Nutrition in pregnancy

Article *in* Obstetrics Gynaecology & Reproductive Medicine · July 2016

DOI: 10.1016/j.ogrm.2016.06.005

CITATIONS
7

READS
14,092

3 authors, including:

Angela C Flynn
King's College London
31 PUBLICATIONS **442** CITATIONS
SEE PROFILE

Dharmintra Pasupathy
King's College London
152 PUBLICATIONS **1,691** CITATIONS
SEE PROFILE

Nutrition in pregnancy

Alison Ho

Angela C Flynn

Dharmintra Pasupathy

Abstract

The pivotal role of nutrition in pregnancy is well established and has important implications on subsequent maternal and offspring health, including outcomes in later adult life. Optimal nutrition periconception, if maintained throughout pregnancy, promotes optimal foetal growth and development. Growth trajectories *in utero* and size at birth are related to the offspring's risk of developing disease in later life, especially chronic non-communicable diseases such as hypertension, diabetes and coronary heart disease (the Barker hypothesis). This article aims to review nutritional requirements in pregnancy, describe their transport mechanisms and highlight the implications of inadequate or inappropriate intake. Nutritional requirements are broadly divided into issues surrounding quality (macronutrients and micronutrients) and quantity of intake with a final summary of current International Federation of Gynaecology and Obstetrics (FIGO) and Royal College of Obstetricians and Gynaecologists (RCOG) recommendations.

Keywords gestational weight gain; healthy eating; macronutrients; micronutrients; nutrient requirements; nutrition; pregnancy

Introduction

The fetus relies on maternal nutrition for growth and development. Additionally, nutrition forms the basis of maternal well-being and equips the mother for delivery and recovery postnatally. Nutrition is recognized to be associated with gestational diabetes and pre-eclampsia and therefore improved nutritional intake has the potential to reduce these complications and their associated short and long term morbidities. During the antenatal period, healthcare professionals have regular contact with pregnant women therefore pregnancy is an opportunity to help establish healthy dietary habits that can potentially be adopted by her family, establishing a beneficial background to optimal health for future generations.

The placenta links maternal and foetal circulation with syncytiotrophoblasts lining placental villi and consisting of two polarized membranes: microvillous membrane facing maternal circulation and basal plasma membrane facing foetal capillary epithelium. Thus, nutrients must pass through these two membranes before crossing the foetal capillary epithelium to enter the foetal circulation. The expression and activity of transporter mechanisms within the placental-foetal unit have been found to be associated with foetal growth restriction, macrosomia, diabetes, obesity and maternal nutrient availability.

Healthy eating in pregnancy

The National Institute for Health and Clinical Excellence (NICE) form the basis of UK healthcare policy and include healthy eating approaches. Calorie restriction is not advised and recommendations focus on achieving and maintaining a healthy weight during pregnancy by basing meals on starchy foods (wholegrain if possible), eating fibre rich foods and consuming at least five portions a day of fruit and vegetables. Food high in fat and sugar (including fried, some drinks and confectionery) should be avoided. Pregnant women are also advised to eat breakfast, and to watch portion sizes and how often they are eating.

The RCOG has provided advice regarding healthy eating in pregnancy in alignment with NICE guidance. Low-fat dairy foods for a source of calcium are encouraged with a daily intake of protein in the form of lean meat, two portions of fish a week (one of which should be oily) or lentils, beans and tofu. The Government's Healthy Start voucher scheme has successfully improved dietary patterns in pregnancy with a reported relative increase in daily portions of fruit and vegetables.

Nutrient requirements in pregnancy

Energy and macronutrients

Energy requirements in pregnancy for individuals vary and guidelines differ between countries, however, it is agreed that additional requirements are relatively small. The RCOG recommends a modest increase of 200 kcal/day in the third trimester — an approximate 10% increase from the 1940 kcal/day recommendation in a non-pregnant adult woman.

Carbohydrate and fibre: carbohydrates form the main substrate for foetal growth, fuelling maternal and foetal organ function, biosynthesis and are additionally used in structural components of cells, co enzymes and DNA. Maternal and foetal brain functions use glucose from carbohydrate as their preferred source of energy with glucose providing at least 75% of foetal energy requirements. Glucose crosses the placenta by facilitated diffusion along a concentration gradient through members of the glucose transporter family (GLUT).

