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Research Article

Umbilical Cord Milking

The Effect Of Umbilical Cord Milking In Reducing ROP Of Preterm Babies

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Background: Recent advances in neonatal care in the last decade have improved the survival rates for premature infants. Consequently, the incidence of ROP has increased in parallel. Prematurity, low birth weight, respiratory distress syndrome, mechanical ventilation, prolonged oxygen treatment and blood transfusion increase the risk of ROP. **Methodology:** Neonates born before 37 weeks of gestation were assigned to either umbilical cord milking or non-milking group at a 1: 1 ratio according to a computer-generated randomized sequence. After delivery of a baby umbilical cord milking was performed by holding the infant at the level of the placenta. The first eye evaluation for ROP was done at 20 days of age for gestational age less than 30 weeks & weight below 1200gm & at 30 days of age for gestational age more than 30 weeks & above weight 1200gm. Follow-up was continued until retinal vascularization was completed. The follow-up schedules were organized depending on the retinal findings. The retinal finding was evaluated according to the International Classification of Retinopathy of Prematurity. The patients were grouped as no ROP, mild ROP (stages I-II ROP without plus disease, showed regression), and severe ROP (zone 1 or zone 2, stage III, aggressive ROP without stages, stage II with plus disease who required treatment). **Results:** 114 newborns were enrolled in this study. Then among 114 preterm neonates 57 were randomized to the umbilical cord milking group and 57 were randomized to no milking group. Baseline characteristics were almost similar between the two groups. There was a significant increase in hematocrit level 57.3 ±3.5 V 47.4 ± 4.5 (P value less than 0.001), reduction in need of blood transfusion 3.5% V 42.1% (P value less than 0.001) & reduction in ROP 3.5% V 19.3% (P 0.007). **Conclusion:** This study concluded that umbilical cord milking after delivery improves hematocrit levels, reduces the need for blood transfusion & reduces the incidence of ROP in preterm infants.

Keywords: Umbilical Cord Milking, Retinopathy of Prematurity, Preterm, Blood Transfusion, RCT

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Introduction

In Bangladesh 14 out of 100 babies are born prematurely before 37 weeks of pregnancy and the rate is rising [1]. The global preterm birth rate is 10% [2]. Retinopathy of prematurity (ROP) is an important cause of preventable blindness in children. Approximately 50,000 children suffer from visual impairment secondary to ROP worldwide [3]. Recent advances in neonatal care in the last decade, have improved the survival rates for premature infants. Consequently, the incidence of ROP has increased in parallel. ROP is under constant epidemiological study around the world. Prematurity, low birth weight, respiratory distress syndrome, and prolonged oxygen treatment increase the risk of ROP development [4]. Additionally, blood transfusion and mechanical ventilation are independent risk factors for predicting the development of ROP disease. When the umbilical cord is clamped immediately after birth (i.e., immediate cord clamping, ICC), a significant amount of the fetal blood remains in the placenta leading to relatively lower red blood cell (RBC) volume in the newborn. Umbilical cord milking is a procedure in which a 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—of which they are deprived when early cord clamping is carried out—completing placental transfusion in a shorter time than delayed cord clamping [5]. Systematic reviews [6] have reported that delayed cord clamping(DCC) when compared with immediate cord clamping reduces the incidence of mortality, intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), Retinopathy of prematurity (ROP) and need for blood transfusions in preterm infants. Hence, many professional organizations have endorsed DCC as a standard delivery room practice for vigorous preterm infants [7]. However, DCC could be difficult to implement in preterm infants in the delivery room needing resuscitation. Hence, Umbilical cord milking has been investigated as a potential alternative to delayed cord clamping because resuscitative measures can proceed shortly after delivery. A recent meta-analysis of 7 randomized controlled trials of umbilical cord milking in infants delivered at 33 weeks demonstrated that infants Who undergo UCM have higher hemoglobin (Hb) and a lower risk for oxygen requirement at 36 weeks and IVH of all grades compared with those who undergo immediate cord clamping [8]. Another study showed patients with ROP who require treatment were a little higher in the non-UCM group [9]. Therefore, based on previous reports, we hypothesized that Umbilical cord milking reduces the incidence of ROP in preterm infants by reducing the need for blood transfusions.

