Duration of cord clamping and physiological jaundice in newborn: A case–control study

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Received - 14 March 2019 Initial Review - 29 March 2019 Accepted - 13 April 2019

ABSTRACT

Introduction: Delayed cord clamping (DCC) in term newborns improves iron stores in infancy, and the most international guidelines now recommend at least 30–60 s of DCC in term and preterm newborns. **Objective:** The objective of this study was to find out the association between neonatal jaundice (physiological) and duration of cord clamping. **Methods:** An observational matched case–control study was conducted from June 1, 2017, to May 31, 2018, in the neonatal unit of a tertiary care hospital in Odisha after getting approval from the institutional ethics committee. Of 3367 neonates, 784 were included in the study (392:392) after satisfying the pre-defined inclusion and exclusion criteria. All the relevant data were collected and validated, and the results were analyzed. Fisher exact test was performed to find out the association. For all statistical purpose, $p<0.05$ was considered to be statistically significant. **Results:** A significant association was found between neonatal jaundice and DCC as evidenced by Chi-square value: 15.62; p=0.0001, relative risk (95% confidence interval [CI]): 1.68 (1.29, 2.18), absolute risk reduction: −0.12 (−0.18, −0.06), and number need to treat (95% CI): −8 (−6, −17). **Conclusion:** Neonatal jaundice appears to be more commonly associated among babies with DCC.

Key words: *Delayed cord clamping, Early cord clamping, Neonate, Phototherapy, Physiological jaundice*

Cord blood is the lifeblood of a baby until its birth. Stem cells and red blood cells (RBC) are the important containers of cord blood, and recently, scientists have discovered that cancer-fighting T-cells are also among the important constituents of umbilical cord blood [1]. The exact timing of cord clamping has been a controversial issue till date. Standard definitions of "early" or "late" cord clamping have not been formulated yet. Policies for the timing of cord clamping vary from 60 s after birth to >60 s after the birth or when cessation of umbilical cord pulsation occurred [2]. Early cord clamping (ECC) is a part of active management of the third stage of labor, which significantly decreases the duration of the third stage and postpartum blood loss [3,4]. The disadvantages of ECC include infant anemia, increased incidence of acidemia, hypoxic-ischemic brain damage, childhood mental disorders, increased risk of hypovolemia, iron loss, several blood disorders, type 2 diabetes, and increase in the likelihood of fetomaternal transfusion as a larger volume of blood remains in the placenta [5-7].

Disadvantages of delayed cord clamping (DCC) are increased risk of hypervolemia, hyperviscosity, polycythemia, respiratory symptoms, and hyperbilirubinemia [2,5,8,9]. DCC is responsible for a moderate increase in blood viscosity which leads to polycythemia. As per a meta-analysis study, no evidence of any significant harm has been noted for phototherapy to treat jaundice by admission to the NICU [2,5,8,9]. Jaundice is almost certain when a baby gets his or her full quota of blood and is due to lysis of the normal excess of blood to produce bilirubin.

At each birth, obstetrical providers decide when to clamp and cut the umbilical cord. Clear evidence to guide a provider's decision for term infants is not sufficient at this time [10]. Fear of hyperbilirubinemia and polycythemia is a concern that has hindered the adoption of DCC as routine care. When cord clamping is delayed at birth or the umbilical cord is milked, infants obtain a placental transfusion resulting in an increase of approximately 20–30% in blood volume and 50% increase in red cell volume [11,12]. Although changes in practice are beginning to favor DCC, evidence of long-term outcomes is limited. From the 2010 University of Granada study: "The clamping of the umbilical cord of newborns from full-term pregnancies, 2 min after the placenta is delivered, there was no difference to hematocrit or hemoglobin levels of the umbilical cord when compared to clamping the cord within 20 s"[1].

Some studies have shown an increased risk of polycythemia (more RBCs in the blood) and jaundice when the cord is clamped later [1]. Although it is confirmed that anemia is less in DCC as compared to ECC [13], some degree of confusion still exists between relation of neonatal jaundice and duration of cord clamping. Till date, there are no studies done in our country and also in our state to fill the existing knowledge gap.

METHODS

An analytical matched case–control study was conducted from June 1, 2017, to May 31, 2018, in the neonatal unit of a tertiary care center in Burla. The hospital is a 900-bedded tertiary care hospital of Western Odisha, serving two neighborhood states (Jharkhand and Chhattisgarh). Ethics committee approval was obtained for this study. As there are no such studies in the past in our center, by statistical convention, we have assumed 50% prevalence of physiological jaundice among DCC neonates. By taking the prevalence of physiological jaundice as 50%, absolute precision of 5%, and confidence interval (CI) of 95%, minimum sample size calculated was 384 using single proportion absolute precision method, with the help of nMaster v 2 (BRTC, Bagayam, Vellore).

All the relevant data were collected from the hospital record in a case report format. Inclusion criteria for cases (DCC neonates) were the neonates admitted to our neonatal unit with documented DCC from the hospital register and physiological jaundice. Inclusion criteria for controls (ECC neonates) were ECC and physiological jaundice. Sepsis, preterm (<37 weeks of gestation), pathological jaundice (1st day jaundice), conjugated hyperbilirubinemia, cephalohematoma, and congenital anomalies were excluded in both cases and controls. Of total 3367 neonates admitted to our neonatal unit only 1561 were included in the study. However, after matching with age in hours, gender, and duration of hospitalization in days from hospital register, only 784 neonates (392:392) were included in the final analysis. The babies were enrolled by simple consecutive sampling technique after satisfying the predefined inclusion and exclusion criteria.

