

Effect of timing of umbilical cord clamping on hemoglobin and hematocrit levels in preterm deliveries

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Abstract

Introduction: Immediate cord clamping (ICC), a fairly new birth practice, is a common routine practice in hospital settings throughout the world, replacing the decade long older practice of delayed cord clamping (DCC). A delay in clamping the cord facilitates a gentle physiologic transition that benefits all neonates, especially to the vulnerable ones, resulting in increased infant's hemoglobin and hematocrit levels.

Objective: To determine the effect of timing of cord clamping on hemoglobin and hematocrit levels in preterm deliveries.

Materials and Method: This was a hospital based prospective cohort study conducted in the department of Obstetrics and Gynecology, JNMC, Aligarh. A total number of 150 cases of preterm deliveries were included, which were randomly allocated to umbilical cord clamping done at <30 seconds i.e. Group A (50 cases), delayed cord clamping done at 60-120 seconds i.e. Group B (50 cases) and delayed cord clamping done at >180 seconds i.e. Group C (50 cases). Hemoglobin and hematocrit levels were assessed at birth, at 24 hours after birth and at discharge. Analysis was done using t- test, chi-square test and ANOVA test (Analysis Of Variance).

Results: Mean hemoglobin and hematocrit levels at birth, 24 hours after birth and at discharge were significantly higher in the delayed cord clamped neonates as compared to the early clamped group. There was a significant rise in mean hemoglobin level in the delayed clamped group B (0.9 ± 1.55 g/dl) and group C (1.82 ± 1.68 g/dl) as compared to the early clamped group A, in which there was a reduction of 0.46 ± 1.66 g/dl, in hemoglobin levels. Statistically insignificant rise in mean hematocrit level was observed in delayed clamped group B (2.21 ± 2.97 %) and group C (1.24 ± 3.22 %), as compared to group A (1.41 ± 6.72 %).

Conclusion: Delayed cord clamping is associated with higher hematocrit and hemoglobin levels at birth, at 24 hours and at discharge in preterm deliveries. This is a low cost intervention and its implementation would be particularly relevant in under-resourced settings, where anemia is still a major challenge.

Keywords: Delayed cord clamping, Hemoglobin, Hematocrit, Placental transfusion, Preterm baby

Introduction

Cord clamping is a part of the third stage of labor, during the time between the delivery of the baby and the placenta. However, the optimal timing for cord clamping after delivery has been a subject of much debate and the ideal timing is yet to be established and needs to be reconsidered.⁽¹⁾ The comparative benefits and shortcomings of early versus delayed cord clamping need further conclusive research in the field. While early cord clamping allows for initiating the immediate resuscitation of the neonate; delaying the cord clamping significantly increases the transfer of blood from the placenta to the infant.^(2,3) A delay of 30 to 45 seconds results in 8% to 24% increase in blood volume (2–16 ml/kg after cesarean birth and 10–28 ml/kg after vaginal birth), which would otherwise be wasted and the baby be deprived of the much needed blood.⁽⁴⁾ Early cord clamping denies the infant of the vital additional blood volume transferred from the placenta (around additional 30%), putting the infant at increased risk of iron deficiency anemia, especially in low resource settings with high prevalence of maternal anemia. Delayed cord clamping results in an increase in blood volume and higher blood pressure,^(5,6) higher hemoglobin and hematocrit levels^(7,8,9) as well as iron

stores of the neonate, thereby reducing the need for subsequent blood transfusions⁽⁸⁾ and decreased incidence of neonatal anemia, more optimal oxygen transport and higher red blood cell flow,⁽¹⁰⁾ fewer days on oxygen and ventilation,⁽¹¹⁾ fewer blood transfusions^(8,11) and lower rates of intraventricular hemorrhage (IVH).^(12,13) Keeping the above points in mind, we had planned this study to determine the effect of delayed umbilical cord clamping in preterm deliveries in terms of neonatal outcome.

