



The Impact of Umbilical Cord Clamping Time on the Infant Anemia: A Randomized Controlled Trial

**Sevil Güner¹, Birsen Karaca Saydam²*

1. Department of Midwifery, Mersin University, 33343, Mersin, Turkey
2. Department of Midwifery, Ege University, Faculty of Health Sciences, 35100, İzmir, Turkey

***Corresponding Author:** Email: sevil.guner@mersin.edu.tr

(Received 04 Oct 2020; accepted 04 Dec 2020)

Abstract

Background: Anemia during infancy causes irreversible physical, cognitive, motor, and behavioral development disorders. This study aimed to determine the effect of delaying umbilical cord clamping time on certain parameters regarding anemia during the infancy.

Methods: This randomized controlled trial was conducted at a university hospital in west of Turkey (Dec 2017-Dec 2018). Overall, 110 participants were evaluated for the research, 65 participants were randomized after excluding those who did not meet the inclusion criteria (intervention=32, control=33). Randomly assigned to delayed clamping (1 min after delivery) or early clamping (in 15 sec after delivery), and followed up until 4 months postpartum. 48th-hour hematocrit, bilirubin values, need for phototherapy and hematocrit, hemoglobin values, diagnosis of anemia at the postnatal fourth month were compared between two groups. The data showing normal distribution were assessed using the parametric tests. The level of statistical significance was determined as $P<0.05$.

Results: The 48th-hour hematocrit and bilirubin levels of the intervention group were significantly higher than the control ($P<0.01$ and $P<0.05$, respectively). No significant difference regarding the need for phototherapy due to postnatal hyperbilirubinemia was observed between the two groups ($P>0.05$). Means of the intervention group hematocrit and hemoglobin levels measured during anemia screening performed at the fourth month were found to be higher than those of the infants in the control group ($P<0.05$ and $P<0.05$, respectively).

Conclusion: Delaying umbilical cord clamping had a positive impact on the haematological parameters of infants. Clamping the cord at least one minute in birth can be performed to prevent the iron deficit anemia that could be seen during the first years of infants' lives.

Keywords: Umbilical cord; Clamping; Infant; Anemia; Midwifery

Introduction

Anemia is globally regarded as an important dietary and public health issue due to its adverse impacts on physical and mental development during infancy and childhood and the prevalence of anemia in the first year of life in Turkey up to 50%

(1). Anemia during infancy causes irreversible physical, cognitive, motor, and behavioral development disorders (2) and it is a significant problem focused on due to these adverse impacts. Nevertheless, the procedures to be performed during



Copyright © 2021 Guner et al. Published by Tehran University of Medical Sciences.
This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (<https://creativecommons.org/licenses/by-nc/4.0/>). Non-commercial uses of the work are permitted, provided the original work is properly cited.

this period are limited. Therefore, clamping the umbilical cord lately during the delivery boosts newborns' iron stores and contributes to the efforts to prevent anemia (3). The extra iron achieved through this practice may contribute to preventing iron deficiency when combined with the already-present iron within the bodies of infants (approx. 75 mg/kg) (4-9).

The Turkish Ministry of Health states that infants should be examined for anemia at the fourth month within the monitoring protocol for the infants and children, and infants with a hemoglobin level of 11 g/dL should be assessed for anemia, resulting in the initiation of treatment protocol when needed (10). Late clamping procedure (for at least 60 sec) should be commonly used in cases where iron deficit anemia is an issue and that this procedure should be studied and supported more (11).

Despite its proven benefits, the common approach in Turkey is that the umbilical cord is early clamped, and the factors determining the cord clamping time include practice-related concerns, information deficiency, personal preferences, and routine hospital practices (12). The relevant studies are quite limited in Turkey where anemia during the infancy and childhood is quite common. We aimed to determine the effect of delaying umbilical cord clamping time on certain parameters regarding anemia during the infancy.

