

Breastfeeding and fatty liver — is there any association?

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ABSTRACT

The campaign to promote the natural feeding of infants, at least for the first six months of life, conducted over recent years has deep justification from a medical point of view. Numerous gynecological and pediatric societies around the world recommend breastfeeding as the most appropriate way of feeding infants. It has been proven that the benefits of this type of nutrition go beyond nutritional aspects, proper growth and development. The list of long-term metabolic benefits, which include reducing the incidence of obesity, allergies, infections and diabetes, is constantly growing. It has been shown that the method of feeding infants using various mechanisms may influence the tendency of the liver to accumulate fatty compounds and develop fatty liver disease with its metabolic consequences leading to liver failure, cirrhosis and hepatocellular carcinoma. This is an important discovery due to the growing obesity epidemic in adults and children. Metabolic dysfunction — associated fatty liver disease (MAFLD) has become the most common cause of chronic liver disease, affecting 25% of the global population. The results of studies conducted in recent years have shown the protective effect of breastfeeding on the risk of developing MAFLD later in life in both children and breastfeeding women. New scientific reports provide the basis for qualifying breastfeeding as a modifiable risk factor for MAFLD.

Keywords: breastfeeding; metabolic diseases; fatty liver

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INTRODUCTION

The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) recommend breastfeeding as the most appropriate way to feed newborns and infants.

It should be the sole method of nutrition for the first six months of life, beginning within the first hour after birth [1]. The same recommendations are also presented by the American College of Obstetricians and Gynecologists (ACOG), the American Academy of Pediatrics (AAP) and the Committee on Nutrition of the European Society of Gastroenterology, Hepatology and Nutrition of Children the European Society for Pediatric Gastroenterology Hepatology and Nutrition, (ESPGHAN) [2, 3]. The benefits of breastfeeding go beyond nutritional aspects. In addition to conditioning

the proper growth and development of the young body, it brings several health benefits. It has been proven that naturally fed children are less likely to suffer from obesity, allergies, infections and diabetes [4]. According to data published by WHO, overweight and obesity occur in 5.7% to 40% of children, depending on the population studied. It has been estimated that obesity may be a problem for up to approximately 40 million children under five years of age, with prevalence in younger children [5].

Obesity-related diseases are a risk factor for the development of metabolic dysfunction associated with fatty liver disease — MAFLD [6]. It is characterized by excessive accumulation of fat in the liver, associated with insulin resistance and obesity, defined as the histological presence of hepatic

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steatosis > 5% of hepatocytes in the absence of alcohol abuse. Initially, the disease was called nonalcoholic fatty liver diseases (NAFLD) — and this term is used in many earlier scientific papers — but recently the nomenclature was changed to MAFLD. Metabolic dysfunction associated with fatty liver disease is a serious public health problem because it is a risk factor for many metabolic diseases, including cardiovascular diseases, which are still the leading cause of death in the world [6], type 2 diabetes, and, except of all, is the most frequently diagnosed liver disease in humans [7]. The excessive accumulation of lipids in the liver leads to impaired functioning of this organ and, consequently, to fibrosis and the development of hepatocellular carcinoma [8, 9].

A characteristic feature of MAFLD is fatty liver as a result of disturbances in lipid homeostasis in the liver. Excessive amounts of free fatty acids accumulated as a result of increased lipolysis of adipose tissue and *de novo* lipogenesis exceed the ability of the liver to oxidize them or secrete in the form of very low-density lipoproteins. This set of metabolic disorders is a consequence of the coincidence of various environmental, genetic and epigenetic factors [6]. MAFLD has become the most common chronic liver disease, affecting 25% of adults in the world [2]. According to the results of general population studies, it is diagnosed in 7.6–9.6% of children. However, studies conducted in pediatric obesity clinics indicate a higher frequency of up to 34.2% [6].

BREASTFEEDING — METABOLIC EFFECT IN CHILDREN

The fetal period and the first few months after birth are the “plastic” age. It is often referred to as a “window of opportunity”. This initial period of life is particularly important because the intensively developing organism is highly susceptible to environmental pressure and must adapt to changing stimuli [10]. The research conducted so far allows us to conclude that prenatal, perinatal and postnatal events may have a significant impact on an individual’s human metabolic health, both in the medium- and long-term perspectives.

Breastfeeding remains the most appropriate alimentary pattern for infants. Breast milk has a unique composition best suited to the baby’s needs. It contains numerous bioactive compounds, including oligosaccharides, which protect against the development of many disorders occurring in childhood, including obesity, type 2 diabetes and other metabolic diseases [5]. The composition of breast milk is not constant. It changes dynamically depending on various variables, such as gestation, the postpartum period and the suckling period. Although the main function of milk is to provide nutrients for the infant’s intensive development, mother’s milk has also been described as the first

probiotic food. It contains over 200 phylotypes of probiotic bacteria [4]. Additionally, human oligosaccharides promote the growth of beneficial bacteria *Bifidobacteria* and *Bacteroides* [5]. Feeding a newborn this way not only enriches the microbiota but also has a real impact on the composition and activity of the intestinal flora. This may be crucial in preventing the development of metabolic syndrome later in life [4]. Scientific research has shown that the composition of the “adult-type” microbiota depends on many factors including perinatal conditions, which include the method of delivery, type of breastfeeding and the use of antibiotics. Additionally, it has been shown that the mother’s diet, age, metabolic status, family genetics and lifestyle have a strong influence on the infant’s intestinal flora [10].

