

The Effect of Delayed Umbilical Cord Clamping on Blood Sugar and Venous Hematocrit levels in Term Infants of Diabetic Mothers

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Abstract: Background: Delayed clamping of the cord after birth enhances the short and long term hematologic status of infants. Although late clamping might increase blood viscosity, there is no evidence of any significant harm. **Objectives:** To investigate the effects of delayed umbilical cord clamping, compared with early clamping on blood glucose, hemoglobin, hematocrit and serum bilirubin in term infants of diabetic mothers. **Methods:** There were 84 infants of diabetic mothers randomized to early or immediate cord clamping (n = 28), 1 minute delayed cord clamping (n = 28), and 2 minutes delayed cord clamping (n = 28). We measured infants hemoglobin, hematocrit, Red Blood Cell (RBC) count, blood glucose and serum bilirubin 1 and 6 hours after delivery. Secondary outcomes as neonatal jaundice and respiratory problems were assessed. **Results:** The mean infants hematocrit at 6 hours after clamping was significantly higher ($p < 0.001$) in the 1 minute (49.6±3.9) and the 2 minutes delayed clamping groups (50±4.9) than in the early clamping group (46.5±4.6). The mean infants Red Blood Cell count and hemoglobin at 6 hours after clamping were significantly higher ($p < 0.001$) in the 2 minutes delayed clamping group (4.7±0.4), (18±1.5 g/dl) than both the 1 minute delayed clamping group (4.6±0.3), (16±1.4 g/dl) and the early clamping group (5.2±1.5), (16.8±1.4 g/dl) respectively. At 6 hours after clamping, infants showed no significant differences in Random Blood Sugar (RBS), serum bilirubin or postnatal outcomes. **Conclusion:** In infants of diabetic mothers, delayed cord clamping resulted in improved hematocrit levels without demonstrable adverse effects.

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1. Introduction

Diabetes with pregnancy is one of the most common medical disorders complicating pregnancy. It has been found that the incidence of diabetes complicating pregnancy has increased approximately 40% between 1989 and 2004.[1] Managing infants of diabetic mothers is an important and challenging issue in current neonatology practice. The combined erythrocyte and storage iron pools are significantly lower in infants of diabetic mothers. These findings are likely due to increased fetal iron utilization during compensatory hemoglobin synthesis in response to chronic hypoxemia and reduced iron transfer during late gestation complicated by diabetes. [2]. During the first six months of life, infants are largely dependent on the iron supply present at birth for growth and hemoglobin (Hgb) production. [3] Iron stores at birth correlate with iron stores at 6 to 12 months of age and are determined by the transplacental iron transferred from the placenta at the time of delivery. This is in turn determined by the timing of umbilical cord clamping. [4.] Iron deficiency anemia is common even in socially advantaged population. In developing countries, prevention of iron deficiency is not easy. [4] Delayed cord clamping provides extra iron to the neonate, which might prevent iron deficiency in the first year of life. The positive effect of delayed cord

clamping could be even more clinically important in developing countries. For those infants a moderate placental transfusion could represent physiological and inexpensive means of increasing iron stores. [5]

The question of when to clamp and cut the umbilical cord has been debated for many years. In the United States, delayed cord clamping was the standard care between the 1930s and 1960s and was advocated by well-respected obstetricians. Overtime, the practice of delayed cord clamping became viewed as dangerous or at least inconvenient without adequate scientific evidence applied to the subject [6]. In our delivery center at Ain Shams University Maternity Hospital, in Cairo, Egypt, immediate clamping of the umbilical cord is the recommended practice. Early cord clamping is believed to be the standard practice in many delivery settings.[7]. In 2007, the World Health Organization removed early cord clamping from its recommendations for active management of the third stage of labor for the prevention of postpartum hemorrhage. [8] The International Federation of Obstetricians and Gynecologists and the International Confederation of Midwives published a joint statement in 2006 for active labor that does not include early clamping. [9]

The hypothesis for this study was that delayed clamping of the umbilical cord would increase hemoglobin and hematocrit levels in infants of diabetic mothers. Those infants are at risk of anemia because of their mothers' diabetes. This study was planned to detect the effect of timing of cord clamping on blood glucose, venous hematocrit, hemoglobin and serum bilirubin in term infants of diabetic mothers.

