Srivastava, Anu, and Swati Jain. 2023. "Appetite Self-Regulation in Infancy - The Role of Direct Breastfeeding." *World Nutrition*, March, 22–27. https://doi.org/10.26596/wn.202314122-27.

Literature Review

Appetite self-regulation in infancy - The role of direct breastfeeding

Anu Shrivastava, Swati Jain[1a]

[1] Department of Food and Nutrition, Lady Irwin College, University of Delhi, India

Keywords: appetite, appetite regulation, infant obesity, breastfeeding, bottle feeding, nutritive sucking, non-nutritive sucking

https://doi.org/10.26596/wn.202314122-27

World Nutrition 2023;14(1):22-27

Infant feeding practices have a vital role to play in shaping the eating behaviour and overall health of individuals in both childhood as well as adulthood. A lesser-known advantage of breastfeeding in the global obesogenic environment, is its role in self-regulation of an infant's appetite. Research demonstrates that children fed exclusively from the breast (that is, they are never bottle fed) develop the capacity for self-regulation of breastmilk intake – after all, mothers cannot possibly observe the quantity of milk the infant ingests. This encourages the infant to gain control, thus avoiding any overconsumption. On the other hand, bottle fed infants (whether mother's milk or formula milk) are subjected to mother's or other caregivers encouragement of bottle emptying. Since the regulation largely lies externally with the parent/caregiver on scheduled or timed feeding versus a cue feeding, this állows the possibility of such children being prevented from developing their own appetite responsiveness independently. Studies do find differences in satiety responses of children fed human milk with a bottle and those who were directly breastfed. Research has shown that directly breast-fed infants do not consume extra milk once their appetite stimulation phase ends. However, the teaching of bottle emptying during early infancy is positively associated with the weight gain. Such distinctions clearly emphasize the importance of breast feeding, but whether it is the milk composition (human or formula) or the mode of feeding (directly from breast or using bottle) that plays a bigger role in signalling appetite control warrants further examination. Considering that an infant's weight gain or growth has a multifactorial causation, this review will highlight the association of direct breastfeeding with appetite signalling in infancy.

INTRODUCTION

Self-regulation consists of automatic (bottom-up) and deliberate (top-down) processes focused on adjustment of one's mental and physiological state, thereby altering emotion, cognition, or behaviour adaptively to context. However, inclusion of homeostatic processes in self-regulation remains debatable (Nigg 2017). Appetite regulation involves homeostatic and hedonic mechanisms through interactions between the brain, gut and the adipose tissue (Russell and Russell 2021). Its biological elements include nutrient sensing and availability, long-term energy reserves, food and taste preferences, metabolic requirements, genetic predispositions, neurocognitive and neuroendocrinological processes, along with the homeostatic processes responsible for energy balance through regulation of intake and expenditures. All of this influences the development of appetite self-regulation (ASR) in children. Both homeostatic and non-homeostatic factors interact. Breastfed infants appear to have a unique ability to self-regulate both the breast milk intake and energy intake from solid foods (Agostoni 2005).

ASR can be conceptualised in terms of a "Satiety cascade" consisting of three phases: (1) pre-consumption, involving hunger cues, food choices and food cue responsiveness; (2) during consumption, involving satiation and habituation; and (3) post-consumption, that includes central and peripheral post-ingestive and post-absorptive mechanisms influencing satiety and satiety cues. Both satiation and satiety are significant processes involved in regulation of appetite. Russell and Russell (2021), have presented six components of ASR: (1) eating when not hungry, (2) delay of gratification, (3) responsiveness to food cues, (4) calorie compensation, and (5) fussy eating (6) dysregulated eating. Similar to general self-regulation (GSR), development of ASR also involves both automatic and deliberate avoidance processes. ASR development across childhood exhibits large inter-individual differences and

a Corresponding author: swati.jain@lic.du.ac.in

seems to decline particularly with respect to regulation of food approach responses, in contrast to GSR which is retained (Russell and Russell 2021). Some children continue to be picky eaters into middle childhood which suggests that they struggle to control their bottom-up avoidance reactions to some foods while some children are able to self-regulate their eating (Francis and Riggs 2018).

