

To Study the Effect of Timing of Umbilical Cord Clamping on Neonatal Outcomes with Special Emphasis on Neonatal Hyperbilirubinemia and Hematocrit Levels in the Early Neonatal Period

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ABSTRACT

Introduction: The umbilical cord of every newborn is clamped and cut at birth, yet the optimal timing for this intervention remains controversial. For at least over 200yrs, multiple controversies have arisen around the timing of umbilical cord clamping. Delayed cord clamping or placental transfusion could be a cost effective intervention to improve the iron status of infants by enhancing their red cell mass. Search in literature reveals that several controlled trials evaluating the short term and long term hematological outcomes of delayed cord clamping have been performed in the past but very few studies have investigated the risk of hyperbilirubinemia especially from this part of the world. Hence this cross-sectional study was conceptualized.

Material and Methods: It was a cross-sectional study conducted among 212 term infants born at Rohilkhand Medical College and Hospital, Bareilly, over a period of 1 year, who fulfilled the inclusion criteria were included in our study.

Results: In the present study, hemoglobin, bilirubin, and hematocrit levels at birth and at 24 hours of birth in Immediate cord clamping and Delayed cord clamping was taken. Mean levels of hemoglobin, bilirubin and hematocrit was found higher in Delayed Cord Clamping group as compared to Immediate Cord Clamping group.

Conclusion: The study was conclusive of the fact that in term infants delayed cord clamping increases hemoglobin, hematocrit and bilirubin levels at birth and at 24 hrs of birth as compared to immediate cord clamping. Moreover, there was no significant associated adverse effects.

Keywords: Immediate Cord Clamping, Delayed Cord Clamping.

at birth.^{2,3}

There are various benefits of delayed cord clamping like increased hemoglobin and hematocrit levels for the neonate with a subsequent reduction in rates of anemia and iron deficiency that may extend into the infant period. Delayed cord clamping or placental transfusion could be a cost effective intervention to improve the iron status of infants by enhancing their red cell mass.^{4,5}

It appears that infants born to anemic mothers benefit more than those born to non-anemic mothers from the additional iron they derive from the blood passed from the placenta as a result of delayed cord clamping. Between 25% and 60% of the fetoplacental circulation blood volume is found in the placenta at term which allow placental transfusion after birth that can provide the newborn with a 30% increase in blood volume and upto a 60% increase in red cell.

The physiologic transfusion is on average between 19 and 40 ml/kg of birth weight which is equal to as much as 2% of the newborn final birth weight.⁶ Such effects is very important for the future of children considering that iron deficiency in the early stages may be harmful to the central nervous system and result in neurocognitive disorders. In addition, iron deficiency is the main cause of anemia, a severe condition is developing countries, although less serious in developed countries.⁷⁻¹¹

That is to say, that placental transfusion is an unavoidable physiological outcome occurring the first minutes of life and resulting from the redistribution of blood between the placenta and the infant. Therefore we must reflect upon the practice in relation to the timing of cord clamping because many health care providers are unaware of the fact that

INTRODUCTION

The umbilical cord of every newborn is clamped and cut at birth, yet the optimal timing for this intervention remains controversial. For at least over 200yrs, multiple controversies have arisen around the timing of umbilical cord clamping. The timing for cord clamping vary from early cord clamping generally done immediately after birth whereas later cord clamping usually involves clamping the umbilical cord greater than 30 seconds after the birth or when cord pulsation has ceased.¹ According to the newer neonatal resuscitation guidelines 2015 (American heart Association for cardiopulmonary resuscitation and emergency cardiovascular care 2015 recommendations, part 13) delayed cord clamping after 30 sec is suggested for both term and preterm neonates who do not require resuscitation

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there is an undesirable physiological basis for delayed cord clamping.¹²⁻¹⁴

In neonates who do not require resuscitation, delayed cord clamping is associated with less intraventricular hemorrhage, higher blood pressure and blood volume, less need for transfusion after birth, and less necrotizing enterocolitis. The only adverse consequence found was a slightly increased level of bilirubin, associated with more need for phototherapy.²⁻⁴

Search in literature reveals that several controlled trials evaluating the short term and long term hematological outcomes of delayed cord clamping have been performed in the past but very few studies have investigated the risk of hyperbilirubinemia especially from this part of the world. Hence this cross-sectional study was conceptualized.

