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Clinical evaluation of delayed cord clamping in outcome in preterm babies admitted in district female hospital, Basti, Uttar Pradesh

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Abstract
The optimal time-point for umbilical cord clamping after delivery has been under debate for several decades. Through this study we endeavoured to look into and compare both the beneficial and adverse effects of delayed and immediate cord clamping. As per 2015 NRP guidelines on clamping of umbilical cord, early clamping is within 30 seconds and delayed cord clamping is more than 30 seconds after birth for a healthy term newborn. Hence based on above findings the present study was planned for Clinical Evaluation of Delayed Cord Clamping in Outcome in Preterm Babies Admitted in District Female Hospital, Basti, Uttar Pradesh.
The study was conducted in District Female Hospital, Department of Paediatrics, Basti, UP from May 2016 to May 2019 on 50 patients. The cases were divided in two study groups as neonates undergoing the Early Cord Clamping and Delayed Cord clamping.
The data generated from the present study concluded that clinical profile of neonates with delayed clamping of cord is also better with less perceived need for blood transfusion. The incidence of hyperbilirubinemia requiring phototherapy was increased in Delayed Cord clamping group. No exchange transfusion was required. There was no significant increase in the number of neonates with polycythaemia in the Delayed Cord clamping group. No beneficial or detrimental effect on the incidence of IVH was noted in the study group.

Keywords: delayed cord clamping, preterm babies, Uttar Pradesh, etc

Introduction
Preterm birth (premature birth) is a significant public health problem across the world because of associated neonatal (first 28 days of life) mortality and short- and long-term morbidity and disability in later life. Preterm is defined by World Health Organization (WHO) as babies born alive before 37 completed weeks of gestation or fewer than 259 days of gestation since the first day of a woman's last menstrual period (LMP). Normally, a pregnancy lasts about 40 weeks.
According to WHO, every year about 15 million babies are born prematurely around the world and that is more than one in 10 of all babies born globally. Almost 1 million children die each year due to complications of preterm birth (2013). Across 184 countries, the rate of preterm birth ranges from 5% to 18% of babies born. In India, out of 27 million babies born every year (2010 data), 3.5 million babies born are premature.
Newborn deaths (those in the first month of life) account for 40 percent of all deaths among children under five years of age. Preterm birth is the world's number one cause of newborn deaths, and the second leading cause of all child deaths under five, after pneumonia.
Many of the preterm babies who survive suffer from various disabilities like cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses. The morbidity associated with preterm birth often extends to later life, resulting in physical, psychological and economic stress to the individual and the family.
Though occurrence of preterm birth is a global problem, but more than 60% of preterm births occur in Africa and South Asia. In the lower-income countries, on average, 12% of babies are born too early compared with 9% in higher-income countries. Within countries, poorer families are at higher risk. Survival of premature babies also depends on where they are born; almost 9 out of every 10 preterm babies survive in high-income countries because of enhanced basic care and awareness, in sharp contrast to about 1 out of 10 in low-income countries.
More than three-quarters of preterm /premature babies can be saved with often inexpensive care such as essential care during child birth, antenatal steroid injections (given to pregnant women at risk of preterm labour under set criteria to strengthen the babies' lungs) and postnatal care like kangaroo mother care (the baby is carried by the mother with skin-to-skin contact and frequent breastfeeding), and basic care for infections and breathing difficulties.
Identification of risk factors in women with improved care before, between and during pregnancies; better access to contraceptives and increased empowerment/ education can further decrease the preterm birth rate (the number of preterm births divided by the number of live births) [1].
In placental mammals, the umbilical cord (also called the navel string, birth cord or funiculus umbilicalis) is a conduit between the developing embryo or fetus and the placenta. During prenatal development, the umbilical cord is physiologically and genetically part of the fetus and (in humans) normally contains two arteries (the umbilical arteries) and one vein (the umbilical vein), buried within Wharton's jelly. The umbilical vein supplies the fetus with oxygenated, nutrient-rich blood from the placenta. Conversely, the fetal heart pumps low oxygen containing

blood, nutrient-depleted blood through the umbilical arteries back to the placenta.

