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Correlation of Early and Late Cord Clamping Time with Hematological Variables: An Observation Study Focusing on The Neonatal Outcomes

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Abstract

Objectives: The purpose of this study was to evaluate the neonatal outcomes in early and delayed cord clamping and to find their correlation in early and delayed cord clamping with different haematological parameters in neonates of Jinnah Postgraduate Medical Centre, Karachi.

Material and methods: This was a cross observational study through convenient sampling technique conducted for a period of six months from 1st July 2016 to 31st December 2016 in the Obstetrics & Gynaecology ward of Jinnah Postgraduate Medical Centre, Karachi after ethical approval. The total of 340 pregnant women devoid of any hemolytic disease and with singleton pregnancy were included in the study. Women with multiple pregnancies, any systemic disease and prior history of postpartum hemorrhage were excluded from the study. Newborns were divided into two groups on the basis of cord clamping time with early clamping group 1(n=170) and late clamping group 2(n=170). SPSS version 20.0 was used and spearman and pearson correlation was applied. T-test and chi square test were applied to assess the differences and association with significance level of < 0.005.

Results: Total of 340 pregnant women were incorporated in this study and their neonates were divided into two groups on the basis of cord clamping time. Group 1 had clamping time of 45±7.92 seconds and group 2 with clamping time of 118±33.26 seconds. Hemoglobin was 13.29±1.33 mg/dl in group 1 and 13.43±1.06 in group 2. Hematocrit was 40.87±3.78 % and 41.36±3.02% in group 1 and 2 respectively. Bilirubin (mg/dl) was 9.15±5.77 in group 1 while 13.14±10.14 in group 2. Anemia was present in 7.1% and 2.9% of infants in group 1 and respectively. Polycythemia was observed in 2.9% of infants of group 1 while 11.25% infants of group 2 presented with it. High bilirubin was seen in 4.1% and 19.4% infants of group 1 and 2 respectively. No correlation exists in any hematological parameter with increasing clamping time in either group.

Conclusion: The present study predicted that no correlation in either group existed between hemoglobin, hematocrit and bilirubin with increasing cord clamping time. Furthermore, there was no association observed in neonates with anemia, low hematocrit, polycythemia and high bilirubin with increasing cord clamping time.

Keywords: correlation, hematological parameters

Introduction

Previously done studies have discovered that, approximately 25% to 60% (54–160 ml) of the overall amount of blood in combined fetal–placental unit at term is found in placental distribution, and about 60% of the fetal red blood cells are observed in placenta [1]. Blood that transfuses from placenta to neonate at delivery is a physiological phenomenon that enhances the instant shift to extra-uterine life [2]. The time of cord clamping, location of the infant in relation to the placenta, the infant's respiratory effort and contraction of uterus are among the numerous factors on which efficient blood transfer from placenta is dependable [3]. Globally, various studies have discovered different views regarding the time of cord clamp in which mother and newborn safety are amongst the chief considerable points of differences. Numerous health care personnel worldwide try to deliver the baby and clamping of the cord as quickly as possible [4].

Umbilical cord clamping time is still an exceedingly controversial matter [5,6]. It can be early cord clamping (ECC) (cord being clamp <10 seconds following delivery) or delayed cord clamping (DCC) (cord being clamped 30-180 seconds subsequent to delivery) [7]. The reduction of 20-40 ml of blood per kilogram of body weight is observed in the newborn with early clamping of the cord (in the first 5 to 15 seconds of birth) in comparison to late clamping (1-3 minutes after birth). It has been under debate that ECC causes amplification of the chances of hypovolemic injury and iron loss in infant, also as a consequence of loss of hematopoietic stem cells [8]. Several studies showed that delayed cord clamping may possibly add in prevention of iron deficiency anemia in the primary year of life. The cause for this outcome is based on the reality that subsequent to birth, 80 ml of blood is transfused from placenta to newborn at 1 minute following birth and 100 ml at 3 minutes after birth [9,10]. This quantity will provide 40 to 50 mg/kg of additional iron to the approximately 75 mg/kg of body iron that newborn term infants have, attaining a total of 115 to 120 mg/kg, which may reduce the chances of iron deficiency in the initial year of life [11,12]. It has often been recommended that DCC in full term infants might result in additional instances of jaundice that require light therapy, but it has not been verified with available data. Additionally to clamping delay, there are further factors that influence the shift of blood from the placenta to the infant [13]. Numerous reviews have revealed the potential benefits and risks linked with late and early clamping of the umbilical cord. A recent study of cord clamping in the preterm population revealed lesser necessity for blood transfusion and risk of intra-ventricular hemorrhage are amongst the few probable advantages of late cord clamping.[14] Reviews to date of studies in term infants provided no strong authentication for the dominancy of either clamping approach. [15] Facts disclose that predominantly for newborn infants who do not demand resuscitation DCC is proven to be favorable.[16] It has been suggested that giving focus only on clamping delay and ignoring other factors such as when the baby starts breathing may possibly be non productive for the newborn and could even as a consequence cause infant-to-placenta shift of blood.[17]

The purpose of this study was to evaluate the neonatal outcomes in early and delayed cord clamping and to find their correlation with different haematological parameters in neonates.

