Pregnancy Nutrition: The Impact of Under- and Overnutrition During Pregnancy

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Optimization of maternal nutritional and fetal status has been a public health goal since records began. The association of low-calorie intake with low birth weight is perhaps best evidenced by reports from the famine-stricken populations of Leningrad and southern Holland during World War II.[1,2] Since the beginning of the 20th century, with the awareness that gestational weight gain was a proxy for maternal nutrition, efforts have been made to ensure adequate gestational weight gain. The effects of fetal nutritional excess also are exemplified by excessive fetal growth in response to suboptimal glucose control in women with gestational diabetes, but recently increasing trends in maternal dietary caloric excess and obesity have led to considerable concern over the myriad of associated adverse maternal and fetal health outcomes. Importantly, we are now aware that maternal nutritional status may have unforeseen influences on the developing child that extend to increased risk of disease in later life. This association, embodied in the Developmental Origins of Disease Hypothesis, has given renewed vigor to investigations of maternal nutritional status in pregnancy.

Protein-Energy Malnutrition

Women in developing countries remain at risk of protein-energy malnutrition and associated low birth weight, major causes of neonatal mortality and morbidity. A recent meta-analysis of women from developed and developing countries suggests that balanced protein-energy supplementation can lead to a 31% (95% CI 15%–44%) reduction in delivery of infants who are small for gestational age.[3] Data from some of the studies in the meta-analysis are shown in Fig 1.

Year of Study	Weight	Risk Ratio IV, Fixed, 95% CI
1973	4.4%	0.56 [0.21, 1.48]
1997	49.4%	0.65 [0.49, 0.87]
1981	14.8%	0.88 [0.52, 1.50]
1984	0.5%	0.09 [0.01, 1.45]
1978	7.5%	0.78 [0.37, 1.65]
1980	23.3%	0.70 [0.46, 1.07]
Total (95% CI)	**100.0%**	**0.69 [0.56, 0.85]**

Heterogeneity: Chi² = 3.31, df = 5 (*P* = 0.65); I² = 0%
Test for overall effect: Z = 3.56 (*P* = 0.0004)

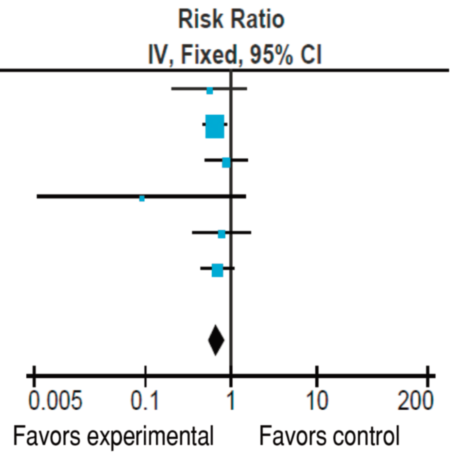

Fig 1. Effect of balanced protein energy supplementation during pregnancy on risk of small-for-gestational age births.[3]

Source: Imdad A, Bhutta ZA. Effect of balanced protein energy supplementation during pregnancy on birth outcomes. *BMC Public Health*. 2011;11(suppl 3):S17.

These findings suggest that this intervention should be scaled up in developing countries. There is hitherto no information, however, as to whether these benefits may reduce risk of disease in the child in later life.

Micronutrient Deficiencies

Pregnant women in both developed and developing countries are at risk of micronutrient deficiency. In developing countries where the incidence of anemia is high, iron/folate supplementation is an effective treatment, but iron and multivitamin supplements have only a modest influence on reducing low birth weight.[4] Iodine deficiency, which is associated with adverse influences on cognitive development and increased infant mortality and morbidity, remains a problem in some parts of the world.[5]

The influence of inadequate periconceptual folate intake on risk of neural tube defects is well known, but increasing evidence for the role dietary folate insufficiency plays in fetal growth restriction, for example, in pregnancy in adolescents,[6] (Fig 2) and in preeclampsia[7] suggests that folate supplementation should be considered throughout pregnancy.

