



The Effectiveness of Delayed Cord Clamping on Infant Outcomes

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ABSTRACT

Introduction: Lately, delayed cord clamping is often used as a method of cutting the umbilical cord which is expected to provide good outcomes for the baby, but this method still needs to be studied in depth through review articles to find out its effect. This study aims to compare the results of studies on the effectiveness of delayed cord clamping methods on bilirubin levels and neurodevelopment of infants and toddlers.

Method: The method in this study is a scoping review with PRISMA guidelines, the data bases used are Pubmed and Google Scholar. The inclusion criteria for this study included randomized control trial, quasi-experimental, and clinical trial designs.

Result: There are 6 articles that discuss the effectiveness of DCC on neurodevelopment. In the Age of stage questionnaire, there are 5 domains that have high average values, which are problem solving, fine motor skills, and communication. On the Bayley Scales of Infant Development questionnaire which has the highest average score is the motor cognitive domain. Most of the articles that discuss the effectiveness of DCC on bilirubin levels show that there is an increase in bilirubin levels after the DCC intervention.

Conclusion: DCC is less effective on neurodevelopment and bilirubin levels. It is necessary to develop further research in Indonesia regarding the effects of DCC on neurodevelopment and bilirubin levels

Keywords: delayed, delay, umbilical cord clamping, cord clamping

INTRODUCTION

At the time of birth, the baby is still connected to the mother with the placenta through the umbilical cord. The baby is separated from the placenta by clamping and cutting the umbilical cord. Umbilical cord clamping in newborns is an intervention that must be carried out, there are several optimal timings for clamping the umbilical cord, namely early cord clamping which is carried out in the first 60 seconds after the baby is born, and delayed cord clamping is carried out in the first 1 minute after the baby is born¹.

World Health Organization (WHO) recommends waiting to clamp and cut the umbilical cord after the baby is born. These recommendations are based on the understanding that clamping is delayed because it allows blood to flow continuously from the placenta to the baby for 1 to 3 minutes after birth. This brief delay is known to increase iron stores in young infants by more than 50% at 6 months of age². Statements from some of the literature show that the time to cut the umbilical cord is still a matter of controversy.

However, many studies have found that delaying clamping and cutting the umbilical cord has proven to have many benefits including preventing anemia, increasing hematocrit levels, reducing the incidence of postpartum hemorrhage, optimizing oxygen transfer to the baby, increasing the closeness of mother and baby and increasing the growth of the baby's brain³. Other benefits include BBL bilirubin levels⁴, and neurodevelopment⁵.

The length of time the delay in clamping the umbilical cord affects the bilirubin levels of newborns, the faster the clamping time, the higher the bilirubin level in the baby⁴.

Healthy neurodevelopment is a maturation process that produces motor skills, perceptual, cognitive, language, psychosocial, and self-regulation skills. The rapid and complex neurodevelopment of the human brain begins in the first 1000 days of life, the period from conception and the first two years after birth⁶. Irreversible neurodevelopmental disorders in children are associated with iron deficiency that occurs during the first 3 years of life, with delayed cord clamping at birth it is expected that the baby's blood volume can increase by 30-40% (25-35 ml/kg) which can provide additional substantial iron⁷.

Anderson et al (2014) in their research found that delays in cutting the umbilical cord lead to a tendency toward positive neurodevelopmental effects, such as communication, gross motor, fine motor, problem solving and personal social domain.

This study aims to analyze the effectiveness of delayed cord clamping method on bilirubin levels and neurodevelopment of infants and toddlers.

