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Breastfeeding impact on kidney health : updated evidence

Impact de l'allaitement maternel sur la santé rénale : mise à jour

Hakim RAHMOUNE.[1,2], *Nada BOUTRID.*[1,3], *Hala BOUTRID.*[1,4]

[1]LIRSSEI Research Laboratory, Faculty of Medicine, University of Setif-1, Algeria. [2]Department of Pediatrics, University Hospital of Setif, Algeria. [3]Department of Pediatrics, EHS El Eulma, Algeria. [4]Department of Obstetrics-Gynecology, M.L. Debaghine University Hospital of Bab-El-Oued, Algiers, Algeria

Corresponding author: rahmounehakim@gmail.com
ORCID: 0000-0002-9604-3675

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Abstract Breastfeeding is extensively acknowledged for its numerous health benefits, particularly during the critical early stages of life. This article synthesizes contemporary evidence regarding the influence of breastfeeding on renal function and health, drawing from a diverse array of international studies. The findings consistently demonstrate that breastfeeding is associated with enhanced renal growth, improved kidney function, and a diminished risk of various renal pathologies. Specifically, breastfed infants exhibit significantly larger renal volumes and elevated glomerular filtration rates, compared to their formula-fed counterparts. Moreover, exclusive breastfeeding correlates with lower incidences of urinary tract infections and nephrotic syndrome. This review reaffirms the critical importance of breastfeeding for both immediate infant health, and its potential to shape renal health throughout life, thereby, supporting the Developmental Origins of Health and Disease (DOHaD) hypothesis, and emphasizing the necessity for ongoing advocacy in this domain.

Key words: Breastfeeding, *Kidney, Infant, DOHaD*

Résumé L'allaitement maternel est reconnu pour ses innombrables bienfaits sur la santé, notamment durant les premières périodes critiques de la vie. Cet article, s'appuyant sur une panoplie d'études internationales, synthétise les plus récentes preuves concernant l'impact positif de l'allaitement maternel sur la fonction et la santé

rénales. En effet, ces études ont démontré systématiquement que l'allaitement maternel est associé à une meilleure croissance rénale, une optimisation de la fonction rénale et un risque réduit de diverses pathologies rénales. Ainsi, les nourrissons allaités au sein présentent des volumes rénaux significativement plus importants et des taux de filtration glomérulaire plus élevés par rapport à ceux nourris au lait artificiel. De plus, l'allaitement au sein exclusif est corrélé à une incidence plus faible d'infections urinaires et de syndrome néphrotique. Cette mise au point met donc en exergue l'importance majeure de l'allaitement maternel dans la santé rénale à court terme, chez les nourrissons et son aptitude à façonner le pronostic néphrologique, tout au long de la vie adulte, soutenant ainsi l'hypothèse des Origines Développementales de la Santé et des Maladies (*Developmental Origins of Health and Disease, DOHaD*) et soulignant la nécessité d'un plaidoyer continu en faveur du lait de mère.

Mots-clés: *Allaitement maternel, Rein, Nourrisson, DOHaD*

Introduction

The significance of breastfeeding extends beyond mere nutrition; it plays a pivotal role in shaping long-term health outcomes, particularly concerning metabolic, cardiovascular and other non-communicable diseases [1,2]. Human milk is uniquely formulated to meet the nutritional needs of infants, providing, not only essential macronutrients, but also bioactive compounds that profoundly influence growth and development [3,4]. In fact, breast milk has a unique composition that differs significantly from artificial milk, including variations in macro- and micronutrient profiles, as well as, exclusive bioactive components that encompass a broad array, including human milk oligosaccharides, lactoferrin, immune mediators, growth factors, cytokines, and stem cells—elements entirely absent in formula milk (3-6). These components, among others, play a crucial role in contributing to the significant benefits of human milk on organ development and physiological functions, with lasting effects that extend from childhood into adulthood. This unique composition further underscores the unparalleled value of breast milk in promoting lifelong health outcomes.

