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A Brief Overview: Breast Milk Colostrum Bioactives

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Abstract

Colostrum is the basic nutrient that is secreted after birth and meets all the needs of the newborn. Colostrum is rich in nutritional micro and macronutrients and bioactive substances such as antimicrobial and growth factors, which are necessary for the development of the newborn's digestive and immune systems. Colostrum differs from mature milk in terms of appearance, amount, and content. It has higher levels of immunoglobulin A, growth factors, and other protective components. Colostrum has a lesser energy, protein, and carbohydrate composition than mature milk, but a higher fat content. This review summarizes the available information on the composition of human colostrum. Furthermore, it provides an overview of growth factors and immune factors found in colostrum.

1. Introduction

Breastfeeding is often regarded as the best cost-effective option for lowering child morbidity and mortality (Nguyen et al., 2018). World Health Organization (WHO) recommends exclusively breastfeeding for the first 6 months, then continuing up to the age of 2 years and beyond (World Health Organization, 2009). The WHO defines early breastfeeding as starting breast milk feeding within one hour of delivery (Abie & Goshu, 2019). Breast milk contains a complex nutritional matrix that includes proteins and amino acids, lipids, lactose and oligosaccharides, vitamins, minerals, and other compounds (Ren et al., 2021).

Colostrum is the milk secreted within the first few days by the mammary gland of female mammals immediately after birth. It is commonly yellow in colour or creamy and its composition significantly differs from the mother's mature milk (El-Loly, 2022a). A mother first produces colostrum, which is highly significant, followed by an increase in milk production over the next 24 to 48 hours, with lactation finally regulated by the newborn infant (Santoro, Martinez, Ricco, & Jorge, 2010). It is rich in nutritional micro and macronutrients, as well as many bioactive substances such as antimicrobial and growth factors, which are required by all newborn mammals to develop the digestive system, resist and improve immune systems (El-Loly, 2022b).

The amount, appearance, and content of colostrum differ from that of mature milk. It is critical in terms of meeting the newborn's needs in the early days (Karakaya Suzan, 2020).

Colostrum not only provides a complete diet with all of the essential nutrients for the newborn during its initial months of life, but it also provides basic immunological protection against pathogens in the environment (El-Loly, 2019). Colostrum contains more immunoglobulin A (IgA), growth factors, and other protective components than mature milk (Karakaya Suzan, 2020). The high content of secretory immunoglobulins suggests that colostrum's primary function is immunologic rather than nutritional (Mosca & Giannì, 2017). As a result, breastfeeding with insufficient colostrum weakens the immune system while also exposing the child to microbial infection (Bagwe-Parab, Yadav, Kaur, Tuli, & Buttar, 2020). This review provides an overview of colostrum's nutrients, growth factors, and bioactive components, potential health implications, and benefits.

2. Breast milk components

Colostrum is rich in nutritional micro and macronutrients and bioactive substances such as antimicrobial and growth factors, which are necessary for the development of the newborn's digestive and immune systems. In this sub-title, nutrients, immune and growth factors of colostrum are summarized (Figure 1).

2.1. Nutrients

Breast milk is the most important nutrient for the growth and development of the baby (Yang, Zhang, Bao, & Rong, 2018). Colostrum volume is typically low due to the newborn stomach's small size after birth; however, it contains a high concentration of