2. Subjects and Methods

This study is a Randomized Controlled Pilot study. Eighty four pregnant women with diabetes mellitus in labor were enrolled in the study. Women were eligible if they had uneventful vaginal or cesarean section delivery with the following characteristics; (1) thirty seven weeks gestation, (2) singleton pregnancy at term and (3) no evidence of congenital malformation by ultrasonography. The study was approved by the Ethical Committee at Ain Shams Children's Hospital.

An informed written consent was taken from the mothers. Then they were subjected to the following: (1) Complete history taking (with special emphasis on the history of diabetes, its type and method of treatment). (2) Complete general examination (with special emphasis on the diabetic complications). (3) Venous blood samples (4ml) were collected in both plain and EDTA (*ethylenediaminetetraacetic acid*) containing tubes to estimate random blood sugar and hematocrit values.

They were randomly divided into one of three groups using allocation concealment method. Sequentially numbered opaque sealed envelopes were used. Twenty eight cases were enrolled for immediate cord clamping ≤ 15 seconds (group 1), 28 cases for 1 minute delayed cord clamping (group 2) and 28 cases for 2 minutes delayed cord clamping (group 3). The physician in charge for cord clamping could not be blinded; however, the neonatologists who made the neonatal evaluation were not aware of the timing of clamping.

The newborns were subjected to complete physical examination, APGAR scoring, Sampling of 4 ml of blood 1 hour and 6 hours after delivery in both plain and EDTA containing tubes to estimate venous hematocrit, hemoglobin (Hgb),

Red Blood Cell count, blood glucose and serum bilirubin.

Hgb was estimated with the use of CellDyne 1800 (Abbot park, il60064, USA). Serum Bilirubin and RBS was done on the Synchron CX-9 autoanalyzer.

The newborns were followed up at the Nursery to detect the effect of delayed cord clamping on neonatal outcome including neonatal jaundice requiring phototherapy and respiratory problems.

Statistical methods

All data were tabulated and statistically analyzed using SPSS for Windows Statistical Package (version 12). Numerical data were expressed as mean \pm standard deviation, while categorical data were expressed as number and percent. A chi squared test was used to compare two groups of categorical data. Unpaired t-student test was used to compare numerical parametric data. One way ANOVA test was used to compare more than two groups as regard quantitative variable in parametric data. Kruskal Wallis test was used instead of ANOVA test in non-parametric data. p value of 0.05 was used as the criterion for significance.

3. Results

All the studied groups were comparable as regards to gestational age at delivery and parity. There was no significant difference between women of the three groups concerning mode of delivery, maternal random blood sugar or obstetric history. (Table 1). There were no significant differences 1 hour after cord clamping between neonates of the three groups concerning; RBS, hematocrit, RBCs count, Hgb or total bilirubin levels. (Table 2). Six hours after cord clamping, there was a significantly higher hematocrit levels, RBC, Hgb in neonates of groups 2 and 3 when compared to group 1 ($p < 0.005$). (Table 3)

However, there were no significant differences between neonates of the three groups concerning RBS or total bilirubin levels. (Figure 1).

There was no significant difference between studied groups regarding neonatal jaundice requiring phototherapy, respiratory distress, neonatal intensive care unit admission or hypoglycemia. (Table 4).

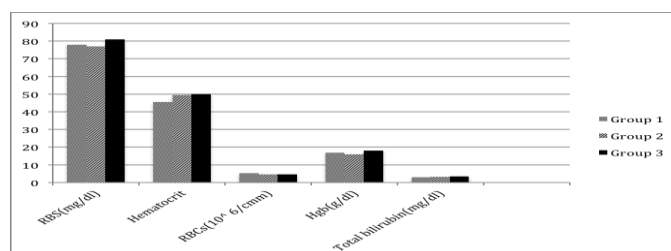


Figure (1) Newborns RBS, Hematocrit, Hemoglobin and total Bilirubin 6 hours after clamping of the umbilical cord in the three groups.

Table (1) Newborns data of the studied groups.