Recent studies have begun to elucidate the specific impacts of breastfeeding on kidney health, revealing both immediate and long-term benefits [7,8].

By synthesizing findings from recent literature, this paper seeks to reinforce the importance of breastfeeding as a foundational element in pediatric healthcare. It also situates breastfeeding within the framework of the Developmental Origins of Health and Disease (DOHaD), emphasizing its potential to influence lifelong renal health, and advocating for continued investment in breastfeeding promotion as a vital public health strategy [9,10].

Particularly, this review aimed to provide a comprehensive overview of the breastfeeding effects on kidney function and health, focusing on various critical aspects, such as renal growth, functional capacity, calcium excretion, infection rates, and risk of nephropathies.

Breastfeeding, DOHaD and kidneys

Developmental Origins of Health and Disease (DOHaD) is a comprehensive framework that posits that environmental factors during critical periods of development, particularly in utero and early life, can significantly influence health outcomes later in life. This concept emerged from the work of David Barker and colleagues, who identified correlations between adverse conditions in early life and the incidence of chronic diseases, such as cardiovascular diseases, diabetes, and obesity in adulthood [11].

The DOHaD hypothesis emphasizes the role of epigenetic mechanisms, which are chemical modifications to DNA that affect gene expression without altering the DNA sequence itself. These modifications can be influenced by various factors, including nutrition, stress, and exposure to toxins during critical developmental windows [11].

Breastfeeding is recognized as a vital component of DOHaD due to its profound impact on infant development and long-term health outcomes [1,2,11]. The composition of breast milk provides essential nutrients, antibodies, and bioactive compounds that support, not only, physical growth, but also, cognitive and immune system development.

Nutritional benefits

Breastfeeding promotes optimal growth and development during infancy. It has been associated with

a reduced risk of obesity, type 2 diabetes, and cardio -vascular diseases later in life [12].

Immunological protection

Breast milk contains immunoglobulins and other immune factors that help protect infants from infections, which can have long-term effects on health. For instance, early exposure to infections can lead to inflammatory responses that may program the immune system in ways that predispose individuals to chronic disease [12].

Psychosocial aspects

The act of breastfeeding also fosters bonding between mother and child, contributing to emotional well-being. This psychosocial aspect is crucial for healthy development and can influence stress responses later in life [13,14].

Additionally, breastfeeding is closely aligned with the United Nations Sustainable Development Goals (SDGs), and plays a crucial role in achieving several of these objectives : it improves nutrition, supporting SDG 2 (Zero Hunger); aids in preventing child mortality and reducing the risk of non-communicable diseases, which corresponds to SDG 3 (Good Health and Well-being); and promotes cognitive development and educational success, linked to SDG 4 (Quality Education). Furthermore, breastfeeding acts as a driving force for eliminating poverty, encouraging economic growth, and decreasing inequalities [15,16].

The optimal duration of breastfeeding is a topic of ongoing debate; however, a growing body of evidence supports the World Health Organization recommendation to breastfeed for up to two years or longer (17,18).

Research indicates that extended breastfeeding correlates with a range of health benefits for both infants and mothers. Notably, a frequently cited ideal duration for breastfeeding is 12 months, which is recognized globally for its significant positive impact on infant health and development (19,20).

In the other hand, kidneys are particularly susceptible to programming effects during early life : research indicates that adverse conditions encountered during fetal development—such as maternal malnutrition or exposure to toxins—can lead to both structural and functional changes in kidneys, a phenomenon known as ‘‘renal programming’’ [21].

One key mechanism involved in renal programming is oxidative stress, which arises from an imbalance between reactive oxygen species (ROS) and antioxidant defenses. This imbalance can result from poor maternal nutrition or environmental exposures during pregnancy. Oxidative stress has been shown to negatively impact kidney development, increasing the risk of hypertension and chronic kidney disease later in life [22].