Methodology

Observational study was conducted in which non-probability convenient sampling method was used with an overall of 340 pregnant women included in the study from the Obstetrics & Gynaecology ward of Jinnah Postgraduate Medical Centre, Karachi. The necessary approval from the Jinnah Hospital's Ethical Review Committee was taken to assemble required data. Collection of data was done in a period of six months from 1st July 2017 to 31st December 2017. An informed approval was taken from women and privacy was maintained. Pregnant women from age of 25 to 45 years and devoid of any haemolytic disease, with prior spontaneous vaginal deliveries, now with a singleton pregnancy diagnosed via ultrasound during the initial trimester and presenting in the 3rd stage of labour with a gestational age of ≥ 37weeks were included in this study. Women with multiple pregnancies, with prior postpartum haemorrhage record, formerly having caesarean section or any systemic disease like diabetes mellitus, hypertension, thyroid disease and cardiac insufficiency were excluded from this study. Two groups were made on the basis on different cord clamping time. Group 1 (n=170) comprised of neonates with cord clamping time of less than 1 min and group 2 (n=170) comprised of those with cord clamping time of greater than 1 min which was recorded by stop watch subsequent to delivery of fetus. Almost immediately after the delivery of placenta, the uterus was massaged either by patient herself or by the caretaker. Researcher gathered the neonatal blood samples through venipuncture subsequent to removal of the fetus and 24 hours after it and were sent to the laboratory for analysis.

Data Analysis

Analysis of data was done via SPSS version 20. Descriptive analysis was done. For quantitative variables such as maternal age, gestational age, hemoglobin level, hematocrit, serum billirubin level, and cord clamp time mean and standard deviation were calculated whereas frequencies and percentages were calculated for qualitative variables i.e. polycythemia, low hematocrit, high serum billirubin, and anemia. Chi-square and t-test were applied and p-value of < 0.05 was taken as significant. Pearson and Spearman tests were applied to see the correlation of cord clamping time with quantitative and qualitative variables respectively.

Results

A total of 340 pregnant females in their third stage of labor were selected for this study. Their infants were taken into two groups on the basis of cord clamping time which in group 1 (n=170) was 45±7.92 seconds while in group 2 (n=170) was 118±33.26 seconds (p-value= < 0.001). The age of mothers in group 1 was 35.57±5.97years while in group 2 was 38.84±5.95 years (p-value=0.260). Gestational age in group 1 and 2 was 38.54±0.94 and 38.45±0.94 weeks respectively (p-value=0.390). Hemoglobin level was 13.29±1.33 and 13.43±1.06 mg/dl in group 1 and 2 respectively (p-value=0.305). Group 1 was found to have

Table 1: Baseline characters of the two groups and their mean difference

Variable n = 340	Group1 (n=170)	Groups 2 (n=170)	P-value
	Mean ± S.D	Mean ± S.D	
Age of Mother(years)	35.57±5.97	38.84±5.95	0.26
Gestational age(weeks)	38.54±0.94	38.45±0.94	0.39
Cord clamping time (seconds)	45.26±7.92	118.70±33.26	< 0.001
Hemoglobin(mg/dl)	13.29±1.33	13.43±1.06	0.305
Hematocrit (%)	40.87±3.78	41.36±3.02	0.189
Billirubin (mg/dl)	9.15±5.77	13.14±10.14	< 0.001

hematocrit of 40.87±3.78% whilst in group 2 was 41.36±3.02% (p-value=0.189). Bilirubin level was 9.15±5.77mg/dl in group 1 and 13.14±10.14 mg/dl in group 2 (p-value= < 0.001). (Table 1)

In group 1 anemia was present in 12(7.1%) infants while 158(92.9%) were anemia free. However 5(2.9%) infants in group 2 were anemic while 165(97.1%) were not. Low hematocrit was seen in 19(11.2%) of infants of group 1 while 151(88.8%) did not had it. On the other hand 8(4.7%) infants of group 2 had low hematocrit while 162(95.3%) did not had it. Polycythemia was present in 5(2.9%) infants in group 1 though 165(97.1%) infants of group 2 had no polycythemia. 19(11.2%) infants of group 2 presented with polycythemia while 151(88.8) were polycythemia free. High bilirubin was seen in 7(4.1%) infants of group 1 though 163(95.9%) did not had it. However 33(19.4%) infants of group 2 presented with elevated bilirubin while 137(80.6%) had no raised bilirubin. (Table 2)