The umbilical cord develops from and contains remnants of the yolk sac and allantois. It forms by the fifth week of development, replacing the yolk sac as the source of nutrients for the embryo. The cord is not directly connected to the mother's circulatory system, but instead joins the placenta, which transfers materials to and from the maternal blood without allowing direct mixing. The length of the umbilical cord is approximately equal to the crown-rump length of the fetus throughout pregnancy. The umbilical cord in a full term neonate is usually about 50 centimeters (20 in) long and about 2 centimeters (0.75 in) in diameter. This diameter decreases rapidly within the placenta. The fully patent umbilical artery has two main layers: an outer layer consisting of circularly arranged smooth muscle cells and an inner layer which shows rather irregularly and loosely arranged cells embedded in abundant ground substance staining metachromatic. The smooth muscle cells of the layer are rather poorly differentiated, contain only a few tiny myofilaments and are thereby unlikely to contribute actively to the process of post-natal closure [2].

The umbilical cord lining is a good source of mesenchymal and epithelial stem cells. Their advantages include a better harvesting, and multiplication, and immunosuppressive properties that define their potential for use in transplantations. Their use would also overcome the ethical objections raised by the use of embryonic stem cells.

The umbilical cord contains Wharton's jelly, a gelatinous substance made largely from mucopolysaccharides which protects the blood vessels inside. It contains one vein, which carries oxygenated, nutrient-rich blood to the fetus, and two arteries that carry deoxygenated, nutrient-depleted blood away. Occasionally, only two vessels (one vein and one artery) are present in the umbilical cord. This is sometimes related to fetal abnormalities, but it may also occur without accompanying problems [3].

It is unusual for a vein to carry oxygenated blood and for arteries to carry deoxygenated blood (the only other examples being the pulmonary veins and arteries, connecting the lungs to the heart). However, this naming convention reflects the fact that the umbilical vein carries blood towards the fetus's heart, while the umbilical arteries carry blood away.

The blood flow through the umbilical cord is approximately 35 ml / min at 20 weeks, and 240 ml / min at 40 weeks of gestation [6]. Adapted to the weight of the fetus, this corresponds to 115 ml / min / kg at 20 weeks and 64 ml / min / kg at 40 weeks.

The umbilical cord enters the fetus via the abdomen, at the point which (after separation) will become the umbilicus (or navel). Within the fetus, the umbilical vein continues towards the transverse fissure of the liver, where it splits into two. One of these branches joins with the hepatic portal vein (connecting to its left branch), which carries blood into the liver. The second branch (known as the ductus venosus) bypasses the liver and flows into the inferior vena cava, which carries blood towards the heart. The two umbilical arteries branch from the internal iliac arteries and pass on either side of the urinary bladder into the umbilical cord, completing the circuit back to the placenta [4].

In absence of external interventions, the umbilical cord occludes physiologically shortly after birth, explained both by a swelling and collapse of Wharton's jelly in response to a reduction in temperature and by vasoconstriction of the blood vessels by smooth muscle contraction. In effect, a natural clamp is created, halting the flow of blood. In air at 18 °C, this physiological clamping will take three minutes or less. In water birth, where the water temperature is close to body temperature, normal pulsation can be 5 minutes and longer.

Closure of the umbilical artery by vasoconstriction consists of multiple constrictions which increase in number and degree with time. There are segments of dilatations with trapped uncoagulated blood between the constrictions before complete occlusion. Both the partial constrictions and the ultimate closure are mainly produced by muscle cells of the outer circular layer. In contrast, the inner layer seems to serve mainly as a plastic tissue which can easily be shifted in an axial direction and then folded into the narrowing lumen to complete the closure. The vasoconstrictive occlusion appears to be mainly mediated by serotonin and thromboxane A2. The artery in cords of preterm infants contracts more to angiotensin II and arachidonic acid and is more sensitive to oxytocin than in term ones. In contrast to the contribution of Wharton's jelly, cooling causes only temporary vasoconstriction [5].