Emerging evidence suggests that interventions such as perinatal antioxidant therapy may help alleviate the detrimental effects of oxidative stress on kidney development. These interventions aim to "reprogram" the kidney response to early-life stressors, potentially preventing the onset of kidney diseases [23].

Thus, the DOHaD framework underscores the importance of early-life factors such as breastfeeding on long-term kidney health, and paves the way to a possible improvement of renal health outcomes across generations [24].

Impact of breastfeeding on renal growth

Breastfeeding has emerged as a critical factor influencing renal development, with far-reaching implications for lifelong health. Nephrogenesis, a process completed by 36 weeks of gestation, determines the nephron endowment, which cannot be replenished postnatally. This finite nephron number underscores the importance of supportive postnatal nutrition to optimize renal growth and function [25-27].

Breast milk provides bioactive peptides and growth factors, such as insulin-like growth factor-1 (IGF-1), and hepatocyte growth factor, which facilitate renal cell proliferation and repair mechanisms [28-29]. Studies in animal models have revealed that milk-derived growth factors promote angiogenesis within the renal cortex, enhancing nutrient delivery and waste filtration efficiency [30-31].

The role of breastfeeding in preserving renal size and structure is supported by robust clinical evidence. A pioneering study initially found that breastfed infants had smaller kidneys than those fed exclusively with infant formula. The mean difference in kidney volume between the high-protein group and the other groups (namely, the breastfed and low-protein groups) was of 10% [32]. A multicenter trial conducted in 2011 (EU Childhood Obesity Project) confirmed that a high protein content in infant formula increases kidney size at six months of age, compared to maternal milk [33]. Later, in 2023, follow-up data from the same trial after an 11-year period indicated that higher protein formula-fed infants had greater renal volume ($\beta = 8.71$, 95% CI 0.09–17.33, $p = 0.048$), and elevated systolic blood pressure ($\beta = 3.43$, 95% CI 0.78–6.08, $p = 0.011$), compared to breastfed infants [34].

Additionally, another study published in 2015 as part of the population-based prospective cohort "Generation R Study" (n=5043) in Rotterdam, the Netherlands, found that children who were never breastfed exhibited smaller combined renal volumes (-2.69 [95% CI, -4.83 to -0.56] cm^3) [35]. Interestingly, from the same 'Generation R Study,' protein intake at one year (n=2968) was not independently associated with kidney size or function at the age of 6 years, highlighting the greater impact of breastfeeding during the first months of life (*i.e.* before introducing solid food) [36].

Collectively, these studies underscore the impact of protein content in infant feeding on renal development and long-term health outcomes. They highlight the importance of breastfeeding and careful formulation of artificial milk in pediatric care; renal growth trajectories in breastfed infants align with natural developmental tempos, minimizing the risk of hypertensive and metabolic complications later in life.

Impact of breastfeeding on renal function

The functional maturation of the kidney is a cornerstone of infant development, with early-life nutrition playing a decisive role in optimizing this process. In the Dutch prospective cohort from the previously mentioned Generation R study, in comparison to children who were breastfed for their entire infancy, those who were never breastfed exhibited lower estimated glomerular filtration rates (−2.42 [95% CI, −4.56 to −0.28] mL/min/1.73 m^2) by the time they reached a median age of 6 years, and this association was explained by the aforementioned effect on kidney volume [35].

In fact, the composition of breast milk—characterized by its balanced macronutrient content and bioactive molecules—helps minimize the metabolic load on immature kidneys. If the protein intake is excessively high during the early infancy (*i.e.* high-protein formula), the glomerular filtration rate may struggle to manage the renal solute load, potentially leading to hypernatremic dehydration. For instance, human milk contains lower protein concentrations than formula, which reduces the solute load and helps prevent nephron damage caused by hyperfiltration [37].

