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UMBILICAL CORD MILKING IN NEWBORNS: SCOPING REVIEW

ORDEÑA DEL CORDÓN UMBILICAL EN RECIÉN NACIDOS: REVISIÓN DE ALCANCE

ORDENHA DE CORDÃO UMBILICAL EM RECÉM-NASCIDOS: REVISÃO DE ESCOPO

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ABSTRACT

Objective: To map the available evidence on umbilical cord milking in newborns. Material and Method: Scoping Review based on the protocol proposed by the Joanna Briggs Institute. A search for full-text articles published in MEDLINE, SCOPUS, WOS and CINAHL was carried out using the following keywords: infant, newborn, umbilical cord milking, placental transfusion and umbilical cord blood. Results: The results indicated umbilical cord milking has superior benefits to the immediate cord clamping, among the main ones are higher levels of Hemoglobin, Hematocrit and Serum Ferritin, and reduction of complications in preterm newborns, such as intraventricular hemorrhage and the need for blood transfusion. When compared to delayed cord clamping, it has similar benefits, but milking is considered a faster method of placental blood transfusion. Conclusions: Umbilical cord milking has similar potential to delayed cord clamping. Therefore, it can be an alternative for obstetric nurses and midwives when delayed cord clamping cannot be performed in order to ensure the benefits of placental transfusion to the neonate.

Key words: Umbilical Cord; Umbilical cord milking; Newborns; Neonatology.

RESUMEN

Objetivo: Mapear la evidencia disponible sobre la ordeña del cordón umbilical en recién nacidos. Material y Método: Revisión de Alcance con base en el protocolo propuesto por el Instituto Joanna Briggs. Se realizó una búsqueda de artículos de texto completo publicados en MEDLINE, SCOPUS, WOS y CINAHL utilizando

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las siguientes palabras clave: lactante, recién nacidos, ordeña cordón umbilical, transfusión placentaria y sangre de cordón umbilical. Resultados: La ordeña del cordón umbilical tiene beneficios superiores al pinzamiento inmediato del cordón, entre los principales se encuentran: mayores niveles de hemoglobina, hematocrito y ferritina sérica y reducción de complicaciones en recién nacidos prematuros, tales como hemorragia intraventricular y necesidad de transfusión sanguínea. En comparación con el pinzamiento tardío del cordón, tiene beneficios similares, pero la ordeña se considera el método más rápido de transfusión de sangre placentaria. Conclusiones: La ordeña del cordón umbilical tiene potencial similar al pinzamiento tardío del cordón, por lo tanto, puede ser una alternativa para enfermeras obstétricas y parteras cuando no se puede realizar el pinzamiento tardío del cordón para asegurar los beneficios de la transfusión placentaria al neonato.

Palabras clave: Cordón umbilical; Ordeña del cordón umbilical; Recién nacido; Neonatología.

RESUMO

Objetivo: Mapear as evidências disponíveis sobre a ordenha de cordão umbilical em recém-nascidos. Material e Método: Revisão de escopo baseada no protocolo proposto pelo Joanna Briggs Institute. A busca de artigos completos publicados na MEDLINE, SCOPUS, WOS e CINAHL foi realizada utilizando as seguintes palavras-chave: lactente, recém-nascido, ordenha do cordão umbilical, transfusão de placenta e sangue do cordão umbilical. Resultados: Os resultados indicaram que a ordenha do cordão umbilical tem benefícios superiores ao clampeamento imediato do cordão, entre os principais estão: níveis mais elevados de hemoglobina, hematócrito e ferritina sérica e redução de complicações em recém-nascidos pré-termo, como hemorragia intraventricular e necessidade de transfusão sanguínea. Quando comparado ao clampeamento tardio do cordão umbilical, tem benefícios semelhantes, mas a ordenha é considerada um método mais rápido de transfusão de sangue da placenta. Conclusões: A ordenha do cordão umbilical tem potencial semelhante ao clampeamento tardio do cordão umbilical, portanto, pode ser uma alternativa às enfermeiras obstetras e parteiras quando o clampeamento tardio do cordão não pode ser executado a fim de garantir os benefícios da transfusão placentária ao neonato.

Palavras-chave: Cordão umbilical; Ordenha de cordão umbilical; Recém-nascido; Neonatologia.

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INTRODUCTION

Placental transfusion is defined as the transfer of residual blood from the placenta to the newborn (NB) in the first minutes of life, a physiological mechanism that plays a short- and long-term essential role in the child's health[1].

Among the recommendations based on scientific evidence for birth assistance that favor placental transfusion, the delayed cord clamping (DCC) stands out[2]. DCC is defined as application of a clamp to the cord ≥30 seconds after birth or based on physiologic parameters (such as when cord pulsation has ceased or breathing has been initiated), without cord milking. The time of DCC can range between 30 and 180 seconds, with a delay of 30 to 60 seconds[3].

DCC offers several benefits to the newborn when compared to the immediate cord clamping (ICC), defined as application of a clamp to the cord <30 seconds after birth, without cord milking[3], including: greater serum ferritin levels[4], increased hemoglobin after birth[3], additional transfer of 15-30 ml/kg blood volume[4], transfer of immunoglobulins and essential stem cells to the tissues and repair of the neonate's organs[2, 5]. Furthermore, in premature NBs, DCC is associated with significant benefits, such as less need for blood transfusion, reduced incidence of necrotizing enterocolitis and intraventricular hemorrhage[2].

Another form of placental transfusion that has been studied and discussed today is umbilical cord milking (UCM). There are two types of UCM, namely: intact-UCM (I-UCM) (also referred to as "stripping" or just UCM), defined as repeated compression of the cord from the placental side toward the infant with the connection to the placenta intact at any time point within the first few minutes after birth; and cut-UCM (C-UCM) (also referred to as "stripping"), defined as drainage of the cord by compression from the cut end toward the infant after clamping and cutting a long segment(3).

The I-UCM, consists of holding the umbilical cord gently and sliding the index finger and thumb on the umbilical cord, at 20 cm from the base of the newborn's navel, with the objective to carry the residual placenta blood present in the cord towards the newborn. Generally, milking is repeated three to four times, but one must wait on average 2 seconds between milking, so the umbilical cord is refilled with blood before being milked again(2).

Another way to do this procedure is the C-UCM, which consists of cutting and clamping 25 cm from the umbilicus immediately after birth; the baby is delivered to the pediatric team and positioned on the radiant warmer, then, the cord is lifted and milked from the end of the cut to the navel, promoting the emptying of all its content towards the newborn(6). UCM allows a faster placental transfusion(7).

It should be noted that often the newborn needs placental transfusion, since it facilitates the neonatal transition/adaptation and the recovery of their health, so UCM can be a viable alternative when there is an impediment to perform the DCC. That is why it is important to have a produced knowledge map about this subject, with the benefits and potential risks well elucidated to guide the practice of nurses and midwives based on current evidence. Thus, these professionals will have accurate information about this technique in order to ensure the best obstetric practices. In this perspective, this study aimed to map the available evidence on UCM in newborns.

MATERIAL AND METHODS

This is a scope review based on the protocol proposed by the Joanna Briggs Institute(8), developed from the following steps: elaboration of the research question; identification of relevant studies, selection of studies; data mapping; separation, summarization and reporting of results; and communicating results. The report of this review followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines(8).

To guide the research, the question 'What is the knowledge produced on the umbilical cord milking by international literature?' was formulated, based on the patient, concept, and context (PCC)(8), defining: P - newborn/infant; C - umbilical cord milking; C - birth.

The articles were searched by people with previous experience in this type of research in the nursing area in the following databases: Medical Literature Analysis and Retrieval System Online (MEDLINE), SciVerse Scopus (SCOPUS), Cumulative Index to nursing and allied health litera-ture databases (CINAHL) and Web of Science (WOS). The search was carried out using the controlled descriptors [Descriptores en Ciencias de la Salud (DeCS), Medical Subject Headings (MeSH) and CINAHL Heading], and uncontrolled (keywords), namely: infant, newborn, umbilical cord milking, placental transfusion and umbilical cord blood. The crossings were performed with the Boolean operators AND and OR.

The first study search process was carried out in October and November of 2019. In February 2022, an update of the search was carried out with studies published between November 2019 and February 2022. The research was carried out by two independent researchers, in order to identify the differences in the findings and include as many studies as possible. Subsequently, the identified articles were compared and, in case of disagreement, sent to a third researcher for a consensus.

The selection of studies was based on the following inclusion criteria: original articles, in English, Spanish or Portuguese, no publishing time limits. We chose not to limit the time to know more comprehensively everything that has already been produced on the theme. Review articles, repeated articles, which were not found in full and did not answer the guiding question, were excluded. The search engine and the number of articles collected in the different databases are shown in Table 1.