Materials and Methods

Study design and participants

This parallel, randomized and controlled study was performed at the delivery room of a university hospital in a western location of Turkey. The intervention group consisted of pregnant women who were between the ages of 19 and 35 yr during the study period (Dec 2017-Dec 2018), whose gestational age was ≥ 37 wk, who had a single and a live fetus at the vertex presentation, who had no medical issues that could pose a risk for postpartum bleeding and who planned vaginal delivery, and the infants who did not need resuscitation

during delivery. The pregnant women who did not accept to participate and infants who received iron support until the postnatal fourth month were excluded.

Before initiating the study, necessary permissions were obtained from the regional Ethics Committee (decision no: 17-5.1/50) and Gynecology and Obstetrics Clinic. In addition, the trial was registered at the clinical trials registry (NCT04463485). The pregnant women meeting the inclusion criteria were informed about the study and informed consent was received. This study was conducted as a doctoral thesis and assessed by a thesis monitoring committee that gathered every six months.

Randomization and allocation concealment

Overall, 110 participants were evaluated. After pregnant women who did not fit the inclusion criteria (n=32) and did not agree to participate in the study (n=6) were excluded, 72 pregnant women were randomized to determine the study group. For the first phase, 36 pregnant women were included in the intervention group and 36 were included in the control group. After the newborns who needed resuscitation during birth were excluded (n=7), the data for the first phase of the study were collected from 65 newborns (32 in the intervention group, 33 in the control group). In the second phase of the study, 13 infants who did not receive anemia scan (5 in the intervention group, 8 in the control group) were lost to follow-up and the study was completed with 52 participants (Fig. 1).

Participants of the study were randomized into two groups, which were intervention (Delayed Cord Clamping-DCC) and control (Early Cord Clamping-ECC) groups. A simple randomization method was used for randomization. Participants' names were written in closed envelopes on the day when study data were collected. Papers that had "intervention" and "control" written on them were put in different envelopes in the same way. The researcher asked delivery room staff to choose one envelope, and their groups were determined in this way.

