

# **Comparison between the Efficacy of Early and Delayed Umbilical Cord Clamping in Preterm Infants**

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## **ABSTRACT**

**Aim:** To compare the efficacy of early and delayed umbilical cord clamping in preterm infants.

**Study design:** Randomized control trial.

**Setting:** Department of Pediatric Medicine, and Labour Room, Services Hospital, Lahore.

**Duration of study:** From 08-01-2009 to 07-07-2009.

**Methods:** Total 80 cases were selected (40 cases of early cord clamping and 40 cases of delayed cord clamping. Umbilical cord was clamped at 30 second of the birth of babies in group-A and at 120 seconds of the birth of baby in group-B.

**Results:** Regarding sex distribution of babies, there were 20 males (50%) and 20 females (50%) in group-A, while 13 males (32.5%) and 27 females (67.5%) in group-B. Mean  $SD \pm$  gestational age in group-A was  $34.3 \pm 1.6$  weeks while in group-B it was  $34.8 \pm 1.6$ . The difference between the gestational age of both groups was found to be statistically non-significant ( $p=0.131$ ). Similarly mean  $SD \pm$  hematocrit in group-A and group-B was  $34.2 \pm 2.4$  and  $45.7 \pm 4.2$  respectively. The difference between the mean hematocrit of both groups was statistically significant ( $p<0.001$ ). In group-A normal hematocrit ( $43.6 \pm 7.2$ ) was observed in 6 cases (15%) and in group-B normal hematocrit was observed in 34 cases (85%). Low hematocrit was found in 34 cases (85%) and 2 cases (5%) in group-A and group-B respectively. High hematocrit (polycythemia) was found in 4 cases (10%) of group-B only.

**Conclusion:** Delayed cord clamping is more effective than early cord clamping regarding preservation of normal hematocrit in preterm infants.

**Keywords:** Pre-term, timing of cord clamping, hematocrit, anemia, polycythemias.

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## **INTRODUCTION**

Hematocrit is the measure of percentage of blood that is comprised of red blood cells. It is used to screen and determine the extent of anemia as well as a guide of number of transfusions needed<sup>1</sup>. The value of hematocrit is different for different pediatric age groups. In a preterm infant of 30-37 weeks of gestation, the normal value is  $43.6 \pm 7.2$ .

Timing of cord clamping and hematocrit are correlated. Early cord clamping may deprive the infant of essential blood volume and create a state of potential circulatory compromise resulting in hypotension and poor perfusion of tissues<sup>3</sup>. While a delay in clamping the cord increases the transfer of blood from placenta to infant, this improves hematocrit (55% of babies had high hematocrit with delayed cord clamping while only 12% had high hematocrit with early cord clamping), haemoglobin and iron stores, so reducing the need for neonatal transfusion (7.69% required neonatal transfusions with delayed cord clamping while 53.84% with early cord clamping)<sup>4,5</sup>.

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The definitions of early and late clamping of umbilical cord have changed over the years. A century ago early clamping was considered to within one minute, whereas late clamping after five minute<sup>6</sup>. Recent studies and observations suggest early and late clamping as less than 30 seconds and between 30-120 seconds after delivery of the baby respectively<sup>4</sup>.

The current obstetric practice in United States is to clamp the umbilical cord immediately after delivery<sup>3</sup>. Although early cord clamping deprive the newborn with some blood but it helps in prevention of polycytemia (1.25% had polycytemia with early cord clamping while 46.42% with delayed cord clamping), hyperbilirubinemia (6% had hyperbilirubinemia with early cord clamping while 38% with delayed cord clamping) and helps to obtain cord blood for pH and blood gases and neonatal resuscitation but it may increase Rh sensitization<sup>5,7</sup>.

Delayed cord clamping causes the placental transfusion of approximately 80ml of blood<sup>7</sup>. One of the studies in preterm infants has shown the association of this practice with higher haematocrit level four hours after birth<sup>4</sup>.

Another study has shown that it improves cerebral oxygenation, reduces the risk of

intraventricular haemorrhage in preterm infants (17% with delayed cord clamping while 26% with early cord clamping), reduces the need for blood transfusion and improves hemodynamic stability by increasing intravascular blood volume<sup>3</sup>. It also improves vascular stability, iron stores, maintain haematocrit at higher level and prevent infant from developing respiratory distress syndrome<sup>5</sup>.

Even mild iron deficiency in infancy may be associated with cognitive deficit and poor mental and motor coordination<sup>8</sup>. Iron deficient infants are also more prone to febrile seizures<sup>9</sup>. Thus effective interventions are needed to reduce the risk anaemia in infants. Delayed cord clamping has been shown to be simple, safe and cost free procedure that augments red cell mass in both term and preterm neonates<sup>10</sup>.

