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Editorial

NUTRITION AND PREGNANCY- CURRENT KNOWLEDGE AND FURTHER PERSPECTIVES

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Nutritional factors play an important role across the life course but also across generations. It is now well-demonstrated that nutrition and other lifestyle behaviours during pregnancy have an impact on pregnancy outcomes for both mother and neonate health, including risk of gestational diabetes mellitus (GDM) and hypertension, preterm delivery, low birth weight, perinatal survival and risk of developing non-communicable diseases (NCDs) in later life [1,2]. Moreover, recent researches demonstrate that nutrition can also influence germ cells through hormone changes and epigenetic mechanisms both in women and males, and thus further modify embryo and fetus development [3].

According to international guidelines [4-6], the outcomes of interest during pregnancy are both maternal and fetal/neonatal and most of them are under the influence of nutritional factors. The main maternal outcomes that should be monitored are infections, anaemia, pre-eclampsia/eclampsia, GDM, mode of delivery, excessive weight gain, other outcomes (intimate partner violence, side-effects, symptomatic relief, maternal mortality, as well as maternal satisfaction and/or women's rating of usefulness of treatment). Fetal/neonatal outcomes include neonatal infections, small or large for gestational age, low birth weight, preterm birth, congenital anomalies, fetal/neonatal mortality.

We shall try below to summarize the main nutritional interventions recommended by international guidelines in line with current evidence and raise some unanswered questions that should be the subject of further research.

#1 Counselling about healthy diet and being physically active should be offered to all pregnant women to maintain their health and avoid excessive weight gain

A Cochrane review including 65 randomized controlled trials (RCTs) and 11,444 women [7] found that diet, exercise or combined diet and exercise interventions reduced the risk of excessive weight gain during pregnancy by 20%. Other favourable effects of such interventions were seen on risk of maternal hypertension,

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caesarean delivery, macrosomia, and neonatal respiratory morbidity.

General consensus on the "normal" weight gain during pregnancy is presented in Table 1 and it depends on pre-pregnancy body mass index (BMI).

Table 1. Targets for weight gain during pregnancy [6].

Pre-pregnancy BMI	Target weight gain during pregnancy
< 18.5 kg/m^2	12.5–18 kg
18.5–24.9 kg/m^2	11.5–16 kg
25–29.9 kg/m^2	7–11.5 kg
≥ 30 kg/m^2	5–9 kg

BMI, body mass index

Dietary intervention was also proved to have a positive trend towards decreased risk of GDM and the interventions had more significant effects in overweight and obese women [8]. The type of diet that would most favourably affect glucose levels during pregnancy is still a matter of discussion, since only a limited number of trials specifically addressed this issue [9].

#2 Energy and protein requirements during pregnancy should be tailored to women's nutritional status

World Health Organization (WHO) guidelines is mainly focused on undernourished pregnant women in whom an increase in energy and protein intake, including protein dietary supplementation but not high-protein supplementation, is recommended to reduce the risk of stillbirths and small-for-gestational-age neonates [6]. This applies in regions where the prevalence of underweight women (BMI<18.5 kg/m^2) is high (20-39%) or very high (≥40%). In Romania, the general prevalence of underweight in women is not a concern [10], nevertheless around one third of pregnant women had a poor or very poor socioeconomic status according to a report from 2005 [11] and could represent a subgroup at risk.

In women with normal pre-pregnancy weight, the recommended increase in energy intake is 0-85 kcal/day in the first trimester, 285-340 kcal/day in the second, and 452-475 kcal/day in the third [4]. An increase of 10-12 g/day in protein intake above the 60 g intake before pregnancy is also recommended. High protein supplementation (>25% of total energy intake) is not recommended and could be even harmful to the foetus [4]. Fat and carbohydrate intake have similar recommendations as in general population with avoidance of saturated fat and high glucose-index (GI) carbohydrates and preference for mono- and polyunsaturated fats and low GI carbohydrates [4,5]. Recommended fiber intake is 28 g/day and can avoid constipation and decrease the risk of GDM and pre-eclampsia [4].

In women with pre-pregnancy obesity, an energy intake of 25 kcal/kg body weight or less, should be recommended. A calorie restriction at around 1800-2500 kcal/day is advisable and was shown to prevent deterioration of glucose metabolism during late pregnancy [4].

#3 Micronutrient supplementation during pregnancy

Iron

Anaemia during pregnancy is a frequent condition, with nearly one out of five pregnant women being affected in developed countries [12]. Iron deficiency and maternal anaemia increases the risk of low-for-gestational age and preterm delivery and, in severe cases, can affect maternal mortality in the event of postpartum haemorrhage [4-6]. Iron requirements increase during pregnancy and it is considered that these high requirements cannot be met by dietary sources only [5]. The daily recommended iron supplementation is 30-60 mg of elemental iron, with the higher dose to be used in regions were maternal anaemia (total haemoglobin<11 g/dl) is

encountered in >40% of pregnancies. If daily supplementation is not tolerated due to side-effects, an intermittent supplementation of 120 mg elemental iron weekly can be used in settings where anaemia is less common (<20% pregnancies) [6]. If anaemia is diagnosed during pregnancy, a daily dose of 120 mg elemental iron should be prescribed until haemoglobin levels reach 11 g/dl [6].