The reference list of included articles was also consulted to identify additional publications that had not been mapped. The full text was read to assess its eligibility and, then, 18 articles were included. The search flowchart is shown in Figure 1, based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart(8).

Table 1. Search engine and number of articles identified in the different databases, period 1949-2022.

Database	Crossing-descriptors	Found articles	Selected articles
MEDLINE	"umbilical cord milking" OR "placental transfusion"	541	19
Scopus	" infant, newborn" AND "umbilical cord blood" OR "umbilical cord milking" OR "placental transfusion"	2.250	26
CINAHL	"infant, newborn" AND "umbilical cord milking" OR "placental transfusion" OR "umbilical cord blood"	5.215	0
Web of Science	"infant, newborn" AND "umbilical cord milking" OR "placental transfusion"	607	10
TOTAL		8.613	55

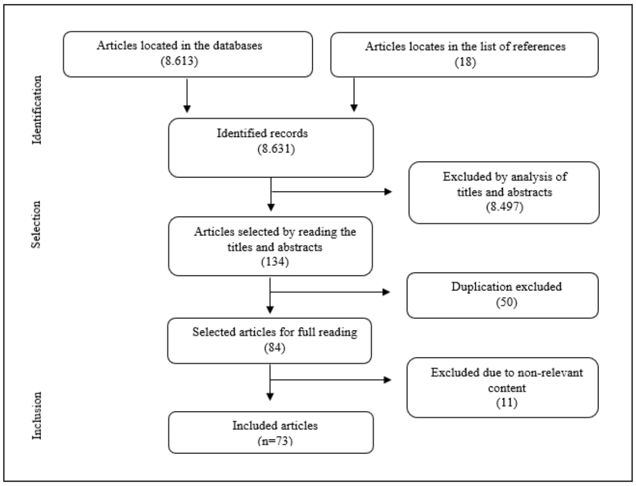

Figure 1. Search flowchart in the databases.

After the selection, the publications were mapped and an analytical table was created containing the characterization data of those included in this review. This data charting form was based on the Joanna Briggs Institute manual for scoping reviews[8].

The data's were extracted and mapped descriptively[8]. Some results were presented in the word cloud format. The word cloud groups and organizes the words graphically depending on their frequency. It is a simpler lexical analysis, however, graphically quite interesting, as it enables the rapid identification of keywords of a corpus[9]. In this sense, the word cloud was used to synthesize the main information found in the studies, interpreting them to describe the available evidence that answered the study question.

As this is a scoping review, according to the adopted methodology, the methodological quality assessment of the included studies is waived. To ensure ethical aspects, the reliability and the fidelity of the information found in the selected publications were guaranteed through appropriate referencing and rigor in the presentation of the findings.

RESULTS

It included 73 articles, 55 of which were identified in the databases and 18 from their references, published in English between the years 1949 and 2022. Most publications are randomized controlled trials (RCT) (49; 67.12%), conducted in the United States of America (USA) (26; 35.61%) and in India (13; 17.80%). As for the authors' degree, most medical authors were pediatricians and neonatologists (47; 64.38%), few were obstetricians and gynecologists (24; 32.87%) and only two nurses (Table 2). Most of the studies found performed a comparison between UCM and ICC, focusing on preterm newborns (PTNB).

Table 2. Articles found in the Research.

