Original Article

DOI: 10.7860/IJNMR/2025/77298.2439

Paediatrics Section

Effect of Early versus Delayed Umbilical Cord Clamping on Neonatal Haemoglobin Status: A Randomised Controlled Trial

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ABSTRACT

Introduction: Anaemia, especially Iron Deficiency Anaemia (IDA), among neonates and young children, is a major public health problem in India. Umbilical cord clamping after the delivery of the foetus plays an important role in preventing neonatal anaemia. The World Health Organisation (WHO) strongly recommends clamping the cord one minute after delivery, a practice known as late or Delayed Cord Clamping (DCC). In contrast, Early Cord Clamping (ECC) involves clamping the umbilical cord within the first 15-30 seconds of birth, a practice that has been followed since ancient times. Compared to ECC, DCC helps minimise iron deficiency and prevent anaemia in both term and preterm infants.

Aim: To study the effect of different cord clamping interventions (DCC and ECC) on neonatal anaemia.

Materials and Methods: A prospective randomised controlled trial was conducted in the Department of Paediatrics, Karwar Institute of Medical Sciences, Karwar, Karnataka, India to compare the effects of ECC and DCC in late preterm, term and post-term neonates, using parameters such as Haemoglobin (Hb), Haematocrit (HCT) and serum bilirubin. The present study was carried out in the Department of Paediatrics at a tertiary care teaching hospital in Karwar from July 2023 to December 2024 over a period of six months. A total of 120 newborns were included and randomly allocated to the ECC group (60, where the cord was clamped within 15-20 seconds after birth) and the DCC group (60, where the cord was clamped within 60 seconds of birth).

Results: The mean birth weights of the ECC and DCC neonates were 2.66±0.4 kg and 2.73±0.39 kg, respectively. The majority of the study participants were female 62 (51.6%) and term neonates (96, or 80%). The mean Hb and HCT levels were significantly higher in the DCC group compared to the ECC group ($p<0.05$). Serum bilirubin levels and instances of clinical jaundice did not differ significantly according to statistical analysis between the groups.

Conclusion: A significant decreasing trend was noted in neonatal anaemia, along with an increase in Hb and HCT levels in DCC compared to ECC neonates.

Keywords: Bilirubin, Haematocrit, Polycythaemia, Preterm neonate, Term neonate

INTRODUCTION

Anaemia in newborns and young children is a major public health issue in India and even in some developed countries [1,2]. According to the National Family Health Survey 5 (2019-21), the prevalence of anaemia among children aged 6 to 59 months was found to be 67.1% [3]. Umbilical cord clamping after the delivery of the fetus plays an important role in preventing neonatal and infant anaemia. Usually, blood continues to flow in the umbilical arteries and veins for a few minutes after birth, which is termed a placental transfusion. This is known to improve neonatal blood volume by approximately 12 ml/kg in the first 30 seconds after birth [4].

The 2012 WHO guidelines on basic newborn resuscitation strongly recommend that the cord should not be clamped earlier than one minute after birth in newborn term or preterm babies who do not require positive-pressure ventilation. This is referred to as late or DCC. In contrast, ECC involves clamping the umbilical cord within the first 15-30 seconds of birth [5]. ECC, or immediate cord clamping, is associated with a high-risk of anaemia, intraventricular haemorrhage, respiratory distress syndrome and late-onset sepsis. Infants may be prone to develop polycythaemia, transient tachypnoea of the newborn, jaundice and elevated blood pressure if cord clamping is delayed beyond one minute [6].

Various organisations, such as the American College of Obstetrics and Gynaecology (ACOG), World Health Organisation (WHO), Neonatal Resuscitation Program (NRP), Royal College of Obstetricians and Gynaecologists (RCOG) and American College of Nurse-Midwives (ACNM), have issued guidelines regarding clamping time, recommending intervals of 30-60 seconds, ≥ one minute, 30-60 seconds, two minutes and 2-5 minutes after birth, respectively. However, there is no uniform recommendation [7]. To date, literature does not show evidence of an increased risk of polycythaemia or jaundice with DCC; however, some studies have noted a slightly higher rate of icterus requiring phototherapy in term infants [7].

The current study seeks to compare the two methods: ECC and DCC, while also exploring the aforementioned observations. This is the first study conducted in the North Kanara region (part of the Western Ghats) of Karnataka, India, with a diverse ethnic background.

Thus, the aim of this study was to examine the effect of ECC versus DCC on preventing anaemia, using Hb and HCT values. Additionally, it aims to investigate the occurrence of Neonatal Hyperbilirubinaemia (NNHB) and polycythaemia in both interventions.