Materials and Methods

Study design: This randomized controlled trial was done in the Department of Obstetrics & Gynaecology & Department of Neonatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, from May 2021 to April 2022, after getting approval from the Institutional Review Board.

Eligibility criteria: All inborn preterm neonates gestational age <37 weeks were eligible for enrolment. Preterm neonates with congenital malformations, birth weight below 1 kg, and Rh-negative mothers were excluded from the study.

Study procedure: This Randomized Control Trial was conducted in the Department of Obstetrics & Gynecology & Department of Neonatology, BSMMU, Dhaka after approval by the Institutional Review Board (IRB) for one year from May 2021 to April 2022. Infants born before 37 weeks of gestation & born of singleton pregnancy were included in this study. Preterm neonates with congenital malformations, Rh-negative mothers and pregnancies with placental abnormalities or complications were excluded from the study. A written informed consent was taken from parents and assurances about confidentiality were given. Neonates born before 37 weeks of gestation were assigned to either umbilical cord milking or no intervention group at a 1:1 ratio according to a computer-generated randomized sequence. The obstetricians were made aware of the randomization by the neonatology team immediately 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 UCM were performed by holding the infant at the level of the placenta. The cord was pinched as close to the placenta

As possible and milked toward the infant over a 2-second duration. The cord was released and allowed to be refilled with blood for 2 seconds. Then milking was done once again. After completion, the cord was clamped and the neonates were shifted for routine care.

First eye evaluation for ROP was done at 20 days of age for gestational age less than 30 weeks & or weight below 1200gm & at 30 days of age for gestational age more than 30 weeks & above weight 1200gm. Follow-up was continued until retinal vascularization was completed. The follow-up schedules were organized depending on the retinal findings. All of the examinations were performed by the same doctor of associate professor level with indirect ophthalmoscopy with a 20 D lens and scleral depression. The retinal findings were evaluated according to the International Classification of Retinopathy of Prematurity [10]. The patients were grouped as no ROP, mild ROP (stages I-II ROP without plus disease, showed regression), and severe ROP (zone 1 or zone 2, stage III, aggressive ROP without stages, stage II with plus disease who required treatment).

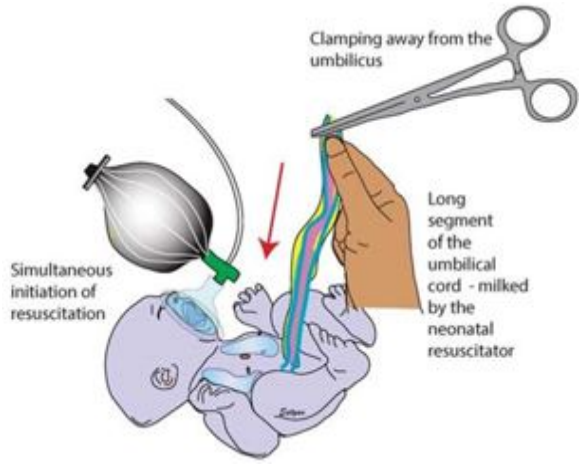

Figure 1: Umbilical cord milking.

Figure 2: Umbilical cord milking after delivery.

Results

A total of 130 preterm neonates were eligible for this study. Among them, 16 newborns were excluded and 114 newborns were included in this study. Among 114 preterm neonates, 57 were randomized to the umbilical cord milking group and 57 were randomized to no milking group.

A total of 130 preterm neonates were eligible for this study. Among them, 16 newborns were excluded and 114 newborns were included in this study. Among 114 preterm neonates, 57 were umbilical cord milking group and 57 were in the no-milking group.

The general characteristics of mothers are shown in **Table 1**. Baseline characteristics are comparable between the two groups. Most of the mothers (71.9%) were in the age group 21 to 30 years. There was no statistically significant difference in parity of mother, maternal morbidities, antenatal visit & antenatal corticosteroid.