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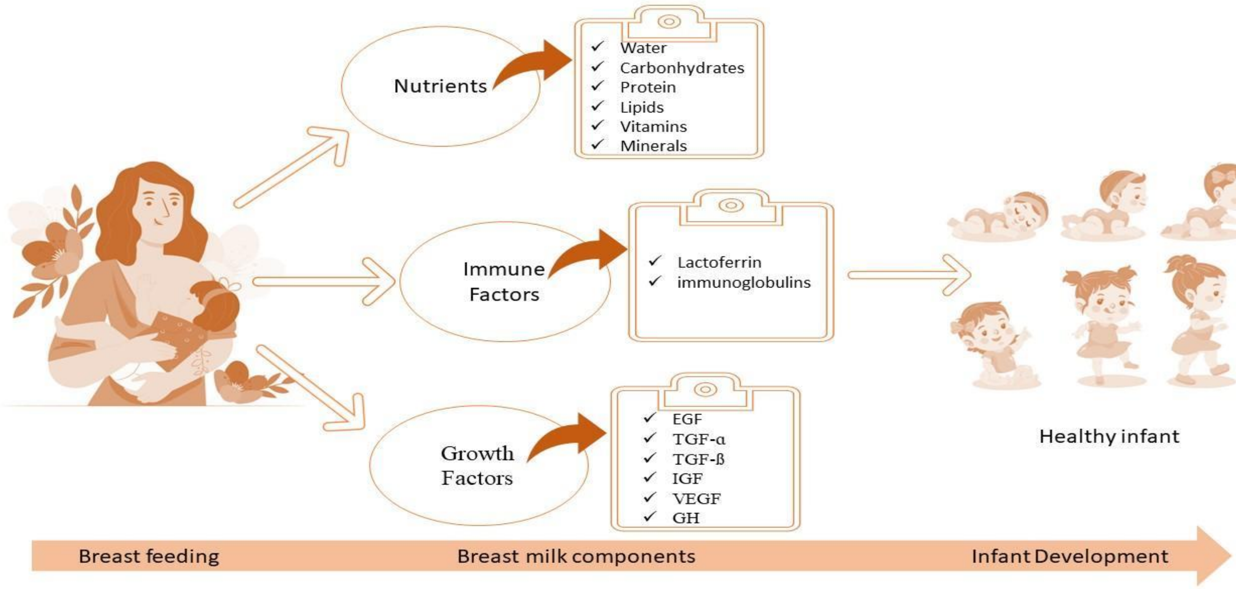

Figure 1. Breast milk components and infants health (Adapted from El-Loly, 2022b)

nutrients, including carbohydrates and proteins, immune system elements such as immunoglobulins, immunocompetent cells and cytokines, several other biologically active compounds, and commensal or potentially probiotic bacteria (Espinosa-Martos et al., 2013).

Breast milk macronutrient composition varies between mothers depending on diet, ethnicity, and other factors (Binte Abu Bakar, Salim, Clulow, Nicholas, & Boyd, 2021). Table 1 compares the nutritional content of colostrum and mature milk (TÜBER, 2022). According to one study, mature milk has significantly higher energy, fat, and lactose contents than colostrum, but lower protein content (Sever et al., 2015).

Breast milk produced immediately after delivery, as well as known as colostrum, differs from milk produced later in lactation. Total proteins in colostrum are high, but they diminish dramatically after around the first month, then more slowly in the following months. Total nitrogen decreases after the first month, although non-protein nitrogen (mostly urea) remains stable at a low level (Lönnerdal, 2013).

The mother's dietary patterns have an impact on the amount of fatty acids in breast milk (Finley, Lönnerdal, Dewey, & Grivetti, 1985). Given the various effects of fatty acids on infant health, the determinants of polyunsaturated fatty acids (PUFA) supply via breast milk must be addressed (Hoppu, Isolauri, Laakso, Matomäki, & Laitinen, 2012). Breast milk contains long-chain (LC) PUFAs, which are essential nutrients involved in growth, the immune system, vision, and cognitive and motor development, particularly docosahexaenoic (DHA) and arachidonic acid (AA) (Martin, Ling, & Blackburn, 2016). A longitudinal cross-sectional study found that AA, DHA, and n-3 LC-PUFA levels were higher in colostrum than in mature milk (de la Garza Puentes et al., 2019). In a French cohort study, it was shown that the level of PUFA in colostrum and the duration of breastfeeding had a mild effect on the intelligence scores of children (Bernard et al., 2017).

