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Effect of early and delayed cord clamping on hemoglobin and hematocrit among full term neonates.

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ABSTRACT… Objective: To compare the mean hemoglobin levels and frequency of polycythemia in full term neonates after early and delayed cord clamping. **Study Design:** Randomized Controlled Trial. **Setting:** KRL General Hospital Islamabad (Labor Room/ Neonatology). **Periods:** December 2017 to June 2018. **Material & Methods:** 190 full term neonates were selected and divided into 2 equal groups randomly: Early cord clamping group after delivery and late cord clamping group. Two hours after clamping the venous blood samples were taken for the hemoglobin and hematocrit levels. Mean and standard deviation were calculated for gestational age, birth weight, hemoglobin and hematocrit. Frequency and proportions were calculated for gender and polycythemia. **Results:** Mean gestational age of the mothers was 39.27 ± 1.50 weeks. Of 190 neonates, 91 (47.9%) were males, 99 (52.1%) were females. Mean birth weight was 3.64 ± 0.72 kg while mean Hb and HCT levels were 16.07 ± 2.30 g/dl and 63.26 ± 5.32% respectively. Keeping cut off value of 13.5 g/dl of Hb to label anemia or no, 35 (18.4%) neonates were anemic in this study. The polycythemia (HCT >65%) was present in 72 (37.9%) of neonates. There was no difference between groups in terms of gender, anemia, gestational age and birth weight (p values 0.663, 0.852, 0.700 and 0.491 respectively). The distribution of polycythemia was different among groups (p value 0.007). The mean hemoglobin level in group A was 15.52 ± 1.90 g/dl while in group B it was 16.62 ± 2.53 g/dl (p value 0.001). Mean Hb levels were statistically not different among some of the groups (gestational age <40 weeks, birth weight <4 kg) while HCT levels are significantly different among male group and category of birth weight >4 kg. Rest of the stratification groups showed significant difference. **Conclusion:** The delayed cord clamping in neonates results in increased mean hemoglobin and hematocrit levels with increased frequency of polycythemia as compared to early cord clamping.

Key words: Hemoglobins, Infant, Newborn, Polycythemia, Prognosis, Umbilical Cord.

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INTRODUCTION

Anemia is common disorder in pediatric population. In poor countries, iron deficiency leading to anemia is most prevalent in children < 5 years old. In Pakistan, overall 62.3% children are anemic out of which 4.1% are severely anemic. Iron deficiency anemia is associated with impaired physical growth and cognitive development in children less than five years of age.[1]

A study in India showed that delayed cord clamping is safe, simple and low-cost procedure in reducing IDA in infants. Mean hemoglobin measured in early cord clamping group was 17.75 ± 1.56 g/dl while it was 19.97 ± 1.511 g/dl in late cord clamping group.[2] As compared to early clamping, a delay of one to three min in cord clamping provides an additional blood of 20-35 ml/kg body weight. This additional amount of blood can supply extra iron amounting to 40-50 mg/kg body weight. A newborn has 75 mg/kg body weight of iron stores which may reach up to 115-125 mg/kg when this additional volume of blood is added due to late cord clamping. This may help to prevent IDA. Moreover, late cord clamping is associated with increased serum ferritin levels at four months of age.[3]

However, a recent local study conducted in India showed that this delay in cord clamping showed in-significant effect on hemoglobin level and iron stores in the infants.[4] In another recent study of Spain frequency of polycythemia was higher in full term newborns in which delayed cord clamping was done. Out of 80 patients exposed to early cord clamping 4 (5%) developed polycythemia whereas out of 131 neonates exposed to delayed cord clamping 21 (16%) developed polycythemia.[5]

The aim of this study was to compare the effect of early and delayed cord clamping on neonatal hemoglobin and hematocrit. As there is limited research regarding frequency of polycythemia. The results of this study would help to adapt a cord clamping technique that has an advantage of improved hematological profile and decreased risk of complications.

MATERIAL & METHODS

This research was done in labor room and neonatology unit of KRL General Hospital Islamabad, six months (December 2017 to June 2018) after approval from the hospital ethical review committee ERC2016/02/01. Patients of both genders male and female including full term neonates, neonates having APGAR score of 8/10 or above at one minute and mothers with Hb ≥ 10 g/dl at time of delivery were included the study. Patients including neonates born to mothers with pregnancy induced hypertension, gestational diabetes, poly or oligohydramnios, heart disease, anemia or preterm labor, neonates with any congenital or acquired illness were excluded from the study.

Early cord clamping was defined as umbilical cord clamping done within 15 seconds just after the delivery. While delayed cord clamping was defined as umbilical cord clamped at 60-180 seconds of birth or immediately after cessation of cord pulsations. Full term neonante was defined as neonate with gestational age of 37-41 weeks. Anemia was defined as central venous hemoglobin level ≤ 13.5 g/dl measured at two hours of life. A neonate was labeled as having polycythemia when central venous hematocrit (HCT) was > 65% measured at two hours of life.