Within the child, the umbilical vein and ductus venosus close up, and degenerate into fibrous remnants known as the round ligament of the liver and the ligamentum venosum respectively. Part of each umbilical artery closes up (degenerating into what are known as the medial umbilical ligaments), while the remaining sections are retained as part of the circulatory system.

The cord can be clamped at different times; however delaying the clamping of the umbilical cord until at least one minute after birth improves outcomes as long as there is the ability to treat the small risk of jaundice if it occurs [6]. Clamping is followed by cutting of the cord, which is painless due to the absence of nerves. The cord is extremely tough, like thick sinew, and so cutting it requires a suitably sharp instrument. While umbilical severance may be delayed until after the cord has stopped pulsing (5–20 minutes after birth), there is ordinarily no significant loss of either venous or arterial blood while cutting the cord. Current evidence neither supports, nor refutes, delayed cutting of the cord, according to the American Congress of Obstetricians and Gynecologists (ACOG) guidelines.

There are umbilical cord clamps which incorporate a knife. These clamps are safer and faster, allowing one to first apply the cord clamp and then cut the umbilical cord. After the cord is clamped and cut, the newborn wears a plastic clip on the navel area until the compressed region of the cord has dried and sealed sufficiently.

The length of umbilical left attached to the newborn varies by practice; in most hospital settings the length of cord left attached after clamping and cutting is minimal. In the United States, however, where the birth occurred outside of the hospital and an emergency medical technician (EMT) clamps and cuts the cord, a longer segment up to 18 cm (7 in) in length is left attached to the newborn [7].

A Cochrane review in 2013 came to the conclusion that delayed cord clamping (between one and three minutes after birth) is "likely to be beneficial as long as access to treatment for jaundice requiring phototherapy is available". In this review delayed clamping, as contrasted to early, resulted in no difference in risk of severe maternal postpartum hemorrhage or neonatal mortality, low Apgar

score. On the other hand, delayed clamping resulted in an increased birth weight of on average about 100 g, and an increased hemoglobin concentration of on average 1.5 g/dL with half the risk of being iron deficient at three and six months, but an increased risk of jaundice requiring phototherapy [8].

In 2012, the American College of Obstetricians and Gynecologists officially endorsed delaying clamping of the umbilical cord for 30–60 seconds with the newborn held below the level of the placenta in all cases of preterm delivery based largely on evidence that it reduces the risk of intraventricular hemorrhage in these children by 50%.In the same committee statement, ACOG also recognize several other likely benefits for preterm infants, including "improved transitional circulation, better establishment of red blood cell volume, and decreased need for blood transfusion". In January 2017, a revised Committee Opinion extended the recommendation to term infants, citing data that term infants benefit from increased hemoglobin levels in the newborn period and improved iron stores in the first months of life, which may result in improved developmental outcomes. ACOG recognized a small increase in the incidence of jaundice in term infants with delayed cord clamping, and recommended policies be in place to monitor for and treat neonatal jaundice. ACOG also noted that delayed cord clamping is not associated with increased risk of postpartum hemorrhage [9].

Several studies have shown benefits of delayed cord clamping: A meta-analysis showed that delaying clamping of the umbilical cord in full-term neonates for a minimum of 2 minutes following birth is beneficial to the newborn in giving improved hematocrit, iron status as measured by ferritin concentration and stored iron, as well as a reduction in the risk of anemia (relative risk, 0.53; 95% CI, 0.40–0.70). A decrease was also found in a study from 2008. Although there is higher hemoglobin level at 2 months, this effect did not persist beyond 6 months of age. Not clamping the cord for three minutes following the birth of a baby improved outcomes at four years of age. A delay of three minutes or more in umbilical cord clamping after birth reduce the prevalence of anemia in infants [10].