Materials and Method

Study design and sampling: The prospective cohort study was conducted in the department of Obstetrics and Gynecology in collaboration with the neonatal section of department of Pediatrics, at Jawaharlal Nehru Medical College and Hospital, AMU, Aligarh. Women with single live intrauterine pregnancies <37 weeks of gestational age, presenting to the hospital with symptoms indicating that they might deliver before 37 weeks were assessed for eligibility. During the study period, a total number of 1253 preterm deliveries were registered. Based on the inclusion and exclusion criteria of our study, cases were selected and were included in the study after taking informed consent. Group

allocation was done when the birth was imminent, and mothers were randomly allocated into three groups according to the timing of cord clamping.

Group A: Umbilical cord clamping done at <30 sec.

Group B: Delayed cord clamping done at 60-120 sec.

Group C: Delayed cord clamping done at > 180 sec.

Time of clamping of umbilical cord was noted after the delivery of baby using a stop watch and the baby was transferred to the neonatology staff.

Evaluation of the mothers: A complete and detailed history, general physical examination and systemic examination were done for each woman, after taking informed consent.

Evaluation of the neonates: The neonatal data was collected at 3 points of time- at birth, 24 hours after birth and at discharge from the hospital. Neonatal hemoglobin and hematocrit were determined by using auto hematology analyzer.

Neonatal hemoglobin and hematocrit values

	Normal Range ⁽¹⁴⁾	Anemia ⁽¹⁵⁾	Polycythemia ⁽¹⁶⁾
Hemoglobin (g/dl)	18.5±2.0	13.0	22
Hematocrit (%)	60±8%	45	65

The three groups were compared for the following parameters:

1. Neonatal hemoglobin levels at birth, 24 hours and at time of discharge.
2. Neonatal venous hematocrit values at 24 hours and at time of discharge.
3. Rise in hemoglobin levels.
4. Rise in hematocrit values.

Statistical analysis: Data was analyzed using the t-test, chi-square test and ANOVA test (Analysis Of Variance). A p-value of <0.05 was considered statistically significant.

Study Duration: The study was conducted for a period of 2 years (2014-2016). The rights of the patients during interview were well respected.

Ethical approval: The study protocol was approved by the institutional research Ethics Committee, Jawaharlal Nehru Medical College, AMU, Aligarh. Furthermore, written consent was obtained prior to participation in the study.

Results

A total number of 150 cases of preterm deliveries were included in the study. Mean age of mothers in our study was 24.54 ±3.56 years with a range of 18-36 years, while the mean gestational age of neonates was found to be 32.18 ±5.01 weeks. Almost half of the cases (43%) were multigravidae. Mean birth weight of neonates in our study was 1.83±0.46 kg and maximum numbers of cases were between 1.6- 2.0 kg group (45.3%). No significant difference in Apgar score at 1 minute and 5 minutes was noted among the three study groups.

In our study, statistically significant difference in mean hemoglobin levels at birth were seen in cases of delayed cord clamping, both at 60-120 seconds (group B) and at >180 seconds (group C), as compared to early cord clamping done at <30 seconds (group A). Similarly, significant difference in mean hemoglobin levels were observed at 24 hours after birth and at the time of discharge; showing that delayed cord clamping has a beneficial effect on neonatal hemoglobin levels. In delayed cord clamped neonates, a statistically significant difference in mean rise in hemoglobin levels, from birth till the time of discharge, was observed. There was a mean rise in hemoglobin levels of 0.90 ±1.55 g/dl in DCC group at 60-120 seconds (group B) and 1.82 ± 1.68 g/dl in DCC group at >180 seconds (group C). However, there was a reduction of -0.46 ± 1.66 g/dl, in hemoglobin levels in neonates in which early cord clamping was done at <30 seconds (Table 1).