	Group 1 [Immediate Clamping] (n=28)	Group 2 [Delayed Clamping after 1 min] (n=28)	Group 3 [Delayed Clamping after 2 min] (n=28)	<i>∩p</i>
Birth weight (kg)	3.9 ± 0.5	3.8 ± 0.7	3.6 ± 0.6	>0.05
1-min Apgar score	6.4±1.3	6.3±1.2	6.7±0.9	>0.05
5-min Apgar score	8.6±0.5	8.4±0.7	8.6±0.9	>0.05
Fetal gender				
Male	16(57.1%)	16(57.1%)	11(39.3%)	0.30
Female	12(42.9%)	12(42.9%)	17(60.7%)	0.87
Jaundice requiring Phototherapy	2(7.14%)	3(3.57%)	1(3.57%)	0.77
Respiratory Distress	2(7.14%)	1(3.57%)	1(3.57%)(congenital heart disease)	1
NICU admission for other reasons	1(3.57%) hypocalcemic convulsions	1(3.577%) (lethargy)	1(3.57%) (trisomy 21, sepsis)	
Hypoglycemia	1(3.57%)	0 (0%)	0 (0%)	0.36

∩p is statistically significant at <0.05.

Table (2) Difference between the three groups regarding maternal RBS, diabetes mellitus type, diabetes control, treatment duration and associated other illnesses.

	Group 1 [Immediate Clamping] (n=28)	Group 2 [Delayed Clamping after 1 min] (n =28)	Group 3 [Delayed Clamping after 2 min] (n =28)	<i>∩p</i> ★
Maternal age (years)	31±3.7	30.4±5.6	30.7±5.2	>0.05
Gestational Age	38±1.5	37.9±1.4	37±0.9	>0.05
Type of delivery				
Cesarean section	20(71.4%)	22(78.65%)	21(75%)	0.83
Vaginal delivery	8(28.65)	6(21.4%)	7(25%)	
Random Blood Sugar (mg/dl)	114(75-490)	108(49-600)	121(60-110)	>0.05
Diabetes Mellitus Type				
Pregestational (types I, II)	9 (32.1%)	16 (57.1%)	21 (75%)	0.01
Gestational	19(67.9%)	12 (42.9%)	7 (25%)	
Diabetes Mellitus Treatment				
Insulin	27(96.4%)	28(100%)	27(96.4%)	0.59
Diet Control	1(3.6%)	0 (0%)	1(3.6%)	
Diabetes Mellitus Control				
Controlled	24(85.7%)	24(85.7%)	25(89.3%)	0.9
Uncontrolled	4(14.3%)	4(14.3%)	3(10.7%)	
Diabetes Mellitus Complications				
Yes	27(96.4%)	27(96.4%)	27(96.4%)	1
No	1(3.6%)	1(3.6%)	1(3.6%)	
Duration of Illness (months)	15 (4 – 24)	21 (4 – 34)	29 (5 – 39)	0.00
Other Illnesses				
No	21(75%)	20(71.4%)	23(82.1%)	0.63
Hypertension	3(10.7%)	3(10.7%)	4(14.3%)	
Preeclampsia	4(14.3%)	3(10.7%)	1(3.6%)	
APS	0 (0%)	1(3.6%)	0 (0%)	
DVT	0 (0%)	1(3.6%)	0 (0%)	

∩p is statistically significant at <0.05

Table (3): Comparison between studied groups regarding RBS, Hematocrit, Hgb and Bilirubin 1 hour after clamping the umbilical cord.

	Group 1 [Immediate Clamping] (n=28)	Group 2 [Delayed Clamping after 1 min] (n=28)	Group 3 [Delayed Clamping after 2 min] (n=28)	\bar{p}
Random Blood Sugar mg/dl)	59 ± 7.2	61 ± 24	61.5 ± 22	0.88
Hematocrit	46 ± 4.3	48 ± 4.5	46.4 ± 5	0.23
RBCs (x 10 ⁶ /cmm)	4.7 ± 1.4	4.3 ± 0.2	4.5 ± 0.3	0.21
Hgb (g/dl)	16.1 ± 1.4	15 ± 1.4	15.7 ± 1.7	0.03
Total bilirubin (mg/dl)	1.89 ± 0.65	2 ± 0.07	2.2 ± 0.7	0.11

\bar{p} is statistically significant at <0.05

Table (4) Comparison between studied groups regarding RBS, Hematocrit, Hgb and Bilirubin 6 hours after clamping the umbilical cord.

