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The impact of breastfeeding on strengthening the infant's immune system and preventing infectious diseases

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Abstract

Human milk is a highly complex biological fluid composed of numerous components that perform diverse and essential roles in infant development. Scientific research continues to reveal new functions and mechanisms associated with its bioactive elements. The immune system of a breastfed infant can be significantly influenced by human milk, as it contains immunological factors that actively interact with the infant's developing immune responses. In addition to enhancing vaccine effectiveness and supporting immune maturation, breastfeeding may sometimes contribute to the modulation or suppression of certain immune reactions, including transplant rejection and the risk of developing specific autoimmune disorders such as type 1-diabetes. Breastfeeding appears to provide the newborn with optimal nutrition, reducing the risk of vitamin A deficiency and supporting an appropriate and well-regulated immune response. Moreover, the regulation of anti-inflammatory properties and the establishment of healthy gut microbiota through breastfeeding further increase the likelihood that the infant will develop a balanced and properly functioning immune system. Nevertheless, the precise roles of growth factors, cytokines, idiotypic and anti-idiotypic antibodies, along with other anti-inflammatory components present in maternal milk, in shaping the infant's immune system still require further detailed investigation and ongoing scientific research.

Key words: Breastfeeding, Human milk, Breast milk, Newborn, Autoimmune disease.

1. Introduction

Human breast milk not only offers the best nutrition for newborns and infants but also boosts immunity against a variety of infections. It is a highly complicated material with many proteins, cells, and other constituents. The consequences of nursing on the newborn, including several direct and indirect effects on the body's response to infection, are constantly being better understood [1].

Breastfeeding offers the child and infant unparalleled natural nutrients. According to earlier research on Human breast milk, thymus gland development, and infant reaction to immunization, it also comprises a variety of protective substances against contagious diseases. It might influence how the immune system develops [2].

Suppose introducing breast milk components significantly improves the immune system's development. Then, stopping breastfeeding too soon may contribute to the development

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of numerous chronic illnesses in later life (autoimmune disorders, for example) [3].

The mucosal membranes of the infant's respiratory and gut, where the majority of infections occur, are shielded by secretory IgA (SlgA). In addition, In addition to IgG and IgM antibodies, mother's milk also contains growth factors, complement factors, hormones, vitamins, cytokines, prostaglandins, granulocytes, macrophages, B and T lymphocytes, and other substances [4].

The majority of these substances in milk influence the typical microbial flora in the gut and aid in the infant's host defense. The immune system, along with other tissues and organs, is also affected [5].

2. Components of Human Breast Milk Immunological

Although they are still developing, the fetus and infant have immunological protections. As a compensatory mechanism, the immunoglobulin (Ig) G antibody produced by the mother provides some protection by overcoming the placental barrier [6].

These antibodies from mothers diminish during the first six to twelve months of a person's life after birth. However, breast milk can provide additional maternal protection for the newborn and infant [7].

Human breast milk has a significant amount of secretory IgA (sIgA). These antibodies are vulnerable to possible infections and stop them from adhering to the baby's cells because they were produced due to the mother's prior exposure to infectious agents [8].

Secretory IgA is designed to withstand proteolytic digestion and live in the mucosal membranes of the intestinal tract and respiratory system. In addition to neutralizing infectious pathogens, secretory IgA reduces the destructive influences of tissue inflammation that other antibody types may cause [9].