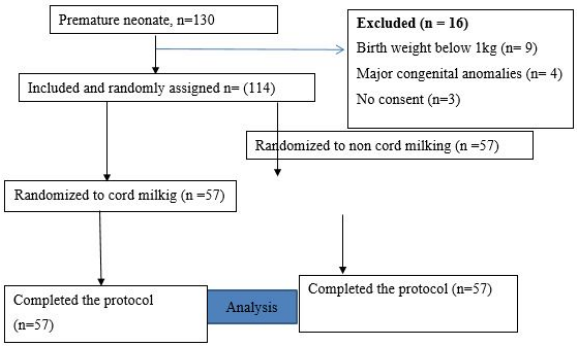

Figure-3: CONSORT flow diagram for study.

Table 1: Baseline characteristics of maternal factors (N=114)

Characteristics	Milking group(n=57)	No milking group(n=57)	Total (N=114)	P – Value
Maternal age				
<20 yrs	0	0	0	0.186
21-30 yrs	37(64.9%)	45(78.9%)	82(71.9%)	
31-40 yrs	19(33.3%)	12(21%)	31(27.2%)	
>40yrs	1(1.7%)	0	1(0.9%)	
Parity				
Primipara	26(45.6%)	28(24.6%)	54(47.4%)	0.708
Multipara	31(54.3%)	29(25.4%)	60(52.6%)	
No of antenatal visits				
<4	8(14%)	8(14%)	16(14%)	1.0
>4	49(86%)	49(86%)	98(86%)	
Maternal DM	6(10.6%)	9(26.4%)	15(13.2%)	0.406
Maternal hypertension	20(35%)	17(29.8%)		0.746
Maternal chorioamnionitis	0	2(0.9%)	2(1.8%)	0.154
Oligohydramnios	20(35.1`%)	21(36.8%)	41(36%)	0.845
Antenatal corticosteroid	47(82.4%)	42(73.6%)	89(78.1%)	0.258

Data are presented as numbers (percentages) unless otherwise indicated.

Statistical test: Chi-square test

Table 2. Baseline characteristics of neonates are comparable between the two groups. Most of the babies (71.1%) were moderate to late preterm (Cord milking group 71.9% & non-milking group70.2% respectively). Birth weight was mostly between 1000gm to 2499gm in both groups. Most of the babies were AGA in both groups. In the cord milking group 36.8% was SGA and in the non-milking group, 22.8% was SGA. Gender distribution reflected slight male predominance which was 52.6%. Most of the infants were born by LUCS which was 90.4%. Resuscitation was needed in 5.3% of babies in the Cord milking group & 07% of babies non the milking group. Only one baby was intubated in the delivery room & cord milking was done on this baby.

Table 2: Baseline characteristics of neonates (N=114)

Characteristics	Milking group(n=57)	No milking group(n=57)	Total (N=114)	P Value
Gestational age Moderate to late preterm (32 to 36 weeks)	41(71.9%)	40(70.2%)	81(71.1%)	0.836
Very preterm (28 to 32 weeks)	16(28.1%)	17(19.8%)	33(28.9%)	
Birth weight n(%),				
Low birth weight (1500gm-2499gm)	26(45.6%)	32(56.1%)	58(50.9%)	0.148
Very low birth weight (1000gm-1499gm)	29(50.8%)	24(42.1%)	53(46.5%)	
Normal birth weight (2500-4000gm)	2(3.5%)	1(1.8%)	03(2.3%)	
Fetal growth, n(%)				
SGA	21(36.8%)	13(22.8%)	34(29.8%)	0.076
AGA	34(59.6%)	44(77.2%)	78(68.4%)	
LGA	2(3.5%)	0	02(1.8%)	
Sex, n(%)				
Male	36(63.2%)	24(42.1%)	60(52.6%)	0.024
Female	21(36.8%)	33(57.9%)	54(47.4%)	
Mode of delivery, n(%)				
LUCS	54(94.7%)	49(86%)	103(90.4%)	0.113
NVD	3(5.3%)	8(14%)	11(9.6%)	
Resuscitation needed	3(5.3%)	4(7%)	07(6.1%)	0.696
Intubation needed in delivery room	1(1.8%)	0	1(0.9%)	0.315
APGAR score at 5th min n(%).				
Excellent condition (7-10)	56(98.2%)	54(94.7%)	110(96.5%)	0.309
Moderately depressed(4-6)	1(1.8%)	3(5.3%)	04(3.5%)	

Data are presented as numbers (percentages) unless otherwise indicated.

