low-birth-weight newborns. These vulnerable infants often face physiological, respiratory, and developmental challenges, as well as nutritional intolerance, requiring frequent painful interventions (Bustani, 2008; Aoyama et al., 2010).

To ensure a safe environment for diagnosis and treatment, various pharmacological and non-pharmacological methods are employed. However, the potential side effects of pharmacological methods have highlighted the importance of non-drug interventions, which are now widely adopted. Non-drug methods include practices such as kangaroo care, breastfeeding, swaddling, positioning, incubator covering, exposure to maternal voice, non-nutritive sucking, and exposure to maternal and breast milk odors (Johnston et al., 2017; Amiri Shadmehri et al., 2020; De Clifford-Faugere et al., 2020; Saberi Louyeh et al., 2020; Taplak & Bayat, 2020).

Among these, exposure to maternal and breast milk odors has been found to be highly effective for newborns. This effectiveness is attributed to the advanced development of the olfactory system at birth. Even without postnatal exposure, newborns can distinguish between various odors, including breast milk (Marlier & Schaal, 2005). For instance, a study involving 21 infants aged 2 to 9 months examined the effects of breast milk odor, odorless air, and non-food odors on EEG wave patterns. The results showed significant changes in the EEG waves of infants exposed to breast milk odor (Gellrich et al., 2021).

The sense of smell begins to develop during the intrauterine period. Odor stimulation emerges by the 11th week of pregnancy and becomes functional by the 28th week, enabling babies to recognize and respond to odors from that point onward (Beker et al., 2019). Both amniotic fluid and breast milk carry odor molecules that reflect the mother's diet, including foods, spices, and beverages. Studies have shown that exposure to these odors during late pregnancy and early infancy influences food preferences, some of which persist into adulthood (Beker et al., 2019).

Research has explored the effects of various odors on newborn responses during different procedures. These odors include breast milk (Taplak & Bayat, 2020), maternal breast and nipple, another mother's breast milk, formula milk (Nishitani et al., 2009), vanilla (Neshat et al., 2016), chamomile (Allam et al., 2006), cinnamon and anise (Van et al., 2018), scented pencils (Van et al., 2018), and lavender (Akcan & Polat, 2016; Usta et al., 2021). Their effects have been studied concerning feeding behavior, transition to oral feeding, pain responses, stress, crying duration, early recovery, and physiological parameters.

Systematic reviews in the literature have primarily focused on specific outcomes. For example, Shah et al. (2012) reviewed the use of breastfeeding or breast milk for procedural pain management in neonates, while Zhang et al. (2018) examined the analgesic effects of breast milk odor. De Clifford-Faugere et al. (2020) analyzed odor stimulation during painful processes, and Muelbert et al. (2019) investigated the role of milk odor and taste in accelerating feeding in preterm infants. These reviews largely emphasized pain relief and feeding outcomes.

This review aims to provide a comprehensive overview of the effects of breast milk odor on various parameters in newborns, including pain, physiological responses, apnea, feeding behavior, crying duration, cortisol levels, comfort, recovery, discharge, and sleep-wake cycles, thereby presenting a broader understanding of its benefits.

Methods

Design

This review incorporates studies on breast milk odor published between January 2005 and October 2024. The design includes a comprehensive description of the search methods, search terms, search limitations, exclusion of duplicate studies, and exclusion criteria.

Sample: Defining the articles reviewed

Studies published over the last 19 years (January 2005–October 2024) were included. Keywords such as "odor," "olfactive," "smell," "scent," "newborn," "infant," "preterm," "breast milk," "breast milk odor," and "olfactive stimulation" were searched collectively and individually across databases, including PubMed, Medline, Web of Science, Google Scholar, ScienceDirect, and the Cochrane Database of Systematic Reviews. Search limitations included studies published in English and those conducted on humans.

Data collection: The search strategy and process

A total of 134 studies were identified through the database research. Using the EndNote X9 application, 14 duplicate records were removed. Exclusions included one study that was inaccessible, four studies published in languages other than English, 14 studies focusing on odor stimulation unrelated to breast milk odor, six review, systematic review, or meta-analysis studies, three studies conducted on non-human subjects, and seven studies published prior to 2005. Only randomized controlled trials, cohort studies, experimental and quasi-experimental studies, and pilot experimental studies were included. Studies with descriptive, cross-sectional, case-control, qualitative, theoretical, protocol designs, or those involving speaking subjects were excluded. Ultimately, 39 studies met the inclusion criteria for this review (Fig. 1).

Measurement

The selected studies were assessed using the Quality Assessment Tool for Quantitative Studies (Jackson & Waters, 2005). Evaluation criteria included selection bias, study design, confounding factors, blinding, data collection methods, and participant withdrawals or dropouts. Each criterion was rated as strong (1), moderate (2), or weak (3). After scoring, an overall global score reflecting the average was calculated (Table 1, Table 2).

For studies lacking clear methodological details, their designs were categorized by the authors based on a thorough evaluation. Due to ambiguities in the methodology sections of some studies, an independent third author conducted a blind re-evaluation of the scores. Agreement on scoring reached 90% after this process (Table 1).

Data analysis

The review included 39 studies. Key data extracted from the studies included:

- Authors and publication order,
- Clinical settings,
- Sample sizes,
- Characteristics of experimental and parallel control groups (gestational age, birth weight, postnatal age),
- Routine hospital procedures performed on newborns (e.g., venipuncture, feeding, heel sticks),
- Delivery method, duration, and frequency of breast milk odor application,
- Focus areas and outcomes of breast milk odor interventions,

The summarized findings highlight the efficacy of breast milk odor interventions (e.g., impact on pain, physiological parameters, and feeding behaviors).

Access-limited articles

Four studies could not be fully accessed due to database restrictions. Therefore, only their abstracts were evaluated (Çakırlı & Açıkgöz, 2024; Deniz & Sarıalioğlu, 2024; Erdoğan & Çamur, 2022; Kim & Choi, 2022).