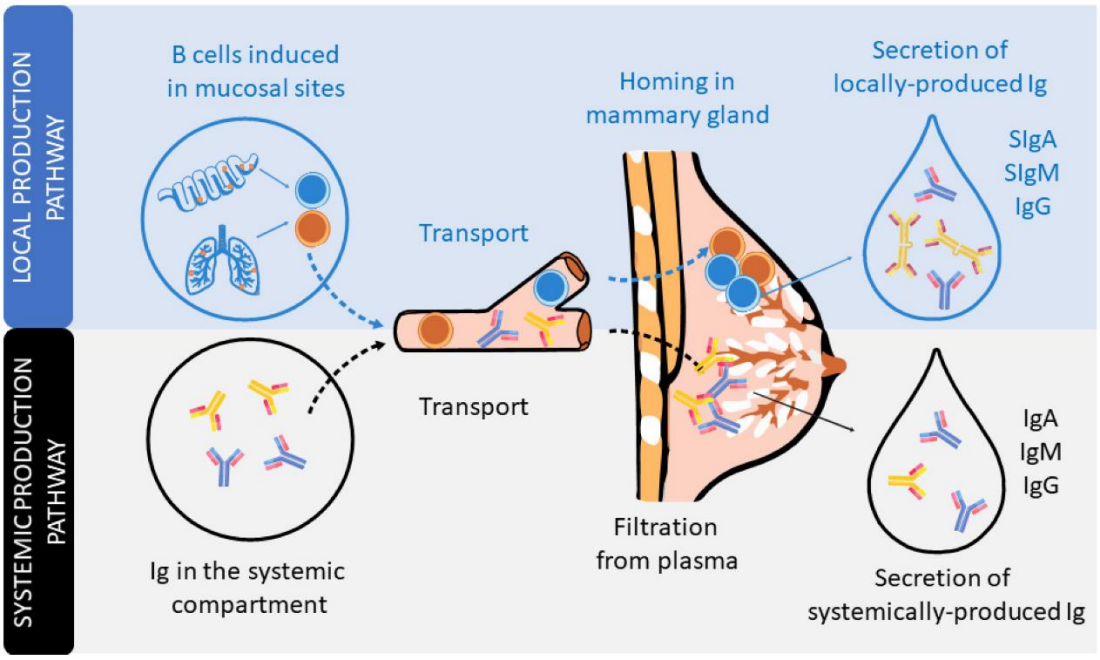

Fig 1. Immunoglobulin is secreted in the milk of humans. Diagram illustrating the local production pathway (including the secretory component and B cell homing to the mammary

gland) and the systemic production pathway (involving the filtration of monomeric IgGs from plasma) [4].

Leukocytes are detectable in human breast milk, particularly in the early colostrum. About 5×106 cells per millilitre are found in colostrum; this number drops by 10 in mature milk. The majority of the leukocytes in question include neutrophils and macrophages that phagocytize microorganisms [10].

Ten percent of the leukocytes found in human milk are lymphocytes, which include B cells that make antibodies, T cells, and natural killer cells. These cells have been shown to pass through the baby's digestive tract, where they are absorbed and have an effect on the immune system [11].

Breast milk includes several nonspecific substances with antibacterial properties and immunologic factors. Among these is the lysozyme enzyme, which prevents the growth of various types of bacteria through rupturing the bacterial cell wall's proteoglycan component [12]. Moreover, lactoferrin, among the most prevalent proteins found in human milk, inhibits the growth of bacteria by eliminating essential iron. Milk of humans has been demonstrated to contain nucleotides that improve an infant's immune system [13]. Although they only occur in tiny amounts in cow's milk, complex sugars comprise many human milk sugars. They can function as decoy receptors that prevent various microbial diseases from attaching [14].