Carbohydrate type and quantity can affect glucose homeostasis via release of insulin. The glycemic index (GI) refers to the area under the curve for blood glucose concentrations during a 2-h period after consuming a test food. A low GI suggests slower rates of digestion and absorption of a food's carbohydrate, potentially relating to a lower insulin demand. It is therefore a modifiable macronutrient in the management of diabetes mellitus (gestational, type 1 and type 2), however, there is no evidence to support a low glycemic index diet for healthy pregnant women.

***Alison Ho** MA MBBS is a Specialist Registrar in Obstetrics and Gynaecology at Kingston Hospital NHS Foundation Trust, London, UK. Conflicts of interest: none declared.*

***Angela C Flynn** BSc MSc is a Research Nutritionist at the Women's Health Academic Centre, Division of Women's Health, King's College London, UK. Conflicts of interest: none declared.*

***Dharmintra Pasupathy** MSc PhD MRCOG is a Consultant/Senior Lecturer in Maternal and Fetal Medicine and Perinatal Epidemiology at the Women's Health Academic Centre, Division of Women's Health, King's College London, UK. Conflicts of interest: none declared.*

Please cite this article in press as: Ho A, et al., Nutrition in pregnancy, Obstetrics, Gynaecology and Reproductive Medicine (2016), http://dx.doi.org/10.1016/j.ogrm.2016.06.005

Fibre affects the postprandial insulin response by influencing the accessibility of carbohydrates and nutrients to digestive enzymes thus delaying their absorption. Fibre supports maternal digestive health, providing bulk to stool and absorbing water to aid transit time. This is especially beneficial as progesterone levels in pregnancy can result in constipation by increasing relaxation of intestinal smooth muscle.

Protein: protein forms the building blocks for both structural and functional components of cells. Requirements are highest during the second and third trimesters due to extra development and growth of both maternal and foetal tissue. It is an alternative energy source when carbohydrate intake is insufficient therefore adequate carbohydrate intake is required in order for cell synthesis to continue. Low socioeconomic status and women with limited dietary variety are at risk of suboptimal protein intake.

Plasma concentrations of most amino acids are higher in foetal circulation. Over 15 different amino acid transporters mediate their transport against a concentration gradient. Systems include System A and System L. System A is sodium dependent for small neutral amino acids while System L is sodium independent for large neutral amino acids with branched or bulky side chains.

Fats and essential fatty acids: fat aids transport of fat-soluble vitamins A, K, D and E and are required for structural (e.g. membrane lipids) and metabolic functions (e.g. precursor for steroid hormones). PUFAs (poly unsaturated fatty acids) are important for neurological development including foetal brain, nervous system and retina. Oily fish, nuts, seeds, vegetable oils, margarines and green leafy vegetables are encouraged to obtain a greater intake of PUFA.

Essential fatty acids linoleic and alpha linolenic acid are precursors for n-6, n-3 LCPUFA and prostaglandins; these are components of the inflammatory process with a role in diseases characterized by inflammation, reproductive health, cervical ripening and initiation of labour. Systematic reviews of RCTs have found little or no effect of n-3 LCPUFA supplementation in pregnancy on cognitive development, birth weight, gestational diabetes mellitus or pre-eclampsia. There is, however, a beneficial effect on increasing gestational length and reducing risk of preterm birth.

Placental triglyceride lipases break down triglycerides into fatty acids. Fatty acids and ketone bodies (produced by maternal lipolysis) cross the placenta by diffusion. Cholesterol-carrying lipoproteins LDL, HDL and VLDL transport cholesterol into foetal circulation. Syncytiotrophoblasts express lipoprotein specific receptors e.g. LDL receptor, scavenger receptor class B type 1 and VLDL receptor. Binding cassette transporter A1 and GI in the foetal endothelium allow cholesterol to enter the foetal circulation. The fetus also synthesizes cholesterol endogenously.