Folic acid

Folic acid is an important micronutrient before and during pregnancy for its properties to prevent neural tube defects, but it also plays a role in maternal anaemia [5,6]. During pregnancy, a daily dose of 400 μg (0.4 mg) folic acid or, alternatively, 2800 μg (2.8 mg) of folic acid once weekly should be administered to all pregnant women [6].

Calcium and Vitamin D

A normal calcium level during pregnancy will prevent occurrence of hypertensive disorders and pre-eclampsia [13,14]. In regions where calcium-deficient diets are not a concern, supplementation is not recommended while in all others a dose of 1.5–2.0 g oral elemental calcium should be taken divided in three doses, taken with meals and several hours apart from iron supplements as the negative interactions could occur between the two supplements [6]. Vitamin D has important roles in pregnancy: regulation of maternal calcium homeostasis, neurological and immune function, or fetus bone development. Vitamin D deficiency can result in low birth weight, neonatal hypocalcaemia and cardiac failure, increased risk of allergy in childhood [15]. In pregnant women at risk for vitamin D deficiency (e.g. dark skin, low sun exposure, vegetarians), vitamin D supplementation should continue at a dose of at least 400 IU/day and the total intake (dietary sources and supplements) should be in the range of 1000–2000 IU [4].

Other micronutrients of concern during pregnancy

Other vitamins and minerals that can have an impact on mother and newborn outcomes are iodine, vitamins B6, B12, A, C, and E, selenium, zinc, choline [4-6]. According to current evidence, no routine supplementation of any of these micronutrients has been shown to improve outcomes and therefore is not recommended.

Multiple micronutrient (MMN) supplements

Use of MMN supplements remains a matter of debate and further research. A Cochrane review including 23 trials (involving 76,532 women) in which MMN supplements containing 13–15 micronutrients (including iron and folic acid) were compared with supplementation with iron and folic acid only, showed similar effects on maternal anaemia and little or no benefits on maternal and fetal outcomes in terms of caesarian delivery, maternal mortality, preterm delivery and neonatal mortality. The only benefit demonstrated with MMN supplements was a 11% reduced risk for low-birth-weight neonate and 13% for small-for-gestational-age as compared with iron and folic acid supplements [16]. The current guidelines do not recommend routine use of MMN supplements unless in regions where nutritional deficiencies are common [6].

#4 Environmental and dietary issues

Food safety and correct food handling and cooking should be closely followed by pregnant women as foodborn illnesses can occur during pregnancy as a consequence of impaired immune response [5]. Use of polycarbonate plastic containers to store and cook foods should be avoided during pregnancy, as a precaution to

prevent possible endocrine disrupting effects on the fetus of the bisphenol A [5].

Fish and seafood are rich in omega 3-fatty acids and consumption of at least 250 g/week is associated with improved visual and cognitive development of the newborn. Nevertheless, possible contamination with mercury and other pollutants is of concern for the foetus development and the source of fish and seafood should be taken into account [4,5].

Caffeine-containing drinks should be restricted during pregnancy to 200 mg of caffeine per day (approximately the amount contained in one cup of coffee) [5]. A recent analysis demonstrated that risk of miscarriage increased by 19% for every increase in caffeine intake of 150 mg/day [17].

Alcohol intake is completely not recommended during pregnancy as it can induce behavioural or neurological defects in the offspring as well as low birth weight and increases the risk of preterm delivery [5,18].

The safety of non-nutritive sweeteners during pregnancy is not yet established neither is their long-term effect on the offspring and therefore should be avoided [19].

#5 Gaps in knowledge

The recently-issued guidelines from World Health Organisation identified several questions that wait for more clear answers [6].

One question is to establish the most effective regimen for supplements that have been already proved their benefits (iron, calcium and folic acid) and if they have significant absorption interactions when combined into a single pill.

Calcium supplementation may have some benefits on preeclampsia, HELLP (haemolysis, elevated liver enzymes, low platelet count) syndrome and preterm birth but the mechanisms and the minimal effective dose are still to be found.

Zinc supplementation, particularly in zinc-deficient populations with no food fortification strategy, could have positive effects on maternal risk of infections and on perinatal outcomes such as preterm birth, small-for-gestational-age, neonatal infections, perinatal morbidity that are waiting for better evidence.

Vitamins C and D could improve maternal and perinatal outcomes but evidence is scarce yet.

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