Editorial

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Breastfeeding and NAFLD from the maternal side of the mother-infant dyad

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Breastfeeding has health benefits for both partners in the mother-infant dyad. Human breast milk provides the infant with optimal nutrition, immune protection, and metabolic regulation. The advantages of breastfeeding for mothers are not as well studied as those for infants, but there is adequate evidence to state that women who breastfeed are likely to have improved health in the short-term, and are at lower risk of developing future diseases.[1]

For infants, human breast milk is the natural and ideal food providing their nutrient and energy needs during the first months of life in the correct quality and amount. Infants who are not breastfed suffer more infectious diseases, such as gastroenteritis and acute otitis media, and more immune-mediated diseases.[2] Moreover, longer breastfeeding periods have been associated with reduced future risk of obesity and non-communicable diseases.[3] However, the mechanism of action by which breastfeeding confers this protective advantage is multifactorial and incompletely understood. While the macro-nutrient composition of human milk is quite stable, human milk is a complex mixture of bioactive factors associated with infant growth and metabolism, including insulin, leptin, adipocyte fatty acid binding protein, multiple growth factors and their binding proteins, and ghrelin, the composition of which varies from mother to mother and over the course of lactation.[4]

In children there are some data regarding breastfeeding and non-alcoholic fatty liver disease (NAFLD). Recently Ayonrinde and colleagues reported perinatal factors associated with greater odds of having NAFLD at age 17; these included exclusive breastfeeding for at least 6 months and maternal obesity at the time of conception.[5] These data suggested that to reduce the risk of NAFLD in late adolescence, one needed to begin before birth by encouraging normal body mass index prior to conception and promoting exclusive breastfeeding for at least the first 6 months of life. Beyond the risk for NAFLD, breastfeeding has also been implicated as a potential protective factor in the severity of NAFLD in children. Among children with NAFLD, those who were breastfed had lower odds of non-alcoholic steatohepatitis (NASH) and lower odds of fibrosis on index biopsy than those who were not breastfed as infants. The data suggested a dose or time dependent protective effect with the duration of breastfeeding.[6]

In the mother, pregnancy, including placental hormones, promotes increased adipose tissue, decreased insulin sensitivity, and increased lipolysis. These metabolic changes can cause gestational diabetes. Pregnancy is also a hyperlipidemic state, with increased concentrations of maternal cholesterol and triglycerides. Thus, pregnancy is associated with changes in glucose and lipid metabolism that are necessary to support the growing fetus but can negatively impact the mother's long-term health.[7]

Lactation and breastfeeding help to restore healthy maternal metabolism. Experimental data from animal models show favorable changes in metabolism associated with lactation. In particular, lactation appears to reverse more quickly, and more completely changes occurring during gestation, *i.e.* visceral accumulation, insulin resistance and increased lipid and triglyceride levels. Epidemiological data support that women who breastfeed have lower long-term rates of chronic disease. Women who do not breastfeed their children have a higher incidence of type 2 diabetes and myocardial infarction.[8] In the CARDIA (Coronary Artery Risk Development in Young Adults) study, women who breastfed longer had lower incidence of metabolic syndrome years later, likely through a lactation dependent lowering effect on blood glucose, lipids and insulin concentrations. Because of the relationship between cardiometabolic health and NAFLD, it is likely that a similar inverse association may exist between lactation and NAFLD.[9] In this issue of *Journal of Hepatology*, Ajmera *et al.* examined the potential association of breastfeeding and future NAFLD. They evaluated 844 women who participated in the long-term CARDIA cohort study and experienced pregnancy, childbirth, and childrearing. The exposure variable was the duration of breastfeeding. The outcome assessed approximately 25 years later, was NAFLD as determined by computed tomography scans. Overall, the rate

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of NAFLD in the cohort was 6%. The main finding was that women who breastfed for >6 months had lower odds of NAFLD in middle age. The strongest risk factors for NAFLD were body mass index and race. However, controlling for these only mildly attenuated the beneficial association of lactation and NAFLD. Thus, lactation may represent a modifiable risk factor for NAFLD, information important for hepatologists in a field where therapeutic options are limited.[10]

Several elements of study design limited the ability to determine the true effect size for breastfeeding. The most important element was likely the selection of individuals and the earlier time period which yielded a low rate of NAFLD, and thus reduced the potential to show benefit. In addition, the presence of NAFLD in the population at baseline was unknown and many nutritional and lifestyle conditions that influence the risk for NAFLD were not evaluated.

The study was also limited to the US. Thus, confirmatory studies in new settings and the current era that assessment established risk factors for NAFLD would be of value. Such future research investigating the prolonged and sustained benefits of lactation should also clarify the mechanisms of action and in turn pave the way to novel strategies for the prevention and treatment of NAFLD.

Future studies should also take into account the complex nature of the pathogenesis of NAFLD and potential protection of lactation and breastfeeding. Some clues were provided by a recent study showing that rats that suckled their pups for 21 days before weaning had higher liver mitochondrial respiration, lower serum glucose concentration, and exhibited changes in liver,[11] skeletal muscle, and white adipose tissue PPARδ protein levels that may, in part, explain the observed lower serum glucose concentration. These novel animal findings provide evidence of differences in metabolic processes that persist months after weaning.[11,12] It is therefore possible that the long-term effect of lactation on a mother's metabolism and mitochondrial function might also play a role also in protection against NAFLD.

Advances in understanding the role of lactation and its relationship with NAFLD will require collaboration across many medical and scientific disciplines. The new data further adds to the immediate importance of continuity of care in order to optimize body mass index pre-conception, pre-natal care throughout pregnancy, and promote and support breastfeeding postnatally throughout the first year of life.

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Conflict of interest

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Authors' contributions

All authors contributed to writing and editing the manuscript.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jhep.2018.10.030.

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