Research demonstrates that children fed exclusively from the breast develop the capability for self-regulation of breastmilk intake, as mothers possibly cannot observe the amount of milk the infant consumes (DiSantis et al. 2011). Breastfed babies have demonstrated short-term and long-term control over their appetite. Images of breast milk ejection of nursing mothers have shown that infants stop ingesting more milk despite the availability of additional milk, as shown by multiple milk ejections after a breastfeeding session. It has been found that only 67% of the available breastmilk is ingested by an infant while feeding from the breast, suggesting that babies do not consume extra milk once the stimulation phase of their appetite cascade ends (Dewey and Lönnerdal 1986; Kent et al. 2006).

In contrast to artificially-fed babies, breast fed babies must expend effort suckling on the breast to initiate the Milk Ejection Reflex (MER) (Nommsen et al. 1991; Pérez-Escamilla et al. 1995). Breastfeeding and bottle feeding, when they have nutritional benefits for the child, are categorised as nutritive sucking. Non-nutritive sucking occurs on the breast and provides comfort to the child. For bottle-feeding infants, this is more likely to take place via thumb sucking or the use of pacifiers (Ling et al. 2018).

There is not much milk available until the MER occurs and therefore in a sense, at first the infant needs to suck non nutritively at the breast (Mepham 1983; Alekseev, Omelianuk, and Talalaeva 2000; Ramsay et al. 2004). On being attached to the breast, infants demonstrate short, rapid bursts of sucking (Inch and Garforth 1989) and this pattern of sucking changes to a long, slow, continuous pattern after the milk begins to flow. On the contrary, with bottle-feeding, an infant obtains milk flow as soon as the teat is inserted into the mouth. Wolff (1968) demonstrated that infants possess a quick ability to switch from NNS to NS and found that sucking frequency was 120 sucks/min during NNS and 60 sucks/min during NS. In addition, the amplitude of sucking in NNS was lower than in NS. Mizuno and Ueda (2006) discovered that, while the suck cycle had the same duration for breast and bottle-feeding during the NNS phase, during the NS period, the duration was shorter and the frequency was higher for breast-feeding. This is likely due to the artificial teat's more rapid milk flow. During NS the sucking pressure was not found to be significantly different between bottle and breast feeding. However, sucking duration is significantly shorter during the NS period for both.

In conclusion, infant sucking behaviour both while breastfeeding and when given a bottle, changed after the milk entered the mouth. Despite industry efforts to create a resemblance between feeding directly from the breast and using a bottle, it is quite clear from the research studies that bottle-feeding is a totally different feeding technique.

APPETITE REGULATING SUBSTANCES IN BREASTMILK

Protein, fatty acids, oligosaccharides and hormones in breast milk can impact infant feeding behaviour (Ballard and Morrow 2013) due to differences in physiologic signalling between the infants fed breastmilk and formula milk (human milk substitute, HMS). Breast milk contains foremilk and hind milk that differ in fat concentration. It is speculated that since hind milk is higher in fat content it might initiate the termination of the feeding session (Karatas et al. 2011). Conversely, the contents in HMS remain the same throughout the feeding episode. Even though mature human milk has a lower protein content than cow's milk and HMS (Franke, Bruhn, and Lawrence 1988; Agostoni 2005), yet it is sufficient for the optimal growth requirements of the infants. The higher protein content of HMS, though it may result in faster growth, may cause adiposity (Taylor et al. 2005). Further, owing to a higher casein-whey ratio, HMS has a slower rate of gastric emptying than breast milk (Van Den Driessche et al. 1999). Many authors have also reported differences in the plasma amino acid pattern between the two groups. The higher plasma levels of the three branched-chain amino acids (leucine, isoleucine and valine) in bottle-fed infants have been associated with increased levels of insulin in plasma and C-reactive peptides in urine, possibly explaining the pro-anabolic effect of the high protein supply (Agostoni 2005).