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
1	McCausland et al. 1949[10] USA	To compare the erythrocyte count and the weight of the full-term newborn in three groups: immediate cutting, late clamping 5min, cord milking.	RCT	127 Term infants	ICC: 41 DCC: 36 UCM: 50	DCC and UCM groups received a significant amount of blood, higher erythrocyte counts, Hb values, initial weights, less weight loss, and less rapid loss of weight
2	Siddall et al. 1952[11] USA	To Investigate the blood of infants born by cesarean section to determine: (1) hemoglobin and red blood cell levels with immediate common umbilical cord tightening and cutting and (2) the effect of rapid extraction or milking of the cord towards the baby before cutting.	RCT	100 Term infants	ICC: 48 UCM: 46	In UCM group the average of Hb and red blood cell count was higher. Moreover, in ICC group a few of the babies had a relative anemia
3	Hosono et al. 2008[12] Japan	To investigate the effects of UCM on the need for red blood cell transfusion and morbidity in very preterm infants.	RCT	40 Preterm infants (born between 24 and 28 weeks of gestation)	ICC:20 UCM:20	UCM group: was more likely not to have needed red cell transfusion and had a decreased number of red blood cell transfusions; Initial mean Hb and blood pressure at admission was higher
4	Hosono et al. 2009[13] Japan	To investigate the effects of UCM on cardiopulmonary adaptation in very low birth weight infants.	Secondary analysis of a RCT	40 Preterm Infants (born between 24 and 28 weeks of gestation)	ICC:20 UCM:20	In UCM group: initial Hb was higher; in first 12h: blood pressure was higher; In 72h: Urine output was higher. There were no significant differences in heart rate, water intake, or ventilatory index values between the groups
5	Rabe et al. 2011[14] United Kingdom	To compare two strategies to enhance placento-fetal blood transfusion in preterm neonates before 33 weeks of gestation.	RCT	58 Preterm infants (born between 24 and 32 completed weeks of gestation)	UCM:27 DCC: 31	DCC group: mean birth weight was 1,263±428g and Mean Hb 17.3 g/L; In UCM group mean birth weight was 1,235±468g and Mean Hb 17.5 g/L.
6	Erickson-Owens et al. 2012[15] USA	To compare hematocrit (Hct) levels at 36 to 48 h of age in term infants delivered by cesarean section exposed to ICC or UCM.	RCT	24 Term infants (>37 weeks of gestation)	ICC:12 UCM:12	UCM group has a smaller placental residual blood volume and higher Hct levels at 36 to 48h. Five infants (42%) in ICC group had a Hct indicative of anemia.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
7	Takami et al. 2012[16] Japan	To investigate the effects of UCM at birth on cerebral perfusion and systemic perfusion in very low birth weight infants	Retrospective cohort	50 Preterm infants (<29 weeks of gestation and birth weight of <1250 g)	ICC: 24 UCM: 26	Hct, left ventricular end-diastolic dimension, left ventricular cardiac output, and superior vena cava flow were higher in UCM group than in ICC group
8	Upadhyay et al. 2013[17] India	To investigate the effect of UCM as compared with early cord clamping on hematological parameters at 6 weeks of age among term and near term neonates.	RCT	200 Term and near-term infants (≥35 weeks of gestation)	ICC:100 C-UCM:100	In C-UCM group: Mean Hb and mean serum ferritin were significantly higher at 6 weeks of age; Mean Hb and Hct at 12 and 48 h was significantly higher; Mean blood pressure at 30 min, 12 and 48 h after birth was significantly higher but within normal range.
9	March et al. 2013[18] USA	To determine whether UCM compared with ICC in extremely preterm deliveries reduces the need for neonatal red blood cell transfusion.	RCT	113 Preterm infants (born between 24 to 28 completed weeks of gestation)	ICC: 57 OCU: 56	UCM group were less likely to require transfusion, higher hematocrits at birth and were less likely to develop an intraventricular hemorrhage.
10	Katheria et al. 2014[19] USA	To describe the effect of UCM on resuscitation interventions and changes in heart rate and SpO_2 immediately after delivery.	RCT	41 Infants born before 32 weeks of gestation	ICC:20 UCM:21	Infants receiving UCM had higher heart rates and higher SpO_2 over the first 5 min of life, were exposed to less FiO_2 over the first 10 min of life than infants with ICC.
11	Patel et al. 2014[20] USA	We hypothesized that UCM would avoid resuscitation delay but improve hemodynamic stability and reduce rates for composite outcome of severe intraventricular hemorrhage, necrotizing enterocolitis, and/or death before discharge.	Retrospective cohort	318 Preterm infants (< 30 weeks of gestation)	UCM:158 ICC:160	UCM group: higher mean blood pressures through 24 h; initial Hct higher and red cell transfusions fewer; presence of the composite outcome less; reductions in severe intraventricular hemorrhage, necrotizing enterocolitis, and death prior to hospital discharge.
12	Alan et al. 2014[21] Turkey	To evaluate the effects of UCM on the need for packed red blood cell transfusion and hematologic and hemodynamic parameters in very-low–birth-weight infants.	RCT	44 Preterm Infants (≤32 weeks of gestation and estimated birth weigth 1500g)	UCM: 24 ICC:24	The number and volume of the need for packed red blood cell transfusions were similar in both groups. Levels of Hb at the first and 24th hour of life were significantly higher in UCM.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
13	Katheria et al. 2014[22] USA	To determine whether UCM improves systemic blood flow and reduces neonatal morbidities compared with ICC.	RCT	60 Preterm infants (<32 weeks of gestation)	UCM: 30 ICC:30	UCM group had greater measures of superior vena cava flow and right ventricular output in the first 6 and 30 h of life, greater serum Hb, fewer blood transfusions and days on oxygen therapy, and less frequent use of oxygen at 36 weeks.
14	Christensen et al. 2014[23] USA	To determine the effect of cord blood milking at preterm delivery on blood viscosity.	Prospective cohort	1st study: 32 Infants (23-40 weeks of gestation) 1nd study: 20 Infants (<32 weeks of gestation)	-	Cord milking at preterm delivery is associated with a low risk of clinical hyperviscosity. Practioners should not refrain from cord milking at preterm delivery because of a concern that it will commonly cause neonatal hyperviscosity.
15	Katheria et al. 2015[24] USA	To determine whether infants < 32 weeks born by cesarean delivery who undergo UCM have higher measures of systemic blood flow than infants who undergo DCC.	RCT	197 Preterm infants (<32 weeks of gestation)	Vaginal delivery: UCM:23 DCC: 20 Cesarean delivery: UCM: 75 DCC: 79	Infants delivered by cesarean randomly to UCM group had higher superior vena cava flow and right ventricular output in the first 12 h of life. UCM group had higher Hb, delivery room temperature, blood pressure over the first 15 h, and urine output in the first 24 h of life. There were no differences for the 43 infants delivered by vaginal delivery.
16	Yadav et al. 2015[25] India	To compare the effect of combined DCC and UCM to either of them had done alone, on hematological parameters at 6 weeks of age in term neonates.	RCT	300 Term infants (>37 weeks of gestation)	C-UCM: 100 DCC: 100 DCC with milking the cut cord: 100	Hemodynamic parameters were comparable in all groups. The median serum ferritin level at 6 weeks was significantly higher in group receiving DCC with milking the cut cord group as compared with the group that received only C-UCM or only DCC.
17	Jaiswal et al. 2015[26] India	To compare the effect of UCM and DCC on hematological parameters (serum ferritin and hemoglobin) at 6 weeks of life in term neonates.	RCT	200 Infants born at >36 weeks of gestation	C-UCM: 100 DCC: 100	Mean serum ferritin and Hb in C-UCM group was comparable to DCC group at 6 weeks of age. There was no difference in hemodynamic status, cranial Doppler indices, and adverse neonatal outcomes among the groups.
18	Jaiswal et al. 2015[27] India	To compare the effect of UCM and DCC on cerebral blood flow in term neonates.	RCT	200 Infants born at >36 weeks of gestation	C-UCM: 100 DCC: 100	Mean Pulsatility Index and Resistive Index in UCM group was comparable in DCC group. Indices among growth retarded babies were not different.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
19	Bora et al. 2015[28] India	To assess the effect of early clamping and milking of a 40-cm umbilical cord LUCM (long umbilical cord and milking) on hemoglobin (Hb) and serum ferritin concentrations at 6 months of age and to evaluate whether the effect is different in infants of anemic and non-anemic mothers.	RCT	200 Term infants of anemic (maternal Hb < 11.0g dl^{-1}) and non-anemic mothers (Hb≥ 11.0g dl^{-1})	Anemic C-UCM:50 ICC:50 Non anemic C-UCM: 50 ICC: 50	Compared with infants of non-anemic mothers, cord Hb was similar, but cord ferritin lower in infants of anemic mothers. Effectiveness of C-UCM did not vary with the maternal anemia status.
20	Hosono et al. 2015[29] Japan	To compare two strategies to potentiate the effects of placental transfusion in infants born at <29 weeks of gestation.	Retrospective cohort	40 Preterm infants (born at <29 weeks of gestation)	C-UCM one time: 20 UCM multiple times: 20	There was no significant difference in the probability of not needing a transfusion during the hospital stay and the mean number of red blood cell transfusions given within the first 21 days of life.
21	Kumar et al. 2015[30] India	To Investigate the effect of UCM on hematological parameters at 6 weeks of age in late preterm infants.	RCT	200 Moderate to late preterm infants (32 0/7 to 36 6/7 weeks of gestation)	C-UCM: 100 ICC: 100	Mean serum ferritin and Hb at 6 weeks was higher in C-UCM group. Higher incidence of jaundice with higher phototherapy rates were noted in C-UCM group.
22	Kilicdag et al. 2016[31] Turkey	To investigate the impact of UCM on the absolute neutrophil counts and neutropenia frequency of preterm infants.	RCT	54 Infants preterms (≤32 weeks of gestation)	UCM: 29 ICC: 25	Absolute neutrophil counts were statistically significantly lower in UCM group on days 1, 3 and 7. The frequency of neutropenia was higher in the UCM group.
23	Rabe, et al. 2016[32] United Kingdom	To study the use of milking of the cord 4 times as an alternative to enhance the redistribution of placental blood into the baby.	RCT	58 Preterm infants (born between 24 0/7 and 32 6/7 completed weeks of gestation)	UCM: 27 DCC: 31	Neurodevelopmental outcomes at 2 and 3.5 years did not significantly differ between the two groups for the three Bayley III composite scores. At 3.5 years there was a trend towards higher scores for girls in the language composite scores and on the motor scale.
24	Agarwal et al. 2016[33] India	To compare the effects of DCC and UCM on haematological and growth parameters at 12 months of age.	RCT	161 Full-term infants (37–41 weeks of gestation)	C-UCM: 83 DCC: 78	There was no significant diferencces between the groups in: mean Hb and serum ferritin at one year, weight, height and mid-upper arm circumference in the groups.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
25	Vatansever et al. 2017[34] Turkey	To compare the antioxidant status of three cord fixation procedures (early fixation, fixation and milking) by analyzing the thiol disulfide balance.	RCT	189 Term infants (37–41 6/7 weeks of gestation)	UCM: 57 DCC: 55 ICC: 77	Native and total thiol levels were significantly lower in the ICC group. The disulfide/total thiol ratio was significantly lower in the DCC and UCM groups.
26	Song et al. 2017[35] Korea	To investigate the safety of UCM in the mother and newborn among very premature deliveries of less than 33 weeks of gestation.	Phase II RCT	66 Preterm infants (born between 24 0/7 and 32 6/7 completed weeks of gestation)	UCM: 34 ICC: 32	Maternal pre- and post-partum Hb levels were 1.35 g/dL in UCM and 1.58 g/dL in ICC group. In UCM group: Hb levels at birth and at 24 h were higher and the mortality rate was significantly lower. In ICC group: required more blood transfusion and inotropic drugs.
27	Piyadigama et al. 2017[36] Sri Lanka	To evaluate whether the effects on Hb, bilirubin and haemodynamic parameters in infants, and blood loss in the mother are better with UCM than with DCC during elective caesarean delivery at term.	RCT	60 Term Infants	UCM: 33 ICC: 27	There were no significant differences between the UCM and DCC groups with regard to mean neonatal Hb, mean neonatal total bilirubin and mean maternal decrease in Hb. All the neonates had birth APGAR of 10 at 5 min. The volume of blood remaining in the placenta was significantly higher in the UCM group.