METHODS

This study uses a systematic literature review method. The object of this research is the effect of delayed

clamping of the umbilical cord on the newborn's outcome (bilirubin and newborn's neurodevelopment). This study used several research stage. Firstly, determining research question (RQ). RQ 1 is distribution of journals/publications discussing delayed cord clamping and its effects on newborn outcomes (clinical hematology, bilirubin, and newborn neurodevelopment). RQ 2 is "How does delayed cord clamping affect newborn outcomes (clinical hematology, bilirubin, and newborn neurodevelopment)?" Inclusion criteria included randomized control trial study designs, quasi-experimental studies, and clinical trials. In addition, criteria for mothers and babies including gestational age at term, preterm, and postmature; pregnancy without disease complications, vaginal delivery and SC, single and twin pregnancies. The exclusion criteria in this study were articles that used research designs such as; cross-sectional studies, case studies, case controls, literature review, scoping review and meta-analysis, clinical trials (animals), RCTs (pilot studies); and articles whose results did not describe perinatal outcomes

Second stage is identification for literature search using keyword. Keyword used in this study is (((delay) OR (delayed)) AND ("umbilical cord clamping")) OR ("cord clamping") Filters: Full text, Clinical Trial, Randomized Controlled Trial.

Third stage is determining the inclusion criteria. The inclusion criteria used the PICOS table below;

Table 1. PICOS

Criteria	Include	Exclude
Population	Studies examine the effect of delayed cord cutting on perinatal outcomes	Population outside the theme studied
Intervention	Delayed cord clamping	Non intervention
Comparison	Early cord clamping	

Outcome	Effects of delayed cord clamping on neonatal outcomes	Does not explain perinatal outcome
Study design	RCT, Quasi-experimental studies, clinical trials	Cross sectional study, case study, case control, Literature review, Scoping review and meta analysis, Clinical trial (animal), RCT (pilot Study)

Fourth stage is screening using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart. the screening result in this study based on The PRISMA flow chart below

RESULT

This Scoping review study investigated the effect of Delayed Cord Clamping on Neurodevelopment and the effect of Delayed Cord Clamping (DCC) on bilirubin levels. The selected articles have gone through a screening process using PRISMA. There are 6 articles that discuss about Neurodevelopment and 10 articles discuss about bilirubin levels. All articles used a randomized control trial design.

