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Original Research Article

## Effect of timing of cord clamping (early vs delayed) on hemoglobin level among newborns: an Indian study

Bikramjit S. Jafra<sup>1</sup>, Sunil K. Mehendiratta<sup>2</sup>, Pooja R. Jafra<sup>3\*</sup>, Anudeep Jafra<sup>4</sup>

<sup>1</sup>Department of Pediatrics, Gian Sagar Medical College and Hospital, Rajpura, Punjab, India

<sup>2</sup>Department of Pediatrics and Neonatology, Venkateshwar Hospital, Dwarka, New Delhi, India

<sup>3</sup>Department of Obstetrics and Gynaecology, Gian Sagar Medical College and Hospital, Rajpura, Punjab, India

<sup>4</sup>Department of Anaesthesia, Post Graduate Institute of Medical Education and Research, Chandigarh, India

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**\*Correspondence:**

Dr. Pooja R. Jafra,

E-mail: drpooja01234@gmail.com

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### ABSTRACT

**Background:** Aim of the current study was to evaluate effect of delayed cord clamping on hemoglobin level among newborns and look for any adverse effects following delayed cord clamping.

**Methods:** Total 60 newborns were enrolled in the study and were randomly allocated to either control (early cord clamping 15 secs) and cases (delayed cord clamping 3 mins). Samples were collected in labor room, during birth to check the hemoglobin, bilirubin and hematocrit levels in two groups. Follow up data were collected in postnatal ward, 24 hours after birth to estimate hemoglobin, hematocrit and bilirubin levels and infants were assessed for the presence of respiratory distress.

**Results:** Hb levels among cases were significantly higher compared to controls at birth. The mean Hb at birth among controls was  $14.90 \pm 1.28$  g/dl and among cases was  $16.06 \pm 2.37$  g/dl (p value 0.023). Hb levels among cases were significantly higher compared to controls at 24 hours. The mean Hb at 24 hours among controls was  $16.16 \pm 1.70$  g/dl and among cases was  $19.28 \pm 2.16$  g/dl (p value <0.001).

**Conclusions:** Hemoglobin and hematocrit levels were significantly increased at birth as well as at 24 hours of age in delayed compared to early clamping group with no significant adverse effects seen in the group with delayed clamping.

**Keywords:** Anaemia, Cord clamping, Hemoglobin levels, Newborn

### INTRODUCTION

In developing countries, anemia being a common disorder is much more prevalent among infants and children. Iron Deficiency Anemia (IDA) in particular has the highest prevalence in children aged less than five years particularly because of poor feeding practices.<sup>1</sup> For overcoming this situation, steps to prevent anemia should be taken starting from birth itself, by practicing institutional deliveries and delayed cord clamping. It is a cost free intervention to enhance the iron quantity of baby.

Delayed cord clamping leads to transfusion of blood from placenta to baby (placental transfusion) and helps in supplementing their mass of red cells.<sup>2</sup>

The total estimated blood volume in the fetoplacental unit is roughly around 120 ml/kg of fetus weight. This blood volume is distributed among placenta and fetus in ratio of 1:2 when cord was clamped immediately after birth. This ratio can be further increased upto 1:5 if delayed cord clamping at 3 minutes is done.<sup>3</sup> This 'Placental transfusion' increases the blood volume by an additional

30% and red blood cells by 60%, thus increasing the oxygen-carrying capacity in the body that would be otherwise lost if cord was to be clamped immediately. This extra volume of blood adds around 40-50 mg/kg body weight of iron to the newborn. Early clamping of cord has been presumed to be among the major causes of anemia in infancy and increased risk of blood disorders such as type 2 diabetes. However, some believe that delayed cord clamping may lead to increased blood pool of the neonatal circulation and may result in increasing the likelihood of neonatal jaundice, respiratory distress and polycythemia. But till date no data suggest any harmful maternal or neonatal influence of delayed cord clamping.

As the data regarding the timing of clamping the umbilical cord and its effect on neonatal outcomes was scarce. Hence present study was conducted to determine the effects, timing of cord clamping (early cord clamping- 15secs and delayed cord clamping-3mins) has on hemoglobin levels at birth and 24 hours and clinical outcome (respiratory distress, need for phototherapy/exchange therapy, hematocrit and bilirubin levels) in newborns.