Negative effects of delayed cord clamping include an increased risk of polycythemia. Still, this condition appeared to be benign in studies. Infants whose cord clamping occurred later than 60 seconds after birth had a higher rate of neonatal jaundice requiring phototherapy.

Delayed clamping is not recommended as a response to cases where the newborn is not breathing well and needs resuscitation. Rather, the recommendation is instead to immediately clamp and cut the cord and perform cardiopulmonary resuscitation. The umbilical cord pulsating is not a guarantee that the baby is receiving enough oxygen. However, where possible, one should perform cardiopulmonary resuscitation with the cord still attached, to receive both benefits of oxygen from the cord and from the intervention [11].

The optimal time-point for umbilical cord clamping after delivery has been under debate for several decades. Through this study we endeavoured to look into and compare both the beneficial and adverse effects of delayed and immediate cord clamping. As per 2015 NRP guidelines on clamping of umbilical cord, early clamping is within 30 seconds and delayed cord clamping is more than 30 seconds after birth for a healthy term newborn. Hence based on above findings the present study was planned for Clinical Evaluation of Delayed Cord Clamping in Outcome in Preterm Babies Admitted in District Female Hospital, Basti, Uttar Pradesh.

Methodology

The study was conducted in District Female Hospital, Department of Paediatrics, Basti, UP from May 2016 to May 2019 on 50 patients. The cases were divided in two study groups as neonates undergoing the Early Cord Clamping and Delayed Cord clamping.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

The inclusion criteria were women with 28 to 34 weeks of pregnancy (shown by ultrasound results at the first or third trimester of pregnancy).

The exclusion criteria were: short umbilical cord (<25 cm), vigorous newborns, those born in meconiumstained amniotic fluid, primary congenital anomalies, umbilical cord prolapse, fetal hydrops, multiple pregnancies, a mother who is ABO or Rh-, a mother with a placenta Previa, placental expulsion, abnormal umbilical cord such as a true umbilical cord knot or a mother with background diseases such as diabetes, hypertension, residence out of the province or lack of follow-up.

Results & Discussion

The definition of early umbilical cord clamping was not clear in most studies except in Rabe, *et al*. (2000)1 early cord clamping was defined as clamping at 20 seconds and there was no immediate clamped group for comparison. We have included this study in this review because we believe that there is close proximity to the immediate clamped groups, and that in clinical practice such delays may occur. Furthermore, it allows the review to focus on at least 20 seconds interval between immediate and late cord clamping. The definition of delayed umbilical cord clamping varied between studies [12].

According to the newer neonatal resuscitation guidelines 2015 (American heart Association for cardiopulmonary resuscitation and emergency cardiovascular care 2015 recommendations, part 13) delayed cord clamping after 30 sec is suggested for both term and preterm neonates who do not require resuscitation at birth [13, 14]. There are various benefits of delayed cord clamping like increased hemoglobin and hematocrit levels for the neonate with a subsequent reduction in rates of anemia and iron deficiency that may extend into the infant period. Delayed cord clamping or placental transfusion could be a cost effective intervention to improve the iron status of infants by enhancing their red cell mass [15, 16].

The theoretical foundation for the study was that the additional blood volume received by placental transfusion, as a result of DCC, would help to reduce neonatal morbidity by providing extra blood volume and improving cardiovascular stability. At any point of time, preterm neonates have lesser feto-placental blood volume as compared to term infants, making them more vulnerable to have a deficit in case of early cord clamping. Delayed cord clamping allows time for adequate placental transfusion to supply the essential blood volume to the neonate.

