

## A Hospital-Based Study to Evaluate the Effect of Umbilical Cord Milking in Improving Hematological and Clinical Outcome in Preterm Babies

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Conflict of interest: Nil

### Abstract

**Aim:** The aim of the present study was to evaluate the effect of umbilical cord milking in improving hematological and clinical outcome in preterm babies.

**Methods:** This randomized controlled trial was done in the Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India from March 2018 to February 2019. A total of 114 mothers anticipated for preterm delivery were admitted in this hospital during the study period who were eligible for this study. Among 114 preterm neonates 57 were umbilical cord milking group and 57 were non milking group.

**Results:** Most of the mothers were in age group 21 to 30 years. There was no statistically significant difference in parity of mother, maternal morbidities, antenatal visit & antenatal corticosteroid. Mean gestational age (weeks) was  $32.5 \pm 1.8$  Vs  $32.6 \pm 2$  in milking & non milking group respectively. Birth weight was mostly between 1000 gm to 2499 gm in both the groups with a mean birth weight (gram)  $1513 \pm 440$  Vs  $1607 \pm 453$  in milking & non milking group respectively. Most of the babies were AGA in both the groups. In cord milking group 36.8% was SGA and in non-milking group 22.8% was SGA. Gender distribution reflected male predominance. Most of the infants were born by LUCS. Resuscitation needed 5.3% babies in cord milking group & 07% babies non milking group. Only one baby of cord milking group was intubated in delivery room.

**Conclusion:** Umbilical cord milking increases hematocrit levels in preterm babies. Newborn who receives cord milking, needs less number of blood transfusion and need of assisted ventilation is less in them. But there is no significant difference in blood pressure, jaundice, need of phototherapy, intraventricular hemorrhage & necrotizing enterocolitis in cord milking & non milking group.

**Keywords:** Umbilical Cord Milking, Hematocrit, Preterm

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### Introduction

Placental transfusion is a transfer of residual placental blood to a newborn after birth till the time of umbilical cord clamping and cutting. Three recent meta-analyses revealed that placental transfusion, compared with ICC, was associated with reduced incidence of mortality, IVH, and need for blood transfusions for infants born preterm. [1-3] This additional blood volume may exert its beneficial effects by enhancing neonatal iron-rich cell volume [4], improving cardiovascular hemodynamics [5] and transferring progenitor stem cells that may replace damaged cells and ameliorate immunocompetence. [6]

Most of clinical practice guidelines endorsed deferred clamping the cord at birth for variable

timing as a standard of care for stable preterm. [7-9] UCM has been considered as an alternative method to deferred cord clamping (DCC) particularly if immediate resuscitation is deemed necessary or in situations with unfavorable fetomaternal circulation hemodynamics. Previous studies showed that UCM in preterm infants provides cardiovascular stability as evidenced by greater systemic blood flow, higher left diastolic function, and improved cerebral perfusion compared to ICC. [10,11] In contrast, an experimental study showed that preterm lambs that underwent UCM had large cerebral blood flow fluctuations and may be susceptible to IVH. However, none of fetal lambs received antenatal steroid. [12]

Preterm neonates with IUGR are more liable to various perinatal complications compared to those adapted for gestational age including hypothermia, hypoglycemia, IVH, NEC, sepsis, hyperbilirubinemia, polycythemia, BPD, and mortality. [13] In addition, they are at high risk to have long term neurodevelopmental disability and cognitive delay. [14] In most of the previously published placental transfusion studies, infants with IUGR or antenatal evidence of placental insufficiency have been excluded for the assumed risks of delayed resuscitation and aggravating polycythemia. Wang et al [15] performed a subgroup analysis of preterm infants with IUGR who were randomized within their original trial of DCC vs. ICC and concluded that DCC has no harmful effects. Furthermore, the results of our previously published randomized controlled trial denoted that DCC in infants with IUGR was associated with mounted stem cell transfusion and greater hemoglobin levels at 2 months of age without higher incidence of polycythemia or need for phototherapy. [16]

The aim of the present study was to evaluate the effect of umbilical cord milking in improving hematological and clinical outcome in preterm babies.

### Materials and Methods

This randomized controlled trial was done in the Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India from March 2018 to February 2019. A total of 114 mothers anticipated for preterm delivery were admitted in this hospital during the study period who were eligible for this study. Among 114 preterm neonates 57 were umbilical cord milking group and 57 were non milking group.