Results

Methodological characteristics of studies

The studies included in this review consisted of randomized controlled trials, experimental studies, quasi-experimental studies, pilot studies, and one near-infrared spectroscopy (NIRS) study (Table 2). In these studies, various experimental groups were exposed to breast milk odor and compared with control groups. The experimental groups included: Non-nutritive sucking (Amiri Shadmehri et al., 2020), white noise, swaddling (Taplak & Bayat, 2020), incubator cover (Alemdar, 2018; Alemdar & İnal, 2020; Saberi Louyeh et al., 2020), odor of another mother's milk (Nishitani et al., 2009; Rad et al., 2021; Cakirli & Acikgoz, 2021), formula milk odor (Nishitani et al., 2009; Badiee et al., 2013; Tasci & Kuzlu Ayyildiz, 2020; Shoaei et al., 2023), sucrose (Modaresi et al., 2024), mother's voice (Ali et al., 2022), breastfeeding (Tavlar et al., 2022), mother and amniotic fluid odor (Akcan & Polat, 2016; Alemdar & Kardaş Özdemir, 2017), lavender odor (Akcan & Polat, 2016), vanilla odor (Rattaz et al., 2005; Jebreili et al., 2015;

Neshat et al., 2016), and odors from the mother's breast, areola, and nipple (Doucet et al., 2007) (Table 2).

The gestational age of infants in the studies varied widely. The earliest gestational age was 25 weeks (Taplak & Bayat, 2020), while the latest was 42 weeks (Doucet et al., 2007; Aoyama et al., 2010; Akcan & Polat, 2016; Amiri Shadmehri et al., 2020; Tasci & Kuzlu Ayyildiz, 2020). Similarly, the weight of the babies varied. The lowest recorded birth weight was 1210 g (Bingham et al., 2007), while the highest was 5070 g (Doucet et al., 2007).

Breast milk odor interventions were applied during a variety of procedures, including vaccinations, oral feeding, gavage feeding, blood sampling, heel blood sampling, peripheral cannulation, and cannula applications (Table 3). Different materials were used to deliver the breast milk odor, such as gauze, filter paper, sterile sponges, and sterile cotton. In one study, the odor was delivered using a diffuser (Baudesson de Chanville et al., 2017), while in another, it was applied in a solution (Nishitani et al., 2009), and in another study, an olfactometer device was used (Bingham et al., 2007). The amount of breast milk ranged from a single drop to 5 ml (Baudesson de Chanville et al., 2017; Beker et al., 2017). The distance from the baby's nose to the source of the breast milk odor varied between 1 mm and 10 cm in the studies (Neshat et al., 2016; Tasci & Kuzlu Ayyildiz, 2020; Deniz & Sarıalioglu, 2024) (Table 3).

The duration and frequency of breast milk odor exposure varied across studies. The shortest intervention lasted for 90 seconds and was applied once (Doucet et al., 2007), while the longest interventions were applied during each feeding until enteral feeding was established (Beker et al., 2017), or during every 3 consecutive feeding for 10 days (Khodagholi et al., 2018) (Table 3).

Main Results of the Studies

Pain

Twenty-one studies examined the effect of breast milk odor on babies' pain. The breast milk odor intervention was applied during various procedures, including vaccination (Amiri Shadmehri et al., 2020; Rad et al., 2021), endotracheal suction (Taplak & Bayat, 2020; Deniz & Sarıalioglu, 2024), blood sampling (Cakirli & Acikgoz, 2021; Erdogan & Camur, 2022), heelstick (Badiee et al., 2013; Akcan & Polat, 2016; Alemdar & Kardaş Özdemir, 2017; Tasci & Kuzlu Ayyildiz, 2020; Tavlar & Karakoc, 2022; Kim & Choi, 2022; Lin et al., 2022; Lan et al., 2021), cannula application (Baudesson de Chanville et al., 2017; Alemdar, 2018), and vein puncture (Jebreili et al., 2015; Asadian et al., 2022).

In 16 of the studies, breast milk odor was found to reduce pain in newborns (Table 2). Additionally, in the study by Cakirli and Acikgoz (2021), breast milk odor positively affected the agitation and sedation parameters of the babies. Baudesson de Chanville et al. (2017) used two pain scales in their study. The Premature Infant Pain Profile (PIPP) score decreased, while the Douleur Aiguë du Nouveau-né (DAN) score did not change. Alemdar and Alemdar et al. (2017) found a lower pain score in the breast milk odor group compared to the control group, although the difference was not statistically significant. However, Taplak and Bayat (2020) determined that breast milk odor was ineffective in reducing pain (Table 2).

Physiological parameters

Seventeen studies investigated the effect of breast milk odor on various physiological parameters in babies. These parameters included heart rate, oxygen saturation, respiration, and hemoglobin oxygenation in the orbito-frontal region.

Five studies examined heart rate, saturation, and respiratory parameters (Alemdar & İnal, 2020; Amiri Shadmehri et al., 2020; Lee & Ra, 2021; Rad et al., 2021; Saberi Louyeh et al., 2020), and nine studies focused on heart rate and oxygen saturation (Akcan & Polat, 2016; Alemdar & Kardaş Özdemir, 2017; Cakirli & Acikgoz, 2021; Neshat et al., 2016; Taplak & Bayat, 2020; Tasci & Kuzlu Ayyildiz, 2020; Erdogan & Camur, 2022; Kim et al., 2022; Lin et al., 2022). One study examined only the heart rate parameter (Maayan-Metzger et al., 2018), while one study focused on hemoglobin oxygenation in the orbito-frontal region (Aoyama et al., 2010).

The studies by Cakirli and Acikgoz (2021), Tasci and Kuzlu Ayyildiz (2020), Akcan and Polat (2016), and Neshat et al. (2016) found that breast milk odor positively affected heart rate and oxygen saturation. Aoyama et al. (2010) reported an increase in hemoglobin oxygenation in the orbito-frontal region of the babies. However, Lee and Ra (2021), Saberi Louyeh et al. (2020), Alemdar and İnal (2020), and Alemdar and Kardaş Özdemir (2017) found no effect on heart rate, saturation, or respiration.

