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Neonatal Outcomes in Cord Clamping; An Observational Study Highlighting the Correlation of Cord Clamping Time with Haematological Parameters

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Abstract

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

Methodology: This was an observational study in which non-probability convenient sampling technique was used after taking ethical approval. The study was conducted on 342 pregnant women in the Obstetrics & Gynaecology ward of Jinnah Postgraduate Medical Centre, Karachi, from 1st July 2016 to 31st December 2016.All the pregnant women from age of 25 to 45 years and without any haemolytic disease, with previous spontaneous vaginal deliveries, with a singleton pregnancy diagnosed via ultrasound during the first trimester and presenting in the 3rd stage of labour with a gestational age of ≥ 37weeks were included in the study. Soon after the delivery of placenta, the uterus was massaged either by patient herself or by the caretaker. Neonatal blood samples were gathered by the researcher through venipuncture following expulsion of the fetus and 24 hours after it and sent to the pathology laboratory of Jinnah Hospital for analysis. Data were analyzed in SPSS Version 20. Descriptive analysis was done. Pearson and Spearman tests were applied to see the correlation of cord clamping time. P-value of < 0.05 was taken as significant.

Results: A total of 342 pregnant females in their third stage of labor were selected for this study. No correlation existed between hemoglobin and hematocrit with cord clamping time (p-value 0.661) and (p-value 0.439) respectively. Weak positive correlation (p=0.002,r = 0.169) existed between billirubin levels with clamping time. No correlation was observed with cord clamping time and anemia, low hematocrit or polycythemia (p-value 0.422), (p-value 0.058) and (p-value 0.20) respectively while weak negative correlation (ρ = -0.221) existed between high bilirubin levels in neonates with increasing cord clamping time (p-value <0.001).

Conclusion: According to our study, no correlation exists between hemoglobin and hematocrit with cord clamping time but weak positive correlation was observed between billirubin levels with clamping time in seconds.

Keywords: cord clamping; correlation; haematological parameters

Introduction

Previous physiological studies have revealed that approximately 25% to 60% (54–160 mL) of the entire blood volume in combined fetal–placental unit at full gestation is present in placental circulation, and about 60% of the fetal red blood cells are found in placenta[1].One of the ancient interventions that humans have performed includes umbilical cord clamping. It can be early cord clamping (ECC) (clamping cord <10 seconds after delivery) or delayed cord clamping (DCC) (clamping cord 30-180 seconds after delivery) [2].A lot of health care personnel globally tend to deliver the baby and clamp the cord as rapidly as possible [3].Reduction of 20 ml to 40 ml of blood per kilogram of body weight is seen in the neonate with early clamping of the cord (within the initial 5 to 15 seconds of birth) as compared to late clamping (1-3 minutes following birth). It has been under discussion that early cord clamping amplifies the risk of hypovolemic damage and iron loss in newborn, also as a result of loss of hematopoietic stem cells the chances of several blood disorders such as type 2

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diabetes increases.[4].Facts reveal that principally for newborn infants who do not necessitate resuscitation, DCC proves to be beneficial. Augmented haemoglobin (Hb) and haematocrit (Hct) levels in the neonate with a consequent drop in rates of anaemia and iron deficiency that may extend into the infancy period are among a few advantages of DCC [5]. On the other side, hyperbilirubinaemia, polycythaemia, and transient tachypnea in the newborn or maternal haemorrhage are among the risk factors that may be enhanced by DCC. One of the study predicted that DCC does not cause a considerable divergence in the haematocrit level of the neonate or neonatal polycythaemia [2]. Others believe that delaying the clamping of cord augments the blood volume to the neonatal circulation that can be detrimental and could lead to congestion therefore escalating the probability of respiratory distress, neonatal jaundice, and polycythemia. [6,7]After delivery, transfusion of fetoplacental blood to the newborn raises the infant's blood volume by 30% to 40% (roughly 25-30 mL/kg), if early cord clamping is not performed. The blood transfused can supply with 75 mg of iron and has been shown to enhance iron stores and provide prevention against iron deficiency in initial infancy to 6 months of life. [8] Neonatal advantages include improved cardiopulmonary adaptation and advanced hemoglobin concentrations to 2 to 3 months of age [9]. DCC is linked with lesser occurrence of all grades of intraventricular haemorrhage (IVH), elevated systemic blood pressure and volume, decrease requirement for blood transfusion, and low occurrence of necrotising enterocolitis. Nevertheless, no dissimilarity has been established in severe IVH, mortality, temperature unsteadiness and long-term outcomes, even though an augment in serum bilirubin coupled with a greater need for phototherapy has been noted. This is regardless of gestational age [10]. In addition to this, early clamping is part of active management of the third stage of labor to support with release of the placenta, and this management has been shown to considerably reduce maternal blood loss soon after birth. [11] According to a recent study of cord clamping in the preterm population, decreased requirement for blood transfusion and lesser risk of intra-ventricular haemorrhage are among the few potential benefits of late cord clamping.[12] one of the systematic review in term infants provided no strong verification for the dominance of either clamping approach.[13]

