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Comparing delayed cord clamping and umbilical cord milking during elective cesarean section for the neonatal outcome

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ABSTRACT

Objectives: to compare between immediate cord clamping, delayed cord clamping, and umbilical cord milking and their effects on hemoglobin and bilirubin level in term infants in cesarean section.
Study design: A randomized clinical trial was conducted from November 2021 to June 2022, including 162 full term pregnant women undergoing elective cesarean section at EL-Shatby Maternity University Hospital. They were randomly assigned (1:1:1 ratio) either to immediate cord clamping just after delivery (Group 1) or delayed cord clamping for 30 s (Group 2) or umbilical cord milking 10 times for 10–15 s (Group 3). The primary outcome measures included hemoglobin and hematocrit levels of the newborn at birth and the secondary outcome was bilirubin level measurement at 72 h of life.
Results: one hundred sixty- two newborns were randomized into 3 groups, fifty-four cases in each, and were investigated on hemoglobin and hematocrit levels; five were lost to follow-up and one hundred fifty-seven were tested for bilirubin. Participants among groups had no significant difference regarding demographic and clinical characteristics, regarding the hemoglobin at birth it was significant higher in the umbilical cord milking group (Group 3) through all groups (14.91 ± 0.91 g/dl vs15.38 ± 0.74 g/dl vs 16.56 ± 1.03 g/dl, p value <0.001), regarding hematocrit level at birth it was significant in the umbilical cord milking group (Group 3) through all groups (44.71 ± 2.94 vs 46.48 ± 2.61 vs 49.74 ± 3.26, p value <0.001). On the other hand, bilirubin level after 72 h had no significant different through the 3 groups (8.80(IQR 4.50–17.20), vs 9.70(IQR3.50–14.70), vs 8.50 (IQR 3.20–19.50), respectively p value= 0.348)
Conclusion: this study showed that umbilical cord milking 10 times for 10–15 s is more effective than delayed cord clamping for 30 s in enhancing hemoglobin and hematocrit levels in newborn delivered by cesarean section with no significant difference on bilirubin level in the newborn.

Introduction

The timing of cord clamping has been a controversial for decades [1]. about 40% of a term newborn's blood volume stays behind in the placental unit when the umbilical cord is early clamped and cut at birth [2] When delayed cord clamping or umbilical cord milking is done at birth, newborns gain a placental transfusion leading to approximately a 20–30% increase in blood volume and a 50% increase in red cell volume [3,4] This vital transfusion of red blood cell stores is essential for anemia prevention, which is a prevalent medical disorder in infants especially in the low and middle-income countries [5]. Iron deficiency anemia remains a major public health problem in young children because of its association with poor neurodevelopment [6], and diminished long-term behavioral and developmental outcomes [7].

According to World Health Organization (WHO), caesarean section use continues to increase globally, it is accounting now for more than 1 in 5 (21%) of all childbirths [8]. This global increase in the number of elective cesarean sections (CS) raises the question about the timing of umbilical cord clamping. [9] Despite the universal call for approving delayed cord clamping (DCC) as the standard of care, the large percentage of neonates born via cesarean are rarely afforded that option, likely because of the concern for maternal bleeding from the uterine incision in the critical minutes that cord clamping is delayed [10]. At the current high rate of cesarean delivery, a lot of newborns are potentially

Abbreviations: ICC, Immediate cord clamping; DCC, Delayed cord clamping; UCM, Umbilical cord milking.

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deprived of the important benefits of DCC.

The American college of obstetricians and gynecologists (ACOG) recommends a delay in umbilical cord clamping in vigorous term infants for 30–60 s after birth, and umbilical cord milking or stripping has been intended as a method of achieving increased placental transfusion to the newborn in a rapid time frame usually less than 10–15 s [11].

The Optimal placental transfusion is feasible in vaginal deliveries due to good uterine tone, and availability for waiting at least 3 min after delivery before cutting the cord [4,12] However, this is not feasible in cesarean section (CS), the placental transfusion is reduced due to maternal hypotension and insufficient uterine contractions[13,14]. In such deliveries, umbilical cord milking (UCM) can be used instead, with UCM increasing blood volume may result in similar benefits as delayed cord clamping (DCC) does in vaginal deliveries.[15,16] including improved blood and red cell volume, red blood cell counts and hemoglobin and hematocrit levels.

