

Article type: Research article

Alteration of Iron, Zinc, Vitamin A Breast Milk Levels During Lactation Period Among Mothers of Low Birth Weight Infant Born at Preterm and Term

Rizky Arisanti Maharani¹, Roedi Irawan², Risa Etika³

¹Researcher, Pediatric Resident, ²Senior staff, Head Division of Nutrition and Metabolic, ³Senior staff, Head Division of Neonatology Faculty of Medicine, Airlangga University, Dr. Soetomo General Hospital, Surabaya, Indonesia

Abstract

Background: Duration of lactation and preterm delivery were noticed as dominant factors affecting breast milk composition, including its micronutrient particularly iron, zinc and vitamin A. This study was to analyze the alteration of iron, zinc, vitamin A levels within colostrum and mature breast milk among mothers of low birth weight (LBW) preterm and term infants.

Methods: This cross-sectional study was conducted between July 2019 and April 2020 among mothers of LBW infant delivered at preterm and term at Dr. Soetomo hospital. Seventeen samples of breast milk were enrolled on each group. Respectively, colostrum and mature milk were collected between day 2 and 4, between day 15 and 20 after delivery.

Results: The iron levels on both groups did not change significantly during lactation period (respectively $p=0,266$ and $p=0,845$). Zinc levels were found significantly higher in colostrum of both groups, as well as vitamin A levels within colostrum in LBW preterm group ($p<0,05$).

Conclusions: Higher levels were found in zinc within colostrum of both groups, similar to vitamin A in LBW preterm group. In contrast, iron did not differ significantly during lactation period.

Keywords: Colostrum, Mature breast milk, Low birth weight

Introduction

Breast milk is the primary nutrition priority recommended to be given to all infants ¹ as it has

been known as an optimal nutrition source for infant growth and development for its macronutrients, micronutrients and unique immunology.² Data in the preclinical studies showed the importance role of breast milk micronutrients in normal brain development during the late fetal and early neonatal periods, however studies related to the role of breast milk micronutrients on preterm brain development are still limited compared to macronutrients.³ Lactation period and preterm birth have been identified as the main causes that can affect the composition of breast milk. Given that exclusive breastfeeding is

Corresponding author:

Roedi Irawan, MD, PhD

Head of Nutrition and Metabolic Division Child Health Department/Faculty of Medicine

Universitas Airlangga.

Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

Email: roedi.dr.rsds@gmail.com

recommended until 6 months of age, it is important to have accurate data regarding the composition of breast milk.⁴

Iron, zinc, and vitamin A are important micronutrients in breast milk.⁵ About 12% mortality of children under 5 years of age are known associated with deficiencies of five common micronutrients and 3 of them are iron, zinc and vitamin A, either one of them or in combination.⁶ Infants with low birth weight (LBW), both preterm and term are significantly more susceptible to zinc deficiency than term infants with normal birth weight as well as iron deficiency.^{7,8} Preterm infants with small for gestational age are also the most vulnerable group for vitamin A deficiency.⁹ Many conflicting statements are found in the literature regarding the impact of preterm birth on nutrient levels, one of which is breast milk micronutrients. In most previous studies have investigated the differences in the micronutrient levels of breast milk for preterm and term infants without adding birth weight. Research on nutrition in term infants which adding birth weight discuss only macronutrient levels and not specifically examine the difference of breast milk levels between LBW and normal birth weight term infants.^{10,11} On the other hand, information regarding the micronutrient levels of breast milk is still lack and inconclusive.

A better understanding of the breastfeeding components will also help in various aspects, one of which is breastfeeding education and better breastfeeding habits, as well as nutritional therapy for high-risk infants, one of which is in preterm infants.¹² On the other hand, information on the composition of both colostrum and mature breast milk in Indonesia is still lack, especially in LBW infants, both preterm and term. Therefore research in colostrum and mature breast milk of LBW, in particular iron, zinc, and vitamin A, preterm and term mother infants is very important.