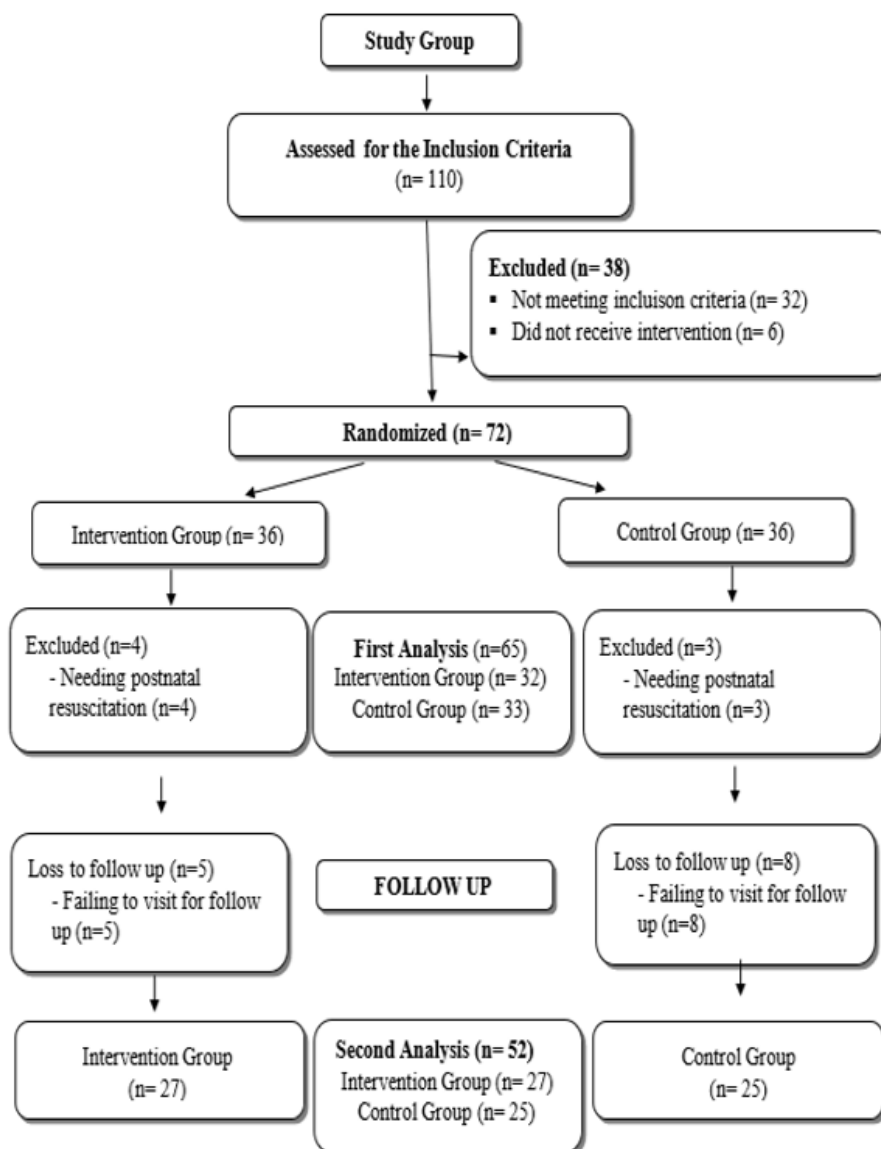


Fig. 1: Consort flow diagram

Procedure

The delivery room staff were informed about the group of participants in all delivery cases in this study. After the completion of the second delivery stage, the umbilical cord was held at the level of the uterus for 60 sec for the infants in the intervention group. After the 60 sec, the umbilical cord was clamped and routine newborn care was provided (the duration was kept by the researcher using the same chronometer). The umbilical cords of the newborns in the control group were clamped within the first 15 sec, and routine newborn care

was provided again. At the postnatal 48th-hour (before the discharge), the hematocrit and bilirubin measurement results seen in the newborn capillary blood sample were noted from hospital records. The researcher provided counseling to all participants in terms of maternal and infant care. The mothers were called through phone at the postnatal 14th day, and data were collected to see whether newborns needed phototherapy owing to hyperbilirubinemia. The data obtained through the anemia screening performed by the family practice unit at the fourth postnatal month (hemoglobin,

hematocrit measurement results, diagnosis of anemia) were assessed, and the data phase was completed. Due to the nature of the practice in this study, blinding could not be performed for the delivery room staff and participants, but blinding was done during the statistical analysis of measurement results.

Outcome variables

Primary outcomes of this study included the 48th-hour hematocrit value, and hemoglobin, hematocrit values and diagnosis of anemia measured at the postnatal fourth month. The secondary outcomes were the bilirubin values measured at the 48th-hour, and the need for phototherapy owing to hyperbilirubinemia at the postnatal period.

Statistical analysis

For the statistical analyses, IBM SPSS Statistics 25.0 (IBM SPSS Statistics for Windows, Version 25.0 Armonk, NY: IBM Corp.) was used. The

constant variables were displayed using the mean, standard deviation, categorical variables and percentage distributions – descriptive statistical methods. At the locations suiting the normal distribution, Student's t-test was used within the inter-group comparisons, while Pearson's chi-square test was used for the categorical variables. The statistical significance level was determined to be $P < 0.05$.

Results

The study groups in this study displayed similar characteristics when compared in terms of demographic and clinical variables such as maternal age, antepartum hemoglobin and hematocrit levels, postpartum hemoglobin level, birth weight, 5th minute APGAR score and first breastfeeding time (Table 1).