28	Katheria et al. 2018[37] USA	To determinate whether UCM is harmful to compromised term/ short-term babies.	Retrospective Cohort	151 Term and near-term infants (35–42 weeks of gestation)	UCM: 36 ICC: 121	There was no significant difference in neonatal outcomes, but fewer infants in UCM group needed resuscitation and ongoing respiratory compared to ICC.
29	Alzaree et al. 2018[38] Egypt	To make a comparison between the effects of UCM versus DCC on hemoglobin level at 6 weeks from delivery among term neonates and which method is most beneficial for them.	RCT	250 Pregnant women starting from ≥ 37 weeks gestational age	UCM: 125 DCC: 125	UCM five times was associated with higher Hb levels at 6 weeks after birth, at physiological anemia of the fetus and significant but clinically there was no difference between the two groups. There was a positive correlation between: Hb of the mother and the newborn during the first day and after 6 weeks; the Hb of the fetus after the first day and at 6 weeks.
30	Ram Mohan et al. 2018[39] India	To evaluate the effect of cord milking on short term morbidity and hematologic parameters at 6 weeks in preterm neonates requiring resuscitation.	RCT	60 Preterm Infants (<37 completed weeks of gestation)	C-UCM: 30 ICC: 30	Infants in the C-UCM group had higher Hb and serum ferritin level.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
31	Lakshimi et al. 2018[40] India	To assess immediate neurological outcome in preterms who received milking of the cord by neurological examination at discharge. To assess neurodevelopmental outcome at six months (corrected gestation) in surviving preterms who received milking of the cord by evaluating for developmental delay.	Prospective cohort	83 Preterm Infants (<34 weeks gestation)	UCM: 42 UCM not done: 41	In UCM group: there was reduction in Amiel-Tison angle abnormalities and neurodevelopmental outcome at 6 months, but the results were not statistically significant.
32	Silahli et al. 2018[41] Turkey	To compare the effect of umbilical cord milking and early cord clamping on thymic size, and neonatal mortality and morbidity in preterm infants.	RCT	90 Infants born before 32 weeks of gestation	UCM: 38 ICC: 37	Hb levels was higher in group UCM, but not significantly. The absolute neutrophil count in UCM group was significantly lower.
33	Girish et al. 2018[42] India	To evaluate the feasibility and safety of UCM in neonates who are depressed at birth.	RCT	101 Infants (≥35 weeks of gestation) depressed at birth	UCM: 50 ICC: 51	There were no significant diferences in resuscitation delay, resuscitation efforts, and short-term outcomes between the two groups
34	McAdams et al. 2018[43] USA	To determine placental transfusion blood volumes with intact and C-UCM in term newborns.	Pilot study	66 Term Infants (≥37 weeks of gestation)	C-UCM: 30 UCM: 30	Mean blood volume with UCM (×4) group was increased. For C-UCM, blood volume increased proportionally to cord length and, by the second milking, 98.1 [±] 4.5% of blood volume was delivered.
35	Katheria et al. 2018[44] USA	To compare the effect of UCM vs DCC on neurodevelopmental and health outcomes in very preterm infants at 22-26 months of corrected age.	RCT	197 Preterm infants (22-26 weeks of gestation)	DCC: 65 UCM: 70	Infants randomized to umbilical cord milking had higher language and cognitive scores compared with those randomized to DCC. There was no difference in rates of mild or moderate to severe neurodevelopmental impairment.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
36	Daskalakis et al. 2018[45] Greece	To compare the levels of tumor necrosis factor a, and interleukins 1, 6, 8 and 10 in the umbilical cord and neonatal circulation among neonates with early and late cord clamping.	Prospective cohort	76 Term Infants (>37 weeks of gestation)	ICC: 36 DCC/UCM: 40	Significant differences were noted in the Hb and Hct levels at 24 h that favored delayed clamping. None of the evaluated markers of inflammation differ between the two groups. Spearman's rho revealed a significant correlation between umbilical cord tumor necrosis factor a (TNF-a) and TNF-a neonatal values at 24 h in the ICC group. Significant correlations were also noted between umbilical cord TNF-a and TNF-a neonatal values at 24 h, umbilical cord interleukins-10 and neonatal interleukins-10 at 24 h and umbilical cord interleukins-1b and neonatal interleukins-1b at 24 h.
37	Katheria et al. 2019[46] USA, Ireland, Germany, Canada	To determine whether the rates of death or severe intraventricular hemorrhage differ among preterm infants receiving placental trans-fusion with UCM vs DCC.	Analysis post hoc of RCT	474 Preterm Infants (21-31 weeks of gestation)	DCC: 238 UCM: 236	There was no statistically significant difference in the rate of a composite outcome of death or severe intraventricular hemorrhage, but there was a statistically significantly higher rate of severe intraventricular hemorrhage in the UCM group.
38	Manoj et al. 2019[47] India	To evaluate the effect of UCM and non-milking technique on the incidence of intraventricular hemorrhage in very preterm neonates (28+1 – 31+6).	Prospective cohort	59 Preterm Infants (21- <32 weeks of gestation)	ICC: 31 UCM: 29	There was no significant difference in the perinatal demographics between the groups. The incidence of Intraventricular hemorrhage was significantly decreased in UCM group as that of that of the ICC group. Further, the mortality, respiratory distress syndrome, need for ventilation support blood transfusion was decreased in UCM groups but not statistically significant as that of the ICC group.
39	El-Naggar et al. 2019[48] Canada	To investigate whether UCM at birth improves systemic blood flow and short-term outcomes, as compared with ICC.	RCT	73 Preterm infants (24-31 weeks' gestation)	UCM: 37 ICC: 36	Haemoglobin on admission was higher in the UCM than in the ICC group . No statistically significant differences were found between groups in superior vena cava flow at 4-6 h or at 10-12 h of age, cardiac output or neonatal morbidities.
40	Rodriguez et al. 2019[49] USA	To evaluate the effect of UCM on outcomes for preterm multiples.	Cohort	149 neonates (120 twins, 29 triplets) (<30 weeks of gestation)	UCM: 98 Controls: 51	Cord milking was associated with a lower rate of adverse composite neonatal outcome in univariable analysis. However, in multivariable modeling, the effect was not significant. Hematocrit was 4.6 unit % higher in the cord milking group, and cord milking was associated with a lower rate of blood transfusion.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
41	Lago Leal et al. 2019[50] Spain	To assess the short and medium-term effects of milking maneuver compared with early cord clamping for infants born before 37 weeks of pregnancy.	RCT	138 Infants (24-36 weeks of gestation)	UCM: 69 ICC: 69	Initial hemoglobin was significantly higher in the UCM group by 1.675 g/dL and initial hematocrit by 5.36% , but no differences in the need of transfusion during the first 30 days after delivery were found. Peak serum bilirubin was similar in both groups. Phototherapy requirements were higher in the UCM group. No differences regarding the need of oral iron supplementation, platelet transfusion, respiratory distress syndrome, patent ductus arteriosus, intraventricular hemorrhage, necrotizing enterocolitis, periventricular leukomalacia, meconium aspiration syndrome, use of surfactant, days of oxygen supplementation, need of vasopressors, length of stay in the neonatal intensive care unit, or postpartum hemorrhage were found.
42	Shirk et al. 2019[51] USA	Primary objective: to compare the effect of DCC vs UCM on the initial hematocrit concentration in preterm births (23-34 weeks gestation). In addition, we sought to compare the effects of DCC vs UCM the incidences of intraventricular hemorrhage, necrotizing enterocolitis, and need for transfusion (secondary objectives).	RCT	282 Preterm infants (23 a 34 weeks of gestation)	DCC:144 UCM: 138	There was not any statistically significant difference in neonatal outcomes between the DCC and UCM groups, the occurrences of transfusion, and ventricular hemorrhage were all lower in UCM group. UCM group had higher initial hematocrit concentration compared with the DCC group, although this was not significant. Peak bilirubin levels and need for phototerapy were similar between groups.
43	Finn et al. 2019[52] Ireland	To compare cerebral activity and oxygenation in preterm infants (<32 weeks of gestation) randomized to different cord clamping strategies.	RCT	44 Preterm Infants (<32 weeks of gestation)	ICC:12 DCC:14 UCM: 18	There were no significant differences between groups for measured of electroencephalogram activity or cerebral near infrared spectroscopy.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
44	Toledo et al. 2019[53] Spain	To demonstrate that UCM would reduce the incidence of intraventricular hemorrhage in this at risk population.	Prospective cohort	69 Preterm Infants (<32 weeks of gestation)	ICC: 36 UCM: 33	No significant differences regarding perinatal characteristics were present between both groups except for chorioamnionitis and preterm rupture of membranes which were more frequent in the UCM group. There was a significant reduction in the incidence of intraventricular hemorrhage in the UCM group as compared to the ICC group and a reduction in the number of transfusions.
45	Tran et al. 2020[54] USA	To assess the current practice of DCC and to determine patient and hospital factors that predict DCC.	Cross-sectional	5332 Infants (22 a 31 weeks of gestation)	-	Infants delivered at <32 weeks or with birth weight <1,500 g were more likely to receive DCC. Cesarean delivery was associated with less likelihood of DCC.
46	Mangla et al. 2020[55] India	To compare the effect of intact umbilical cord milking and DCC on venous hematocrit at 48 (±6) hours in late preterm and term neonates (35 0/7- 42 6/7 week).	RCT	144 Preterm and Term Infants (35-42 weeks of gestation)	UCM: 72 DCC: 72	Hematocrit at 48 h in UCM group was higher than in DCC group. Venous hematocrit at 6 weeks was higher in UCM than in DCC group. Other parameters were similar in the two groups.
47	El-Naggar et al. 2020[56] Canada	To evaluate the rates of practice, and the associations between different cord management strategies at birth (DCC, UCM, and ICC) and mortality or major morbidity, rates of blood transfusion, and peak serum bilirubin in a large national cohort of very preterm infants.	RCT	9729 Preterm Infants (<33 weeks of gestation)	UCM: 394 DCC: 4419 ICC: 4916	Mortality or major morbidity were higher in ICC group when compared with UCM group; Mortality and Intraventricular Hemorrhage were associated with ICC as compared with DCC. Severe intraventricular hemorrhage were higher with UCM compared with DCC. Rates of blood transfusion were higher with UCM compared with UCM and DCC.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
48	Simonin et al. 2020[57] USA	To determine if UCM performed on a cut umbilical cord segment increased the hemoglobin/hematocrit, with a reduction in the incidence of intraventricular hemorrhage, need for blood transfusions, and pressor requirement in infants with <35-weeks gestation.	Cohort	403 Preterm Infants (<37 weeks of gestation)	C-UCM: 106 Control: 297	There were no statistically significant differences between the two groups in hemoglobin/hematocrit, peak bilirubin values, the incidence of intraventricular hemorrhage, need for blood transfusion, and the use of pressors.
49	Katheria et al. 2020[58] USA, Ireland, Germany, Canada	To evaluate changes in cerebral oxygenation, peripheral arterial oxygenation, respiratory status and administered fraction of inspired oxygen (FiO2) during the first 10 min of life in premature infants receiving UCM compared with DCC.	RCT	474 Preterm Infants (23-31 weeks of gestation)	DCC: 238 UCM: 236	There was a increase incidence os severe intraventricular hemorrhage in infants who received UCM compared with DCC. SpO2 was higher in the UCM group in the firt 4 min; mean airway pressures were lower in the UCM group after the firt 7 min. No statistical differences were observed for FiO2, StO2 or heart rates.
