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Breast Milk Application as a Natural Method for Umbilical Cord Care: A Community-Label 3-Arm Pilot Clinical Trial

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Abstract

Objective: To compare the effects of human breast milk with those of chlorhexidine and the dry method on umbilical cord separation in Ethiopia.

Methods: This open-label 3-arm nonrandomized pilot clinical trial was conducted among 45 neonates (15 in each arm) with more than 630 home visits. After a standard cord cut, human breast milk, chlorhexidine, or nothing was applied once per day for 7 days. The primary outcome was the duration of cord separation, while the secondary outcomes were umbilical cord infection, neonatal fever, jaundice, feeding and breathing difficulty, and persistent crying.

Results: There were statistically significant differences in the time-to-cord separation between the human breast milk group and the chlorhexidine ($P < 0.001$) and dry alone ($P = 0.038$) groups. Compared to those of chlorhexidine, the rates of cord separation among human breast milk and the dry-alone group were 16.02, with 95% confidence intervals (3.81, 37.43; $P < 0.001$) and 3.15 (0.99, 10.00; $P = 0.052$), respectively. One (6.7%) cord site infection was observed in the dry-alone groups only.

Conclusion: This community-label study indicated that human breast milk application significantly shortened the length of umbilical cord separation time compared to chlorhexidine and dry methods. A large-scale randomized controlled trial is needed to confirm these results.

Registration: PACTR202310902873290; https://pactr.samrc.ac.za

Keywords: Chlorhexidine; Human breast milk; Neonatal care; Trial; Umbilical cord

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Introduction

The umbilical cord is a fragile entity consisting of a chorionic membrane and vascular components, namely, the umbilical vein and umbilical arteries. Its primary function is to facilitate the transportation of vital nutrients and oxygen from the maternal source to the developing fetus in the womb while simultaneously eliminating waste products from the offspring.[1] The structure undergoes carving at birth, and subsequent desiccation and detachment are anticipated. Nevertheless, this remnant structure serves as a conduit for neonatal infections, namely, omphalitis and sepsis, after delivery.[2] Umbilical cord separation time delay is not only associated with infection but also leads to prolonged bleeding, which leads to hypovolemia, anemia, and death in the neonate. Thus, it is imperative to provide meticulous care for the umbilical cord by facilitating physiological drying and separation using easily accessible, affordable, and feasible agents to avert neonatal mortality and morbidity.[3]

In 2019, 29 to 33 neonatal deaths per 1000 live births occurred in Ethiopia.[4] One of the major causes of mortality is infection, including umbilical cord infection (omphalitis) (34.3%).[5] Various attempts, including hand washing before and after handling the newborn, cutting the umbilical cord with a sterile instrument, baby bathing with antimicrobial agents, and antimicrobial application on the umbilical cord,[6–8] have been made to facilitate the early drying and physiological separation of the umbilical cord. Traditionally, a variety of substances, such as oils, herbs, minerals, and

dung, are being used as cord care agents.[3,9] Additionally, chlorhexidine, salt, and vaselinean were used as a cord care agent.[10] However, all these agents have their drawbacks, and some have no known scientific evidence to support their use in practice.[11] The recommendation of the World Health Organization is to keep the umbilical cord dry and apply chlorhexidine in areas where high-quality delivery and postpartum care are not possible.[12,13] However, there are many discrepancies regarding whether these methods can be considered the best for umbilical cord care. A review article published in 2019 revealed that in areas where there is a high burden of neonatal mortality, chlorhexidine utilization has a statistically significant effect on preventing neonatal infection.[14] Another review paper, on the other hand, recommended topical application of human breast milk on the umbilical cord as an effective and safe way to shorten the cord separation time.[15] Studies conducted in Iran and Turkey[2,7] also recommend the use of human breast milk for early umbilical cord care. Breast milk contains immunoglobulins, interferons, α-fetoprotein, antistaphylococcal factors, cytokines, chemokines, and antioxidants, and these factors may help to facilitate umbilical cord drying and cord separation.[16] A recent systematic review and meta-analysis summarized interventional studies on the effect of milk application on the separation time of the umbilical cord and concluded that breast milk intervention is effective.[15] However, the included studies were hospital based and had shorter follow-up times.[2,17–22]