Table 1: Maternal and neonatal descriptive variables

<i>Variable</i>	<i>Intervention (n=32) Mean±SD</i>	<i>Control (n=33) Mean±SD</i>
Maternal age (yr)	26.9±4.4	27.4±5.4
Antepartum hemoglobin (g/dL)	12.9±0.6	13.1±0.7
Antepartum hematocrit (%)	38.1±1.7	38.5±1.7
Postpartum hemoglobin (g/dL)	12.3±0.4	12.4±0.6
Birth weight (gr)	3333.7±348.9	3325.1±327.3
5th minute APGAR score	9.4±0.5	9.5±0.5
First breastfeeding time (min)	28.1±13.4	29.2±18.7

The 48th-hour neonatal hematocrit level – one of the main variables in this study was 62.06% (SD: 2.77) in the intervention group, and 49.30% (SD: 5.04) in the control group. According to the anemia screening performed at the postnatal fourth month, the venous hemoglobin level was 11.91 g/dL (SD: 0.74) in the delayed clamping group while the hematocrit level was 34.70% (SD: 2.08), and in the early clamping group, hemoglobin level was 11.38 g/dL (SD: 0.58) while the hematocrit level was 33.47% (SD: 2.32). The difference regarding three variables was found to be statistically significant during the inter-group comparisons. The 48th-hour hematocrit level and fourth month

hemoglobin and hematocrit levels were significantly higher in the group of delayed clamping ($P < 0.01$, $P < 0.01$ and $P < 0.05$ respectively).

After the examination toward the variable of anemia diagnosis made within the screening activity performed at the family practice unit, 18.5% of the infants in the intervention group were diagnosed with anemia while 24% had the same disorder in the control group. The comparison made between two groups indicated that anemia was more common in the control group, but the difference was not statistically significant ($X^2: 0.234$, $P > 0.05$) (Table 2).

Table 2: Comparison of primary outcome variables between the two groups

Variable	Intervention		Control		Test value	P value
	N	n (%) / Mean \pm SD	N	n (%) / Mean \pm SD		
Hematocrit 48 th h (%)	32	62.06 \pm 2.77	33	49.30 \pm 5.04	-12.582*	.00
Hemoglobin 4 th month (g/dL)	27	11.91 \pm 0.74	25	11.38 \pm 0.58	-2.846*	.00
Hematocrit 4 th month (%)	27	34.70 \pm 2.08	25	33.47 \pm 2.32	-2.006*	.05
Diagnosis of anemia 4 th month	27	5 (18.5)	25	6 (24.0)	0.234**	.62

Values expressed as mean \pm SD or as n (%) *t-test value **X² test value

Secondary outcome results of this study indicated that the 48th-hour bilirubin level of the newborns in the intervention group was 62.06 mg/dL (SD: 2.77) while the same level of those in the control group was 49.30 (SD: 5.04), and the difference was

statistically significant ($t = -2.087$, $P < 0.01$). Both groups' need for phototherapy due to postnatal hyperbilirubinemia indicated that the difference between the two groups was not statistically significant ($X^2: 0.004$, $P > 0.05$) (Table 3).

Table 3: Comparison of secondary outcome variables between the two groups

Variable	Intervention		Control		Test value	P value
	N	n (%) / Mean \pm SD	N	n (%) / Mean \pm SD		
Bilirubin 48 th h (mg/dL)	32	62.06 \pm 2.77	33	49.30 \pm 5.04	-2.087*	.00
Phototherapy requirement	32	7 (21.9)	33	7 (21.2)	0.004**	.94

Values expressed as mean \pm SD or as n (%) *t-test value **X² test value

Discussion

The hematocrit values, measured at the postnatal 48th-hour of newborns whose umbilical cords were delayed clamping group were statistically and significantly higher than those whose umbilical cords were clamped earlier. The hematocrit measurements of newborns were performed at the postnatal sixth and 48th-h in a study conducted with three groups to examine the impact of umbilical cord clamping time on the hematocrit level and clinical results of newborns, and that study indicated that the hematocrit levels of two groups where umbilical cords were clamped lately were significantly higher than those of the group where umbilical cords were clamped earlier (13), a result similar to the ones found in the present study. The hemoglobin and hematocrit levels of newborns whose umbilical cords were clamped lately were

higher than those of the control group, and the procedure of clamping the umbilical cord later could be beneficial for preventing iron deficiency and anemia during the infancy period (14). The studies conducted after 2000 focus on the impact of cord clamping time on the haematological parameters in the short and long term and their results generally show that the hemoglobin, hematocrit and ferritin levels of the newborns in the late clamping group were significantly higher than those of the newborns whose umbilical cord was clamped earlier (3, 4, 15-20).