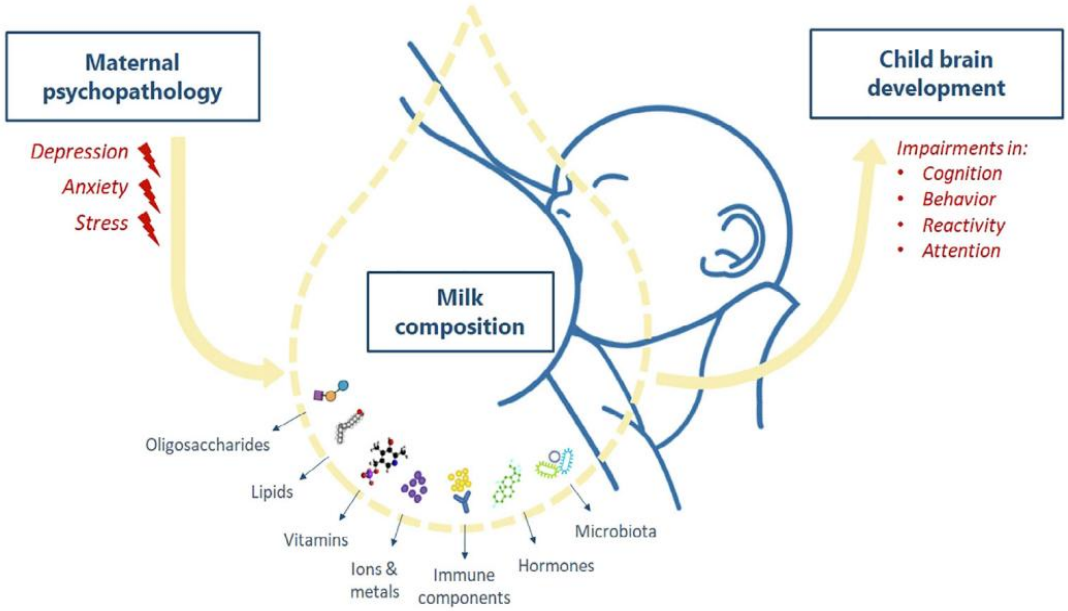

Fig. 2. Breast milk composition as a mediating factor between baby brain development and prenatal psychopathology. Depression, anxiety, and stress are examples of maternal perinatal psychopathologies that cause significant biological changes in the bodies of afflicted women. These changes can then cause changes in the typical makeup of breast milk. Breast milk is the best option for nursing since it gives the baby a variety of vital nutrients and bioactive substances that support the baby's healthy growth, including his neurodevelopment. Given its crucial role, a change in milk's composition can have a serious

negative effect on a child's brain development, affecting basic processes linked to behavior, cognition, attention, and response [15].

3. Breastfeeding and the Evolution of the Immune System

The thymus is a vital component regarding the immune response and is responsible for the healthy growth of T cells. The thymus selects immature T cells, or thymocytes, to eliminate cells that might be self-reactive [16]. Fewer about five per-cents how many thymocytes survive this "education" and are released as fully developed, T cells that are in circulation [17]. The thymus gland's pivotal involvement during the maturation the repertoire of T-cells raises the possibility of immediate influences of nursing in a vital the organ of the developing immunological system, even though It is unknown if thymic size has any clinical significance [18].

When they were four months old, breastfed babies had noticeably greater thymus glands compared to individuals who were only fed formula or occasionally breastfed, measuring the thymic index size with an ultrasonography approach. The three research teams' thymic sizes when born did not differ significantly [19].

By assessing at autopsy, thymic weights in children who lost their lives due to SIDS (sudden infant death syndrome) [20].

Later, attempted in order to make the findings of, hypothesizing that the organ's intrinsic plasticity is why thymic size in vivo varies from that measured at autopsy [21].

In a recent publication, Hasselbalch's group showed an association between breastfeeding and CD8+ T cells, supporting their earlier findings of increased thymus size with breastfeeding [22].

4. Human milk has anti-inflammatory properties

Numerous anti-inflammatory substances with antioxidant properties found in mother's milk can prevent granulocyte chemotaxis and suppress the synthesis of peroxidase, free radicals, and other chemicals. By reducing inflammation, these processes could improve the newborn's health [23]. Tumor necrosis factor-α (TNF-α), interleukin-1 (IL-1), and IL-6 are among the inflammatory, catabolic, and appetite-reducing cytokines that may be produced by the gram-negative bacteria that invade the neonate's gut and produce endotoxins [24]. Breastmilk may have the ability to stop this cytokine production. This could be one reason babies who are not breastfed lose much additional weight in the initial week of life as opposed to those who are [25]. Intriguingly, a key milk protein called lactoferrin can prevent endotoxins from causing human cells to generate IL-6. However, the antibacterial peptide lactoferricin and unnatural cow milk lactoferrin produce a comparable result. TNF-α, IFN-γ, transforming growth factor-ß (TGF-ß), IL-6, IL-10, and IL-1 are among the cytokines found in human milk. It is also possible to promote the generation of cytokines from milk cells [26]. Thus, the macrophages may create the milk T cells that can generate IL-2, IL-3, IL-4, IL-10, IFN-γ, and TNF-α, while IL-1α, IL-1p, IL-1ra (IL-1 receptor analogue), IL-6, IL-8, and IL-10. It is still uncertain if these cytokines, which can significantly affect immunological responses, can likewise affect a breastfed newborn's immune reactivity [27]. Their possible actions and presence are probably strictly regulated. As discussed above, one such control function would be the lactoferrin's cytokine-modulating impact [28].