Micronutrients

Iron and vitamin C: iron is a component of haemoglobin required for foetal development, placental growth and expansion of maternal red blood cell mass. Vulnerability to iron deficiency occurs, especially in late pregnancy as iron transfer to the fetus becomes marked in order to meet increased demands. Deficiency has been associated with a higher risk of preterm delivery, low birth weight, infant iron deficiency and long-term cognition and brain function. Replete stores are required in preparation for childbirth as significant blood loss may occur intrapartum. Iron transfer to the fetus is facilitated through placental transferrin receptors for endocytosis of transferrin-bound iron.

Vitamin C aids iron absorption and competes for placental receptors with glucose, however maternal hyperglycaemia does not result in foetal hypovitaminosis C. A recent Cochrane review suggested that vitamin C might have a role in preventing placental abruption (RR 0.64, 95% CI 0.44−0.92) and prelabour rupture of membranes (RR 0.98, 95% CI 0.70−1.36). However, women supplemented with vitamin C alone or in combination with other supplements were more likely to self-report abdominal pain. Gestational age at birth was increased amongst these women. Supplementation with vitamin C alone reduced the risk of preterm PROM and term PROM but the risk of term PROM was increased when supplementation included vitamin C with vitamin E. The risk of stillbirth, neonatal death, IUGR and pre-eclampsia were not affected by vitamin C supplementation.

Folate and vitamin B12: the prevention of neural tube defects with periconceptional folic acid is well established. Folic acid supplementation has no clear effect on cleft palate/lip or congenital cardiovascular defects. Five percent of the general population has marginal to severe folate deficiency and therefore all women are advised to take 400 mcg/day folic acid prior to conception until the 13th week of pregnancy with higher doses in certain circumstances (Table 1).

Folate binding receptors maintain a high foetal−maternal concentration gradient for DNA synthesis while vitamin B12 is transported via placental receptors. Both micronutrients are associated with a reduction in megaloblastic anaemia, placental vascular disorders, preterm birth, low birth weight and SGA via regulation of circulating homocysteine levels. Homocysteine levels are influenced by the activity of methylene tetrahydrofolate reductase (MTHFR). The C6777T variant has impaired MTHFR function and its presence is associated with an increased risk for pre-eclampsia and recurrent pregnancy loss, potentially via elevated homocysteine levels. Low dietary intake of folic acid can exacerbate this but evidence is lacking with regard to whether pregnant women carrying the C6777T variant should take a higher folic acid supplement.

Vitamin D and calcium: vitamin D is required for immune and nervous system function and mediates the accumulation of foetal calcium from maternal stores in skeletal growth. Vitamin D deficiency can result in rickets, craniotabes and osteopenia. Calcium supplementation reduces the development of hypertensive disorders of pregnancy and an increasing body of evidence demonstrates a relationship between vitamin D deficiency

Please cite this article in press as: Ho A, et al., Nutrition in pregnancy, Obstetrics, Gynaecology and Reproductive Medicine (2016), http://dx.doi.org/10.1016/j.ogrm.2016.06.005

Dietary recommendations in pre-pregnancy and pregnancy (per day)