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Table 1. Nutritional composition of colostrum and mature breast milk (TÜBER, 2022)

Energy and nutrient components	Colostrum	Mature breast milk	Energy and nutrient components	Colostrum	Mature breast milk
Energy (kkal)	58	70	Tiamin (mcg)	15	16
Lactose (g)	5.3	7.3	Riboflavin (mcg)	25	35
Protein (g)	5.3	7.3	Niacin (mcg)	25	200
Lipid (g)	2.9	4.2	Folic acid (mcg)	-	5.2
Cholesterol (mg)	27	16	Vitamin B_6 (mcg)	12	28
Vitamin A (mcg)	89	47	Vitamin B_{12} (mcg)	200	26
Vitamin C (mg)	4.4	4.0	Calcium (mg)	23	28
Vitamin D (mcg)	-	0.04	Iron (mcg)	45	40
Vitamin E (mcg)	1280	315	Zinc (mcg)	540	166
Vitamin K (mcg)	0.2	0.21	Potassium (mg)	74	58

Lactose, a disaccharide, is the primary carbohydrate in breast milk. Lactose concentration in breast milk is the least variable among the macronutrients, however larger amounts of lactose are observed in the milk of mothers producing higher quantities of milk (Ballard & Morrow, 2013).

The amount of oligosaccharide, another type of carbohydrate, in breast milk varies depending on the lactation stage and genetics (Ballard & Morrow, 2013). Some human milk oligosaccharides have many activities, including promoting the growth of beneficial bacteria, inhibiting harmful bacteria, modifying immunological function, and increasing gut barrier functions (Cheng, Akkerman, Kong, Walvoort, & de Vos, 2021; Kong, et al., 2019; Cheng, Kiewiet, Groeneveld, Nauta, & de Vos, 2019).

It was stated that the content of thiamine, riboflavin, niacin, vitamin B6, and pantothenic acid was lower in the first 7 days of milk secretion and increased in the following days (Ren et al., 2015). In a cross-sectional study, the concentration of alpha-tocopherol in colostrum was found to be 1,147.6 ± 582.9 μg/dL (Grilo et al., 2013). Another study found that antioxidant vitamins E, C, and A had colostrum concentrations of 21.34 8.47, 148.92 43.64, and 0.79 0.42 mol/l, respectively. Copper, zinc, and iron antioxidant mineral contents were 19.17 11.73, 63.69 12.82, and 11.44 1.46 mol/l, respectively (Ahmed et al., 2004). Martysiak-Zurowska et al. (2013) reported that alpha-tocopherol concentration decreased from colostrum (999.0 ± 151.0 μg/dL) to mature breast milk (1st month: 292.0 ± 84.0 μg/dL; 3rd month: 207.0 ± 66.0 μg/dL) (Martysiak-Zurowska et al., 2013). It has been determined that the level of vitamin B12 is highest in colostrum and decreases as time progresses towards the 3-4th months (Dror ve Allen, 2018). Vitamin D is also present in low concentrations in human milk, particularly when mothers are not exposed to sunlight, which is now typical in many populations throughout the world (Ballard & Morrow, 2013; Dawodu et al., 2012). According to the results of a review investigating the

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concentration of vitamin E in breast milk, it was stated that the concentration of alpha-tocopherol in milk decreased until it reached mature milk (Lima et al., 2013). Similar results were found in another study. Plasma levels of lutein, zeaxanthin, and cryptoxanthin, as well as -tocopherol and cholesterol, were significantly lower later in lactation than shortly after birth (Schweigert et al., 2004). In the study evaluating the breast milk content of Chinese women over the years, it was determined that the protein, potassium, zinc, and copper content decreased and the lipid content increased as they went from colostrum to mature milk (Yang et al., 2018)

2.2. Immune Factors

Colostrum contains more immune and growth factors than mature breast milk, as well as other bioactive substances. These factors work to protect newborns from illnesses and infections, activate the innate immune system and gut function, and promote the development of a healthy gut microbiome during the first few days after birth (Li et al., 2022).