MATERIAL AND METHODS

It was a cross-sectional study conducted among 212 term infants born at Rohilkhand Medical College and Hospital, Bareilly, over a period of 1 year, who fulfilled the inclusion criteria were included in our study and was conducted in the department of Pediatrics in the collaboration with the department of Obstetrics and gynecology, Rohilkhand Medical College, Bareilly. All consecutively admitted pregnant females in the Obstetrics and Gynecology department and fulfilling the inclusion and the exclusion criteria was enrolled for the study. These mothers was contacted while in their first stage of labor to obtain informed consent and they were assured that patient's personal information would be kept safe and will only be used for research.

After obtaining consent, and prior to delivery, the forthcoming newborn was randomly assigned to either delayed cord clamping (DCC) or immediate cord clamping (ICC) group. In the DCC group the umbilical cord was clamped after 30 seconds or when it stops pulsating. The exact time was recorded by use of a stopwatch, with complete expulsion of the infant as starting point. In the ICC group clamping was done within 10 seconds after delivery. A

sample of cord blood was collected from the placental side after clamping and ligating the fetal side for Hemoglobin and Hematocrit estimations. Before discharging home (usually at 36-48hrs of life) the babies was assessed for clinical signs of polycythemia, hyperviscosity or hyperbilirubinemia. Finally, an infant venous sample was taken for Hematocrit and Bilirubin analysis. (EDTA sample for Hematocrit and analysed by SYSMEX, XS-1000i 5 part cell counter and plain vial sample for bilirubin analysis by EM360 automatic analyser.)

Infant baselines characteristics and study outcomes was recorded in a pre-designed proforma.

STATISTICAL ANALYSIS

After reviewing the records, data was filled in the proforma. The data was entered in MS Excel spreadsheet and analyzed with appropriate statistical method. The data were entered on a Microsoft Excel spreadsheet and imported into Statistical Package for Social Sciences (SPSS) version 22 for statistical analysis. Frequency distribution tables were produced, and the chi square test was used to assess associations of variables. Data was present in mean and standard deviation. Independent t-test was performed to find significant difference in different variables in between two groups. A P-value less than 0.05 was considered statistically significant.

RESULTS

There were total 212 babies taken for study in two groups 107 in immediate group (< 10 Sec) and 105 in Delayed group (>30 Sec). Mean Hemoglobin at birth in immediate group was 17.27 ± 0.84 g/dl and Delayed group was 18.69 ± 0.75 g/dl. There was significant difference in mean Hemoglobin at birth in immediate group and Delayed group. Mean Hematocrit % at birth in immediate group was $52.41 \pm 5.40\%$ and Delayed group was $56.81 \pm 2.24\%$. There was significant difference in mean Hematocrit % at birth in immediate group and Delayed group.

There was no significant difference in clinical plethora at 24 hr in between Immediate group and Delayed group. Out of 107 baby 's 4.67% have required phototherapy who have clinical jaundice at 24 hr in Immediate group and out of 105 baby's 6.67% have required phototherapy who have clinical jaundice at 24 hr in Delayed group. There was no significant difference in requirement of phototherapy at 24 hr in between both the groups.(Table-1)

Mean hematocrit in Immediate group was 53.11 ± 2.36 and Delayed group was 55.01 ± 5.43 and there was significant difference in mean hematocrit at 24 hr in Immediate group and Delayed group. Mean bilirubin in Immediate group was

Clinical plethora (at 24 hr)	Yes	No	Total
ICC	2(1.87%)	105(98.13%)	107(50.5%)
DCC	2(1.90%)	103(98.10%)	105(49.5%)
TOTAL	4(1.9%)	208(98.1%)	212(100.0%)
X ² -Value	0.236		
P-Value	0.627(NS)*		

Table-1: Comparison of clinical plethora at 24 hr in ICC Group and DCC Group

Investigations	ICC					DCC				
	at birth		at 24 hr		mean diff	at birth		at 24 hr		mean diff
	Mean	S.D	Mean	S.D		Mean	S.D	Mean	S.D	
hemoglobin (cord blood) (g/dl)	17.27	0.84	17.11	0.76	0.16	18.69	0.75	18.43	0.77	0.26
hematocrit (cord blood)(%)	52.41	5.4	51.53	2.36	0.88	56.81	2.24	55.01	5.43	1.8
Bilirubin (cord blood) (mg/dl)	1.27	0.4	5.45	1.74	4.18	1.35	0.52	6.52	1.89	5.17

Table-2: Comparison of investigation at birth and at 24 hr in ICC Group and DCC Group.