Starting the life with sufficient blood volume has a great impact on the medical statuses of newborns in the following periods of their lives (21). The haematological parameters examined in the relevant studies reviewing the long-term effect of cord clamping duration among babies are generally the hemoglobin, hematocrit and serum ferritin

levels examined in the period from the postnatal third to 12th months. An iron amount of approximately 60 mg transferred when cord clamping time is delayed will help meet babies' needs in the first three months and prevent the iron deficit disorder that may be developed in the first year (7, 13). In Turkey, elementary iron is administered at the prophylactic dose to babies after the fourth month, as a part of "Turkey Like Iron" program (10). In addition, the impact of using supplementary on the results was considered, and babies' control data were assessed at the fourth month. According to the assessment performed at the fourth month, the mean hematocrit and hemoglobin levels of the babies in the intervention group were significantly higher than those of the babies in the control, similar to the literature. Ferritin-related comparison was not performed due to any infant was not examined for ferritin level. Hematocrit (6, 24-48 h, 5th day and 2 months) and hemoglobin concentration (24-48 h, 7th day, 3-6 months, 1 year) were higher in the groups where the umbilical cord was delayed (22). In a meta-analysis where 15 randomized controlled studies were examined, the impact of early and late clamping on the health of 3911 term newborns was assessed. Additionally, hemoglobin and hematocrit levels covering the sixth hour, 24th-48th-hour and first six months were found to be higher in the group where late clamping was performed (18). In our study, the elementary iron supplement was provided to all babies whose hemoglobin level was under 11 gr/dL but ferritin measurement was not needed for any babies owing to the issues experienced in conducting the primary care services in Turkey, to the higher prices of this test compared to the hemogram test, and to the fact that this test required taking a blood sample from babies twice. The hemoglobin value examined within the full blood test is commonly utilized as a test where erythrocyte index is read photometrically, but serum ferritin level is used as a test reflecting the stored iron less frequently (23). A relevant study conducted to determine the effectiveness of routine blood test and ferritin measurement performed simultaneously in diagnosing the iron def-

icit in newborns indicated that ferritin measurement performed in addition to hemogram measurement was more effective than the measurement of the latter agent in terms of diagnosis (24). However, in Turkey, use of ferritin level was more limited, and the RDW values examined within the hemogram test could be considered to treat the iron deficit (25). Although no significant difference regarding the diagnosis of anemia among the babies in the intervention and control groups was determined, the hemoglobin and hematocrit levels of the babies in the intervention group were significantly higher than those of the babies in the control group. Delaying the umbilical cord clamping time is believed to have positively affected the babies in this study considering because hemoglobin is a molecule carrying iron in the body and a parameter helping experts estimate the iron storage in infants' bodies (26, 27).

The studies conducted to determine the impact of umbilical cord clamping time on neonatal results indicated that the negative results examined the most included newborn hyperbilirubinemia and related need for phototherapy (28). The 48th-hour bilirubin values of newborns whose umbilical cords were delay clamped were statistically and significantly higher than those of the control group. However, according to the comparison made in accordance with the postnatal phototherapy need, the difference between the newborns in the intervention and control groups was not statistically significant. The guide issued by WHO (11) in 2014 to detail the procedure of delaying umbilical cord clamping time indicated that the bilirubin levels of newborns whose cord clamping time was delayed were significantly higher than those whose cords were clamped earlier and that no significant difference regarding the need for phototherapy treatment was present between the groups. A study reviewing the randomized controlled studies performed in this regard reflected that asymptomatic polycythemia of newborns whose cords were clamped later was high and polycythemia created a risk of hyperbilirubinemia among the newborns (22). A study conducted with three newborn groups reported no significant difference between the 24th-48th-bilirubin measurements of these three