Immunological factors in colostrum protect against microorganisms. Colostrum contains trypsin inhibitors, and the unchanged colostrum that travels down the gastrointestinal tract helps to maintain healthy epithelial linings and the immune system. Colostrum thus protects against gastrointestinal disorders (Godhia & Patel, 2013). When breastfed, the child is protected against diseases such as sudden infant death syndrome, sepsis, necrotizing enterocolitis, infections (such as respiratory, gastrointestinal tract, otitis media, meningitis), overweight, obesity, diabetes, hypercholesterolemia, allergic diseases or the disease progresses in a milder course (Bernardo, Cesar, & Organization, 2013; Chrustek, Dombrowska-Pali, & Olszewska-Słonina, 2021).

Lactoferrin is a glycoprotein found in breast milk that has antimicrobial and anti-inflammatory properties (Villavicencio, Rueda, Turin, & Ochoa, 2017). Lactoferrin can tolerate proteolysis in the gastrointestinal tract and potentially improve infant iron absorption (Cai et al., 2018). Human lactoferrin, in particular, can neutralize endotoxin activity, prevent mononuclear cell activation, and, eventually, prevent cytokine secretion that contributes to inflammation (Nolan, Parks, & Good, 2019). Colostrum contains approximately three times the amount of lactoferrin found in mature milk (Cai et al., 2018). Lactoferrin levels in colostrum ranged from 5.0 to 6.7mg/mL and from 0.2 to 2.6mg/mL in mature milk (Queiroz, Assis, & R Júnior, 2013). The lactoferrin content of breast milk is determined by factors such as maternal age, parity, socioeconomic status, nutritional status, maternal infections, and smoking status (Villavicencio et al., 2017). Significant amounts of intact lactoferrin were found in infant stools in investigations, even in babies as young as 4 months old, indicating that lactoferrin can survive being active in the small intestine (Siqueiros-Cendón et al., 2014). Lactoferrin levels were found to be highest in colostrum and lowest in mature milk in a study of the milk content of mothers of low birth weight infants (Turin et al., 2017).

Colostrum's bioactive components are crucial for a newborn's overall health, development, and vitality. Colostrum includes immune cells and antibodies such as immunoglobulins A, G, and M, which are essential parts of the adaptive immune system, as well as lysozyme, lactoferrin, and lactoperoxidase,

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which are significant parts of the innate immune system (Giansanti, Panella, Leboffe, & Antonini, 2016; Li et al., 2022).

Among the many factors involved in the infant's mucosal defenses, IgA, IgM, and IgG found in colostrum and milk provide passive protection for the gastrointestinal system (Demers-Mathieu et al., 2019; Permanyer et al., 2010). IgG can bind to mucus, prevent viruses from attaching to the mucosal surface, and catch pathogens. SIgA was more effective than IgG at changing attachment and catching pathogens in mucin. Despite the discovery of IgM-secreting cells in the infant's gut, it is unknown what role IgM plays in infant mucosal immune defense (Demers-Mathieu et al., 2019).

2.3. Growth Factors

Colostrum contains high levels of proteins, amino acids, growth factors, Igs, cytokines, vitamins, minerals, carbohydrates, fatty acids, and lipids. Colostrum is a valuable product in this context because of its unique components which boost both the immune system and lean muscle mass, promote healthy digestion, and reduce allergy symptoms (Ahmadi et al., 2017; El-Loly, 2022a). Furthermore, because it contains a variety of growth factors, colostrum is an excellent substance for the repair and regeneration of body cells (El-Loly, 2022a).

Breast milk growth factors protect the intestinal mucosal barrier by assisting in its maturation (Nolan et al., 2019). Epidermal growth factor (EGF) is important in the maturation and healing of the intestinal mucosa, as well as nutrient absorption and protein synthesis (Gila-Diaz et al., 2019; Nolan et al., 2019). Breast milk growth factors protect the intestinal mucosal barrier by assisting in its maturation (Nolan et al., 2019). Epidermal growth factor (EGF) is important in the maturation and healing of the intestinal mucosa, as well as nutrient absorption and protein synthesis (Gila-Diaz et al., 2019; Nolan et al., 2019). Colostrum contains 2000 times more EGF than mature breast milk and 100 times more than maternal serum (Puryatni, Ismail, Juniantika, & Kurniawan, 2021). The EGF content of preterm colostrum was found to be between 22.8 and 373 µg/L, and that of term colostrum was found to be between 27.7 and 209 µg/L (Gila-Diaz et al., 2019).