In this study, 190 mothers going to deliver were selected from Obstetrics labor room of KRL General Hospital, Islamabad after fulfilling the inclusion and exclusion criteria. Mothers were divided into two equal groups by table of random numbers. Hospital registration numbers and informed written consent was taken from all mothers. In group A after delivery the cord clamping was done early while in group B the late cord clamping was done. The researcher was kept blind of the group identity. Hemoglobin and hematocrit were measured at two hours of life in the laboratory of KRL General Hospital, Islamabad that was verified by hematologist. All the data was entered on specially designed proforma.

Data was analyzed using SPSS version 17 for windows. Quantitative data like gestational age, birth weight, hemoglobin, hematocrit, and qualitative data like gender and frequency of polycythemia was analyzed. Mean and standard deviation were calculated for quantitative data. Frequency and percentages were calculated for analysis of qualitative data. Both groups were compared in terms of mean hemoglobin levels, hematocrit levels (independent sample t-test) and frequency of polycythemia (Chi square test). Effect Modifiers like gestational age, gender and birth weight were controlled by stratification. Post-stratification independent sample t test and Chi square test were applied. A p-value of ≤ 0.05 was considered significant.

RESULTS

In this study, 190 neonates were enrolled after fulfilling inclusion and exclusion criteria. In group A, 44 out of 95 (46.3%) patients were males and rest of 51 (53.6%) were females; while in the group B, 47 of 95 (49.5) were male and rest 48 (51.5) were females. Frequency of anemia was 18.9% in group A and 17.9% in group B. But the frequency of polycythemia in group A was seen in 27 of 95 neonates (28.4%) while it was seen in 45 of 95 cases in group B (47.4%) (p = 0.007), shown in Table-II. Table-III. showing the mean + SD of all the quantitative variables seen in both the groups (n=190). Both groups, A and B were

compared among each other in terms of various quantitative variables. The results have been shown in Table-III. The results showed that both the Hb and hematocrit are significantly different among groups.

The data was stratified according to gestational age, neonatal gender and birth weight as shown in tables. The following table shows the comparison between groups for mean hemoglobin (Hb) levels after stratification. The results showed that mean Hb levels are statistically not different among some groups (gestational age <40 weeks, birth weight <4 kg).

The following table shows the comparison between groups for mean HC levels after stratification. The difference is not statistically significant among male group and category of birth weight >4 kg. The following table shows the comparison between groups for polycythemia prevalence after stratification.

Parameter		Group		Total	P-Value
		A	B		
Anaemia	Yes	18 (18.9%)	17 (17.9%)	35 (18.4%)	0.852
	No	77	78	155	
Total		95	95	190	

Table-I. Showing comparing the frequency of anemia in both groups (n=190).

Parameter		Group		Total	P-Value
		A	B		
Polycythaemia	Yes	27 (28.4%)	45 (47.4%)	72	0.007
	No	68	50	118	
Total		95	95	190	

Table-II. Showing the frequency of Polycythemia among both groups (n=190).

Parameter	Group		P-Value
	A	B	
Gestational age (wks)	39.23 ± 1.49	39.32 ± 1.52	0.700
Birth weight (kg)	3.68 ± 0.74	3.61 ± 0.71	0.491
Hemoglobin (g/dl)	15.52 ± 1.90	16.62 ± 2.53	0.001
Hematocrit (%)	62.09 ± 4.75	64.43 ± 5.62	0.002

Table-III. Showing mean + SD of all the quantitative variables among groups (n=190).

Parameter		Group		P-Value
		A	B	
Gestational age	<40 weeks	15.58 ± 1.83	16.16 ± 2.46	0.131
	>40 weeks	15.34 ± 2.08	17.57 ± 2.43	<0.0001
Gender	Male	15.85 ± 1.86	16.90 ± 2.53	0.027
	Female	15.23 ± 1.90	16.34 ± 2.52	0.015
Birth weight	< 4 kg	15.84 ± 1.74	16.50 ± 2.48	0.097
	> 4 kg	15.05 ± 2.03	16.841 ± 2.65	0.002

Table-V. Hemoglobin level comparison after stratification of gestational age, gender, birth weight.

Parameter		Group		P-Value
		A	B	
Gestational age	<40 weeks	61.97 ± 4.96	64.11 ± 5.17	0.017
	>40 weeks	62.41 ± 4.25	65.10 ± 6.48	0.071
Gender	Male	62.95 ± 4.93	62.87 ± 5.59	0.941
	Female	61.35 ± 4.50	65.96 ± 2.26	<0.0001
Birth weight	< 4 kg	61.91 ± 4.68	64.43 ± 5.56	0.009
	>4 kg	62.36 ± 4.90	64.44 ± 5.83	0.107

Table-VI. Hematocrit comparison after stratification of gestational age, gender, birth weight.