## MATERIAL AND METHODS

This randomized control trial was carried out over a period of six months from 08-01-2009 to 07-07-2009 in the Department of Pediatric Medicine, Services Hospital, Lahore and labour room, Services Hospital, Lahore. Sample size was calculated sample with 3% margin of error, 80% power of study taking expected percentage of normal haematocrit level that is 55% in delayed cord clamping and 12% in early cord clamping is forty cases in each group. Sampling technique was non-probability purposive sampling. Preterm babies (on clinical examination) with gestation age between 30 weeks and before 37 completed weeks of gestation were included in the study. Preterm babies with congenital anomalies (on clinical examination) and delivered to Rh negative mothers (laboratory evaluation of blood grouping of mother) were excluded.

Demographic information of the babies including name, age, sex and address was recorded. Parents were explained about the procedure of the study. An informed consent was taken from their parents before including them in the study. Antenatal information (like blood group, blood sugar and blood pressure record of the mother) was obtained from the obstetrician. There was not risk involved to the babies and an approval sought for study by ethical committee of the hospital. They were assigned to group-A and group-B randomly by using random number table. Umbilical cord was clamped (by the obstetrician) at 30 seconds of the birth of babies in group-A and at 120 seconds of the birth of babies in group-B. Blood sample was obtained at four hours of age to obtain haematocrit level; efficacy was labeled if normal haematocrit value i.e.  $43.6 \pm 7.2$  was

achieved. All the information was recorded in pre-designed proforma (copy attached).

All collected information was entered in SPSS version 10 and analyzed. Quantitative variables in demography like haematocrit were presented as mean and standard deviation. Qualitative variables like sex presented as percentage. Outcome of two groups were compared for any difference in terms of their mean and standard deviation values. For comparison of normal and abnormal haematocrit (Yes/No) Chi square was applied for estimating significance. The p-value of 0.05 or less was considered statistically significant.

## RESULTS

Group A comprised of 40 babies in which early cord clamping (30 seconds) was carried out, whereas group-B comprised of 40 babies in which late cord clamping (120 seconds) was carried out.

Regarding sex distribution of babies, in group-A there were 20 males (50%) and 20 females (50%), while in group-B there were 13 males (32.5%) and 27 females (67.5%). (Table 1)

Mean  $\pm$  SD gestational age in group-A was  $34.3 \pm 1.6$  while  $34.8 \pm 1.6$  in group-B. Difference between two groups was found to be statistically non-significant ( $P=0.131$ ). Similarly, mean haematocrit  $34.2 \pm 2.4$  and  $45.7 \pm 4.2$  was found in group-A and B, respectively. The difference is statistically significant ( $P<0.001$ ) (Table 2).

Normal hematocrit ( $43.6 \pm 7.2$ ) was observed in 6 out of 40 cases (15%) and 34 out of 40 cases (85%) in group-A and B, respectively. Low haematocrit was found in 34 cases (85%) in group-A and 2 cases (5%) in group-B. Polycythaemia was present in group-B only, i.e. in 4 patients (10%). There was statistically significant difference between two groups ( $P<0.001$ ) (Table 3).

Table1: Distribution of case by sex (n=80)

Gender	Group A	Group B
Male	20(50%)	13(32.5%)
Female	20(50%)	27(67.5%)

Table 2: Distribution of case by gestational age (n= 80)

Variables	Group-A		Group-B	
	Mean	SD	Mean	SD
Gestational age	34.3	$\pm 1.6$	34.8	$\pm 1.6$
T value			-1.525	
P value			0.131	
Hematocrit	34.2	$\pm 2.4$	45.7	$\pm 4.2$
T value			-16.093	
P value			< 0.001	

Table 3: Distribution of case by hematocrit (4 hours of life) (n=80)

Hematocrit	Group A	Group B	P value
Low (<36.4)	34(85%)	2(5%)	<0.001
Normal (43.6±7.2)	6(15%)	34(85%)	<0.001
Polycythemia (>50.8)		4(10%)	

## DISCUSSION

Umbilical cord clamping has been performed since the beginning of mankind but the timing and advantages of early versus delayed clamping are still controversial. Early cord clamping is usually justified for immediate treatment of newborn and for potential prevention of postpartum hemorrhage but it deprives the newborn from large quantity of blood and iron. This is particularly important in preterm babies who are more prone to develop anemia especially in early infancy. In contrast, delayed cord clamping causes transfusion of blood from placenta to neonate and this amount of blood seems to protect the baby from childhood anemia.

Iron stores at birth are variable and are positively correlated to each infant with iron stores at 6, 9 and 12 months of age. Iron content in the diet is the major factor influencing the iron status during the first year of life. Thus an elevated iron deposit at birth is associated with an adequate iron status at 12 months of age.