## METHODS

This was a prospective, randomized, case control study, conducted in Mata Chanan Devi Hospital, Janakpuri, New Delhi from January 2015 to June 2016. Approval of institutional ethical committee was taken along with informed and written consent of all mothers willing to participate in the study. 60 newborns were enrolled in the study. Newborns included in the study were more than 34 weeks gestational age, born via normal vaginal delivery or operative vaginal delivery, caesarean section, those who cried at birth and had cephalic presentation. Newborns who had congenital disorders, twins, tight nuchal cord necessitating early cord clamping or need for resuscitation at birth were excluded also those newborns where mother had gestational diabetes, pregnancy induced hypertension, poly or oligo hydraminos, Antepartum hemorrhage, heart disease, on drugs, pre term labour or HIV infected were also excluded. Newborns were randomly allocated to either cases (delayed cord clamping 3 mins) and controls (early cord clamping 15 secs) using computer generated random number tables. In delayed clamping group, infant was placed on abdomen of the mother following vaginal delivery and on mother's lap in case of cesarean delivery. Blood sample was retrieved from cut end of the neonatal side of umbilical cord. Collection of data was performed in two areas. In labor room, during childbirth to check the hemoglobin, bilirubin and hematocrit levels for two groups (control and cases). After that follow up data was collected in postnatal ward at 24 hours after birth for estimation of hemoglobin, hematocrit and bilirubin levels in both the study groups. The method used for Hb estimation was non cyanide method, for Billirubin, Jendrassik Grof method, for hematocrit, DC detection method and for Ferritin, chemiluminisence method was used. Infants were assessed in the postnatal ward for the presence of respiratory distress defined as respiratory rate

>60 breaths/minute, grunting, nasal flaring or retractions between or below the ribs. For billirubin interpretation and need for phototherapy and exchange transfusion, guidelines from American academy of paediatrics subcommittee on hyperbillirubinemia were used.<sup>4</sup>

## Statistical analysis

The primary variable tested was hemoglobin levels at birth and 24 hours, sample size of 20 per group was calculated based on a mean difference of 2.22 in Hb between the two groups, at two-sided alpha of 0.05, and a power of 90%. But we included 30 per group, to counteract any dropout or refusal. Secondary variable tested were respiratory distress, hematocrit at birth and 24 hours, bilirubin levels at birth and 24 hours and need for phototherapy or exchange transfusion in both groups. Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0 Statistical analysis was performed using Students t test, Chi-square test and Mann Whitney U test. Results were regarded as statistically significant for p value of <0.05.

## RESULTS

Total 60 newborns were enrolled in our study, 30 controls (cord clamped within 15 seconds) and 30 cases (cord clamped at 3 minutes of birth or immediately after discontinuation of pulsation of cord). Mean gestation age, mode of delivery, sex distribution and birth weight were comparable between the two groups.

**Table 1: Demographic factors.**

Variable	Control	Cases	P value
<b>Mode of delivery</b>			
LSCS	20	16	0.292
NVD	10	14	
<b>Sex</b>			
Female	13	15	0.605
Male	17	15	
<b>Birth weight (Kg)</b>	3.03±0.29	2.92±0.39	0.247
<b>Gestation (weeks)</b>	38.10±1.16	38.00±0.91	0.711

Hb levels among cases were significantly higher compared to controls at birth. The mean Hb at birth among controls was 14.90±1.28 g/dl and among cases was 16.06±2.37 g/dl (p value 0.023). Hb levels among cases were significantly higher compared to controls at 24 hours. The mean Hb at 24 hours among controls was 16.16±1.70 g/dl and among cases was 19.28±2.16 g/dl (p value <0.001).

There was a significant rise in hematocrit levels in cases when compared to controls at birth. The mean hematocrit value at birth for controls was 45.34±3.59 % and for cases was 49.28±7.28 % (p value 0.011). There was a significant

rise in hematocrit levels in cases as compared to controls at 24 hours. The mean hematocrit values at 24 hours for

controls was 49.06±4.99 % and for cases was 57.72±5.77 % (p value <0.001).