Materials and Methods

A cross-sectional study was conducted from July 2019 to April 2020 at Department of Child Health

Dr. Soetomo General Hospital Surabaya. The sample were breast milk of mothers who gave birth at preterm and term gestational age by spontaneously, c-section and instrumental vaginal delivery. Colostrum samples were collected between day 2 and 4 and mature breast milk between day 15 and 20 after delivery. Data were analysed by homogeneity test using Shapiro-Wilk test, then analyzed using paired T-test for homogenous data distribution and Wilcoxon for heterogenous data. Two groups then being tested for the difference using the Independent T-test for homogenous data distribution and Mann-Whitney for heterogeneous. IBM SPSS 21.0 was used for all statistical analyses.

Results

During the research period (July – December 2019), there were a total of 215 LBW infants who were born preterm and 39 LBW infants who were born at term in the delivery room and operating room of Dr. Soetomo General Hospital. Based on the sample size calculation formula, the minimum sample size in each group is 17, so that a total of 34 patients were included in this study consisting of 17 mothers who gave birth to LBW preterm infants and 17 mothers who gave birth to LBW term infants who met the inclusion and exclusion criteria. The number of samples was taken from the minimum sample size due to the limited research funding. During the study period, 1 were excluded (the mother died) and 4 mothers were dropped out (the infant died) in the LBW preterm infants and 2 mothers were excluded (the mother was on a ventilator) and 3 mothers were dropped out (the mother resigned) in LBW term infants group. The average age of mothers who gave birth to LBW preterm infants was 22-35 years with an average infant weight of 1000-2000 grams, while the average age of mothers who gave birth to LBW term infants was 28-36 years with an average infant weight 1800 – 2300 grams. The results of the homogeneity test on the basic characteristics of subjects explained in table 1 show a homogeneous distribution in the sex and mode of delivery of the mother, while the data distribution is not homogeneous in the two groups

found on the maternal age, gestational age, birth weight, and combination of gestational age and birth weight.

The mean iron levels in colostrum and mature breast milk in the two groups listed in table 2 show insignificant differences ($P > 0.05$) while in table 3

shows that zinc levels in colostrum are significant ($P < 0.05$) higher than mature breast milk, meanwhile in Table 4 shows that mean levels of vitamin A in the colostrum in LBW preterm infants were significantly higher than in the mature breast milk, while in the group of LBW term infants was not significantly different.

Tabel 1 Basic Characteristics of Subjects

Characteristics	LBW preterm babies (n=17)	LBW term babies (n=17)	P-Value
Mother's Age (mean±SD), years old	28,18±6,66	32,06±3,75	0,047
Gestational age (mean±SD), weeks	33,35±2,52	37,76±0,75	<0,001
Birth weight (mean±SD), grams	1555±480,85	2087,76±291,98	<0,001
Combination of gestational age and birth weight, n (%) Small for Gestational Age Appropriate for Gestational Age	6 (35,3%) 11(64,7%)	13 (76,5%) 4 (23,5%)	0,016
Sex, n (%) Male Female	7 (41,2%) 10 (58,8%)	7 (41,2%) 10 (58,8%)	1,000*
Mode of delivery, n (%) Spontaneous vaginal delivery CS / assisted delivery	3 (17,6%) 14 (82,4%)	6 (35,3%) 11(64,7%)	0,338*

* homogenous P-Value >0.05

Tabel 2 Comparison of Iron Levels in Colostrum and Mature Breast Milk

Gestational Age	Iron		P-Value
	Colostrum (Mean ± SD), mcg/dL	Mature breast milk (Mean ± SD), mcg/dL	
LBW preterm babies	95,41 ± 36,93	107,18 ± 42,39	0,266
LBW term babies	116,06 ± 64,17	119,29 ± 44,05	0,845

Tabel 3 Comparison of Zinc Levels in Colostrum and Mature Breast Milk

Gestational Age	Zinc		P-Value
	Colostrum (Mean ± SD), mcg/dL	Mature breast milk (Mean ± SD), mcg/dL	
LBW preterm babies	789,12 ± 358,67	527,29 ± 122,07	0,027*
LBW term babies	529,65 ± 171,80	367,76 ± 114,91	0,010*

* significant P-Value <0.05

Tabel 4 Comparison of Vitamin A Levels in Colostrum and Mature Breast Milk

Gestational Age	Vitamin A		P-Value
	Colostrum (Mean ± SD), mcg/dL	Mature breast milk (Mean ± SD), mcg/dL	
LBW preterm babies	100,24 ± 15,55	91,41 ± 11,88	0,015*
LBW term babies	87,76 ± 15,95	92,47 ± 10,92	0,207