Clinical jaundice (at 24 hr)	Yes	No	Total
ICC	5(4.67%)	102(45.33%)	107(50.5%)
DCC	7(6.67%)	98(43.33%)	105(49.5%)
TOTAL	12(5.7%)	200(94.3%)	212(100.0%)
X ² -Value	0.395		
P-Value	0.529(NS)*		

Table-3: Comparison of clinical jaundice at 24 hr in ICC Group and DCC Group

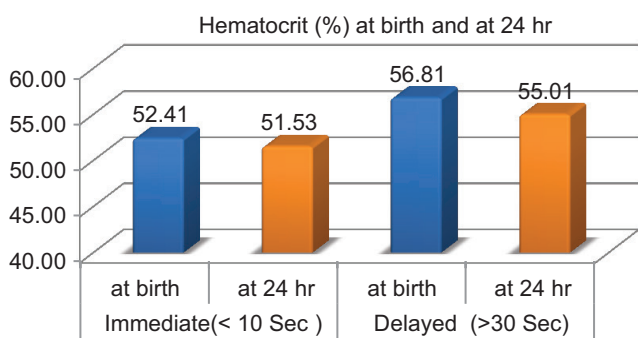


Figure-1: Comparison of hematocrit at birth and at 24 hrs in ICC group and DCC group

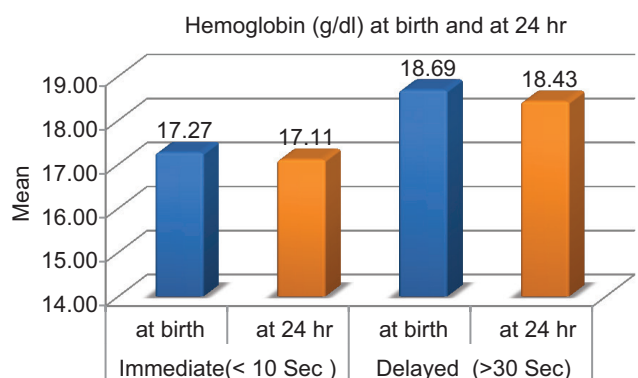


Figure-2: Comparison of hemoglobin at birth and at 24 hrs in ICC group and DCC group

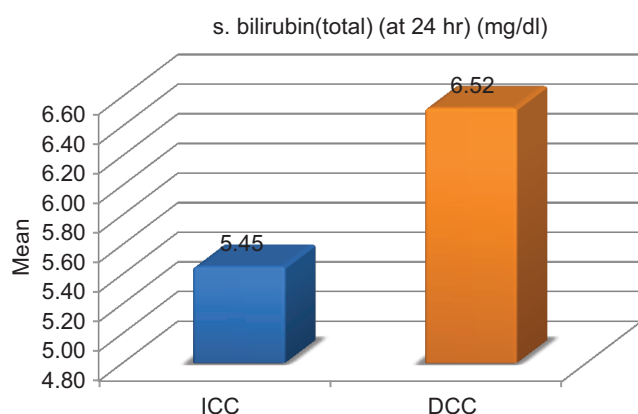


Figure-3: Comparison of serum bilirubin at 24 hrs in ICC group and DCC group

5.45±1.74 and Delayed group was 6.52±1.89 and there was significant difference in mean bilirubin at 24 hr in Immediate group and Delayed group.(Table-2) (figure-1) There was some reduction in hemoglobin (cord blood) (g/dl) and hematocrit (cord blood)(%) from birth to 24 hr and

increase in Bilirubin (cord blood) (mg/dl) from birth to 24 hr in both the groups. Clinical jaundice was not found in any baby in both the group at birth. Out of 107 babies 4.7% had clinical jaundice at 24 hr in Immediate group and out of 105 babies 6.5% had clinical jaundice at 24 hr in Delayed group. There was no significant in clinical jaundice at 24 hr in between Immediate group and Delayed group. Out of 107 babies 1.87% had clinical pleothora at 24 hr in Immediate group and out of 105 babies 1.90% had clinical pleothora at 24 hr in Delayed group. (Table-2,3) (figure-2,3)

