

Nutritional risks among not exclusively breastfed infants in the first 6 months of life

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ABSTRACT

Breast milk is the ideal food for infants and its benefits can be observed in the short and long term. In crisis situations, breastfeeding should be promoted the most because it is one of the most cost-effective interventions aimed at reducing infant morbidity and mortality. In addition to the multiple advantages of breast milk in the mother-child bond and biological and immune properties, the most relevant characteristic of breast milk is that it covers all nutritional needs. When breastfeeding is not possible, the World Health Organization recommends infant formula as the first option. The second option is diluted cow's milk, which entails the risk for nutritional deficiency that should be strictly monitored and timely resolved. When infants are fed with diluted cow's milk, they are mainly at risk for iron, zinc, vitamin A, D, C, and E, amino acid, and essential fatty acid deficiency.

Key words: *breastfeeding, infant nutritional physiological phenomena, breast milk substitutes, micronutrients/deficiency, macronutrients.*

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changes in the quality of feeding, a situation that health care providers should be alert to.

Breast milk is the ideal food since birth, and its benefits can be seen in the short and long term. It has an impact on children's comprehensive health, growth, and development, and creates a protection against future diseases. Breastfeeding is considered one of the most cost-effective interventions aimed at reducing infant morbidity and mortality.³

Argentina has established legal instruments to promote breastfeeding from different perspectives; however, they do not seem to be enough to warrant their practice.⁴ According to the latest National Survey on Nutrition and Health (2019), 96.9% of infants started breastfeeding, and with no significant differences in the analyzed sociodemographic factors.⁵ This is a high prevalence compared to global epidemiological data and is consistent with the positive consideration of breastfeeding among the Argentine population.³⁻⁶ In spite of this, exclusive breastfeeding is maintained until 6 months of life only in 43.7% of infants.⁷

Among infants who are not exclusively breastfed, it is important to know the type of milk received given the important impact it may have on health. According to the National Survey on Breastfeeding of 2017, among infants younger than 6 months not exclusively breastfed, the first option is infant formula (59%), followed by milk from the mother and child plan (MCP) or powder cow's milk fortified with iron, zinc, and vitamin C (20%), and, lastly, unfortified cow's milk (8%).⁷

Breast milk is the "gold standard" and hard to mimic due

INTRODUCTION

The first year of a child's life is one of the most vulnerable stages of the life cycle and encompasses the 1000 days from conception until 2 years old. This is a strategic period in terms of public health prevention, a window for opportunities to identify risks and act accordingly. Delayed interventions, especially in relation to nutrition, are one of the greatest threats to human health and development due to their effect on growth, neurocognitive development, and noncommunicable diseases (NCDs). The social and economic crisis resulting from the coronavirus disease 2019 (COVID-19) pandemic is most likely associated with negative

to its special characteristics and the emotional bond represented by breastfeeding, beyond its composition: it is a “biological dialog” whereby an infant conveys information to their mother about their needs and the mother responds by altering milk’s amount and composition. In addition, it is a vehicle for immune, microbiological, and psychological communication between the mother and her child.⁸ It is a live, unique food that varies from mother to mother, provides macro- and micronutrients, more precisely, oligosaccharides, bacteria, and bacterial metabolites that modulate the gut microbiota composition, which, in turn, modulates gastrointestinal tract and immune system development.⁹⁻¹⁰

In recent years, the evidence suggests that breastfeeding also plays a major role in noncommunicable diseases programming in the long term.³

Organizations like the World Health Organization (WHO), the United Nations International Children’s Emergency Fund (UNICEF), the American Academy of Pediatrics (AAP), and the Spanish Society of Pediatrics (*Asociación Española de Pediatría*, AEP) recommend exclusive breastfeeding on demand during the first 6 months of life.¹¹⁻¹⁴ If breastfeeding is not possible, infant formula should be indicated.

According to the United Nations’ Codex Alimentarius, breast milk substitutes are food products proposed as partial or total breast milk substitutes. Infant formula is defined as liquid or powdered form product for use as a substitute of breast milk in meeting the normal nutritional requirements of infants. It should have proven safety and nutritional suitability to favor an adequate growth and development. Based on this definition, whole cow’s milk is not considered a breast milk substitute in the first 6 months of life due to its potential harmful effects on health.¹⁵

The Food Guidelines (2001) and the Infant Nutrition Guidelines by the Ministry of Health (2006), published by the *Sociedad Argentina de Pediatría*, propose, for the first 6 months of life and in the case of not being able to continue with breastfeeding, infant formula as the first option, diluted cow’s milk (in half) with 5% sugar and 2% oil as the second option, and diluted cow’s milk (in two-thirds) fortified or enriched with iron and vitamins A and C, if possible, as the third option.^{16,17}

Micronutrient deficiency, including vitamin A, iron, zinc, amino acids, and essential fatty acids, are the most relevant deficiencies worldwide.¹⁸

When breastfeeding or the administration of an adequate breast milk substitute are not possible, the nutritional status worsens.