* significant P-Value <0.05

Discussion

The mean comparison results of iron, zinc, and vitamin A levels in colostrum and mature breast milk in preterm and full-term infants in this study showed mixed results. Lönnerdal states that many differences in the breast milk content of preterm and term infants are probably due to decreased blood flow and differentiation of mammary epithelial cells and the absence of tight junctions between epithelial cells in the mammary glands of preterm infants.¹⁶

There was no significant difference in iron levels in both colostrum and mature breast milk on LBW preterm and LBW term infants. This finding is in line with the results of a study by Sabatier et al in Switzerland which examined 27 mothers with preterm infants and 34 mothers with term infants which the

mean iron levels in mothers' breast milk with preterm infants was 36 ± 23 mcg/dL, while in mothers with term infants was 44 ± 15 mcg/dL, however this study did not divide the studied breast milk by lactation period.¹⁷

The mean levels of zinc in colostrum were significantly higher than in mature breast milk for both LBW preterm infants and LBW term infants. The results of this study are in line with the study by Ting et al. which showed that there was a significant dynamic in zinc composition based on the lactation period, namely colostrum, transitional breast milk, and mature breast milk, each of which was 660 ± 390 mcg/dL; 330 ± 140 mcg/dL; and 220 ± 130 mcg/dL as well as a study by Erick which found that zinc levels in breast milk decreased with increasing lactation

period, however these studies did not group based on gestational age or birth weight.^{18,19} Meanwhile, the results of this study are not in line with the study by Sabatier et al. which reported no significant difference in zinc levels in breast milk for mothers with preterm infants and mothers with term infants.¹⁷

Low birth weight preterm infants showed that means level of vitamin A in colostrum was significantly higher than mature breast milk. This in line with a study conducted by Lima et al. on breast milk from mothers with preterm infants who concluded that vitamin A levels were significantly more based on the lactation period ($p < 0.001$) with mean concentrations of the colostrum period. And mature breast milk respectively 81.38 ± 30.09 mcg/dL and 58.17 ± 17.48 mcg/dL.²⁰ Meanwhile, insignificant results were obtained in the LBW term infants group. This might happen because of many factors that affect vitamin A levels in breast milk, namely vitamin A intake, anthropometric status, socioeconomic status, and maternal education according to research from Dror and Allen.²¹

The findings of this study showed significantly higher levels of zinc and vitamin A in the colostrum of mothers who gave birth to preterm babies, this could be used as an education regarding colostrum nutrient levels and the importance of breastfeeding at the beginning of the lactation period as early as possible.

Conclusion

Iron levels in colostrum and mature breast milk changed insignificantly for both preterm and term infants with LBW, while zinc levels in colostrum are significantly higher than in mature breast milk both in mothers of LBW preterm and term infants. Levels of vitamin A in colostrum were significantly higher than in mature breast milk in mothers with LBW infants, however it was not applied in the group of mothers with LBW term infants.

Acknowledgement: The authors are very grateful for the support and help from the nurses, laboratory

analyst and also mothers who were willing to join this research.

Ethical Clearance: The identity of the subject was guaranteed confidentiality. This study was conducted after obtaining ethical clearance from the Ethics Committee of Dr. Soetomo General Hospital in Surabaya, Indonesia with certificate number 1213/KEPK/V/2019. Before the subject recruitment, the researchers had explained to the parents about the general research information and the consent.