Mean Bilirubin mg/dl at birth in Immediate group was 1.27±0.40 mg/dl and Delayed group was 1.35±0.52 mg/dl. There was no significant difference in mean Bilirubin mg/dl at birth in Immediate group and Delayed group. Mean Hemoglobin at 24 hr in Immediate group was 17.11± 0.76 g/dl and Delayed group was 18.43± 0.77 g/dl there was significant difference in mean Hemoglobin at 24 hr in Immediate group and Delayed group. (Table-2) (figure-3)

DISCUSSION

The optimal time-point for umbilical cord clamping after delivery has been under debate for several decades. Through this study we endeavoured to look into and compare both the beneficial and adverse effects of delayed and immediate cord clamping.

As per 2015 NRP guidelines on clamping of umbilical cord, early clamping is within 30 seconds and delayed cord clamping is more than 30 seconds after birth for a healthy term newborn.³ In present study we also followed the NRP guidelines and delayed cord clamping was done 30 seconds after birth.

In our study the timing of immediate cord clamping was taken as less than 10 seconds. Dash, et al. (2014)¹⁴ in their study also had undertaken immediate cord clamping as less than 15 sec.

The definition of early umbilical cord clamping was not clear in most studies except in Rabe, et al. (2000)¹ early cord clamping was defined as clamping at 20 seconds and there was no immediate clamped group for comparison. We have included this study in this review because we believe that there is close proximity to the immediate clamped groups, and that in clinical practice such delays may occur. Furthermore, it allows the review to focus on at least 20 seconds interval between immediate and late cord clamping. The definition of delayed umbilical cord clamping varied between studies. McDonnell et al. (2008)¹⁵ had a mean timed delay of 31 seconds, Rabe et al. (2000)¹ 45 seconds, Hofmeyr et al. (1993)²⁴ 60 and 120 seconds respectively.

My current study revealed that the hemoglobin levels in the ICC group were less than the hemoglobin levels in the DCC group. There was statistically significant difference of hemoglobin levels at birth (17.27 ± 0.84 & 18.69 ± 0.75 for ICC group & DCC group respectively) and at 24 hours (17.11 ± 0.76 & 18.43 ± 0.77) for ICC group & DCC group respectively (p value <0.001).

Approximately 40% of the fetal cardiac output goes to the placenta per minute, whereas 8% to 10% goes to the fetus’s

lungs. There is a dramatic change in the blood flow to the lung from 8% of the cardiac output in fetal life to 45% immediately after birth.¹² Immediate cord clamping limits access to the blood volume.^{12,13}

Emhamed M. O et al. (2004)¹¹ conducted a study to evaluate the hematological “effects of the timing of umbilical cord clamping in term infants” 24 hours after birth in Libya. 104 Mother-infant pairs were randomly assigned to early cord clamping (within 10s after delivery, n=46.) or delayed clamping (after the cord stopped pulsating, n=58).

Infant’s hematological status was evaluated in cord blood and 24 hr after birth. The mean infant hemoglobin level was significantly higher in the delayed clamping group (18.5 g/dL versus 17.1 g/dL; P=0.0005). This result also supports the present study result.

Shirvani. F et al (2010)²⁷ 2010 conducted a study “ to evaluate the hematological effects of umbilical cord clamp timing on newborn’s iron status and its relation to delivery type” in term infants 48 hours after birth in Iran.

Hundred mother-infant pairs were divided into two groups: early cord clamp time within 15 s(n=70) or delayed cord clamp time [15 s after delivery (n=30)]. The mean infant hemoglobin (Hgb; 16.08 gm/dL vs. 14.5 gm/dL; P<0.001) and hematocrit (Hct 47.6 vs. 42.8; P<0.001) levels were significantly higher in the delayed clamping group.

