

Full Length Research Paper

Delayed Cord Clamping: The Potential Effects on The Maternal Postpartum Blood Loss and Neonatal bilirubin and Hemoglobin Concentrations

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Background: The optimal timing of umbilical cord clamping has been debated in the scientific literature. There are positive and negative outcomes of delayed cord clamping so, the need for an evidence-based, optimal cord clamping time is growing. **The work aims** to explain the impact of delayed umbilical cord clamping on neonatal hemoglobin and bilirubin and maternal post-partum hemorrhage. **Methods:** 200 cases were enrolled in this research and were split into two groups (I) containing 100 women treated by early cord clamping (30 seconds) and group (II) containing 100 women treated by delayed cord clamping (3 minutes). **Results:** Birth weight ranged from 2.630 to 3.600 kg, with a mean 3.300 ± 0.160 in group I and 3.284 ± 0.186 kg group II, respectively. Maternal blood loss ranged from 300 to 550 cc, with an average of 414.50 ± 58.47 vs. 425.00 ± 57.04 cc in group I and II, respectively. Neonatal hemoglobin ranged from 12.90 to 19.0 g/dl, and there was a significant low level of hemoglobin in early compared to the late cord clamping group (14.49 ± 0.75 vs. 16.14 ± 1.16 respectively). Serum bilirubin ranged from 1.2 to 9.5, and a statistically significant decrease in early compared to the late-cord clamping group was found (2.80 ± 1.47 vs. 4.92 ± 1.88 respectively). **Conclusions:** delayed cord clamping is an easy, effective, and safe procedure. It resulted in decreased anemia and increased blood volume, and increased iron-rich red cell volume in infants.

Keywords: Delayed clamping; neonatal hemoglobin; neonatal bilirubin; postpartum hemorrhage; third stage of labor

Introduction

The best umbilical cord clamping time has been controversial in the scientific literature for nearly 2 decades; many theories have been told about the best umbilical cord clamping time^[1]. "Early" clamping of the umbilical cord is commonly performed in the 1st minute post-delivery (within the first 15–30 seconds), while "delayed" clamping of umbilical cord is done more than 60 seconds after the birth or when the cord ceased pulsation^[2]. The early clamping has the disadvantages of increased risk of hypovolemia, high incidence of acidemia, infant anemia, development of type ii diabetes, hypoxic-ischemic childhood mental disorders, several blood disorders, brain damage, iron loss, and an elevation in the probability of feto-maternal transfusion as the volume of blood that remains in the placenta is large^[3].

The routine practice in the last decade is delayed umbilical cord clamping because its has a good effect on stability of the neonatal cardiovascular function, hematocrit and decreased rates of hypochromic anemia that develop in the first 3 months after birth, which occurs due to the iron deficiency in the exclusively breastfeed infants^[4]. The English physician Erasmus Darwin in the early 19th century mentioned "another thing very injurious to the child is the tying and cutting of the navel string too soon, which should always be left till the child has not only repeatedly breathed but till all pulsation in the cord ceases. As otherwise, the child is much weaker"^[5]. "Active management of the third stage (AMTSL) is a group of procedures which appeared in the 1960s, and was done to decrease postpartum hemorrhage. This group of procedures consists of three components: 1) immediate cord clamping, 2) delivery of the placenta by controlled cord traction and 3) administration of uterotonic drugs. These procedures were practiced around the world in both developing and developed countries as an sufficient procedure to reduce mothers' death from postpartum hemorrhage^[6].

Also, in a recent study on the delay of the cord clamping, placental transfusion improved the status of the infant's iron for about six months as this allows enough iron reserves for the first 6–8 months after birth. This hinders or postpones the appearance of iron deficiency until other treatment method –such as the use of iron-fortified foods– can be applied^[7].

In the full term newborns, umbilical cord clamping at 1 or 3 minutes after birth leads to elevation in the levels of venous hematocrit obtained at 6 hours, within physiological levels, and the neonatal anemia was decreased without injury to mothers or infants^[8]. After early cord clamping, marked bradycardia occurred and a brief rise in carotid arterial pressure occurred at the same time. This was sequenced by decrease in the blood pressure, and a reduction in cerebral circulation and cardiac output^[9]. The delayed clamping of the umbilical cord has raised concern after worldwide application. Delayed umbilical cord clamping might postpone the resuscitation efforts, if wanted, particularly in preterm infants. On the other hand, the placenta continues its function

to exchange gas post-delivery. As a result, sick and preterm newborns may profit from extra blood obtained from persistent placental transfusion^[10].