In the study by Taplak and Bayat (2020), heart rate was not affected, but oxygen saturation was negatively impacted (Table 2).

Feeding

Ten studies examined the effect of breast milk odor on babies' feeding behavior (Alemdar & Kardaş Özdemir, 2017; Alemdar, 2018). In five of these studies, babies transitioned to oral feeding more quickly (Aboli et al., 2015; Iranmanesh et al., 2015; Khodagholi et al., 2018; Davidson et al., 2019; Alemdar & İnal, 2020). One study found that the breast milk odor group transitioned to enteral feeding faster (Beker et al., 2017), and another study showed improved feeding competence (Saberi Louyeh et al., 2020). In one study, breast milk odor accelerated oral feeding, but the result was not statistically significant (Yildiz et al., 2011).

Regarding weight gain, two studies found that breast milk odor was effective (Beker et al., 2017; Khodagholi et al., 2018), while three studies did not show an effect (Aboli et al., 2015; Alemdar & İnal, 2020; Yildiz et al., 2011).

Two studies found that breast milk odor prolonged the sucking duration of babies (Bingham et al., 2007; Raimbault et al., 2007), and one study reported that babies consumed more milk (Raimbault et al., 2007). Another study observed that babies licked and sucked their mother's breast more (Doucet et al., 2007). In contrast, one study found no change in burst sucking behavior (Bingham et al., 2007), and another study showed no difference in rooting reflexes compared to the control group (Doucet et al., 2007). Additionally, one study found no effect of breast milk odor on babies' risk of necrotizing enterocolitis or intestinal perforation (Beker et al., 2017) (Table 2).

Babies' crying duration

Nine studies investigated the effect of breast milk odor intervention on babies' crying duration. The studies examined how breast milk odor influenced crying during blood sampling (Cakirli & Acikgoz, 2021), heelstick (Rattaz et al., 2005; Nishitani et al., 2009; Alemdar & Kardaş Özdemir, 2017; Tasci & Kuzlu Ayyildiz, 2020; Lin et al., 2022), and venipuncture (Baudesson de Chanville et al., 2017; Asadian et al., 2023).

In five of the seven studies that measured crying duration, babies in the breast milk odor group showed a shortened crying duration (Rattaz et al., 2005; Nishitani et al., 2009; Baudesson de Chanville et al., 2017; Cakirli & Acikgoz, 2021; Tasci & Kuzlu Ayyildiz, 2020; Lin et al., 2022). In the study by Alemdar and Kardaş Özdemir (2017), the crying duration was also shorter, although the result was not statistically significant (Table 2).

Cortisol release

Four studies examined the effect of breast milk odor intervention on newborns' cortisol levels. Three of these studies investigated cortisol levels during heelstick (Nishitani et al., 2009; Badiee et al., 2013; Tasci & Kuzlu Ayyildiz, 2020). In all four studies, breast milk odor intervention was found to lower cortisol levels in newborns compared to the control group (Nishitani et al., 2009; Badiee et al., 2013; Maayan-Metzger et al., 2018; Tasci & Kuzlu Ayyildiz, 2020) (Table 2).

Other parameters

Six studies examined various parameters in babies, including discharge duration (Iranmanesh et al., 2015; Khodagholi et al., 2018), comfort (Alemdar, 2018), grimacing (Rattaz et al., 2005; Nishitani et al., 2009), motor activity (Nishitani et al., 2009), sleep-wakefulness, eye-opening duration (Doucet et al., 2007), and head movement (Rattaz et al., 2005).

Khodagholi et al. (2018) and Iranmanesh et al. (2015) found that babies in the breast milk odor group were discharged earlier from the hospital. Lee and Ra (2021) observed that infants in the breast milk odor group experienced less apnea (Lee & Ra, 2021).

Nishitani et al. (2009) and Rattaz et al. (2005) found that babies in the breast milk odor group exhibited less grimacing during heelstick, as well as reduced motor activity (Nishitani et al., 2009) and head movements (Rattaz et al., 2005). Doucet et al. (2007) found that breast milk odor prolonged babies' eye-opening duration but had no effect on their sleep-wakefulness patterns (Doucet et al., 2007).

In a study by Alemdar (2018), breast milk odor intervention during cannula application did not affect the comfort level of babies (Alemdar, 2018) (Table 2).

Discussion

In this review, breast milk odor was investigated for its effects on various behaviors of newborn babies, such as pain response, physiological parameters, feeding, crying duration, sedation, stress, and other factors. The studies included different clinical settings. For example, the studies by Tasci and Kuzlu Ayyildiz (2020), Badiee et al. (2013), Modaresi et al. (2024), and Tavlar et al. (2022) lacked a control group, with comparison groups consisting of babies exposed to formula milk odor (Badiee et al., 2013; Tasci & Kuzlu Ayyildiz, 2020) or to breastfeeding and the mother's heart sound (Tavlar et al., 2022). Similarly, the studies by Doucet et al. (2007) and Maayan-Metzger et al. (2018) did not include independent control groups, and their results were compared within the same baby experimental group (Doucet et al., 2007; Maayan-Metzger et al., 2018). Because of these study designs, definitive conclusions regarding the exact effects of breast milk odor cannot be drawn.

Breast milk odor was often compared with other odor stimulations, such as vanilla, amniotic fluid, lavender, and maternal odor (Table 2). Additionally, in studies by Amiri Shadmehri et al. (2020), Taplak and Bayat, Saberi Louyeh et al. (2020), and Alemdar (2018), other groups were used that did not involve odor stimulation, such as non-nutritive sucking, white noise, swaddling, and incubator covers (Alemdar, 2018; Amiri Shadmehri et al., 2020; Taplak & Bayat, 2020; Saberi Louyeh et al., 2020). It is important to note that the groups without odor stimulation should be interpreted separately and cannot be directly compared with the odor stimulation groups.