Aim of the study

The aim of this study is to compare between immediate cord clamping, delayed cord clamping and umbilical cord milking and their effects on hemoglobin and bilirubin level in term infants delivered by cesarean section.

Patients and methods

This prospective, randomized study was conducted at EL-Shatby Maternity University Hospital in Alexandria from November 2021 to July 2022. We obtained an approval to our study protocol from Ethics Committee of the faculty of Medicine at Alexandria University with a registration serial number:0106748 IRB NO:00012098 -FWA NO:00018699 as well as all study participants signed an informed written consent after being informed regarding the trial interventions. We included a total of 162 full term pregnant women undergoing cesarean section who were admitted to hospital for delivery.

Mothers were screened for eligibility. The eligibility criteria included: pregnancy with a healthy singleton, gestational age of 38–41 0/7 weeks, an uncomplicated pregnancy and The mother's age (20−40) years. Exclusion criteria included were maternal and fetal criteria. The maternal criteria were: any medical or obstetrical complications like hypertension, pre-eclampsia, diabetes, smoking, and substance abuse, Rh-negative mothers. while fetal criteria involve fetus with evidence of intrauterine growth restriction, and infant with serious congenital anomalies.

Methods

All cases in the 3 studied groups were subjected after admission to full history taking and general examination,Obstetric ultrasound to confirm fetal presentation, assess fetal growth status, amniotic fluid index, fetal biometry including biparietal diameter, head circumference and femur length for IUGR identification and exclusion if found, Laboratory investigations for all pregnant females including: Complete blood counts (CBC) at the time of admission,Measurement of coagulation profile including prothrombin time (PT), activated partial thromboplastin time (APTT) and international normalized ratio (INR), determination of ABO blood grouping and Rh by blood typing tests to exclude mothers with negative Rhesus. The mothers were randomly divided and allocated to immediate cord clamping(ICC), delayed cord clamping (DCC) for 30 s, and umbilical cord milking (UCM) at random 1:1:1 ratio after choosing a card from three cards in a bowl.

Group 1(ICC group)

include 54 pregnant women receive immediate cord clamping we defined that immediate cord clamping was done directly after delivery.

Group 2 (DCC group)

include 54 pregnant women receive delayed cord clamping we defined delayed cord clamping is done 30 s after delivery of the newborn. the newborn is covered with sterile towels and held by the obstetrician in prone position on the maternal abdomen and the time was measured for 30 s during which rubbing of newborn back to promote crying to take place then cut the cord.

Group 3 (UCM group)

include 54 pregnant women receive cord milking in which stripping of the umbilical cord 10 times in the direction of the infant in time frame of 10–15 s the newborn is covered with sterile towel and milking of the umbilical cord is done by the obstetrician 10 times from maternal side to the fetal side in time frame of 10 s and then the cord is cut.

the time between uterine incision and delivery of the newborn, and the timing for clamping of the umbilical cord was measured using a stopwatch.

All the newborns (n = 162) were compared among the three groups, in which cord blood sample for complete blood count is taken from the cord after resuscitation of the newborn by the neonatologist to assess the hemoglobin and hematocrit level at birth. A total serum bilirubin test (TSB) is done at day 3 of delivery, 5 cases were dropped out because they didn't catch up with follow-up in the total serum bilirubin results, and the number of new born become (n = 157). A flow diagram describing the participants flow through the study is shown in Fig. 1.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Qualitative data were described using number and percentage. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Chi-square test for categorical variables, to compare between different groups F-test (ANOVA) for normally distributed quantitative variables, to compare between more than two groups, and Post Hoc test (Tukey) for pairwise comparisons. Kruskal Wallis test for abnormally distributed quantitative variables, to compare between more than two studied groups, and Post Hoc (Dunn's multiple comparisons test) for pairwise comparisons. Significance of the obtained results was judged at the 5% level.

Results

During the study period, 249 women were assessed for eligibility, following which 162 were eligible. Of these 162 women who were eligible, 54 newborns were randomized into each group and 5 were lost to follow-up.

