Molecular and Cellular Endocrinology 435 (2016) 40–47

Contents lists available at ScienceDirect

Molecular and Cellular Endocrinology

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

How maternal malnutrition affects linear growth and development in the offspring

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ARTICLE INFO

Article history:
Received 29 September 2015
Received in revised form
21 January 2016
Accepted 22 January 2016
Available online 26 January 2016

Keywords:
Maternal malnutrition
Birth length
Offspring development
Food supplementation
Low birth weight

ABSTRACT

Maternal malnutrition is common in the developing world and has detrimental effects on both the mother and infant. Pre-pregnancy nutritional status and weight gain during pregnancy are positively related to fetal growth and development. Internationally, there is no agreement on the method of diagnosis or treatment of moderate or severe malnutrition during pregnancy. Establishing clear guidelines for diagnosis and treatment will be essential in elevating the problem. Possible anthropometric measurements used to detect and monitor maternal malnutrition include pre-pregnancy BMI, weight gain, and mid upper arm circumference. Food supplements have the potential to increase gestational weight gain and energy intake which are positively associated with fetal growth and development. Overall more studies are needed to conclude the impact of food/nutrient supplements on infant growth in undernourished pregnant women in developing countries. Currently, a study underway may provide much needed documentation of the benefits of treating malnutrition in pregnancy.

1. Malnutrition in pregnancy is a global health problem

Malnutrition during pregnancy is common in low-income women in the developing world due to inadequate dietary intake combined with increased nutrient requirements; the potential for complications for the mother and child in this at risk population is manifest in increased maternal and infant mortality (2000, Rush, 2000; Black et al., 2008; Lartey, 2008; Bloomfield, 2011) and the lifelong effects of fetal malnutrition (Barker, 2006; Victora et al., 2008). HIV infection, prevalent in some of these populations, exacerbates the risk of poor outcomes associated with malnutrition during pregnancy (Kupka et al., 2004; O'Brien et al., 2005; Mehta et al., 2010; Marazzi et al., 2011; Mehta et al., 2011).

Undernutrition during pregnancy results in maternal complications such as anemia, increased risk of life-threatening hemorrhage and hypertensive disorders of pregnancy such as preeclampsia (Wu et al., 2012). Hemorrhage and hypertension in pregnancy are the leading causes of maternal mortality worldwide (Firoz, Sanghvi et al.). Hemorrhage is associated with anemia and iron deficiency anemia while inadequate calcium intake is associated with the development of gestational hypertensive disorders (Buppasiri, Lumbiganon et al., Firoz, Sanghvi et al.). Infant complications from maternal undernutrition include intrauterine growth retardation (IUGR), low birth weight (LBW), pre-term delivery and birth defects such as neural tube defects (Wu et al., 2012). Additional complications include: poor cognition, academic performance, professional achievement and lower wages as adults (de Onis et al., 2012; Martorell and Zongrone, 2012). In addition, poor nutritional and socioeconomic status during pregnancy affects growth and development in subsequent generations (Martorell and Zongrone, 2012; Gigante et al., 2015).

Pre-pregnancy nutritional status and weight gain during pregnancy are positively related to fetal growth, development and birth weight. As early as 1975, observational studies of the Dutch Famine in 1944–45 identified a relationship between maternal undernutrition and fetal growth (Stein et al., 1978). Maternal undernutrition especially during the second and third trimester reduced birth weight and length (Stein et al., 2004). The first 1000 days, beginning at conception, are considered a critical time for prevention of childhood stunting, since growth failure begins in utero and continues until about two years of age (Victora et al., 2010).

Stunting, or poor linear growth, results primarily from inadequate nutrient availability and poverty that mainly affects low income countries. In a review of trends in stunting amongst pre-

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http://dx.doi.org/10.1016/j.mce.2016.01.024
0303-7207/

school children worldwide, World Health Organization (WHO) estimated that there were 171 million children with stunting in 2010, with 97.6% of them living in developing countries. Although stunting has decreased globally from 39.7% of children under five years in 1990–26.7% in 2010, stunting in Africa has remained unchanged at 40% while it is decreasing in Asia and Latin America. Despite this general global decrease, stunting remains a significant public health concern with more than 132 million children estimated to be stunted in 2020 (de Onis et al., 2012).

The requirement for macro- and micronutrients increase during pregnancy; in many socioeconomically disadvantaged populations, nutrients from available foods are not sufficient to meet these increased needs. Foods consumed by pregnant women in developing countries are commonly low in micronutrients such as iron, zinc and vitamin A due to low intake of animal products (Ramakrishnan et al., 2012). Micronutrients needed inadequate amounts for fetal growth and development and prevention of IUGR include minerals phosphorus, potassium, iron and zinc; vitamins thiamin, riboflavin, niacin, folic acid and pantothenic acid (Wu et al., 2012), which are commonly deficient in undernourished populations. In their review of mechanisms for nutrient regulation during pregnancy, Wu et al. note that maternal undernutrition results in deficiencies of glucose, amino acids, fatty acids and micronutrients which lead to the metabolic changes including reduced placental growth, vascularity and function, oxidative stress, impaired cell signaling and regulation of protein synthesis causing fetal growth restriction (Wu et al., 2012).

