Nutritional Control of Fetal Growth

Chittaranjan Yajnik, MD

Maternal micronutrient nutrition is an important determinant of size and body composition of the fetus. Maternal iron, iodine, calcium, folate, vitamin A, and vitamin C nutrition all influence offspring size. The Pune Maternal Nutrition Study was designed to study the relationship between maternal nutrition and fetal growth, size at birth, and postnatal growth. Maternal circulating folate and vitamin C concentrations predicted larger offspring size, while higher ferritin levels predicted smaller-sized babies. Subclinical vitamin B_{12} deficiency is common in India, especially in vegetarians, and children born to mothers with the lowest vitamin B_{12} but the highest folate status were the most adipose and the most insulin resistant. Furthermore, the relationship between maternal nutrition, fetal growth, and risk of type 2 diabetes and coronary heart disease appears to be much more complex than the simplistic postulates of the "fetal origins" hypothesis.

Key words: fetal growth, micronutrients, nutrition

doi: 10.1301/nr.2006.may.S50–S51

Interest in fetal growth and development was heightened when Barker proposed the "fetal origins" hypothesis, which said that small size at birth (weight, length, ponderal index, etc.) was associated with later risk of type 2 diabetes and coronary heart disease. It was proposed, therefore, that increases in fetal size would reduce the risk of these disorders, and it was assumed that improving maternal nutrition would reduce the incidence of these disorders in the coming generations.

The fetus derives all of its nutrition from its mother, and in this sense is entirely dependent on her for its growth. However, there are a number of factors that control transfer of nutrition from the mother to the fetus, including the mother's nutritional status; her vascular, endocrine, and metabolic response to pregnancy; and placental size and function. Thus, feeding the mother is not equivalent to feeding the fetus. Fetal growth and size are also limited by the size of mother's pelvis, which it has to negotiate for a safe delivery.

In epidemiological studies, common determinants of fetal growth are: maternal size before pregnancy (especially height and fat mass), food intake, physical activity, and weight gain during pregnancy, size of the placenta, gestational length at birth, and some "disease" conditions such as anemia, infections, preeclampsia, and diabetes. Fetal gender is also an important determinant, as is the size of the father.

A number of studies have reported on the size and body composition of the fetus in relation to maternal nutrition. The majority have been observational studies, some using specific interventions. Both macronutrients and micronutrients have been studied. Overall, maternal macronutrients are not a strong determinant of fetal size at birth, although an imbalance in carbohydrates and proteins in early and late pregnancy has been shown to be a determinant of infant thinness. Many studies have failed to demonstrate a major effect of maternal macronutrient supplementation on offspring birth size (with the notable exception of one study in Gambia). Micronutrient nutrition of the mother may be a more important determinant of size and body composition of the fetus. Maternal iron, iodine, calcium, folate, vitamin A, and vitamin C nutrition have been shown to influence offspring size. There are relatively few studies that have studied offspring body composition.

The Pune Maternal Nutirition Study was designed to study the relationship between maternal nutrition and fetal growth, size at birth, and postnatal growth. Over 800 pregnancies were studied in six villages near Pune, India. The children have been followed up regularly. They were studied at 6 years of age for body size and composition, insulin resistance, and cardiovascular risk factors. A higher frequency of intake of micronutrient-rich foods (green leafy vegetables, fruits, and milk) predicted larger offspring size at birth, with variable effects on different body measurements. Maternal circulating folate and vitamin C concentrations predicted larger offspring size, while higher ferritin levels pre-

Dr. Yajnik is director of the Diabetes Unit, King Edward Memorial Hospital and Research Centre, Pune, India.

Please address all correspondence to: Dr. C.S. Yajnik, Director, Diabetes Unit, King Edward Memorial Hospital and Research Centre, Pune, India 400-011; Phone: 91-20-5603-7366; Fax: 91-20-2612-5603; E-mail: diabetes@vsnl.com.

dicted smaller-sized babies. Frequency of maternal intake of micronutrient-rich foods and her circulating micronutrient status were also associated with circulating metabolites (glucose, insulin, triglycerides, cholesterol, homeostasis model assessment-estimated insulin resistance, etc.), overall indicating an association with higher insulin resistance. We measured plasma vitamin B_{12} concentrations later, when it was discovered that subclinical vitamin B_{12} deficiency is common in India, especially in vegetarians. Maternal vitamin B_{12} status was not a predictor of offspring size at birth.

The offspring were studied at 6 years of age for their body size, body composition, insulin resistance markers, and other cardiovascular risk factors. Maternal macronutrient intake during pregnancy was not a significant predictor of offspring size, insulin resistance, or cardiovascular risk factors. Maternal physical activity predicted smaller size and lower insulin resistance. Higher frequency of maternal intake of green leafy vegetables during pregnancy predicted higher adiposity in the offspring during childhood; higher maternal folate status predicted higher adiposity and insulin resistance in the offspring. Higher maternal vitamin B_{12} status predicted lower adiposity in the offspring. Children born to mothers who had the lowest vitamin B_{12} status but the highest folate status were the most adipose and the most insulin resistant.

The relationship between maternal nutrition and fetal growth and risk of type 2 diabetes and coronary heart disease appears to be much more complex than the "fetal origins" hypothesis. Our findings should promote more research in this area to find nutritional factors to help control the growing epidemic of type 2 diabetes and coronary heart disease.