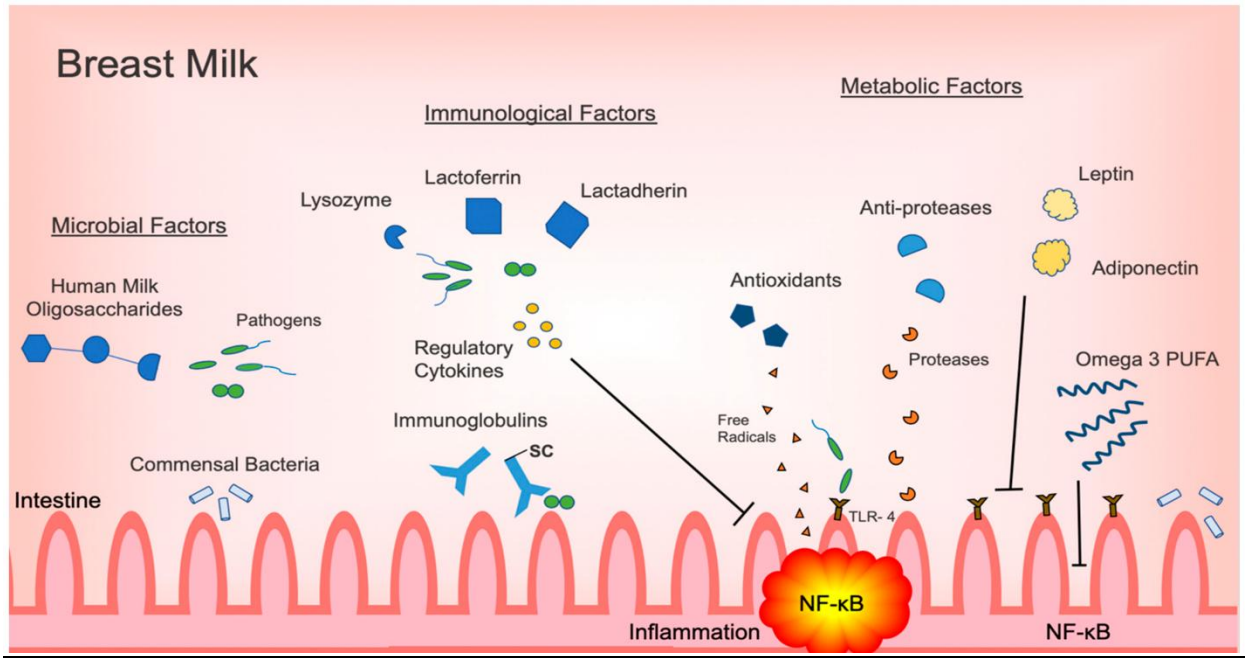

Fig 3. An overview of the metabolic, immunological, and microbiological aspects of breast milk that affect the control of inflammation of the intestines. Abbreviations include nuclear factor kappa B (NF-κB), polyunsaturated fatty acid (PUFA), secretory component (SC), and Toll-like receptor 4 (TLR4) [29].

5. Intestinal flora and breastfeeding

The impacts of breastfeeding on the intestinal flora are likely to have additional indirect consequences on the infant's host defense. Several potentially harmful aerobic bacterial strains rapidly colonize nonbreastfed neonates in underdeveloped areas, exhibiting a constant flux in the gut. Conversely, Swedish new-borns who are solely breastfed exhibit a stable, slower-developing gut flora, with a solitary *E. coli* strain or occasionally *Klebsiella* predominating among the aerobes [30]. Other European nations have similarly seen this variation at the richness of enter-bacterial flora between fed breast milk and non-breastfed new-borns [31]. Breastfeeding may favour some *E. coli* and the development of the adhesion known as type 1 fimbriae, which is not linked to virulence like other *E. coli* adhesions. This could be because type 1 fimbriae directly attach to phagocyte mannose residues, facilitating phagocytosis. Breastfeeding decreases other adhesions that could be virulence factors [32]. Specific milk components can stop some *E. coli* from adhering to host tissues, likely affecting the immunological response. *Pneumococci*, *H. influenzae*, *E. coli*, *V. cholerae* enterotoxin, and *Vibrio cholerae* are all bound by SlgA antibodies and various mimics of epithelial receptors are examples of anti-adherence chemicals found in milk [33]. It has recently been demonstrated that a milk component, most likely a glucosaminoglycan, prevents HIV from attaching to lymphocytes' CD4 receptor [34]. *E. coli* constant exposure to milk contents in the stomach of the breastfed child causes on-going surface structure alterations likely related to a decline in virulence [35]. Compared to non-breastfed new-borns, Infants who are breastfed have increased gut quantities of *Staphylococcus enterococcus*, *Staphylococcus epidermidis*, and *Staphylococcus aureus* [36]. Contrary to

popular belief, breastfed infants do not have greater bifidobacteria numbers. It appears likely that the immune response may differ between nonbreastfed new-borns, they are more susceptible to diarrhea and other diseases because of their diverse flora, which contains a variety of pathogens, for newborns who are breastfed, whose gut flora is steady, *E. coli* of little or no virulence dominates the aerobes [37]. It is also possible that different milk ingredients alter how some antigens are presented to the baby's immune system or how they are exposed to them [38].

