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Mini Review

# From Plate to Pulse: Unleashing the Epigenetic Potential of Maternal Nutrition for Lifelong Cardiovascular Health Across Generations

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**ISSN: 2578-0204**


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**Submission:** May 16, 2023

**Published:** May 30, 2023

Volume 4 - Issue 2

**How to cite this article:** Irfa Rizwan* and Adil Muhammad. From Plate to Pulse: Unleashing the Epigenetic Potential of Maternal Nutrition for Lifelong Cardiovascular Health Across Generations. Open J Cardiol Heart Dis. 4(2). OJCHD.000583. 2023. DOI: 10.31031/OJCHD.2023.04.000583



## Abstract

Cardiovascular Health (CVH) is a multifaceted outcome that is influenced by a complex interplay of genetic and environmental factors. Maternal nutrition during preconception and pregnancy is recognized as a crucial factor that affects cardiovascular health in offspring. This mini review provides an overview of the current scientific evidence supporting the impact of maternal nutrition on lifelong cardiovascular health across generations, with a particular emphasis on the epigenetic mechanisms involved. Epigenetic modifications, including DNA methylation, histone modifications, and non-coding RNAs, play a vital role in mediating the effects of maternal nutrition on cardiovascular outcomes. Several specific nutrients, such as folate, omega-3 fatty acids, and antioxidants, have been demonstrated to influence epigenetic modifications, thereby affecting gene expression patterns relevant to cardiovascular health. Intervention studies have demonstrated the potential to improve cardiovascular health through targeted maternal nutrition interventions. A comprehensive understanding of the intricate relationship between maternal nutrition, epigenetics, and cardiovascular health has critical implications for developing preventive strategies and personalized approaches to promote lifelong cardiovascular well-being. Further research is warranted to fully elucidate these mechanisms and inform public health policies and interventions.

**Keywords:** Cardiovascular health; Maternal nutrition; Epigenetics

## Maternal Nutrition and CVH Across Generation

Maternal nutrition plays a critical role in the long-term health outcomes of both mothers and their offspring. In recent years, accumulating evidence has highlighted the link between maternal nutrition during pregnancy and cardiovascular health across generations. Poor maternal nutrition can lead to fetal programming of the cardiovascular system, resulting in an increased risk of hypertension, coronary heart disease and stroke in adulthood [1]. The World Health Organization (WHO) [2] has antenatal care recommendations, but there aren't any detailed guidelines for the nutritional requirements of women during the entire reproductive process, from conception to pregnancy and lactation. The role of adequate nutrition from pre-conception till adolescence has previously received inadequate attention from clinicians, researchers, and policy experts. However, it has recently become an essential topic of discussion, including a recent workshop organized by the National Academies of Science, Engineering and Medicine [3]. Surprisingly, the 2020-2025 Dietary Guidelines contain advice for infants, toddlers and pregnant women for the first time, which will assist both healthcare professionals and the public.

In December 2020, the US Department of Agriculture (USDA) released its final guideline document (USDA 2020-2025 Dietary Guidelines) [4]. Nationwide data on food intake among pregnant women in the United States are insufficient. However, research has revealed that most of pregnant women consume low-quality diets [5,6]. For instance, between 2010 and 2013, the researchers investigated the diet quality of around 7500 nulliparous women belonging to 8 medical facilities in the United States (US) using the Healthy Eating Index (HEI)-2010. Half of the women stated that they didn't eat enough of the various food groups. It was further assessed that 39% of the total caloric intake was comprised of added sugars, alcohol, and saturated fats. Additionally, the HEI score was only 63 out of 100 [6].

## The Role of Epigenetic Mechanisms in Mediating the Effects of Maternal Nutrition on CVH

Understanding the inherent epigenetic mechanisms is crucial for unravelling the complex interplay between maternal nutrition and cardiovascular health across generations [7]. Epigenetic modifications provide a molecular link between the maternal environment and long-term cardiovascular outcomes in offspring. Targeting these mechanisms may offer potential strategies for intervention and prevention of cardiovascular disease [8]. A strong association has been investigated between maternal nutrition and DNA methylation patterns in genes related to cardiac development and function in infants. It was found that maternal vitamin B12 levels were positively correlated with DNA methylation patterns of cardiac genes in infants, suggesting a link between maternal nutrition, epigenetic modifications, and cardiac health outcomes in offspring [9]. Additionally, molecular markers of cardiac hypertrophy i.e., Nppa and Myh7 were elevated in the rat models fed on High Fat Diet (HFD). Also, Agtr2 mRNA and protein levels increased, whereas Agtr1 and protein levels decreased in HFD neonatal hearts [10]. Similarly, rats fed on obesogenic diet (33% sugars and 16% fat) delivered offspring with impaired glucose homeostasis, hypertension, increased resistance artery endothelial function and abnormal adiposity [11]. Similarly, the protein-restricted offspring had decreased cardiac DNA methylation and altered histone acetylation, leading to increased expression of genes involved in cardiac hypertrophy and decreased expression of genes involved in cardiac contractility. These epigenetic changes were associated with increased susceptibility to hypertension and cardiac dysfunction in adulthood [12].