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

Methodology

This was an observational study in which non-probability convenient sampling technique was used. The study was conducted on 342 pregnant women in the Obstetrics & Gynaecology ward of Jinnah Postgraduate Medical Centre, Karachi. The essential approval from the Jinnah Hospital's Ethical Review Committee was obtained to gather necessary data. Compilation of data covered a period of 6 months from 1st July 2016 to 31st December 2016.An informed consent was taken from women and confidentiality was maintained. All the pregnant women from age of 25 to 45 years and without any haemolytic disease, with previous spontaneous vaginal deliveries, with a singleton pregnancy diagnosed via ultrasound during the first trimester and presenting in the 3rd stage of labour with a gestational age of ≥ 37weeks were included in the study. Women with multiple pregnancies, with previous postpartum haemorrhage history, previously done caesarean section or any systemic disease like diabetes mellitus, hypertension, thyroid disease and cardiac insufficiency were excluded from the study. Cord was clamped on different timings from as low as 45 to as high as 118 seconds recorded by stop watch following delivery of fetus. Soon after the delivery of placenta, the uterus was massaged either by patient herself or by the caretaker. Neonatal blood samples were gathered by the researcher through venipuncture following expulsion of the fetus and 24 hours after it and sent to the pathology laboratory of Jinnah Hospital for analysis. All other aspects of obstetric care were done according to standard practice in the hospital.

Data Analysis

Data were analyzed in SPSS Version 20. Descriptive analysis was performed. 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 while frequencies and percentages were calculated for qualitative variables i.e. polycythemia, low hematocrit, high serum billirubin, and anemia. Pearson and Spearman tests were applied to see the correlation of cord clamping time with quantitative and qualitative variables respectively. p-value of < 0.05 was taken as significant.

Results

A total of 342 pregnant females in their third stage of labor were selected for this study. The mean age of mother was 35.2±5.98 years while that of gestation was 38.5±0.94 weeks. The mean cord clamping time was found to be 81.9±43.90 seconds. Anemia was found in 17(5%) neonates while 325(95%) were anemia free. Low hematocrit was present in 27(7.9%) while 315(92.1%) neonates did not have it. Polycythemia appeared in 24(7%) whereas 318(93%) were normal. Only 40(11.7%) neonates were found to have high billirubin while 302(88.3%) had no such issue. Mean hemoglobin and hematocrit were 13.3±1.20 mg/dl and 41.1±3.42% respectively while mean billirubin was found to be 11.1±8.46 md/dl. (Table: 1) No correlation existed between hemoglobin and hematocrit with cord clamping time (p-value 0.661) and (p-value 0.439) respectively. Weak positive correlation (p-vlaue=0.002,r = 0.169) existed between billirubin levels with clamping time (Table:2). No correlation was observed with cord clamping time and anemia, low hematocrit or polycythemia (p-value 0.422), (p-value 0.058) and (p-value 0.20) respectively while weak negative correlation ($\rho = -0.221$) existed between high bilirubin levels in neonates with increasing cord clamping time (p-value <0.001). (Table:3)

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Table1: Baseline characteristics of the two groups and their mean difference

Variable n = 342	Mean ± S.D/Frequency (%)
Age of Mother(years)	35.2+5.98
Gestational age(weeks)	38.5+0.94
Cord clamping time (seconds)	81.9+43.90
Hemoglobin(mg/dl)	13.3±1.20
Hematocrit (%)	41.1±3.42
Billirubin (mg/dl)	11.1±8.46
Anemia	
Yes	17(5%)
No	325(95%)
Low Hematocrit	
Yes	27(7.9%)
No	315(92.1%)
Polycythemia	
Yes	24(7%)
No	318(93%)
High billirubin	
Yes	40(11.7%)
No	302(88.3%)

Table 2: Pearson correlations between cord clamping time and haemoglobin, hematoctit and billirubin.