Impact of breastfeeding on calcium excretion

Optimal calcium metabolism during infancy is critical, not only for bone health, but also for renal function. Human milk provides calcium in a form that is readily absorbed, making it highly effective for meeting infant nutritional needs. This assertion is supported by several studies. One relevant study indicates that calcium, along with other minerals such as iron and zinc, is highly bioavailable in human milk, suggesting optimal conditions for absorption, compared to infant formulas [38].

A report from the European Childhood Obesity Project (CHOP) in 2017 found that feeding methods in the early months of life influence calciuria, with breastfed infants exhibiting the highest levels. The authors recommended establishing new cut-off values based on feeding types to prevent the overdiagnosis of hypercalciuria in breastfed infants. These findings highlight the differences in renal processing influenced by diet, specifically comparing breastfeeding to artificial milk during early life [39].

Nevertheless, while breastfeeding offers significant advantages for calcium metabolism, additional supplementation may be necessary for preterm infants to meet their increased mineral requirements [40].

Future investigations are warranted to clarify the optimal duration and exclusivity of breastfeeding for preventing mineral imbalances.

Impact of breastfeeding on the risk of developing nephropathies

The impact of breastfeeding extends to the prevention of early-life nephropathies, particularly nephrotic syndrome and IgA nephropathy.

Nephrotic syndrome

A very recent report from a national cohort study conducted in South Korea found that exclusive breastfeeding was associated with a 20% reduction in the risk of developing nephrotic syndrome [41].

IgA nephropathy

A Turkish monocentric study indicated that infants with IgA nephropathy had shorter median durations of breastfeeding compared to healthy controls (6 months *vs* 12 months), suggesting that early-life nutrition plays a significant role in kidney disease susceptibility [42].

These findings open new avenues for understanding how breastfeeding influences the lifelong risk of nephropathies. Further research should investigate the complex interplay between breastfeeding, genetic predispositions, and environmental factors in the development of various nephropathies

Impact of breastfeeding on the risk of urinary tract infections

Urinary tract infections (UTIs) are a common pediatric condition that can have long-term consequences for renal health. Recurrent UTIs and upper urinary tract

infections, such as pyelonephritis, significantly increase the risk of renal scarring and chronic kidney disease [43,44].

Breastfeeding has emerged as a key protective factor against UTIs, offering immunological benefits that extend beyond infancy. Human milk is rich in antimicrobial and immunomodulatory components, including secretory immunoglobulin A, lactoferrin, and human milk oligosaccharides. These components work synergistically to inhibit bacterial adherence to the urinary epithelium, neutralize toxins, and enhance the infant innate immunity [45-47].

Strong evidence supports the protective effect of breastfeeding against UTIs. A recent meta-analysis that included 16 studies involving over 10,000 infants found that breastfeeding reduced the risk of UTIs by 58%. This "shield effect" was most pronounced in exclusively breastfed infants, with the odds ratio for UTI incidence dropping to 0.4. Furthermore, the study highlighted that the duration of breastfeeding had a dose-dependent effect; longer breastfeeding periods provided greater protection [48].

Breastfeeding should be considered an efficient primary preventive strategy against UTIs, particularly in high-risk populations such as infants with vesicoureteral reflux or congenital urinary tract anomalies. By enhancing immunity and reducing pathogen load in the gastrointestinal and urinary tracts, breastfeeding plays a crucial role in safeguarding renal health in infants.

Conclusion

Breastfeeding provides significant long-term benefits that extend into both childhood and adulthood, aligning with the principles of Developmental Origins of Health and Disease (DOHaD). This overview presents robust and recent evidence indicating that maternal breastfeeding is positively correlated with renal health outcomes, showcasing a nephro-protective effect. Conversely, the increased risk of renal complications in children who are not breastfed should be considered alongside other risk factors, such as obesity and infections, which breastfeeding can also help mitigate. Continued research is essential to fully elucidate the long-term benefits of breastfeeding on renal health.

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Authors contributions

Conceptualization: HR; Data curation: HR; Supervision and validation: NB; Writing - original draft, review & editing: HR, NB and HB.

Conflict of interests

The authors have nothing to disclose.

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