Gestation represents 25% of the critical first 1000 days, thus it is a window of opportunity to optimize growth potential and prevent stunting by improving maternal nutritional status, both before and during pregnancy.

2. Evidence that mother's anthropometry and micronutrient status is associated with infant size and growth

Birth size is important for infant morbidity and mortality and for later adult health. Studies have identified indirect and direct effects of maternal age and height, genetic, demographic, socio-economic, behavioral and nutritional factors on birth size (Zhang et al., 2015). The US Institute of Medicine (IOM) established guidelines for weight gain during pregnancy based on pre-pregnancy BMI, as shown in Table 1, with the aim to optimize birth outcomes, including the prevention of LBW (Institute of Medicine (U.S.). Subcommittee on Nutritional Status and Weight Gain during Pregnancy. and Institute of Medicine (U.S.). Subcommittee on Dietary Intake and Nutrient Supplements during Pregnancy. 1990). WHO does not have recommendations on total weight gain or rate of weight gain at this time.

Currently there is no agreement on which anthropometric measurement method(s) should be used to detect, monitor and treat mild, moderate or severe undernutrition during pregnancy. Ideally an indicator would be simple to measure, valid and be universally applicable to pregnant women no matter the location or context.

Table 1
Institute of Medicine (IOM) weight gain recommendations in pregnancy.

Pre-pregnancy BMI (kg/m^2)	Total weight gain recommended (kg)	Gain/wk in 2nd and 3rd trimesters (g)
>18.5	12.7–18.2	450–590
18.5–24.5	11.4–15.9	365–420
25–29.9	6.8–11.4	227–320
>30.0 kg	5.0–9.1	180–270

Multiple micronutrient deficiencies are common in poor women in developing countries and contribute to LBW, IUGR and other adverse pregnancy outcomes. Several meta-analysis on the impact of multiple micronutrient supplementation on birth size have been conducted. Fall et al. looked at randomized control trials in 12 low income countries that mainly compared the standard of care, iron and folic acid supplementation, with one-times recommended dietary allowances (RDA) amounts of multiple micronutrient supplementation (Fall et al., 2009). They found that the multiple micronutrient supplementation was associated with improved birth weight of 22.4 g (95% CI 8.3–36.4) and a reduction in LBW risk (OR 0.89, 95% CI 0.81–0.97). Interestingly, the effect on birth weight (22.0–56.1 g) was stronger in women with a BMI higher than 20 kg/m^2 compared to mothers with BMI <20 kg/m^2 (Fall et al., 2009) which was also found in another study (Roberfroid et al., 2012). These authors suggested that although one-times RDA micronutrient supplement significantly reduces LBW, this amount of increased birth weight may not be sufficient to warrant this type of intervention and that better evidence of functional benefits are needed. Alternately, the amount of nutrients in the micronutrient supplement might not have been adequate in the undernourished women since the RDA is based on healthy populations rather than undernourished ones and that micronutrients might not have been fully utilized concurrent with inadequate energy intake (Roberfroid et al., 2012). In the meta-analysis by Ramakrishnan et al., 16 micronutrient randomized control trials were included to study the effect of micronutrient supplementation on pregnancy outcomes. It included one study of HIV-positive mothers and the content and dose of the micronutrient supplements varied; the control was usually iron and folic acid. In pooled analysis, they found overall a significant 14% reduced risk of LBW (95% CI, 0.81–0.91), similar to the Fall et al. meta-analysis. Birth weight in the multiple micronutrient groups was 53 g higher (95% CI. 41.6–63.7) than the control, (Ramakrishnan et al., 2012) which was nearly twice what Fall et al. found. In general, effects seemed strongest if the supplements contained 60 mg iron rather than 30 mg, but this was not statistically significant.

When prenatal food was fortified with multiple micronutrients in a study of 1296 pregnant women in Burkina Faso, Huybregts, et al. found an increase in birth weight (31 g) but this was not significantly more than the comparison group (Huybregts et al., 2009). The supplement provided 372 kcal, 14.7 g protein and one times RDA micronutrients and was compared to the control of one times RDA micronutrient supplement without macronutrients. Sixty to seventy percent of the enrolled women were anemic or vitamin deficient. After adjustment for gestational age at delivery, birth weight was not different between groups. In mothers who were underweight, however, birth weights increased by 111 g, but this was not statistically significant compared to the control group. Again, this may be the case of not enough nutrient support to have an impact.

2.1. Pre-pregnancy BMI

The pre-pregnancy BMI measurement is a reflection of maternal nutritional status while gestational weight gain is the aggregate change of mother's, child's and placental mass in the physiologic state of pregnancy. Ay et al. followed 8451 pregnant women in the Netherlands and measured fetal growth in relation to maternal anthropometry (Ay et al., 2009). They found an increased effect of BMI on fetal weight in the second half of pregnancy and the largest effects on fetal weight were near the end of pregnancy. The fetal growth rate difference between the lowest quintile BMI and the highest was 4.49 g/wk (95% CI: 3.48–5.29). Pre-pregnancy BMI was associated with birth weight difference (−88 g, 95% CI-120,-57)