Table 1: Maternal Details

Group	Group A	Group B
Parameters	**Early Cord Clamping**	**Delayed Cord clamping**
No. of Cases	**25**	**25**
Maternal Age years	21 – 30	22 – 29
Parity	1 – 3	1 – 3
Maternal Hb gm/dl	10.1 – 11.9	10.5 – 12.3

Table 2: Neonatal Parameters

Group	Group A	Group B
Parameters	**Early Cord Clamping**	**Delayed Cord clamping**
No. of Cases	**25**	**25**
Birth Weight gm	2240- 2865	2489 – 3115
Gestational Age weeks	32 – 37	33 – 38
Length cm	45 – 49	46 - 50
OFC cm	29 – 34	27 – 33
APGAR		
1 min	8	9
5 min	9	10
Mean Bilirubin gm/dl	10.5 – 14.8	11.5 – 15.6

Table 3: Morbidity

Group	Group A	Group B
Parameters	**Early Cord Clamping**	**Delayed Cord clamping**
No. of Cases	**25**	**25**
Polycythaemia	0	1
IVH	1	0
Sepsis	0	0
Jaundice	3	7
Exchange Transfusion	0	0
Blood Transfusion	3	2
Feeding Problems	5	2
Patent Ductus Arteriosus	1	0
Respiratory Distress Syndrome		
Apnoea	1	1
Hypoglycaemia	2	1
Transient Tachypnoea of Newborn	1	1
Necrotizing Enterocolitis	1	1

All the participants in this research were healthy pregnant women who had either a vaginal or surgical delivery. However, in Gupta's research [2], anaemic mothers participated. Another investigation by Van Rheene [17] was set in a malaria-endemic region. The study conducted by Middleton [18] was only focused on vaginal deliveries.

An increased concentration of hemoglobin and consequently higher blood volume raises the risk of hyperbilirubinemia and lengthened hospitalization for phototherapy. Moreover, delayed clamping might cease early and timely CPR. Overall, delayed umbilical cord clamping does not reduce the Apgar's score, PH of the cord blood and the RDS induced by polycythemia [17]. A cofactor of delayed clamping is polycythemia which is often unmarked [19].

DCC was not associated with any increased risk for significant polycythaemia and this finding was consistent with study done by Kinmond *et al*. [20] In our study among all the neonates, only one had a haematocrit >65% in the DCC group. But the neonate was asymptomatic and didn't need any intervention. Furthermore, we did not find any significant difference in overall neonatal morbidity in both groups. There are some studies that have found an improved respiratory status and function in neonates with delayed cord clamping which was reflected by improved firstday oxygen saturation (SPO2) and median duration of supplemental oxygen required by these neonates [21, 22].

According to AAP (2004) additional red blood cells can improve the infant's iron stores and there is only a small risk in group of neonatal jaundice requiring phototherapy as per the review. In our study there was no significant difference in requirement of phototherapy at 24 hr in between the ICC group and DCC group. McDonald *et al*. (2008) concluded on the other hand that increasing iron stores in infants through delayed cord clamping may be particularly beneficial in resource poor settings where severe anaemia is common [23].

One of the limitations of this study was that we did not measure effects of delayed cord clamping on blood volume. However, we checked the indirect manifestations of increased blood volume such as initial hematocrit, blood pressure and urinary output. Recording of only short-term effects of delayed clamping could be another limitation. Outcomes of delayed cord clamping were not studied in cases of growth retarded babies and in non-vigorous neonates requiring resuscitation. Apart from timing of cord clamping, position of infants and use of ergometrine after delivery, other factors which affect the placental transfusion i.e. mode of delivery (vaginal versus caesarean), were not compared. Single-center based study and small sample size were other limitations.

Delayed cord clamping is a relatively inexpensive and safe intervention that could provide significant benefits to the preterm neonates, especially in an underresourced setting, where access to good nutrition is limited during childhood and anemia is still a major challenge.

Conclusion

The data generated from the present study concluded that clinical profile of neonates with delayed clamping of cord is also better with less perceived need for blood transfusion. The incidence of hyperbilirubinemia requiring phototherapy was increased in Delayed Cord clamping group. No exchange transfusion was required. There was no significant increase in the number of neonates with polycythaemia in the Delayed Cord clamping group. No beneficial or detrimental effect on the incidence of IVH was noted in the study group.

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