Statistical test: Chi-square test

SGA: small for gestational age; AGA: appropriate for gestational age**; L**GA: Large for gestational age**.** LUCS: Lower Uterine Cesarean Section; NVD: Normal vaginal delivery

A comparison of the clinical outcome between the cord-milking and no-milking groups is shown in **Table 3.** Our study showed a significant reduction in the need for blood transfusion in the cord-milking group. 3.5% V 42.1% in the Cord milking group & non milking group (P less than 0.001) No statistical differences were found in the incidence of feed intolerance, NEC and intraventricular hemorrhage.

Table 3: Clinical outcomes between the milking group and no milking group (N=114)

Characteristics	Milking group(n=57)	No milking group(n=57)	Total (N=114)	P-Value
Jaundice n(%)	48(84.2%)	51(89.5%)	99(86.8%)	0.406
Phototherapy needed n(%)	48(84.2%)	51(89.5%)	99(86.8%)	0.406
Blood transfusion n(%)	2(3.5%)	24(42.1%)	26(22.8%)	0.001
Blood pressure				
Normal	57(100%)	56(98.2%)	113(99.1%)	0.315
Low	0	1(1.8%)	01(0.9%)	
Feed intolerance, n(%)	16(28.1%)	20(35.1%)	36(31.6%)	0.420
NEC , n(%)	06(10.5%)	08(14%)	14(12.3%)	0.568
IVH, n(%)	03(5.3%)	05(8.8%)	08(07%)	0.463

Data are presented as numbers (percentages) unless otherwise indicated.

Statistical test: Chi-square test

RDS: respiratory distress syndrome; HHHFNC: Heated humidified high-flow nasal cannula;

CPAP: continuous positive airway pressure; MV: Mechanical ventilator

A comparison of the haematological outcomes between the milking group and the no-milking group is shown in **Table 4** Our study showed a significant increase in hematocrit level in the cord milking group. Hematocrit level was 57.3±3.5 V 47.4 ±4.5 in Cord milking group & non milking group (P less than 0.001)

Table 4: haematological outcomes between the milking group and no milking group (N=114)

Characteristics	Milking group(n=57)	No milking group(n=57)	P-Value
Haematocrit(%),mean ± SD	57.3± 3.5	47.4 ±4.5	.001

TSB 9.8±2.7 9.9±2.5 0.86

All values were given as mean±SD.

Statistical test: Independent Sample

Table 5 Comparison of ROP, severity of ROP & treatment modalities between the milking group and the No milking group showing a significant number of patients experienced ROP & needed treatment. (3.5% V 19.3%) in Milking group and No Milking group, (P 0.007).

Table-5: Comparison of ROP, severity of ROP & treatment modalities between milking group and no milking group (N=114)

ROP	Milking group(n=57)	No milking group(n=57)	Total (N=114)	P value
ROP, n(%)	2(3.5%)	11(19.3%)	13(11.4%)	0.007
Severity of ROP				
Mild ROP	0	1(0.9%)	1(0.9%)	0.046
Severe ROP	2(3.5%)	10(17.5%)	12(21%)	
Need of treatment				
LASER	0	4(07%)	4(3.5%)	0.035
Bevacizumab	2(3.5%)	6(10.5%)	8(07%)	

Qualitative data are presented as the number and percentage, Statistical test: The Chi-square test was used for categorical data, and $p < 0.05$ was considered significant. Quantitative data are presented as mean ± SD, Statistical test: One sample T-test was done, and $p < 0.05$ was considered significant.