6. Autoimmune disorders and breastfeeding

It is well recognized that T1D, or type 1 diabetes, is an immunologically mediated condition that destroys pancreatic β cells, ultimately resulting in total and permanent reliance on exogenous insulin [39]. Genetic susceptibility variations mainly influence the development of T1D, but the rise in prevalence over the previous 50 years clearly points to the significance of non-genetic variables [40]. More than 30 years have passed since the theory that breastfeeding might have prevented type 1 diabetes was first put forth, and other mechanisms have subsequently been suggested [41]. Although many theories have been put forth to explain breastfeeding's preventive effects, which include a stronger gut microbiome, later exposure to dietary antigens, and a decreased risk of infections that could cause diabetes, and proper gut maturing in the newborn, the exact explanation for why human milk may offer protection against type 1 diabetes is still unknown [42].

An endocrine pathological condition that affects both Type 2 diabetes in both youngsters and adults (T2D) has significantly increased in the past 30 years, especially in children around the world [43]. The ethology is very diverse and includes both environmental and genetic variables [44]. These environmental factors, such as food, can be changed to stop the disease from starting and progressing [45]. One of the main contributing factors to the progression of obesity and metabolic syndrome in the future is the lack of breastfeeding or its incorrect pattern [46]. In fact, prior research linked adequate breastfeeding to a 24% lower incidence of type 2 diabetes in children [47]. A systematic research found a direct correlation between the length of nursing and the newborn's risk of developing childhood Diabetes type 2 and obesity [48].

The most prevalent autoimmune inflammatory joint disease in the world, rheumatoid arthritis (RA), is distinguished through a unique structure of the joint and bones degradation [49]. Numerous researches have looked into the relationship between breastfeeding as well as the chance of having RA, only the findings have been mixed [50]. According to a study by Colebatch [51], positive result for rheumatoid factor new-borns were fewer possibilities than rheumatoid factor-negative infants to have been breastfed for more than three months in HLA-DR4-negative kids; however, this result wasn't observed in HLA-DR4-positive infants. A recent meta-analysis found of 1672 RA patients, [52] sought to determine the relationship link with the possibility of RA and breastfeeding. They discovered an opposite relationship within the population under study as a whole, linking a lower risk of RA regardless of whether breastfeeding lasted more than 12 months or less [53].

The most prevalent immune-mediated condition affecting multiple sclerosis (MS) affects young individuals' central nervous systems [54]. There may be a prodromal phase of multiple sclerosis (MS), as

evidenced by the fact that environmental influences affect long before symptoms appear [55]. Recent research has linked nursing for at least four months to a lower risk of developing multiple sclerosis (MS); nevertheless, other studies continue to question how extended breastfeeding affects MS risk [56].

In people who are genetically predisposed, eating gluten-containing cereals can result in celiac disease (CD), an immune system-mediated illness [57]. Although the tendency to celiac disease is determined mainly by genetic background, breastfeeding CD patients have been shown to have improved long-term health [58]. This may be because of the delayed addition of gluten to the regular diet, which increases the interval between the commencement of the illness and the introduction of gluten, prevents gut dysbiosis, and decreases the prevalence of gastrointestinal disorders in breastfed newborns [59]. Compared to newborns that were not breastfed when gluten was first introduced, breastfed newborns had a 52% lower risk of getting CD, according to a comprehensive review and meta-analysis that included all research conducted between 1966 and 2004 [60].

Ulcerative colitis and Crohn's disease are the two prominent symptoms of inflammatory bowel diseases (IBD), which are characterized as long-lasting inflammatory illnesses of the digestive system [61]. Although the precise cause of IBD is still unknown, it is thought that in genetically predisposed individuals, an irregular host immune response to gut flora is a contributing factor in the underlying process [62]. Having a family history of IBD is the leading risk factor for the condition. Since the young adult population has the highest probability of IBD, initial exposures may force future susceptibility [63]. Compounds found in human milk affect an infant's immunological tolerance and gut bacterial colonization in addition to providing infection protection [64]. Numerous studies discovered that breastfeeding protected against IBD, mostly in cases of early onset [65]. Other research, however, did not find a link between nursing and IBD [66]. Disparities in the duration of breastfeeding and its characterization (exclusive versus nonexclusive) may account for this result variability [67].

