

In light of recent discoveries: Breastfeeding is more than nutrition for term and preterm babies

Gözdem Kaykı¹✉, Şule Yiğit¹✉

¹Division of Neonatology, Department of Pediatrics, Hacettepe University, Ankara, Türkiye.

Human milk is universally recognized as the ideal source of nutrition for infants in their early stages of development. Its safety, accessibility, constant readiness, optimal temperature, and affordability contribute to its exceptional status. The American Academy of Pediatrics (AAP) and the World Health Organization (WHO) recommend exclusive breastfeeding for around six months post-birth, followed by continued breastfeeding with complementary foods until two years of age.¹ Moreover, breastfeeding provides not only vital nutrition for the baby but also plays a role in fostering a strong bond between parent and child. In spite of these recommendations, the exclusive breastfeeding rate through 6 months has been shown to be 37% in low-and middle-income countries and lower than 20% in most high-income countries.² In this regard, as a reminder of the importance of breastfeeding, we aimed to highlight some important points based on recent insights. These insights underscore the lifelong health effects of breast milk, showing its influence on the microbiome and immune development through its prebiotic contents, stem cells, and other bioactive components.

Known advantages and distinct effects on preterm infants

Breastfeeding offers a range of protective benefits, leading to reduced incidences of infections, obesity, diabetes mellitus, inflammatory bowel disease, childhood

leukemia, asthma, atopic dermatitis, dental caries, malocclusion and postneonatal mortality.^{1,2} Furthermore, breastfeeding has been associated with higher levels of intelligence in children.²⁻⁵

Notably, for very low birth weight infants, the provision of mother's expressed milk has been linked to a decreased occurrence of necrotizing enterocolitis (NEC), late-onset sepsis, chronic lung disease, and retinopathy of prematurity.^{1,6} It also shortens hospital stays and rehospitalization rates, and facilitates complete enteral feeding.

New insights

Breastmilk has unique contents with anti-inflammatory, antimicrobial, immunoregulatory agents, as well as live leukocytes and their effect on the developing immune system of the child.¹ Exploration into the human milk microbiome commenced as early as 2003,⁷ uncovering a multitude of bacteria that contribute to the infant's intestinal microbiome.^{7,8} This colonization process plays a pivotal role in fostering appropriate immune system development and functionality in infants.

Moreover, human milk oligosaccharides, which are composed of five fundamental monosaccharides (glucose, galactose, N-acetylglucosamine, fucose, and sialic acid), operate as prebiotics, antiadhesive antimicrobials, modulators of intestinal epithelial cell responses, and immune modulators.⁵

In addition to that, human milk contains extracellular vesicles (EVs), which are particles

✉ Gözdem Kaykı
gozdemkayki@hotmail.com

Received 11th October 2023, revised 30th November 2023,
accepted 26th December 2023

released from cells to transmit intracellular signals.⁹ These vesicles are cell-derived membrane bound vesicles functioning as a means of cell to cell communication. It has been shown that human breast milk derived exosomes significantly promote intestinal stem cell proliferation and viability.¹⁰ Human milk EVs cargo (comprising DNA, RNA, micro-RNA and proteins) can have anti-inflammatory, immunomodulatory, or neurodevelopment effects and improve the barrier function of the intestinal epithelium.¹¹ A recent study has shown that human milk exosomes could improve experimentally NEC-induced intestinal injury, restored intestinal regeneration, inhibited inflammation, and NEC-related complications better than amniotic fluid stem cell derived exosomes.^{12,13} These findings may explain why breastfeeding regimens in neonatal intensive care units decrease the incidence of NEC. Proteomic studies have also suggested that proteins derived from breast milk EVs may play a role in the regulation of gastrointestinal tract development.^{13,14}

Breastfeeding challenges

On the other hand, breastfeeding can introduce an additional layer of stress during a period characterized by rapid life changes. Parenting, baby care responsibilities, physical transformations, and feelings of isolation can collectively contribute to these potential stressors.¹⁵ For example, a doctor described the difficulties she faced through her own breastfeeding journey as a mother.¹⁶ Upon careful reading of this referenced article, the difficulties which she faced mostly originated from a lack of appropriate breastfeeding consultation within three days after birth. In addition to that, other factors such as using nipple guards or bottle feeding might have complicated the problem. Finally, her experience ended with her continuing to feed her baby formula. This entire process reveals how essential breastfeeding consultation and education are. Namely, in healthcare facilities with robust breastfeeding support, immediate

skin-to-skin contact after birth, early initiation of breastfeeding within the first hours, active promotion of exclusive breastfeeding, avoidance of pacifier use, and timely provision of breastfeeding information are key practices.¹

In conclusion, these newfound insights emphasize that breast milk transcends being solely a source of nourishment, warranting increased attention to its multifaceted significance. Additionally, it should be noted that during a time of significant life changes such as a child birth, difficulties with breastfeeding is not the sole cause of a mother's stress. Increasing the social support of a new mother during these periods may be a more rational solution than not recommending breastfeeding. There's a need to bolster social policies that promote and support breastfeeding practices.¹⁷⁻¹⁹