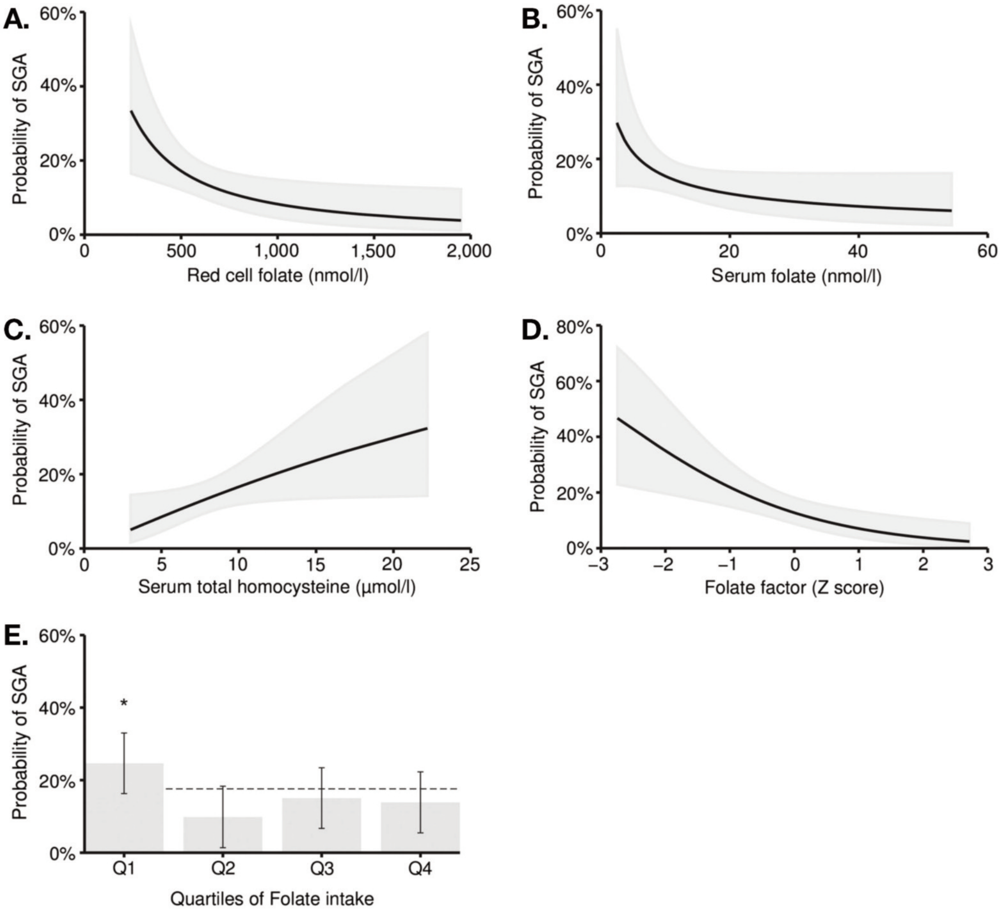

Fig 2. Folate status and folate intake measured in pregnant adolescents during the 3rd trimester and relations with small-for-gestational age (SGA) birth.[6] Shaded areas represent 95% CIs. Data adjusted for confounding variables (multiple logistic regression). A: Relation between red blood cell folate and SGA birth (n=263). Curve obtained by multiple logistic regression (MLR) of log-transformed biomarkers. B: Relation between serum folate and SGA birth (n=280). Curve obtained by MLR of log-transformed biomarkers. C: Relation between serum total homocysteine and SGA birth (n=290). Curve obtained by MLR of log-transformed biomarkers. D: Relation between folate factor score and SGA birth (n=290). Folate factor score defined by factor analysis of red blood cell folate, serum folate, and serum total homocysteine. Curve obtained by MLR of log-transformed biomarkers. E: Relation between quartiles of folate intake and SGA birth (n=288). Subjects in the lowest quartile of folate intake (<187 µg/day) were more likely to deliver an SGA infant than were subjects with higher intakes (odds ratio: 2.71; 95% CI: 1.28, 5.71; *P*=0.009, energy-adjusted). Columns represent the probability of SGA birth, determined by MLR of folate intake and SGA birth, adjusted for energy intake. Error bars represent 95% CIs. The dashed line indicates the incidence of SGA birth in the sample as a whole.