MATERIALS AND METHODS

A prospective randomised control trial was conducted in the Department of Paediatrics, Karwar Institute of Medical Sciences, Karwar, Karnataka, India from December 2023 to November 2024, lasting for 12 months after obtaining ethical clearance from the Institutional Ethical Committee (approval no: IEC/KRIMS/O/32/2023-24 dated 8th December 2023). It was a single-blinded study in which the mother was not informed about which of the two methods of

cord clamping would be used after delivery, while the investigator was not blinded.

Inclusion criteria:

- Singleton live pregnancy
- Term, late preterm and post-term gestations
- Adequate cord length (minimum of 25 cm)
- Not requiring resuscitation

Exclusion criteria:

1. Maternal conditions:

- Maternal Rh-negative blood type
- Positive anti-Human Immunodeficiency Virus (HIV) and Hepatitis B surface antigen (HBsAg)
- Pre-eclampsia
- Forceps or vacuum-assisted delivery
- Unstable maternal condition
- Placental abruption or placenta previa
- Toxoplasmosis, Rubella Cytomegalovirus, Herpes simplex and HIV (TORCH) infections
- Multiple gestation

2. Foetal conditions:

- Antenatally diagnosed major congenital anomalies of the fetus or diagnosed at the time of birth
- Intrapartum foetal distress
- Newborn with meconium-stained liquor (MSL)
- Neonate with unstable vitals (e.g., NB depression, BA, Respiratory Distress Syndrome (RDS), Hypoxic-ischaemic Encephalopathy (HIE), etc.,

Sample size calculation: The sample size was calculated by a statistician using hospital data similar to the study by Enyinna KP et al., [8] with the formula:

$$n = \frac{r+1}{r} * \frac{(Z\alpha_{/2}+Z\beta)^2 * SD^2}{(\mu 1-\mu 2)^2}$$

where,

- μ1= 13.2- Mean Hb level in the ECC group (based on hospital records)

- μ2= 13.8- Mean Hb level in the DCC group

- SD= 1.15- Combined standard deviation [8]

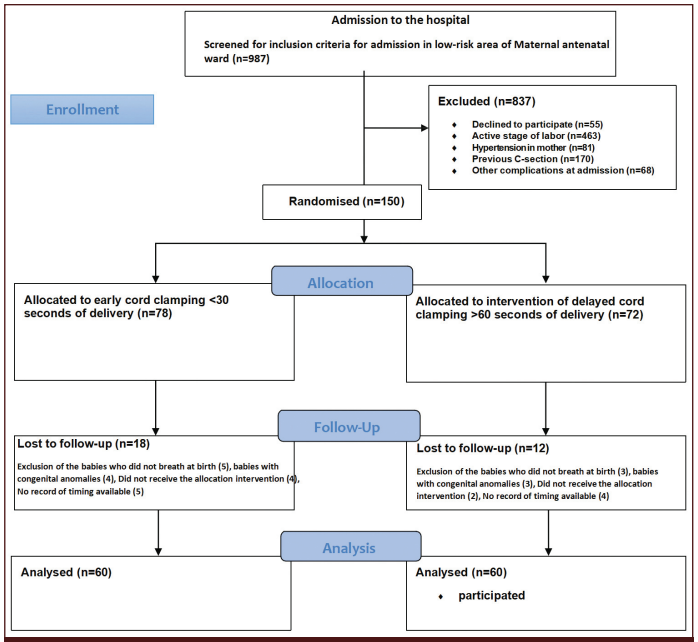
- r= 1:1- Ratio of cases to controls

- aZα/2"= 1.96 at the 5% level of significance

Using the above formula, at 90% power, Zβ= 1.28, the minimum sample size required in each group was 58, meaning a total of 116 neonates were studied.

Study Procedure

During the study period, 987 pregnant mothers who met the inclusion and exclusion criteria were informed in advance and written consent was obtained. After delivery, 120 neonates who fulfilled the inclusion and exclusion criteria were allocated to the ECC or DCC group using simple randomisation [9] and the chit method [Table/Fig-1]. The time between the delivery of the fetus and the clamping of the umbilical cord was documented using a timer. Epidemiological data, detailed history and physical examination findings were recorded. Blood investigations, including Hb, HCT, Red Blood Cells (RBC), White Blood Cell (WBC), platelet counts and Total Bilirubin (TB) and Direct Bilirubin (DB), were performed 48 to 72 hours after birth. Simultaneously, the neonates were examined for clinical icterus and those requiring phototherapy or exchange transfusion were also recorded. Haematological parameters were estimated using the Sysmex XN500 automated haematology analyser, while TB and DB were measured using the Walter and Gerarde method in the automated analyser, with values referenced from Henry's Clinical Diagnosis and Management, 24th edition [10].



[Table/Fig-1]: Flowchart depicting enrollment of study participants.

STATISTICAL ANALYSIS

All the data were compiled in a Microsoft Excel sheet and analysed using Statistical Package for the Social Sciences (SPSS) version 27.0. An unpaired t-test was applied to determine the statistical significance between the two groups. Results were considered statistically significant for a p-value of <0.05.