In addition, researchers have also raised interest regarding increased risks for diseases such as polycythemia in these newborns^[11, 12]. Even though, in some studies, there is a mild increase in the development of jaundice that needs phototherapy in full-term newborns so, benefits and drawbacks of delayed cord clamping are becoming well known within the medical field and the need for an evidence-based, optimal cord clamping time is growing^[13].

Aim of this study

The study aims to explain the impact of delayed clamping of umbilical cord on neonatal hemoglobin and bilirubin and maternal post partum hemorrhage.

Patients and methods

This study is a prospective case-controlled performed in Al Azhar University Hospital's casualties, Department of Obstetrics and Gynecology, New Damietta. This study included 200 women and the cases were selected in the period from 1st of May 2018 to the end of May 2019.

The study was conducted according to the Ethical Committee, and After explanation of the study to the patients and before sharing in the study a written consent was taken from all cases, medical history in details was taken and a general physical examination was performed.

Inclusion criteria:

Singleton pregnancy.

Cephalic presentation.

Expected vaginal delivery at term.

The absence of history of medical disease (hypertension, preeclampsia and diabetes) or complications; and the absence of intrauterine growth restriction or congenital malformations.

Exclusion Criteria:

Women with any of the following criteria were excluded from the study:

Preterm labour.

Instrumental delivery.

Caesarean section (previous or planned in current pregnancy).

Anaemia (Hb less than 8gm/dl). The presence of surgical/medical disease, or any other complications including obstetric complications that require early cord clamping (Rh multiple pregnancy, sensitized pregnancy and severe preeclampsia/eclampsia).

If the circulation of the placenta is malfunctioning as in placental abruption, umbilical cord avulsion or abnormal placentation.

The need for immediate resuscitation of the newborn or maternal hemodynamic instability.

Patients:

200 cases were enrolled in this research and were split into two groups:

Group (I):100 women will undergo early cord clamping (30 seconds).

Group (II):100 women will undergo delayed cord clamping (3 minutes).

Outcome Measures

The infant hematocrit at 24 hours after birth.

Plasma level of bilirubin at 24 hours after birth.

The postpartum maternal blood-loss volume, the assistant records the evaluated maternal blood loss postpartum in about two hours after delivery by weighing sheets, pads and other fabrics, and by estimating the blood volume collected in a pan.

Pediatricians assessing the outcomes were unaware of the assigned interventions. The time was calculated using a stopwatch and the time starts with complete delivery of the infant. During this time, the infant was hold supine at the level of the introitus. In the late cord clamping group, the infant was placed on a table at the level of the introitus, and the infant was dried and wiped with a sterile warm towel.

Statistical analysis

Data were tabulated and analyzed using Statistical Program for Social Science (SPSS Inc. USA) version 24. Qualitative data were expressed as frequency and percentage. Quantitative data were expressed as mean± standard deviation (SD). T-tests was used when comparing between two means. A one-way analysis of variance (ANOVA) when comparing between more than two means. Chi-square test was used when comparing between non-parametric data. P-value < 0.05 was considered significant. P-value > 0.05 was considered insignificant.

Results

In the present study, the maternal age ranged from 20 to 34 years and the results showed no significance among early cord clamped and late cord clamped infants (27.92±2.32 vs 28.08±2.75 years respectively). Gestational age at delivery ranged from 37

to 41 years, and no significance was found among early cord clamped and late cord clamped infants (38.66±1.08 vs 38.42±1.02 weeks, respectively). Neonatal birth weight ranged from 2.630 to 3.600 kg and no significance was found among early cord clamped and late cord clamped infants (3.300±0.160 vs 3.284±0.186 kg respectively) (table 1).

The neonates were 96 males (48.0%) and females were 104 (52.0%) and no significance was found among early cord clamped and late cord clamped infants (males represented 52.0% and 44.0% of early and late groups respectively) (table 2). Maternal blood loss ranged from 300 to 550 cc and there no significance was found among early cord clamped and late cord clamped infants (414.50±58.47 vs 425.00±57.04 respectively) (table 3).

Regarding APGAR score at first minute ranged from 7 to 9 and no significance was found among early cord clamped and late cord clamped infants (7.85±0.72 vs 7.96±0.58 respectively). In addition, at the fifth minute, APGAR score ranged from 8 to 10 and there no significance was found among early cord clamped and late cord clamped infants (9.38±0.55 vs 9.52±0.52 respectively) (table 4).

Neonatal hemoglobin ranged from 12.90 to 19.0 g/dl and there was statistically significant decrease of hemoglobin in early when compared to late cord clamping group (14.49±0.75 vs 16.14 ± 1.16 respectively). Neonatal hematocrit ranged from 46.44 to 68.40 and there was statistically significant decrease in early when compared to late group (52.18±2.70 vs 58.15±4.17 respectively) (table 5).