The Ethiopian government identified umbilical cord care as one of the components of essential newborn care and endorsed chlorhexidine as an alternative method of care.[23] Conversely, delayed umbilical cord separation and associated complications including bleeding and infection are common in rural settings where clinical services are limited. Chlorhexidine application incurs additional medical costs and may restrict its use in resource-limited settings. There are also community rumors that can cause blindness if chlorhexidine is mistakenly applied to the eye or cause inflammation of the newborn's genitalia.[24] The World Health Organization has included the application of human breast milk to the cord as a harmless practice.[25] Human breast milk does not imply any cost, is readily available to the baby, and has antiseptic potential. However, the possibility of topically applying human breast milk to shorten umbilical cord separation time at the community level in developing countries is plausible.[26] To the best of our knowledge, this is the first 3-arm interventional study that aimed to assess the effect of human breast milk in comparison with chlorhexidine or dry alone on the separation of the umbilical cord through community-level follow-up over an extended 2-week period.

Methods

Study area

This study was conducted in Debre Markos town public health institutions in the East Gojjam zone, Amhara region, Northwest, Ethiopia.

Study design and period

An open-label 3-arm nonrandomized pilot clinical trial was conducted to determine the effect of topical application of human breast milk in comparison with chlorhexidine gel and dry alone methods on the separation time of the umbilical cord among newborns in Debre Markos town public health institutions from March 2020 to September 2022. Since the routine cord care methods used are not similar across the 2 institutions (in the hospital, dry care is routine; and in the health center, chlorhexidine is routinely applied), we cannot run a randomized controlled trial. Although cord care during the neonatal period differs among these setups, the provision of essential newborn care is the same in hospitals and health centers. This study included 3 groups of newborns who received umbilical cord care via milk, chlorhexidine, or dry alone at a 1:1:1 ratio. The milk group and dry-alone group participants were recruited from Debre Markos Comprehensive Specialized Hospital (DMCSH), whereas the chlorhexidine group participants were recruited from the Debre Markos Health Center (DMHC), where chlorhexidine is routinely provided. For the participants in the DMCSH, the first eligible mother-newborn pair was assigned to the milk group, the second was assigned to the dry alone group, and so on. Eligible chlorhexidine group participants in the DMHC were enrolled consecutively. Chlorhexidine was dispensed from the health center pharmacy unit, whereas breast milk was obtained from each mother to help them apply to their own baby. The first breast milk expression and application to the cord were assisted by health professionals and thereafter by mothers themselves. Breastmilk and chlorhexidine were applied once per day for 7 consecutive days.

Subjects

Mother-newborn pairs delivered at the selected health institutions in Debre Markos town were invited to participate in the study. The inclusion criteria included singleton and term pregnancies (37 to 41 weeks of gestation) and uncomplicated newborns. The exclusion criteria included complications such as prematurity (born before 37 weeks of gestation), low birth weight (less than 2500 g), congenital anomalies, born by cesarean section or instrumental delivery, maternal genital tract infection, premature rupture of membrane, chorioamnionitis, and maternal rectovaginal group B *Streptococcus* colonization. All eligible mother-newborn pairs from the respective health institutions were approached for voluntary participation. The cord clamp, cut, and length were managed for all participants following the national cord care management guidelines in Ethiopia.[27] On average, after 1 minute of birth, the umbilical cord of each baby was clamped with sterile forceps at 3 cm (2 fingers) from the umbilicus, and then another clamp was applied 3 cm away from the first clamp and cut in between. This yields an average length of 4.5 cm. Therefore, the clamping time, length of the retained cord, sterile techniques used, and even bathing soap were the standard throughout the follow-up.