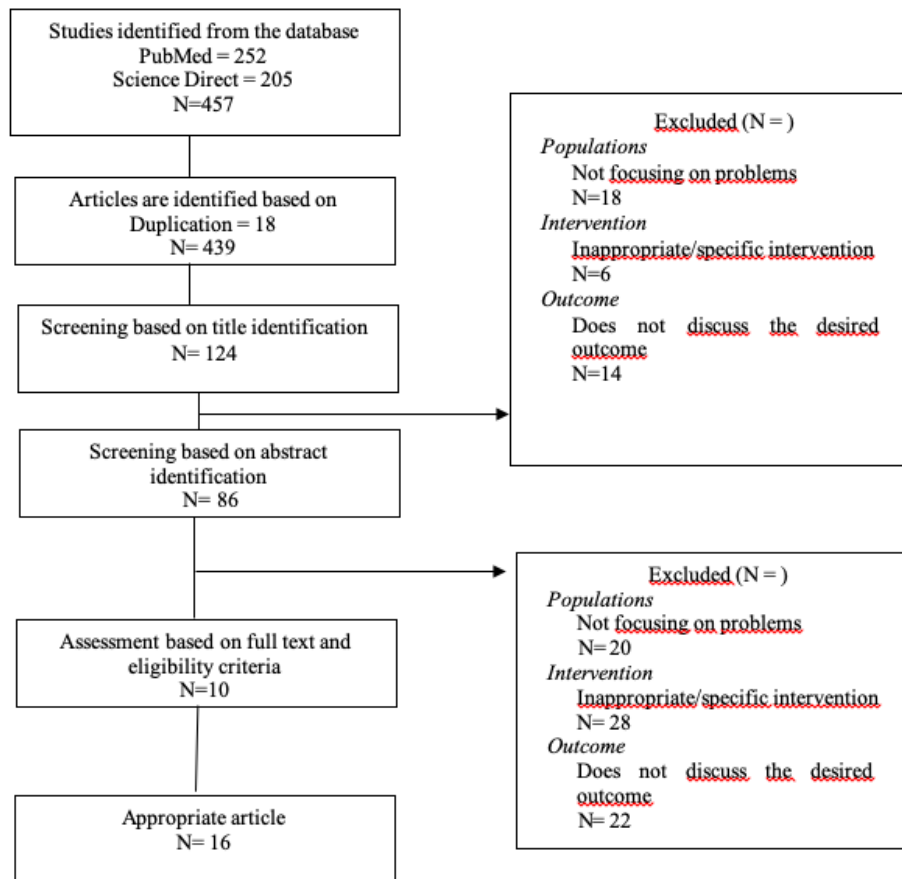


Figure 1. PRISMA flowchart

Table 2. The Effectiveness Of Delayed Cord Clamping On Neurodevelopment

NO	Study	Year, Methods, Measuring Instruments, Research Sites	Inclusion and Exclusion Criteria	Duration of Delayed Cord Clamping	Analysis Time	Result
1	Effects of delayed cord clamping on neurodevelopment and infection at four months of age: A randomised trial ⁸	<ul style="list-style-type: none"> • 2013 • randomised trial • Age & Stages Questionnaire-II • Hospital in Halland Sweden 	uncomplicated pregnancy, vaginal delivery, term	≥ 180 second	4 months after delivery	DCC has a higher mean score (SD) in the problem solving domain, namely 55.3 (7.2) p=0.03 and the fine motor domain has a lower score, namely 48.7(10) p=0.4
2	Effect of delayed vs early umbilical cord clamping on iron status and neurodevelopment at age 12 months a randomized clinical trial ⁵	<ul style="list-style-type: none"> • 2014 • randomized clinical trial (analisis ke dua) • Age & Stages Questionnaire • Hospitals in areas of Sweden 	Aterm, uncomplicated pregnancy	≥ 180 second	12 months after delivery	DCC has a higher mean (SD) score in the fine motor domain, namely 52.1 (18.1) p=0.81, and the communication domain has a lower score, namely 40.4 (12.7) p= >0.99
3	Randomised trial of cord clamping at very preterm birth: Outcomes at 2 years ⁹	<ul style="list-style-type: none"> • 2020 • Randomised trial • Ages and Stages Questionnaire-3. • Several hospitals in England 	Very premature baby (32 weeks)	≥ 2 minute	2 years after delivery	DCC has adverse neurodevelopmental outcomes for very premature newborns compared to ECC. Adverse neurodevelopment, namely speech/language and cognitive domains
4	Effect of Delayed Cord Clamping on Neurodevelopment at 3 Years: A Randomized Controlled Trial ¹⁰	<ul style="list-style-type: none"> • 2021 • randomized-controlled trial • Ages and Stages Questionnaire (ASQ) • Hospital in Kathmandu, Nepal • 	Uncomplicated pregnancy, vaginal delivery, 34-41 weeks' gestation, singleton pregnancy	≥ 180 second	3 years / 36 months after delivery	DCC has a higher mean (SD) score in the communication domain (57.4) p=0.69, and the personal-social domain has a lower score (48) p=0.83
5	A Randomized Clinical Trial of Umbilical Cord Milking vs Delayed Cord Clamping in Preterm Infants: Neurodevelopmental Outcomes at 22-26 Months of Corrected Age	<ul style="list-style-type: none"> • 2018 • Randomized Clinical Trial • Bayley Scales of Infant Development, third edition, • San Diego, USA 	Gestational age 23- 31 weeks, gemelli (2 or 3)	45-60 second	22-26 months after delivery	DCC has a higher average score (SD) in the motor domain (97; p=0.349), cognitive (95; p=0.031), and the lowest domain value is Language (87; p=0.013)