Regarding the number of RBCs, it ranged from 4.45 to 6.55 x 10⁶ and there was statistically significant decrease in early when compared to late group (5.00±0.26 vs 5.57±0.40 respectively). On the other hand, no significance was found among early cord clamped and late cord clamped infants as regard to mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC). The platelets ranged from 220 to 270 x 10³ and there was no significance among early cord clamped and late cord clamped infants (243.90±9.70 vs 242.69±10.21 respectively). WBCs ranged from 12 to 19 x 10³ and no significance was found among early cord clamped and late cord clamped infants (14.81±1.58 vs 14.84±1.57 respectively) (table 5).

The serum bilirubin ranged from 1.2 to 9.5 and there was statistically significant decrease in early when compared to late-cord clamping group (2.80±1.47 vs 4.92±1.88 respectively) (table 5).

Table (1): Relation between groups regarding maternal age (year), gestational age at delivery, and birth weight (kg)

		Mean	SD	Min	Max	t	p
Maternal age (year)	Early	27.92	2.32	24	33	0.44	0.66
	Late	28.08	2.75	20	34		
	Total	28	2.54	20	34		
Gestational age at delivery	Early	38.66	1.08	37	41	1.62	0.11
	Late	38.42	1.02	37	40		
	Total	38.54	1.05	37	41		
Birth Weight (kg)	Early	3.3	0.16	2.89	3.6	0.64	0.51
	Late	3.284	0.186	2.63	3.54		
	Total	3.292	0.173	2.63	3.6		

Table (2): Comparison between studied groups regarding neonatal gender

Neonatal sex		Group				Total	
		Early		Late		No.	%
		No.	%	No.	%		
Male	52	52.0%	44	44.0%	96	48.0%	
Female	48	48.0%	56	56.0%	104	52.0%	
Statistics		X ² = 1.28				p = 0.25	

Table (3): Comparison between studied groups regarding maternal blood loss (cc)

	Mean	SD	Min	Max	t	p
Early	414.50	58.47	300.00	550.00	1.28	0.20
Late	425.00	57.04	350.00	550.00		
Total	419.75	57.85	300.00	550.00		

Table (4): Comparison between studied groups regarding neonatal APGAR score at first and fifth minutes

		Mean	SD	Min	Max	t	p
APGAR 1 st minute	Early	7.85	0.72	6.00	9.00	1.18	0.23
	Late	7.96	0.58	7.00	9.00		
	Total	7.91	0.65	6.00	9.00		
APGAR 5 th minute	Early	9.38	0.55	8.00	10.00	1.85	0.07

Late	9.52	0.52	8.00	10.00
Total	9.45	0.54	8.00	10.00

Table (5): Comparison between studied groups regarding neonatal hematological parameters and serum bilirubin

		Mean	SD	Min	Max	t	p
Hemoglobin	Early	14.49	0.75	12.9	16.2	11.95	<0.001*
	Late	16.14	1.16	13.8	19		
	Total	15.32	1.28	12.9	19		
Hematocrit	Early	52.18	2.7	46.44	58.32	12.02	<0.001*
	Late	58.15	4.17	49.68	68.4		
	Total	55.16	4.61	46.44	68.4		
RBCs	Early	5	0.26	4.45	5.59	11.97	<0.001*
	Late	5.57	0.4	4.76	6.55		
	Total	5.28	0.44	4.45	6.55		
MCV	Early	82.2	1.4	80	85	0.14	0.88
	Late	82.23	1.48	80	86		
	Total	82.22	1.43	80	86		
MCH	Early	32.52	1.94	29	36	0.31	0.75
	Late	32.43	2.1	27	36		
	Total	32.48	2.02	27	36		
MCHC	Early	35.82	1.78	33	39	0.4	0.68
	Late	35.92	1.73	33	40		
	Total	35.87	1.75	33	40		
Platelets	Early	243.9	9.7	227	270	0.85	0.39
	Late	242.69	10.21	220	270		
	Total	243.3	9.95	220	270		
WBCs	Early	14.81	1.58	12	19	0.13	0.89
	Late	14.84	1.57	12	19		
	Total	14.83	1.57	12	19		
Bilirubin	Early	2.8	1.47	1.2	7.1	8.89	<0.001*
	Late	4.92	1.88	1.2	9.5		
	Total	3.86	1.99	1.2	9.5		

Discussion

For many decades early cord clamping (ECC) has been performed. However, recent findings preferring delayed cord clamping (DCC) in terms and preterm newborns made many professional organizations like the American Academy of Pediatrics, World Health Organization, Royal American College of Nurse-Midwives and College of Obstetricians and Gynecologists, accrediting DCC as the recommended procedure for delivery and labor. Many benefits can be achieved to the newborn by a short delay in clamping of the cord, as the placenta can add about 100 mL of blood to the newborn, 80 mL of these delivered within the first minute^[14]. DCC is beneficial to term and preterm infants. Term infants experienced increased levels of hemoglobin at birth and improved iron stores for the six to seven months after birth^[15].