50	Katheria et al. 2020[59] USA	To study the content of umbilical cord blood from a series of healthy full-term infants assigned at random to receive UCM or DCC	RCT	25 Term Infants (>37- 42 weeks of gestation)	DCC: 12 UCM: 13	In comparing placental transfusion strategies, blood obtained from an umbilical cord that has been "milked" vs one in which clamping was simply delayed contains mesenchymal stromal cells in addition to solely hematopoietic stem cells, a composition more favorable for hematopoiesis, as suggested by its superior rescue of lethally irradiated bone marrow–depleted mice.
51	Chaowawanit et al. 2020[60] Thailand	To measure the blood volume in the umbilical cord of preterm infants at a certain length and to identify the correlation among blood volume, length, and circumference of umbilical cord, gestational age (GA), birth weight and placenta.	Cross-sectional	75 Preterm Infants (24-36 weeks of gestation)	C-UCM: 75	The mean length, diameter, and circumference were 23.31 ± 7.66, 1.10 ± 0.18, and 3.56 ± 0.75 cm, respectively. The mean residual blood volume was 11.58 ± 4.99 mL or 0.50 ± 0.18 mL/cm. Total residual blood volume had a significant positive strong correlation with umbilical cord length.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
52	Li et al. 2020[61] China	To investigate whether intact umbilical cord milking can aggravate infection or result in other undesirable complications in preterm infants with premature prolonged rupture of membranes.	RCT	102 Preterm Infants (28 a 37 weeks of gestation)	UCM: 48 ICC: 54	There was no significant differences between the two groups regarding hematological parametes (platelet count, white blood count, netrophil ratio, and C-reactive protein) or neonatal outcomes (probable or certain neonatal infection, respiratory distress syndrome, necrotizing enterocolitis, and ventricular hemorrhage). However in C-UCM group had higher serum Hb and Hct, and received fewer blood transfusions than those in the ICC group.
53	Harer et al. 2020[62] USA	To determine if DCC is associated with a reduction in neonatal acute kidney injury.	Retrospective cohort	278 very low birth weight neonates	DCC: 125 ICC: 116 C-UCM: 37	The incidence of Acute Kidney injury in the first week was 20.1% with no difference between groups.
54	Josephsen et al. 2020[63] USA	To assess potential benefits of UCM when compared with ICC in extremely preterm infants.	RCT	56 Preterm Infants (24-27 weeks of gestation)	ICC: 27 UCM: 29	No differences were seen in initial hemoglobin or number of blood transfusions. Umbilical cord milking may be an alternative to delayed cord clamping, but its safety and efficacy are not established in extremely premature infants.
55	Chiruvolu et al. 2020[64] USA	To identify and describe current cord clamping practices and evaluate factors associated with variations.	Cross-sectional	517 neonatologists	-	More than half of the providers responded not performing any UCM in their practice. Significant associations were detected between performance of UCM and all queried demographic variables independently. Clinicians with >20 years of experience were more likely from institutions performing UCM compared to the providers with fewer years of experience. However, teaching hospitals were less likely to perform UCM compared to non-teaching hospitals. Similarly, practices with level IV neonatal intensive care uni were less likely to perform UCM compared to practices with level III units. Significant variations were also noticed for not providing placental transfusion in higher-risk deliveries. Demographic and professional factors were noted to be associated with these differences.
56	Panburana et al. 2020[65] Thailand	To study the effect of intact umbilical cord milking procedure in comparison with the procedure of DCC in term neonates.	RTC	168 Term infants (37-42 weeks of gestation)	UCM: 84 DCC: 84	Both UCM and DCC revealed a comparable effect on hematologic status without deleterious effects on neonatal and maternal outcomes at the age of 48-72 h in term neonates.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
57	Al-Wassia et al. 2020[66] Saudi Arabia	To compare the efficacy and safety of DCC and UCM for term infants and their mothers.	RCT	82 Term Infants	DCC: 39 UCM: 43	There were no significant differences between groups with regards to maternal outcomes. There were no differences in the need for resuscitation, apgar scores at one and five minutes and admission to intensive care unit between groups. The results showed the efficacy and safety of UCM compared to DCC in term infants. The adoption of UCM may be considered as an alternative care treatment, especially in cases that are not candidates for DCC.
58	Leslie et al. 2020[67] USA	To learn how midwives today manage the umbilical cord at birth.	Cross-sectional	1106 members of the American College of Nurse-Midwives	-	Cord milking was practiced by 37% of participants. Cord milking is not as widely practiced as DCC, and respondents were less likely to be convinced by the evidence for cord milking.
59	Kumbhat et al. 2021[68] USA	To compare short-term outcomes after placental transfusion DCC or UCM versus ICC among extremely preterm infants.	Retrospective cohort	3116 infants (<29 weeks of gestation)	ICC: 1870 DCC/UCM: 1246	In this extremely preterm infant cohort, exposure to placental transfusion was not associated with the composite outcome of mortality or major morbidity, though there was a reduction in mortality by 36 weeks' postmenstrual age.
60	Chiruvolu et al. 2021[69] USA	To evaluate the short-term effects of UCM on term infants delivered by cesarean section.	Retrospective cohort	387 term infants (37 weeks or greater gestation)	UCM: 141 ICC: 246	There were no significant differences in other maternal or neonatal characteristics. Although this study was not powered to detect differences in outcomes, the occurrence of hyperbilirubinemia needing phototherapy, symptomatic polycythemia, neonatal intensive care uni admissions, or readmissions for phototherapy was similar between the groups.
61	Chiruvolu et al. 2021[70] USA	To examine the short-term effects of placental transfusion on late preterm infants born between 35 0/7 and 36 6/7 weeks of gestation.	Retrospective cohort	279 Late preterm infants (35-36 weeks of gestation)	ICC: 118 DCC/UCM: 161	The mean hematocrit after birth was significantly higher in the DCC/UCM group. Fewer infants had a hematocrit <40% after birth in the DCC/UCM group compared with the ICC group. The incidence of hyperbilirubinemia needing phototherapy, neonatal intensive care unit admissions, or readmissions to the hospital for phototherapy was similar between the groups. Fewer infants in the DCC/UCM group were admitted to the neonatal intensive care unit primarily for respiratory distress. Symptomatic polycythemia did not occur in either group.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
62	Kilicdag et al. 2021[71] Turkey	To compare the effects of three different methods of umbilical cord management on hematological parameters in term and late-preterm infants.	RCT	587 infants (>35 weeks' gestation)	UCM: 197 C-UCM: 190 ICC: 200	Mean hemoglobin and hematocrit levels at 48 h of age were higher in UCM group compared with the ICC group. Therefore UCM is more beneficial choice.
63	Shen et al. 2021[72] Taiwan	To evaluate whether a shorter length (20 cm) of C-UCM has potential benefits, compared to ICC, in very preterm babies.	RCT	76 Preterm infants (< 30 week's gestation)	C-UCM: 37 ICC: 39	A 20-cm C-UCM showed no effect on reducing the incidence of packed red blood cell transfusion in preterm babies with gestacional age less than 30 weeks compared with ICC.
64	Aydogan Kirmizi et al. 2021[73] Turkey	To evaluate obstetricians' practices of umbilical cord clamping, milking, and skin-to-skin contact applications and to determine the related variables.	Cross-sectional	522 obstetricians	-	It was determined that 510 (99.7%) of the participants included in the study knew what cord milking was, 132 of them (25.3%) did not use the cord milking method at all, 210 (40.2%) used it sometimes, and 180 (34.5%) applied it always, and no significant difference was found between physicians working in the public and private sector. Umbilical cord milking was performed by 174 physicians (33.3%) in all term, preterm, and fetuses requiring resuscitation, by 54 physicians (10.3%) only in term fetuses, by 90 physicians (17.2%) only in preterm fetuses, and by 108 (20.7%) physicians only in fetuses requiring resuscitation in order not to lose time. One-hundred and eighty (34.5%) of the physicians who applied cord milking stated that they applied it once in every birth, 96 (18.4%) did it two times, and 114 (21.8%) did it three or more times.
65	George and Isac 2021[74] India	To analyse the effects of UCM on the neonatal haematological parameters at 72 h and 6 weeks of age and its association with any adverse effects.	RCT	125 term and 19 late preterm infants (≥34 weeks of gestation)	UCM: 73 ICC: 71	In the intervention arm, the mean haemoglobin and haematocrit were significantly higher as compared to the control arm, at 72 h of age. There was also significant increase in the mean haemoglobin and haematocrit compared to the controls, at 6 weeks. No statistical difference was found in the incidence of post-partum haemorrhage and duration of third stage. There was no significant rise in hyperbilirubinaemia, phototherapy requirement and polycythaemia among neonates in the intervention group.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
66	Zanardo et al. 2021[75] Italy	To evaluate whether UCM is more effective than ICC in enhancing placental transfusion after elective cesarean delivery.	RCT	130 Term Infants (39-40 weeks of gestation)	UCM: 65 ICC: 65	There were no significant differences in cord blood mean Hct values at birth. Conversely, at 48 h of age, the UCM group had significantly higher capillary heel Hct values, supporting a higher placental transfusion volume, despite comparable neonatal body weight decrease.
67	El-Naggar et al. 2021[76] Nova Scotia	To compare the effect of UCM vs. early cord clamping on cerebral blood flow.	RCT	73 Preterm Infants (24- <31 weeks of gestation)	UCM: 37 ICC: 36	There were no significant differences between groups in middle or anterior cerebral blood flow velocities and resistive indices at either study time point. Cerebral blood flow variables were not correlated with mean blood pressure, systemic blood flow, or intraventricular hemorrhage
68	Sura et al. 2021[77]) Kenya	To compare preterm (< 37 weeks) neonatal haemoglobin, haematocrit, polycythaemia, anaemia, clinical jaundice and maternal primary post-partum haemorrhage following UCM versus DCC.	RCT	260 Preterm Infants (28- <37 weeks of gestation)	DCC: 128 UCM: 133	The mean neonatal haemoglobin, haematocrit, anaemia were similar between UCM and DCC respectfully. However, neonatal polycythaemia and neonatal jaundice were statistically significantly lower in UCM compared to DCC.
69	Orpak et al. 2021[78] Turkey	To investigate the effect of C-UCM, which permits resuscitation during immediate transition period.	RCT	62 Term Infants (≥37 weeks of gestation)	C-UCM: 31 UCM: 31	There were no significant differences in terms of mean gestational age, birth weight, Apgar scores at the 5th min, first breathing time, arterial oxygen saturation, cerebral regional oxygen saturation, blood pressure, hemoglobin levels, and residual placental blood volume between C-UCM and UCM groups.
70	Kumbhat et al. 2021[79] USA	To compare short-term outcomes after placental transfusion (DCC or UCM) versus ICC among extremely preterm infants.	Retrospective cohort	3116 Infants <29 weeks of gestation)	DCC: 895 UCM: 291 DCC + UCM: 60 ICC: 1870	Among 3116 infants, 40% were exposed to placental transfusion, which was not associated with the primary composite outcome of mortality or major morbidity by 36 weeks postmenstrual age. However, exposure was associated with decreased mortality by 36 weeks postmenstrual age and decreased hypotension treatment in first 24 postnatal hours.
71	Consonni et al. 2020[80] Italy	To evaluate the effect of different strategies to improve placental transfusion in cesarean section.	Retrospective cohort	223 term infant (≥37.0 weeks of gestation)	DCC: 137 ICC without milking: 53 UCM: 33	At multivariate analysis, UCM was associated with neonatal Hct. In elective UCM led to higher neonatal Hct compared to UCC without milking and DCC. Therefore, UCM could be a valid option to favor placental transfusion.