Interventions

For the breast milk group, mothers were provided practical counseling on how to collect breast milk and apply it to the cord. After breastfeeding their baby, the participants/mothers expressed the remaining breast milk and applied it to the cord of their babies. They were taught to wash their hands with soap and water before and after expressing breast milk and applying it to the cord. A routine baby bath

was used to keep the body clean. An estimated 1–2 mL of breast milk was applied to the whole part of the remnant cord, which was subsequently allowed to air dry for 10 minutes. This procedure was performed once per day for 7 consecutive days until 1 week after birth. Mothers were advised not to apply anything other than breast milk.

Reference groups

Chlorhexidine or dry-alone methods were applied in other groups as a reference. For the chlorhexidine group, approximately 1 mL of chlorhexidine gel was applied to the cord within 24 hours after birth. Then, chlorhexidine was applied to the cord once per day for 7 days. After application, the cord was kept open to allow the gel to dry. Mothers were also reminded not to apply anything other than chlorhexidine. For the dry-alone group, the umbilical cord was kept air-dry without anything for the same days. The hygienic practices used were like those used in the breast milk and chlorhexidine groups. Among all groups, the assessment of the cord was conducted by trained female midwives twice daily to record any signs of infection (for example, redness, swelling, or pus/discharge) within 14 days after birth.

The umbilical cord separation time was defined as the time from birth to complete sloughing off to the umbilical cord. The follow-up started on the first day of birth and continued until the 14th postnatal day, 2 times per day at the home visit. Neonates who developed infection or whose cord was not separated until the 14th postnatal day were censored. Among all groups, the assessment of the cord was conducted twice daily to record any signs of infection until 2 days after the sloughing off to the cord within 14 days after birth.

Outcome measures

The primary outcome was umbilical cord separation time, while the secondary outcomes were umbilical cord infection/omphalitis, neonatal fever, breathing difficulty, neonatal jaundice, breastfeeding difficulty, and persistent crying. The data collectors were trained female midwives who could detect each outcome in each participant. The trained midwives evaluated babies in their respective groups at each visit. Only midwives assigned to the milk group were included, and similarly, other teams of midwives were assigned to the chlorhexidine and dry groups. Therefore, there was no cross-evaluation, and the midwives in 1 group were not aware of the other groups. The cord was observed twice per day until the day of cord separation. Furthermore, the babies were followed for 2 more days to assess signs of infection and any complications after cord separation. At every follow-up, the midwives completed the pretested checklist for signs of cord separation, signs of infection, or other danger signs.

Sample size

The sample size was determined using the effect size obtained from a study conducted in Iran.[26] We used superiority trial hypothetical assumption including effect size 6.13 days (difference of average time of cord separation in the milk and chlorhexidine group), standard deviation (*SD*) of 4.47 (the average of the 2 groups in the abovementioned study), power of 90%, α of 5%, and dropout rate of 10%.[28] The calculated minimum sample size was 30 participants (15 in 2 groups) based on a 1:1 intervention-to-reference ratio, given our hypothesis regarding the differential effects of breast milk versus chlorhexidine and dry methods for 2 comparison groups. Consequently, we have increased the sample size of the reference group 2-fold. Finally, 45 singleton and term pregnancies and healthy mother-newborn pairs (15 in each group) were included in the study; approximately 630 home visits were made (2 visits per day for each participant for 14 days).

Statistical analysis

Quantitative data are presented as mean ± *SD* for normally distributed continuous variables. Categorical data are presented as frequency and percentages. The umbilical cord separation time (in days) was the dependent variable, while the independent variables included treatment group characteristics, obstetric characteristics, and neonatal outcomes. The data were subsequently entered into Microsoft Excel and exported to Stata 17 software (StataCorp LLC, College Station, TX) for analysis. We transformed the continuous variables such as maternal age and gestational age into clinically meaningful categories, and a Cox proportional hazard regression model was fitted. The maternal age was categorized by considering pregnancy at an advanced maternal age.[29] Although gestational age was one of the inclusion criteria and only term babies were included in this study, we wanted to determine the difference between those term and postdate groups of participants and dichotomized them into term and postdate groups.[30] To compare the differences in categorical variables between the intervention groups, the Pearson chi-square test was used, for which the assumptions were fulfilled. When the chi-square test failed, the Fisher exact test was computed. One-way analysis of variance (ANOVA) was performed for normally distributed data. Since neither the chi-square test nor the Fisher exact test nor the Kruskal-Wallis test handle censored data, we also performed survival data analysis. The Kaplan-Meier survival curve was used to estimate survival, and the log-rank test was used to compare the survival time between different groups of explanatory variables. All variables that could have a reasonable effect on umbilical cord separation time were selected and entered into a multivariate Cox proportional hazards regression analysis to identify predictors of the time to separation of the umbilical cord. The adjusted hazard ratio (AHR) was used to determine the strength of the association, and a P value <0.05 was used to indicate statistical significance.

