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Breast milk: its components and special effects on newborns and infants

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Abstract

Background. Breastfeeding is the gold standard of infant nutrition, ensuring optimal growth, development, and formation of the immune system during the first six months of life. Breast milk is a unique biological medium that contains both macro- and micronutrients, and bioactive components such as bacteria, immunoglobulins, lactoferrin, oligosaccharides, stem cells, and microRNAs. These compounds play a key role in the formation of the intestinal microbiota of newborns, affecting immunity, metabolism, neurodevelopment, and psychoemotional state. Changes in the microbiome due to the type of feeding are associated with long-term risks of allergies, obesity, type 2 diabetes, autoimmune and infectious diseases.

Despite significant progress in the study of breastfeeding, the mechanisms of interaction between its bioactive components and the intestinal microbiota remain poorly understood, necessitating a systematic analysis of current data. **The aim** of the study was to evaluate the relationship and impact of breastfeeding on the formation of the gut microbiome, immune system and neurodevelopment of infants, with a detailed look at the bioactive components of breast milk, such as microbiota, oligosaccharides, complement, immunoglobulins, stem cells and microRNAs. **Materials and methods.** To achieve this goal, a systematic literature review was conducted using PubMed, Scopus and Google Scholar databases. The search was carried out using the following keywords: ‘human milk’, “milk microbiota”, “newborn's immune system”, “breastfeeding”. Preference was given to systematic reviews, clinical trials, and analytical articles published in English. The analysis covered current, verified data on the composition of breast milk and its impact on the microbiota and infant health. **Results.** A systematic review found that breast milk is a dynamic biological medium that adapts to the needs of the infant through gradual changes in composition from colostrum to mature milk. Colostrum, which is rich in immunoglobulins (including IgA), lactoferrin, leukocytes and epidermal growth factor, provides primary immune defence by stimulating tissue regeneration and intestinal barrier function. Transitional milk, which appears on days 4-14, increases the energy value due to increased lactose and fat content, promoting weight gain and microbiota development. Mature milk stabilises the nutritional profile, supporting growth and metabolism due to its high content of lipids, carbohydrates, and micronutrients such as vitamins A, B and D, depending on the mother's diet. The microbiota of milk, which includes hundreds of bacterial species (Streptococcus, Staphylococcus, Bifidobacterium, Lactobacillus), forms the intestinal microbiome, reducing the risk of dysbiosis and infections by competitively displacing pathogens and stimulating anti-inflammatory cytokines. Milk oligosaccharides act as prebiotics, promoting the growth of beneficial bacteria and preventing pathogen adhesion, which strengthens the intestinal barrier. Short-chain fatty acids (SCFAs), metabolites of bacteria, modulate the immune system, reducing the risk of atopic diseases, although their levels are reduced in mothers with allergies. Lactoferrin has antimicrobial, antifungal, and immunomodulatory effects, supporting the growth of beneficial microorganisms. Complement components selectively regulate the microbiota, destroying gram-positive bacteria, which contributes to microbial balance. Immune cells (neutrophils, macrophages, lymphocytes) and peptides (α-lactalbumin, casein, lysozyme) provide protection and digestion, while stem cells and microRNAs influence epigenetic regulation, promoting neurodevelopment and immune maturation. **Conclusions.** Breastfeeding, through the synergy of bioactive components,

promotes a healthy intestinal microbiota, supports immunity and neurodevelopment, reducing the risk of allergies, metabolic and neurological disorders. However, the mechanisms of action of individual components, such as microRNAs, stem cells and the impact of maternal diet, require further research. The results highlight the importance of supporting breastfeeding for infants, as there is currently no infant formula that reproduces the bioactive properties of breast milk.

Keywords: "human milk"; "milk microbiota"; "newborn's immune system"; "breastfeeding".

Introduction

Breastfeeding is the gold standard in infant nutrition for at least 6 months, ensuring optimal growth, development, and immune system formation. In cases where the mother's milk is unavailable, donor's milk is recommended, while artificial feeding should be the last choice [1]. Breast milk contains many micro- and macronutrients, and it also contains biologically active components, including bacteria, immunoglobulins, lactoferrin, and microRNAs, which play a significant role in the formation of the intestinal microbiota in infants [2].

The intestinal microbiome of newborns begins to form from the first days of life and significantly impacts the immune system, metabolism, psycho-emotional state and overall health [3].

A growing body of evidence suggests that changes in the infant microbiome caused by the type of feeding influence the susceptibility to allergies, obesity, type 2 diabetes, autoimmune reactions and infectious diseases in childhood and adulthood.

Despite significant progress in the study of breastfeeding, the mechanisms of interaction between the bioactive components of breast milk and the intestinal microbiota of infants remain poorly understood, which requires a systematic analysis of the literature.

The aim of the study

To evaluate the relationship and impact of breastfeeding on the formation and composition of the intestinal microbiome, immunity, neurodevelopment of infants, focusing on the bioactive components of breast milk.