Two studies included babies who were not yet 28 weeks old (Maayan-Metzger et al., 2018; Taplak & Bayat, 2020). It has been found that odor stimulation begins to develop in the 11th week of pregnancy and becomes functional at the 28th week, when babies are capable of identifying and reacting to odors (Beker et al., 2019). In the study by Taplak and Bayat (2020), which examined pain and physiological parameters, the pain scores of babies did not change, and their oxygen saturation was negatively affected (Taplak & Bayat, 2020). In the quasi-experimental pilot study by Maayan-Metzger et al. (2018), which measured cortisol levels and heart rate, it was reported that babies' cortisol levels decreased, but their heart rate remained unchanged (Maayan-Metzger et al., 2018). This suggests that babies born before 28 weeks may not respond adequately to odor stimulation.

Breast milk odor was found to reduce pain in babies. Pain reduction was observed in 16 out of 21 studies (Table 2). In two studies, pain scores decreased, though not statistically significant (Alemdar & Kardaş Özdemir, 2017; Alemdar, 2018). In one study, pain decreased on one of two pain scales (Baudesson de Chanville et al., 2017), and in another study, the mean pain score did not change (Taplak & Bayat, 2020). Theoretically, it can be said that breast milk odor reduced pain in 90% of the studies.

Although there were no studies specifically examining how odor stimulation affects pain, skin-to-skin contact has been shown to have a positive effect on pain in babies. Skin-to-skin contact involves multiple dimensions, such as maternal closeness, touch, and olfactory stimuli, which allow babies to smell their mothers. This situation is also relevant during breastfeeding, making it an effective intervention for term babies (De Clifford-Faugere et al., 2020). We assume that babies exposed to the smell of breast milk recognize it, which makes them feel safe and relaxed. For premature babies, studies where the intervention was performed only once or for a short duration showed either no decrease or a minimal decrease in pain (Alemdar & Kardaş Özdemir, 2017; Alemdar, 2018; Taplak & Bayat, 2020). To enhance the effect of breast milk odor on pain, it is suggested that babies with older gestational ages should be selected, and the frequency and duration of the breast milk odor intervention should be prolonged.

Seventeen studies examined the effect of breast milk odor on physiological parameters. In eleven studies, breast milk odor had a positive effect, in five studies it had no effect, and in one study, it had a negative effect (Table 2). Aoyama et al. (2010) used near-infrared spectroscopy (NIRS) to measure hemoglobin oxygenation in the orbitofrontal regions of babies exposed to breast milk odor.

The study found significantly higher oxygenation levels in these areas, suggesting that babies can recognize and distinguish the smell of breast milk (Aoyama et al., 2010). This result may indicate that babies calm down and develop a positive response to familiar odors. However, some studies found no effect of breast milk odor. Upon closer inspection, it was noted that these studies included babies with lower gestational ages compared to others (Alemdar & Kardaş Özdemir, 2017; Maayan-Metzger et al., 2018; Alemdar & İnal, 2020; Saberi Louyeh et al., 2020). For example, in the study by Taplak and Bayat (2020), where oxygen saturation was negatively affected, some of the babies were born before the 28th week of gestation. This may explain why these babies did not react positively to the odor stimulation (Taplak & Bayat, 2020).

Ten studies in the review examined the effect of breast milk odor on feeding behaviors. Babies exposed to breast milk odor switched to oral or enteral feeding faster, gained weight more rapidly, consumed more milk, and developed feeding behaviors such as burst sucking and rooting reflexes (Table 2). Odor stimulation is known to affect feeding behavior in infants. Beker et al. (2019) stated that amniotic fluid and breast milk contain receptors that reflect the foods, spices, and beverages consumed by the mother. Babies exposed to these odors during late pregnancy and early infancy may develop a preference for these foods that persist into adulthood (Beker et al., 2019). Additionally, olfactory stimuli trigger a cephalic phase response, which includes saliva production, insulin secretion, and increased stomach acid production (Muelbert et al., 2019). This response may lead to gastrointestinal reactions to the breast milk odor. In three studies, weight gain did not differ between babies in the breast milk odor group and the control group. However, in all three of these studies, babies in the breast milk odor group transitioned to oral feeding more quickly (Yildiz et al., 2011; Aboli et al., 2015; Alemdar & İnal, 2020). Weight gain is a long-term process, so the impact of breast milk odor may not be immediately visible in such short periods.

In studies examining the effect of breast milk odor on the crying duration of babies during procedures such as blood sampling, venipuncture, and heelstick, it was found that the crying duration was significantly shortened (Table 2). This result suggests that breast milk odor has a calming effect on babies.

Several studies investigated the impact of breast milk odor on cortisol release during painful procedures. Babies exposed to breast milk odor had lower cortisol levels, indicating a reduced biochemical response to pain (Nishitani et al., 2009; Badiee et al., 2013; Maayan-Metzger et al., 2018; Tasci & Kuzlu Ayyildiz, 2020). Since cortisol levels are a marker of pain response, lower cortisol levels suggest that breast milk odor may help reduce pain levels in babies.

Additionally, babies exposed to breast milk odor showed less motor activity, grimaced less, and had shorter discharge periods following painful procedures (Rattaz et al., 2005; Doucet et al., 2007; Iranmanesh et al., 2015; Khodagholi et al., 2018). The reduction in motor activity during pain indicates that breast milk odor helps babies remain calmer. This finding is supported by the study of Hym et al. (2020), where babies exposed to their mother's odor showed less movement and remained calmer, as observed through computer software analysis. This further confirms that exposure to breast milk odor has a soothing effect on babies during stressful situations.

Table 1.
Global scores of studies.