	Pre-pregnancy	Pregnancy	Food sources
Macronutrients			
Energy	1940 kcal	+200 kcal in third trimester only	Carbohydrates in starchy vegetables, grains, sugars. Fat in nuts, seeds, vegetable oils, poultry, eggs, fish, meat
Fibre		No quantitative recommendation	Beans, wholegrain, wholemeal, pulses, nuts, oats, fruit and vegetables
Protein	45 g	+6 g	Meat, poultry, fish, eggs, dairy products, legumes, rains, nuts, seeds
Micronutrients			
Thiamin	0.8 mg	+0.1 mg[a]	Vegetables (peas), fruit, eggs, wholegrain breads, some fortified breakfast cereals, liver[e]
Riboflavin	1.1 mg	+0.3 mg	Milk, eggs, fortified breakfast cereals, rice
Vitamin C	40 mg	+10 mg	Fruit, vegetables
Folate	200 μg	+100 μg[b]	Broccoli, Brussels sprouts, liver[e], spinach, asparagus, peas, chickpeas, fortified breakfast cereals
Vitamin D	—	+10 μg[c]	Oily fish, eggs, fortified fat spreads, fortified breakfast cereals, some powdered milks
Vitamin A	600 μg	+100 μg	Cheese, eggs, oily fish, fortified low-fat spreads, milk, yoghurt
Niacin	13 mg	[d]	Meat, fish, wheat flour, eggs, milk
Vitamin B6	1.2 mg	[d]	Pork, poultry, fish, bread, whole cereals, eggs, vegetables, soya beans, peanuts, milk, potatoes, some fortified breakfast cereals
Vitamin B12	1.5 g	[d]	Meat, salmon, cod, milk, cheese, eggs, some fortified breakfast cereals
Calcium	700 mg	[d]	Dairy products, green leafy vegetables, soya beans, tofu, nuts, bread with fortified flour, sardines and pilchards
Phosphorus	550 mg	[d]	Red meat, diary foods, fish, poultry, bread, brown rice, oats
Magnesium	270 mg	[d]	Green leafy vegetables, nuts, brown rice, bread (especially wholegrain), fish meat, dairy foods
Sodium	1600 mg	[d]	Sodium chloride naturally low levels in all foods but added to processed foods e.g. ready meals, meat products (bacon), cheese, some bread, breakfast cereals, savoury snacks, tinned vegetables
Chloride	2500 mg	[d]	
Potassium	3500 mg	[d]	Fruit (bananas), some vegetables (broccoli, parsnips, brussel sprouts), pulses, nuts, seeds, fish, shellfish, beef, chicken turkey
Iron	14.8 mg	[d]	Liver[e], meat, beans, nuts, dried fruit, wholegrains, fortified breakfast cereals, soybean flour, dark-green leafy vegetables

(*continued on next page*)

Please cite this article in press as: Ho A, et al., Nutrition in pregnancy, Obstetrics, Gynaecology and Reproductive Medicine (2016), http://dx.doi.org/10.1016/j.ogrm.2016.06.005

Table 1 (*continued*)

	Pre-pregnancy	Pregnancy	Food sources
Zinc	7.0 mg	[d]	Meat, shellfish, dairy foods, bread, cereal products
Copper	1.2 mg	[d]	Nuts, shellfish, offal
Selenium	60 μg	[d]	Brazil nuts, fish, meat, eggs
Iodine	140 μg	[d]	Sea fish, shellfish, cereals, grains

Other points to note

Oily fish (source of omega 3 fatty acids): Two portions of fish a week, one of which should be oily.

Caffeine: <200 mg/day (=roughly two mugs of instant coffee).

[a] In third trimester only.

[b] 400 μg folic acid/day supplement pre conception until 13 weeks. Higher dose of 5 mg folic acid/day supplement pre conception until 13 weeks if patient or partner has a neural tube defect or family history of neural tube defects, previous pregnancy affected by neural tube defect, BMI >30 kg/m^2, coeliac disease, diabetes or on anti-epileptic medication, sickle-cell anaemia or thalassaemia.

[c] 10 μg supplement is required as this level is not usually achievable through diet. Especially important for those most at risk of deficiency: women of South Asian, African, Caribbean or Middle Eastern family origin, limited exposure to sunlight, diet low in vitamin D (e.g. those women who consume no oily fish, eggs, meat, vitamin D-fortified margarine or breakfast cereal), prepregnancy body mass index >30 kg/m^2.

[d] No increment.

[e] Liver is high in vitamin A and high consumption is not recommended in the periconceptional period due to the teratogenic risk.

Obtained from Nutrition in Pregnancy Scientific Impact Paper No. 18 2010. RCOG 2010 and www.nhs.uk

Table 1

and low birth weight, preterm delivery, gestational diabetes mellitus and pre-eclampsia. Individuals particularly at risk for vitamin D deficiency include those of South Asian, African, Caribbean or Middle Eastern origin, a body mass index >30 kg/m^2 and low sun exposure.

Iodine: iodine is required for foetal thyroid function and neurological development. Iodine deficiency has been linked to mental retardation and cognitive deficit. Periconceptional and antenatal supplementation in regions of severe iodine deficiency have been found to reduce the risk of cretinism and improve motor function. Reports of gestational iodine deficiency and potential benefits of iodine supplementation are emerging.

Vitamin E: more evidence regarding vitamin E supplementation in pregnancy is required, as a recent Cochrane review suggested an advantageous role in reducing the risk of placental abruption (RR 0.64, 95% CI 0.44–0.93). However, supplementation with vitamin E was associated with an increased risk of self-reported abdominal pain and term prelabour rupture of membranes. There was no difference in vitamin E supplementation on the risk of stillbirth, pre-eclampsia, preterm birth and IUGR.