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6	Effect of delayed cord clamping of term babies on neurodevelopment at 12 months: A randomized controlled trial ¹²	<ul style="list-style-type: none"> • 2019 • randomized controlled trial • Ages and Stages Questionnaire (ASQ) • USA 	Aterm, uncomplicated pregnancy vaginal delivery	≥ 180 second	12 months after delivery	DCC has a higher average score in the communication domain (59.3; p=0.008) and personal social (59; p=0.008). The lowest domain value is problem solving (56.3; p=0.20)
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Table 3. The Effectiveness of Delayed Cord Clamping On Bilirubin Levels

NO	Study	Year, Methods, Measuring Instruments, Research Sites	Inclusion and Exclusion Criteria	Duration of Delayed Cord Clamping	Analysis Time	Result
1	Delayed Cord Clamping versus Early Cord Clamping in Elective Cesarean Section: A Randomized Controlled Trial ¹³	<ul style="list-style-type: none"> • 2019 • Randomized Controlled Trial • Padua Teaching Hospital, Italia 	Single pregnancy, term, caesarean delivery, no abnormalities in the fetus	≥ 60 second	72 hours after delivery	transcutaneous bilirubin on day 3 was higher in DCC (7.6 mg/dl) compared to ECC (6.4 mg/dl) (Difference MD = 1.2 mg/dl; 95% CI -0.0 to 2.5; p= 0.05)
2	A randomized controlled study of immediate versus delayed umbilical cord clamping in infants born by elective caesarean section ¹⁴	<ul style="list-style-type: none"> • 2020 • randomized controlled • Brescia, Italia 	<ul style="list-style-type: none"> • Newborn criteria: 37-42 weeks gestatio, weight appropriate for gestational age • pregnant women: BMI > 19 and < 25, age ≥ 37 years 	≥ 60 second	72 hours after delivery	There was an increase in bilirubin (MD= 8.54 ; p= 0.004) in newborns born with DCC but without the need for phototherapy.
3	Placental transfusion: Umbilical cord clamping and preterm infants ¹⁵	<ul style="list-style-type: none"> • 2000 • prospectively randomized. • New Orleans, USA 	premature newborns	20 second	5 minutes after the baby is born	The average peak serum bilirubin in DCC was higher than that in the ECC group (6.6 mg/dl and 6.2 mg/dl; p= 0.56)
4	Comparison of two types of intervention to enhance placental redistribution in term infants: randomized control trial ¹⁶	<ul style="list-style-type: none"> • 2015 • randomized control trial • India 	Aterm>36 weeks, vaginal delivery and Sectio caesarea,	60-90 second	48 hours after delivery	The average serum bilirubin in DCC was higher compared to the group UCM/ Umbilical Cord Milking (6 mg/dl dan 5,84 mg/dl, p= 0,61)