Materials and methods

To achieve this goal, a systematic literature review was conducted using the PubMed, Scopus, and Google Scholar databases, which made it possible to comprehensively analyse the current state of research in the field and identify verified data. Preference was given to systematic reviews, clinical trials and analytical articles published in English. The search was conducted using the following keywords: ‘human milk’, “milk microbiota”, “newborn's immune system”, “breastfeeding”.

Results and discussion

Breast milk is a unique biological medium that combines nutrients, immunological components and bioactive molecules adapted to the infant's needs at different stages of its development. Its composition is not static, but changes dynamically from the first days after birth to the period of mature lactation, reflecting the evolution of the baby's physiological requirements. The first fluid a newborn receives is colostrum, a thick, nutritious substance secreted in limited amounts during the first few days after birth. Colostrum is distinguished by its composition, which is rich in immunological components such as secretory immunoglobulin A (IgA), lactoferrin and leukocytes, as well as growth factors, including epidermal growth factor (EGF), which plays a key role in tissue regeneration, intestinal epithelial development and maintaining the barrier function of mucous membranes [4].

Unlike mature milk, colostrum contains significantly less lactose, emphasizing its primary role in protecting and stimulating development rather than providing calories. It is also characterised by a higher content of sodium, chloride and magnesium, while the concentration of potassium and calcium is lower, which ensures an optimal ionic balance for the newborn during the period of adaptation to the environment [5]. These features of colostrum make it indispensable in the first days of life, when the infant is most vulnerable to pathogens such as bacteria or viruses, which it encounters for the first time [6].

Approximately four days after delivery, colostrum is replaced by transitional milk, which is secreted for up to 14 days and is characterised by a rapid increase in volume and changes in composition, namely the concentration of proteins and immunoglobulins decreases, while the content of fats and lactose increases, increasing caloric content, decreasing the number of leukocytes, decreasing sodium levels, increasing the content of calcium, potassium and B vitamins, contributing to energy needs, microbiota development and gradual transition to the next period of nutrition [7].

After two weeks, mature milk is secreted to replace transitional milk, which acquires a stable composition adapted to support the baby's rapid growth and development. Mature milk contains a lower percentage of proteins and minerals, but higher concentrations of lipids and carbohydrates, provide the necessary energy for active metabolism [4, 8]. Its composition includes macronutrients (proteins, fats, lactose), the concentration of which depends on the stage of lactation and the mother's physiological characteristics, as well as micronutrients such as vitamins A, B1, B2, B12 and D, which vary depending on the mother's diet and nutrient reserves [9].

For example, a deficiency of vitamin D in the mother's diet can reduce its milk content, affecting the mineralisation of the baby's bones. In addition, mature milk contains growth factors that actively act on the endocrine, nervous, vascular and intestinal systems, contributing to their maturation. Immunological components, such as antibodies and cytokines, remain important, although their concentration is slightly reduced compared to colostrum, while continuing to provide protection against infections and inflammation [9].

The bioactive components of breast milk come from different sources, the mammary epithelium secretes some, others are extracted from maternal serum and transported across the mammary epithelium by a receptor-mediated transport mechanism [4, 10].

One of the most important elements of breast milk is its microbiota, which includes more than 200 different bacterial species and plays a key role in the formation of the primary intestinal microbiota of infants [9].

Breast milk contains bacteria at a concentration of approximately 1000 colony forming units per millilitre, which provides up to 800,000 microorganisms per day to the infant's digestive tract [11] The most common are members of the genera Streptococcus and Staphylococcus, followed by Bifidobacterium, Lactobacillus, Propionibacteria, Enterococcus and members of the Enterobacteriaceae family [12, 13, 14] These microorganisms not only colonise the gut but also create a stable microbial environment that significantly reduces the risk of dysbiosis compared to infants fed formula [15].

Breast milk bacteria are involved in modulating the immune response by stimulating the production of anti-inflammatory cytokines, which reduces the likelihood of developing allergic conditions such as asthma or atopic dermatitis, as well as other immune-mediated pathologies [9].

In particular, Lactobacillus strains isolated from milk exhibit antimicrobial properties, inhibiting the adhesion and growth of pathogenic bacteria such as Escherichia coli, Shigella spp, by competitive displacement and stimulation of mucin synthesis in intestinal enterocytes, which forms a protective barrier [16, 17, 18]. In a double-blind controlled study, the use of Lactobacillus strains in infants aged 6 to 12 months led to a 46% reduction in gastrointestinal infections, 27% in respiratory infections and 30% in general infections, confirming their protective potential [19].

In addition to live bacteria, breast milk also contains metabolites of bacterial origin, in particular short-chain fatty acids (SCFAs) such as formate, acetate, propionate, butyrate and valerate. These compounds are the end products of fibre fermentation in the mother's intestine and can be transported systemically, in particular to the mammary glands during lactation.

SCFAs have a pronounced immunomodulatory effect: they stimulate the development of regulatory T cells, promote the formation of immune tolerance, activate the synthesis of dendritic cell precursors and maintain the integrity of the intestinal epithelial barrier.