Gestational weight gain and obesity in pregnancy

To achieve appropriate gestational weight gain, the provision of energy is balanced against physical activity, pre-pregnancy weight, age, nutritional status, percent of body fat to fat free mass, basal metabolic rate with energy expenditure to support growth and development of the placental-foetal unit. The relationship between gestational weight gain and pregnancy outcomes is difficult to establish, as it is a reflection of multiple components: fetus, placenta, uterus, amniotic fluid, maternal adipose tissue, blood volume expansion and mammary glands. NICE have not published recommendations on weight gain during pregnancy due to lacking evidence, however, the recommendation of the Institute of Medicine (2009) are detailed in Table 2.

A high pre-pregnancy BMI carries adverse maternal and foetal outcomes – gestational diabetes mellitus, pre-eclampsia,

IOM recommendations on total weight gain during pregnancy for singleton fetuses

	Pre-pregnancy body mass index (BMI) (kg/m^2)	Total weight gain during pregnancy (lbs)	Total weight gain during pregnancy (kgs)
Underweight	<18.5	28–40	13–18
Normal weight	18.5–24.9	25–35	11–16
Overweight	25.0–29.9	15–25	7–11
Obese	≥30	11–20	5–9

Obtained from Weight Gain During Pregnancy: Reexamining the Guidelines IOM report May 2009

Table 2

Please cite this article in press as: Ho A, et al., Nutrition in pregnancy, Obstetrics, Gynaecology and Reproductive Medicine (2016), http://dx.doi.org/10.1016/j.ogrm.2016.06.005

caesarean section, assisted delivery, postpartum haemorrhage, infection and thrombosis, large for gestational age (LGA) growth, birth defects and stillbirth. Periconception and antenatally, these women should be warned of these increased risks and encouraged to make lifestyle changes to support weight management. Randomized controlled trials of physical activity and dietary intervention in obese women have failed to demonstrate an effect on the risk of gestational diabetes and LGA. Further research is required to determine the optimal gestational weight gain in different BMI categories.

Special considerations

Smoking, alcohol and caffeine consumption and recreational drug use can have a detrimental effect on foetal nutrition, growth and development. Physical activity is beneficial by managing weight gain, preparing for labour and aiding glucose homeostasis especially in diabetic women.

Pregnant women are at risk of food borne illness e.g. listeriosis in unpasteurized milk, cheese or pate, salmonella in partially cooked eggs, poultry and shellfish and toxoplasmosis in undercooked meat or salad vegetables contaminated with soil or contamination with cat faeces. Methylmercury in fish is teratogenic, affecting development of the foetal nervous system, and therefore should be restricted to two portions a week. Consuming high levels of vitamin A is also teratogenic and therefore multi-vitamins containing vitamin A, liver, pate, fish liver oils and other food fortified with vitamin A should be avoided.

FIGO recommendations in pregnancy

Obtained from Hanson MA, Bardsley A, De-Regil LM et al. The International Federation of Gynaecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First". Int J Gynaecol Obstet 131 S4(2015) S213–S253.

1. Promotion of a varied, healthy diet with supplementation or fortification of foods when necessary
2. Encouraging the adoption of healthy dietary habits pre-pregnancy
3. Early access to prenatal care to provide the following:
    a. nutrition counselling
    b. recognition and appropriate intervention of micronutrient deficiencies
    c. treatment of co-existing conditions e.g. malaria, TB, HIV, gastrointestinal infections and non-communicable disease
4. Importance of pre-pregnancy BMI
    a. Both low and high BMIs may lack either nutritional quality or quantity balance, resulting in poorer pregnancy outcomes
5. Avoidance of detrimental behaviours including smoking, alcohol intake and recreational drug use before, during and after pregnancy as well as food borne illness and teratogens
6. Exercise and energy requirement recommendations
    a. dietary energy intake should only involve a moderate increase of 340–450 kcal per day in the second and third trimester
    b. moderate exercise of 30 minutes per day and avoidance of hard physical labour during late pregnancy
7. Monitoring of appropriate gestational weight gain

Box 1

FIGO recommendations

The recent FIGO recommendations in adolescent, pre conception and maternal nutrition have emphasized that healthcare promotion is the cornerstone of optimizing nutritional status (Box 1).