Parameter		Polycythaemia	Group		P-Value
			A	B	
Gestational age	<40 weeks	Yes	20 (29.4%)	28 (29.4%)	0.087
		No	48	36	
	>40 weeks	Yes	07 (25.9%)	17 (54.8%)	0.026
		No	20	14	
Gender	Male	Yes	17 (38.6%)	18 (38.3%)	0.974
		No	27	29	
	Female	Yes	10 (19.6%)	27 (56.2%)	<0.0001
		No	41	21	
Birth weight	< 4 kg	Yes	15 (26.8%)	29 (46%)	0.037
		No	41	34	
	>4 kg	Yes	12 (30.7%)	16 (50%)	0.143
		No	27	16	

Table-VII. Polycythaemia comparison after stratification of gestational age, gender, birth weight.

DISCUSSION

The clamping of the umbilical cord in fundamental step during the third stage of labor. The discussion over the timing of clamping of the cord has been controversial. Initial attempts to quest for this are in the literature since start of the nineteenth century but insufficient results are available. The residual blood in the placenta is the focus in this issue. Long before around 2 decades back a study related to this topic was done and meta-analysis was done using its data with some other studies, it was concluded that after 40 seconds net-flow between placenta and infant reverses. And cord-clamping if delayed further 40 seconds can end up into a rise in the RPBV (residual placental blood volume) back to the level found when the cord was clamped before 20 seconds.[6]

Later on when the timing of cold clamping was studied on larger scale with more variables in focus then it came to recognition that cord clamping timing in normal deliveries may have no significant effect but late clamping in premature neonates is beneficial because it reduces the incidence of respiratory distress syndrome.[7] In 2005 a literature review showed almost similar observations i.e. late cord clamping for full term neonates has no extra advantage.[8] The late cord clamping increases the blood viscosity by 40% initially which may revert to near normal after 24 hours.[9]

Van Rheenen P and Brabin BJ, et al concluded that delayed cord-clamping in infants, with anemic mothers can decrease the risk of anemia in infants till 2-3 months age, without an associated rise in the chances of perinatal complications. This step just after the birth of a neonate in countries where fetal anemia is a common condition can improve the morbidity and mortality of neonates and infants.[10]

In 2008, Jahazi, A., et al.[11] showed that there is no difference between the early and late clamping groups in terms of HCT levels (61 ± 4.9 versus 61.6 ± 4.5% for early and later groups respectively, p value >0.05). This is contrary to the results of our study which showed that HCT in early and late clamping group is 62.09 ± 4.75 and 64.43 ± 5.62% respectively with p value of 0.002. These conflicting results may have arisen due to two major differences. First the sample size of our study was 190 in total while above mentioned study had sample size of 64 only. Second difference was the timing of clamping. For our study, the early clamping was done at 15 seconds while in this study the early clamping was done at 30 seconds. In the same year another study had similar results as compared to my study. This study showed that late cord clamping coincides with an increased placental transfusion, expressed by higher hematocrit and emoglobin values, and larger left ventricle diameter at the end of the diastole, with no changes in peripheral perfusion or oxygen metabolism.[12] Improvement in Hb, HCT with increased risk of polycythemia after delayed cord clamping in neonates was shown by Rincon D, et al and Salari Z, et al. with

no effect on the APGAR score and duration of third stage of labor.[5,13]

Even the chances of maternal postpartum hemorrhaging and/or neonate jaundice are also no affected, as was seen by Chien, PC, et al. in a study in 2015.[14] Similar conclusions were made in a study in 2017. In our study, we limited to only single time hematological measurements in the immediate postnatal time, but the late cord clamping may have the beneficial effects later also.

One study by Andersson, O., et al. (2011) showed the delayed cord clamping, compared with early lamping, resulted in improved iron status and reduced prevalence of iron deficiency at 4 months of age, and reduced prevalence of neonatal anemia, without demonstrable adverse effects.[3] Another recent study showed that serum ferritin levels are raised in late cord clamping group even at the end of six months of life.[15] Somewhat conflicting results were shown by Agarwal, S., et al. (2016).[4] It showed that at the end of one year there was no difference between groups in terms of iron stores, hemoglobin levels or growth parameters. These conflicting results may be due to the selection of participants as in 2017, Kc, A., et al. showed that delayed cord clamping reduces anemia at 8 and 12 months of age in a high-risk population, which may have major positive effects on infants' health and development.[16] So for low risk infants the early or late clamping might have no impact. Even after 6 months, mean Hb, HCT, serum iron levels were higher in delayed cord clamping group with no evidence of polycythemia or jaundice.[15]

Studies have shown that delayed clamping and cord milking should be done routinely in all deliveries.[17-20] In our study, we stratified the data to counteract the effect of confounders. The stratification results showed the results showed that mean Hb levels are statistically not different among some of the groups (gestational age <40 weeks, birth weight <4 kg) while HCT levels are significantly different among male group and category of birth weight >4 kg.

CONCLUSION

The delayed cord clamping in neonates results in increased mean hemoglobin and hematocrit levels with increased frequency of polycythemia as compared to early cord clamping. The results should be ascertained on large scale to establish as protocol for late clamping of cord.

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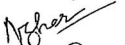
3	M. Azhar Farooq	Discussion writing, Data Analysis.	
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