Intestinal dysbiosis, *i.e.* permanent modification of the microbiome, has been recognized, based on the results of research in experimental adult murine models and adult patients, as an important factor in the development of many systemic diseases, for example obesity and MAFLD. Unfortunately, it has been poorly documented in the pediatric population so far [6]. It has been proven that intestinal flora affects the use of nutrients supplied with food, the immune system, and the expression of host genes. Therefore, it is reasonable to assume that microbiota may influence the development of MAFLD at a young age.

Although there is not enough data supporting the relationship between neonatal feeding and the development of MAFLD later in life, the type of infant feeding, and the duration of breastfeeding may have a profound impact on the risk of developing MAFLD. The protective effect of breast-feeding on the development of NAFLD was observed in 2009 by Nobili et al. [11], which examined the relationship between infant feeding pattern (breastfeeding vs formula feeding and duration of breastfeeding) and the development of fatty liver in children aged from 3 to 18 years. Of the 191 study participants with confirmed NAFLD, 91 were naturally breastfed and the duration of breastfeeding was usually around 8 months. It was noted that the probability of developing non-alcoholic steatohepatitis (NASH), a more severe form of NAFLD, and liver fibrosis was lower in breastfed children and decreased with the length of breastfeeding. The benefit of breastfeeding was also demonstrated in the Western Australian Pregnancy (Raine) Cohort Study, where just over 15% of 1170 adolescents aged 17 years were diagnosed with fatty liver by ultrasound. It was estimated that breastfeeding for at least 6 months without starting formula before 6 months of age was independently associated with a 40% lower risk of developing NAFLD in adolescence. On the other hand, early introduction of formula feeding, before 6 months of age, was associated with a 70% higher risk of NAFLD [7]. The results of the Ragama Health Study, a cohort study of 499 14-year-olds living in an urban area

of Sri Lanka, indicated a short period of breastfeeding (less than 4 months) as a factor significantly associated with a higher risk of NAFLD [12]. The association of artificial infant feeding with the severity of adverse liver changes in children aged 5–12 years with biopsy-proven NAFLD was reported in a cross-sectional study of 182 patients at the Bambino Gesù Children's Hospital in Rome. The results of an extensive analysis considering many factors, including pregnancy, genetic, familial, nutritional and lifestyle factors have identified the lack of breastfeeding among the significant factors predisposing to the development of NASH and liver fibrosis [13]. Ayonrinde et al. [7], analyzing a group of 1170 adolescents aged 17 years in the Western Australian Pregnancy (Raine) Cohort Study, concluded that to reduce the risk of NAFLD being diagnosed during adolescence, it is recommended to breastfeed for at least 6 months, avoid early feeding with complementary milk and achieving the mother's normal BMI before pregnancy. These data suggest that infants who breastfed for less than six months were much more likely to develop NAFLD later in life. The latest systematic review on the relationship between breastfeeding and the development of NAFLD in later life has led to the conclusion that breastfeeding may be a protective factor for the development of NAFLD if it lasts long enough, *i.e.* at least 6 months [14]. On the other hand, Abeysekera et al. [10] in their parental negative control study did not replicate previous work that found a strong association between neither any nor exclusive over six months breastfeeding nor NAFLD.

Except of breastfeeding, extensive studies were focused on assessing the relationship between the mother's nutritional status and the occurrence of metabolic diseases, such as obesity, type 2 diabetes and non-alcoholic fatty liver disease (NAFLD) in her offspring [10].

BREASTFEEDING

— METABOLIC EFFECTS IN MOTHERS

The relationship between infant feeding and the risk of developing chronic diseases in mothers has been the subject of numerous studies for many years. During recent studies, the protective effect of breastfeeding on the development of NAFLD in the mother has also been documented. In a study by Ajmera et al. [15] with the participation of 844 women, it was shown that a longer duration of lactation, especially longer than 6 months, is associated with a significantly lower probability of NAFLD in middle age. Similar conclusions were drawn from the results of a nationwide study by Goh et al. carried out on a cohort of nearly 7,000 Korean women. It was noted that women who breastfed for more than one month were less likely to develop NAFLD. Moreover, a gradual decrease in the risk of NAFLD was shown with the extension of the lactation period [16].

The benefits of breastfeeding for the mother have not been as extensively documented as in the case of infants. Future research should determine the effect of lactation on the development of NAFLD and other liver diseases.

SUMMARY

Metabolic dysfunction associated with fatty liver disease is an increasing cause of cirrhosis and hepatocellular carcinoma and the most common liver disease in children, which can represent an aggressive phenotype of the disease and lead to the requirement for liver transplantation. The constantly growing incidence of MAFLD in Western countries and Asia in the absence of effective therapy prompts the search for modifiable risk factors. The evidence of a protective effect of breastfeeding on MAFLD for both mothers and their offspring, cited in this article, extends the list of potential long-term benefits of breastfeeding and may be an argument to include breastfeeding as a weapon in the fight against the growing MAFLD epidemic.

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Author contributions

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Conflict of interest

The authors declare that they have no competing interests.

Supplementary material

None.

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