APPETITE REGULATING HORMONES IN BREASTMILK

Aside from the fat content of human milk, some hormones in human milk have roles in energy metabolism, appetite, and food intake. Indeed, breastmilk is a source of several bioactive compounds that are responsible for metabolic balance (Savino et al. 2011). It contains substances that are appetite regulatory hormones in adults, including leptin, ghrelin, adiponectin, resistin, cystokinin, and others (Agostoni 2005; Mazzocchi et al. 2019). The serum profile of appetite regulatory hormones in infants is not only different depending on milk type but also by the mother's serum concentrations of these hormones. There is a complex interplay of signals and hormones regulated by ghrelin that lead to differences in the neurometabolic pattern of breastfed and formula fed infants and thereby their growth curves. In addition, it is not only the gastrointestinal organs but an existence of unequivocal involvement of adipose tissue and brain (Agostoni 2005).

Vásquez-Garibay et al. (2019) showed that appetite-regulating hormones are significantly and directly correlated in mother-infant dyads that practiced exclusive breastfeeding, but not in those who received HMS. In addition, breastfed infants had higher levels of GLP-1 and peptide YY as compared to infants fed HMS. Also, there are significantly higher leptin levels in mothers belonging to the HMS group compared to breastfed group, which may be due to higher adiposity typically seen in the HMS group. Further, leptin levels are higher and hunger hormone, ghrelin and IGF-1 levels are lower in breastfed infants when compared to HMS-fed infants (Savino et al. 2005). In the first few months after birth, the serum levels of the orexigenic hormone, ghrelin, is higher in HMS-fed infants than in breast fed infants, leading to a higher appetite (Savino et al. 2011).

A network or linkage extends between the gastrointestinal organs to adipose tissue and brain, denoting the complex nature of appetite regulation. Recent research has shown that adiponectin and IGF-1 have positive correlations with weight gain and BMI in infants; however, this warrants further research (Weyermann, Brenner, and Rothenbacher 2007; Savino et al. 2005). The level of adiponectin in breast milk has been found to be higher than other hormones and has shown a significant role in regulation of weight gain in new-borns even going forward in their early years of life (Woo et al. 2012). Obestatin present in breastmilk could also be associated with less overfeeding and suppression of the new-borns' appetite (Aydin et al. 2008).

Ghrelin is another hormone found in human milk. It is produced in the gastrointestinal tract and acts on the central nervous system to regulate appetite and weight. The presence of ghrelin in human milk was first described by Aydin et al. (2006). A portion of ghrelin has a unique fatty acid modification (n-octanoylation) at Ser 3. Of the two forms of ghrelin, acylated and deacylated ghrelin, the acylated form (known as active ghrelin) is thought to be essential for binding to the growth hormone secretagogue receptor 1a. Deacylated ghrelin, however, is not totally inactive. It has influences on both cell proliferation and adipogenesis and counteracts the metabolic effects of active ghrelin. The total ghrelin level is the sum of the acylated and deacylated ghrelin levels.

Reduced levels of both total and active ghrelin in the hindmilk may cause satiety, reduce appetite, and indicate the completion of breastfeeding (Karatas et al. 2011). The cause of this decrease in breast milk during feeding is unclear. According to several researchers, a glucose infusion and higher-than-normal fat levels reduce ghrelin levels. Low levels of total ghrelin, which employs HDL-C as a transporter, are caused by low levels of high-density lipoprotein cholesterol (HDL-C), which coincides with low levels of total cholesterol, according to one theory (Karatas et al. 2011). Recent studies have shown that the mother's breast tissue or maternal plasma are two potential sources of ghrelin in human milk

Leptin is a signalling protein that informs the brain about body fat stores and, at the hypothalamic level, is a hormone that increases the metabolic rate and decreases appetite. Leptin may be produced by different cell types in mammary tissue. In addition to leptin synthesis, mammary tissue epithelial cells may transfer leptin from the blood, and these two mechanisms may account for the presence of leptin in milk. Even if ghrelin were added to HMS, it would be at constant levels during feeding and thus might not affect appetite control. Similarly, like fat, leptin concentrations in HMS would be stable during feeding. Gastric leptin is involved in the short-term regulation of digestion; in contrast, the leptin that is secreted by white adipocytes primarily acts on the hypothalamus for the long-term regulation of food intake (Karatas et al. 2011). Savino et al. (2005) have reported higher leptin and lower ghrelin and IGF-1 levels in infants being breastfed than in HMS-fed infants.