Variables	Cord clamping time (sec)	
	r	p-Value
Hemoglobin (mg/dl)	0.024	0.661
Hematocrit (%)	0.042	0.439
Billirubin (mg/dl)	0.169	0.002

Table 3: Spearman correlations between cord clamping time and different haematological variables.

Variables	Cord clamping time (sec)	
	ρ	p-Value
Anemia	0.044	0.422
Low Hematocrit	0.103	0.058
Polycythemia	-0.126	0.20
High Billirubin	-0.221	< 0.001

Discussion

This study is one of its own kind in a way that no study has been found to be related to the correlation of cord clamping time with hematological parameters.

There is wide variation in the accurate explanation of immediate and late cord clamping time. This may lead to differences in the correlation of haematological parameters in association with the cord clamping time. Study of published data is complex due to short of agreement on the definition of DCC which, in various studies, ranges from 2-10 minutes or till the cessation of cord pulsation after birth. ECC generally means cord clamping within 10 seconds following birth.[14] A study done by Andersson O et al. on 400 full term infants and comparing DCC (>180 sec after delivery) vs. ECC (< 10 seconds after delivery) revealed no considerable differences in hemoglobin concentration among the two groups after 4 months but reduced prevalence of anemia at second day of birth(P-value=0.02) was noticed in infants of DCC group. However, no differences in polycythemia or bilirubin levels needing phototherapy was seen.[15]Similarly study done on Peruvian infants with cord clamping varying from 57 ± 32 seconds (ICC) to 107 ± 87 seconds (DCC) and followed after 8 months showed that in ICC 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.[16]These above mentioned studies are consistent with our study with respect to hemoglobin concentration and polycythemia but contradicts with respect to bilirubin levels and infants being anemic. In accordance to the previously mentioned study, another study conducted by Philip Lanzkowsky on a series of 133 infants in which 63 cases were those in which cord was clamped straight away the infant was born (group 1), and in 70 cases the cord was clamped only after it had been stripped off (group 2). The mean hemoglobin levels in the late-clamped infants were considerably elevated statistically than in the early-clamped infants. The mean hemoglobin levels between birth and 12 hours, 13 and 24 hours, and 72 and 96 hours were 19.80, 18.20, and 18.13 g./100 ml. respectively in the infants of group 1, whereas 20.14, 19.86, and 19.74 g./ 100 ml. respectively in the infants of group 2.[17] Similarly, a totality of 242 patients were incorporated in a study of Rincon D et al. in which three groups according to cord clamping time (g1 = 80) <60s, (g2 = 31) 1-2 min and (g3 = 131)2-3 min were evaluated. It was observed that the values 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 statistically superior in delayed clamping group. Meanwhile, a considerable enhancement was seen in the number polycythemic infants in group 3.[18]Contrary to this, infants were followed-up at 4 (n=207) and 8 months (n=184) post-partum period in a study conducted by Blouin B et al. at hospital Iquitos, Peru in which no considerable fluctuations in hemoglobin levels between infants born to anaemic mothers and those born to non-anaemic mothers at either 4 or 8 months of age was noticed. However, timing of cord-clamping did modify the status of anemia in infant who were born to anemic mothers. Noteworthy effects of delayed cord-clamping in prevention of anaemia were established in infants born to anaemic mothers at both 4 months and 8 months of age.[19]Through a study done by Tanmoun M et al., in which 148 term infants were elected out of which 72 received early cord clamping and 76 received delayed cord clamping, after 48 hours of delivery, the infant's hemoglobin, and