Conclusion

Nutrition in pregnancy requires a careful balance of both quality and quantity of intake in order to optimize foetal growth and development in addition to reducing maternal morbidity. MTHFR genotypes, vitamin C, vitamin E and iodine supplementation are emerging areas of research. The RCOG and FIGO recommendations have centered around early intervention through healthcare promotion of a varied, healthy diet, beneficial lifestyle behaviours and the use of supplementation or fortified foods as necessary. Such changes are also valuable if carried out in the long term by both the mother and her family. ◆

FURTHER READING

Barker DJ. Maternal nutrition, fetal nutrition and disease in later life. *Nutrition* 1997 Sep; **13:** 807–13.

Bothwell TH. Iron requirements in pregnancy and strategies to meet them. *Am J Clin Nutr* 2000 Jul; **72**(suppl 1)**:** 257s–64.

De-Regil LM, Pena-Rosas JP, Fernandez-Gaxiola AC, Rayco-Solon P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database Syst Rev* 2015 Dec 14. Issue 12. Art. No.:CD007950.

Hanson MA, Bardsley A, De-Regil LM, et al. The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First". *Int J Gynaecol Obstet* 2015 Oct; **131**(suppl 4)**:** S213–53.

Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev* 2014 Jun 24. Issue 6. Art. No.:CD001059.

National Institute for Health and Care Excellence. Weight management before, during and after pregnancy. NICE guidelines published July 2010. PH27. https://www.nice.org.uk/guidance/ph27/resources.

Royal College of Obstetricians &Gynaecologists. Nutrition in pregnancy (Scientific Impact Paper No. 18). RCOG published 2010. https://www.rcog.org.uk/en/guidelines-research-services/guidelines/sip18/.

Rumbold A, Ota E, Nagata C, Shahrook S, Crowther CA. Vitamin C supplementation in pregnancy. *Cochrane Database Syst Rev* 2015. Issue 9. Art. No.:CD004072.

Rumbold A, Ota E, Hori H, Miyazaki C, Crowther CA. Vitamin E supplementation in pregnancy. *Cochrane Database Syst Rev* 2015. Issue 9. Art. No.:CD004069.

Please cite this article in press as: Ho A, et al., Nutrition in pregnancy, Obstetrics, Gynaecology and Reproductive Medicine (2016), http://dx.doi.org/10.1016/j.ogrm.2016.06.005

Practice points

- Advice regarding nutrition in pregnancy centers around a healthy, varied diet pre-pregnancy, antenatally and post-natally
- Important components include macronutrients (carbohydrate, fibre, protein, fats) and micronutrients (iron, folate, vitamin B12, vitamin D, calcium, iodine)
- Energy requirements in pregnancy require a modest increase of 200 kcal/day in the third trimester
- A high fibre, low glycemic index diet aids glucose homeostasis in diabetic women
- PUFAs may beneficially increase gestational length and reduce risk of preterm birth through their role in inflammation
- Increased vulnerability to iron deficiency occurs in the 3rd trimester and replete stores are required in preparation for intrapartum blood loss
- The role of vitamin C and E supplementation in reducing placental abruption and prelabour rupture of membranes requires further research
- Calcium supplementation reduces the development of hypertensive disorders of pregnancy
- Vitamin D deficiency has been found to be associated with low birth weight, preterm delivery, gestational diabetes mellitus and pre-eclampsia
- Potential benefits of iodine supplementation are emerging
- Obesity and excessive gestational weight gain are associated with adverse maternal and foetal outcomes, however, optimal gestational weight gain in different BMI categories are yet to be determined by NICE
- Food can carry teratogens (mercury, lead) and pathogens (listeriosis, salmonella, toxoplasmosis)
- Smoking, alcohol intake and recreational drug use are detrimental behaviours that should be avoided

Please cite this article in press as: Ho A, et al., Nutrition in pregnancy, Obstetrics, Gynaecology and Reproductive Medicine (2016), http://dx.doi.org/10.1016/j.ogrm.2016.06.005