Continuation of Table 2

Corr	Author /Year / Country	Objective	Methodological design	Participants	Intervention	Outcomes
72	Kartal et al. 2022[81] Turkey	To show the relationship between ICC, DCC, C-UCM techniques with total oxidant capacity, total antioxidant capacity, and peroxynitrite levels.	RCT	69 Term infants	ICC: 23 DCC: 23 C-UCM: 23	The 5-minute Apgar's score of the babies in ICC group was significantly lower than the babies in DCC and C-UCM group. The total oxidant capacity, oxidative stress index, and peroxynitrite measurements of three groups did not differ statistically. The total antioxidant capacity value of the C-UCM group was significantly higher than the patients with the ICC and DCC groups
73	Xie et al. 2022[82] China	To investigate whether UCM prevents and controls anemia in preterm infants, as compared with ICC.	RCT	242 Preterm infants (<34 weeks' gestation)	ICC: 127 UCM: 115	Neonates receiving UCM had significant higher levels of Hb, hematocrit, and serum iron. Lower prevalence of anemia and lower need for transfusions were noted in UCM group. Although UCM was associated with prolonged duration of phototherapy, the maximum levels of bilirubin were similar between two groups.

Note: RCT= Randomized controlled trial; ICC= immediate cord clamping; UCM= umbilical cord clamping; DCC= delayed cord clamping; C-UCM= cut umbilical cord milking; Hb= Hemoglobin; Hct= Hematocrit

The UCM has been part of the practice of few professionals who care for the newborn[64, 67, 73]. However, the protocol for carrying it out varied among the included studies, in some of them the infant was placed on sterile drape at or below the level of the placenta (between the mother's thighs in vaginal delivery or to the mother's side in cesarean delivery)[12, 14, 18-24, 27, 29-36, 39-41, 42, 43, 45-49, 53, 58, 66, 69, 74, 76-78].

For neonates that underwent I-UCM, the cord was pinched as close to the placenta as possible with the thumb and index fingers of the left hand and about 30 cm of the umbilical cord was vigorously milked towards the umbilicus. Speed of milking was approximately 5 or 10 cm/s each within the initial 5 min of life. The cord was then released at the placental end and allowed to refill with blood for a brief 1 to 3 seconds pause between each milking motion[12, 14, 18-24, 27, 29-36, 39-41, 42, 43, 45-49, 53, 58, 66, 69, 74, 76-78]. In general, the entire procedure was completed in not more than 30 s. After this, the umbilical cord was clamped and cut at 2-3 cm from the umbilicus and the infant taken to the warmer for routine newborn care[20, 23, 26, 35, 43, 48, 50, 61, 69, 74, 77].

In cases of C-UCM, the 20-30 cm length of umbilical cord was clamped and cut (within 10 s), and then milked[15, 17, 25, 26, 28, 44, 59]. Concerning the number of times that cord milking was performed, it varied between one to eight, but in most studies, it was performed three times [12,13, 16-21, 25-30, 32-34, 36, 39-41, 43-45, 46-49, 52, 53, 57-59, 63, 65, 66, 70, 74, 76, 80].

Also was found comparisons between the types of milking C-UCM and I-UCM[29, 43, 57, 78]. Other studies performed other types of comparison, such as: UCM x 'non-milking'[34, 40], ICC x DCC x UCM[71] and UCM x DCC x DCC with UCM[25, 79].

The main benefits of UCM compared with ICC in preterm neonates are described in Figure 2. However, other studies have compared UCM with ICC in term newborns (TNB), whose main benefits of UCM are shown in Figure 3. Another type of comparison found in the articles was between DCC and UCM, and the results show that there are no differences between the two procedures as described in Figure 4.

In addition the UCM was analyzed in a study that evaluated the neonates requiring resuscitation[39], infants with acidosis at birth[6] and with depressed at birth[42]. Most studies have not found adverse events resulting from UCM. However, the existing adverse event appears to be the same as that of DCC: higher incidence of hyperbilirubinemia requires phototherapy[30]. In PTNB, some publications evidenced a lower number of neutrophils in the groups submitted to UCM compared to the DCC group[31, 41]. Also in PTNB studies found that there was an increased incidence of severe intraventricular hemorrhage in infants who received UCM compared with DCC [45, 56, 58]. However, research has found that there was a significant reduction in the incidence of intraventricular hemorrhage in the UCM group as compared to the ICC group [18, 47, 53, 56].