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hematocrit were considerably higher in delayed cord clamping than early cord clamping (17.8 g/dl vs. 16.1 g/dl; p< 0.001 and 54.5% vs. 50.3%; p<0.001 , respectively). However, in early cord clamping the prevalence of neonatal anemia was comparatively superior than delayed cord clamping but the difference was not statistical significant (n=11, 15.3% vs. n=4, 5.3%; p=0.08, respectively). Polycythemia and mean serum total bilirubin were comparatively higher in delayed cord clamping than early cord clamping but not significant (4.0% vs. 1.4%; p=0.25 and 13.3 mg/dl vs. 12.7 mg/dl; p=0.21, respectively).[20] Similarly, although the facts are observed from small clinical trials, delayed umbilical cord clamping in premature neonates is coupled with reduction in the need for red blood cell transfusions, and augmentation in hemoglobin and hematocrit levels.[21] In support of this, Ashish KC et al., reported in their study of 540 infants in which 270 each were randomized to the delayed and early clamping groups. 212 infants (78.5%) from the delayed group and 188 (69.6%) from the early clamping group who returned at 8 months of age were blood sampled. After various analysis, infants who underwent delayed clamping had elevated levels of hemoglobin (10.4 vs 10.2 g/dL; difference, 0.2 g/dL; 95% CI, 0.1 to 0.4 g/dL). Also delayed cord clamping decreased the prevalence of anemia (hemoglobin level <11.0 g/dL) at 8 months in 197 (73.0%) vs. 222 (82.2%) infants.[22] Thawinkum S. et al. randomized 47 infants to receive ECC and 47 DCC. At 48 hrs after delivery, the mean infant hematocrit was statistically considerably advanced in DCC group (56.2 and 49.6 percent, respectively).Also the percentage of anemic infants was significantly elevated in the ECC (15.9 %) vs. the DCC (2.2 %) group. No considerable differences were noticed in the amount of polycythemic infants, hyperbilirubinemia and the use of phototherapy between both groups.[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 found elevated hemoglobin levels (19.4 vs. 17.8 g /dl, P=0.002) at 24 to 48 h, with no dissimilarity in bilirubin levels or symptomatic polycythemia. [24]According to study conducted in April 2013, umbilical cord clamping between 30 and 180 seconds subsequent to birth in term infants resulted in advanced concentration of hemoglobin and hematocrit throughout the neonatal period, and amplified serum ferritin levels and a lesser incidence of iron deficiency anemia at 4-6 months of age. [25] Study of Mungkornkaew S et al., reported 100 cases, randomized to each groups to perform 1 minute versus 2 minutes of delayed cord clamping. Baseline characteristics were similar in both groups. Fetal hematocrit, hemoglobin and microbilirubin were considerably increased in 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)observed at 48 hours following 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 requirement were superior in 2 minutes cord clamping group. Moreover the study revealed no prevalence of fetal anemia, polycythemia and exchange transfusion in both. [26]These aforementioned studies revealing enhancement in hemoglobin levels, increasingly polycythemic and anemic infants are inconsistent with our study. Contrary to our results, one of the study predicted slightly high hematocrit and hemoglobin level at birth chiefly amongst late cord clamping group as compared to early group with no considerable differences while a noteworthy differences were noticed concerning these levels following 24 hours. Furthermore, no significant difference was observed in total Billirubin levels, polycythemia and anemia The frequency of infants with a hematocrit level of less than 45% at birth and following 24 hours amongst early and late group was indefinitely superior in the early cord clamping group vs. late cord clamping but with no statistically major differences (3%, 3% &1%, 0.0% respectively).[27]

The qualitative approach of our study has assured that we have assessed the extensive range of outcomes of cord clamping and its correlation with hematological parameters. However, the study might not be protected from observer and selection bias. Taking into account the views of our observations and to what extent they are steady with the early and late cord clamping would be illuminating to discover more facts about neonatal outcomes which will help clinicians in reducing the frequency of anemia at the preliminary level.

Conclusion

According to our study, no correlation exists between hemoglobin and hematocrit with cord clamping time but weak positive correlation was observed between billirubin levels with clamping time in seconds. Moreover, no correlation was seen in neonates with anemia, low hematocrit or polycythemia while weak negative correlation existed between high bilirubin levels in neonates with cord clamping time.

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