**Table 2: Hemoglobin and hematocrit levels.**

Hb (g/dl)	Control (n=30)		Cases (n=30)		P Value
	Mean±SD	Range Min-Max	Mean±SD	Range Min-Max	
<b>At Birth</b>	14.90±1.28	13.2 - 19.0	16.06±2.37	12.0 - 22.0	0.023
<b>24 Hrs</b>	16.16±1.70	13.6 - 21.5	19.28±2.16	15.8 - 23.2	<0.001
Hematocrit (%)	Control (n=30)		Cases (n=30)		P Value
	Mean±SD		Mean±SD		
<b>At Birth</b>	45.34±3.59		49.28±7.28		0.011
<b>24 hrs</b>	49.06±4.99		57.72±5.77		<0.001

There was significant rise in bilirubin level in cases compared to controls at 24 hours, however, the need for phototherapy was comparable between the two groups and the difference was insignificant and none of the newborns in either group required exchange transfusion. There was no increase in adverse effects following delayed cord clamping which were measured in terms of APGAR, respiratory distress and polycythemia requiring partial exchange.

**Table 3: Secondary variables.**

Variable	Control	Cases	p value
<b>APGAR at 1 min</b>	8.03±0.49	8.03±0.49	1.000
<b>APGAR at 5 min</b>	8.80±0.41	8.90±0.31	0.286
<b>Bilirubin (mg/dl)</b>			
At birth	1.84±0.71	1.91±1.43	0.799
24 hrs	4.95±1.64	6.21±1.98	0.009
<b>Need for phototherapy</b>			
Absent	26	25	1.000
Present	4	5	

**DISCUSSION**

Ideal time as when to clamp the umbilical cord has been an issue of controversies for decades.<sup>5</sup> Physiological studies show that total amount of blood in the combined fetal-placental pool of circulation is 54-160 ml, which is approximately 25% to 60% at term gestation and has 60% of fetal red blood cells. Placental transfusion via delayed cord clamping could prove to be an intervention that is cost-effective and enhances the iron level status in infancy by improving red cell mass.<sup>2</sup>

In a study done by Dash et al, the hemoglobin estimation in the Group I (cord clamp at 15 sec of birth) were lesser compared with Group II (cord clamp immediately after cessation of pulsation or at 3 mins of birth). This difference in hemoglobin was significant at birth (17.75±1.56 g/dl and 19.97±1.5 g/dl, p value <0.001 for group I and II respectively) and at 24 hours (16.97±1.23 g/dl and

19.59±1.39 g/dl, p value <0.001 for group I and II respectively). Placental transfusion if allowed to continue three minutes resulted in greater volume of blood in fetus (fetus: placenta ratio 5:1, as against a ratio of 2:1 in early clamping). At the end of three minutes some 20 ml/kg of blood remained in placenta. Clamping the cord immediately when compared with a delaying till 3 minutes provided an extra 20-35 ml/kg body weight of blood. This study thus, supported the results of our study.<sup>6</sup>

In this study, for both the groups, the mean 1 minute APGAR score was 8.03±0.49. For controls the mean 5 minute APGAR score was 8.80±0.41 and for cases, was 8.90±0.31. The difference in APGAR score at 5minute was not clinically significant (p value 0.286). This was possibly because the time interval between cord clamping and measurement of APGAR was short and beneficial effects of delayed cord clamping could not have occurred till then and also because newborns requiring resuscitation (with possible low APGAR scores) were already excluded from the study. These results are in agreement with a study done by Stauss et al.<sup>7</sup>

In this study, we looked for respiratory distress in terms of respiratory rate >60 breaths/minute, nostril flaring, grunting and retractions between or under the ribs in both the groups. But we did not find any significant difference (p value 0.195). This was possibly because all the high risk newborns were excluded from the study. Even in a study done by Cernadas et al, three groups were compared; group 1 (cord clamped within the first 15 seconds), group 2 (cord clamped at 1 minute) and group 3 (cord clamped at 3 minutes); the results were similar. The respiratory disorder after birth was transient with no need of oxygen supplementation beyond 24 hours of life.<sup>8</sup> A systemic review has also reported similar results mentioning that the insignificant increase in tachypnea in some studies was just a part of physiologic compensatory mechanism.<sup>9</sup>