Ethical approval

This study was conducted in accordance with the *Declaration of Helsinki*. Ethical clearance was obtained from the Debre Markos University College of Health Sciences Ethical Review Committee (Ref. no. HSC/R/C/Ser/Co/139/11/11) on January 14, 2020. Written informed consent was obtained from the mothers of each neonate included in the trial. To maintain the confidentiality of the participants' information, data were collected using codes instead of names, and the data were kept confidential and not accessible to anyone else. Furthermore, the data were used for this research purpose only, and no individual data were used for dissemination of findings.

Results

In this study, 45 mother-newborn pairs were included. Among the 45 mothers, more than 53% were primiparous. The minimum and maximum gestational ages were 37 and 42 weeks, respectively, while the median gestational age was 39 weeks. All births were spontaneous vaginal deliveries, and none of the mothers had developed chorioamnionitis or prolonged rupture of the membrane during labor. Approximately half (48.9%) of the newborns were male. The birth weight of the neonates ranged from 2500 to 4000 g. The majority (64.4%) of the newborns weighed between 2500.0 g and 3000.0 g, and the mean weight was 3057.8 g. The Apgar score of all included newborns ranged from 5 to 9 in the first minute. No statistically significant differences were detected among the study groups in terms of their Apgar scores or the abovementioned characteristics (Tables 1 and 2). All the babies were cord-clamped and cut via sterile techniques. All patients were exclusively breastfed throughout the follow-up. None of the babies had a fever, jaundice, breastfeeding or breathing difficulty, persistent crying, or other danger signs. One neonate (6.7%) from the dry group developed cord infection on the sixth day of follow-up and was transferred to DMCSH for evaluation and management; this patient was censored because of the survival data analysis in the Cox regression model. She had only some discharge from the side of the cord. After evaluation, she returned to her home with no medication, was scheduled for follow-up every other day, and was confirmed to be healthy throughout the neonatal period. The milk and chlorhexidine groups did not show signs of infection. In the chlorhexidine group, the umbilical cords of 2 neonates did not fall off until the 14th follow-up day, and these patients were censored.

Since one-way ANOVA was not used, we performed a Kruskal-Wallis test to assess umbilical cord separation time among the breast milk, chlorhexidine, and dry-alone groups and found that there was a statistically significant difference among the groups. A Bonferroni post hoc correction was performed and revealed a statistically significant difference between the breast milk and chlorhexidine groups and between the breast milk and dry-alone groups. The breast milk group participants had a shorter cord separation time than the chlorhexidine and dry-alone groups ($P < 0.001$ and $P = 0.038$, respectively). However, there was no significant difference between the chlorhexidine and dry group ($P = 0.542$) (Supplementary Fig. 1, http://links.lww.com/MFM/A54). Taking the censored data into consideration, we fitted the data with a survival function model. The overall median time to cord separation was 7 days, with an IQR of 5–10 days. The median times to umbilical cord separation among the human milk, chlorhexidine, and dry alone groups were 5 (4–6 days), 10 (6–13 days), and 7 (6–8 days), respectively (Fig. 1).

To determine predictors of the time to separation of the umbilical cord, we performed a multivariable Cox proportional hazard regression analysis and found that breast milk application was significantly more strongly associated with

Table 1

Comparison of study participants' (mothers') characteristics in each group.