5	Delayed Cord Clamping in Newborns Born at Term at Risk for Resuscitation: A Feasibility Randomized Clinical Trial ¹⁷	<ul style="list-style-type: none"> • 2017 • randomized control trial • San Diego, USA 	Aterm, vaginal delivery	1 and 5 minutes	24 hours after delivery	The mean level of bilirubin (serum or transcutaneous) in the 1 minute DCC was higher than the 5 minute DCC (6.09 mg/d; 5.7 mg/dl; p=0.56)
6	Immediate versus delayed umbilical cord clamping in premature neonates born < 35 weeks: A prospective, randomized, controlled study ¹⁸	<ul style="list-style-type: none"> • 2007 • prospective, randomized, controlled • Haifa, Israel • 24-34 weeks of gestation, babies born without congenital abnormalities and problems 	24-34 weeks of gestation, babies born without congenital abnormalities and problems	30-45 second	72 hours-1 week after delivery	The average peak bilirubin level was 10.7 mg/dl (p= 0.07), the peak bilirubin level in vaginal delivery was 12.5 mg/dl (p=0.09), the peak bilirubin level in caesarean delivery was 9.3 mg/dl (p=0.11), and peak bilirubin level in neonates <1500 g is 8.4 mg/dl (p=0.93)
7	Effects of delayed cord clamping on residual placental blood volume, hemoglobin and bilirubin levels in term infants: a randomized controlled trial ¹⁹	<ul style="list-style-type: none"> • 2017 • randomized controlled trial • Rhode Island, USA 	Uncomplicated pregnancy, no gemelli, vertex position, gestational age 37-41 weeks	≥ 5 minutes	24-48 hours after delivery	The average value of total serum bilirubin in Intention-to-treat/intent to provide treatment was 9 mg/dl (p=0.5) and Actual treatment/actual treatment was 8.5 mg/dl (p=0.45)
8	A randomized controlled clinical trial on peripartum effects of delayed versus immediate umbilical cord clamping on term newborns ²⁰	<ul style="list-style-type: none"> • 2021 • randomized controlled clinical trial • Nigeria 	Singleton pregnancy, 37-42 weeks, vaginal delivery, uncomplicated pregnancy, newborns born without congenital abnormalities and problems	60 second	At birth and 48 hours after after delivery	The mean value of bilirubin in the DCC at birth was 3.13 mg/dl (p=0.815), in DCC 48 hours after the baby was born it was 3.88 mg/dl (p=0.380)
9	Delayed cord clamping was not associated with an increased risk of hyperbilirubinaemia on the day of birth or	<ul style="list-style-type: none"> • 2020 • randomised clinical trial • Kathmandu, Nepal 	Vaginal delivery, pregnancy without complications or without chronic medical conditions, single pregnancy, 34-41	≥ 180 second	At birth and 24 hours after after delivery	The average value of transcutaneous bilirubin in DCC at birth was 85.4 (p=0.6), in DCC 24 hours after birth was 104.8 (p=0.8)

	jaundice in the first 4 weeks <small>21</small>		weeks' gestation			
10	Delayed cord clamping in South African neonates with expected low birthweight: A randomized controlled trial <small>22</small>	<ul style="list-style-type: none"> • 2015 • randomized clinical trial • KwaZulu-Natal, Afrika Selatan 	Maternal age ≥ 18 years, vaginal delivery, estimated low birth weight baby	Between 120 and 180 seconds	24 hours after delivery	The average total serum bilirubin level was above the threshold for DCC, which was 6% lower than the ECC result, which was 16% (p=0.12).

Table 2 shows the search results for articles about the effect of Delayed Cord Clamping on Neurodevelopment, obtained articles published in 2013-2021. Most of the research locations were conducted in 3 European regions, 2 USA regions, and 1 Asian region. Umbilical cord clamping is 45 - ≥ 180 seconds. The time used to perform a Neurodevelopmental analysis was at the age of 4 - 36 months. Almost all articles use the Age & Stages Questionnaire, there is one article that uses the Bayley Scales of Infant Development. 4 articles have conditions for mothers with term pregnancies, while 2 articles have conditions for mothers with pregnancies term, whereas 2 articles have conditions for mothers with preterm pregnancies. 4 articles used the terms of an uncomplicated pregnancy, while 2 articles did not clearly state the conditions. 3 articles allow vaginal delivery, while 3 other articles allow vaginal delivery and caesarean section. All articles exclude congenital abnormalities in their study.

Articles that use the Age & Stages questionnaire have different results in the main result which has a higher average score (SD), namely in the problem solving, fine motor, and communication domains. One article described DCC as having detrimental effects on neurodevelopment in the very premature newborn compared to ECC. One article that used the Bayley Scales of Infant Development measuring tool had a higher average score in the motor and cognitive domains.

Table 3 shows the search results for articles about the effect of Delayed Cord Clamping on bilirubin levels, found articles published in 2000-2021. Research locations were conducted in the USA 3 articles, 2 articles in Europe, 3 articles in Asia, 2 articles in Africa. The duration of cord clamping is 20 seconds - ≥ 5 minutes. The time to do the analysis of bilirubin levels is from birth to 1 week after the baby is born. Almost all articles use a

bilirubin analysis tool, except for 2 articles that use transcutaneous bilirubin, namely the articles Cavallin et al., 2019 and Rana et al., 2020. 6 articles have full term pregnancy, 2 articles have preterm conditions and full term pregnancy, 1 articles with preterm pregnancy requirements, 1 article without clarity on gestational age requirements. 6 articles with vaginal delivery, 1 article with cesarean delivery, 1 article with vaginal and cesarean delivery, 2 articles without clear delivery method requirements.