A study done by Emhamed et al, supported our results. Results of the study showed that cord hematocrit values were comparable in the two groups (p value 0.37) but the

hematocrit value was greater in delayed clamping group at 24 hours ( $P=0.0037$ ) and this difference was statistically significant. The study suggested that in infants born at full term gestation, placental transfusion due to delayed clamping can raise mass of red cells by 25-33%.<sup>10</sup>

In a study done by Jaleel et al, bilirubin in umbilical cord blood sample was 1.8 mg/dl in group A (umbilical cord clamped immediately after birth) and 1.9 mg/dl in group B (clamping delayed until discontinuation of pulsations in the cord), with p value of 0.206 which was clinically insignificant. Serum bilirubin levels, 6 hours after birth was 2.5 mg/dl in group A compared to 2.7 mg/dl in group B, with p value of 0.095 which was clinically insignificant. Although serum bilirubin on both these timed samples were more in the delayed clamping group when compared to the other group, but this rise was insignificant ( $P = 0.186$  for bilirubin rise in group B versus group A).<sup>11</sup>

In this study, the percentage of newborns who needed phototherapy among controls were 13.3% and among cases were 16.7% but the difference was not significant. The results of our study were supported by other studies as well.<sup>12,13</sup>

In this study, none of the newborns among control or cases required exchange transfusion. This was in agreement with previous studies, such as a study done by Rheenens et al which showed that despite the fact that peak bilirubin concentrations tended to be higher after delayed cord clamping, the phototherapy threshold was never exceeded and none of the neonates required exchange transfusion.<sup>14</sup> Although the peak bilirubin concentrations tended to be higher after delayed cord clamping, the phototherapy threshold was never exceeded and none of the newborns required exchange transfusion.

In this study, among controls, 12 out of 30 newborns and among cases, 15 out of 30 newborns came for follow up at 2 months. Although the mean Hb at 2 months among cases that came for follow up tended to be on a higher side when compared with controls that came for follow up. There was a large number of loss to follow up cases so the significance could not be commented upon due to small number of cases.

But in a study done by Grajeda et al, Hb at 2 months of newborns in the three groups (early clamping, delayed clamping at the level of placenta and delayed clamping with infant kept below the level of placenta) were studied. Group 2 showed significant increase in Hb as compared to group 1 with a p value of 0.03. Whereas in another study by Andersson et al (50), the mean Hb at 4 months of age for early cord clamping group ( $\leq 10$  s after delivery) and in delayed cord clamping group ( $\geq 180$ s) was studied. Although Hb was higher in delayed cord clamping group but the difference was not statistically significant. The lack of a substantial difference between the two groups was explained by the fact that Hb concentration declines and

approaches each person's unique, genetically determined "set point" around 2 months of birth.<sup>15</sup>

We also studied mean ferritin value at 2 months. Although mean ferritin at 2 months among cases that came for follow up was on a higher side when compared with controls but the significance could not be calculated because of large number of loss to follow up cases. Different results are reported in literature in respect to ferritin levels on follow up, but an increase in ferritin level is seen on follow up in infants with delayed cord clamping further supporting the beneficial role for the same.<sup>13,15</sup>

There were some limitations for this study. The amount of blood that was really transfused from the placenta into the newborn kid could not be quantified. The infants in the group that had the delayed cord clamping, however, had higher Hb and hematocrit at birth and at 24 hours of age, which showed that there had been more placental transfusion in this group. The study was done in newborns that were healthy and  $>34$  weeks gestation. So the results could not be applied to preterm deliveries ( $<34$  weeks) and high risk deliveries. Among those newborns who were followed up at 2 months and tested for ferritin, we could not rule out the possibilities of involvement of other factors like infant feeding, iron supplementation, infant health and socioeconomic indicators. In few cases the results obtained at 2 months were not satisfactory due to loss to follow up.

## CONCLUSION

Hemoglobin and hematocrit levels were significantly increased at birth and at 24 hours of age in delayed compared to early clamping group. No adverse effects were seen in the delayed clamping group as: None of the polycythemic newborns were symptomatic or received any partial exchange. Although bilirubin levels were higher in delayed clamping group at 24 hours but this was clinically insignificant as there was no significant difference for need for phototherapy between the two groups and none of the newborns received exchange transfusion. Respiratory distress was not increased significantly and APGAR scores were comparable in both the groups.

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