Variable	Milk group ($n = 15$)	Chlorhexidine group ($n = 15$)	Dry group ($n = 15$)	Statistical value	*P*
Maternal age (years), mean ± *SD*	24.4 ± 3.41	26.7 ± 6.62	26.9 ± 5.45	1.63	0.208*
Marital status, *n* (%)				NA	>0.999†
Married	14 (93.33)	14 (93.33)	13 (86.67)		
Others‡	1 (6.67)	1 (6.67)	2 (13.33)		
Maternal education, *n* (%)				NA	0.275†
No formal education	3 (20.00)	5 (33.33)	1 (6.67)		
Primary education	1 (6.67)	4 (26.67)	4 (26.67)		
Secondary education	4 (26.67)	4 (26.67)	5 (33.33)		
Tertiary education	7 (46.67)	2 (13.33)	5 (33.33)		
Paternal education, *n* (%)				NA	0.024†
No formal education	2 (13.33)	1 (6.67)	2 (13.33)		
Primary education	0	8 (53.33)	5 (33.33)		
Secondary education	5 (33.33)	1 (6.67)	4 (26.67)		
Tertiary education	8 (53.33)	5 (33.33)	4 (26.67)		
Mothers' occupation, *n* (%)				NA	0.142†
Government employee	6 (40.00)	1 (6.67)	2 (13.33)		
Private employee	0	3 (20.00)	2 (13.33)		
Housewife	6 (40.00)	7 (46.67)	4 (26.67)		
Merchant	3 (20.00)	4 (26.67)	7 (46.67)		
Parity, *n* (%)				2.14	0.343§
Primiparous	10 (66.67)	6 (40.00)	8 (53.33)		
Multiparous	5 (33.33)	9 (60.00)	7 (46.67)		
GA at birth (weeks), mean ± *SD*	39.9 ± 1.68	39.1 ± 1.62	39.8 ± 1.57	0.67	0.676*

*One-way analysis of variance.

†Fisher exact test.

‡Others: single, widowed, and divorced.

§Pearson chi-square test.

GA: Gestational age; NA: Not applicable; *SD*: Standard deviation.

Table 2

Comparison of characteristics of participants (neonates) in each study group.

Variable	Milk group (n = 15), n (%)	Chlorhexidine group (n = 15), n (%)	Dry group (n = 15), n (%)	Statistical value	P
Newborn gender					
Female	8 (53.33)	8 (53.33)	7 (46.67)	0.18	0.915*
Male	7 (46.67)	7 (46.67)	8 (53.33)		
First minute Apgar score				NA	>0.999†
>7	11 (73.33)	12 (80.00)	12 (80.00)		
≤7	4 (26.67)	3 (20.00)	3 (20.00)		
Fifth minute Apgar score				NA	>0.999†
>7	15 (100.0)	14 (93.3)	15 (100.0)		
≤7	0	1 (6.67)	0		
Birth weight, g				NA	0.791†
2500–3000	10 (66.67)	10 (66.67)	9 (60.00)		
3001–3500	2 (13.33)	4 (26.67)	3 (20.00)		
3501–4000	3 (20.00)	1 (6.67)	3 (20.00)		
Umbilical cord infection	0	0	1 (6.67)	NA	>0.999†

*Pearson chi-square test.

†Fisher exact test.

NA: Not applicable.

a shorter umbilical cord separation (AHR 16.02 with 95% confidence interval: 3.81, 37.43; $P < 0.001$) than was chlorhexidine application (Fig. 2). All the other explanatory variables fitted in the multivariable Cox proportional hazard analysis model were not significantly different.

Discussion

The median duration of cord separation in the breast milk group was 5 days shorter than that in the chlorhexidine group and 2 days shorter than that in the dry-alone group. Moreover, there was no statistically significant difference between the chlorhexidine group and the dry-alone group. These findings revealed that the ability of human breast milk to shorten the umbilical cord separation time is much better than that of both chlorhexidine and dry bone alone (Fig. 3).

