



Influence of Famine in Women with Non-Alcoholic Fatty Liver Disease

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In the last decades the keyword non-alcoholic fatty liver disease (NAFLD) was increasingly evoked in research frameworks and in clinical practice.¹ NAFLD is an umbrella term that includes different entities, in particular the simple hepatic fat accumulation, non-alcoholic steatohepatitis characterized by steatosis with necroinflammation, fibrosis and finally cirrhosis and its complications.¹

Globally, the NAFLD prevalence among liver diseases and in general population, is recently rising along with its associated conditions, as obesity, insulin resistance, metabolic syndrome and diabetes.² This increment is related to dietary habits and the increase of sedentary lifestyle. Its diffusion seems to be pandemic, given that it is beginning to affect also the populations in the developing world and rural areas, due to the spread of Western lifestyle.³ Even if the real rate of worldwide incidence of NAFLD are not known, is estimated that its prevalence in general population has reached 20-30% in Western Countries and 5-18% in Asia and it is increasing over time.⁴ Currently, NAFLD pathogenesis can be explained by a "multiple hit" hypothesis, that considers multiple factors acting together on genetically predisposed subjects, to induce NAFLD development and progression.⁵

In this issue of *Annals of Hepatology*, the authors of the article entitled The Great Chinese Famine Exposure in Early Life and the Risk of Nonalcoholic Fatty Liver Disease in Adult Women, describe a retrospective study that aims to elucidate the relationship between great Chinese famine (years 1959-1962) exposure and the risk of NAFLD in adult women.⁶ The study include a total of 8,752 women, 4,476 (51.1%) exposed to famine during gestation or early childhood, 1,873 (21.4%) exposed to famine prenatally, and 2,403 (27.5%) exposed to famine post-natally. The authors found that the prevalence rates of NAFLD among non-exposed, prenatally and post-natally

exposed women were 17.3, 23.0, and 22.9%, respectively. Pre-exposed and postnatally exposed women had higher risks of NAFLD, exhibiting ORs (95% CI) of 1.33 (1.04-1.70) and 1.26 (1.03-1.55), respectively. Prenatally but not post-natally exposed women, had significantly higher risks of having abnormal transaminase levels, with ORs of 1.30 (1.05-1.61). Interesting were the data on NAFLD severity, categorized as mild, moderate and severe according to ultrasound features. The prevalence rates of mild steatosis among non-exposed, prenatally and postnatally exposed women were respectively 16.6, 21.5, and 21.1%. The prevalence rates of moderate and severe steatosis among non-exposed, prenatally and postnatally exposed women were respectively 0.7, 1.6, and 1.7%. The Authors concluded that adult women who were prenatally and postnatally exposed to famine, had higher risks to develop NAFLD and hypothesize that intrauterine restriction may influence in the adult life liver function and metabolism.⁶

This study of Zheng, *et al.* provides valuable information on the relationship between exposure to starvation and NAFLD pathogenesis. A preclinical study has shown that nutritional restriction in early life, may permanently change hypothalamic circuits regulating energy homeostasis, a key step in the development of metabolic diseases.⁷ In this context, undernutrition during the critical early periods of developmental plasticity, may increase the susceptibility to NAFLD by increased activation of both de novo lipogenesis and hepatic lipid storage.^{8,9} Finally, maternal and early postnatal malnutrition is linked with epigenetic changes observed in many pathways involved in energy metabolism, hormone functions, hepatic steatosis, and inflammatory processes.¹⁰ The authors also found that prenatally exposed women had significantly higher risks not only of transaminase high blood levels, but also displayed the highest prevalence and risk of NAFLD and mild, moderate and severe steatosis.

This paper also confirm the data recently reported by Wang, *et al.* on the influence of famine exposure to adult Chinese women with NAFLD.¹¹ In fact, to better understand the data here reported, is important for the reader to take into consideration the period of great Chinese famine, the largest famine in human history and the traditional Chinese culture and in particular the legacy of “son preference”, who considers sons more important and more valuable than daughters. The result of this preference may have influenced hepatic and metabolic outcomes in adulthood.

CONFLICT OF INTEREST

The author declare no conflict of interest.

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