Table 1: Comparison of hemoglobin levels among groups A, B and C

	Mean Hemoglobin (g/dl)			p value
	Group A	Group B	Group C	
At birth	14.14±1.5	15.02±1.4	16.36±2.2	<0.001
At 24 hours after birth	13.45±1.5	15.34±1.6	17.28±2.2	<0.001
At discharge	13.68±1.8	15.92±2.0	18.18±2.2	<0.001
Rise in hemoglobin (g/dl)	-0.46±1.66	0.9±1.55	1.82±1.68	<0.001

In neonates with delayed cord clamping done at 60-120 seconds (group B) and at >180 seconds (group C), we found statistically significant differences in hematocrit levels, as compared to the early clamped group (group A). The difference in hematocrit levels were highly significant, both at 24 hours and at the time of discharge. There was a mean rise of 1.41±6.72% in hematocrit levels in early clamped group A; 2.21±2.97% in group B and 1.24±3.22% in group C. There was a statistically insignificant rise in the hematocrit levels from birth till discharge, in both the early cord clamped group as well as in neonates with delayed cord clamping done at 60-120 seconds and at >180 seconds (Table 2).

Table 2: Comparison of hematocrit levels among groups A, B and C

	Mean Hematocrit (%)			p value
	Group A	Group B	Group C	
At 24 hours after birth	43.86±5.2	46.56±4.8	47.42±6.1	0.003
At discharge	45.27±6.5	48.78±5.4	48.66±6.0	0.005
Rise in hematocrit (%)	1.41±6.72	2.22±2.97	1.24±3.22	0.532

Discussion

The theoretical foundation for the study was that the additional blood volume received by placental transfusion, as a result of DCC, would help to reduce neonatal morbidity by providing extra blood volume and improving cardiovascular stability. At any point of time, preterm neonates have lesser fetoplacental blood volume as compared to term infants, making them more vulnerable to have a deficit in case of early cord clamping.⁽¹⁷⁾ Delayed cord clamping allows time for adequate placental transfusion to supply the essential blood volume to the neonate. In our study, mean hemoglobin levels noted at birth in group A, B and C were 14.14 ±1.5 g/dl, 15.02 ±1.4 g/dl and 16.36 ±2.2 g/dl, respectively (p<0.05), which was found to be statistically significant, both in DCC at 60-120 seconds (group B), and at >180 seconds (group C), as compared to early cord clamping done at <30 seconds (group A). Similarly, mean hemoglobin levels at 24 hours after birth in groups A, B and C, were 13.45 ±1.5 g/dl, 15.34 ±1.6 g/dl and 17.28 ±2.2 g/dl, respectively (p<0.05) and at time of discharge were 13.68 ±1.8 g/dl, 15.92 ±2.0 g/dl and 18.18 ±2.2 g/dl, respectively (p<0.05), showing that hemoglobin levels in delayed clamped groups were significantly higher than early clamped neonates at 24 hours after birth and at discharge. This shows that delayed cord clamping increases placental transfusion and has a beneficial effect on neonatal hemoglobin levels. Ibrahim et al. (2000), Ultee et al. (2008) and Elimian et al. (2014) demonstrated a similar significant increase in mean hemoglobin levels in their studies.^(6,18,19) (Table 3)

There was a mean rise in hemoglobin levels of 0.90 ±1.55 g/dl in DCC group at 60-120 seconds (group B) and 1.82 ± 1.68 g/dl in DCC group at >180 seconds (group C). However, there was a reduction of -0.46 ±1.66 g/dl, in hemoglobin levels in neonates in which early cord clamping was done at <30 seconds. There

was a significantly higher rise in hemoglobin levels in delayed cord clamped neonates as compared to the early clamped neonates, from birth till the time of discharge. This initial rise in hemoglobin levels in preterm neonates reduces the need for blood transfusions and its subsequent complications, improves tissue perfusion and increases iron stores in the neonate, lasting up to 2-3 months of age. A similar rise in hemoglobin levels by 0.9 g/dl was noted in a study done by Popat et al. (2016).⁽²⁰⁾

