

7. Kannan L, Lodha R, Vivekanandhan S, Bagga A, Kabra SK, Kabra M. Intravenous fluid regimen and hyponatraemia among children: A randomized controlled trial. *Pediatr Nephrol.* 2010;25:2303-9.
8. Neville KA, Sandeman DJ, Rubinstein A, Henry GM, McGlynn M, Walker JL. Prevention of hyponatremia during maintenance intravenous fluid administration: A prospective randomized study of fluid type versus fluid rate. *J Pediatr.* 2010;156:313-9.
9. Arikan AA, Zappitelli M, Goldstein SL, Naipaul A, Jefferson LS, Loftis LL. Fluid overload is associated with impaired oxygenation and morbidity in critically ill children. *Pediatr Crit Care Med J.* 2012;13:253-8.
10. Shamin A, Afzal K, Ali SM. Safety and efficacy of isotonic (0.9%) vs. hypotonic (0.18%) saline as maintenance intravenous fluids in children: A randomized controlled trial. *Indian Pediatr.* 2014;51:969-74.
11. National Patient Safety Agency. Reducing the risk of hyponatraemia when administering intravenous infusions to children. 28 March 2007. Available from: <http://www.nrls.npsa.nhs.uk/resources/?entryid45=59809>. Accessed November 7, 20014.

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## Changes in Preterm Breast Milk Composition with Advancing Infant Age

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**B**reast milk has a dynamic and a variable composition during a single feed, diurnally, and differs in composition according to gestation, chronological age of the infant, and health status of the mother. The timing of expression of milk and storage can also alter this composition [1]. The difference between preterm and term milk has been studied in great detail by researchers; a few studies have focused on the changes that occur in these two kinds of milk over a longitudinal period of time. A recent systematic review of these studies did not find any study on preterm milk composition beyond two months of chronological age [2]. The pilot study by Dutta, *et al.* [3], in this issue of *Indian Pediatrics*, explores an important area that has not been evaluated well in previous studies, i.e. change in composition of breast milk as the chronologic age advances and the other feeds are added. The study provides some more information regarding composition at 90 and 180 days [3]. The duration of exclusive breastfeeding in preterm infants is likely to be foreshortened due to delay in initiation of breastfeeding, intensive care in neonatal period and prolonged hospitalization. These infants are more likely to have complementary feeding introduced before 6 months of corrected age and hence are likely to be bereft of benefits of exclusive breastfeeding. In this study, analysis of serial breast milk samples reveals that as the chronologic age advances, there is an increase in the triglyceride and sodium levels and progressive decline in the protein content. However, to suggest that there is a possible cause-effect relationship in sodium and triglycerides between exclusive breastfeeding mothers

compared to those who have introduced mixed feeding is a speculation, because of low numbers and some methodology related issues. Limitations of the study include sample collection time as fat content beyond three minutes is expected to be more, and with increasing age the lipid concentration in the initial milk is higher due to efficient breast emptying. The information related to milk volume and other components of milk such as trace elements, bioactive proteins, or anti-inflammatory substances have not been collected. Future studies would benefit from tracking caloric intake of infants, breastfeeding frequency in mothers, and anthropometric data of infants. These parameters would inform us about infant health and other important modifiers in addition to changes in breast milk composition over a period of time. Authors speculate on the pathophysiology behind differences in composition as the chronologic age advances, such as involution of mammary gland or changes in the cellular permeability. Although this is possible theoretically, one cannot make a strong case for these physiologic attributes, unless there are data on milk volumes, secretory rates, and the concentration of components measured and analyzed using regression analysis. Human milk is species-specific and it is uniquely superior for infant feeding [4]. This basic understanding raises the question whether the compositional changes that occur over time are nature's way of adapting the milk constituents to suit the infant needs. The compositional changes in term infants during weaning have been reported earlier in other studies [5-7], but the pathophysiologic mechanisms that lead to these changes have not been

explored well. Various biologically active proteins such as secretory immuno-globulin A, lysozyme, lactoferrin, adiponectin, and beta endorphin with the exception of leptin are seen in higher amounts in preterm milk in the first month as compared to term neonates [8]. Whether this composition gives the preterm a better chance for combating infection, can only be speculated but it will be interesting to detect levels of these components in the first six months of life. Understanding of RNA, DNA, gene expression of epithelial cells from breast milk (including genes for cytokines, and other interleukins), and genome wide evaluations would give better understanding of reasons behind differences in composition. Breast milk is a rich source of maternal genetic information. RNA and DNA from breast milk is an appropriate source for conducting gene expression or epigenetic study [9]. Scientists interested in research in this area would be well served by forming a coalition to conduct studies across communities with a centralized laboratory given the task of analyzing bioactive components as well as genomic data.

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#### REFERENCES

1. Ballard O, Morrow AL. Human milk composition: Nutrients and bioactive factors. *Pediatr Clin North Am.* 2013;60:49-74.
2. Gidrewicz DA, Fenton TR. A systematic review and meta-analysis of the nutrient content of preterm and term breast milk. *BMC Pediatr.* 2014;14:216.
3. Dutta S, Saini S, Prasad R. Changes in preterm human milk composition with particular reference to introduction of mixed feeding. *Indian Pediatr.* 2014;51:997-9.
4. Underwood MA. Human milk for the premature infant. *Pediatr Clin North Am.* 2013;60:189-207.
5. Neville MC, Allen JC, Archer PC, Casey CE, Seacat J, Keller RP, *et al.* Studies in human lactation: Milk volume and nutrient composition during weaning and lactogenesis. *Am J Clin Nutr.* 1991;54:81-92.
6. Allen JC, Keller RP, Archer P, Neville MC. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr.* 1991;54:69-80.
7. Garza C, Johnson CA, Smith EO, Nichols BL. Changes in the nutrient composition of human milk during gradual weaning. *Am J Clin Nutr.* 1983;37:61-5.
8. Mehta R, Petrova A. Biologically active breast milk proteins in association with very preterm delivery and stage of lactation. *J Perinatol.* 2011;31:58-62.
9. Baumgartel KL, Conley YP. The utility of breastmilk for genetic or genomic studies: A systematic review. *Breastfeeding Med.* 2013;8:249-56.