Authors	A	B	C	D	E	F	Global Score
Modaresi et al., 2024	3	3	3	3	3	3	3
Deniz et al., 2024 Access Limited	AL	AL	AL	AL	AL	AL	AL
Shoaei et al., 2023	2	2	3	3	2	3	2
Asadian et al., 2023	2	2	3	3	2	3	3
Ali HM et al., 2022	3	3	3	3	3	3	3
Tavlar et al., 2022	3	2	2	3	2	2	2
Erdogan et al., 2022 Access Limited	AL	AL	AL	AL	AL	AL	AL
Kim et al., 2022 Access Limited	AL	AL	AL	AL	AL	AL	AL
Lin et al., 2022	1	1	2	1	1	2	1
Lan et al., 2021	2	2	1	2	1	2	2
Cakirli et al., 2021 Access Limited	AL	AL	AL	AL	AL	AL	AL
Rad et al., 2021	1	2	1	1	2	3	2
Lee et al., 2021	1	2	2	2	2	2	2
Shadmehri et al., 2020	2	1	1	3	1	3	2
Taplak et al., 2020	1	2	1	1	2	2	2
Louyeh et al., 2020	3	3	2	3	2	3	3
Çakırlı. et al., 2020	2	2	1	3	2	2	2
Taşçı et al., 2020	2	3	3	2	2	2	2
Davidson et al., 2019	3	3	2	2	2	3	2
Alemdar et al., 2019	2	2	1	3	3	2	2
Khodagholı et al., 2018	2	3	2	1	2	3	2
Metzger et al., 2018	3	3	3	3	3	3	3

Alemdar, 2018	2	2	1	3	2	2	2
Beker et al., 2017	3	3	2	3	3	2	3
Alemdar et al., 2017	2	2	1	3	2	2	2
Chanville, 2017	1	2	2	1	2	2	2
Akcan, 2016	2	1	1	2	3	2	2
Neshat, 2015	3	3	2	3	3	3	3
Aboli, 2015	3	3	2	3	3	3	3
Jebreili, 2015	3	3	2	3	3	3	3
Iranmanesh et al. 2015	3	3	2	3	3	3	3
Badiee et al. 2013	3	3	3	3	3	3	3
Yildiz et al. 2011	2	1	2	2	2	2	2
Aoyama et al. 2010	2	2	2	2	1	1	2
Nishitani et al. 2009	3	2	1	3	2	3	2
Bingham et al. 2007	3	3	3	3	3	3	3
Doucet et al. 2007	2	3	2	3	2	3	3
Raimbault et al. 2006	2	3	2	3	2	2	3
Rattaz et al. 2005	2	3	2	2	2	2	3
Quality codes	1-Strong			2-Moderate		3-Weak	

Notes: Labels: A, Selection bias; B, Study design; C, Confounders; D, Blinding; E, Data collection methods; F, withdrawals, and drop-outs.

Limitations and strengths

One limitation of this study is the small number of clinical trials, which results in a limited sample size for properly evaluating the effects of breast milk odor. Additionally, the quality of the included studies varied in terms of methodology, and there were inconsistencies in the methods used for scoring outcomes. To provide more reliable evidence, it is recommended that future clinical trials with higher methodological rigor be conducted. This should include measures such as allocation concealment, blinding of outcome assessment, and consideration of intention-to-treat analysis.

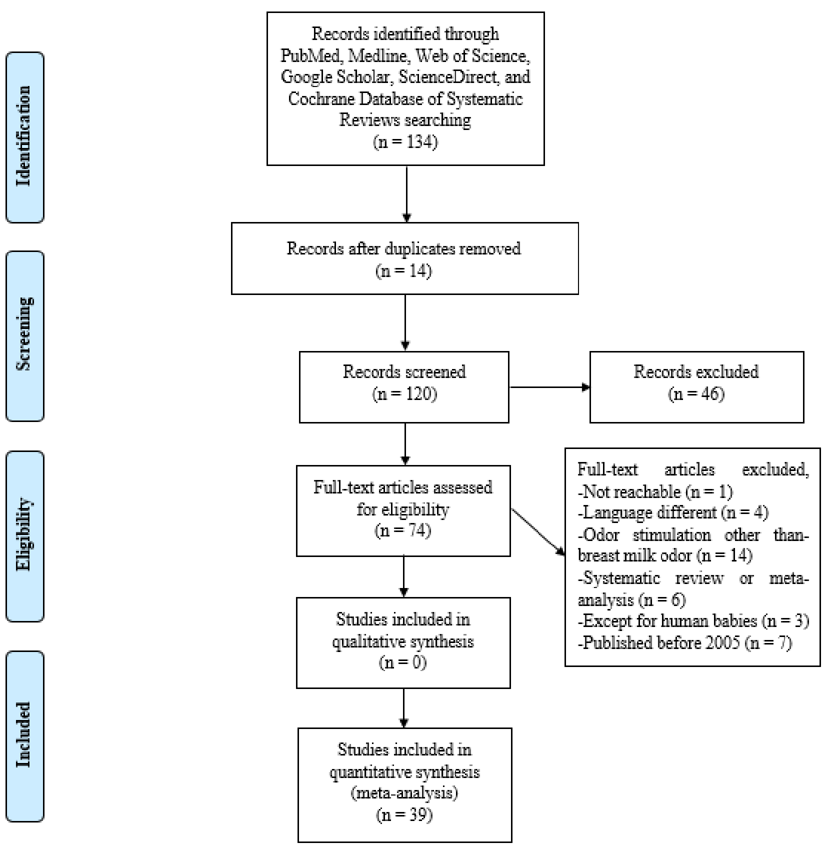

Fig. 1. Flow diagram of research.

Table 2.
Main results of studies.

