Diabetes & Metabolic Syndrome: Clinical Research & Reviews xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Review

Maternal and paternal periconceptional nutrition as an indicator of offspring metabolic syndrome risk in later life through epigenetic imprinting: A systematic review☆

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ARTICLE INFO

Article history:
Available online xxx

Keywords:
Periconceptional
Nutrition
Metabolic syndrome
Epigenetics
Methylation

ABSTRACT

Aims: This review examined whether maternal and paternal periconceptional nutrition effects an offspring's likelihood of developing chronic metabolic related conditions due to epigenetic imprinting.
Methods: A literature search was conducted in multiple science databases and limited to studies published after 2012, in English language and peer reviewed. The data from selected articles were extracted and a qualitative approach was employed due to heterogeneity of results.
Results: Newborns from obese fathers showed altered methylation overall and significant hypomethylation at the Insulin-like Growth Factor 2 (*IGF2*) gene. High maternal pre-pregnancy body mass index (BMI) was associated with altered offspring DNA methylation levels and gestational diabetes mellitus induced significantly increased methylation levels in offspring. Gestational weight gain was not associated with differentially methylated cord blood. Birth weight was higher in offspring exposed to famine in early gestation. Offspring born post maternal bariatric surgery showed a lower percentage of body fat and improved fasting insulin levels compared to siblings born pre-maternal bariatric surgery.
Conclusions: The available evidence suggests that poor maternal and paternal periconceptional nutrition can increase the risk of metabolic syndrome in offspring, through epigenetic imprinting. Potential parents should be advised that maintaining a healthy diet and BMI is likely to reduce the risk of metabolic syndrome in offspring.

Contents

☆ This study did not receive a grant from any funding agency in the public, commercial or not-for-profit sectors.

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http://dx.doi.org/10.1016/j.dsx.2017.04.021
1871-4021/

1. INTRODUCTION

1.1. Epigenetics, DNA Methylation and Gene Expression

Epigenetics relates to phenotypic trait variations, the modification of gene expression rather than DNA alteration itself. DNA methylation is an important mechanism regulating gene expression. It occurs when a methyl group is added to the cytosine at the five position in a pyrimidine ring in a cytosine-phosphate-guanine (CpG) dinucleotide [1,2]. DNA methylation is a mechanism used by cells to 'lock off' or 'silence' genes. When methylation does not occur as it should there can be devastating consequences including inappropriate gene silencing at the tumour suppressor genes in cancer cells [3]. Methylation was thought to only prevent gene expression; however, it has been shown that the function of methylation can vary with context [4]. Thus, depending on the site of methylation, expression can be down regulated or promoted. The epigenetic state of an individual's genome is both inheritable and receptive to environmental factors [5].

1.2. Metabolic Syndrome

Metabolic syndrome is a growing cause of ill-health worldwide, contributing an enormous burden to healthcare systems [6]. Metabolic syndrome is diagnosed when at least three of the following conditions are present: hypertension, impaired fasting glucose (or impaired glucose tolerance or insulin resistance), central adiposity, systemic inflammation, decreased high density lipoproteins and elevated triglycerides [7]. Together, these conditions significantly increase an individual's risk of cardiovascular disease and type 2 diabetes [8]. In addition to a genetic cause [9], the development of metabolic syndrome is influenced by the environment and pre-existing diseases (Fig. 1).

1.3. Nutrition and Epigenetics

Nutrition is important for proper genetic and epigenetic processes to occur during human development [10]. Foetal and infant development processes rely on the presence of the correct quantity and quality of nutrients. Variation or deficiency of nutrients during key developmental stages can effect developing tissue and the phenotype [11]. These effects, known as 'programming', may impact on risk factors for non-communicable diseases, including metabolic syndrome.

It is accepted that maternal prenatal nutrition has an impact on the health of the offspring during foetal development [12]. Maternal malnourishment can result in intrauterine growth restriction, preterm birth, low birth weight and defects including iodine deficiency disorders and neural tube defects [13]. These disorders and defects occur in part due to altered DNA methylation and other epigenetic changes at imprinted genes, secondary to maternal over-nourishment or malnourishment [14]. Epigenetic links have been shown between the prenatal diet of mice and the increased incidence of obesity, type 2 diabetes and other metabolic syndrome related conditions in their offspring [6]. Although the effects of human maternal and paternal periconceptional nourishment have been studied in humans, there is little literature on the effect of periconceptional nutrition on DNA methylation, childhood development and health outcomes in human offspring [15]. Observations of the effect of post-war famine on offspring of undernourished mothers suggest there is an increased likelihood of such offspring developing chronic disease in adulthood [16]. However, there is a need to better understand the impacts of undesirable diets around the time of human conception and their effects on the risk of chronic disease in offspring so that, if necessary, appropriate advice can be given to men and women planning families [17]. This review aims to systematically evaluate the literature to determine whether maternal and/or paternal periconceptional nutrition effect an offspring's likelihood of developing metabolic syndrome related conditions due to epigenetic imprinting.

2. METHOD

2.1. Eligibility Criteria

Any study of men or women over 18 years of age at conception, that investigated sub-optimal or over-optimal maternal or paternal periconceptional diets or periconceptional BMI, and that examined outcomes relating to genetic or epigenetic changes or metabolic related disease or symptoms in the offspring, were eligible for inclusion in the review.

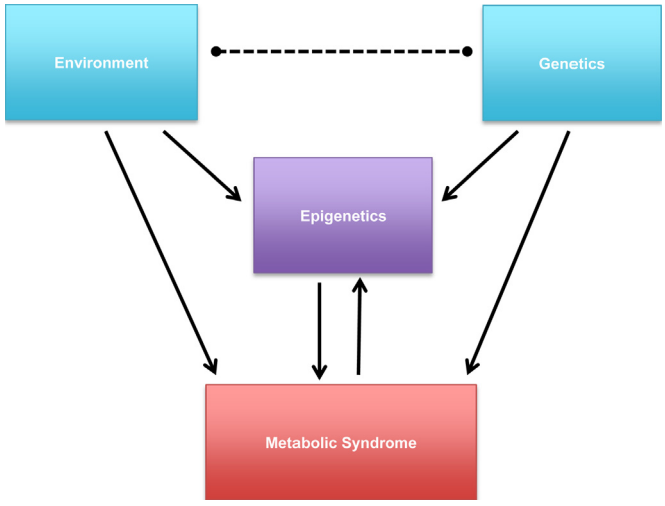

Fig. 1. Suggested mechanism for developing metabolic syndrome.
Adapted from *Handbook of Obesity – Volume 1: Epidemiology, Aetiology, and Physiopathology, Third Edition* (p. 122), by Bray GA, 2014, Boca Raton: CRC Press. Copyright 2014 by Taylor & Francis Group.

Please cite this article in press as: A.R. Dunford, J.M. Sangster, Maternal and paternal periconceptional nutrition as an indicator of offspring metabolic syndrome risk in later life through epigenetic imprinting: A systematic review, Diab Met Syndr: Clin Res Rev (2017), http://dx.doi.org/10.1016/j.dsx.2017.04.021