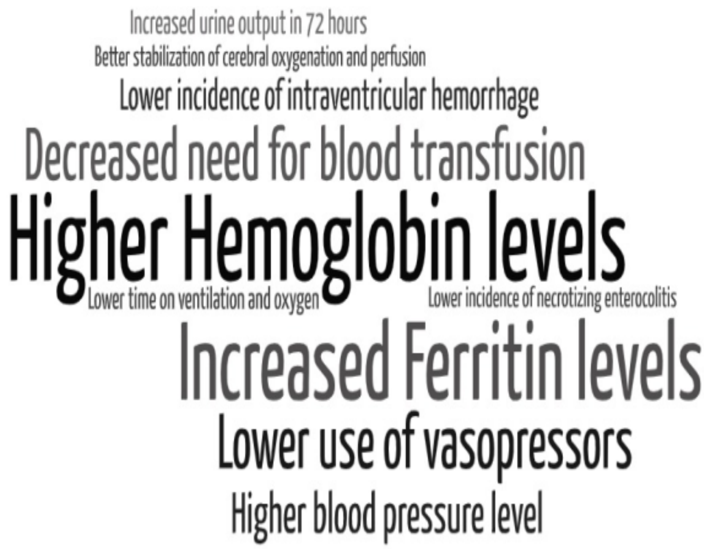

Figure 2. Benefits of umbilical cord milking compared to immediate cord clamping in preterm newborns.

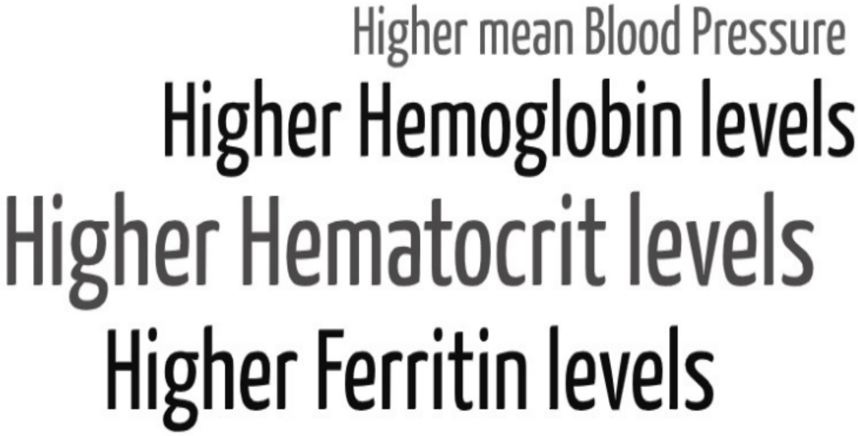

Figure 3. Benefits of umbilical cord milking compared to immediate cord clamping in term newborns.

Figure 4. Results of umbilical cord milking compared to delayed cord clamping in newborns.

DISCUSSION

This mapping allowed us to know how UCM has been performed in obstetric practice and its benefits and risks for the neonate, mainly compared to the ICC and the DCC. Most of the publications are results of RCT aiming to prove the advantages of UCM and providing evidence for its use. Through this review, it was possible to verify that UCM is more beneficial to neonates than ICC and that it can be used as an alternative to DCC, since it is a quick method to obtain placental transfusion to the newborn, as it is usually performed in less than 30 seconds the entire procedure.

About the use of UCM in the assistance to the NB, it was identified that a few professionals have used this technique. A survey conducted with neonatologists in the USA(64) and a study with obstetricians' practices in Turkey(73), identified that more than half of them do not perform UCM. This also was found in a research with nurse-midwives(67). These results indicate that evidence related to this practice should be widely disseminated among these professionals in order for neonates to benefit from this practice.

An important aspect to highlight from the analysis of the publications is that there is no standardization in the protocol used in the milking.

The vast majority share the same position of the infant at or below the level of the placenta, the milking of about 30 cm of the cord towards the navel in approximately 5 or 10 cm/s each, and the conclusion in not more than 30 s.

About the technique, some studies used the intact milking technique and others, the cut. Researchers, when comparing the cut with the intact milking, identified that the average blood volume of the intact UCM was higher than in the cut. Despite being a pilot study, with a small sample and without randomization, clinical benefits are important, however further studies are needed to compare these two techniques for further clarification. Although milking the cut umbilical cord may allow a faster onset of resuscitation in the newborn, the smaller total amount of transfused blood volume compared to intact milking raises questions about the general benefits of cut UCM(43).

However, other studies have identified that there were no significant differences in terms of mean gestational age, birth weight, Apgar scores at the 5th min, first breathing time, arterial oxygen saturation, cerebral regional oxygen saturation, blood pressure, hemoglobin levels, and residual placental blood volume(78) hemoglobin/hematocrit, peak bilirubin values, the incidence of intraventricular hemorrhage, need for blood transfusion, and the use of pressors(57) between C-UCM and I-UCM groups.

Another aspect related to the milking technique is the number of times that must be performed, which is not yet standardized. In this review, most studies performed three times; however, more studies are necessary to clarify this issue. A study found no differences between the milking of the cut cord performed once, with the milking of the cord intact performed three times, since both groups showed similar benefits such as probability of not needing transfusion during hospitalization and number of administrations of red blood cell transfusion in the first 21 min of life. Although this study has some limitations, such as a small sample size not being a prospective randomized study, it demonstrated that the cutting of UCM performed only once seems to be a less demanding and easier method to be performed(29).

Other comparisons were made between the types of milking. A study compare UCM x 'non-milking', demonstrated benefits in the neurological development of newborns submitted to milking(34, 40). Others that compared ICC x DCC x UCM, finding higher levels of hemoglobin and hematocrit in the last two groups(71), and greater oxidative stress(13), higher mortality or major morbidity(56), lower 5-minute Apgar's score in those submitted to ICC. Also was identified that there were no significant differences between groups for measures of electroencephalogram activity or cerebral near infrared spectroscopy(52), total oxidant capacity, oxidative stress index, and peroxynitrite measurements(81).

Still in relation to the type of milking, the technique of milking after DCC has been used, such as a study carried out with TNB, which compared this procedure with DCC and with milking separately and demonstrated that the iron reserve in this group was significantly higher than in the other two. Cord milking after DCC can increase the volume of extra blood that remains in the non-pulsatile cord, in addition to the usual placental transfusion and, thus, improve hematological parameters in the newborn. Despite these results, further studies are needed to better elucidate these findings(25).

Among the benefits of UCM, when compared to ICC, there is an increase in the levels of Hemoglobin, Hematocrit and Serum Ferritin, according to the articles analyzed(11-13, 17, 19, 35, 41). Placental transfusion contributes to 30 mL/kg of blood to the neonate, in extremely preterm infants with ICC about one-half of their normal circulating in utero blood volume are left in the placenta(83). The increase in these levels helps prevent childhood anemia(1). This is important for the PTNB, which is a population at risk for anemia, especially the small for gestational age and extremely low birth weight infants(83). In this sense, the ICC can be one of the probable causes for anemia in preterm infants, as it deprives them of blood from the placenta.

In more recent studies included in this review, which compared UCM to DCC in TNB and PTNB, similar levels of hemoglobin, hematocrit and serum ferritin were found between the two groups(14, 27, 33, 65). It should be noted that, at term birth, the newborn has an iron reserve of 75 mg/kg and, when submitted to DCC, an additional 40 mg occurs in one minute and 50 mg in three minutes. This means an iron reserve of 115-125 mg/kg, which is sufficient to prevent iron deficiency between the fifth and twelfth month of life[1].

Some analyzed publications[24, 38, 55] demonstrated that the newborns submitted to UCM had higher levels of serum hemoglobin, hematocrit and Ferritin when compared to those in which DCC was performed. This can be explained because some factors may influence the amount and speed of placental transfusion at DCC, such as the time of clamping of the umbilical cord, uterine contractions, umbilical blood flow, beginning of breaths and the positioning of the newborn after birth[84].

Especially in low and middle income countries, whose population is deficient in food and has a higher prevalence of anemia, the placental transfusion, whether by DCC or UCM procedure is advantageous and may have clinical value, since it reduces the incidence of neonatal and childhood anemia[85]. Considering that, in some studies[24, 38, 55], UCM presented higher levels of hemoglobin and hematocrit when compared to DCC, it is deduced that this procedure may also reduce the incidence of neonatal and childhood anemia.