A meta-analysis study done by Hutton and Hassan at 2007 found that a period of 2 min or more of delayed clamping decreased the risk of iron store deficiencies by 33% and the risk of anemia by 47% at ages 2–3 months^[3]. In addition, it has been suggested that DCC elevates the supply of stem and progenitor cells and might be beneficial and non-invasive procedure for transplanting these cells to the infant to fight age-related and neonatal diseases^[16, 17]. Some studies have found that DCC in preterm infants leads to decreased demand for blood transfusions and decreased incidences of intraventricular hemorrhage and necrotizing enterocolitis^[9, 15]. The mentioned benefits were explained due to improved transitional circulation because clamping of the cord prior to the start of sufficient infant ventilation can lead to malfunction in cardiovascular function that may be harmful to the infant, especially for the pressure passive neonatal brain^[18]. On the other hand, some drawbacks for DCC infants include neonatal jaundice requiring phototherapy and an increase in polycythemia. The presence of polycythemia has been without symptoms, and the case is assumed harmless^[19]. DCC seems to mildly elevate the likelihood of developing severe neonatal jaundice that is treated by phototherapy but does not affect clinical jaundice's total risk as a disease^[15].

A study included 1634 preterm neonates proposed that DCC does not lead to a decrease in the likelihood of combined outcome mortality or significant morbidity at 36-week gestation than ECC neonates^[20]. Moreover, there wasn't increase in the incidence of increased maternal blood loss at delivery, postpartum hemorrhage, decreased levels of hemoglobin or requirement of blood transfusions, and the use of uterotonic drugs showed no significant difference^[15]. Delayed cord clamping is not widely performed in our daily practice, and its effect on neonates and mothers is not sufficiently addressed in our scientific community. So, the current research was designed to determine the Impact of DCC on fetal hemoglobin, bilirubin, and maternal post-partum blood loss. It included 200 females with a singleton, non-complicated pregnancy, cephalic presentation, and who expected to deliver at term. They were allocated randomly to equal groups; the first underwent early cord clamping (30 seconds) and the second

underwent delayed cord clamping (3 minutes). The study outcome included neonatal hematocrit, plasma bilirubin (at 24 hours), and postpartum blood loss (at two hours after delivery). Besides, the fetal outcome was documented. In previous literature, it was reported that umbilical cord clamping ≥ 60 s after delivery, were noticed to decrease anemia in newborns^[7] and highlighted as a very cost-effective procedure^[21, 22]. Furthermore, DCC has been found to improve social skill and the development fine motor function at 4 years of age^[23]. DCC also apparently protects against disability of motor function in very low birth weight male neonates, may be due to elevation in blood stem cell and red cell volumes^[24].

The guidelines of World Health Organization (WHO) in 2013 regarding maternal, newborn, child, and adolescent health recommend clamping the umbilical cord at 1–3 min after delivery^[25].

According to these guidelines, we choose to delay cord clamping to more than 3 minutes in the present work. Also, the rationale to investigate full-term neonates was based on the fact that, when neonates need an intervention for stabilization, the cord is quickly clamped to permit for such interventions.

This rationale was emphasized by **Nelin et al.**^[26] who reported that in the circumstances where the neonate underwent any intervention, DCC was not done. This is because in the conditions where the infant requires help for stabilization, the cord is clamped early to facilitate supplying care to the infant. **Hutchon**^[27] reported that DCC wasn't performed in neonates who underwent any interventions, as the infants who were requiring urgent resuscitative measures or asphyxiated were not included due to issues about their medical condition and health outcomes.

The early cord clamped and late cord clamped infants showed no significance in the present work regarding maternal and neonatal demographics. These results agree with **De Paco et al.**^[28] who reported that the late and early cord clamped groups in the maternal or fetal demographic data showed no significant differences. The present work results revealed that delayed cord clamping was accompanied with a favorable effect such as increased hematocrit, hemoglobin, and red blood cells, which collectively could guard against anemia in early life. On the other hand, there was a significant increase in serum bilirubin, which may load on the health care system of increased the need for phototherapy.