Authors	Research Design	Sample of Experimental and Control Groups	Postnatal Age	Baby Weight (Mean±SD or Range) gr	Routine Intervention Applied to The Babies	Duration and Frequency of Intervention	Focus	Main results of the Breast Milk Odor Group
Modaresi et al., 2024	Experimental	Breast milk odor: 31 Sucrose: 34 Breast milk taste: 34	2-29 days	BMO: 3189.03 590.16 SG: 3044.71 599.98 BMT: 3089.12±572.19	Venipuncture	2 minutes before procedure	Pain	The smell of breast milk has been reported to be effective in reducing pain
Deniz et al., 2024 Access Limited	RCT	Breast milk odor: 44 Control group: 44	AL	AL	Endotracheal Suction	From 5 minutes before to 5 minutes after endotracheal suction	Pain Stress	Breast milk odor group's pain and stress score averages were lower than the control group during and after the endotracheal suction procedure
Shoaei et al., 2023	RCT	Breast milk odor: 32 Formula odor: 32 Control group: 32	1-5 days	BMO: 2492.24±331.53 FO: 2373.5±355.59 CG: 2362.3±290.52	Routine follow-up	Twice a day for four days	Respiratory distress and oxygen saturation	Although not statistically significant, human milk group infants had less respiratory distress than the control group. There was no change in oxygen saturation
Asadian et al., 2023	RCT	Breast milk odor: 20 Control group: 20	3-5 days	-	Venipuncture	Started 3 minutes before blood sampling until the completion of the procedure	-Pain (Modified behavioral pain scale) -Crying -Movements	This study found that the odor of breast milk was effective in reducing infants' procedural pain
Ali et al., 2022	Quasi Experimental	Breast milk odor: 50 Mother voice: 50 Control group: 50	3-7 days	1476.60±307.12-1399.60±310.38	Peripheral Cannulation	15 minutes before procedure	Pain and Comfort	It was determined that discomfort and pain in the breast milk odor group decreased statistically compared to the control group
Tavlar et al., 2022	RCT	Breast milk odor: 30 Breastfeeding: 30 Mother's heart beat sound: 30	1-2 days	BMO: 3218.83±447.74 BF: 3191.16±352.16 MHBS: 3258.66±401.99	Heel lance	From 3 min before to 3 min after the procedure	ALPS-Neo Pain	Breast milk odor was found that not effective for pain
Erdogan et al., 2022	RCT	Breast milk odor, taste and	AL	AL	Blood drawing procedure	AL	Pain,	The lowest pain score during the procedure was

Access Limited		control group, separate or combined					SpO2 levels, Heart Rate	found in the infants to whom breast milk taste and smell were administered together
Kim et al., 2022 Access Limited	A quasi experimental	Breast milk odor: 24 Control group: 34	AL	AL	Heel stick	30 seconds before the start of heel stick sampling	Pain Heart rate Oxygen saturation	The pain scores of the breast milk group were found significantly lower than those of the control group
Lin et al., 2022	Prospective RCT	Breast milk odor, Breast milk odor+taste, Control Group Totally 114 infants	-	BMO: 3105.39±385.47 BMOT: 3066.45±345.80 CG: 3120.92±355.69	Heel stick	2 min prior to the heel prick, until the collection of the blood sample	Biobehavioral responses to pain (Heart rate and saturation), crying time	In the study, babies who smelled breast milk had less pain response, and their crying time was shorter
Lan et al., 2021	RCT	Gentle Touch, Breast milk odor, Breast milk odor+taste, Totally 120 infants	2-3 days	3100.25±352.61	Heel stick	Routinely, Three minutes prior to the heel stick to the 5th minute of recovery	Pain	The smell and taste of breast milk was found to be effective in reducing pain
Cakirli et al., 2021 Access Limited	RCT	Breast milk odor: 30 Another mother's milk: 30 Control group: 30	AL	AL	AL	AL	Pain Crying time	Babies who received breast milk odor had less pain and shorter crying times compared to the control group
Rad et al., 2021	RCT	Breast milk odor: 30 -Another mother's milk odor: 30 Control group: 30	1-4 days	**1620±425-1806±553	Hepatitis B vaccine administration	Started 3 min before vaccination and continued until the vaccination was completed/once	-Pain (PIPP) -Physiological parameters	-Pain decreased compared to other groups -Blood pressure and saturation did not change -The heart rate is positively affected
Lee et al., 2021	Experimental	-Breast milk odor: 13 -Control group: 18	-	1456±226-1552±248	In the stable times of babies	3 times a day with 2 hours of intervention/for 5 days in a row	Normal and abnormal physiological parameters	-No change in pulse, respiration and saturation -No difference was observed between the groups in tachycardia, bradycardia, tachypnea and desaturation

								There was a statistically significant reduction in apnea
Shadmehri et al., 2020	RCT	-Breast milk odor: 30 -Non-nutritive suction:30 -Control group: 30	1-3 days	2500-3500 **3091±230-3134±332	Hepatitis B vaccine administration	3 minutes/once	-Pain (MBPS) -Physiological parameters	-Pain decreased -Saturation has not changed -Heart rate and respiration were positively effected
Taplak et al., 2020	RCT	-Breast milk odor: 20 -White noise: 20 -Swaddling: 20 -Control group: 20	1-7 days	*1000>	Endotracheal suction	5 minutes before the intervention until 5 minutes after the intervention/once	-Pain (PIPP-R) -Physiological parameters	-Pain not affected -Saturation negatively effected -Heart rate did not change
Louyeh et al., 2020	Quasi Exp.	-Breast milk odor: 35 -Incubator cover: 35 -Control group: 35	-	1500-2200 **1442±71-1446±63	During feeding	15 minutes/once	Nutritional adequacy	-Respiration, heart rate, saturation have not affected -Nutrition adequacy improved
Çakırlı et al., 2020	RCT	-Breast Milk Odor: 30 -Another mother's milk odor: 30 -Control group: 30	1-6 (2-6.25) days	*2873–3486	Blood sampling	-2 minutes before the blood sample is taken -1.5-2 minutes while taking blood sample -A while after blood sample is taken/once	Pain (N-PASS) (Agitation, Sedation) -Cry -Physiological parameters	-Pain decreased -Agitation and sedation were positively affected -Crying duration shortened -Saturation and heart rate were positively affected
Taşçı et al., 2020	RCT	-Breast milk odor: 42 -Formula milk odor: 42	-	*2500-4000	Heel stick	-3 minutes before the heel stick, during, and 9 minutes after/once	-Pain (NIPS) -Physiological parameters -Crying duration -cortisol release	-Pain decreased -Saturation and heart rate affected positively -Crying duration decreased -The cortisol level decreased
Davidson et al., 2019	Randomized Pilot Study	-Breast milk odor: 17 -Water odor control: 16	1-8 days	Ns	Oral feeding	15 minutes/4-6 times a week until the baby transited to oral feeding	Transition to oral feeding	-Babies before 31 weeks transited faster to oral feeding -Babies after 31 weeks transited later to taking feeding