The objective of this study is to provide updated information about the nutritional risk of infants younger than 6 months who are not exclusively breastfed.

This study analyzes the following aspects:

- Proteins in breast milk, baby formula, and cow’s milk.
- Fatty acids.
- Micronutrients.
- Cow’s milk and iron deficiency.

Proteins in breast milk, infant formula, and cow’s milk

Breast milk proteins are the ideal source of amino acids for infant growth, have a higher biological value and, being homologous, they lack antigenic ability.

Protein content in breast milk varies during breastfeeding; from 1.4-1.6 g/100 mL in the first months to 0.8-1.0 g/100 mL after this period. Serum proteins (PS) account for 80% of total proteins; the remaining 20% is casein. Such ratio is also modified over time and reaches 50%:50% during late breastfeeding.¹⁹

The main serum proteins in breast milk are alpha-lactalbumin (critical for lactose synthesis), lactoferrin and IgA (important bioactive and immune molecules).^{20,21}

Lactoferrin accounts for 15-20% of serum proteins, plays a major antibacterial role (by inhibiting bacterial growth, adhesion, and translocation), and modulates epithelial growth.^{22,23} IgA is the main immunoglobulin present in breast milk and confers an important antimicrobial protection. Other immune factors found in breast milk include leukocytes, cytokines, lysozymes, and these warrant an adequate gut microbiota development, thus favoring food tolerance.²⁴

Protein fat content in cow’s milk (3.5%) is 3 times higher than that of breast milk. The main protein in cow’s milk is casein (80%). It can be categorized into sub-classes: alpha-casein, the main type in cow’s milk, and beta-casein, the main type in breast milk.

The lactoferrin in cow’s milk has lower antibacterial effects and does not favor iron absorption, like that present in breast milk. In cow’s milk, the total amount of immunoglobulins is lower than in breast milk, and the main immunoglobulin is IgG.²⁵

Given its high protein and sodium content, the intake of unmodified cow's milk causes a high renal solute load and a risk for increased water loss in urine and dehydration in infants.²⁶

Protein content in infant formula is approximately 1.5 g/100 mL.⁹ For infant formula to have a similar quality to breast milk, they contain 60% of serum proteins and 40% of casein. Serum proteins in infant formula contain beta-lactoglobulin. The addition of bovine lactoferrin to infant formula has improved its function in recent years because it prevents contamination.^{27,28}

Carbohydrates

The main carbohydrate in breast milk is lactose (90%), and its fat content is approximately 7 g/100 mL. Lactose favors calcium and mineral absorption and is the precursor of oligosaccharide production.

Breast milk contains small amounts of glucose and galactose and more than 200 structures of oligosaccharides, whose composition and proportion varies depending on different factors.

Human milk oligosaccharides (HMO) are the third component, following lactose and lipids, and its concentration varies depending on the different breastfeeding periods (5-20 g/L in mature milk and 20-25 g/L in colostrum). HMO are minimally digested in the small intestine and the undigested fraction serves as a prebiotic. The presence of different HMO stimulates specific bacterial growth that have beneficial effects and inhibits the development of harmful ones. HMO affect cell responses and modulate epithelial apoptosis and cell proliferation and differentiation. Certain HMO reduce proinflammatory cytokine expression and have an impact on the development of diseases related to the immune system.²⁹

Several bacteria have been detected in breast milk, thus forming a true seeding by providing more than 10⁵ bacteria per day from the maternal gut, an effect of the entero-mammary pathway.^{30,31}

Cow's milk contains 4.5 g/L of lactose and only scarce amounts of glucose, galactose, and oligosaccharides.

Most infant formulas contain lactose (5.4-8.2 g/100 mL) and a lower proportion of maltodextrins. Infant formula contains added fructooligosaccharides and galactooligosaccharides as complex oligosaccharides that function as prebiotics.³²

Some infant formulas currently include some fucosylated HMO that have been identified in breast milk.