Human breast milk, particularly colostrum, contains insulin-like growth factors (IGFs) such as IGF-I and IGF-II (Gila-Diaz et al., 2019). IGF-I is an anabolic hormone with mitogenic, metabolic, differentiation, and anti-apoptotic properties (Alzaree et al., 2019; Puryatni et al., 2021; Sridharaswari, Irmawati, Suryawan, & Retnowati, 2019). IGF-I also regulates vascularization, which is mediated by vascular endothelial growth factor (VEGF) (Gila-Diaz et al., 2019). The higher levels of EGF and IGF-1 contained in colostrum reduced the incidence of necrotizing enterocolitis in neonates (Puryatni et al., 2021). Hepatocyte Growth Factor (HGF) has been shown to regulate VEGF production from endothelial cells and to complement VEGF biological activity in the infant's gut (Munblit et al., 2016). HGF levels in colostrum are 20 to 30 times higher than in maternal serum (Yamada, Saito, & Morikawa, 1998).

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Table 2. Immune Factors and Growth Factors in Human Colostrum (Ballard & Morrow, 2013; Gila-Diaz et al., 2019; Godhia & Patel, 2013; Polidori et al., 2022)

Immune Factor	Human Colostrum	Function
Lactoferrin	700 mg/mL	Acute phase protein, chelates iron, antibacterial, antioxidant
IgA	17.35 mg/mL	Inhibition of pathogen binding
secretory IgA (sIgA)	540 mg/mL	Inhibition of pathogen binding
IgG	0.43 mg/mL	Anti-microbial, phagocytosis activation; anti-inflammatory, allergen response
IgM	1.59 mg/mL	Complement activation, agglutination
Growth Factor		
Epidermal growth factor (EGF)	200 mcg/L	Stimulation of cell proliferation and maturation
Transforming growth factor alfa (TGF-ɑ)	2.2-7.2 mcg/L	Angiogenesis stimulator and cell migration and proliferation regulator
Transforming growth factor beta (TGF-ß)	20-40 mg/L	Anti-inflammatory, stimulation of T cell phenotype switch
Insulin like growth factor (IGF)	18 mg/L	Retinal vascularization, brain maturation
Vascular endothelial growth factor (VEGF)	75 mcg/L	Angiogenesis and tissue repair stimulation
Growth hormone (GH)	41 ng/L	Healing of injuries and accelerating bone regeneration

Transforming growth factor (TGF-ß) is an anti-inflammatory cytokine found in colostrum that is primarily produced by parenchymal cells and infiltrating cells (Gila-Diaz et al., 2019). In human milk, three TGF-ß isoforms (TGF-ß1, TGF-ß2, and TGF-ß3) are present, with TGF-ß2 being the most prevalent (Khaleva et al., 2019; Sakaguchi et al., 2018). Diet, birth weight, gestational age, baby's age, location, and probiotic use all affect TGF-ß1 levels in breast milk (Alsharnoubi, Ishaak, Elsheikh, & Ezzat, 2019). According to a study of 389 lactating mothers' milk, the concentration of HGF, TGF-ß1, and TGF-ß3 was significantly higher in colostrum than in mature milk (Munblit et al., 2016).

3. Conclusion

Breast milk is a unique food that meets all of the newborn's needs. Colostrum, the mother's first milk, is called the baby's first vaccine. Colostrum is a unique nutrient with its nutritional value, immune factors, and growth factors. When colostrum macronutrients are compared to mature breast milk, the fat concentration is higher and the energy, protein, and carbohydrate contents are lower. Colostrum contains more growth and bioactive components than mature breast milk, according to research. Colostrum, which is extremely crucial for the baby's immune system, must be consumed.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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