Discussion

Retinopathy of prematurity is a devastating morbidity in preterm babies which may lead to blindness. Approximately one-quarter of a newborn's blood volume is wasted by clamping the umbilical cord immediately after birth Therefore, the World Health Organization and American College of Obstetricians and Gynecologists recommend standard delayed cord clamping in the delivery room for newborns who do not need resuscitation [11]. However, there are concerns about this procedure in neonates needing resuscitation & preterm babies having a chance of hypothermia. In such patients, an alternative that can provide the newborn with the desired additional volume of blood is called UCM [11]. In this study, it was found a decreased need for blood transfusion in preterm babies in whom cord milking was done. In a systemic review [12] it was seen Cord milking, when compared with immediate cord clamping, reduced the need for packed RBC Transfusions. A vast majority of research found delayed umbilical cord clamping effective in preventing the occurrence of anemia. With this concern, it should be reminded that preterm children 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 [13]. This study showed a significantly higher level of haematocrit in cord cord-milking group. Previous studies [14] support this study showing higher levels of birth haemoglobin and haematocrit levels in those babies who underwent cord milking. The greatest barrier to the clinical application of placental transfusion is the long-held belief that over-transfusion can lead to symptomatic polycythaemia and hyperbilirubinemia. In this study, jaundice was found in both groups all of them needed phototherapy but no one needed exchange transfusion but there was no significant difference in both groups. Research done by Erickson-Owens showed similar findings that there was no report of symptomatic polycythaemia and no significant differences between the immediate cord clamping and cord milking groups in the incidence of clinical jaundice, peak TSB levels, hyperbilirubinemia requiring hospitalization or readmission for phototherapy. This study did not show a significant difference between initial respiratory distress & need for oxygen. However, a significant number of patients in the non-milking group needed assisted ventilation later on. But in another study [14] umbilical cord milking managed to significantly reduce the frequency of RDS. In Middleton's study [15], the number of infants hospitalized in NICU due to RDS was about the same in both groups (1-3 cases).

In Spear's investigation, a similar number of neonates showed to have symptoms of RDS [16]. Postpartum respiratory care is currently changing from intubation to Continuous Positive Airway Pressure ventilator (CPAP) or intubation and prescription of surfactant, immediate removal of the tube and CPAP [17].

Cord milking appears to be a viable alternative to delayed cord clamping when timing is critical. In our study, we found that milking the cord took <20s. It demonstrated significantly higher haematocrit levels within 6 hours of life when compared with infants with no milking.

These findings suggest that cord milking is easy to implement and takes only a few seconds to improve an infant's hematologic status [18]. The pathogenesis of ROP is multifactorial. Blood transfusion increases the risk of ROP in newborns. This effect has been attributed to increased delivery of oxygen, iron, and free radicals of oxygen to the retina [19]. Recently, with improvement in neonatal care, the survival rate of extremely premature infants, who are in the high-risk group for ROP development, has increased [20]. The previous study showed no significant correlation between Umbilical cord milking & ROP but more neonates required laser treatment in the non-UCM group. This single-center, RCT showed a lower incidence of ROP in premature babies who underwent Umbilical cord milking after delivery. Only two patients from the Milking group developed ROP & needed treatment. On the other hand, 11 patients in the non-milking group developed ROP. Among them in one patient ROP regressed spontaneously, rest ten needed treatment either inj. Bevacizumab or LASER. A previous study showed that birth haemoglobin and hematocrit levels, neonatal blood pressure and clinical symptoms including neonatal jaundice requiring phototherapy and polycythemia 48 hours after the birth were higher in the cord milking group than the non-milking group [14]. In this study, it was seen that there was a higher level of hematocrit done within 6 hours of birth. The need for blood transfusion was significantly lower in the milking group. By cord milking extra amount of blood was transferred to the baby, which increased the level of hematocrit & reduced the need for blood transfusion. Ultimately ROP was reduced.

Limitations

Single-centre study.

Conclusion

This study concluded that umbilical cord milking after delivery improves haematocrit levels, reduces the need for blood transfusion & reduces the rate & severity of ROP in preterm infants.

So umbilical cord milking helps preterm babies improve their hematocrit level and reduces the need for blood transfusion & assisted ventilation. By reducing all of these risk factors it reduces ROP.

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