The basic demographic and clinical data of the three studied groups maternal age, gestational age, parity, mode of previous delivery show insignificant difference between the three studied group (Table 1). The maternal investigation of the three studied groups showed that complete blood count (which include hemoglobin, hematocrit and platelets) and coagulation profile (which include PT, P activity %, INR) show insignificant difference between the three studied groups, as shown in (Table 2). The Time taken from uterine incision till the neonatal team receive the fetus show significant difference between the three groups the median was 55.0 (IQR 33.0 – 75.0) in the ICC group, in the DCC group was 79.0 (IQR 47.0 – 155.0) and in the UCM group 58.50 (IQR 40.0 – 150.0). as shown in (Table 3). The neo natal laboratory findings showed that hemoglobin was significantly higher in UCM with mean 16.56 ± 1.03 than ICC group with mean 14.91 ± 0.91and DCC group with mean15.38 ± 0.74 (p value <0.001). Also, the hematocrit level was significant higher in the UCM group with mean 49.74 ± 3.26 than ICC group with mean 44.71 ± 2.94 and DCC group mean 46.48 ± 2.61 (p value <0.001), on the other hand the bilirubin level showed no significant difference between the three groups [ICC 8.80(IQR

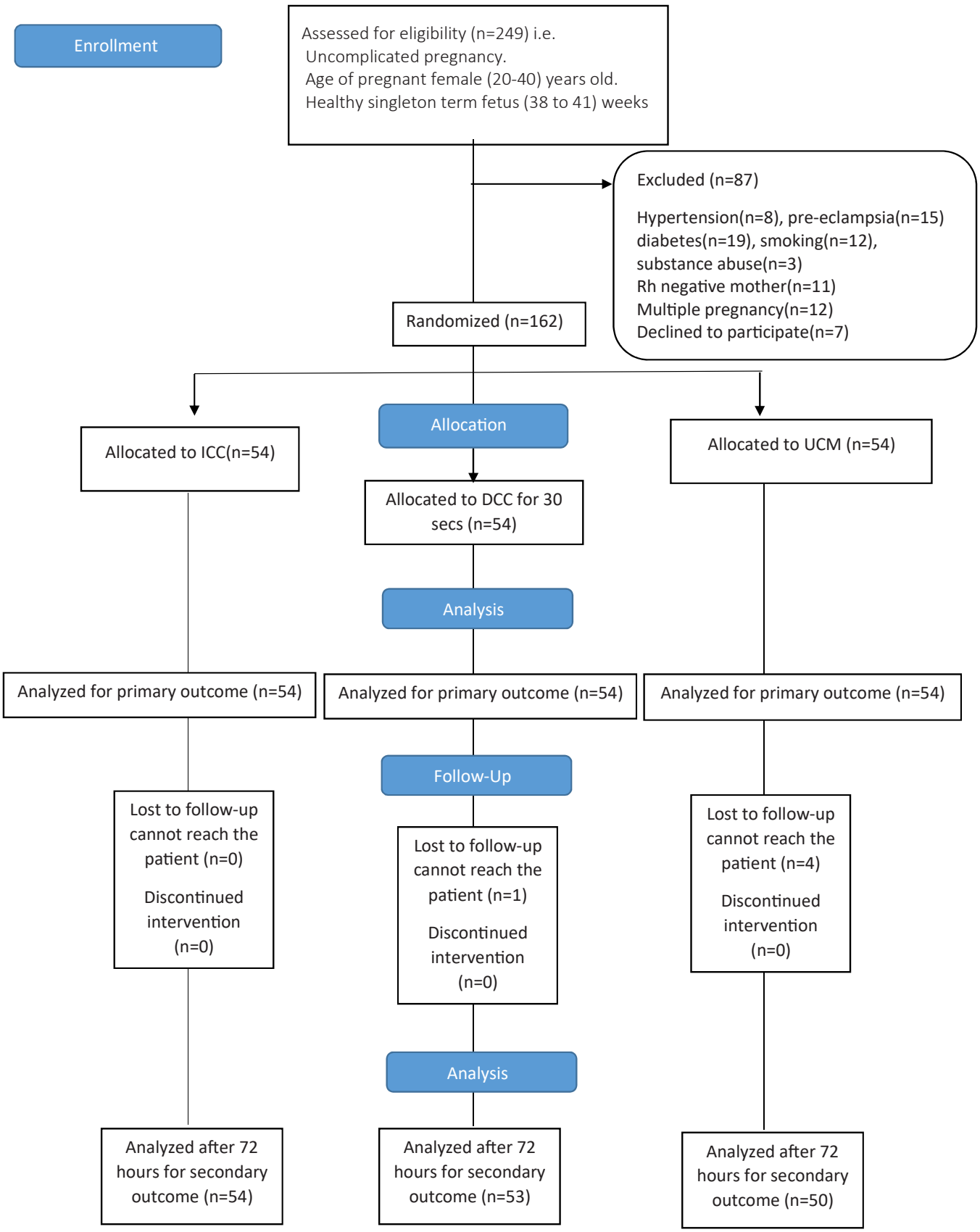

Fig. 1. CONSORT participants' included in the study.

Table 1
Baseline demographic and clinical data of the participants.

Parameters	ICC (n = 54)	DCC (30 s) (n = 54)	UCM (n = 54)	p
Maternal age (mean ± SD)	27.59 ± 5.28	26.52 ± 5.65	26.33 ± 5.24	0.426