## Transgenerational Influence of Maternal Nutrition on CVH

The nutritional status of a mother can impact the CVH of not only her offspring but also subsequent generations. The epigenetic alterations acquired during pregnancy can be inherited and contribute to long-term cardiovascular health outcomes in subsequent generations [7]. This phenomenon has been observed in both animal and human studies, providing authentic evidence of the transgenerational influence of maternal nutrition on CVH. The offspring of undernourished mothers exhibited altered cardiac gene expression and increased susceptibility to cardiovascular diseases, such as hypertension. Importantly, these detrimental effects were observed in the grand-offspring and great-grand-offspring, indicating a transgenerational impact of maternal nutrition on CVH [13]. It was investigated after the severe famine during World War II that the offspring of mothers who were pregnant during this famine had an increased risk of cardiovascular diseases, such as coronary heart disease and hypertension, compared to individuals born before or after the famine. Remarkably, these effects were observed not only in the first generation but also in the second generation, indicating a transgenerational transmission of adverse CVH outcomes related to maternal undernutrition [14]. It has been indicated that the poor maternal nutrition also resulted in transgenerational alterations in DNA methylation patterns in the offspring's cardiovascular tissues. These modifications were associated with cardiovascular dysfunction and increased susceptibility to cardiovascular disease in subsequent generations [8]. Also, maternal undernutrition during pregnancy led to increased DNA methylation at the promoter region of the peroxisome proliferator activated receptor α (PPARα) gene in the hearts of adult offspring, which was associated with impaired cardiac function [15]. Likewise, pregnant mice fed on protein-restricted diet resulted in vascular dysfunction [16], impaired glucose tolerance [17], increased oxidative stress [18], impaired immunity [19], disturbed feeding behavior and increased fat deposition [20].

## Targeted Nutrients for Improving CVH

Antioxidants, such as vitamins C and E, play a crucial role in safeguarding against oxidative stress, a factor that can contribute to cardiovascular impairments. Maternal micronutrient status, including iron, zinc, and vitamin D, can influence fetal cardiac development. Adequate intake and balance of these micronutrients through diet or supplementation may support optimal cardiovascular health in the developing fetus [21]. Favorable effects on Cardiovascular Health (CVH) outcomes in offspring were found when mothers received antioxidant supplementation during pregnancy. The improvement in endothelial function and reduced risk of hypertension was also observed [22]. Supplementation of high dose of vitamin E (120-160mg/kg) in maternal diet enhanced antioxidant potential and reduced overall oxidative stress in chick models [23]. Similarly, balanced maternal macronutrient intake, including appropriate protein, carbohydrates and healthy fats, is crucial for optimal CVH in offspring. Balanced macronutrient intake during pregnancy has been linked to reduced risk of metabolic disorders and improved CVH outcomes in children [24]. Several components of cardiovascular function, including inflammation, peripheral artery disease and anticoagulation, may be affected by omega-3 fatty acids (Eicosatetraenoic Acid [EPA] and Docosahexaenoic Acid [DHA]). In those with extremely mild Alzheimer's disease, EPA and DHA have been related to promising results in prevention, weight control and cognitive performance [25]. Folic acid also plays a crucial role in the prevention of detrimental birth defects i.e., spina bifida and anencephaly [26]. Although there is some evidence that folate supplementation may have varying effects on different subtypes of congenital heart defects, it is unclear whether the preventative time window is the same as for neural tube defects. There are no RCTs that show that folic acid doses in the mg range are more helpful than the currently recommended 400-800g/d taken at least 2-3 months before conception through the end of the first trimester [27]. Maternal exposure to certain substances, such as alcohol, tobacco and excessive caffeine, has been associated with an increased risk of fetal cardiac abnormalities. Avoiding or minimizing the consumption of these substances during pregnancy can contribute to improved fetal cardiac health [28].

## Conclusion and Future Directions

Maternal nutrition has a profound impact on fetal cardiac health, with potential consequences that can extend across generations. The epigenetic mechanisms underlying these effects provide a fascinating insight into the intricate interplay between nutrition, gene expression and cardiovascular health. By understanding and harnessing the epigenetic potential of maternal nutrition, we can unlock lifelong cardiovascular health benefits for future generations. Through targeted interventions such as omega-3 fatty acid supplementation, folic acid supplementation, antioxidant support, balanced macronutrient intake and glycemic control, we can optimize maternal nutrition to improve fetal cardiac development and reduce the risk of adverse cardiovascular outcomes. These interventions hold the promise of mitigating the impact of maternal undernutrition or overnutrition, as well as preventing conditions like congenital heart defects, hypertension and metabolic disorders in offspring.

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