groups where early clamping was performed in the first 15 sec while the late clamping was done at the 60th second and third minute (13). A cochrane review showed that newborns whose umbilical cords were clamped early needed less phototherapy than those whose cords were clamped later due to hyperbilirubinemia, and that late clamping could be performed for cases where phototherapy conditions were suitable (18). However, the studies examined within the present study indicated that the non-standardized properties of inclusion criteria for phototherapy were interesting in terms of questioning the results (8, 11). The studies performed at a later period indicated no significant difference regarding the need for phototherapy between two groups due to hyperbilirubinemia (8, 19, 29, 30).

There were some limitations in our study. Firstly, it was aimed to evaluate the whole sample group in terms of anemia at the 4th month, but could not be performed due to loss of follow-up. This problem frequently encountered in prospective studies is also valid for our study. In addition, the fact that ferritin test was not performed in the units screened for anemia due to institutional policies and spending limitations is another limitation for our study.

Conclusion

Delaying the umbilical cord clamping time for at least 60 sec after the delivery is a suitable approach for preventing anemia during infancy. The implication for the practice; developing a national guide for health workers will provide standardization in practice. Moreover, professional training for the hospital staff will make great contributions to the efforts of spreading the procedure in Turkey. We emphasize that it is also necessary to provide training on this subject to families preparing for birth in order to spread the procedure whole country.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

We extend our gratitude to the members of thesis monitoring committee, all staff of the obstetrics clinic and participants all of whom contributed to this study as a doctoral thesis. This trial was presented at 3rd International & 4th National Istanbul Midwifery Days Congress 8-10 October 2020 and it was rewarded as 3rd oral presentation.

Funding

No financial support was received from any institutions.

Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Turkish Hematology Association (2011). Diagnosis and treatment guide for iron deficiency anemia in children. Istanbul: Turkish Hematology Association.
2. Andersson O, Lindquist B, Lindgren M, et al (2015). Effect of delayed cord clamping on neurodevelopment at 4 years of age: A randomized clinical trial. *JAMA Pediatr*; 169 (7): 631-8.
3. Chaparro MC, Neufeld LM, Alavez GT, et al (2006). Effect of umbilical cord clamping on iron status in Mexican infants: a randomised controlled trial. *Lancet*, 367(9527):1997-2004.
4. Gokmen Z. Effects of delayed umbilical cord clamping on peripheral haematological parameters and peripheral blood haematopoietic stem cells in premature neonates [PhD thesis]. Faculty of Medicine, Department of Pediatrics, Division of