Maternal gestational age (weeks)	38.0 (37.0 – 40.0)	38.36 (37.0 – 40.0)	38.14 (36.71 – 40)	0.474
Previous mode of delivery				
i. Primi	18 (33.3%)	18 (33.3%)	16 (29.6%)	0.253
i. Previous caesarian section	33 (61.1%)	29 (53.7%)	27 (50%)	
i. NVD	3 (5.6%)	7 (13%)	11 (20.4%)	
Parity				
i. Primi	15 (27.8%)	18 (33.3%)	15 (27.8%)	0.766
i. Multi	39 (72.2%)	36 (66.7%)	39 (72.2%)	

IQR: Inter quartile range SD: Standard deviation
p: p value for comparing between the different studied groups

Table 2
Maternal investigations among studied groups.

Maternal investigations	ICC	DCC (30 s)	UCM	p
	(n = 54)	**(n = 54)**	**(n = 54)**	
Mean hemoglobin (g/dl)	11.38 ± 1.20	11.44 ± 1.12	11.01 ± 1.12	0.115
	(n = 54)	**(n = 54)**	**(n = 54)**	
Mean hematocrit (%)	33.51 ± 2.82	33.74 ± 2.77	33.31 ± 2.87	0.721
	(n = 54)	**(n = 54)**	**(n = 54)**	
Platelets (x10^3)	231.93 ± 53.64	238.06 ± 55.85	229.56 ± 46.49	0.683
	(n = 54)	**(n = 54)**	**(n = 54)**	
PT /sec	11.60 (9.70 – 13.80)	11.60 (11.1 – 12.6)	11.60 (10.8 – 13.4)	0.778
	(n = 54)	**(n = 54)**	**(n = 54)**	
P activity %	100 (74.10 – 113.0)	100.0 (87.0 – 107.0)	100.0 (84.2 – 112.0)	0.413
	(n = 54)	**(n = 54)**	**(n = 54)**	
INR	1.0 (0.90 – 1.20)	1.0 (0.96 – 1.08)	1.0 (0.93 – 1.11)	0.391
Blood group				
A	22 (40.7%)	15 (27.8%)	17 (31.5%)	$^{MC}p = 0.536$
B	13 (24.1%)	16 (29.6%)	13 (24.1%)	
AB	4 (7.4%)	1 (1.9%)	3 (5.6%)	
O	15 (27.8%)	22 (40.7%)	21 (38.9%)	

IQR: Inter quartile range SD: Standard deviation
MC: Monte Carlo test
p: p value for comparing between the different studied groups

4.50–17.20), vs DCC 9.70(IQR3.50–14.70), vs UCM 8.50(IQR 3.20–19.50), p value= 0.348].