	Group 1 [Immediate Clamping] (n=28)	Group 2 [Delayed Clamping after 1 min] (n=28)	Group 3 [Delayed Clamping after 2 min] (n=28)	\bar{p}
RBS (mg/dl)	78 ± 9	77 ± 12.9	81 ± 13	0.42
Hematocrit	46.5 ± 4.6	49.6 ± 3.9	50 ± 4.9	0.01
RBC(10 ⁶ /cmm)	5.2 ± 1.5	4.6 ± 0.3	4.7 ± 0.4	0.04
Hgb (g/dl)	16.8 ± 1.4	16 ± 1.4	18 ± 1.5	0.00
Total bilirubin (mg/dl)	2.9 ± 1.5	3.2 ± 1.5	3.5 ± 1.4	0.31

\bar{p} is statistically significant at <0.05

4. Discussion

The optimal time to clamp the umbilical cord for all infants regardless of gestational age or fetal weight, is when the circulation in the cord has ceased, the cord is flat and no pulse is evident [10]. Delayed cord clamping is not widely practiced in the United States because favorable clinical endpoints of delayed umbilical cord clamping trials have been inconsistent [11-13].

This study showed a significantly elevated hematocrit measured six hours after birth in infants of diabetic mothers underwent delayed cord clamping either at 1 or 2 minutes after birth. Meanwhile, the mean hematocrit remained within physiological limit in all studied groups. The equivalence of the groups at maternal age, gestational age, and parity supports the conclusion that the effect may be causal. These data are in agreement with Shirvani *et al.*, 2010[10], who found that delayed cord clamping increases the hematocrit in healthy term infants. Ultee *et al.*, 2008[14] also found higher hematocrit in preterm infants delivered 34-36 weeks gestation with delayed cord clamping more than 180 seconds. These findings go also in agreement with studies in India & Guatemala in addition to other well designed well randomized trials, which showed higher hematocrit level six hours after birth in infants with delayed cord clamping. In these studies sustained effect of late cord clamping has been demonstrated by other indicators of infant hematologic status (iron stores and ferritin) at age

of six months.[13,16,17] However, our results are in contrast with Chaparro *et al.*, 2006[16] who found no significant hematological difference between immediate and delayed clamping of the cord. This might be because they studied the hematocrit three to six months after birth. For term infants, concerns have been raised that delayed clamping results in hypervolemia with respiratory distress, erythrocytosis with plethora and hyperviscosity, and hyperbilirubinemia. Our results showed no significant differences between early and late clamping of the umbilical cord in postnatal respiratory symptoms.

Hutton and Hassan, 2007 reported in their meta-analysis study that delayed clamping of the umbilical cord for at least 2 minutes after birth consistently improves both the short and long term hematologic status of infants. They stated that late clamping was associated with a moderate increase in blood viscosity and increased rates of polycythemia, yet there was no evidence of any significant harm [17]. However, in this study none of the infants showed polycythemia either uncomplicated or complicated.

Our results confirm that there are no significant statistical differences between the studied groups as regard the secondary outcome including jaundice and need for phototherapy. This is supported by Cernades *et al.*, 2006 findings [18], who showed no significant differences in bilirubin level between studied groups with cord clamping 15, 60 and 180 seconds after birth.

Our findings are in contrast to McDonald and Middleton, 2008 [19]. They reported a significant increase in infants needing phototherapy for jaundice in the late compared with early clamping groups. They found that increase in newborn hemoglobin levels in late compared with early cord clamping, although this effect didn't persist past six months.

Larger studies are needed to have conclusive recommendations on timing of clamping of the umbilical cord in this high risk group of infants of diabetic mothers.

Conclusion

Delayed cord clamping in infants of diabetic mothers increases the hematocrit levels but within physiological ranges. It is a simple procedure that might be incorporated in integrated programs aimed at reducing iron deficiency anemia. This might be important especially for infants of diabetic mothers in developing countries.

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