

Review Article**Review of Breastfeeding on Hypothyroidism in Infants and Early Childhood**

Pooya jafari doudaran.¹ Rasool Karimi Matloub². Abnoos mokhtari ardekani³. Saeed Karimi Matloub⁴

1 - Faculty of Medicine, Qom University of Medical Sciences, Qom, Iran.

2 - Students Research Committee, Arak university of Medical Sciences, Arak ,Iran.

3- Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Science, & Physiology Research Center, Kerman University of Medical Sciences, Kerman, I.R. Iran.

4 - Students Research Committee, Qom university of Medical Sciences,Qom ,Iran

***Corresponding Author:** Saeed Karimi Matloub, Students Research Committee, Qom university of Medical Sciences, Qom, Iran. ORCID: <https://orcid.org/0000-0002-0258-3137>

Abstract:

Introduction: Deficiency of thyroid hormones at any time from the first weeks of life to two years after birth can impair the growth and activity of brain cells and affect brain function and intelligence. Numerous pieces of evidence show the benefits of breastfeeding in the prevention of many medical conditions for the child. While congenital hypothyroidism is linked to prenatal circumstances, mostly related to maternal factors, later hypothyroid diseases in infants might be associated with the nutritional status of the newborn. In this study, we reviewed different aspects of breastfeeding or formula feeding concerning hypothyroidism in early childhood.

Methods: This was a narrative review study.

Results: our review abstracted the link between breastfeeding with hypothyroidism in three main topics of (i) iodine concentrations of the maternal milk and hypothyroidism in the infant; (ii) comparison of breastfeeding and bottle feeding for incidence of hypothyroidism or thyroid autoimmunity; and (iii) role of breastfeeding in treatment of the congenital hypothyroidism.

Conclusion: our study discussed the gain-a victory benefits of breastfeeding over the formulas and disadvantages of the soy-based formulas. In case of indications of formula nutrition in infants, iodine intake and supplementation should be considered.

Keywords: breastfeeding, thyroid hormones, infancy, formula, hypothyroidism

Submitted: 2 May 2022, Revised: 16 June 2022, Accepted: 3 July 2022

Introduction

Breast milk is ideal nutrition for the infant and contains a combination of vitamins, proteins, and fats and actually contains all the compounds needed for normal growth and development (1). It is best to start breastfeeding immediately after birth. This can guarantee successful breastfeeding in the future. In the last weeks before birth and a few days after birth, the breasts produce the first ideal milk called colostrum. This milk contains many antibodies, sugars, proteins, and minerals (1). One of the benefits of this milk is that it helps to improve the infant's digestive system and prepares it for digesting breast milk (2). The decision to breastfeed is a personal matter and the opinions of others can be involved and reputable centers recommend breastfeeding (4). But every mother and neonate is a unique human being, so it is up to the individual to decide based on the condition. Breastfeeding reassures parents that the baby is growing and developing properly. It also affects the baby in terms of mental development and increasing IQ (3). Numerous studies from around the world have shown that diarrhea, lower respiratory tract (lung) problems, and ear infections are less common and less severe in breastfed babies (5). Researchers have found that immune factors in colostrum or colostrum (the first milk produced in the mother's body) protect the baby against pathogens by creating a protective layer on the lining of the intestines, nose, and throat (6). The main immune factor here is secretory IgA (immunoglobulin A). This substance is present in large amounts in colostrum (colostrum), but it is also present in milk in smaller amounts in the following days. Due to the importance of colostrum in the health of the baby's mammary system, breastfeeding should be started immediately after the baby is born (7). Breast milk also protects the baby against inflammatory bowel disease at an older age. Several studies have shown that there is a link between not consuming breast milk in infancy

and developing inflammatory bowel diseases such as Crohn's disease and ulcerative colitis in adulthood (8). Another benefit of breastfeeding is that it protects against diseases such as eczema and asthma. Findings from several studies show that breastfeeding for 6 months or more reduces the risk of respiratory or food allergies (9,10); while shreds of evidence about the relationship between hypothyroidism and breastfeeding are less discussed.†

Despite the importance of timely and ongoing treatment of hypothyroidism, which necessitates continuous follow-up of these patients, there are reports even from developed countries that confirm the lack of treatment and care for infants and children with congenital hypothyroidism (11). It might contribute to a decrease in IQ and varying degrees of mental retardation, especially during adolescence and youth. In order to prevent any disorders and shortcomings in the proper treatment of these patients, it is necessary to educate parents on how to care for and follow the treatment of their children (12). Any change in maternal thyroid activity in early pregnancy and fetal thyroid activity in the second and third trimesters of intrauterine life and the first two years of life may be associated with adverse effects on pediatric brain development (13,14). Even babies who have a temporary increase in TSH at birth, which normally decreases in the weeks after birth, may have lower IQs than control babies (15).†