Studies have demonstrated that breast milk and formula milk also elicit different responses with respect to insulin secretion, adipose tissue deposition and inflammation (Ailhaud and Guesnet 2004; Bergeron et al. 2007; Ailhaud et al. 2006). Gastric emptying (GE) influences satiety, so the human milk components that influence emptying such as adiponectin, whey protein, casein:whey ratio, lactose, total CHO and oligosaccharides potentially influence milk intake thereby impacting growth and development in the early phase of life. In breastfed infants, appetite regulating hormones, macronutrients along with feed volume influences GE and feeding patterns. Breast milk components such as adiponectin, whey protein, casein:whey ratio influence GE; wherein feed volume tends to determine effect of casein:whey ratio and lactose concentrations on GE such that, faster GE rate results from larger feed volumes. Hence, both feed volume as well as the composition of the milk play a significant role in appetite regulation through their effect on gastric function (Gridneva et al. 2016).

Infants who are breastfed exhibit different feeding behaviours than those who are bottle-fed, in part because breastfed babies are more likely to start and stop feeding sessions (Crow, Fawcett, and Wright 1980). This impact prompts the essential question of how much infants who freely suckled at the breast differ from infants who were fed formula in terms of their intake of macronutrients (Lucas, Lucas, and Baum 1980). Infants who freely suckled at the breast appear to self-regulate intake. Breast milk contains a high number of proteins, cytokines, growth factors and potentially bioactive hormones, which give rise to changes that go far beyond those caused by the macronutrient composition (Gale et al. 2012). In addition, the CHILD study researchers show that consuming only breast milk reduces the risk of obesity the most. Bottles of expressed human milk added to direct breastfeeding reduce the protective effects of breastfeeding (Holmes 2018).

CONCLUSIONS

This review reinforces the need for formulation of infant feeding guidelines addressing the behavioural factors linked with exclusive breastfeeding, emphasising on infant led feeding with minimal influence of the caregiver and avoidance of pressurising feeding styles. Also, novel strategies are needed for effective early life interventions and to improve maternal feeding practices (such as type of bottle while bottle feeding infants) in order to reduce the global paediatric obesity pandemic and promote well-being (Azad et al. 2018; DiSantis et al. 2011; Ventura and Pollack Golen 2015). Further, longitudinal studies in natural settings are required to study the impact of the caregiver's behaviour in the formation of food preferences and anthropometric measures of the infant in later life. Precise causal mechanisms associated with feeding practices and obesity risk need to be explored (Azad et al. 2018).

The present review summarised the multitude of effects on infant's appetite self-regulation caused by a myriad of factors like the feeding style, composition of milk and maternal control. Thus, in addition to choosing the method of feeding perhaps mothers should also start paying close attention to the infant initiated bottle emptying feeding behaviour. Given children are living largely in a global obesogenic environment and it is known that individuals suffering from obesity in their childhood tend to become obese adults, this could play a minor yet significant role in reducing the paediatric obesity epidemic.

Submitted: September 21, 2022 BRT, Accepted: January 17, 2023 BRT

REFERENCES

Agostoni, Carlo. 2005. "Ghrelin, Leptin and the Neurometabolic Axis of Breastfed and Formula-Fed Infants." *Acta Paediatrica* 94 (5): 523–25. https://doi.org/10.1111/j.1651-2227.2005.tb01931.x.

Ailhaud, G., and P. Guesnet. 2004. "Fatty Acid Composition of Fats Is an Early Determinant of Childhood Obesity: A Short Review and an Opinion." *Obesity Reviews* 5 (1): 21–26. https://doi.org/10.1111/j.1467-789x.2004.00121.x.

Ailhaud, G., F. Massiera, P. Weill, P. Legrand, J. Alessandri, and P. Guesnet. 2006. "Temporal Changes in Dietary Fats: Role of N−6 Polyunsaturated Fatty Acids in Excessive Adipose Tissue Development and Relationship to Obesity." *Progress in Lipid Research* 45 (3): 203–36. https://doi.org/10.1016/j.plipres.2006.01.003.