These results are supported by the findings of several studies, which showed that human breast milk has a shorter umbilical cord separation time than dry food alone or povidone-iodine.[7,18,21,26,31,32] Even though the quality of the included studies was poor, a systematic review also revealed that human breast milk application is the most safe and effective approach for umbilical cord separation.[15] Nonetheless, the exact mechanism of umbilical cord separation is unknown, and factors such as bacterial colonization,

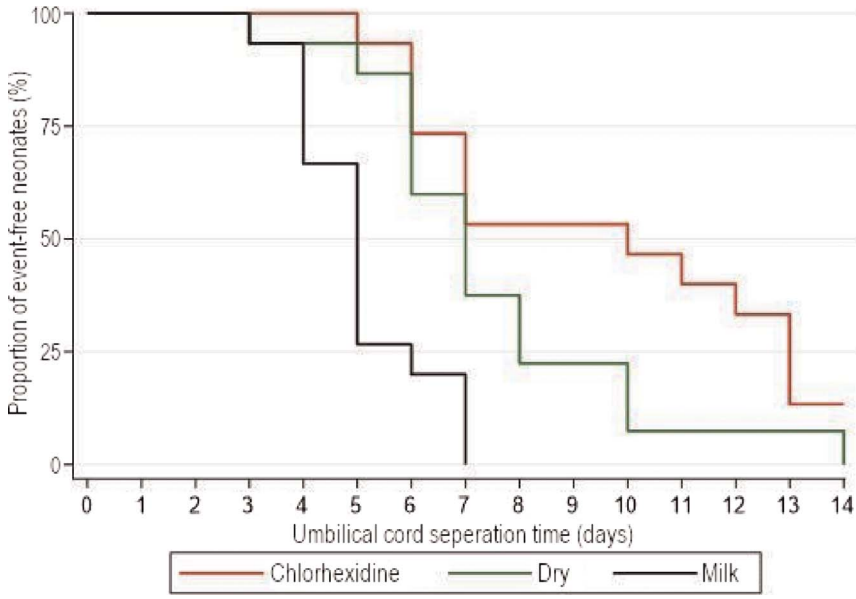

Figure 1. Kaplan-Meier survival estimate of time to separation of umbilical cord among the 3 intervention groups. For 1 participant in the chlorhexidine group, the cord was not separated until the 14th day of follow-up.