Mean hematocrit levels observed at 24 hours of birth, in group A, B and C, were 43.86±5.2%, 46.56±4.8% and 47.42±6.1%, respectively (p=0.003); while, at discharge were 45.27±6.5%, 48.78±5.4% and 48.66±6.0%, respectively (p=0.005). In neonates with delayed cord clamping done at 60-120 seconds (group B) and at >180 seconds (group C), we found statistically significant differences in hematocrit levels, as compared to the early clamped group (group A), both at 24 hours and at the time of discharge. This improved hematocrit level results in improved iron stores of the neonate, and hence, a beneficial effect on overall neonatal outcome. Elimian et al. (2014), Song et al. (2015) and Chun et al. (2016) also reported similar findings of a significant increase in hematocrit levels in delayed cord clamped neonates.^(19,21,22) (Table 4)

There was a mean rise of 1.41 ± 6.72% in hematocrit levels in early clamped group A; 2.21 ± 2.97% in group B and 1.24 ± 3.22% in group C, which is a statistically insignificant rise in the hematocrit levels from birth till discharge, in both the early cord clamped group as well as in neonates with delayed cord clamping done at 60-120 seconds and at >180 seconds. This result may be due to variations in plasma volume that occur shortly after delivery, that either concentrate or dilute the RBCs in the blood stream, to either increase or decrease hematocrit values, respectively.

Table 3: Mean hemoglobin values in various studies

Study and Year	Mean hemoglobin level (g/dl)		p value and Inference
	Early clamping	Delayed clamping	
Elimian et al (2014)	16.3±2.3	17.4±2.6	0.001, Significant
Ultee et al (2008)	11.1±1.7	13.4±1.9	<0.05, Significant
Ibrahim et al (2000)	12.9±0.6	16.8±0.4	0.001, Significant
Our study (2016)	13.45±1.5	17.28±2.2	<0.05, Significant

Table 4: Mean hematocrit values in various studies

Study and Year	Mean hematocrit level (%) in		p value and inference
	Early clamping	Delayed clamping	
Our study (2016)	43.86±5.2	47.42±6.1	0.003, Significant
Chun et al (2016)	47.2±7.5	54.0±6.2	<0.05, Significant
Elimian et al (2014)	47.4±7.3	51.3±7.3	0.001, Significant
W Oh et al (2011)	40.2±5.1	44.9±7.8	<0.05, Significant
Strauss et al (2008)	53.0±1.1	56.0±1.3	0.188, NS
Mercer et al (2006)	46.0±6.0	49.0±6.0	0.06, NS
Mercer et al (2003)	42.0±9.8	44.0±10.8	0.59, NS
Ibrahim et al (2000)	39.0±1.4	50.3±1.3	0.001, Significant

Conclusion

Delayed cord clamping is a relatively inexpensive and safe intervention that could provide significant benefits to the preterm neonates, especially in an under-resourced setting, where access to good nutrition is limited during childhood and anemia is still a major challenge.

Our study demonstrates the beneficial effects of delayed cord clamping in preterm neonates as compared to early clamping. Delayed cord clamping resulted in significantly higher hemoglobin and hematocrit levels, and thereby, improved hemodynamic stability; without putting the neonate at increased risk of deleterious effects of placental over-transfusion.

It is time to rethink the management of umbilical cord clamping in preterm neonates and change our practices.