Discussion

The timing of the clamping and cutting of the umbilical cord has a significant impact on the infant's blood and red cell volume and early iron stores.[4,17,18] The placenta serves as the blood reservoir designed to meet this immediate demand for increased blood volume. A delay in cord clamping or cord milking increases placental transfusion and results in a 20–30% increase in whole blood and a 50–60% increase in red blood cell volume.[4]UCM may be a better alternative when DCC is not feasible in case of cesarean section delivery.

Our study was randomized controlled trial which include 162 pregnant women who were randomized by ration 1:1:1 in to 54 cases received ICC,54 received DCC for 30 s and 54 received UCM for 10–15 s, our aim was to compare hemoglobin and hematocrit level in the

Table 3
Time of cord clamping, Infant characteristics at birth and outcomes.

Parameter	ICC (n = 54)	DCC (30 s) (n = 54)	UCM (n = 54)	P
	No. %	No. %	No. %	
Time from uterine incision till clamping of cord/ sec(median)	55.0 (33.0 – 75.0)	79.0 (47.0 – 155.0)	58.50 (40.0 – 150.0)	< 0.001*
Sig. bet. grps	$p_1 < 0.001$*, $p_2 = 0.096$, $p_3 < 0.001$*			
Infant gender				
i. Male	32 (59.3%)	19 (35.2%)	28 (51.9%)	0.037*
i. Female	22 (40.7%)	35 (64.8%)	26 (48.1%)	
Mean infant hemoglobin at birth (g/dl)	14.91 ± 0.91	15.38 ± 0.74	16.56 ± 1.03	< 0.001*
Sig. bet. grps	$p_1 = 0.022$*, $p_2 < 0.001$*, $p_3 < 0.001$*			
Mean infant hematocrit at birth (%)	44.71 ± 2.94	46.48 ± 2.61	49.74 ± 3.26	< 0.001*
Sig. bet. grps	$p_1 = 0.006$*, $p_2 < 0.001$*, $p_3 < 0.001$*			
Infant blood group				
A	24 (44.4%)	11 (20.4%)	17 (31.5%)	$^{MC}p = 0.165$
B	11 (20.4%)	14 (25.9%)	13 (24.1%)	
AB	1 (1.9%)	4 (7.4%)	1 (1.9%)	
O	18 (33.3%)	25 (46.3%)	23 (42.6%)	
Rh				
Positive	54 (100%)	52 (96.3%)	52 (96.3%)	$^{MC}p = 0.543$
Negative	0 (0%)	2 (3.7%)	2 (3.7%)	
	(n = 54)	**(n = 53)**	**(n = 50)**	
Infant bilirubin 72 hrs after birth(median)	8.80 (4.50 – 17.20)	9.70 (3.50 – 14.70)	8.50 (3.20 – 19.50)	0.348

IQR: Inter quartile range SD: Standard deviation
MC: Monte Carlo
p: p value for comparing between the different studied groups
p_1: p value for comparing between ICC and DCC (30 s)
p_2: p value for comparing between ICC and UCM
p_3: p value for comparing between DCC (30 s) and UCM
* : Statistically significant at $p \leq 0.05$

neonates at birth in the 3 groups and their bilirubin level after 72 hrs. We found that the hemoglobin and hematocrit levels were the highest in the UCM group in comparison to the other two groups and the bilirubin level has no significant difference among the three groups.

No static factors for hemoglobin and hematocrit measurements were obtained in studies, most of the studies showed a different time in DCC group, studies in Consonni S et al. [19], Cavallin F [20], De Bernardo et al. [21], the DCC was at 60 s, Shao et al. [22] the DCC was 30–60 s in one group and the other group DCC 60–120 s

In study by Erickson-Owens, D. A.[23] it was reported that Hematocrit level at 36–48 h was higher in UCM when compared with ICC (57.5% ± 6.6 vs 50.0% ± 6.4 respectively P = 0.01), in his trial on 24 women scheduled were delivered by elective cesarean section and randomized to either immediate clamping (<10 s) or UCM 5 times at birth. Another study by Zandros et al. [24] had measured the hematocrit level at birth and after 48 hr of delivery they reported that on comparison between UCM and ICC groups (n = 130) in newborns delivered by elective cesarean section that hematocrit level in cord blood at delivery was measured (UCM, 44.5 ± 4.8 vs. ICC, 44.9 ± 4.2, p = 0.74),which mean no difference in the hematocrit level between the 2 groups, which was against results in our study, but on measuring hematocrit level at 48 h of age, a capillary heel sample was taken and showed the UCM group had significantly higher hematocrit values (UCM, 53.7 ± 5.9 vs.