RESULTS

Out of 120 neonates, 60 underwent ECC and 60 underwent DCC. The majority of the neonates were term infants, with 49 (81.7%) in the ECC group and 47 (78.3%) in the DCC group. They were born through Normal Vaginal Delivery (NVD), with 32 (53.3%) in the ECC group and 34 (56.7%) in the DCC group. Most of the newborns in the ECC group were female (55%), while the majority in the DCC group were male (51.7%) [Table/Fig-2].

The mean birth weights of the ECC and DCC neonates were 2.66±0.4 kg and 2.73±0.39 kg, respectively. The most common blood group among the mothers in the present study population was O-positive [ECC: 22 (36.7%) and DCC: 25 (41.7%)]. The most common blood group of the neonates was also found to be O-positive and was equally distributed in both study groups (25 in each group, 41.7%) [Table/Fig-2].

The mean HB and HCT values were significantly higher in the DCC group compared to the ECC neonates, with the difference being statistically significant, having a p-value of <0.001 [Table/Fig-3]. The mean RBC count in the ECC and DCC groups was 4.84±0.73 and 5.02±0.68, respectively.

Study parameters		Cord clamping n (%)		p-value
		Early (n=60)	Delayed (n=60)	
Birth weight (kg) (Mean±SD)		2.66±0.4	2.73±0.39	0.349
Gestation	Late preterm	6 (10.0%)	7 (11.7%)	0.901
	Post-term	5 (8.3%)	6 (10.0%)	
	Term	49 (81.7%)	47 (78.3%)	
Delivery	LSCS	28 (46.7%)	26 (43.3%)	0.714
	NVD	32 (53.3%)	34 (56.7%)	
Mother's blood group	A^+	16 (26.7%)	11 (18.3%)	0.461
	AB^+	5 (8.3%)	3 (5.0%)	
	B^-	0	1 (1.7%)	
	B^+	17 (28.3%)	18 (30.0%)	
	O^-	0	2 (3.3%)	
	O^+	22 (36.7%)	25 (41.7%)	
Gender of the baby	Female	33 (55.0%)	29 (48.3%)	0.465
	Male	27 (45.0%)	31 (51.7%)	
Baby's blood group	A^+	15 (25.0%)	10 (16.7%)	0.365
	AB^+	3 (5.0%)	2 (3.3%)	
	B^-	1 (1.7%)	1 (1.7%)	
	B^+	16 (26.7%)	19 (31.7%)	
	O^-	0 (0%)	3 (5.0%)	
	O^+	25 (41.7%)	25 (41.7%)	
Clinically icteric	Yes	10 (16.7%)	7 (11.7%)	0.432
	No	50 (83.3%)	53 (88.3%)	
Phototherapy	Yes	9 (15.0%)	11 (18.3%)	0.624
	No	51 (85.0%)	49 (81.7%)	

[Table/Fig-2]: Distribution of birth weights and major mothers' blood groups between the groups.
* Significant association; Significance calculated using; Chi-square test

Study parameters	Cord clamping (Mean±SD)		Unpaired t-test	p-value
	Early (n=60)	Delayed (n=60)		
Hb (gm/dL)	16.19±1.61	17.4±1.95	3.734	<0.001*
RBC (/dL)	4.84±0.73	5.02±0.68	1.35	0.18
HCT (L/L)	46.16±4.88	49.71±6.65	3.312	0.001*
TB (mg/dL)	11.18±3.54	11.51±3.33	0.528	0.599
DB (mg/dL)	0.42±0.20	0.41±0.18	0.31	0.757

[Table/Fig-3]: Haematological parameters in the two study groups.
* Significant difference; Hb: Haemoglobin; RBC: Red blood corpuscles count; HCT: Haematocrit; TB: Total bilirubin; DB: Direct bilirubin

Clinical icterus was observed predominantly in ECC neonates (10 out of 60), whereas seven out of 60 DCC neonates were icteric. A total of 9 (15.0%) ECC neonates and 11 (18.3%) DCC neonates received phototherapy, indicating no statistical significance (p=0.624) concerning the timing of umbilical cord clamping in relation to the appearance of clinical jaundice and the need for phototherapy. No statistically significant difference was observed in the mean TB and DB values of ECC and DCC neonates in the present study, as depicted in [Table/Fig-3].

DISCUSSION

In the present study, the mean birth weight of the ECC and DCC neonates was found to be 2.66±0.4 kg and 2.73±0.39 kg, respectively, where the birth weight of the DCC group neonates was higher compared to the ECC group. Similarly, in a study conducted by Gonnade NV et al., the mean birth weight in the DCC group (Group-B) was 2.78 kg, which was slightly higher than that of the ECC group (Group-A) at 2.64 kg [11]. In a study conducted by Jafra BS et al., the mean birth weight among cases was 2.92±0.39 kg, which was lower compared to the control group at 3.03±0.29 kg [12].