Fatty acids

Breast milk contains 3-5% of lipids that provide 40-50% of total energy and essential fatty acids. Triglycerides (TG) account for 98% of total lipids.³³ Phospholipids (PL) are not abundant but very relevant: they are part of milk fat globule membrane, contain essential fatty acids, and are positively associated with neurodevelopment, immune system modulation, and antimicrobial properties.^{34,35}

Fatty acids are derived from endogenous synthesis in the mammary gland and uptake from maternal plasma.³³

The most abundant fatty acids in breast milk are monounsaturated fatty acids (MUFA) (43%) and saturated fatty acids (SFA) (40%). Total n-3 and n-6 polyunsaturated fatty acids (PUFA) account for 2.3% and 14.7%, respectively, whereas docosahexaenoic acid (DHA) accounts for 0.18-0.30% and arachidonic acid (ARA), 0.38-0.45%.³⁶

Cow's milk contains more than 60% of SFA, 30% of MUFA, and only 4% of PUFA, but no DHA.³⁷ This is a very important limitation for cow's milk as a breast milk substitute due to the effect of PUFA on neurodevelopment. DHA and ARA are essential fatty acids due to the limited enzymatic maturation necessary to synthesize them in the first months of life.³⁸ DHA accounts for 25% of total fatty acids in the human brain cortex, 30% in the retina, and 60% in photoreceptor cells.³⁹

The industry of infant formula as a breast milk substitute has modified its fatty acid profile. The percentage of SFA and PUFA was adapted to international recommendations and maintain the DHA:ARA ratio.^{15,40} Their absorption and entrance into the bloodstream have been measured in the levels observed in breast milk.^{41,42}

Diluted cow's milk at 50% with the addition of 2 g of oil and 5 g of sugar per 100 mL should be the last option, and every effort should be made to supplement any potential deficiency. For example, the addition of 2 g of sunflower oil would provide linoleic oil (54%) and oleic oil (33%), but only 0.2% of linolenic oil and no DHA. Diluted cow's milk at 50% provides 1.65 g of lipids per 100 mL and only traces of n-3.

The profile of fatty acid malnutrition has been described and demonstrated an increase in n-6 and n-9, to the detriment of n-3, particularly DHA, with the consequences described above.⁴³

Micronutrients

Breast milk is an accurate source of micronutrients, some of which are modified depending on the maternal nutritional status.⁴⁴

Vitamins A and B12 require an adequate maternal intake to reach the desired levels for infant nutrition.⁴⁵

Vitamin D level is low in breast milk and should be supplemented preventively during the first month of life (400 IU/day).⁴⁶ If the breastfeeding mother restricts animal products in her diet, she should receive supplementation for vitamin B12, zinc, iron, etc. to prevent the negative consequences on infant development.⁴⁷

Vitamin and mineral intake from infant formula is regulated by the Codex Alimentarius; in general, it refers to the ideal composition of breast milk.¹⁵

The level of vitamin D in unfortified cow's milk is low, and even lower if diluted. The level of vitamins A and C in unfortified whole cow's milk is

low (31 retinol equivalents [RE] and 0.94 mg/100 g, respectively) and minimal when diluted. Breast milk contains 64 RE and 5 mg/100 g, respectively.³⁷

Breast milk provides a calcium:phosphorus ratio of 2:1,¹¹ thus ensuring its optimal use. The ratio in cow's milk is 1:1, which may lead to hypocalcemia due to secondary hyperparathyroidism.⁴⁸

Cow's milk and iron deficiency

A negative aspect of cow's milk consumption among infants is its association with iron deficiency. Iron plays a major role in the body, especially in relation to oxygen transport, immune system, and the brain.^{49,50}

Iron stores at birth are enough until approximately 4 months old.

Without preventive supplementation or fortification, it is difficult to achieve an adequate iron nutrition.⁵¹ Bioavailability in breast milk is high.⁵²

TABLE 1. Composition of breast milk, infant formula, whole cow's milk, and diluted cow's milk

Nutrient/100 mL	Breast milk	Infant formula*	Whole cow's milk**	Diluted cow's milk + 5% sugar + 2% oil***
Energy (Kcal)	70	60-70	61	68
Proteins (g)	0.9-1	1.3-2	3.4	1.7
Casein (%)	20	40	80	80
Serum proteins (%)	80	60	20	20
Carbohydrates (lactose) (g)	6.9	4-6	4.6	2.3
Fat (g)	3.8 (3.5)	2.6-4.2	3.4	2.7 (with added oil)
Iron (mg)	0.05	0.3	0.05	0.025
Zinc (mg)	0.17	0.32	0.38	0.19
Sodium (mg)	16	13-36	49	25
Potassium (mg)	53	36-108	152	76
Calcium (mg)	32	32	119	59
Phosphorus (mg)	14	16	93	47
Calcium/phosphorus	2-1	2-1	1-1	1-1
Vitamin A (RE)****	30-64	42-126	31	15.5
Ascorbic acid (mg)	5	7	0.94	0.47
Vitamin D (IU)	15-20	28-56	5-10	2.5-5
Vitamin E (mg of alpha-tocopherol)	1.38	0.5-1.25	0.1	0.05
Vitamin B12**** (mg)	0.58	0.30	0.35	0.18
Osmolality (mOsm)	286	258-309	350	187