Alekseev, N.P., E.V. Omelianuk, and N.E. Talalaeva. 2000. "Dynamics of Milk Ejection Reflex during Continuous Rhythmic Stimulation of the Areola-Nipple Complex of the Mammary Gland." *Ross Fiziol Zh Im I M Sechenoval* 86: 711–19.

Aydin, Suleyman, Suna Aydin, Yusuf Ozkan, and Selahattin Kumru. 2006. "Ghrelin Is Present in Human Colostrum, Transitional and Mature Milk." *Peptides* 27 (4): 878–82. https://doi.org/10.1016/j.peptides.2005.08.006.

Aydin, Suleyman, Yusuf Ozkan, Fazilet Erman, Bilgin Gurates, Nermin Kilic, Ramis Colak, Tugba Gundogan, et al. 2008. "Presence of Obestatin in Breast Milk: Relationship among Obestatin, Ghrelin, and Leptin in Lactating Women." *Nutrition* 24 (7–8): 689–93. https://doi.org/10.1016/j.nut.2008.03.020.

Azad, Meghan B., Lorena Vehling, Deborah Chan, Annika Klopp, Nathan C. Nickel, Jonathan M. McGavock, Allan B. Becker, et al. 2018. "Infant Feeding and Weight Gain: Separating Breast Milk from Breastfeeding and Formula from Food." *Pediatrics* 142 (4): 20181092. https://doi.org/10.1542/peds.2018-1092.

Ballard, Olivia, and Ardythe L. Morrow. 2013. "Human Milk Composition: Nutrients and Bioactive Factors." *Pediatric Clinics of North America* 60 (1): 49–74. https://doi.org/10.1016/j.pcl.2012.10.002.

Bergeron, Karen, Pierre Julien, Teresa A. Davis, Alexandre Myre, and M. Carole Thivierge. 2007. "Long-Chain n-3 Fatty Acids Enhance Neonatal Insulin-Regulated Protein Metabolism in Piglets by Differentially Altering Muscle Lipid Composition." *Journal of Lipid Research* 48 (11): 2396–2410. https://doi.org/10.1194/jlr.m700166-jlr200.

Crow, R. A., J. N. Fawcett, and P. Wright. 1980. "Maternal Behavior during Breast- and Bottle-Feeding." *Journal of Behavioral Medicine* 3 (3): 259–77. https://doi.org/10.1007/bf00845051.

Dewey, K. G., and B. Lönnerdal. 1986. "Infant Self-Regulation of Breast Milk Intake." *Acta Paediatrica Scandinavica* 75 (6): 893–98. https://doi.org/10.1111/j.1651-2227.1986.tb10313.x.

DiSantis, Katherine Isselmann, Bradley N. Collins, Jennifer O. Fisher, and Adam Davey. 2011. "Do Infants Fed Directly from the Breast Have Improved Appetite Regulation and Slower Growth during Early Childhood Compared with Infants Fed from a Bottle?" *International Journal of Behavioral Nutrition and Physical Activity* 8 (1): 89. https://doi.org/10.1186/1479-5868-8-89.

Francis, Lori A., and Nathaniel R. Riggs. 2018. "Executive Function and Self-Regulatory Influences on Children's Eating." In *Pediatric Food Preferences and Eating Behaviors*, edited by J. Lumeng JCF, 183–206. London: Academic Press. https://doi.org/10.1016/b978-0-12-811716-3.00010-5.

Franke, Antoine A., John C. Bruhn, and Charles M. Lawrence. 1988. "Distribution of Protein in California Milk in 1983." *Journal of Dairy Science* 71 (9): 2373–83. https://doi.org/10.3168/jds.s0022-0302(88)79821-5.

Gale, Chris, Karen M Logan, Shalini Santhakumaran, James RC Parkinson, Matthew J Hyde, and Neena Modi. 2012. "Effect of Breastfeeding Compared with Formula Feeding on Infant Body Composition: A Systematic Review and Meta-Analysis." *The American Journal of Clinical Nutrition* 95 (3): 656–69. https://doi.org/10.3945/ajcn.111.027284.