DCC is defined as umbilical cord clamping for >60 s and for ECC <60 s [13]. Physiological jaundice represents physiological immaturity of the neonates to handle increased bilirubin production [13]. Physiological jaundice was assessed clinically by Kramer rule [14] and serum bilirubin (T) by laboratory investigation and was put into the normogram [14] for phototherapy range detection.

All the collected data were exported to the Excel sheet. Data cleaning and validation were done manually, and the results were analyzed in terms of odds ratio and risk ratio (RR) with the help of Dxt software 1.0 (BRTC, Vellore). Chi-square test was performed to find out the association. For all statistical purpose, $p<0.05$ was considered to be statistically significant.

RESULTS

In the study population of 392 cases, 116 patients received phototherapy, and of 392 controls, 69 neonates received phototherapy. Their baseline characters were analyzed and are represented in Table 1. Phototherapy and duration of cord clamping were associated significantly as evidenced by Chi-square value: 15.62; p=0.0001. Other supporting factors were RR (95% CI): 1.68 (1.29, 2.18) and number need to treat (95% CI): −8 (−6 and −17). Among DCC neonates (physiological), the risk of developing neonatal jaundice was 1.68 times higher as compared to ECC neonates. If 100 neonates were to be exposed to DCC, then 12 neonates will develop neonatal jaundice.

DISCUSSION

Some of the previous studies observed that more infants needed phototherapy and longer stay in the hospital after DCC was implemented [15]. The bilirubin concentration was significantly higher in the DCC group and the peak occurred later. When cord clamping is delayed at birth or the umbilical cord is milked, infants obtain a placental transfusion resulting in approximately 20–30% increase in blood volume and 50% increase in red cell volume [15]. This will further lead to polycythemia and excess RBC breakdown to produce hyperbilirubinemia. The finding was in concordance with a previous study where meta-analysis comparing DCC versus ECC in term infants was also demonstrated an increased risk for hyperbilirubinemia and phototherapy among DCC babies [15]. It was argued that the benefits at later age outweigh the risk for hyperbilirubinemia, which matches with our study.

Garabedian *et al*. found that DCC improved hemoglobin levels at birth, so the need for postnatal exchange transfusion was less and there was no increase in severe hyperbilirubinemia [16]. The improved hemoglobin levels were not sufficient to cause polycythemia but lead to mild neonatal jaundice. However, in the current study, neonatal jaundice requiring phototherapy was more in DCC as compared to ECC. The increased blood volume leads to lysis more and produces phototherapy range of neonatal jaundice.

Mercer *et al*. observed no relation of the duration of cord clamping and the incidence of hyperbilirubinemia or symptomatic polycythemia [17]. Chidre and Chirumamilla also observed no significant difference (p=0.1460) between the duration of cord clamping and neonatal hyperbilirubinemia requiring phototherapy [18]. Some other previous studies also observed only a trend toward higher bilirubin levels and no difference in phototherapy needs in these neonates [19-21]. Although peak bilirubin was reported to be higher previous data in the literature on phototherapy were scarce. The studies could not find an increased risk of hyperbilirubinemia in DCC [19-21].

Table 1: Baseline characters of study population

Parameters (Mean±SD)	Cases (DCC)	Controls (ECC)	t-value	Chi-square value	p-value
Age (h)	34.61±6.42	35.46±6.60	−0.923	-	0.357
Duration of hospitalization	2.29±0.53	2.31±0.54	−0.133	-	0.894
SBT (mg/dl)	13.84±0.76	13.77±0.73	0.676	-	0.504
Sex (Male:female)	1.08:1	1.04:1	-	0.002	0.989

SD: Standard deviation, DCC: Delayed cord clamping, ECC: Early cord clamping, SBT: Serum bilirubin total, p<0.05 is considered statistically significant

The clinical significance of the differences in bilirubin levels in DCC as well as ECC was found unclear and also there was no excess increase of RBC volume in DCC which leads to phototherapy range hyperbilirubinemia by lysis [19-21]. Furthermore, bilirubin at a certain range may even be protective as an antioxidant. However, in this study, there was a significant (p=0.0024) correlation between DCC and neonatal jaundice.

As our study is a case–control study, the strength of evidence was low, which adds on to the limitation of this study. Further, we have adopted a non-probability sampling technique as the data were collected retrospectively, though we have tried to avoid the confounding factors and biases as much as possible by matching the data. We have just found an association but the causality could not be explained. As this study was poor in terms of resources such as manpower and funding, the lack of follow-up was a major limitation to this study.

CONCLUSION

DCC has a pivotal role in increasing the incidence of neonatal jaundice. We have found an association of physiological jaundice among DCC neonates. However, more research and robustic approach are recommended in future for reaching out the definite role of duration of cord clamping on neonatal physiological jaundice.

ACKNOWLEDGMENT

We are thankful to our colleagues, department, and at last but not the least the patients without whom this study would not have been possible.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Bhoi S, Mishra NR, Rout S. Duration of cord clamping and physiological jaundice in newborn: A case–control study. Indian J Child Health. 2019; 6(4):186-188.

Doi: 10.32677/IJCH.2019.v06.i04.010