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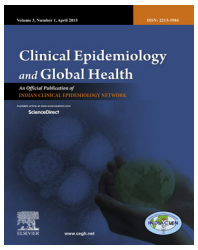

Continuing education

Protein quality in early infancy and long-term health outcomes

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ABSTRACT

Nutrition in early life plays vital role in development of metabolic diseases in adulthood, especially obesity and its complications. Conventional infant formulas having protein supply of 55–80% as compared to breastfed infants could enhance early weight gain and later obesity risk. An improved amino acid profile along with a recommended protein quantity of 1.8 g protein per 100 kcal enables whey predominant starter formula to meet requirement of normal term infants during the first four months of life. Therefore infant formulae with reduced protein contents, high protein quality and the whey-predominant are recommended in infants who are not completely breastfed.

1. Introduction

Globally, childhood obesity is one of the major public health concerns in the 21st century with its increase in prevalence at an alarming rate. It has been estimated that, globally the number of overweight children under the age of five is greater than 42 million. Among them, nearly 31 million of these children reside in developing countries.[1] Prevailing evidence suggest that childhood obesity is associated with the development of metabolic diseases like diabetes, obesity, hypertension and cardiovascular diseases at a younger age. As the metabolic diseases related with overweight and obesity is usually preventable, prevention of childhood obesity is very essential in this context.[2]

The prevalence of overweight and obesity among children has increased rapidly in many low- and middle-income countries.[1] Moreover, in the developing countries, children of high socioeconomic status are affected more than the low socioeconomic status. However, in developed countries, children in lower socioeconomic status are affected more than the children in higher socioeconomic status.[3]

Genetic factors affect the vulnerability of a given child to an obesogenic environment; however, it is not the only factor that

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affects childhood and adult obesity. It is the net outcome of factors like genetic influence, early life programming, individual lifestyle choices and the environment that results in childhood and adult obesity.[4]

The purpose of this article is to review the role of early life metabolic programming and the impact of protein intake in early life on long term health outcomes.

2. Early metabolic programming and long term health outcome

The Barker's or Fetal Origins of Adult Disease'' (FOAD) hypothesis suggest that prenatal exposures affect the fetus' development and consequently, it increases the risk of specific diseases in adult life. Initially, this association was observed for adult coronary heart disease, later it was demonstrated with a range of chronic conditions including Type II diabetes mellitus (T2DM), cancer, and osteoporosis to various psychiatric illnesses. The FAOD hypothesis is based on the evidence that certain intrauterine exposures can influence a single genotype to produce different phenotypes at specific developmental periods.[5]

Epigenetics, which is defined as somatically heritable states of gene expression resulting from changes in chromatin structure without alterations in the DNA sequence, also plays an important role in the metabolic make up of an individual. Prevailing evidence suggest that metabolic events during limited and sensitive windows of prenatal and postnatal development have marked modulating effects on health in later life, which is a concept often referred to as programming or metabolic programming.[6] In addition, environmental exposures during the acute time window can affect the profile of epigenetics and results in obesity. It has been observed that nutrition in early life, an environmental factor, play a vital role in the development of metabolic diseases in adulthood, especially the obesity and its complications (see Fig. 1).[7]

Transgenerational transmission of epigenetic markers was first demonstrated by Morgan and colleagues using the Avy-dependent coat color mouse. Although methylation of the intra-cisternal A particle retrotransposon (IAP) region was associated with a wild-type coat color phenotype, the mice were genetically agouti. In addition, it has been observed that DNA methylation markers could be transmitted across multiple generations.[8] Other studies also showed that methyl supplemented diets during pregnancy were adequate to increase methylation of the Avy-allele and produce offspring of pseudoagouti appearance regardless of the parents phenotype and this phenotype was then passed on to the F2 generation.[9] These studies suggest that manipulations of the maternal condition potentially cause epigenetic modifications in the offspring and produce a variety of phenotypic outcomes even if the offspring were genetically identical.[8,9]

Maternal protein restricted diet during pregnancy, which induces an altered phenotype in the offspring, involves alterations in DNA methylation and histone modifications in particular genes. For example, the honeybees that grow to be either queens or workers based on if they are feed on royal jelly or beebread demonstrated the epigenetic effects of diet on the honeybee phenotype. In the honeybee model, the different

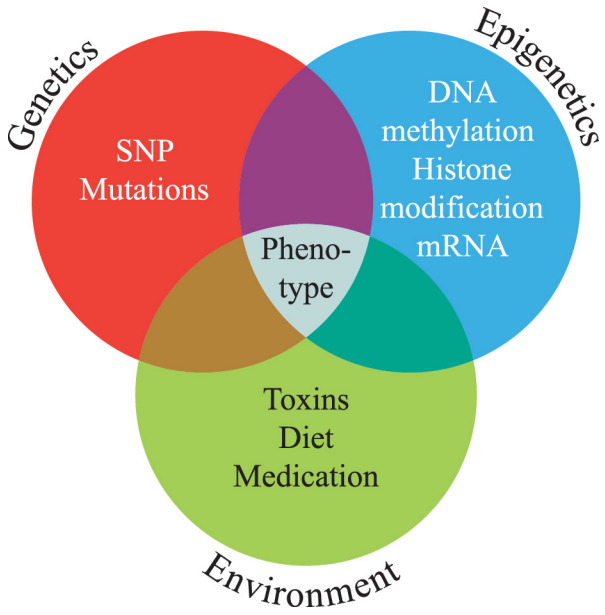

Fig. 1 – Interplay of genetic, environmental and epigenetic factors in the metabolic programming. SNPs, single nucleotide polymorphisms; DNA, Deoxyribonucleic acid; mRNA, messenger ribonucleic acid.

types of honey that induced the epigenetic changes in DNA methylation pattern resulted in different honeybee phenotype. Therefore, diet can alter DNA methylation and thereby, alter gene expression that possibly affects both physiologic and pathologic pathways.[7]

Accelerated early postnatal growth which occurs as a result of relative over nutrition in infancy has been suggested to increase the risk of later obesity. A study by Singhal et al. assessed the effect of early growth promotion on later body composition in two randomized trials of infants born small for gestational age who have been assigned at birth randomly to receive either a nutrient-enriched formula or a standard formula. The study demonstrated that the fat mass was lower in children assigned to the standard formula as compared with the children who received the nutrient enriched formula with a mean (95% CI) difference after adjustment for sex for study 1 was −38% (−67%, −10%), $P = 0.009$ and for study 2 was −18% (−36%, −0.3%), $P = 0.04$. The study has provided the evidence that there is a causal link between faster early weight gain and a later risk of obesity. The prevailing evidence suggests that early nutritional environment interacts with an individual's genetic disposition to program metabolism and development.[10]

Adipogenesis which is regulated by peroxisome proliferator-activated receptor (PPAR) that is activated by cytosine-adenosine-adenosine-thymidine (CAAT) enhancer binding proteins (C/EBPs) and regulatory element-binding protein 1 (SREBP-1) occurs predominantly during late fetal and early postnatal life. However, it can also occur at later stages of life under certain conditions like obesity. During early life, nutritional environment greatly influence adipocyte proliferation and differentiation, especially the concentrations of circulating hormones and nutrients such as insulin-like