Gridneva, Zoya, Sambavi Kugananthan, Anna Hepworth, Wan Tie, Ching Lai, Leigh Ward, Peter Hartmann, and Donna Geddes. 2016. "Effect of Human Milk Appetite Hormones, Macronutrients, and Infant Characteristics on Gastric Emptying and Breastfeeding Patterns of Term Fully Breastfed Infants." *Nutrients* 9 (1): 15. https://doi.org/10.3390/nu9010015.

Holmes, Alison Volpe. 2018. "Is Breast Still Best From a Bottle?" *Pediatrics* 142 (4). https://doi.org/10.1542/peds.2018-2297.

Inch, S., and S. Garforth. 1989. "Establishing and Maintaining Breastfeeding." In *Effective Care in Pregnancy*, edited by I. Chalmers, M. Enkin, and M. Keirse.

Karatas, Zehra, Sultan Durmus Aydogdu, Ener Cagri Dinleyici, Omer Colak, and Nesrin Dogruel. 2011. "Breastmilk Ghrelin, Leptin, and Fat Levels Changing Foremilk to Hindmilk: Is That Important for Self-Control of Feeding?" *European Journal of Pediatrics* 170 (10): 1273–80. https://doi.org/10.1007/s00431-011-1438-1.

Kent, Jacqueline C., Leon R. Mitoulas, Mark D. Cregan, Donna T. Ramsay, Dorota A. Doherty, and Peter E. Hartmann. 2006. "Volume and Frequency of Breastfeedings and Fat Content of Breast Milk throughout the Day." *Pediatrics* 117 (3): e387–95. https://doi.org/10.1542/peds.2005-1417.

Ling, Hiu Tung Bonnie, Fung Hou Kumoi Mineaki Howard Sum, Linkun Zhang, Cindy Po Wan Yeung, Kar Yan Li, Hai Ming Wong, and Yanqi Yang. 2018. "The Association between Nutritive, Non-Nutritive Sucking Habits and Primary Dental Occlusion." *BMC Oral Health* 18 (1): 145. https://doi.org/10.1186/s12903-018-0610-7.

Lucas, Alan, Penny J. Lucas, and J.David Baum. 1980. "The Nipple-Shield Sampling System: A Device for Measuring the Dietary Intake of Breast-Fed Infants." *Early Human Development* 4 (4): 365–72. https://doi.org/10.1016/0378-3782(80)90041-9.

Mazzocchi, Alessandra, Maria Lorella Giannì, Daniela Morniroli, Ludovica Leone, Paola Roggero, Carlo Agostoni, Valentina De Cosmi, and Fabio Mosca. 2019. "Hormones in Breast Milk and Effect on Infants' Growth: A Systematic Review." *Nutrients* 11 (8): 1845. https://doi.org/10.3390/nu11081845.

Mepham, T.B. 1983. "Physiological Aspects of Lactation." In *Biochemistry of Lactation*, edited by T.B. Mepham, 5. New York: Elsevier.

Mizuno, Katsumi, and Aki Ueda. 2006. "Changes in Sucking Performance from Nonnutritive Sucking to Nutritive Sucking during Breast- and Bottle-Feeding." *Pediatric Research* 59 (5): 728–31. https://doi.org/10.1203/01.pdr.0000214993.82214.1c.

Nigg, Joel T. 2017. "Annual Research Review: On the Relations among Self-Regulation, Self-Control, Executive Functioning, Effortful Control, Cognitive Control, Impulsivity, Risk-Taking, and Inhibition for Developmental Psychopathology." *Journal of Child Psychology and Psychiatry* 58 (4): 361–83. https://doi.org/10.1111/jcpp.12675.

Nommsen, L.A., C.A. Lovelady, M.J. Heinig, B. Lönnerdal, and K.G. Dewey. 1991. "Determinants of Energy, Protein, Lipid, and Lactose Concentrations in Human Milk during the First 12 Months of Lactation: The DARLING Study." *American Journal of Clinical Nutrition* 53 (2): 457–65. https://doi.org/10.1093/ajcn/53.2.457.