Source of Funding – Self

Conflict of Interest – Nil

References

1. American Academy of Pediatrics Committee on Nutrition. Nutritional needs of low-birth-weight infants. *Pediatrics*. 1985;75(5):976-986.
2. Mohd-Taufek N, Cartwright D, Davies M, et al. The effect of pasteurization on trace elements in donor breast milk. *J Perinatol*. 2016;36(10):897-900. doi:10.1038/jp.2016.88
3. IDAI. *Konsensus Asuhan Nutrisi Pada Bayi Prematur*. 1st ed. (Kadim M, Roeslani RD, Nurmalia LD, eds.). Ikatan Dokter Anak Indonesia; 2016.
4. Chung MY. Factors affecting human milk composition. *Pediatr Neonatol*. 2014;55(6):421-422. doi:10.1016/j.pedneo.2014.06.003
5. EFSA. Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union. *EFSA J*. 2013;11(10). doi:10.2903/j.efsa.2013.3408
6. Saleem AF, Bhutta ZA. 3.2 Micronutrient Deficiencies in Children. In: *World Review of Nutrition and Dietetics*. Vol 113. S. Karger AG; 2015:147-151. doi:10.1159/000375276
7. Jyotsna S, Amit A, Kumar A. Study of serum zinc in low birth weight neonates and its relation with maternal zinc. *J Clin Diagnostic Res*. 2015;9(1):SC01-SC03. doi:10.7860/

JCDR/2015/10449.5402

8. Berglund S, Westrup B, Domellöf M. Iron supplements reduce the risk of iron deficiency anemia in marginally low birth weight infants. *Pediatrics*. 2010;126(4). doi:10.1542/peds.2009-3624
9. Kositamongkol S, Suthutvoravut U, Chongviriyaphan N, Feungpean B, Nuntnarunit P. Vitamin A and E status in very low birth weight infants. *J Perinatol*. 2011;31(7):471-476. doi:10.1038/jp.2010.155
10. Dizdar EA, Sari FN, Degirmencioglu H, et al. Effect of mode of delivery on macronutrient content of breast milk. *J Matern Neonatal Med*. 2014;27(11):1099-1102. doi:10.3109/14767058.2013.850486
11. Mangel L, Ovental A, Batscha N, Arnon M, Yarkoni I, Dollberg S. Higher fat content in breastmilk expressed manually: A randomized trial. *Breastfeed Med*. 2015;10(7):352-354. doi:10.1089/bfm.2015.0058
12. Kim SY, Yi DY. Components of human breast milk: from macronutrient to microbiome and microRNA. *Clin Exp Pediatr*. 2020;63(8):301-309. doi:10.3345/cep.2020.00059
13. Dahlan MS. *Besar Sampel Dan Cara Pengambilan Sampel Dalam Penelitian Kedokteran Dan Kesehatan*. 3rd ed. Salemba Medika; 2013.
14. C, kalsum V, Majiding CM, Rahman TAA, Kurniati Y. Mineral Concentrations in Breast Milk across Infant Birth Weight. *Pakistan J Nutr*. 2019;19(1):32-37. doi:10.3923/pjn.2020.32.37
15. Lawlor DA, Mortensen L, Andersen AMN. Mechanisms underlying the associations of maternal age with adverse perinatal outcomes: A sibling study of 264 695 danish women and their firstborn offspring. *Int J Epidemiol*. 2011;40(5):1205-1214. doi:10.1093/ije/dyr084
16. Lönnerdal B. Nutritional and physiologic significance of human milk proteins. *Am J Clin Nutr*. 2003;77(6). doi:10.1093/ajcn/77.6.1537s
17. Sabatier M, Garcia-Rodenas CL, De Castro CA, et al. Longitudinal changes of mineral concentrations in preterm and term human milk from lactating swiss women. *Nutrients*. 2019;11(8). doi:10.3390/nu11081855
18. Yang T, Zhang L, Bao W, Rong S. Nutritional composition of breast milk in Chinese women: A systematic review. *Asia Pac J Clin Nutr*. 2018;27(3):491-502. doi:10.6133/apjcn.042017.13
19. Erick M. Breast milk is conditionally perfect. *Med Hypotheses*. 2018;111:82-89. doi:10.1016/j.mehy.2017.12.020
20. Lima MSR, da Silva Ribeiro KD, Pires JF, et al. Breast milk retinol concentration in mothers of preterm newborns. *Early Hum Dev*. 2017;106-107:41-45. doi:10.1016/j.earlhumdev.2017.01.006
21. Dror DK, Allen LH. Retinol-to-fat ratio and retinol concentration in humanmilk show similar time trends and associations with maternal factors at the population level: A systematic review and meta-analysis. *Adv Nutr*. 2018;9(suppl_1):332S-346S. doi:10.1093/advances/nmy021