Table 2: Association of hematological parameters in two groups

Variable n = 34		Group 1 (n=170)	Group 2 (n=170)	P-Value
		Frequency(%)	Frequency(%)	
Anemia	Yes	12(7.1)	5(2.9)	0.082
	No	158(92.9)	165(97.1)	
Low Hematocrit	Yes	19(11.2)	8(4.7)	0.027
	No	151(88.8)	162(95.3)	
Polycythemia	Yes	5(2.9)	19(11.2)	0.003
	No	165(97.1)	151(88.8)	
High billirubin	Yes	7(4.1)	33(19.4)	< 0.001
	No	163(95.9)	137(80.6)	

No Pearson correlation in either group existed between hemoglobin, hematocrit and bilirubin with increasing cord clamping time (p-value=0.176),(p-value=0.467) and (p-value=0.818) respectively in group 1 while (p-value=0.533),(p-vlaue=0.620) and (p-value=0.409) respectively in group 2. (Table 3)

Table 3: Pearson correlations between early and late cord clamping time with haemoglobin, hematocrit and billirubin.

Variables	Cord clamping time (sec)			
	Group 1		Group 2	
	R	p-Value	R	p-Value
Hemoglobin (mg/dl)	-0.104	0.176	-0.048	0.533
Hematocrit (%)	-0.056	0.467	-.038	0.620
Billirubin (mg/dl)	0.018	0.818	-0.064	0.409

Similarly no spearman correlation was seen in neonates to have anemia, low hematocrit, polycythemia and high bilirubin with increasing cord clamping time in either group (p-value=0.104),(p-value=0.926),(p-value=0.307) and (p-value=0.327) respectively in group 1 while (p-value=0.858), (p-value=0.812), (p-value=0.978) and (p-value=0.871) respectively in group 2. (Table 4)

Table 4: Spearman correlations between early and late cord clamping time with haemoglobin, hematocrit and billirubin

Variables	Cord clamping time (sec)			
	Group 1		Group 2	
	ρ	p-Value	P	p-Value
Anemia	-0.125	0.104	-0.014	0.858
Low Hematocrit	0.007	0.926	-0.018	0.812
Polycythemia	0.079	0.307	0.002	0.978
High Billirubin	-0.076	0.327	-0.013	0.871

Discussion

Study of available data is multifarious due to disagreement on the description of DCC which, in a range of studies, range from 2-10 minutes or until the termination of cord pulsation following birth. ECC in general means what it says although some studies includes cord clamping within ten seconds following birth. [18] A study of Andersson O et al. on 400 full term infants and having comparison of DCC (>180 sec following delivery) vs. ECC (< 10 seconds subsequent to delivery) provided no substantial differences in hemoglobin levels between the two groups after 4 months but decreased prevalence of anemia at 2nd day of birth [2(1.2%) vs. 10(6.3%), P = 0.02] was observed in infants of DCC group. On the other hand, no differences in polycythemia or bilirubin levels necessitating phototherapy was seen.[19] Likewise study conducted on Peruvian infants with variation in cord clamping time from 57 ± 32 seconds (ECC) to 107 ± 87 seconds (DCC) and followed after 8 months revealed that in ECC vs. DCC groups 79.1% vs. 63.4% (hemoglobin 9.9 ± 1.39 g/dL vs. hemoglobin 10.7 ± 0.9 g/dL, p<0.05) respectively were anaemic. [20] Correspondingly, a total of 242 patients were included in a study of Rincon D et al. in which three groups in accordance to cord clamping time (g1 n= 80) <60s, (g2 n= 31) 1-2 min and (g3 n= 131) 2-3 min were evaluated. In the analysis the levels of hemoglobin (g1: 17.3 g/dl, g2: 18.9 g/dl, g3: 19.2 g/dl; p < 0.01) and hematocrit (g1: 53.4%, g2: 58%, g3: 59%; p < 0.01) were found to be significantly higher in DCC group. However, , a substantial augmentation was seen in the frequency of polycythemic infants in group 3.[21] A study by Tanmoun M et al., in which 148 term infants were chosen out of which 72 got ECC and 76 received DCC. After 48 hours of birth, the infant's hemoglobin, and hematocrit were significantly advanced in DCC vs ECC (17.8 g/dl vs. 16.1 g/dl; p< 0.001 and 54.5% vs. 50.3%; p<0.001 and 54.5% vs. 50.3%; p<0.001, respectively).Conversely, in early cord clamping the prevalence of neonatal anemia was greater than delayed cord clamping but the difference was not considerable (N=11, 15.3% vs. N=4, 5.3%; p=0.08, respectively). Polycythemia and mean serum total bilirubin were reasonably higher in DCC than ECC but not noteworthy (4.0% vs. 1.4%; p=0.25 and 13.3 mg/dl vs. 12.7 mg/dl; p=0.21, respectively).[22] Likewise, although the facts appear chiefly from small trials, delayed umbilical cord clamping in premature neonates is coupled with lesser requirement for red blood cell transfusion, enhancement in hemoglobin and hematocrit values. [23] In accordance with this, J S Mercer et al. reported 73 females with term (37 to 41 weeks) singleton