- Neonatology, Baskent University, Ankara; 2010.
5. Yigit MB, Kowalski WJ, Hutchon DJR, et al (2015). Transition from fetal to neonatal circulation: modeling the effect of umbilical cord clamping. *J Biomech*, 48(9):1662-70.
 6. Kluckow M, Hooper SB (2015). Using physiology to guide time to cord clamping. *Semin Fetal Neonatal Med*, 20(4):225-31.
 7. Pisicane A (1996). Neonatal prevention of iron deficiency. *BMJ*, 312(7024): 136-137.
 8. Chaparro MC (2011). Timing of umbilical cord clamping: effect on iron endowment of the newborn and later iron status. *Nutr Rev*, 69 Suppl 1:S30-6.
 9. Todorich B, Pasquini JM, Garcia CI, et al (2009). Oligodendrocytes and myelination: the role of iron. *Glia*, 57(5):467-78.
 10. Republic of Turkey Ministry of Health (2012). Infant and Child Monitoring Protocols. Access: https://dosyaisam.saglik.gov.tr/Eklenti/9010_bebek-cocuk-izlem-protokolleripdf.pdf
 11. World Health Organization (WHO). (2014). Guideline: delayed umbilical cord clamping for improved maternal and infant health and nutrition outcomes. Geneva: World Health Organization.
 12. Karatas Baran, G, Sahin S (2019). Effect of Delayed Umbilical Cord Clamping on Newborn Health. *Journal of Düzce University Health Sciences Institute*, 9 (2): 95-101.
 13. Ceriani Cernadas J, Guillermo C, et al (2006). The effect of timing of cord clamping on neonatal venous hematocrit values and clinical outcome at term: a randomized, controlled trial. *Pediatrics*, 117 (4): e779-86.
 14. Ahmad K, Aly SA, Zahran, SA (2012). Effect of early versus late umbilical cord clamping of term infants on maternal and neonatal outcomes. *J Am Sci*, 8 (9): 1935-1941.
 15. Emhamed MO, van Rheenen PF, Brabin BJ (2004). The early effects of delayed cord clamping in term infants born to Libyan mothers. *Trop Doct*, 34 (4): 218-22.
 16. Venancio, SI, Levy RB, Saldiva SRDM, et al (2008). Effects of delayed cord clamping on hemoglobin and ferritin levels in infants at three months of age. *Cad Saude Publica*, 24 (2): S323-31.
 17. van Rheenen PF, Gruschke S, Brabin BJ (2006). Delayed umbilical cord clamping for reducing anaemia in low birthweight infants: implications for developing countries. *Ann Trop Paediatr*, 26 (3): 157-67.
 18. McDonald SJ, Middleton P, Dowswell T, et al (2008). Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Cochrane Database Syst Rev*, 2013(7):CD004074.
 19. Rincon D, Foguet A, Rojas M, et al (2014). Time of cord clamping and neonatal complications, a prospective study. *An Pediatr (Barc)*, 81(3):142-8.
 20. Nourai S, Amir Ali Akbari S, Vameghi R, et al (2019). The effect of the timing of umbilical cord clamping on hemoglobin levels, neonatal outcomes and developmental status in infants at 4 months old. *Iran J Child Neurol*, 13 (1): 45-55.
 21. Korukcu O, Avgoren G (2016). The effect of delayed umbilical cord clamping and cord milking on health of newborn. *Journal of Anatolia Nursing and Health Sciences*, 19 (Special Issue): 46-52.
 22. Hutton EK, Hassan ES (2007). Late vs early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. *JAMA*, 297 (11): 1241-52.
 23. Gedikoglu G, Agaoglu L (1993). Haematological Diseases. In: Paediatrics Vol 2. Ed, O Neyzi, T Ertugrul. Nobel Medical Publishers, İzmir, Turkey, pp: 347-363.
 24. Arsan S, Cullas Ilarslan NE, Gunay F (2016). The importance of iron prophylaxis in the first two years of life and the measurement of ferritin in anemia screening with hemogram: can it be part of routine screening? Ankara University Scientific Research Project Final Report, pp: 1-16.
 25. Akgunes, E. Examination of erythrocyte index RDW and MCV as iron deficiency screening test in children [Master thesis]. Republic of Turkey Ministry of Health Bakirkoy Dr. Sadi Konuk Training and Research Hospital, İstanbul; 2004.
 26. Giardina B, Messana I, Scatena R, et al (1995). The multiple functions of hemoglobin. *Crit Rev Biochem Mol Biol*, 30 (3): 165-96.
 27. Kayiran SM, Gurakan B (2010). Effect of iron deficiency on motor development and

- cognitive functions in children. *TAF Preventive Medicine Bulletin*, 9 (5): 529-534.
28. Ouellette Landynn E (2016). Delayed umbilical cord clamping: a state of the science. *Senior Honors Projects*, 253. <https://commons.lib.jmu.edu/honors201019/253/>
29. Rabe H, Diaz-Rossello JL, Duley L, et al (2012). Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. *Cochrane Database Syst Rev*, 9(9):CD003248.
30. Begley CM, Gyte GML, Devane D, et al (2015). Active versus expectant management for women in the third stage of labour. *Cochrane Database Syst Rev*, (3):CD007412.