Source: Baker PN et al. A prospective study of micronutrient status in adolescent pregnancy. *Am J Clin Nutr.* 2009;89:1114-1124. Reprinted by permission of the American Society for Nutrition.

A new randomized controlled trial (the FACT trial) is addressing the potential for prevention of preeclampsia by folate supplementation in early pregnancy. Although there is little evidence of a prolonged effect of folate on childhood risk of disease, a recent study of Indian mothers and their children suggests that folate status in pregnancy may have an independent influence on cognitive function in young children.[8] Since folate metabolism plays an important role in gene methylation status and epigenetic regulation of gene expression, influences of maternal dietary folate on later risk of disease may occur through persistently altered gene methylation status in the child. Further studies are required to address the genome-wide or candidate gene methylation status of children born to folate-deficient and folate-replete women.

Vitamin D insufficiency in pregnant women is prevalent worldwide and observational studies have suggested links with gestational diabetes and preeclampsia.[9] While a relationship between vitamin D insufficiency and increased risk of infant rickets is well established, it now appears that maternal vitamin D status may have consequences for a child's bone density in later life.[10,11]

Obesity

Obesity in pregnancy represents an increasing challenge to health care professionals. Obesity is associated with increased risk of miscarriage, thromboembolism, preeclampsia, gestational diabetes, and a high cesarean section rate, among many other problems (Table). An infant born to an obese mother is more likely to develop congenital malformations, to be born large for gestational age, and to die in stillbirth.[12]

Table. Maternal and Fetal Risks Associated With Maternal Obesity

Maternal Risk	Fetal/Infant Risk
Gestational diabetes	Macrosomia
Preeclampsia	Shoulder dystocia
Venous thromboembolism	Brachial plexus damage
Genital infection	Intrauterine death
Urinary tract infection	Spina bifida
Wound infection	Heart defects
Postpartum hemorrhage	
Induction of labor	

An intervention is needed that reliably reduces the risk of these complications, in both mother and child. One approach is to devise strategies to limit gestational weight gain in obese pregnant women; however, a meta-analysis of recent small studies suggests that the strategies that have been tried have been unable to achieve the weight-gain restrictions recommended by the USA Institute of Medicine (5–9 kg).[13] However, approaches that specifically concentrate on improvement of maternal glucose tolerance and consequent reduction of macrosomia may be more apposite, although these require much larger studies to achieve adequate power. Such a study, the UPBEAT Trial, is now underway in the United Kingdom.

References

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Q & A

Q: Thank you, Dr Poston, for a wonderful presentation to kick off this meeting. I would like to add to your skeptical view on using gestational weight gain as the holy grail. Some data from a large national trial that was recently published in Germany showed that obesity prevalent among 70,000 children was positively related to gestational weight gain. The effect size, however, was small—1 kilogram of weight gain on average with only 1% increase in obese prevalence in the child population. To be realistic, how many kilograms could we ever change in terms of gestational weight gain? This would have a very small effect on child obesity. On top of that, the effect was only seen in normal-weight pregnant women. There was no effect in obese women.

I also have a question. I noticed in your pilot trial, you saw no effect of the glycemic load change on gestational age at birth. I am sure you are aware of the data that has been published on a small controlled trial last year in which the investigators reported a remarkable increase of 1½ weeks in gestational age related to glycemic load compared to a low-fat diet. Is there any reasonable hypothesis why there should be such an effect?

Dr Poston: I do not know why you would get an alteration in gestational age. On the other hand, obese populations have a high incidence of preeclampsia, which can reduce gestational age at delivery. But we need to distinguish between elective preterm delivery and spontaneous preterm births: The births among women with preeclampsia would not necessarily be spontaneous preterm births.