The majority of the neonates were born through NVD, with 32 (53.3%) in the ECC group and 34 (56.7%) in the DCC group. Similar results were observed in a study conducted by Gonnade NV et al., where the majority were born through NVD, with 29 (58%) in Group-B and 38 (76%) in Group-A [11]. In contrast, Jafra BS et al., found that most of the neonates were born through Lower Segment Caesarean Section (LSCS) in both the control 20 (66.6%) and case (16, 53.3%) groups [12]. In the current study, the majority of female neonates in the ECC group accounted for 33 (55%), while males accounted for 31 (51.7%) in the DCC group. Jafra BS et al., identified the majority of male neonates in the control group (17, 56.6%) and an equal proportion of males and females in the case group 15 (50%) [12].

In the current study, a statistically significant increase in the mean Hb level of DCC group neonates (17.4±1.95 gm/dL) was observed in comparison to the ECC group (16.19±1.61 gm/dL), with a p-value of <0.001. Similarly, Gonnade NV et al., found a significant difference in the mean Hb of the DCC group at 15.02 gm/dL compared to the ECC group at 11.69 gm/dL, with a p-value of <0.0001 [11]. Jafra BS et al., also observed a statistically significant difference between the mean Hb levels in the control group (16.16±1.70 gm/dL) and the cases (19.28±2.16 gm/dL) investigated 24 hours after birth [13]. In the study by Jaiswal J et al., significantly higher mean Hb values were observed in the DCC group (16.8±1.5 gm/dL) compared to ECC neonates (15.1±1.2 gm/dL), with a level of significance at <0.001 [13]. Another study conducted by Fawzy AEMA et al., found no significant difference between the mean Hb levels of the ECC (14.82±1.98 gm/dL) and DCC (14.99±1.87 gm/dL) groups [14]. In the study of Qian Y et al., it was observed that neonates had significantly higher Hb levels when umbilical cord clamping was done 61-90 seconds after birth compared to the ECC group [15].

In the present study, a higher mean HCT was found in DCC neonates (49.71±6.65 L/L) compared to ECC neonates (46.16±4.88 L/L). Gonnade NV et al., found a higher HCT in the DCC group with a mean of 48.67 in comparison to the ECC group (42.36), with a p-value of 0.002 [11]. Jafra BS et al., also observed a statistically significant difference between the mean HCT levels of the control group (49.06±4.99 L/L) and the cases (57.72±5.77 L/L) investigated 24 hours after birth [12]. In the study by Qian Y et al., significantly higher HCT levels were observed in neonates when umbilical cord clamping was done 61-90 seconds after birth (61.24±6.89 L/L) compared to the ECC group (57.92±7.92 L/L) [15].

In the present study, no statistically significant difference was observed in TB and DB values between DCC (11.51±3.33 mg/dL, 0.41±0.18 mg/dL) and ECC (11.18±3.54 mg/dL, 0.42±0.20 mg/dL) neonates. Similarly, Fawzy AEMA et al., also observed no significant difference in the serum bilirubin levels of Group-1 (ECC, 6.95±2.01 mg/dL) and Group-2 (DCC, 7.01±2.31 mg/dL) neonates [14]. According to Ricon D et al., no significant difference in TB levels was observed among ECC and DCC neonates [16]. In contrast, Gonnade NV et al., documented a statistically significant difference in the mean TB levels of Group-A (2.06±0.53 mg/dL) and Group-B (4.92±6.64 mg/dL) neonates, with a p-value of 0.003 [11].

Limitation(s)

Preterm babies were not included in the present study. The long-term effects of DCC compared to ECC were not studied.

CONCLUSION(S)

The DCC significantly improves neonatal Hb and HCT levels, thereby preventing anaemia. It poses no significant risk of NNH, nor does it increase the need for phototherapy or exchange transfusion. Therefore, DCC should be considered a routine practice rather than an exception in normal and uncomplicated situations. Large multicentric trials are required to explore the additional advantages and possible adverse effects of DCC in various co-morbid and complicated scenarios.

Acknowledgement

The authors would like to express their sincere gratitude to professors, colleagues, juniors, house surgeons, nurses and non teaching staff of the Departments of Paediatrics, Obstetrics and Gynaecology and Community Medicine along with technical staff from the central laboratory of Karwar Institute of Medical Sciences, Karwar for their unwavering support throughout the present study.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Dec 13, 2024
- Manual Googling: Jan 11, 2025
- iThenticate Software: Jan 24, 2025 (14%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Dec 11, 2024**
Date of Peer Review: **Jan 02, 2024**
Date of Acceptance: **Jan 25, 2025**
Date of Publishing: **Mar 31, 2025**