Literature review:†

Primary reports in the late 80s show pieces of evidence that breastfeeding is associated with considerably higher T4 and T3 levels than formula-fed babies (16). Latest studies also confirm that in comparison to human milk, infant formulae lack thyroid hormones (17).†

In comparison to mothers' milk from those without hypothyroidism, the nutritional content of mothers' milk from those with hypothyroidism might be different (18). breast milk is indeed an infant's primary supply of

iodine, and the amount of iodine in breast milk is highly influenced by the mothers' iodine consumption during lactation time (19). Breast milk iodine concentration (BMIC) in mothers and urine iodine concentration (UIC) in newborns and toddlers are the best ways to determine iodine status (20). The BMIC and iodine content of formula preparations used to feed babies determines the infant's iodine intake (21). Studies propose that a BMIC ranging from 100–150 µg/dl would be optimal for infancy neurodevelopmental growth (22). Higher levels of iodine exposure might cause hypothyroidism (23). A preterm newborn whose first screening thyroid function test findings were normal developed hypothyroidism after getting exposed to high levels of maternal iodine in breastmilk (24). In a 2021 study in Japan, for most newborns, iodine treatment for mothers who were previously diagnosed with Grave's disease had no effect on thyroid function. About 10% of newborns developed moderate subclinical hypothyroidism, however plasma TSH levels normalized after ceasing iodine treatment (25). Lewis et al. evaluated animal model of Baboons monkey for the difference between breastfeeding and formula in thyroid hormones concentrations in infants in the 90s. They found that formula-fed infants had greater plasma T3 levels than breast-fed infants (26). A study in premature infants showed that feeding with the milk of the mother of the premature newborn was linked to substantially greater thyroid hormone levels than those fed with formula, at around 4 weeks of age (27). Later, Conrad et al. bring the finding that babies fed soy formula exhibited longer spikes in TSH levels compared to non-soy formula (28). This negative consequence of soy-based formula was attributed to the similarity of its isoflavones with endogenous estrogens that might disrupt hormonal regulation of the newborn (29). Retrospective study of children with autoimmune thyroid disease showed that soy-based formula feeding was 31% in those

children compared to the 12-13% in healthy controls (30).¹

Congenital hypothyroidism and breastfeeding:¹ Congenital hypothyroidism is a relatively common disease. The disorder may be detected shortly after birth by neonatal screening tests or other diagnostic tests. In order to prevent the spread of complications such as mental retardation, learning disabilities and growth retardation, treatment should be started in the first week after the baby is born (11,12). The disease can be treated with oral thyroid hormone medications, including congenital heart disease, neonatal, premature infant death syndrome (13), and an increased risk of congenital malformations (11-13). Most babies with hypothyroidism have a normal appearance at birth and have no specific clinical symptoms, so if the diagnosis is based solely on clinical signs, the baby will suffer irreversible complications such as deafness and mental retardation. This disease can be prevented only when the disease is diagnosed in infancy (11-13). As a result, screening measures are necessary for early and timely diagnosis of the disease. Congenital hypothyroidism is the most common endocrine disorder of infants and the most common preventable causes of mental retardation in infants are: Deficiency of thyroid hormone in the fetus leads to disorders in important organs such as the central nervous system and skeletal system. Although most of these infants appear normal at birth, but new scientific information has shown that the delay in treatment, leads to severe developmental disorders and irreversible mental retardation. Loss of IQ due to this disease can be prevented only when the disease is diagnosed very early and ideally in the first days of life (11-13). Congenital hypothyroidism in infants and rapid initiation of pre-levothyroxine treatment significantly increase the mental development and linear growth of these children and is considered one of the preventive medicine programs in which the profit-to-cost ratio is positive (34). Genetic

factors in the transient type and environmental factors in the permanent type are more prevalent. The identification of these factors is very helpful in controlling the disease and its complications. In some countries of the world, screening tests for newborns are mandatory at birth (31).¹

Congenital hypothyroidism can be divided into permanent and transient groups. Congenital hypothyroidism refers to the time when TSH is greater than 5 L / μu of the foot sample in a 3- to 7-day-old infant and is confirmed by intravenous TSH was 5.6 g / dl. Less T4 and 10 μu / L and transient hypothyroidism, normalization of TSH (less than 5 L / μu) intravenously in neonatal congenital hypothyroidism before the age of three (32).¹ Congenital hypothyroidism screening began for the first time in 1972 in North America and gradually spread to other countries. Today, in most developed countries of the world, this test is performed routinely. Reduce the socio-economic burden of the disease (33) The results of psychometric psychiatric tests showed that the IQ of children with congenital hypothyroidism treated at the time was similar to the normal population.¹