This randomized controlled study compared the potential placental transfusion effect in the newborns in terms of hematocrit with early and delayed umbilical cord clamping. A total of 80 preterm newborns meeting the inclusion and exclusion criteria were selected after the informed consent from parents. They were assigned to group-A and group-B randomly by using random number table. In group-A umbilical cord was clamped at 30-seconds of birth of baby and in group-B it was clamped at 120 seconds of birth of baby. Babies in both the groups were comparable in terms of gestational age.

Blood samples were drawn at 4 hours of age to obtain hematocrit level. In group A (early cord clamping) the mean hematocrit of the newborns was  $34.2 \pm 2.4$  which was below the desired physiological range ( $43.6 \pm 7.2$ ). While in group B (delayed cord clamping) the mean hematocrit was  $45.7 \pm 4.2$ . Thereby confirming our hypothesis i.e. delayed cord clamping increases the hematocrit level of preterm babies.

Thus preterm babies in group A with early cord clamping were more prone to anemia as compared with babies in group B with delayed cord clamping. These results are comparable with the study done by Ultee et al<sup>11</sup>. They included 37 premature infants and randomly assigned them into one of the two groups.

The late cord clamped group showed consistently higher hemoglobin levels, both at the age of one hour (mean  $13.4 \text{ mmol/l}$  SD $\pm 1.9$  versus mean  $11.1 \text{ mmol/l}$  SD $\pm 1.7$ ) and at 10 weeks (mean  $6.7 \text{ mmol/l}$  SD $\pm 0.75$  versus mean  $6.0 \text{ mmol/l}$  SD $\pm 0.65$ ).

The results of our study are also in comparison with meta-analysis carried out by Hutton and Hassan<sup>12</sup>. They assessed the eligibility and quality of trials. It included 15 controlled trials (1912 newborns). Infants with delayed cord clamping were followed up for 2-6 months of age, they showed improved hematological status measured as hematocrit, improved iron status measured by ferritin concentration and stored iron and a clinically important reduction in the risk of anemia.

In the current study, normal hematocrit was observed in 6 cases (15%) in group-A (early cord clamping) and 34 cases (85%) in group B (delayed cord clamping). Low hematocrit was found in 34 cases (85%) in group A and only 2 cases (5%) in group B. Thus in group A (early cord clamping) only 15% of newborns showed normal hematocrit while in group B (delayed cord clamping) 85% had normal hematocrit. This is also comparable with other studies<sup>4,10,13</sup>.

Rabe et al<sup>4</sup> reviewed the literature to determine the impact of early and delayed cord clamping as outcomes in preterm infants. They found 7 randomized controlled trials that compared early and delayed cord clamping in 297 preterm infants. Delayed cord clamping upto 2 minutes was associated with higher hematocrit at four hours of life than early cord clamping, fewer blood transfusions for anemia (28 versus 52%), hypotension (20 versus 50%) and fewer intraventricular hemorrhages (17 versus 26%).

A randomized clinical trial done by Strauss et al<sup>13</sup> on 105 preterm neonates at 30-36 weeks of gestation. They found that, with delayed cord clamping, circulating RBC volume increased ( $P=0.04$ ) and weekly hematocrit values were higher ( $P<0.005$ ).

Although late cord clamping prevent the development of anemia but there is risk of polycythemia and hyperbilirubinemia. We have not studied these factors but Van Rheenen et al<sup>10</sup> reviewed the literature on delayed cord clamping in 190 term infants and 40 preterm infants and showed a 12% increase risk of hyperbilirubinemia. No other study has shown this increased risk of hyperbilirubinemia.

In current study, low hematocrit was present in 85% of newborns in group A (with early cord clamping) while only 5% of newborns in group B (with delayed cord clamping). Similarly oxford midwives research group<sup>14</sup> in one of their studies found a remarkable increase of anemia in group with early

cord clamping at 6,24 and 48 hours of life.

In this study 4 babies (10%) with delayed cord clamping were observed to have polycythemia whereas none from early cord clamping had high hematocrit value. All these babies were asymptomatic. This result is in comparison with the meta-analysis done by Hutton and Hassan [50] in 7 studies with 403 neonates. The meta-analysis showed that all the neonates with polycythemia were asymptomatic and did not have any pathological effects of polycythemia.

Present study was limited only to check hematocrit level at 4 hours of age. I did not measure the hematocrit level later in neonatal life to monitor for anemia. I also did not measure the serum bilirubin level as Van Rheenen et al<sup>10</sup> showed 12% increase risk of hyperbilirubinemia with delayed cord clamping.

## CONCLUSION

In preterm babies delayed cord clamping (at 120 seconds after birth of baby) results in an increase of hematocrit level measured at 4 hours of life within physiological ranges. Thus delayed cord clamping is more effective than early cord clamping regarding preservation of normal hematocrit in preterm infants.

More studies need to be carried out to look for hyperbilirubinemia and polycythemia in delayed cord clamping and monitoring of anemia during infancy in early cord clamping.

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