One significant method in which asthmatic patients' airways get inflamed has been identified as the allergic reaction that occurs to allergens that are prevalent in the environment [68]. Some asthmatic patients' sera included antibodies against β-adrenergic receptors, suggesting an autoimmune component to reducing βadrenergic responsiveness [69]. Numerous studies have up to this point indicated that extended, only breastfeeding lowers the incidence of asthma and wheeze during the early years of life [70]. The immunoglobulins, immunoglobulins specific to allergens, immunosuppressive cytokines, and immune complexes found in human milk may alter the immunological replies to allergens and reduce vulnerability to immune-dependent diseases [71].

Breastfeeding is common among patients with autoimmune thyroid disease (ATD), and it may help prevent the condition from developing, as evaluated by Fort in 1990 [72]. The results showed early infancy feedings with soy-containing formulas were more common, but there was no association between the duration and history of breastfeeding and the onset of ATD [73]. The Health Study of Nurses and the Health Study II of Nurses are two prospective cohort studies that [74] recently examined to determine the relationship between systemic lupus erythematosus (SLE) and breastfeeding. However, they could not find a statistically significant correlation between length and the incidence of SLE. More research may result in new connections and

approaches between immunological illnesses and breastfeeding [75].

7. Conclusion and perspectives

Worldwide, the advantages of breastfeeding are widely acknowledged. Several immune-mediated disorders benefit from breastfeeding, according to current scientific research, albeit some precise mechanisms are still unclear. Recent technological advances have made it possible to characterize the composition of human milk better, expanding our understanding of its potential and providing evidence for potential protective mechanisms against a wide range of illnesses that can have long-term adverse health effects. However, there is disagreement regarding the advantages of nursing for moms who have autoimmune illnesses. Unquestionably, prolactin plays a part in immune system modulation, and new research has linked hyperprolactinemia to lupus symptoms, disease activity, and relapses. Bromocriptine medication is helpful in situations of non-responsive lupus and in preventing postpartum flare-ups.

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تأثير الرضاعة الطبيعية على تقوية جهاز المناعة لدى الرضيع والوقاية من الأمراض المعدية

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الملخص

حليب الأم سائل بيولوجي شديد التعقيد يتكون من مكونات عديدة تؤدي أدوارًا متنوعة وأساسية في نمو الرضيع. ولا يزال البحث العلمي يكشف عن وظائف وآليات جديدة مرتبطة بعناصره النشطة بيولوجيًا. يمكن أن يتأثر الجهاز المناعي للرضيع الذي يرضع رضاعة طبيعية بشكل كبير بحليب الأم، لاحتوائه على عوامل مناعية تتفاعل بنشاط مع استجابات الرضيع المناعية النامية. بالإضافة إلى تعزيز فعالية اللقاحات ودعم نضج الجهاز المناعي، قد تساهم الرضاعة الطبيعية أحيانًا في تعديل أو كبح بعض الاستجابات المناعية، بما في ذلك رفض الأعضاء المزروعة وخطر الإصابة بأمراض المناعة الذاتية مثل داء السكري من النوع الأول. ويبدو أن الرضاعة الطبيعية توفر للمولود الجديد التغذية المثلى، مما يقلل من خطر نقص فيتامين (أ) ويدعم استجابة مناعية مناسبة ومنظمة جيدًا. علاوة على ذلك، فإن تنظيم الخصائص المضادة للالتهابات وتكوين ميكروبات معوية صحية من خلال الرضاعة الطبيعية يزيد من احتمالية أن يطور الرضيع جهازًا مناعيًا متوازنًا ويعمل بشكل سليم. مع ذلك، لا تزال الأدوار الدقيقة لعوامل النمو، والسيتوكينات، والأجسام المضادة الذاتية والمضادة لها، إلى جانب المكونات الأخرى المضادة للالتهابات الموجودة في حليب الأم، في تشكيل جهاز المناعة لدى الرضيع، بحاجة إلى مزيد من البحث العلمي المعمق

الكلمات المفتاحية: الرضاعة الطبيعية، حليب الأم، حديث الولادة، أمراض المناعة الذاتية