ICC, 49.8 ± 4.6%, $p < 0.001$). Furthermore, Consonni S et al. [19] reported in their study that UCM significantly increased hematocrit level after 48 hrs when compared to ICC (61.82% ± 5.19 in UCM vs 57.14% ± 5.96 in ICC, $P = 0.001$) while the delayed cord clamping did not increase hematocrit level after 48 hrs (57.61% ± 6.22 in DCC vs 57.14% ± 5.96 in ICC, $P = 0.66$). Also, Cavallin F [20] reported in his study that hematocrit at day 2 was significantly higher in the DCC 60 s than in the ICC (DCC 54 ± 6 vs ICC 48 ± 5 $p < 0.0001$). Also, De Bernardo et al. [21]reported in their study on 132 newborns that DCC after 60 s has higher hematocrit after 72 h than ICC with mean (56.71 ± 6.663 vs 51.56 ± 6.929 respectively; $p < 0.05$).

Nevertheless, in a study by Shao et al. [22] serial measurement of hemoglobin and hematocrit levels from day 0 to day 3 after birth were done and it showed no significant difference in the hematological values with p value > 0.05,and they found that Increasing the duration of cord clamping from 60 s to 120 did not increase hemoglobin and hematocrit levels but led to a decreasing trend, which may be the result of placental blood flow reflux. Clamping the cord at 30–60 s in cesarean section was a better choice rather than 61–120 s

In concern with the bilirubin levels, in our study we measured the bilirubin levels at 72 hrs after delivery and it showed no significant difference in the bilirubin level between the three groups. Some studied measured TSB at 48 hrs, Zandros et al. [24] reported in their study that the mean of TSB levels at 48 hrs among the UCM and ICC groups (7.40±2.12 vs. 7.17±1.87) p=0.57 which showed no significant difference, and only one infant in UCM group received a brief course of phototherapy and no further treatment was necessary.

Other studies measured TSB after 72 hrs, Cavallin F [20] reported that bilirubin at day 3 was slightly higher in the DCC 60 s (DCC 7.6 ± 2.9 vs ICC 6.4 ± 2.6 p value= 0.05) and no infants needed phototherapy for hyperbilirubinemia during their hospital stay. Also, Consonni S et al. [19] reported that bilirubin level has no significant difference between groups (ICC 7.69 ± 3.65,DCC 8.19 ± 3.54 with p value 0.439) and (ICC 7.69 ± 3.65, UCM 9.05 ± 3.32 with p value 0.103).

On the other hand De Bernardo et al. [21]reported an increase in bilirubin after 72 hrs in DCC 60 s but without need of phototherapy (DCC 60 sec 8.54 ± 2.90 vs ICC 7.06 ± 2.76; $p < 0.05$). Also, in a Cochrane study by McDonald SJ [25] it was reported that delaying cord clamping was associated with an increased bilirubin level and the need for phototherapy, but Cavallin F [20] reported that bilirubin was slightly higher in the DCC than in the ICC but no infant needed phototherapy. Also, in a study by Machiko Nakagawa et al. [26] they reported that Newborns with high cord blood hemoglobin had a high incidence of phototherapy.

The effect of our study that umbilical cord milking is a quick, easy method to deliver placental blood transfusion for the infant after delivery in a rapid short time, which is not influenced by the situation of the cesarean section where opened surgical wound, bleeding, maternal hypotension and decreased uterine contractions took place. Also, the cord blood sample that is taken at birth is easy, quick, non-injurious for the infant and give an idea about the hematological status of the infant with the same results like central venous sample or heel capillary sample which are more uncomfortable and injurious to the infant.

Conclusion

umbilical cord milking 10 times for 10–15 s help in enhancing hemoglobin level with no effect on bilirubin level in the newborn this short time serve an easy way in the protection of newborn from anemia and improve iron stores in the first months of life and so the umbilical cord milking is an effective strategy for placental transfusion in elective cesarean section.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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