fetuses randomized to DCC (5 min; n=37) or ICC (<20 s; n=36) and established prominent enhancement in hemoglobin levels (19.4 vs 17.8 g dl−1, P=0.002) at 24 to 48 h, with no divergence in bilirubin levels or symptomatic polycythemia.[24] According to a study conducted in April 2013, umbilical cord clamping between 30 to 180 seconds following birth in term infants resulted in higher levels of hemoglobin and hematocrit throughout the neonatal period and a lesser incidence of iron deficiency anemia in 4 to 6 months of age. [25] The above mentioned studies are consistent with our results predicting that there is enhancement of hematological parameters with delayed cord clamping but no considerable difference or correlation seen among the two groups. Study of Mungkornkaew S et al., reported 100 cases, randomized to each groups to perform 1 minute versus 2 minutes of delayed cord clamping. Fetal hematocrit, hemoglobin and microbilirubin considerably augmented in 2 mins of delayed cord clamping time (53.44% vs. 52.39 % (p = 0.041) 16.33 g/dL vs. 14.74 g/dL (p = 0.001) and 11.04 mg/dL vs. 10.17 mg/dL (p = 0.011) noticed at 48 hours subsequent to birth. (53.44% vs. 52.39 %) (p = 0.041) 16.33 g/dL vs. 14.74 g/dL (p = 0.001) and 11.04 mg/dL vs. 10.17 mg/dL (p = 0.011). Neonatal jaundice and phototherapy necessity were higher in 2 minutes cord clamping group. Moreover the study observed no prevalence of fetal anemia, polycythemia and exchange transfusion in either group.[26] One of the study reported high hematocrit and hemoglobin level at birth mainly among DCC in comparison to ECC group with no substantial differences whereas a notable differences were noticed regarding these levels after 24 hours. Additionally, no vital difference was seen in total billirubin value, polycythemia and anemia. The incidence of infant with a hematocrit level of < 45% at birth and following 24 hours amongst early and late group was indistinctly greater in ECC vs. DCC but with no significant differences (3%, 3% &1%, 0.0% respectively).[27] Salae R et al. analyzed 86 neonates in their study. Neonates in the DCC group had appreciably higher hematocrit value than the ECC group (55.4% and 47.6%, respectively: p = 0.02). The microbilirubin level in the DCC group was also notably elevated than in the ECC group (9.4% and 8.6 mg %, respectively: p = 0.04). On the other hand, phototherapy and length of hospitalization in both groups were not dissimilar. [28] In a study in which total 200 women were randomized; 99 to the delayed cord clamping and 101 to the early clamping group. The mean early hemoglobin (17.4±2.5 versus 16.3±2.3 g/dL, P = 0.001) and hematocrit (51.3±7.3 versus 47.4±7.3, P = 0.001) were considerably greater in the delayed clamp group. 36.4% (36/99) of neonates in the delayed cord clamp group were diagnosed with anemia compared to 47.5% (48/101) in the immediate clamp group, (P = 0.11).[29] The mean hematocrit (27.3 ± 3.8 % vs. 31.8 ± 3.5 %, p value 0.00) at 6 wk of age was considerably superior in the infants of DCC group. The DCC group required extensive duration of phototherapy (55.3 ± 40.0 h vs. 36.7 ± 32.6 h, p value 0.016) and had a trend towards elevated risk of polycythemia.[30] These above mentioned studies are in line with results of this study however no significant correlation noticed with any of the hematological parameters with enhancing the clamping time.

The qualitative approach of our study has declared that we have illustrated the extensive range of outcomes of cord clamping time. However the study might not be free from observer and selection bias. Considering the interpretations of our study and to what range the neonatal outcome might be consistent with the hematological profile of the mothers during the last trimester of pregnancy would be enlightening to reveal more facts about the neonatal outcomes.

Conclusion

The present study predicted that no correlation in either group existed between hemoglobin, hematocrit and bilirubin with increasing cord clamping time. Furthermore, there was no association observed in neonates with anemia, low hematocrit, polycythemia and high bilirubin with increasing cord clamping time.

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