Eligibility criteria: All inborn preterm neonates gestational age from 28 weeks to 34 weeks were eligible for enrolment. Preterm neonates with congenital malformations, Rh- negative mothers and born to monochorionic multiple pregnancy were excluded from study.

Pregnant mothers anticipated to preterm delivery from 28 weeks to 34 weeks were eligible for this study. Women were enrolled at the onset of spontaneous labor (cut off point >7 cm cervical dilation) if they were in labor, or when the decision had been made for caesarean delivery for those not in labor. Preterm neonates with major congenital malformations & Rh-negative mothers were excluded from study. A written informed consent was taken from parents and assurance about confidentiality were given. Neonates born between 28 to less than 34 weeks were randomly allocated to either umbilical cord milking or non-milking group. Delivery attending doctors were trained about the

procedure by hands on training & video demonstration. Attending doctor was made aware of the randomization by the researcher before delivery of the infant. In one group no intervention was done. In another group umbilical cord milking was done. After delivery of a baby umbilical cord was clamped away from the umbilicus keeping a distance about 25cm (about 10 fingers). Long segment of cord was milked toward the infant over two seconds duration each time by neonatal resuscitation team. Thus, milking was done for two times. Then the cord was clamped close to umbilicus & cut accordingly. Then routine umbilical cord care was ensured.

All required information for each neonate was recorded in a data collection form. The questionnaire was developed by reviewing evidence from books and scientific articles. The subjects were evaluated clinically & biochemically up to their hospital stay.

At 6 hours of age blood sample (1 mL) was taken in EDTA (ethylene diamine tetra acetic acid) tube. Hematocrit (Hct) level was assessed in clinical pathology department of BSMMU by fully automated blood cell counter (Sysmex, XN-2000 model, Japan). Different modes of respiratory support were initiated in patients following NICU protocol according to their respiratory severity score. Respiratory support was titrated according to infant's clinical condition, percent saturation of oxygen and arterial blood gas as per NICU protocol.

Blood pressure was measured by non-invasive Oscillo metric method in all neonates at 24 hours of age. Blood pressure cuff was applied to the right upper extremity. Bladder length covered 75% to 80% (2/3rd) of arm circumference and bladder width was measured by measuring mid upper arm circumference. Three successive blood pressure readings were taken at 2- minute intervals. Final blood pressure was considered as the mean of three readings. The study neonates were clinically assessed for jaundice. Total serum bilirubin was measured at 48 hour of age or earlier if clinically jaundice appeared. 1ml of venous blood was sent in a tube. The bilirubin concentration was determined by using an automated diazo method in department of biochemistry. Requirement of phototherapy was decided as per unit protocol.

Necrotizing enterocolitis (NEC) was diagnosed clinically if any infant presenting with the triad of feeding intolerance, abdominal distension and gross bloody stool. Diagnosis was confirmed by abdominal Xray. Bell staging was used to classify necrotizing enterocolitis (NEC).

Bed side Ultra sonogram of brain was done by qualified radiologist or neonatologist of associate professor level to find out IVH (from grade I to IV) by 72 hour of age or any time if any clinical feature of IVH developed.

Data analysis: After collection, data were entered into a personal computer then edited, analyzed, plotted and were presented in graphs and tables. Qualitative data were expressed in proportion or percentage & statistical test were done by chi-square test and quantitative data were expressed as mean &

SD and statistical test were done by student t test. All data were analyzed by SPSS software for windows, version 20. P value <0.05 was considered as level of significance.

### Results

**Table 1: Baseline characteristics of maternal factors**

Characteristics	Milking group (n=57)	Non milking group(n=57)	Total (N=114)	p Value
<b>Maternal age, n (%)</b>				
21-30 yrs	37(64.9)	45(78.9)	82(71.9)	
31-40 yrs	19(33.3)	12(21)	31(27.2)	0.186ns
>40yrs	1(1.7)	0	1(0.9)	
<b>Parity, n (%)</b>				
Primipara	26(45.6)	28(49.1)	54(47.4)	0.708ns
Multipara	31(54.3)	29(50.9)	60(52.6)	
<b>Antenatal visits, n (%)</b>				
Less than 4	8(14)	8(14)	16(14)	1.0ns
4 or more	49(86)	49(86)	98(86)	
Maternal DM, n%	6(10.5)	9(15.8)	15(13.2)	0.406ns
Maternal HTN, n%	20(35)	17(29.8)	37(32.4)	0.746ns
Oligohydramnios	20(35.1)	21(36.8)	41(36)	0.845ns
ACS	47(82.5)	42(73.6)	89(78.1)	0.258ns

Most of the mothers were in age group 21 to 30 years. There was no statistically significant difference in parity of mother, maternal morbidities, antenatal visit & antenatal corticosteroid.