Comparison of hypothyroid newborns who were breastfed or formula-fed revealed that the negative consequences of congenital hypothyroidism are not lessened by breastfeeding (34).¹

Conclusion:

Our review summarized the relationship between breastfeeding and hypothyroidism in three main areas: (i) maternal milk iodine concentrations and infant hypothyroidism; (ii) comparison of breastfeeding and bottle feeding for hypothyroidism or thyroid autoimmunity; and (iii) role of breastfeeding in the treatment of congenital hypothyroidism. Our research looked at the advantages of nursing over formulas as well as the drawbacks of soy-based formulas. When newborns show signs of

formula feeding, iodine consumption and supplements should be evaluated.¹

References:

1. Lyons KE, Ryan CA, Dempsey EM, Ross RP, Stanton C. Breast milk, a source of beneficial microbes and associated benefits for infant health. *Nutrients.* 2020 Apr;12(4):1039.¹
2. Blesa M, Sullivan G, Anblagan D, Telford EJ, Quigley AJ, Sparrow SA, Serag A, Semple SI, Bastin ME, Boardman JP. Early breast milk exposure modifies brain connectivity in preterm infants. *Neuroimage.* 2019 Jan 1;184:431-9.¹
3. Ojo-Okunola A, Nicol M, Du Toit E. Human breast milk bacteriome in health and disease. *Nutrients.* 2018 Nov;10(11):1643.¹
4. Erick M. Breast milk is conditionally perfect. *Medical hypotheses.* 2018 Feb 1;111:82-9.¹
5. Boix-Amorós A, Collado MC, Van't Land B, Calvert A, Le Doare K, Garssen J, Hanna H, Khaleva E, Peroni DG, Geddes DT, Kozyrskyj AL. Reviewing the evidence on breast milk composition and immunological outcomes. *Nutrition reviews.* 2019 Aug 1;77(8):541-56.¹
6. Bardanzellu F, Peroni DG, Fanos V. Human breast milk: bioactive components, from stem cells to health outcomes. *Current Nutrition Reports.* 2020 Mar;9(1):1-3.¹
7. Ramiro-Cortijo D, Singh P, Liu Y, Medina-Morales E, Yakah W, Freedman SD, Martin CR. Breast milk lipids and fatty acids in regulating neonatal intestinal development and protecting against intestinal injury. *Nutrients.* 2020 Feb;12(2):534.¹
8. Xu L, Lochhead P, Ko Y, Claggett B, Leong RW, Ananthakrishnan AN. Systematic review with meta-analysis: breastfeeding and the risk of Crohn's disease and ulcerative colitis. *Alimentary pharmacology & therapeutics.* 2017 Nov;46(9):780-9.¹
9. Lodge CJ, Tan DJ, Lau MX, Dai X, Tham R, Lowe AJ, Bowatte G, Allen KJ, Dharmage SC. Breastfeeding and asthma and allergies:

a systematic review and meta-analysis. *Acta Paediatrica*. 2015 Dec;104:38-53.†

10. Oddy WH. Breastfeeding, childhood asthma, and allergic disease. *Annals of Nutrition and Metabolism*. 2017;70(Suppl. 2):26-36.†
11. Rovet J, Daneman D. Congenital hypothyroidism. *Pediatric Drugs*. 2003 Mar;5(3):141-9.†
12. Rastogi MV, LaFranchi SH. Congenital hypothyroidism. *Orphanet journal of rare diseases*. 2010 [Dec];5(1):1-22.†
13. Kempers MJ, van Tijn DA, van Trotsenburg AP, de Vijlder JJ, Wiedijk BM, Vulsmma T. Central congenital hypothyroidism due to gestational hyperthyroidism: detection where prevention failed. *The Journal of Clinical Endocrinology & Metabolism*. 2003 Dec 1;88(12):5851-7.†
14. Vulsmma T, Gons MH, de Vijlder JJ. Maternal-fetal transfer of thyroxine in congenital hypothyroidism due to a total organification defect or thyroid agenesis. *New England Journal of Medicine*. 1989 Jul 6;321(1):13-6.†
15. Elmlinger MW, Kühnel W, Lambrecht HG, Ranke MB. Reference intervals from birth to adulthood for serum thyroxine (T4), triiodothyronine (T3), free T3, free T4, thyroxine binding globulin (TBG) and thyrotropin (TSH). *Clinical Chemistry and Laboratory Medicine (CCLM)*, vol. 39, no. 10, 2001, pp. 973-979. <https://doi.org/10.1515/CCLM.2001.158>†
16. Hahn HB, Spiekerman AM, Otto WR, Hossalla DE. Thyroid function tests in neonates fed human milk. *American journal of diseases of children*. 1983 Mar 1;137(3):220-2.†
17. Vass RA, Kiss G, Bell EF, Miseta A, Bódis J, Funke S, Bokor S, Molnár D, Kósa B, Kiss AA, Takács T. Thyroxine and Thyroid-Stimulating Hormone in Own Mother's Milk, Donor Milk, and Infant Formula. *Life*. 2022 Apr 14;12(4):584.†
18. Lopes FD, Soares FV, Silva DA, Moreira ME. Do Thyroid Diseases during Pregnancy and Lactation Affect the Nutritional Composition of Human Milk?. *Revista Brasileira de Ginecologia e Obstetrícia*. 2020 Dec 21;42:752-8.†
19. Andersson M, Braegger CP. The Role of Iodine for Thyroid Function in Lactating Women and Infants. *Endocrine reviews*. 2021 Nov 17.†
20. Ares S, Quero J, Sáenz-Rico B, Morreale de Escobar G. Hypothyroidism and thyroid function alterations during the neonatal period. A New Look at Hypothyroidism. D. Springer (Ed.), InTech. 2012 Feb 17.†
21. Azizi F, Smyth P. Breastfeeding and maternal and infant iodine nutrition. *Clinical endocrinology*. 2009 May;70(5):803-9.†
22. Azizi F, Smyth P. Breastfeeding and maternal and infant iodine nutrition. *Clinical endocrinology*. 2009 May;70(5):803-9.†
23. Andersson M, Braegger CP. The Role of Iodine for Thyroid Function in Lactating Women and Infants. *Endocrine reviews*. 2021 Nov 17.†
24. Smith VC, Svoren BM, Wolfsdorf JI. Hypothyroidism in a breast-fed preterm infant resulting from maternal topical iodine exposure. *The Journal of pediatrics*. 2006 Oct 1;149(4):566-7.†
25. Hamada K, Mizokami T, Maruta T, Higashi K, Konishi K, Momotani N, Tajiri J. Thyroid function of infants breastfed by mothers with Graves disease treated with inorganic iodine: a study of 100 cases. *Journal of the Endocrine Society*. 2021 Feb;5(2):bvaal87.†
26. Lewis DS, McMahan A, Mott GE. Breast feeding and formula feeding affect differently plasma thyroid hormone concentrations in infant baboons. *Neonatology*. 1993;63(5):327-35.†
27. Oberkotter LV, Pereira GR, Paul MH, Ling H, Sasanow S, Farber M. Effect of breast-feeding vs formula-feeding on circulating

thyroxine levels in premature infants. *The Journal of pediatrics (USA)*. 1985;.

28. Conrad SC, Chiu H, Silverman BL. Soy formula complicates management of congenital hypothyroidism. *Archives of disease in childhood*. 2004 Jan 1;89(1):37-40.†

29. Setchell KD, Zimmer-Nechemias L, Cai J, Heubi JE. Exposure of infants to phytoestrogens from soy-based infant formula. *The Lancet*. 1997 Jul 5;350(9070):23-7.†

30. Fort P, Moses N, Fasano M, Goldberg T, Lifshitz F. Breast and soy-formula feedings in early infancy and the prevalence of autoimmune thyroid disease in children. *Journal of the American College of Nutrition*. 1990 Apr 1;9(2):164-7.†

31. Heyerdahl S, Oerbeck B. Congenital hypothyroidism: developmental outcome in relation to levothyroxine treatment variables. *Thyroid*. 2003 Nov 1;13(11):1029-38.†

32. Grüters A, Krude H. Update on the management of congenital hypothyroidism. *Hormone Research in Paediatrics*. 2007;68(Suppl. 5):107-11.†

33. Fisher DA, Dussault JH, Foley Jr TP, Klein AH, LaFranchi S, Larsen PR, Mitchell ML, Murphey WH, Walfish PG. Screening for congenital hypothyroidism: results of screening one million North American infants. *The Journal of pediatrics*. 1979 May 1;94(5):700-5.†

34. Letarte J, Guyda H, Dussault JH, Glorieux J. Lack of protective effect of breast-feeding in congenital hypothyroidism: report of 12 cases. *Pediatrics*. 1980 Apr;65(4):703-5.†