The present work results are comparable to those reported by **Nesheli et al.**^[29] who reported that DCC increases full term newborns' levels of hemoglobin and hematocrit. They attributed their findings to the relative transfer of plasma and red blood cells from the placenta to the neonate in the two groups. Also, they reported no significant difference between both groups as regard RBCs indices. Also, **Mcdonald et al.**^[15] reported that DCC improves iron storage, increases hemoglobin at birth, and reduces iron deficiency anemia in the first 12 months after birth when correlated to ECC.

Furthermore, in preterm neonates, **Popat et al.**^[30] reported that, newborns in the DCC group had a higher baseline Hb (16.7 g/dL vs 15.8 g/dL, $P < .001$) and higher hemoglobin at 6 hours (17.4 g/dL vs 16.0 g/dL, $P < .001$). Another study included 61 term neonates- 30 in Group I (during the first 15 seconds after birth the cord was clamped) and 31 in Group II (cord clamped immediately after cessation of pulsation or at 3 min of birth). Level of hemoglobin was obtained and measured from blood of cord post delivery immediately and one day after by heel prick method. The average level of hemoglobin of cases immediately after delivery was 17.15 ± 1.56 and 19.97 ± 1.51 in Group I and Group II, respectively ($p < 0.000$). The average level of hemoglobin one day after delivery was 16.97 ± 1.13 Group I and 19.59 ± 1.39 in and Group II ($p < 0.000$)^[31]. **Shirvani et al.**^[32] presented research on the timing of the cord clamping and its effect on infant's iron condition among 100 mother-infant pairs. They split the cases into 2 groups: early cord clamp time or delayed cord clamp time. The mean infant hemoglobin (Hgb; 16.08 g/dL vs. 14.5 g/dL; $P < 0.001$) levels were significantly increased in the DCC group. The Pan American Health Organization recommend DCC over immediate cord clamping. This procedure was found to be cost-effective, making it suitable and sustainable practice for developing countries.

The results of the present study reported that DCC in term neonates is accompanied by a significant rise in bilirubin and the need for phototherapy^[33]. A 2012 Cochrane review by **Rabe et al.** revealed that peak concentration of bilirubin was increased for neonates subjected to DCC because of increased placental transfusion; however, they also note that bilirubin levels at which treatment is initiated are likely to differ between centers and studies usually do not state criteria for treating hyperbilirubinemia^[9].

These infants have an increase in hematocrit within hours of delivery, and the increase in the red blood cells breakdown may contribute to the bilirubin load increase^[34]. Despite the risk of increased bilirubin load, delayed cord clamping benefits outweigh that risk in term neonates, as long as phototherapy is available to treat jaundice^[35].

The present work results revealed no significance among early cord clamped and late cord clamped infants regarding maternal blood loss (414.50 ± 58.47 vs. 425.00 ± 57.04 , respectively). These results are comparable to those reported by **Andersson et al.**^[36] who reported that the maternal hemorrhage in the two groups revealed no significant differences [median (range) 350 (100–6500) mL in the ECC group and 400 (150–2000) mL in the DCC group ($p = 0.3$)]. Also, **Mcdonald et al.**^[15] reported that there was no relation between DCC and need for blood transfusion, the risk to the mother to develop postpartum hemorrhage or blood loss at delivery. Furthermore, **Ruangkit et al.**^[37] did not find a higher level of loss of blood regarding the mother and bleeding complications in DCC applied in multiple pregnancies in relation to ECC. **De Paco et al.**^[28] reported that the blood test performed at 48 h after birth in all women to estimate postpartum loss of blood showed no significance between hematological tests. This test is not completely precise but it shows any maternal complications and can be used to decide if blood transfusion is required. Other

studies^[8, 36] have noted comparable findings on applying further objective methods to measure quantity of blood loss from the mothers during the third stage of delivery.

Finally, and collectively, **Argyridis**^[38] concluded that DCC seems to be useful for both preterm and term infants and should be performed, except when there is a maternal or neonatal indications that necessitates immediate cord clamping. DCC in term infants increases ferritin and hemoglobin for the first months of life, with possible benefits of development of the nervous system later in life. When delayed clamping is practiced, jaundice that requires phototherapy is increased. Therefore, phototherapy equipment should be available. Preterm infants may also profit from DCC, as studies reported that there is improvement of hemoglobin and neonatal circulation and a decrease in the need for transfusion. There is a decrease in the likelihood of intraventricular hemorrhage and better long-term outcomes. There maternal complications, such as the increased risk of postpartum hemorrhage showed no difference.

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