**Table 2: Baseline characteristics of neonates**

Characteristics	Milking group (n=57)	Non milking group (n=57)	Total (N=114)	P Value
<b>Gestational age, n (%)</b>				
28 to less than 32 weeks	16(28.1)	17(29.8)	33(28.9)	
32 to 34weeks	41(71.9)	40(70.2)	81(71.1)	0.836 <sup>ns</sup>
Mean GA (weeks), Mean $\pm$ SD	32.5 $\pm$ 1.8	32.6 $\pm$ 2	32.55 $\pm$ 1.9	
<b>Birth weight, n (%)</b>				
1000g-1499g	29(50.8)	24(42.1)	53(46.5)	
1500g-2499g	26(45.6)	32(56.1)	58(50.9)	0.148 <sup>ns</sup>
2500g-4000g	02(3.5)	01(1.8)	03(2.3)	
Mean BW(g), Mean $\pm$ SD	1513 $\pm$ 440	1607 $\pm$ 453	1560 $\pm$ 446	
<b>Fetal growth, n (%)</b>				
SGA	21(36.8)	13(22.8)	34(29.8)	
AGA	34(59.6)	44(77.2)	78(68.4)	0.076ns
LGA	2(3.5)	0	02(1.8)	
<b>Gender, n (%)</b>				
Male	36(63.2)	24(42.1)	60(52.6)	0.024 <sup>s</sup>
Female	21(36.8)	33(57.9)	54(47.4)	
<b>Mode of delivery, n (%)</b>				
LUCS	54(94.7)	49(86)	103(90.4)	0.113ns
VD	3(5.3)	8(14)	11(9.6)	
Resuscitation needed, n (%)	3(5.3)	4(7)	07(6.1)	0.696ns
Intubation in delivery room	1(1.8)	0	1(0.9)	0.315ns
<b>APGAR score at 5th min n (%)</b>				
Excellent condition (7-10)	56(98.2)	54(94.7)	110(96.5)	0.309ns
Moderately depressed (4-6)	1(1.8)	3(5.3)	04(3.5)	

Mean gestational age (weeks) was  $32.5 \pm 1.8$  Vs  $32.6 \pm 2$  in milking & non milking group respectively. Birth weight was mostly between 1000 gm to 2499 gm in both the groups with a mean birth weight (gram)  $1513 \pm 440$  Vs  $1607 \pm 453$  in milking & non milking group respectively. Most of the babies were AGA in both the groups. In cord milking group

36.8% was SGA and in non-milking group 22.8% was SGA. Gender distribution reflected male predominance. Most of the infants were born by LUCS. Resuscitation needed 5.3% babies in cord milking group & 07% babies non milking group. Only one baby of cord milking group was intubated in delivery room.

**Table 3: Comparison of hematological outcomes between the milking group and non-milking group**

Characteristics	Milking group(n=57)	Non milking group(n=57)	p-Value
Hematocrit (%), Mean $\pm$ SD	57.3 $\pm$ 3.5	47.4 $\pm$ 4.5	.001
Blood transfusion 1st week, n (%)	2(3.5)	12(21.1)	0.001
TSB (mg/dl), Mean $\pm$ SD	9.8 $\pm$ 2.7	8.9 $\pm$ 2.5	0.86

This study showed significant increase in hematocrit level ( $57.3 \pm 3.5$  Vs  $47.4 \pm 4.5$  in cord milking group & non milking group) in cord milking group. This study also showed significant reduction in need of blood transfusion in first week of life in cord milking group.

**Table 4: Comparison of need of initial respiratory support between the milking group and non-milking group**

Characteristics	Milking group (n =57)	No milking group (n=57)	Total (N=114)	p-Value
Supplemental oxygen, n(%)	48(84.2)	49(86)	97(85.1)	0.793ns
Assisted ventilation, n(%)	22(38.5)	36(63.2)	58(50.8)	<b>0.024*</b>
<b>Mode of assisted ventilation, n (%)</b>				
HHHFNC	0	1(1.8)	1(0.9)	0.049
CPAP	18(31.6)	26(45.6)	44(38.6)	
MV	04(7)	09(15.8)	13(11.4)	

No significant difference found in need of supplemental oxygen but requirement of assisted ventilation was significantly higher in non-milking group.