* Food and Agriculture Organization of the United Nations, World Health Organization. Standard for infant formula and formulas for special medical purposes intended for infants. In Codex Alimentarius. International Food Standards. 2007. [Accessed on: June 30th, 2021]. Available at: http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https://253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXS%2B72-1981%252FCXS_072e.pdf

** Jenssen RG, Kroger M. The importance of milk and milk products in the diet. In: Miler GD, Jarvis JK, McBean LD (eds). Handbook of Dairy Foods and Nutrition. 2nd ed. Boca Raton (Fla): CRC press; 1999:1-55.

*** Ministerio de Salud. Dirección Nacional de Maternidad e Infancia. Sucédáneos de la Leche Materna. In Guías Alimentarias para la población infantil. Buenos Aires: MINSAL; 2006: 27.

**** Variables according to maternal intake.

Infants fed with cow's milk have a higher risk for iron deficiency.^{26,53-55} The replacement of breast milk with cow's milk has a negative association with iron deficiency and a positive association with infant formula;⁵⁶ this is attributed to their fortification. In addition, studies of unfortified infant formula showed a better iron nutrition compared with subjects who received cow's milk, which evidences that other mechanisms are involved in it.⁵⁷

The different types of amino acid combinations in proteins also account for the effects on iron absorption. Cysteine is the only amino acid capable of increasing iron absorption.⁴⁹ Casein (80% in cow's milk) has a low level of cysteine (3 mg/g of protein), but a level 10 times higher (30 mg/g of protein) in serum proteins (80% in breast milk).⁵⁸

In alpha-lactalbumin (22% of serum proteins in breast milk but only 3.5% in cow's milk), the level of cysteine is 48 mg/g of proteins.⁵⁸ Therefore, such benefit is also observed in infant formula.

The state of iron stores regulates its absorption, which is also affected by diet factors: ascorbic acid favors absorption, while calcium hinders it.⁴⁹

A high level of calcium in cow's milk inhibits iron absorption. For breast milk and cow's milk, iron absorption was 48% and 19.5%, respectively. The addition of calcium to breast milk inhibits iron absorption. The differences in calcium content account for 70% of the difference in iron bioavailability.⁵⁹ In infant formula, calcium levels are similar to those of breast milk.

Iron requirements for infants in the second trimester are 0.7 mg/day. The iron level in infant formula is 6-12 mg/L. Such high intake covers the requirements.²⁶

Another concern in relation to cow's milk consumption in the first year of life is blood loss through the digestive tract. Healthy infants have a minimal blood loss in feces. Such blood loss was estimated using labeled substances at 0.59 mL/day.⁵⁷ Infants fed with cow's milk have a higher induced loss: 1.7 mL/day; in the same infants but fed with infant formula, it reduced to 0.3 mL/day. A blood loss of 1.7 mL/day equals an iron loss of 0.53 mg/day, which hinders the possibility of a net balance of 0.7 mg/day that is necessary to prevent iron deficiency.⁵⁷ It has been estimated that, in 40% of infants fed with cow's milk, blood loss increases significantly.

Higher losses have been reported at a lower prevalence (< 1%), e.g., hemorrhagic proctocolitis

associated with allergic immune reactions.⁶⁰

Table 1 shows the composition of breast milk, infant formula, whole cow's milk, and diluted cow's milk.

Final remarks

Breastfeeding is the ideal food for infants.

When the indication of breast milk substitutes is justified, the most adequate option should be selected based on age, socioeconomic conditions, and local availability. Infant formula is the first option when breastfeeding is not possible.

Whole cow's milk is contraindicated in the first year of life, and suggested diluted cow's milk pose a risk for nutritional deficiencies in the infant that should be closely monitored and timely supplemented.

The main risks for infants fed with diluted cow's milk include iron, zinc, vitamin A, D, C, and E, amino acid, and essential fatty acid deficiency.

In this group of infants, full supplementary feeding is recommended before 6 months old (but not before 4 months old) to improve micronutrient intake, accompanied with iron and vitamins A, C, and D supplementation as per recommendations.⁶¹⁻⁶³ ■

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