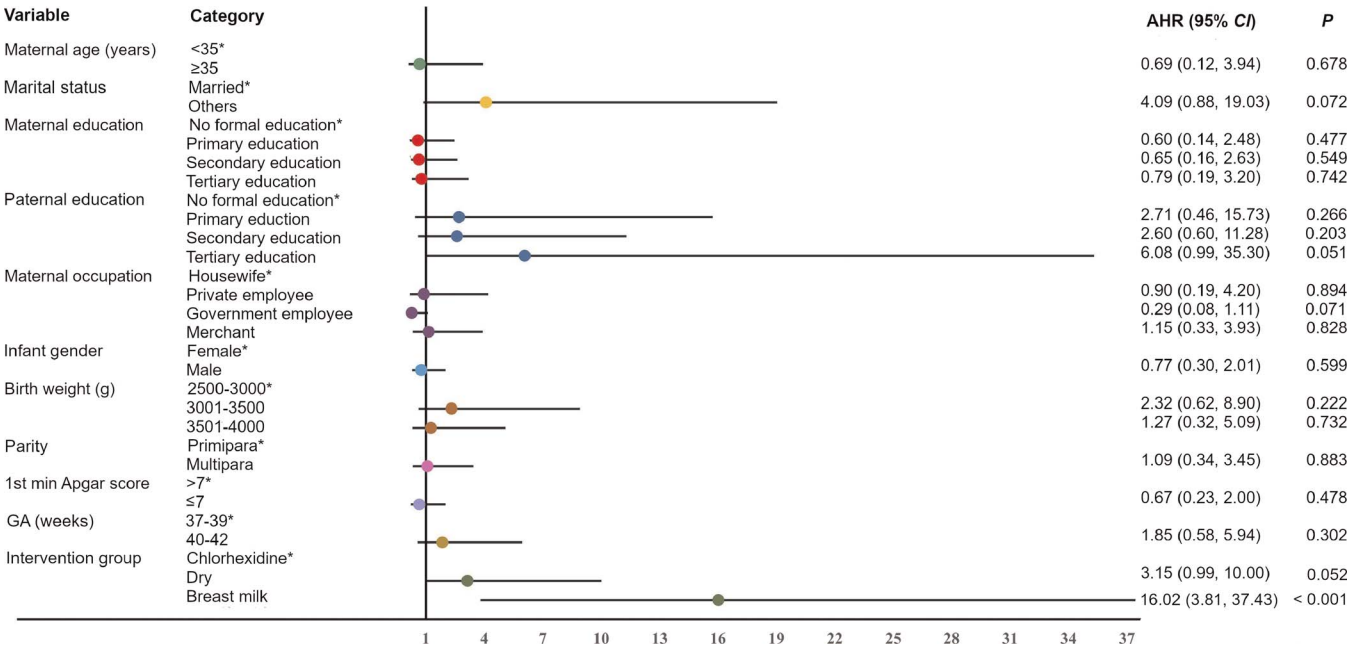

Figure 2. Forest plot for a multivariable Cox proportional hazard regression analysis (* reference category). AHR: Adjusted hazard ratio; GA: Gestational age.

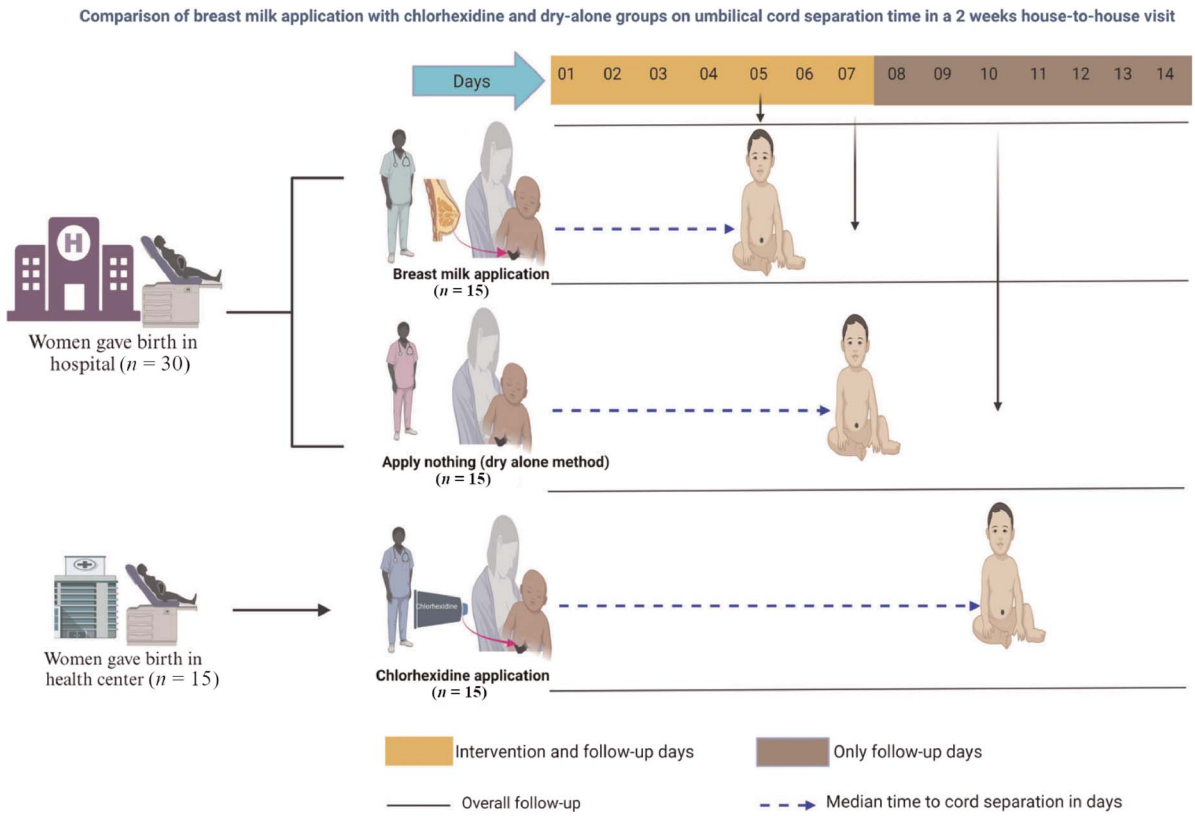

Figure 3. Effect of breast milk on time to separation of umbilical cord compared to chlorhexidine and dry methods. Figure created using BioRender.com, license agreement number: PS270TU9RW.