In Cochrane database systemic review in (2008) on effects of cord clamping by McDonald, Middleton P, Dowswell T et al. the hemoglobin levels measured at 24 and 48 hours of life were found significantly high and statistically significant (p value <0.001) in the group of babies subjected to delayed cord clamping than group of babies subjected to early clamping.¹⁵ Since the delayed cord clamping group had higher range of hemoglobin levels, delayed clamping can be considered to improve the hemoglobin levels in subjects. There are many benefits of delayed cord clamping including prevention of neonatal anemia and incidence of anemia later. This intervention has not only been proven effective, but it is cost-free, making it a particularly appropriate and sustainable intervention for low-resource areas of the world. The normal value of haematocrit in newborn till one month is in the range of 42-65%. In present study mean Hematocrit at birth in ICC group was 52.41 ± 5.40 and DCC group was 56.81 ± 2.24 respectively and there was significant difference in ICC group and DCC group and mean haematocrit at 24 hr in ICC group was 51.53 ± 2.36 whereas in DCC was 55.01 ± 5.43 respectively, showing statistically significant difference. There has been a concern of polycythaemia and hyperbilirubinaemia with DCC. Polycythemia is defined as Hct level >65% and occurs in about 2% to 5% of term newborns. The primary concern with polycythemia is related to the development of blood hyperviscosity.³⁶

Ricon D, Fouguet A et al. (2006)²⁸ found significant increase of polycythemia related clinical features in a number of newborns delivered with delayed cord clamping. Out of the 50 cases of DCC we found 6 cases (12%) of polycythaemia with haematocrit >65%, but none of them required any active management.²² In our study also none of the cases

required any active management due to polycythemia and increased hematocrit >65% levels. The risk of developing hyperbilirubinemia is another issue of concern in delayed cord clamping.

Rabe H et al. (2012)¹ found that none of the neonates with elevated bilirubin levels required phototherapy treatment or exchange transfusions. In our study there was no significant difference in requirement of phototherapy at 24 hr in between the ICC group and DCC group. In present study the mean total bilirubin level at 24 hr is 5.45 ± 1.74 in ICC group and 6.52 ± 1.89 in DCC group. 4.7% in ICC group and 6.5% in DCC group have clinical jaundice at 24 hr and there was no statistically significant difference in between ICC group and DCC group.

Saigal et al. (1977)²⁶ found that ‘Symptomatic neonatal clinical pleothora’ (tachypnoea, mild cyanosis, plethoric skin colour and neurological depression persisted on average for 30 hr after birth) were caused by large placental transfusions associated with delayed clamping of the umbilical cord. In our study 1.87% in ICC group and 1.90% in DCC group have symptomatic neonatal clinical pleothora at 24 hr, showing no statistically significant difference in between ICC group and DCC group.

According to AAP (2004) additional red blood cells can improve the infant's iron stores and there is only a small risk in group of neonatal jaundice requiring phototherapy as per the review. In our study there was no significant difference in requirement of phototherapy at 24 hr in between the ICC group and DCC group. McDonald et al.(2008) concluded on the other hand that increasing iron stores in infants through delayed cord clamping may be particularly beneficial in resource poor settings where severe anaemia is common.¹⁵ The difference we found in the mean hemoglobin and hematocrit levels of infants at 24 hr after delivery in favour of the the DCC group is possibly of clinical importance. DCC, which is safe, simple and low-cost delivery procedure, should be incorporated in the routine labour management. It could serve as an additional cost-effective intervention within integrated programmes aimed at reducing iron deficiency anemia (IDA) in infants in developing countries.

CONCLUSION

Term and preterm infants appear to derive benefit from delayed umbilical cord clamping; therefore, delayed umbilical cord clamping for at least 30–60 seconds is recommended in term infants. In term infants, delayed umbilical cord clamping increases hemoglobin levels at birth and improves iron stores in the first several months of life. There is a small increase in jaundice requiring phototherapy in term infants undergoing delayed umbilical cord clamping. Consequently, obstetrician–gynecologists and other obstetric care providers adopting delayed cord clamping in term infants should ensure that mechanisms are in place to monitor for and treat neonatal jaundice. Clamping and cutting of the umbilical cord at birth is the oldest and most prevalent intervention in humans. Various studies have advocated the practice of DCC which was found to be true in our study as well. Moreover

there were no significant associated adverse effects. It is a safe, simple and low cost delivery procedure that should be incorporated in integrated programs.

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