Author contribution

The authors confirm contribution to the paper as follows: study conception and design; draft manuscript preparation; G. K, S. Y. All authors reviewed the results and approved the final version of the manuscript.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Meek JY, Noble L; Section on Breastfeeding. Policy statement: breastfeeding and the use of human milk. *Pediatrics* 2022; 150: e2022057988. <https://doi.org/10.1542/peds.2022-057988>
2. Victora CG, Bahl R, Barros AJ, et al; Lancet Breastfeeding Series Group. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *Lancet* 2016; 387: 475-490. [https://doi.org/10.1016/S0140-6736\(15\)01024-7](https://doi.org/10.1016/S0140-6736(15)01024-7)

3. Belfort MB, Rifas-Shiman SL, Kleinman KP, et al. Infant feeding and childhood cognition at ages 3 and 7 years: effects of breastfeeding duration and exclusivity. *JAMA Pediatr* 2013; 167: 836-844. <https://doi.org/10.1001/jamapediatrics.2013.455>
4. Deoni SCL, Dean DC, Piryatinsky I, et al. Breastfeeding and early white matter development: a cross-sectional study. *Neuroimage* 2013; 82: 77-86. <https://doi.org/10.1016/j.neuroimage.2013.05.090>
5. Karpen H, Poindexter B. Enteral nutrition. In: Gleason CA, Sawyer T, editors. *Avery's Diseases of the Newborn*. 11th ed. Philadelphia: Elsevier; 2024: 871-887. <https://doi.org/10.1016/B978-0-323-82823-9.00059-3>
6. Moukarzel S, Bode L. Human milk oligosaccharides and the preterm infant: a journey in sickness and in health. *Clin Perinatol* 2017; 44: 193-207. <https://doi.org/10.1016/j.clp.2016.11.014>
7. Murphy K, Curley D, O'Callaghan TF, et al. The composition of human milk and infant faecal microbiota over the first three months of life: a pilot study. *Sci Rep* 2017; 7: 40597. <https://doi.org/10.1038/srep40597>
8. Ames SR, Lotoski LC, Azad MB. Comparing early life nutritional sources and human milk feeding practices: personalized and dynamic nutrition supports infant gut microbiome development and immune system maturation. *Gut Microbes* 2023; 15: 2190305. <https://doi.org/10.1080/19490976.2023.2190305>
9. Admyre C, Johansson SM, Qazi KR, et al. Exosomes with immune modulatory features are present in human breast milk. *J Immunol* 2007; 179: 1969-1978. <https://doi.org/10.4049/jimmunol.179.3.1969>
10. Dong P, Zhang Y, Yan DY, et al. Protective effects of human milk-derived exosomes on intestinal stem cells damaged by oxidative stress. *Cell Transplant* 2020; 29: 963689720912690. <https://doi.org/10.1177/0963689720912690>
11. Jiang X, You L, Zhang Z, et al. Biological properties of milk-derived extracellular vesicles and their physiological functions in infant. *Front Cell Dev Biol* 2021; 9: 693534. <https://doi.org/10.3389/fcell.2021.693534>
12. Hu X, Zhang R, Liang H, et al. Comparison and investigation of exosomes from human amniotic fluid stem cells and human breast milk in alleviating neonatal necrotizing enterocolitis. *Stem Cell Rev Rep* 2023; 19: 754-766. <https://doi.org/10.1007/s12015-022-10470-5>
13. Martin C, Patel M, Williams S, Arora H, Brawner K, Sims B. Human breast milk-derived exosomes attenuate cell death in intestinal epithelial cells. *Innate Immun* 2018; 24: 278-284. <https://doi.org/10.1177/1753425918785715>
14. van Herwijnen MJ, Zonneveld MI, Goerdayal S, et al. Comprehensive proteomic analysis of human milk-derived extracellular vesicles unveils a novel functional proteome distinct from other milk components. *Mol Cell Proteomics* 2016; 15: 3412-3423. <https://doi.org/10.1074/mcp.M116.060426>
15. Ayers S, Crawley R, Webb R, Button S, Thornton A; HABiT collaborative group. What are women stressed about after birth? *Birth* 2019; 46: 678-685. <https://doi.org/10.1111/birt.12455>
16. Kennedy AJ. Breast or bottle - the illusion of choice. *N Engl J Med* 2023; 388: 1447-1449. <https://doi.org/10.1056/NEJMp2300346>
17. Pérez-Escamilla R, Tomori C, Hernández-Cordero S, et al. Breastfeeding: crucially important, but increasingly challenged in a market-driven world. *Lancet* 2023; 401: 472-485. [https://doi.org/10.1016/S0140-6736\(22\)01932-8](https://doi.org/10.1016/S0140-6736(22)01932-8)
18. Rollins N, Piwoz E, Baker P, et al. Marketing of commercial milk formula: a system to capture parents, communities, science, and policy. *Lancet* 2023; 401: 486-502. [https://doi.org/10.1016/S0140-6736\(22\)01931-6](https://doi.org/10.1016/S0140-6736(22)01931-6)
19. Baker P, Smith JP, Garde A, et al. The political economy of infant and young child feeding: confronting corporate power, overcoming structural barriers, and accelerating progress. *Lancet* 2023; 401: 503-524. [https://doi.org/10.1016/S0140-6736\(22\)01933-X](https://doi.org/10.1016/S0140-6736(22)01933-X)