The studies analyzed also showed that the NB submitted to milking compared to the ICC technique had higher mean arterial pressure levels[13, 17, 20] and that, in PTNBs, UCM was associated with higher blood pressure in 15 hours of life when compared to DCC[24]. It is noted that in term newborns, this increase may not be clinically significant, but in hypotensive neonates, the gain of 4 mmHg derived from circulatory blood by placental transfusion may be sufficient to prevent hypovolemia[13, 17].

This research also showed that there is no difference in the average number of transfusions in the first 42 days of life between PTNBs submitted to UCM and DCC[13] and that UCM reduced the need for blood transfusion when compared to ICC [7, 20, 34]. Placental transfusion promotes autotransfusion of the volume of residual blood volume in placenta available to the newborn. Already the ICC don't allow it, so it can contribute to the loss of organ-specific vascular competence in the lung, gastrointestinal tract, brain, kidney, and other organs[83].

As well, UCM contributes to the growth of the newborn (weight, height and average arm circumference) and does not impair the neurological development in the long run[32]. Infants undergoing UCM showed higher language and cognitive scores compared to those undergoing DCC[44]. The child's largest iron reserve, offered through UCM or DCC, certainly contributes to child development, since the iron-deficiency anemia in infants affects neuro-cognitive functions of learning and memory which can result in fatigue and low economic productivity[83].

It was also observed that UCM helps reduce morbidities due to prematurity such as intraventricular hemorrhage and necrotizing enterocolitis, compared to ICC in PTNB, in the publications covered in this review[18, 20]. Such benefit may be due to the considerable amount of umbilical cord blood stem cells received through placental transfusion[5].

According to the selected studies, UCM is a procedure that reduces the need for respiratory support in premature infants. In addition, it reduces the time of mechanical ventilation and the use of supplemental oxygen in PTNBs, compared to those who underwent DCC[12, 19]. This result may also be associated with the placental blood that is a rich source of fetal stem cells[84].

Stem cells play a fundamental role in the development and maturation of various organs and systems, mainly in the central nervous, respiratory, endocrine, immune and hematological systems. Moreover, they are involved in anti-inflammatory and anti-infectious actions, reducing the appearance of several diseases, including anemia of prematurity, intraventricular hemorrhage, sepsis and periventricular leukomalacia, in addition to reducing complications in respiratory distress syndrome. They also seem to have a beneficial effect on chronic lung diseases, apnea of prematurity, retinopathy of prematurity and necrotizing enterocolitis[5].

Another factor associated with the reduced morbidities due to prematurity identified in this research was the better cerebral[13] and systemic[16] oxygenation provided by the greater blood flow promoted by milking. A study carried out in PTNB randomized to UCM had greater measures of superior vena cava flow and right ventricular outlet in the first 6 h and 30 h of life[19]. In very low birth weight infants (<29 weeks, birth weight <1250g), milking provided stabilization of oxygenation and cerebral perfusion by increasing the left ventricular diastolic function by increasing the left ventricular preload[16].

If the umbilical cord is cut before the start of spontaneous breaths, it can negatively affect cerebral perfusion during the transition from the fetal to the neonatal period. This is probably due to the increased afterload observed in the left ventricle and the decreased preload provided by the umbilical vein. Air entering the newborn's lungs increases the pulmonary blood flow, which provides most of the preload for the left ventricle. In this sense, hemodynamic stabilization after delivery, which allows the maintenance of cerebral blood flow, is particularly important to preserve the vascular germinal matrix and reduce severe intraventricular hemorrhages in the newborn[84].

One of the studies examined showed differences in systemic blood flow between newborns and preterm infants, and preterm infants born through cesarean delivery and submitted to UCM had greater flow from the superior vena cava and ventricular outflow in the first 12 hours of life, showing higher systemic blood flow than in those in which the DCC was performed[24]. However, a study carried out with TNB showed that UCM was similar to DCC in terms of blood flow speed and Doppler indices in the middle cerebral artery[27].

In addition, another study demonstrated that PTNBs submitted to UCM have a higher heart rate and oxygen saturation and require smaller amounts of oxygen after delivery when compared to babies undergoing ICC. In this sense, it can be said that blood transfusion provided by both DCC and UCM improves pulmonary blood flow and helps with lung expansion[19].

The transition from fetus to neonate is a physiological process that includes numerous adaptations in their organ systems. There is a sudden transition to air breathing that involves complex changes in pressure, circulatory system and pulmonary blood flow. To facilitate this adaptation, adequate blood volume is necessary to ensure full perfusion to all of the infant's organs in adapting to extra-uterine life[83].

When compared to ICC, UCM reduces the need for support immediately after delivery and in situations where resuscitation was needed immediately, milking has the advantage of being completed in a very short period of time to improve stability after delivery[19]. Thus, it can be indicated in situations where the NB requires resuscitation immediately at birth to provide placental transfusion.

About resuscitation, the studies showed that UCM practice has benefits for newborns. One of the studies evaluated premature infants who needed resuscitation and found that UCM provides better cardiovascular results during the neonatal transition and better stabilization of blood pressure than in those submitted to ICC[39]. In cases of neonates with acidosis at birth, those who received UCM required less resuscitation and continuous respiratory support[6]. Furthermore, UCM is extremely beneficial for newborns and late preterm infants (≥35 weeks) who are born depressed. It was assessed that milking does not delay neonatal resuscitation or resuscitation efforts, compared to those who received ICC[42].

During neonatal resuscitation in term and late preterm infants, UCM can prevent or reduce brain damage, since, when performing this procedure, there is an increase in intravascular volume, cerebral blood flow and oxygen supply[42]. In this sense, this intervention can be valuable, especially in places with scarce resources, where there is no access to technological support and unavailability of blood components[6].

Regarding oxidative stress, the comparison between the three umbilical cord management procedures (ICC, DCC and UCM) detected that the ICC increases the production of disulfide titers and decreases the thiol levels in the newborn. Low plasma thiol levels and increased disulfide levels may be indicative of oxidative stress, which would contraindicate the performance of this procedure in newborns[34].

As for the adverse events resulting from the UCM, these seem to be the same as the DCC, which is the increased incidence of hyperbilirubinemia in neonates requiring phototherapy. However, as some studies have not found this outcome, it is necessary further research is needed for clarification. Despite the increased risk of jaundice, the benefits associated with UCM outweigh it. In this sense, professionals who provide assistance to the NB must guarantee the use of strategies to monitor and treat neonatal jaundice[86].

In premature newborns, in some studies, lower numbers of neutrophils in the groups submitted to UCM compared to the DCC group. However, neutropenia is an expected event in newborns submitted to umbilical cord blood transfusion and can be explained by the delayed recovery of neutrophils in these situations[31, 41].

Another adverse event reported was severe intraventricular hemorrhage, in PTNB. This outcome can be justified because extremely premature newborns do not have adequate self-regulation of the brain system compared to more mature neonates. Due to this system immaturity, changes in the systemic blood flow obtained with the UCM can be transferred to the cerebral blood flow causing rupture of the vessels[87]. In addition, in extreme preterm newborns, the maternal condition of chorioamnionitis releases inflammatory mediators that cross the blood-brain barrier, promoting a neuroinflammatory cascade, which increases the fragility of the germinal matrix and the cerebral blood vessels[46].

Although there is evidence on the reduction of intraventricular hemorrhage in preterm neonates submitted to late cutting of the umbilical cord, there are few studies on the UCM as an alternative to decrease intraventricular hemorrhage in extremely low birth weight newborns. In this sense, further studies on the safety and efficacy of UCM are needed as an approach for performing placental transfusion in these neonates[87].

Given all that has been presented, it can be said that UCM is a proven safe intervention that guarantees adequate placental transfusion at birth for TNB and PTNB, with several benefits well described in the literature[24].

Because it is a scope review, the studies included in that review have not been formally assessed for methodological quality. In this sense, despite the inclusion of a range of studies, which allowed us to know the nuances of UCM, care should be taken as to the incorporation of the interventions described in the studies in clinical practice.

CONCLUSION

Through this scoping review, it was possible to map the available evidence on UCM in newborns to support birth care. Most of the studies evidenced the benefits of using UCM instead of ICC, or as an alternative to DCC, in situations where rapid placental transfusion is required. The superior benefits to the ICC evidenced were: higher levels of Hemoglobin, Hematocrit and Serum Ferritin, and reduction of complications in preterm newborns, such as the need of blood transfusion. When compared to DCC, it has similar benefits; however, UCM is considered a faster method of placental blood transfusion. Therefore, it can be an alternative when delayed cord clamping cannot be performed.

In addition, this study enabled the identification of gaps that still need to be investigated on UCM, such as the number of times milking should be performed, what is the best type of milking and long-term results.

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