References

- Rabe H, Diaz-Rossello JL, Duley L, Dowswell T. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. *Cochrane Database of Systematic Reviews* 2012;(8):CD003248.
- Yao AC, Lind J, Tiisala R, Michelsson K. Placental transfusion in the premature infant with observation on clinical course and outcome. *Acta Paediatr Scand* 1969;58:561-6.
- Yao AC, Moinian M, Lind J. Distribution of blood between infant and placenta after birth. *Lancet* 1969;2(7626):871-3.
- Narendra A, Beckett C, Aitchison T, Kyle E, Coutts J, Turner T, et al. Is it possible to promote placental transfusion at preterm delivery? *Pediatr Res* 1998;44:453.
- Rabe H, Wacker A, Hulskamp G, Hornig-Franz I, Jorch G. Late cord clamping benefits extrauterine adaptation. *Pediatr Res* 1998;44:454.
- Ibrahim H, Krouskop R, Lewis D, Dhanireddy R. Placental transfusion: umbilical cord clamping and preterm infants. *J Perinatol*. 2000;20:351-4.
- Oh W, Carlo W, Fanaroff AA, Mc Donald S, Donovan EE, Poole K, et al. Delayed cord clamping in extremely low birth weight infants: a pilot randomized controlled trial. *Pediatr Res*. 2002;51(suppl):365-6.
- Rabe H, Wacker A, Hulskamp G, Hornig-Franz I, Schulze-Everding A, Harms E, et al. A randomized controlled trial of delayed cord clamping in very low birth weight preterm infants. *Eur J Pediatr*. 2000;159:775-7.
- McDonnell M, Henderson-Smart DJ. Delayed umbilical cord clamping in preterm infants: a feasibility study. *J Pediatric Child Health*. 1997;33:308-10.
- Nelle M, Fischer S, Conze S, Beedgen B, Brischke EM, Linderkamp O. Effects of later cord clamping on circulation in prematures. *Pediatr Res*. 1998;44:420.
- Kinmond S, Aitchison TC, Holland BM, Jones JG, Turner TL, Wardrop CA. Umbilical cord clamping and preterm infants: a randomized trial. *Br Med J*. 1993;306:172-5.
- Hofmeyr GJ, Bolton KD, Bowen DC, Govan JJ. Periventricular/ intraventricular haemorrhage and umbilical cord clamping. Findings and hypothesis. *S Afr Med J*. 1988;73:104-6.
- Hofmeyr GJ, Gobetz L, Bex PJ, Van der Griendt M, Nikodem C, Skapinker R, et al. Periventricular/intraventricular hemorrhage following early and delayed umbilical cord clamping: a randomized controlled trial. *Online J Curr Clin Trials*. 1993;Doc No 110.
- Gallagher PG. The neonatal erythrocyte and its disorders. In: Nathan and Oski's Hematology and Oncology of Infancy and Childhood, 8th ed, Orkin SH, Fisher DE, Look T, Lux SE, Ginsburg D, Nathan DG (Eds), WB Saunders, Philadelphia 2015;52.
- Kumari S, Gupta AK, Dadhich JP. Anemia in the neonates. *Recent advances in pediatrics*. 2000;5(2):212-9.
- Ramamurthy, RS. Neonatal polycythemia and hyper viscosity; state of the art. *Perinatol Neonatol*. 1979;3:38.
- Linderkamp OL. Placental transfusion: determinants and effects. *Clin Perinatol* 1982;9:599.
- Ultee CA, Van Der Deure J, Swart J, Lasham C, Van Baar AL. Delayed cord clamping in preterm infants delivered at 34-36 weeks' gestation: a randomised controlled trial. *Arch Dis Child Fetal Neonatal Ed*. 2008;93(1):F20-F23.
- Elimian A, Goodman J, Escobedo M, Nightingale L, Knudtson E, Williams M. Immediate compared with delayed cord clamping in the preterm neonate: a randomized controlled trial. *Obstet Gynaecol*. 2014;124(6):1075-9.
- Popat H, Robledo KP, Sebastian L, Evans N, Gill A, Kluckow M et al. Effect of Delayed Cord Clamping on Systemic Blood Flow: A Randomized Controlled Trial. *J Pediatr*. 2016;178:81-6.
- Song D, Jegatheesan P, DeSandre G, Govindaswami B. Duration of cord clamping and neonatal outcomes in very preterm infants. *PloSOne*. 2015;10(9):e0138829.
- Chun JY, Yoon S, Kim JS, Ho YH, Ahn SY, Yoo HS et al. Delayed Cord Clamping Compared with Cord Milking in Preterm Neonates. *Neonat Med*. 2016;23(2):74-80.