Thus, breast milk affects the infant's healthin two ways: on the one hand, through the direct colonisation of the infant's microbiota with bacteria, and on the other hand, through the action of metabolites produced by the mother's intestinal microflora. According to the latest data, SCFAs can also reduce the risk of developing atopic diseases in infants [34, 35]. However, a study by Geddes D. T. (2021), found that the content of short-chain fatty acids (SCFAs) in the breast milk of mothers with atopy was significantly lower compared to the milk of healthy women [36].

In addition, milk bacteria contribute to the development of peyer's patches in the intestine by increasing the number of plasma cells producing IgA, which, together with absorbed milk sIgA, in the intestinal lumen are part of the protective function of the epithelial barrier in the intestine by neutralising food antigens, preventing pathogen adhesion to the mucosa and exhibiting immunomodulatory effects, promoting immune tolerance [20].

Epidermal growth factor (EGF), present in both amniotic fluid and breast milk, is important in the maturation and regeneration of the intestinal mucosa. EGF is resistant to acidic environments and digestive enzymes, which allows it to pass to the intestine via the stomach, where it stimulates enterocytes to actively divide, enhances DNA and protein synthesis, and improves water and glucose absorption. EGF implements a number of protective mechanisms in the newborn's intestine, in particular, it inhibits apoptosis and restores the structure of proteins of tight junctions between the intestine and liver, which are disrupted by the pro-inflammatory factor TNF-α [4].

Equally important are breast milk oligosaccharides , which are not digested by the infant digestive system but act as prebiotics, selectively stimulating the growth of beneficial bacteria, in particular Bifidobacterium infantis [21], that prevent pathogens from adhering to the intestinal epithelium, reducing the risk of invasion and infectious complications [22]. They contribute to the strengthening of the intestinal barrier by protecting epithelial cells from oxidative stress, regulating their proliferation and reducing inflammatory responses, which is critical for gut health in the first months of life [23].

One of the most important components of breast milk is lactoferrin, a glycoprotein with the ability to bind iron, which is found in high concentrations in breast milk, especially in colostrum (3.16 g/l), while in mature milk its level decreases to 1.73 g/l. Thanks to its ability to bind iron, which is essential for the growth of pathogens, lactoferrin has antimicrobial, anti-inflammatory, antibacterial, antifungal and antiviral effects, while promoting the growth of beneficial bacteria such as Lactobacillus and Bifidobacterium. In addition, it has an immunomodulatory effect by stimulating the production of NK cells, IL-10, TNF-α and IgG, resulting in increased immune defence in newborns [24].

Among breast milk's lesser-known but exciting components is the complement system present in many mammals, including humans [25]. Complement components such as C1q and C3 are able to selectively kill Gram-positive bacteria, e.g. Staphylococcus lentus, through an antibody-independent mechanism that activates the membrane-attacking complex and causes bacterial lysis [26]. This mechanism plays an important role in the formation of a balanced microbiota, promoting the dominance of beneficial microorganisms and reducing the risk of pathogenic infections.

The immunological protection of breast milk is also provided by a wide range of peptides and proteins, such as α-lactalbumin, casein, lysozyme and secretory IgA, which are involved in digestion, protection against infection and growth stimulation, in particular through epidermal growth factor [27]. Milk contains immune cells, such as neutrophils, macrophages, lymphocytes and myeloid-derived suppressor cells (MDSCs), which suppress the overactivity of monocytes and T cells, providing fine-tuning of the immune response [28].

Of particular interest are stem cells, which are present in greater numbers in colostrum compared to mature milk, indicating their important role in the early development of tissues and organs [29], in particular exosomes, which carry bioactive molecules such as proteins, DNA, mRNA and microRNAs - more than 1400 species, affecting the expression of up to 60% of genes [30], being higher in colostrum, and depends on the type of milk (anterior or posterior), indicating their adaptive function [31]. These molecules, which are resistant to digestion, reach the systemic circulation by crossing the blood-brain barrier and affect neurodevelopment, while stem cells, in particular nestin-positive cells, can differentiate into neural cells or act as epigenetic regulators [30, 32].

The milk microbiota also contributes to epigenetic modifications by affecting signalling molecules that regulate gut and brain development [33].

Conclusions

Breastfeeding is the foundation for infant health, in particular through its influence on the gut microbiota.The composition of breast milk is dynamic and adaptive, reflecting the stages of infant development, as confirmed by this systematic review. Breast milk provides both protection in the first days of life and supports the growth and stability of the gut microbiota. The microbiota in breast milk plays a major role in creating a healthy gut environment. However, many of its biologically active components and their effects are unexplored and remain at the research level.

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Conflict of interest

The authors declare that the study was conducted with no conflicts of interest, financial, authorship, or other nature that could have influenced the course and results of the research in this article.

Author Contributions

All authors contributed equally to the conceptualization, methodology, literature analysis, and writing of this review article.

Institutional Review Board Statement

This is a narrative review article and does not involve human or animal subjects; therefore, IRB approval was not required.

Data Availability Statement

No new data were generated or analyzed in this study. All information is derived from publicly available literature sources.

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