Alemdar et al., 2019	RCT	-Breast Milk odor: 30 -Mother voice: 30 -Incubator cover: 31 -Control group: 32	-	1000> **1,404±99-1,503±194	Routine care	Until the babies transited to oral feeding/until the babies are discharged	-Physiological parameters -Transition to oral feeding	-Saturation, heart rate, respiration were not affected -There was no difference in weight, height, and head diameter during discharge -Babies transited to oral feeding faster
Khodagholı et al., 2018	Quasi Exp.	-Breast Milk odor: 16 -Control group: 16	4-6 days	1000> **1320±148-1311±159	Gavage feeding	3 consecutive feedings daily/every day for 10 days	Transition to oral feeding -Discharge time -Daily weight gain	-Transited to oral feeding faster -Weight gain was faster -Discharge duration decreased
Metzger et al., 2018	Pilot Quasi Exp.	Breast milk odor: 15 -2 days odor free/2 days breast milk odor/2 days odor free	7-54 days	*835-1643	-	For 2 days with the pad changed every 3 hours	-Cortisol release -Heart rate	-Salivary cortisol level decreased -There was no change in heart rate
Alemdar, 2018	RCT	-Breast milk odor: 30 -Mother voice: 30 -Incubator cover: 31 -Control group: 32	-	**1404±99, 1503±194	Peripheral cannula application	during and up to the fifth minute after the intervention/once	-Pain (PIPP) -Comfort	-Pain decreased although not statistically -Comfort score did not change
Beker et al., 2017	Randomized Control Pilot Trial	-Breast milk odor: 28 -Control group: 33	-	**937±252, 942±179	Tube feeding	During each feeding/every day until transition to enteral feeding	-Transition to enteral feeding -Weight gain -Discharge -NEK rate, -Intestinal perforation	-Enteral feeding was not affected -Weight gain increased Discharge duration not affected -No change in the NEK rate and intestinal perforation
Alemdar et al., 2017	RCT	-Breast milk odor: 22 -Mother's odor: 20 -Amnion fluid odor: 21	-	**1,939±836-2,235±801	Heel stick	15 minutes before the intervention until 15 minutes after the intervention (approximately 31 minutes)/once	-Pain -Physiological parameters -Crying duration	-Pain decreased, although not statistically -No change in the crying duration -No difference in heart rate

		-Control group: 22						
Chanville et al., 2017	RCT	-Breast milk odor: 16 -Control group: 17	0-10 (6-8) days	*1647-1947	Venipuncture	3 minutes before the intervention until 9 minutes after the intervention/once	Pain (PIPP and DAN) -Crying duration	-PIPP pain score decreased -DAN pain score did not change -Crying duration shortened
Akcan et al., 2016	Exp.	-Breast milk odor: 24 -Amniotic fluid odor: 27 -Lavender odor: 24 Control group: 25	-	2500> *2,640-4200	Heel stick	5 minutes before the intervention and 5 minutes after the intervention/once	-Pain (NIPS) -Physiological parameters	-Pain decreased -Heart rate and saturation were positively affected
Neshat et al., 2015	Quasi Exp.	-Breast milk odor: 45 -Vanilla odor: 45 -Control group: 45	3-28 days	**1575±322-1587±365	Venipuncture	5 minutes before the intervention and 30 seconds after the intervention/once	Physiological parameters	Heart rate and saturation positively affected
Aboli et al., 2015	Exp.	-Breast milk odor: 46 -Control group: 46	-	**1469±295-1601±412	Gavage feeding	4 times in a day/every day until transition to oral feeding	-Transition from gavage feeding to oral feeding -Weight gain	-Transition to oral feeding was faster -No difference was observed in weight gain
Jebreili et al., 2015	Quasi Exp.	-Breast milk odor: 45 -Vanilla odor: 45 -Control group: 45	3-28 days	**1575±322-1587±365	Venipuncture	5 minutes before the intervention and 30 seconds after the intervention/once	-Pain (PIPP)	-Pain decreased
Iranmanesh et al., 2015	Exp.	-Breast milk odor: 46 -Control group: 46	-	**1469±295-1601±412	Gavage feeding	4 times a day/every day until transition to oral feeding	-Transition from gavage feeding to oral feeding -Discharging	-Transition to oral feeding was faster -Discharge duration shortened
Badiee et al., 2013	Quasi Exp.	-Breast milk odor: 25 -Formula milk odor: 25	1-30 days	**2098±527-2287±105	Heel stick	3 minutes before the intervention until 9 minutes after the intervention/once	-Pain (PIPP) -Crying duration -Cortisol release	-Pain decreased -Crying duration shortened -Cortisol decreased
Yildiz et al., 2011	Exp.	-Breast milk odor: 40	(0-2) days	**1466±294-1606±383	Gavage feeding	3 times in a day during	-Transition from gavage	-Although not statistically, oral feeding