Pérez-Escamilla, R., R.J. Cohen, K.H. Brown, L.L. Rivera, J. Canahuati, and K.G. Dewey. 1995. "Maternal Anthropometric Status and Lactation Performance in a Low-Income Honduran Population: Evidence for the Role of Infants." *American Journal of Clinical Nutrition* 61 (3): 528–34. https://doi.org/10.1093/ajcn/61.3.528.

Ramsay, Donna T., Jacqueline C. Kent, Robyn A. Owens, and Peter E. Hartmann. 2004. "Ultrasound Imaging of Milk Ejection in the Breast of Lactating Women." *Pediatrics* 113 (2): 361–67. https://doi.org/10.1542/peds.113.2.361.

Russell, Alan, and Catherine G. Russell. 2021. "Appetite Self-Regulation Declines across Childhood While General Self-Regulation Improves: A Narrative Review of the Origins and Development of Appetite Self-Regulation." *Appetite* 162: 105178. https://doi.org/10.1016/j.appet.2021.105178.

Savino, Francesco, Maria F Fissore, Erica C Grassino, Giuliana E Nanni, Roberto Oggero, and Leandra Silvestro. 2005. "Ghrelin, Leptin and IGF-I Levels in Breast-Fed and Formula-Fed Infants in the First Years of Life." *Acta Paediatrica* 94 (5): 531–37. https://doi.org/10.1111/j.1651-2227.2005.tb01934.x.

Savino, Francesco, Stefania Alfonsina Liguori, Miriam Sorrenti, Maria Francesca Fissore, and Roberto Oggero. 2011. "Breast Milk Hormones and Regulation of Glucose Homeostasis." *International Journal of Pediatrics* 2011: 803985. https://doi.org/10.1155/2011/803985.

Taylor, Rachael W, Andrea M Grant, Ailsa Goulding, and Sheila M Williams. 2005. "Early Adiposity Rebound: Review of Papers Linking This to Subsequent Obesity in Children and Adults." *Current Opinion in Clinical Nutrition and Metabolic Care* 8 (6): 607–12. https://doi.org/10.1097/01.mco.0000168391.60884.93.

Van Den Driessche, Mieke, Kristel Peeters, Paul Marien, Yvo Ghoos, Hugo Devlieger, and Gigi Veereman-Wauters. 1999. "Gastric Emptying in Formula-Fed and Breast-Fed Infants Measured with the 13C-Octanoic Acid Breath Test." *Journal of Pediatric Gastroenterology & Nutrition* 29 (1): 46–51. https://doi.org/10.1097/00005176-199907000-00013.

Vásquez-Garibay, Edgar M., Alfredo Larrosa-Haro, Elizabeth Guzmán-Mercado, Nelly Muñoz-Esparza, Samuel García-Arellano, Francisco Muñoz-Valle, and Enrique Romero-Velarde. 2019. "Serum Concentration of Appetite-Regulating Hormones of Mother–Infant Dyad According to the Type of Feeding." *Food Science & Nutrition* 7 (2): 869–74. https://doi.org/10.1002/fsn3.938.

Ventura, Alison K., and Rebecca Pollack Golen. 2015. "A Pilot Study Comparing Opaque, Weighted Bottles with Conventional, Clear Bottles for Infant Feeding." *Appetite* 85: 178–84. https://doi.org/10.1016/j.appet.2014.11.028.

Weyermann, Maria, Hermann Brenner, and Dietrich Rothenbacher. 2007. "Adipokines in Human Milk and Risk of Overweight in Early Childhood: A Prospective Cohort Study." *Epidemiology* 18 (6): 722–29. https://doi.org/10.1097/ede.0b013e3181567ed4.

Wolff, Peter H. 1968. "The Serial Organization of Sucking in the Young Infant." *Pediatrics* 42 (6): 943–56. https://doi.org/10.1542/peds.42.6.943.

Woo, Jessica G., M. Lourdes Guerrero, Fukun Guo, Lisa J. Martin, Barbara S. Davidson, Hilda Ortega, Guillermo M. Ruiz-Palacios, and Ardythe L. Morrow. 2012. "Human Milk Adiponectin Affects Infant Weight Trajectory during the Second Year of Life." *Journal of Pediatric Gastroenterology & Nutrition* 54 (4): 532–39. https://doi.org/10.1097/mpg.0b013e31823fde04.