drying, necrosis, infarction, and granulocyte influx may be involved independently or synergistically.[33] Human breast milk contains abundant levels of tumor necrosis factor-alpha (TNF-α), which is an inflammatory cytokine that is amenable to a diverse range of signaling events within cells, leading to necrosis or apoptosis.[34,35] Since colonization occurs during cord separation, the application of chlorhexidine suppresses bacteria that facilitate cord drying and separation because chlorhexidine contains massive amounts of alcohol, while human breast milk contains many bacteria that promote cord drying separation.[13,36]

Additionally, the difference in their effect on cord separation between breast milk and chlorhexidine may be attributed to their composition. Human breast milk contains immunologic bioactive components such as α-lactalbumin, lactoferrin, lysozyme, and secretory immunoglobulin A (sIgA), which have anti-infectious effects.[37] Lactoferrins are effective at constraining the influence of bacterial adherence and biofilm formation in neonates and preventing group B *Streptococcus*–associated disease.[38] Additionally, breast milk contains cytokines, polyunsaturated fatty acids, immune-stimulating proteins, glycoproteins, glycated components such as mucins, human milk oligosaccharides (HMOs), and extracellular vesicles, which provide a comprehensive continuum of antiviral properties.[39,40] However, chlorhexidine is composed of 0.12% chlorhexidine gluconate, 11.6% alcohol, glycerin, PEG-40 sorbitan diisostearate, flavor, sodium saccharin, and FD&C Blue.[36] Therefore, alcohol decreases beneficial bacterial colonization, which facilitates physiological shrinkage of the remnant cord. In general, breast milk is an easily accessible, affordable/cost-effective, natural, easy to apply, harmless, and effective body fluid for shortening the umbilical separation time compared with chlorhexidine, which is a pharmaceutical product that incurs cost, with conceivable side effects.[31]

This study was conducted on community labels with frequent visits to ensure proper application of the provided intervention. Similar hygienic material was also used to control intergroup hygiene variation. Since this was a pilot trial, it may lead researchers to perform other large-scale community-label randomized controlled trials. Although it was a pilot study, the limitation of this study was the small sample size. Additionally, this study is open-label and may not be as strong as double-blind trials for inferring the results. Despite these limitations, our findings were comparable to those of previously published articles.

Conclusion

Instead of using chlorhexidine gel or the dry-alone method for umbilical cord care, the use of human breast milk shortens the length of cord separation. The use of chlorhexidine or the dry method did not significantly reduce the median time of umbilical cord separation. These findings can be useful for other large-scale studies with larger sample sizes to address the clinical benefits of human breast milk including omphalitis and skin rush due to diaper use.

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Author Contributions

B.K.A. conceived the study. B.K.A., L.Y.W., and Y.B. designed the study, provided training for the data collectors, and monitored the study. B.K.A., L.Y.W., and K.G.T. analyzed the data. B.K.A. drafted the manuscript. T.M.L., A.A.M., G.N.M., A.S., M.L.E., G.G.A., W.F.L., and G.G.W. revised the drafted manuscript. C.C.W. and Y.W. supervised the analysis and manuscript writing and revised the manuscript. All the authors approved the final version of the manuscript and decided to submit it for publication.

Conflicts of Interest

None.

Data Availability

The supporting data are available among authors' data stores and can be accessed based on formal request.

Editor Note

Chi Chiu Wang is one of the Editorial Board Members of *Maternal-Fetal Medicine*. The article was subject to the journal's standard procedures, with peer-review handled independently of this editor and the associated group.

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