Bilirubin levels with a duration of DCC $\geq 60 - 180$ seconds almost all show increased levels of bilirubin after DCC intervention but are still within normal limits. In the article Tiemersma et al., 2015 showed that the average total serum bilirubin level above the threshold in DCC was lower, which was 6% compared to the ECC result, which was 16%.

DISCUSSION

Brain development in children depends on neurodevelopment. It happened when neurons form connections with other neurons, and develop networks appropriate to various skills²³. For example, if a child is learning to crawl, the skills needed to crawl, such as balance, moving the arms and legs. These activities will be stored in the brain's memory so that they can be repeated to practice these skills. If the child crawls again on another day or time, the developed network will be activated.

Children's neurodevelopment can be monitored using several measurement scales, in this Scoping review there are two measurement scales used, which are the Age & Stage Questionnaire and the Bayley Infant Development Scale. The Age & Stages Questionnaire is an early-stage developmental screening tool that is filled out by parents. There are 5 domains that are assessed, namely personal-social, gross motor, fine motor, problem solving,

and communication for children aged 2 - 66 months ²⁴.

Scoping review articles using the Age & Stages Questionnaire, obtained different results in each domain which had a higher average score (SD), namely in the domains of problem solving, fine motor skills, and communication ^{5,8,10,12}. One article explains that Delayed Cord Clamping (DCC) has a detrimental effect on neurodevelopment in very premature newborns compared to Ealy Cord Clamping (ECC) ⁹.

The Bayley Scales of Infant Development (BSID) is an extensive formal developmental assessment tool for diagnosing developmental delays in early childhood. There are 5 domains measured through the BSID, namely: cognitive, language, motor, social emotional and adaptive behavior. The results found in the use of the BSID measurement scale, namely DCC, had a higher average score (SD) in the cognitive-motor domain and the lowest domain value, namely language ¹¹.

Even though some of the domain mean values are high, the effectiveness of DCC still needs to be tested again, because half of the several articles show that DCC has no significant effect on children's neurodevelopment. Research in scoping review articles on the effects of DCC on neurodevelopment is mostly carried out in Europe and the USA, while Asia is only in the South Asia region, while Southeast Asia is still very small, especially in Indonesia. We hope that health researchers in Indonesia can develop this DCC intervention for neurodevelopment and bilirubin levels in infants.

On the other hand, bilirubin levels that exceed normal levels will be described as pathological jaundice. The appearance of pathological jaundice is within 24 hours due to an increase in serum bilirubin ≥ 5 mg/dl/day. Physiological jaundice usually appears between the ages of 24-72 hours and

peaks between days 4 and 5 and 7 in premature infants. Normal bilirubin levels in newborns are ≤ 15 mg/dl and the latest recommendations based on the American Academy of Pediatrics (AAP) normal bilirubin levels are up to 17-18 mg/dl ²⁵.

The results of a Scoping review of several articles on the effectiveness of DCC on infant bilirubin levels show that the effectiveness of DCC still needs to be re-tested. This is based on most of the articles which show that after DCC there is an increase in bilirubin levels although still within normal limits, this indicates that DCC is less effective on bilirubin levels. Research related to DCC on bilirubin levels in Indonesia is still few. It is hoped that researchers in Indonesia can develop this DCC intervention on bilirubin levels in infants.

CONCLUSION

DCC is less effective on neurodevelopment and bilirubin levels. However, we hope that health researchers in Indonesia can develop this DCC intervention for neurodevelopment and bilirubin levels in infants and other outcomes in infants and children.

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