		-Control group: 40				feeding/every day until the baby is discharged	feeding to oral feeding	increased, the duration of discharge was shortened -Weight gain has not changed
Aoyama et al., 2010	NIRS study	-Breast milk odor: 14 -Mixed group: 12	2-9 days	*1548-3496	-	60 seconds basic period, 30 seconds warning period, 60 seconds relaxation period/totally 15 minutes including other intervention	Orbito-frontal cortical activation	Blood oxidation increased in the orbito frontal area
Nishitani et al., 2009	Exp.	-Breast milk odor: 12 -Another mother's milk odor: 15 -Formula milk odor: 9 -Distilled water control group: 12	5 days	**3163±48-3188±70	Heel stick	3 minutes before the intervention until 9 minutes after the intervention/once	-Crying duration -Grimace -Motor activity -Cortisol release	-Crying duration shortened -Babies less grimaced -Motor activity decreased -The cortisol level decreased
Bingham et al., 2007	Quasi Exp.	-Breast milk odor: 6 -Control group: 6	10-17 days	*1210-2353	Tube feeding	Ten minutes each at 3-hour intervals/each day until babies show sucking behavior	Nutrition Behavior	-Suction duration prolonged -Bursts suction unchanged
Doucet et al., 2007	Exp.	-Breast milk odor: 12 -Breast odor: 15 -Nipple odor: 15 -Areola odor: 13 -Control group: 12/15/15/13	3-4 days	*2755-5070	-	90-second intervention/once for each group	-Sleep-wakefulness, crying -Sucking, rooting, licking -Eye-opening	-Aurosal symptoms unchanged -Crying duration shortened -Rooting reflex unchanged -Licking and sucking duration prolonged -Eye opening duration prolonged
Raimbault et al., 2006	Exp.	-Breast milk odor: 7 -Control group: 6	-	**2010±278-2036±211	During breastfeeding	Once in a day 2 minutes/each day for 5 days	-Feeding behavior (sucking, nipple grasping, amount of milk consumed)	-Suction duration prolonged -Milk consumption increased -No change was observed in the nipple grip behavior

Rattaz et al., 2005	Exp.	-Breast milk odor: 11 -Vanilla odor: 11 -Unfamiliar vanilla: 11 Control group: 11	3-4 days	*2310–4300	Heel stick	Before and during the intervention/once	-Crying duration -Grimace -Head movement	-Crying duration shortened -Babies less grimaced -Head movement decreased

*Note: * Range in findings ** Min-max Mean and SD values between group.*

Table 3.
Usage of breast milk.

Research	Material	Quantity of Breast Milk	Distance to Baby's Nose
Modaresi et al., 2024	Cotton balls	2 ml	Placed near the nose
Deniz et al., 2024 Access Limited	Sterile sponge	1 ml	10 cm
Shoaei et al., 2023	Gauze	3 ml	2 cm
Asadian et al., 2023	Napkin	2 ml	3 cm
Asadian et al., 2023			
Ali HM et al., 2022	Sterile sponge	-	5 cm
Tavlar et al., 2022	Sterile odorless cloth	5 ml	3 cm
Erdogan et al., 2022 Access Limited	AL	AL	AL
Kim et al., 2022 Access Limited	AL	AL	AL
Lin et al., 2022	Cotton balls	2.5 ml	3 cm
Lan et al., 2021	Cotton balls	-	Near the newborn's nostrils
Cakirli et al., 2021 Access Limited	AL	AL	AL
Rad et al., 2021	Cotton swab	2 ml	3cm
Lee et al., 2021	Gauze	5 ml	2 cm
Shadmehri et al., 2020	Gauze	2 ml	3 cm
Taplak et al., 2020	Filter paper	1 ml	10 cm
Louyeh et al., 2020	Gauze	1.5 ml	1.5 cm
Çakırlı et al., 2020	Gauze	20 drop	15 cm
Taşçı et al., 2020	Filter paper	2 ml	10 cm
Davidson et al., 2019	Sterile cotton	3 drop	1-2 cm
Alemdar et al., 2019	Sterile sponge	5 ml	5 cm
Khodagholı et al., 2018	Cotton pad	Ns	2-3 cm
Metzger et al., 2018	Cotton pad	1.5 ml	10 cm
Alemdar, 2018	Sterile sponge	5 ml	5 cm
Beker et al., 2017	Gauze	1 drop	Very close
Alemdar et al., 2017	Sterile sponge	5 ml	5 cm
Chanville et al., 2017	Scent diffuser with air flow that releases 6 liters of fragrance per minute	5 ml	-
Akcan et al., 2016	-	5 ml of breast milk in a 20 ml tube	10 cm
Neshat et al., 2015	Cotton	Ns	1 mm
Aboli et al., 2015	Cotton	1 ml	1.5-2 cm
Jebreili et al., 2015	Cotton	Ns	1 mm
Iranmanesh et al., 2015	Cotton	1 ml	1.5-2 cm
Badiee et al., 2013	Filter paper	2 ml	Ns
Yildiz et al., 2011	Sterile pad	Ns	2 cm
Aoyama et al., 2010	Sterile gauze	A few drops	1 cm
Nishitani et al., 2009	2-4 ml breast milk in solution	2-4 ml	10 cm
Bingham et al., 2007	Olfactometer device	Ns	Ns
Doucet et al., 2007	Breast milk poured on the mother's breast	1 ml	2-3 cm
Raimbault et al., 2006	Cotton	Ns	1 cm
Rattaz et al., 2005	Gauze	20 drops	Close

Conclusion

The studies on breast milk odor were conducted in various clinical settings and involved babies with different gestational ages. The key findings regarding breast milk odor include:

- Reducing pain in babies during painful procedures.
- Positively affecting physiological parameters, including heart rate, oxygen saturation, respiration, and hemoglobin oxygenation.
- Supporting feeding behaviors, such as facilitating the transition to oral or enteral feeding, promoting weight gain, and encouraging sucking and licking.
- Lowering cortisol levels during painful procedures.
- Shortening the duration of crying in babies.
- Reducing the length of the discharge process.

A standardized breast milk odor intervention for premature infants in the NICU can be applied during painful interventions, to address nutritional deficiencies, manage unstable vital signs, and alleviate stress during medical procedures.

Ethics approval statement

We declare that this study is one of those that do not require ethics committee approval.

Patient consent statement

N/a.

Consent for publication

N/a.

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CRediT authorship contribution statement

S. Dertli: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **M. Özcan:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization.

Data availability statement

N/a.

Declaration of competing interest

The authors declare that they have no competing interests.

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