**Table 5: Comparison of clinical outcomes between the milking group and no milking group**

Characteristics	Milking group(n=57)	Non milking group(n=57)	p-Value
Mean systolic BP (mmHg), Mean $\pm$ SD	43.8 $\pm$ 3.9	43.7 $\pm$ 3	0.895
Jaundice n (%)	48(84.2)	51(89.5)	0.406
Phototherapy needed n (%)	48(84.2)	51(89.5)	0.406
NEC, n (%)	06(10.5)	08(14)	0.568
IVH, n (%)	03(5.3)	05(8.8)	0.463

No statistically significant differences were found in systolic blood pressure, jaundice, need of phototherapy, NEC & Intraventricular hemorrhage.

## Discussion

Umbilical cord milking is a procedure in which clamped or unclamped umbilical cord is grasped and blood is pushed ("stripped") two times towards the newborn, in a rapid time frame, usually within 10 seconds. The target of umbilical cord milking is to provide infants with their whole potential blood volume. Systematic reviews [17] have reported that delayed cord clamping (DCC), when compared with immediate cord clamping reduces the incidence of mortality, intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC) and need for blood transfusions in preterm infants. Hence, many professional organizations have endorsed delayed

cord clamping as a standard delivery room practice for vigorous preterm infants. [18]

Most of the mothers were in age group 21 to 30 years. There was no statistically significant difference in parity of mother, maternal morbidities, antenatal visit & antenatal corticosteroid. Mean gestational age (weeks) was  $32.5 \pm 1.8$  Vs  $32.6 \pm 2$  in milking & non milking group respectively. Birth weight was mostly between 1000 gm to 2499 gm in both the groups with a mean birth weight (gram)  $1513 \pm 440$  Vs  $1607 \pm 453$  in milking & non milking group respectively. Most of the babies were AGA in both the groups. In cord milking group 36.8% was SGA and in non-milking group 22.8% was SGA. Gender distribution reflected male predominance. Most of the infants were born by LUCS. Resuscitation needed 5.3% babies in cord milking group & 07% babies non milking group. Only one baby of cord milking group was intubated in

delivery room. Study done by Yu-Jie Xie et al [19], neonates receiving cord milking had significant higher levels of hematocrit in preterm babies below 34 weeks of gestation. This study showed newborn who received cord milking, needed less number of blood transfusion. In a systematic review [20] it was seen cord milking, when compared with immediate cord clamping, reduced the need for packed RBC transfusions. In fact, a vast majority of research found delayed umbilical cord clamping is effective in preventing the occurrence of anemia. With this concern, it should be reminded that preterm babies are exposed to the risk of anemia. They do not enjoy sufficient iron as a term infant does. The importance of iron insufficiency lies not only in the fact that it leads to anemia, but also in its adverse effects on child behavior and cognition. [21]

This study showed significant increase in hematocrit level ( $57.3 \pm 3.5$  Vs  $47.4 \pm 4.5$  in cord milking group & non milking group) in cord milking group. This study also showed significant reduction in need of blood transfusion in first week of life in cord milking group. No significant difference found in need of supplemental oxygen but requirement of assisted ventilation was significantly higher in non-milking group. No statistically significant differences were found in systolic blood pressure, jaundice, need of phototherapy, NEC & Intraventricular hemorrhage. Another study done by Nagano [22] also showed no significant difference in necrotizing enterocolitis. In this study, there was no significant difference in need of supplemental oxygen but significant difference in need of assisted ventilation. Literature evidence shows that cord milking immediately improves pulmonary blood flow and assists lung expansion at breathing onset. [23,24] Katheria et al [24] reached conclusions infants who had received cord milking, ongoing respiratory support were fewer in number than those who received immediate cord clamping.

### Conclusion

Umbilical cord milking increases hematocrit levels in preterm babies. Newborn who receives cord milking, needs less number of blood transfusion and need of assisted ventilation is less in them. But there is no significant difference in blood pressure, jaundice, need of phototherapy, intraventricular hemorrhage & necrotizing enterocolitis in cord milking & non milking group.

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